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A novel device to suppress electrical stimulus artifacts in electrophysiological experiments

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ABSTRACT

Electrophysiological studies of the effects of electrical brain stimulation have to contend with stimulus artifacts, which complicate both the maintenance of recorded neuron waveforms at recording time, and the post-hoc analysis of the data. The artifacts can be removed by digitally averaging some or all of the (stereotypic) artifact waveforms across artifacts, and then subtracting the resulting template from the recorded waveform at the time of artifact production. Available software-based approaches to this problem are effective but time consuming, and do not help with the problem of maintaining the recording quality at recording time. Alternative hardware-based methods are effective as well, but relatively inflexible and very expensive.

We here provide a detailed description of a simple high-performance artifact removal device based on a multi-processor microcontroller as well as analog-to-digital and digital-to-analog converters. This device provides the benefits of self-adapting online-removal of stimulus artifacts for a fraction of the price of the commercially available devices. The device is fully customizable, and can be easily adjusted to various stimulation conditions, as well as AC line noise removal.

1. Introduction

In recent years there has been renewed interest in the evaluation of responses of single neurons to electrical stimulation at nearby or distant locations in *in vivo* preparations (e.g., Erez et al., 2009; Hashimoto et al., 2003; McCairn and Turner, 2009; Nanda et al., 2009). These studies provide information about conduction properties of neurons or axons, and help us to characterize synaptic transmission between the recorded neurons. In addition, brain stimulation has become a treatment for movement disorders and other conditions, and a large number of studies have examined the mechanisms that may underlie the beneficial therapeutic effects (e.g., Hashimoto et al., 2003; McCairn and Turner, 2009).

Such studies of stimulation effects are often complicated by the presence of stimulus artifacts which can be sufficient to render the first few milliseconds after a given stimulus unusable for analysis. Several previous studies have described methods to minimize this problem, usually relying on the fact that the artifacts have a relatively stable waveform to which the irregular neuronal signal is linearly added (Arslan et al., 2001; Blogg and Reid, 1990; Erez et al., 2010; Harding, 1991; Hashimoto et al., 2002; Heffer and Fallon, 2008; Hines et al., 1996; Montgomery et al., 2005; O'Keeffe et al., 2001; Wichmann, 2000). These methods generally generate an 'expected' average artifact template which is then subtracted from the recorded signal in order to reconstruct the neuronal signal.

The available software-based methods to do this are highly effective, but have the disadvantage that post-hoc removal of artifacts does not help with the recording itself, in which the presence of stimulus artifacts in oscilloscope displays or audio monitoring greatly interferes with attempts to judge and maintain the quality of the recorded neuronal signals on line. Furthermore, a practical problem with stimulus artifact removal systems that rely on post-processing is that they tend to be time-consuming.

These limitations can be addressed with *online* artifact removal performed prior to oscilloscope display or amplification and storage of the data. This insight has led to the development of commercially available hardware artifact removal devices. These devices are, indeed, effective, but are also prohibitively expensive and inflexible. Similar devices for removing stable line noise artifacts are also available, and also expensive.

We here report on the design and practical use of a simple and easy to build microcontroller-based artifact removal device (ARD) that very effectively removes artifacts of stable waveforms, as they occur during electrical stimulation experiments or from line inter-

Abbreviations: ADC, analog-to-digital converter; ARD, artifact removal device; DAC, digital-to-analog converter; STN, subthalamic nucleus; VL, ventrolateral nucleus of the thalamus.

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ference. The ARD is more flexible and far less expensive than the commercially available devices.

2. Methods

2.1. Device development

2.1.1. General principle of operation

The new device samples analog input that includes recurrent monotonous artifact waveforms. It generates and updates templates of these waveforms, and subtracts the waveform template on subsequent occurrences of the artifact, thereby creating an artifact-corrected version of the input signal which is converted back into an analog signal.

2.1.2. Hardware

A schematic diagram of the hardware is shown in Fig. 1. The ARD was designed using the P8X32A microprocessor (Parallax Inc., Rocklin, CA). The architecture of this chip allows for multitasking of up to eight independently operating processors ('cogs'). Each of the processors has its own RAM, with cog-specific code and variables. In addition, the cogs have shared access to central ('hub') RAM which can be used to pass information between the cogs and to store digitized artifact waveforms. All cogs are simultaneously clocked at 80 MHz. The microprocessor can be programmed in Parallax's interpreter language SPIN, and/or in assembly language. Large portions of the code were written in assembly language to maximize the speed and temporal predictability of code execution.

