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Comparison of Common Artifact Rejection Methods applied to Direct Cortical and Peripheral Stimulation in Human ECoG

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***Abstract*—Invasive and non-invasive electrical stimulation are increasingly being used for the diagnosis and treatment of neurological disorders, and for characterizing neural circuits involved in a range of behaviors. However, there are substantial challenges in understanding the effects of stimulation on brain activity due to contamination of electrophysiological recordings by electrical stimulation artifacts. Here, we compare the performance of several artifact removal methods on electrocorticographic (ECoG) recordings with simultaneous cortical or peripheral stimulation in humans. We systematically evaluated the effects of stimulation modality, stimulation frequency, and neural recording frequency on the ability to reconstruct neural activity amplitude and phase data. We found that no single method was most effective for all situations, however it was possible to reconstruct key neural data features in every case. The development of optimized artifact removal procedures will facilitate clearer understanding of the biological effects of electrical stimulation and allow for improved therapeutic applications.**

I. Introduction

The use of electrical stimulation to modulate brain function and behavior is of great interest for clinical and scientific endeavors, including as a therapeutic treatment for disease [1-3], reinstatement of lost function [4-7], and for enhancement of function beyond normal baseline performance [8-10]. Recent efforts have tested the effects of stimulation using both invasive (direct electrical stimulation [11-12], deep brain stimulation [13], vagus nerve stimulation [14-15]) and non-invasive (transcranial current stimulation, peripheral/transcutaneous nerve stimulation [16]) methods. Although each of these applications has been used successfully in certain subject populations, our ability to refine and extend the utility of electrical stimulation has been hindered by difficulties in evaluating its effects on cortical and subcortical neurophysiology, due to contamination of electrophysiology recordings by the electrical stimulation itself.

Among the crucial outstanding questions, it is unknown how the application of current directly affects neural circuits and networks, and for how long the effects of stimulation outlast its application. Therefore, conducting neurophysiological recordings immediately before and after stimulation is insufficient. A number of artifact rejection techniques have been developed and applied in an attempt to recover usable physiological signals during stimulation. At the scale of neuronal networks (on the order of millimeters to centimeters), amplitude and phase of brain oscillations are commonly studied, obtained by calculating the FFT or other frequency domain transform of the timeseries. Here, we systematically applied commonly-used signal processing and artifact rejection techniques to human electrocorticography (ECoG) data and directly compared their effects on the ability to recover amplitude and phase information during stimulation. Artifacts were taken from application of direct cortical stimulation and peripheral nerve stimulation in patients undergoing ECoG monitoring for epilepsy. However, instead of applying the artifact rejection technique directly to these data with stimulation artifacts, we added the artifacts to periods of ECoG recordings during which no stimulation was delivered, and subsequently applied artifact rejection. Thus, we were able to evaluate the effects of the artifact rejection procedure itself on amplitude and phase representations of the signals, the metrics which are most commonly used to assess biological effects of electrical activity in the brain.

II. Experimental Procedures

Stimulation was administered during concurrent ECoG recording in 4 patients undergoing inpatient monitoring for the localization of seizure foci in epilepsy. The experimental protocol was approved by the Committee for Human Research at the University of California, San Francisco and the University of Iowa. Written informed consent was obtained from all subjects. ECoG data were acquired at sampling rates of 3kHz ('low Fs', peripheral stimulation and direct cortical stimulation) and 24.4kHz ('high Fs', direct cortical stimulation; Tucker-Davis Technologies, PZ5M-512, RZ2), and at 24.0kHz ('high Fs') during peripheral stimulation (NeuraLynx ATLAS). Direct cortical stimulation was delivered through ECoG electrodes (100Hz, 3mA, biphasic pulses, 100μs pulsewidth, IZ2MH, Tucker-Davis Technologies), and peripheral nerve stimulation was delivered non-invasively through a bipolar electrode attached to the cymba concha of the left ear (30Hz, 0.6mA, biphasic pulses, 250μs pulse width, BioPac STMISOLA Constant Current and Constant Voltage Isolated Linear Stimulator) (Fig 1A).

