A Hybrid Hardware and Software Approach for Cancelling Stimulus Artifacts During Same-electrode Neural Stimulation and Recording

Stanislav Culacli1, Brian Kim1, Yi-Kai Lo2, and Wentai Liu2

Abstract—Recovering neural responses from electrode recordings is fundamental for understanding the dynamics of neural networks. This effort is often obscured by stimulus artifacts in the recordings, which result from stimuli injected into the electrode-tissue interface. Stimulus artifacts, which can be orders of magnitude larger than the neural responses of interest, can mask short-latency evoked responses. Furthermore, simultaneous neural stimulation and recording on the same electrode generates artifacts with larger amplitudes compared to a separate electrode setup, which inevitably overwhelm the amplifier operation and cause unrecoverable neural signal loss. This paper proposes an end-to-end system combining hardware and software techniques for actively cancelling stimulus artifacts, avoiding amplifier saturation, and recovering neural responses during current-controlled in-vivo neural stimulation and recording. The proposed system is tested in vitro under various stimulation settings by stimulating and recording on the same electrode with a superimposed pre-recorded neural signal. Experimental results show that neural responses can be recovered with minimal distortion even during stimulus artifacts that are several orders greater in magnitude.

I. INTRODUCTION

Simultaneous electrical stimulation and recording of evoked neural responses is integral for understanding the dynamics of neural networks and developing closed-loop neural interfaces. However, a common problem to such systems is the stimulus artifact, which occurs when the current stimulus applied to activate neurons passes through the electrode-tissue interface and is sensed by recording electrodes. Stimulus artifacts, which are often several orders of magnitude larger than the recorded action potentials, can saturate the recording amplifier and confound the detection of neural responses [1].

Although past research has aimed to reduce the artifacts by circuit designs and digital post-processing, current recording systems are unable to record neural responses for 2 ms on the stimulating electrode and 0.5 ms on a neighboring non-stimulating electrode following the stimulus, due to amplifier saturation [1]. Since action potentials can be evoked as early as 100 μs in response to a stimulus pulse [2], stimulus artifacts, which can be on the order of a millisecond, can hinder the detection of fast neural responses.

Previous methods that address the stimulus artifact cancellation problem can be fundamentally divided into hardware and software approaches. Analog filtering has been applied to neural recordings for removing frequencies associated with the stimulus artifacts. However, underlying neural responses can be distorted by this process, as they often overlap in frequency spectrum with artifacts [3]. Another method is blanking, which is applied by temporarily disconnecting the recording electrode from the amplifier during stimulation to avoid saturation [4]. Nonetheless, this approach inevitably leads to signal loss during the blanking window and introduces the challenge of choosing the optimal window size. Finally, electrode discharging can diminish the duration and size of stimulus artifacts through an active feedback circuitry [5] but cannot completely remove artifacts from recordings and is mainly limited by the impedance of the electrode-tissue interface.

A common software technique for stimulus artifact removal is template subtraction, which generates a representative template of the artifact and subtracts the template from the contaminated neural signal to recover the underlying neural response. One efficient method for generating templates is averaging the periodic artifact shapes, which relies on the assumption that artifacts have stable forms onto which irregular neural signals are linearly added [6]. Other means of generating templates include polynomial function-fitting, and wavelet filters [7]. Although template subtraction can potentially recover signals during stimulation, its performance heavily depends on the accuracy of the template. Most importantly, software-based approaches cannot recover signals during stimulation if the amplifier has saturated during this period.

This paper proposes a system that combines the advantages of both hardware and software principles to solve the problem of stimulus artifact cancellation. The hardware module reduces the stimulus artifact to a value that prevents amplifier saturation during recordings, while the software module performs template averaging and subtraction to recover the underlying neural responses.

II. SYSTEM ARCHITECTURE AND SPECIFICATIONS

A. System Architecture

The system-level setup is illustrated in Fig 1. A constant current stimulator injects periodic pulses into the stimulation site of the cell, which results in the superimposition of a neural response and a large stimulus artifact on the same electrode. This summed signal is processed by the artifact
cancellation device, and the neural response is recovered artifact-free at the system output.

Fig. 2 shows the block diagram of the proposed system, which is divided into a hardware and software module, connected by a data acquisition (DAQ) card. Both hardware and software modules rely on the assumption that periodically incoming stimulus artifacts are similar in shape and amplitude, which is often the case during neural stimulation.