In addition to the microcontroller, 16-bit analog-to-digital and digital-to-analog converters (ADC and DAC, respectively) were used. The ADC chip (AD977, Analog Devices, Norwood, MA) is controllable via a three-wire serial interface, and allows for conversion speeds of up to 100 ks/s. It allows for a variety of mono- or bipolar input ranges which are internally offset and voltage-divided to the ADC's conversion range. We chose a ±5 V input range. The DAC chip (MAX541, Maxim Integrated Products, Sunnyvale, CA) is also controlled via a three-wire serial protocol. In some situations it may be advisable to buffer input and outputs of the ARD with unity-gain followers and to couple inputs and outputs capacitatively. These additional components are not shown in Fig. 1. The MAX541 operates in unipolar mode which is simple and sufficient for most laboratory situations. A worthwhile alternative to this is the MAX542 chip which allows bipolar operation in conjunction with a dual-supply precision operational amplifier.

The microprocessor is available on pre-soldered prototype boards which also offer USB connectivity, a 5-MHz crystal that is used by the microcontroller clock, as well as 3.3 V and 5 V power regulators. The circuit described here was implemented on such a prototype board. For clarity, the wiring diagram in Fig. 1 does not show the power and crystal connections. In addition to the integrated circuits, only a few external components are needed, including resistors, capacitors, and an LED which is used to indicate out-of-range sampling in the input signal (see Table 1). The

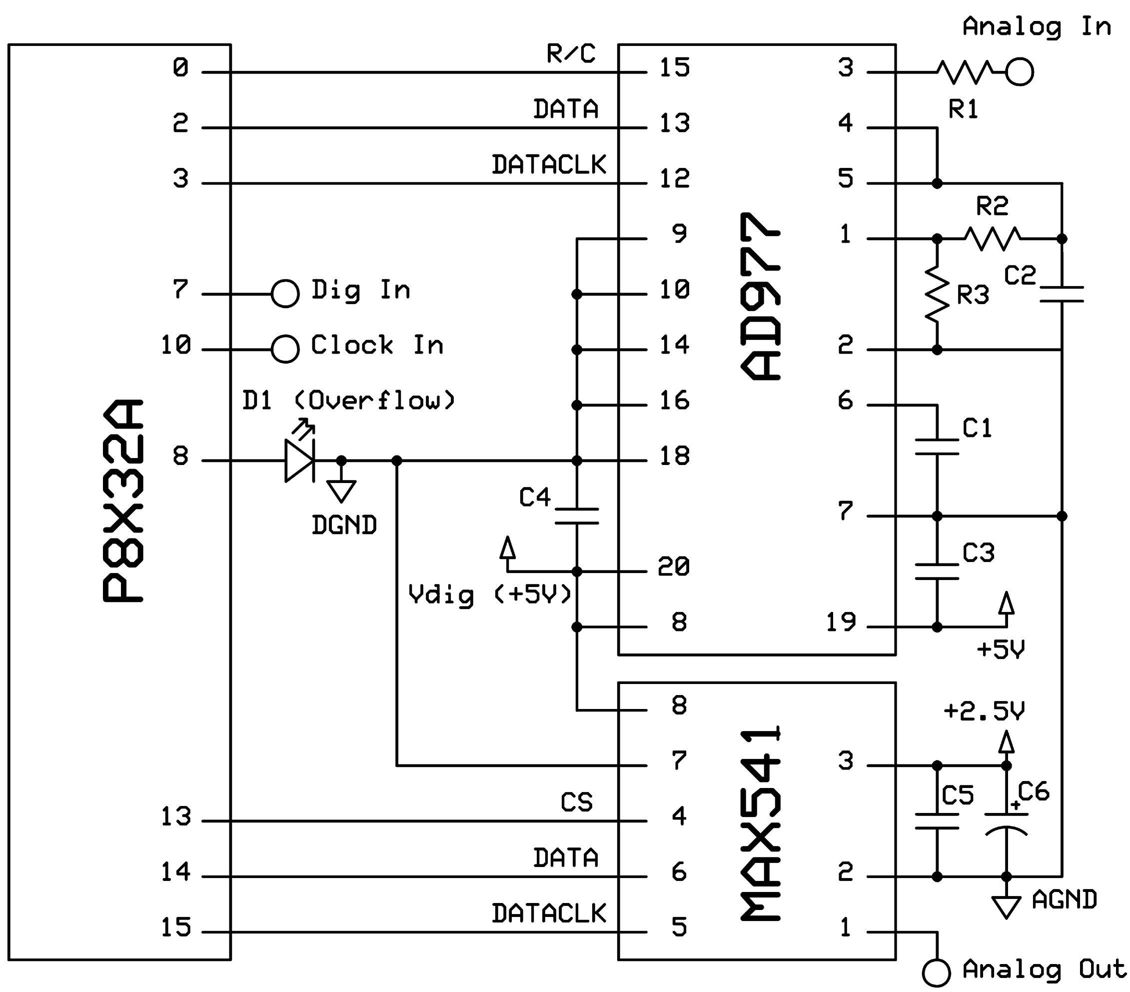

Fig. 1. Wiring diagram of the described device. Note that the pin out numbering on the integrated circuits does not follow the physical positions of the pins. This was done to simplify the diagrammatic representation, and was (partly) forced by the arrangement of components on the circuit board.