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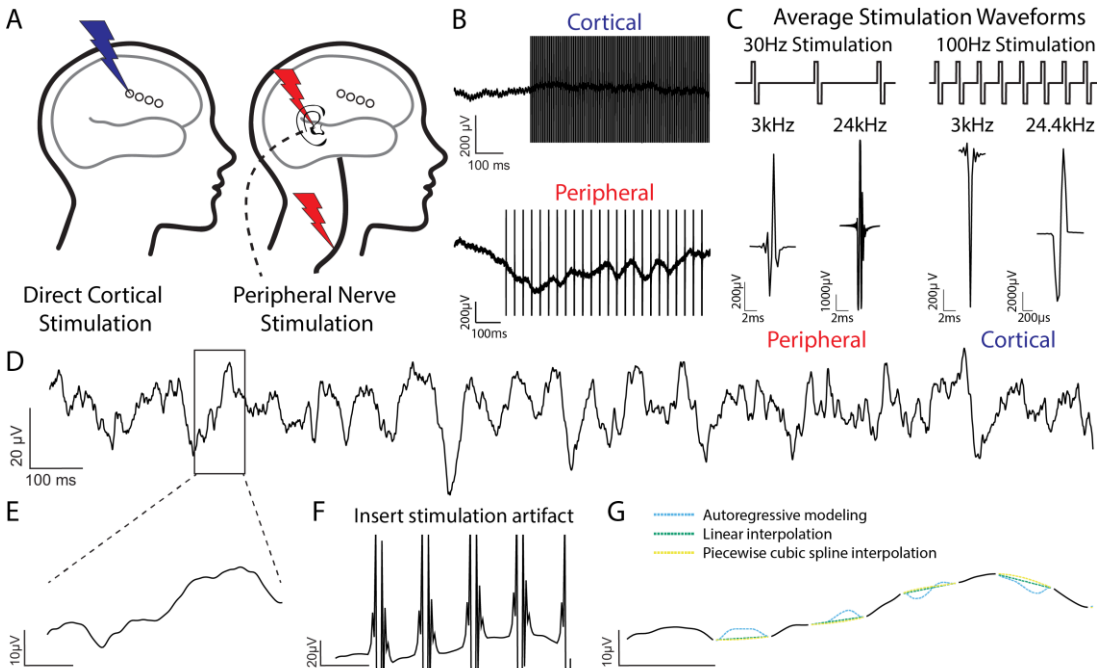

Figure 1. Overview of experimental and artifact cleaning procedures. (A) Stimulation artifacts recorded from four patients receiving either direct cortical (blue) or peripheral nerve (red) stimulation. (B) Example ECoG time-courses with recorded electrical artifacts; y-axis truncated. (C) Average stimulation waveform extracted for each type of stimulation in recordings acquired with low and high sampling rates. (D) Sample 'original signal' free of stimulation artifact. (E) Data segment from (D). (F) Same data segment as (E) after insertion of a 100Hz cortical artifact; y-axis truncated. The notch-filtering method was applied to this artifact-inserted time series. (G) Three additional artifact rejection procedures were tested and compared on the same data.

III. Methodology

A. ECoG Processing

One hundred one-second trials of clean data were extracted from an ECoG channel during a low Fs recording and a high Fs recording (Tucker-Davis Technologies), representing the 'original signal'. Channel amplitude was normalized to 1, and the signals underwent notch filtering at line noise frequencies (± 2Hz), bandpass filtering [2 250Hz], and downsampling to 512Hz. Zero-phase digital filtering was used in order to prevent phase distortion. These signals represent the 'clean original signal'. Average artifacts were extracted from recordings with each stimulation condition (Figs 1B and C) and the artifact amplitudes were normalized to 1. These artifacts were then applied to copies of the original signal (Figs 1D, E, and F) by multiplying the artifact with a Hanning window of the same size and a scaling factor of 40 (determined through empirical observation of the relative amplitude between signal and artifact), and replacing the samples in the original signal with the generated artifact. Peripheral stimulation artifacts were 8ms long, while cortical stimulation artifacts were 5.6 and 0.98ms when acquired at 3kHz and 24.4kHz sampling, respectively. Artifact durations were determined using visual inspection.

Four artifact rejection procedures were tested, detailed below. Following the procedure-specific processing steps, all signals underwent the same line noise notch filtering, bandpass filtering, and downsampling as was used to obtain the clean original signal. We applied artifacts whose sampling rate (low or high Fs) matched the sampling rate of the original signal. Each type of artifact (cortical and peripheral) was applied at each of the empirically tested stimulation frequencies (30Hz and 100Hz) in different test sets. Together, this allowed us to investigate the effects of sampling rate, stimulation frequency, and morphology of stimulation artifact. Finally, amplitude and phase were extracted from all test sets by applying the Hilbert transform to bandpass filtered signals using logarithmically spaced center frequency bands between 2 and 200Hz. Performance of artifact rejection techniques was assessed by computing squared Pearson correlations between matched trials of the original clean signal and each artifact rejection technique, for each frequency bin, separately for amplitude and phase. Plotted results show the mean (± sem) R^2 value across trials. All analyses were conducted in MATLAB and R.

