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Real-time artifact detection and removal for closed-loop EEG–TMS

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Abstract. Transcranial magnetic stimulation (TMS) combined with electroencephalography (EEG) is a non-invasive tool for studying brain connectivity and excitability. However, the EEG signals are often hindered by artifacts. Several signal-processing methods have been developed for correcting these artifacts offline. Yet, new promising EEG–TMS applications, such as closed-loop stimulation, would greatly benefit from artifact correction in real time. We present an algorithm for real-time attenuation of extracranial noise and removal of ocular artifacts from EEG–TMS data. Two established offline cleaning methods were implemented in a real-time setting: the source-estimate-utilizing noise-discarding (SOUND) algorithm and ocular-artifact removal with independent component analysis (ICA). This procedure cleans streamed raw data by multiplying every EEG sample with SOUND and ICA spatial filters, with a delay of less than 0.1 ms. The SOUND filter is constantly updated in a parallel process to react to changes in noise characteristics. In tests with pre-recorded EEG–TMS data, the proposed algorithm was fast enough for real-time use, removed ocular artifacts efficiently, and detected and cleaned contaminated channels automatically, leaving the noiseless channels intact. The algorithm can be used to detect and remove extracranial noise and ocular artifacts in real-time EEG and EEG–TMS experiments.

Keywords: transcranial magnetic stimulation, electroencephalography, artifact removal, closed-loop stimulation, real-time signal processing

1. Introduction

Transcranial magnetic stimulation (TMS) is a tool for probing cortical excitability and connectivity (Tremblay et al., 2019). It also has several therapeutic applications, such as depression treatment. TMS could be further enhanced by timing it during specific brain states, informed by real-time electroencephalography (EEG) (Zrenner et al., 2016). Unfortunately, raw EEG–TMS data can be severely contaminated by extracranial signal sources, such as cranial muscle activity, ocular artifacts, and electrode-related noise (Ilmoniemi et al., 2015). Effective real-time cleaning of EEG would help to identify brain states more precisely and improve the robustness of closed-loop EEG–TMS applications.

Here, we present a real-time artifact-removal algorithm for EEG–TMS. The algorithm removes ocular artifacts in a data-driven manner, and noise from other extracranial sources by using the conductivity profile of the head. To this end, two established offline cleaning methods, the source-estimate-utilizing noise-discarding algorithm (SOUND) (Mutanen et al., 2018) and independent component analysis (ICA) (Vigário, 1997), were modified for real-time use. SOUND uses the EEG forward model to cross-validate the EEG traces across channels. As a result, a linear spatial filter that suppresses noise is formed. The assumption of SOUND is that due to the effects of the low-conductivity skull and the well-conducting skin, intracranially generated EEG signals are more correlated across channels than extracranially generated artifacts. Independent component analysis (ICA), a common method for removing EEG and EEG–TMS artifacts (Vigário, 1997; Rogasch et al., 2017), is based on the assumption that the EEG data can be represented as a linear combination of temporally independent neuronal and artifactual components (Vigário, 1997).

2. Methods and materials

2.1 The algorithm

The algorithm removes extracranial noise and ocular artifacts in real time by multiplying every EEG data sample with SOUND and ICA spatial filters. The SOUND filter was estimated and updated based on 500-ms-long data segments allocated in a buffer. This operation did not slow down the real-time sample-by-sample cleaning because it ran in a parallel process. We built the ICA filter by using 200 s of data from the beginning of the measurement as calibration data and visually identifying ocular-artifact topographies. The same ICA filter was used throughout the real-time process. The working principle of the algorithm is illustrated in Fig. 1.

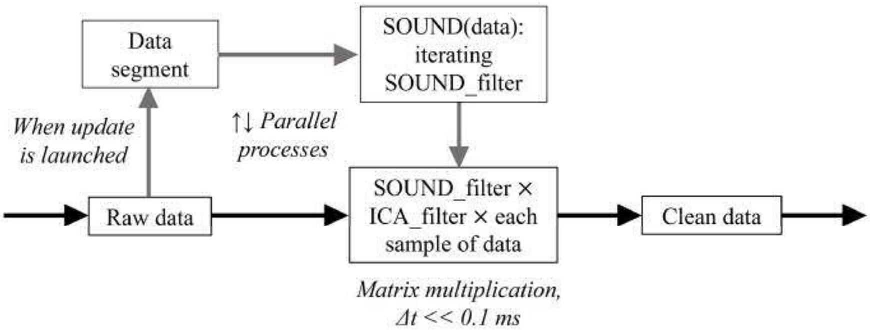

Figure 1. *The working principle of the real-time cleaning algorithm with the source-estimate-utilizing noise-discarding (SOUND) algorithm and independent component analysis (ICA). Each raw data sample is cleaned by multiplying it with the SOUND and ICA spatial filters. The SOUND filter is regularly updated in a parallel process based on short data segments.*

The filters were different for resting-state and post-pulse (0–500 ms after each TMS pulse onset) data due to distinct noise distribution and statistical properties. In addition to cleaning the data, the algorithm digitally blocked the high-amplitude TMS-pulse artifact for 10 ms, and baseline-corrected every data sample with a sliding window of the latest 500 ms of resting-state data. The resulting real-time implementation was based on the open-source SOUND tools (Mutanen et al., 2020) and the FASTICA package (Hyvärinen & Oja, 2000).

