Universal serial bus powered and controlled isolated constant-current physiological stimulator

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We have developed a compact, isolated, physiological, constant-current stimulator that is powered and controlled by a universal serial bus (USB) interface. The stimulator is designed to be used in *ex vivo* cardiac experiments but is suitable for a wide variety of settings. The cost and features compare very favorably with commercial stimulators usually used in research and student laboratories. In addition to being USB powered, other novel aspects of our stimulator include the ability to produce large currents, up to 100 mA through a typical 1 k Ω load, by means of a single high-voltage dc-to-dc converter; user-specified variable period, magnitude, and duration of complex monophasic or biphasic sequences; and easy integration via hardware or software into existing experimental setups. © 2008 American Institute of Physics. [DOI: 10.1063/1.3030861]

Many cardiac electrophysiology studies require some forms of electrical stimulation. The stimulator described here was specifically designed to be used in cardiac studies of isolated rabbit hearts, but is generally applicable to a large class of physiological stimulation requirements. It is not intended for use on humans.

Other custom stimulators that produce constant voltage, and constant voltage and small constant currents, were described by Land *et al.*¹ and Brasil *et al.*,² respectively, among others. Both of these stimulators are geared toward pacing or single pulse generation. A more sophisticated multiple channel stimulator by Cheever *et al.*³ is used for skeletal muscle cardiac assist.

In the past we used commercial stimulators (Bloom) to produce constant current stimuli, hereafter called legacy stimulators. In the following discussion a load of 1 k Ω is assumed, which is typical in our experiments on small hearts. The magnitude of the output current from our legacy stimulators is set by an analog control on the enclosure. The duration of the stimuli is controlled by external transistor-transistor logic (TTL) pulses generated using a peripheral component interconnect counter/timer card (6602, National Instruments) and a host personal computer. The legacy stimulators have numerous shortcomings: (1) they require high-voltage batteries that need to be changed frequently and are difficult to obtain, (2) there is approximately 25 μ A of leakage current when the stimulator is inactive, (3) the stimulators are unable to provide over 80 mA, and (4) there are no means to change magnitude or polarity during a rapid

stimulation sequence. Also, legacy stimulators, like most other commercial stimulators, are not well suited for modification or optimization for a specific application. We have built stimulators that address these shortcomings and add other useful features: (1) all power comes from the host computer via a universal serial bus (USB) connection, (2) there is no measurable output when the stimulator is inactive, (3) 100 mA can be delivered to a typical load, (4) nearly any desired stimulus sequence with variable period, magnitude, and polarity can be generated, and (5) the output is isolated electrically from the computer and ground.

A USB controller module (MT-USB, Molex) comprises a 40-pin 20 MHz programmable intelligent computer (PIC) 18F452 microcontroller (Microchip), a 16 $\times$ 2 liquid crystal display, and a USB connector and circuitry that are used to communicate with the host personal computer (PC) and control the stimulator. The MT-USB has two ten-pin headers connected to our custom printed circuit board (PCB). The PIC module uses the USB connection as a virtual serial port to communicate with the host PC. The PIC control program is written in C and compiled with the CCS PCWH version 3.236 compiler.

The stimulator uses a classic, buffered, voltage-controlled current source (VCCS) with a few modifications. Figure 1 shows a schematic of the circuit. A constant set-point voltage provided by a 12 bit digital to analog converter (DAC) (U7) and a digital enable signal (both described below) control the set point and activation of the VCCS. In order to prevent any output from the stimulator when it is inactive, we implemented an unconventional operational-amplifier (op-amp) power supply. The digital enable signal is fed into the optoisolator (U6). When the digital enable signal is low, the emitter and base of Q1 are at the same potential and no current flows, which effectively disconnect the power to U1A, ensuring zero output. When the digital enable signal is high, the voltage drop across R5 causes Q1 to saturate and

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FIG. 1. (Color online) Stimulator schematic. A list of parts is provided in the supplement.⁴

provide power to U1A. (The effectiveness of this approach is further discussed in the supplement.⁴) This unconventional op-amp supply does introduce rise-time delays: we measured 5 and 15 μs rise times for currents of 10 and 100 mA, respectively. In cardiac experiments, pulses generally are at least several hundreds of microseconds in duration; therefore this minor increase in rise time is an acceptable trade-off to eliminate any leakage current. R1 (100 Ω) is a current limiting resistor. C1 (0.1 μF) is in parallel with the load and serves to reduce the output noise. D1 helps to ensure current will only flow one way through the circuit. The VCCS is a common circuit and will not be discussed further.

A table of the pin connections between the custom PCB and the MT-USB module is given in the supplement.⁴ A picture of the assembled PCB is shown in Fig. 2. The PIC module, and therefore the host PC, is electrically isolated from the stimulation circuitry. The 5 V supply provided by

the USB powers three dc-to-dc converters, which provide power isolation and produce voltages of 5, 12, and 200 V (U9, U8, and U10, respectively). Four digital lines from the PIC control the DAC (U7) by means of a four-wire serial peripheral interface, and are isolated by optoisolators (U2–U5). In the following discussion, “local” refers to the stimulation circuitry side of isolation, and “remote” refers to the PIC/PC side of the isolation.

The dc-to-dc converters all require a minimum load. The 5 V components, which are always on, consume enough current to provide an adequate load for the 5 V converter. R9 and R10 ensure a minimum load for the 12 and 200 V converters, respectively. The 200 V converter has a maximum output of 6.6 mA, and R11 ensures the current is always below this amount.