B. Artifact Cleaning Methods

- Notch: 4th order Butterworth filter applied at stimulation frequency and harmonics up to 1kHz (center frequency ± 2Hz).
- Autoregressive Modeling (ARM): Artifact periods interpolated using a forward and backward autoregressive model, with the number of samples used for estimation set to half the artifact duration and a model order of 5. Samples during the artifact were not included in modeling [17].
- Linear Interpolation: Linear interpolation between samples adjacent to each stimulation artifact [18].
- Piecewise Cubic Hermite Interpolating Polynomial (PCHIP): Data between samples containing artifacts were interpolated by fitting a cubic polynomial with query points at the edges of each artifact. [19].

IV. RESULTS

By calculating the R^2 values between the clean original signal and signals with artifact added and artifact rejection methods applied, we could assess the performance of each method (Fig 2). Overall, lower sampling rate (3kHz) ECoG suffered more corruption in amplitude and phase reconstruction relative to higher sampling rate data (see https://github.com/ChangLabUcsf/StimulationArtifactRejectionMethods). Thus, we focused our analyses on data and artifacts acquired at high sampling rates (24.0 and 24.4 kHz).

The performance of each artifact removal method varied across frequencies for each artifact condition. For example, when looking across all frequencies, ARM performed best for 100Hz peripheral and cortical stimulation. However, at high gamma frequencies (70-150Hz), notch filtering was superior for 100Hz cortical stimulation but the poorest method for 100Hz peripheral stimulation. Linear interpolation consistently outperformed PCHIP. Notch filtering generally did poorly, with some specific exceptions (high frequency activity during 100Hz cortical stimulation; select frequencies during 30Hz peripheral stimulation).