The hardware module consisting of an analog-to-digital converter (ADC), a digital-to-analog converter (DAC), a microcontroller unit (MCU), and analog amplifiers sufficiently reduces the input artifact size to avoid saturating the output amplifier. An artifact template acquired by the hardware module is then subtracted from all incoming artifacts, and the result is amplified. The output of the hardware module, \( o_{hw}(t) \), can be described as:

\[
    o_{hw}(t) = (\Delta a(t) + s(t)) \times G
\]

(1)

where \( \Delta a(t) \) is the residual artifact, \( s(t) \) is the neural response of interest, and \( G \) is the output amplifier gain. The amplified residual artifact, \( \Delta a(t) \times G \), is minimized to avoid saturation.

The software module consisting of a graphical user interface (GUI) and template subtraction algorithm eliminates the residual artifacts from the hardware module output via template averaging (Fig. 2). The output of the software module, \( o_{sw}(t) \), is described as:

\[
    o_{sw}(t) = o_{hw}(t) - \frac{1}{k} \sum_{i=1}^{k} o_{hw}(t-Ti) = s(t) \times G
\]

(2)

where the sigma term represents the averaging of \( k \) previous hardware output values, each separated by the stimulation period \( T \). This term captures the residual artifact, \( \Delta a(t) \times G \), of the hardware output, while minimizing the nonperiodic neural response component, such as an action potential (AP) or local field potential (LFP). Even in the case where the stimulus-evoked neural response is time-locked to the stimulation event, some random variance in the time lag of the neural response still exists and averaging is sufficient to minimize the time-locked signal [6].

Fig. 3 illustrates the simulated hardware and software signals during artifact cancellation. The hardware input is the sum of the periodic stimulus artifacts and a ground truth neural signal, where the amplitude of the artifact component is several orders of magnitude larger than that of the neural signal. The hardware output is the sum of the periodic residual artifacts, shaped by the data converter quantization at a finite sampling frequency, and the underlying neural response, which after amplification is still within the amplifier supply rails. The software module applies template averaging on the hardware output to recover the neural response sans artifact.

B. Design Implementation

System-level specifications are designed to cancel the large stimulus artifacts, while preserving the integrity of the neural signal during the recovery process. The system’s input range is determined by the expected maximum artifact amplitude in intended applications. In-vivo examples, such as rat cortex stimulation with a 0.8 mm diameter electrode and 50 µs pulses of 10 mA current [8], sciatic nerve stimulation with a 0.005 mm² electrode and 200 µs pulses of 50 µA [9], and deep brain stimulation (DBS) [10], result in artifact amplitudes of 4.99 V, 0.198 V, and 3.40 V, respectively. The amplitudes are calculated using the equations in [11], with electrode material parameters described in [12]. Considering this range of artifact sizes, the input signal limit, \( V_{sig,max} \), is set to 5 V, which determines the specification for the ADC and DAC full-scale voltage.

In comparison, neural signals, such as extracellular APs and LFP can have an amplitude range of 50 µV-5 mV at a frequency range of 1 Hz-10 kHz [13]. The system’s noise floor requirement, \( V_{sig,min} \), is thus set to be < 50 µV. The resulting dynamic range, \( V_{sig,max}/V_{sig,min} \), is 100 dB. ADC
and DAC sampling rates are set to be 100 kHz, which is sufficiently high to allow filtering of the high-frequency switching noise while still preserving signals of interest up to 10 kHz. The data converter resolution is set to digitize the artifact without digitizing the neural signal. A 12-bit resolution at 5 V full-scale results in a least significant bit (LSB) value of 1.22 mV, while a 10-bit resolution results in a LSB of 4.88 mV. These resolutions accommodate both AP and LFP signals, respectively. An ADC and DAC with 12 bits of resolution are chosen to allow adjustment of resolutions, by discarding the last two bits when not needed. Finally, the hardware output gain is designed to be programmable between 40 dB and 60 dB.

The hardware analog signal subtraction and multiplication is performed by three operational amplifiers. The first subtracts the reference electrode (RE) from the working electrode (WE), the second executes the core functionality by subtracting the MCU’s stored artifact template from the output of the first stage, and the third amplifies the residual artifact by the selected gain to output to the software module.

The MCU performs artifact cancellation in three phases, each initiated by a trigger signal that is synchronized to each stimulus pulse. Phase 1 digitizes and stores the initial artifact as a template, phase 2 iteratively updates the template based on the difference measured by the ADC until the template converges within maximum hardware resolution, and phase 3 subtracts the final template from all following artifacts. Periodic template calibration, by re-entering phase 2, ensures an accurate waveform shape to handle artifact drift.