The USB 2.0 specification states that a maximum of 500 mA may be drawn by a connected device. The maximum current drawn when the stimulator is connected to the USB connector is approximately 400 mA, which is well below the maximum. This is the peak current when the stimulator is first connected; the steady-state current is about 300 mA.

The output polarity is controlled by a latching micro-relay (K1). Since the relay control pins are isolated from the inputs and outputs, the relay is switched directly by two output pins on the PIC and the remote 5 V supply. The digital outputs of the PIC are connected through 1 k Ω resistors (R7, R8) to the bases of two NPN transistors (Q3, Q4). The transistors reduce the required source current from the PIC and protect the digital outputs from the back-emf of the relay coil. The specifications state that the relay has a maximum switching time of 5 ms with 3.3 ms being typical.

FIG. 2. (Color online) Custom PCB. The PIC module is mounted on the enclosure front panel (not shown) and connected to the PCB via the ten-pin header located in the lower left-hand corner of the picture.

Rather than try to achieve output accuracy by selecting expensive precision components, we chose a software calibration. The DAC voltage reference (Z1) and sense resistor (R2) are the components that fundamentally determine the precision of the output. Calibration information is stored in the PIC's EEPROM. The two calibration values are set via software command and are retained indefinitely. Details of the calibration procedure are given in the supplement.⁴

The 12 bit DAC introduces small quantization errors, especially at low currents. The stimulator provides small currents, less than 1 mA, with an accuracy of approximately 3%. Larger currents are produced with an accuracy of approximately 1%. Detailed testing and calibration procedures and data are provided in the supplement.⁴

In order to make the stimulator as versatile as possible, all communication is accomplished via text commands, which offer a variety of advantages. For example, LABVIEW, MATLAB, EXCEL, or any other program that can write to a serial port can control the stimulator without the need for specialized libraries or software tools. The stimulator accepts currents in tenths of milliamperes and durations in tenths of milliseconds. Descriptions of the nine acceptable commands with examples are included in the supplement.⁴

The stimulus on-off control is done with a TTL pulse generated either externally or by the PIC. The signals from both remote sources are routed through the same optoisolator (U6), which is the sole TTL input to the local stimulator circuitry. The external TTL input is also connected to a pin on the PIC, which allows the PIC to detect the falling edge of the TTL input. This is used for Enhanced mode.

The device has five modes of operation: *Compatibility*, *Manual*, *Wavetrain*, *Enhanced*, and *Standalone*. These five modes allow simple autonomous (no external TTL control pulses needed) pacing sequences to complex biphasic sequences with variable period and duration. A detailed description of each of the modes is given in the supplement.⁴

Enhanced mode is specialized for our purposes and adds the ability to change the magnitude, polarity, period, and duration during a rapid stimulation sequence that is synchronized with high-speed charge coupled device (CCD) cameras. The Enhanced mode stimulation sequence in Fig. 3 spells "VU" in rectangular current pulses.

The total cost in parts, including the custom PCBs, is approximately \$200, making this stimulator an attractive device for use in either research or student laboratories. Similar stimulators from a prominent commercial vendor range from approximately \$1000 with simple pacing functionality, to over \$6000 for one that offers features similar to Enhanced mode, although only to 10 mA output current. Neither of these options is USB powered. 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 USB stimulators lack, such as multiple channels and continuous waveforms; 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

FIG. 3. (Color online) Example of an enhanced mode stimulation sequence. (a) The letters VU are spelled with rectangular current pulses measured on an oscilloscope (TDS5034B, Tektronix) with a differential probe (DP-25, AMEC Instruments) across a 1 k Ω resistor.

is not intended for use on humans. A more in-depth discussion of component costs and possible design variations is included in the supplement.⁴

The high-voltage dc-to-dc converter generates 25 kHz noise, which can be picked up near the stimulator with an oscilloscope or electrodes on the heart. Even though the rms value of the 25 kHz component is negligible, this noise could be a significant problem when making electrode measurements, and filtering may be required to improve signal quality. However, the 25 kHz noise does not affect our optical measurements of cardiac action potentials and tissue responses to electrical stimulation,^{5,6} and hence we did not pursue further noise reduction. The information required to reproduce the PCB and the code will be provided upon request.

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¹B. R. Land, B. R. Johnson, R. A. Wytenbach, and R. R. Hoy, J. Undergrad. Neurosci. Ed. **3**, A30 (2004).

²R. O. Brasil and J. H. Leal-Cardoso, Braz. J. Med. Biol. Res. **32**, 767 (1999).

³E. A. Cheever, D. R. Thompson, B. L. Cmolik, W. P. Santamore, and D. T. George, IEEE Trans. Biomed. Eng. **45**, 56 (1998).

⁴See EPAPS Document No. E-RSINAK-79-009812 for a supplement that gives additional details and discussion of the stimulator. For more information on EPAPS, see <http://www.aip.org/pubservs/epaps.html>.

⁵D. W. Evertson, M. R. Holcomb, M. Eames, M. Bray, V. Y. Sidorov, J. Xu, H. Wingard, H. M. Dobrovolsky, M. C. Woods, D. J. Gauthier, and J. P. Wikswo, IEEE Trans. Biomed. Eng. **55**, 1241 (2008).

⁶V. Y. Sidorov, M. R. Holcomb, M. C. Woods, R. A. Gray, and J. P. Wikswo, Basic Res. Cardiol. **103**, 537 (2008).