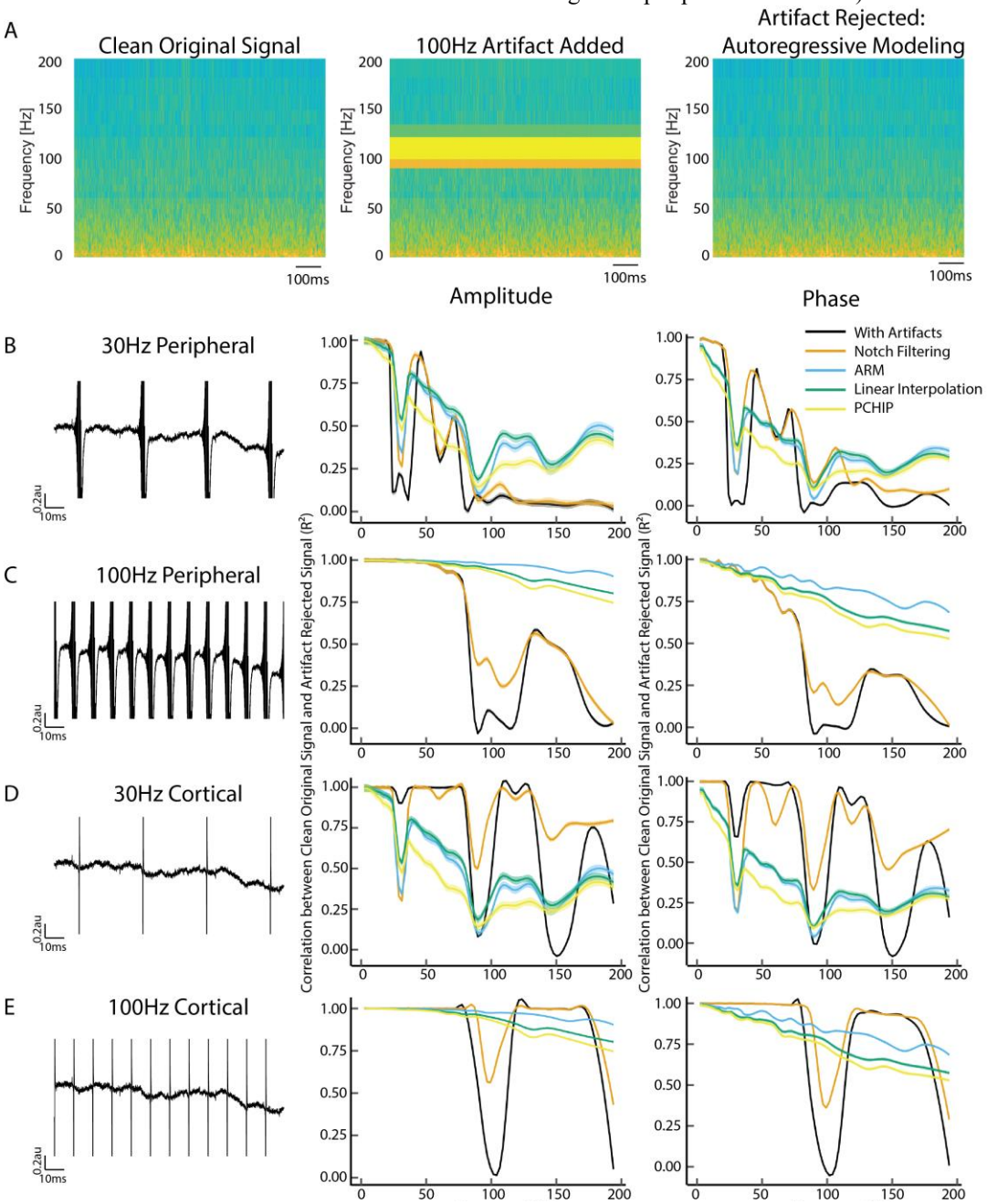

Figure 2. Evaluation of artifact rejection techniques for high sampling rate data. (A) Analytic amplitude spectrograms of the clean original signal (left), the same data with 100Hz stimulation artifact added (center), and the same signal with reconstructed data using ARM (right). (B-E). Left: Sample time courses of ECoG with artifacts inserted. Center: LOESS (LOcal regrESSion) lines fit using 100 trials, representing central trend ± standard error of squared Pearson correlation (R^2) between the clean original and reconstructed analytic amplitude (obtained via Hilbert transform), plotted separately for each method. Right: LOESS lines ± standard error of squared Pearson correlation (R^2) between clean original and reconstructed phase.

V. DISCUSSION

Amplitude and phase of neurophysiological signals are commonly used to understand brain activity. However, calculation of these metrics is sensitive to missing values in the timeseries and sharp voltage fluctuations, which are associated with electrical stimulation artifacts. We applied different artifact removal methods to dampen stimulation frequency harmonics or estimate underlying samples corresponding to the timing of electrical stimulation artifacts and compared how much these techniques affected the calculation of amplitude and phase relative to the original clean data. We found that high sampling rate during acquisition was critical for faithful representation of amplitude and phase data, likely because higher sampling rates were better able to capture short duration stimulation pulses and high-frequency components due to edges of the rectangular waves. Lower frequency activity was reconstructed more accurately than higher frequency activity. Interestingly, performance of artifact removal was much more sensitive to the frequency of stimulation, rather than the width of each stimulation artifact. This may result from multiple harmonics of the stimulation frequency corrupting data within frequencies of interest. Generally, the artifact removal techniques performed equally well for amplitude and phase at a given frequency.

Our study demonstrates that there may not be a one-size-fits-all best approach for stimulation artifact removal, but rather the specific metrics of interest must be considered when planning electrophysiological recording parameters and cleaning data. We were primarily interested in frequency-domain metrics (amplitude and phase), and thus how the interpolated data influenced results of a time-frequency transform. ARM, linear interpolation, and PCHIP each resulted in high R^2 values between the original clean signal LFP and the reconstructed LFP time series. Thus, considerations for the optimal method may differ if staying in the time domain or converting to the frequency domain.

The comparisons conducted here were not exhaustive, and did not comprehensively search the parameter space. We note the following limitations: For all methods, we chose parameters that were based on theoretical and empirical considerations; we did not assess topological effects of stimulation artifact with varying distances from the stimulation location; insertion of stimulation artifacts into recorded signal does not fully incorporate long-term capacitive changes that may occur at the electrode-tissue interface; the results may differ with other stimulators or different electrode types; we focused investigation on artifacts generated by electrically -isolated stimulators commonly employed for safe cortical, peripheral, and non-invasive neurostimulation; we did not utilize or test specialized hardware with analog front-end modifications to suppress stimulation artifact during data acquisition. More comprehensive future study into these questions will be critical to develop well-motivated and practical techniques.

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