The power supply used for the system directly powers the amplifiers at 15 V for a high output signal swing to take advantage of the full input range of the DAQ card that digitizes and relays the signal to the software module. The DAQ card digitizes the hardware output signal at a relaxed resolution requirement, since the output signal is already amplified by a gain of 40 to 60 dB.

The hardware circuit is realized on a standard four-layer printed circuit board (PCB), designed to avoid analog and digital trace signal coupling. A National Instruments NI 6259 M-series DAQ card is used to relay the output of the PCB board to the GUI-based software algorithm.

A custom-designed GUI provides an intuitive interface for users to apply the template subtraction algorithm on the hardware output. Template averaging segments the device output into individual artifact instances and subtracts the averaged artifact shape from each instance to recover the underlying neural response, as described in (2). A 3rd order Butterworth band-pass filter with a band of 350-5000 Hz for AP data and 10-100 Hz for ECoG data extracts the neural signals of interest.

III. EXPERIMENTAL RESULTS

The prototype device is tested in-vitro with stainless steel wire electrodes immersed in saline (0.90% NaCl) based on the same-electrode stimulation and recording setup shown in Fig. 1. A custom current mode stimulator built by this lab [1] is used, and a pre-recorded neural signal is superimposed on the working electrode during each of the stimulation tests.

A. Test Results

The functionality of the prototype device is demonstrated by recovering ground truth AP signals from 20 Hz biphasic artifacts with 200 µA and 5 ms pulse-width and ECoG signals from 20 Hz biphasic artifacts with 200 µA and 10 ms pulse-width. Fig. 4 shows segments of the hardware input (ground truth + stimulus artifact), hardware output (residual artifact), and software output (recovered signal). The hardware output resembles the simulated signal in Fig. 3, adopting a sawtooth waveform from the quantization errors of the digitized artifact template. In Fig. 4a, AP spikes are fully recovered from the overlapping stimulus artifact, showing minimal distortion of the ground truth input. In Fig. 4b, fast gamma oscillations during an onset of seizure are recovered, preserving the key amplitude changes in the ground truth.
neural signals with frequency filtering alone is insufficient for the recovery of the neural signal. System noise increases the noise level in the recovered signals compared to the ground truth, but does not affect the features of interest in each test case.

B. Frequency Spectrum Analysis

The Fourier transform plots in Fig. 5 show the frequency content of the signals throughout the various stages of the artifact cancellation system. Since the periodic, high edge rate artifact waveform contaminates the neural signals with harmonics at all frequencies, as shown in the hardware input and output, frequency filtering alone is insufficient for the recovery of the signal of interest. In comparison, the software output illustrates the frequency content of the recovered neural signal, which is free of such harmonics. In addition, the similarity between the Fourier transformations of the ground truth and the recovered signal indicates that the neural signal is preserved with minimal distortion, as was the case in the time domain analysis in the previous section.

C. Comparison to Previous Works

Recent and past works demonstrating results with artifact cancellation by use of hardware or software techniques are summarized in Table I. To the best of the authors’ knowledge, the proposed work is the first to achieve full online neural response recovery during a large artifact event, while stimulating and recording on the same electrode.

IV. CONCLUSION

The proposed system allows simultaneous neural stimulation and recording on the same electrode by cancelling stimulus artifacts in real-time. This design uses both hardware and software techniques and is implemented using off-the-shelf components, custom PCB, and custom GUI-controlled software algorithms. In-vitro test results with pre-recorded neural signals demonstrate the ability to fully recover neural responses before, during, and after stimulus artifact events, even if the artifact amplitudes are orders of magnitude greater than that of the neural signals. This study has various clinical applications, such as DBS, which uses high-frequency stimulus pulse trains to treat motor disorders, but the mechanisms of which are still poorly understood due to the contamination of artifacts in neural recordings.

![Fig. 5. Frequency content during the signal processing stages. After software recovery, the frequency content matches that of the ground truth.](image-url)

<table>
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<th>Table I: System Comparison</th>
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<tbody>
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<td>Approach</td>
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<td>Prevent saturation?</td>
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<tr>
<td>Same-electrode setup?</td>
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<td>Recover signal during artifact?</td>
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<td>Large artifact-to-signal ratio?</td>
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REFERENCES