2.2 Assessing the algorithm

We tested the algorithm with streamed pre-recorded TMS-evoked EEG measured from a 25-year-old right-handed healthy female who had given her written consent. The experiment was accepted by the local ethics committee at the medical faculty of the University of Tübingen (protocol 716/2014BO2) and conducted in accordance with the Declaration of Helsinki. In the measurement, single-pulse TMS was applied to the left primary motor cortex with a randomized inter-stimulus interval of 2 ± 0.25 s. Simultaneous 126-channel EEG was recorded with a sampling frequency of 5000 Hz with a 24-bit biosignal amplifier in DC mode (NeurOne, Bittium, Oulu, Finland) and a TMS-compatible 128-channel cap with Ag/AgCl sintered ring electrodes (EasyCap BC-TMS-128, EasyCap, Herrsching, Germany), placed according to the International 10-5 system. Streaming and all tests were run on MATLAB r2020b on a computer with a dual-core Intel Core i7-7500U processor and 8 GB of RAM.

Real-time SOUND cleaning was performed by updating the SOUND filter in one parallel process every 500 ms. The quantitative tests of the noise-removal quality of real-time SOUND were based on comparing real-time-SOUND-cleaned data with the raw[1] and with the offline-SOUND-cleaned data. We ran these tests with 100 pre-determined 2-s trials (from 1 s before to 1 s after each TMS pulse), which were randomly chosen from the entire 42-minute-long session. We assessed the quality of real-time SOUND by computing the relative root-mean-square difference (RMSD) between offline- and real-time-cleaned data, raw and real-time-cleaned data, and by estimating the change in signal-to-noise ratio (SNR) due to real-time SOUND cleaning.

Ocular-artifact removal was tested quantitatively in the frequency domain. We visually located resting-state blinks from the data. A time period of 500 ms was assigned for each blink (starting from the first EEG onset of the blink), along with a 500-ms adjacent pre-blink period. Successful real-time-ICA-cleaning should exclusively remove the ocular-signal-related low frequencies, making blink- and pre-blink spectra more alike compared to the raw data, while the pre-blink spectrum should not change from the raw data.

[1] The term raw refers to the data corrected only for the baseline and TMS-pulse artifact.

3. Results

Visual inspection of the streamed EEG data (Fig. 2) suggested that the real-time ICA suppressed the ocular deflections and that SOUND restored signals in the noisy channels while leaving other channels unaltered. The mean sample-processing durations in Table 1 demonstrate that the algorithm is capable of real-time cleaning, since processing one sample of data took less time than the inter-sample interval of 0.2 ms. The median update duration can be understood as the minimum inter-update interval: with one parallel process (Fig. 1), a new update can be started every 40 ms for 60-channel 5000-Hz data.

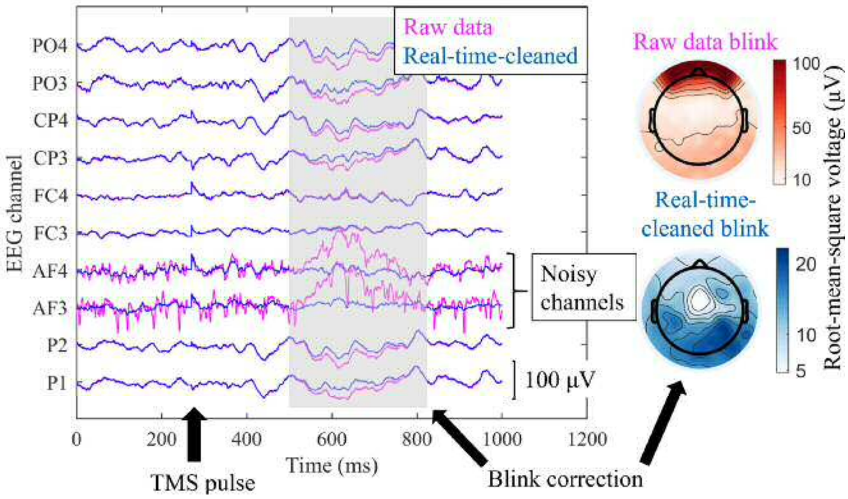

Figure 2. *Example of real-time visualization of the cleaning algorithm showing raw (baseline-corrected) and real-time-cleaned data after cleaning TMS-pulse artifacts, blink artifacts, and noise. The noise in channels AF3 and AF4 is due to frontal muscle activity. The right panel shows how the blink-related EEG topography was attenuated.*

Table 1. *SOUND-update durations and mean sample-processing times of the algorithm for two different numbers of channels.*

N:o of channels	*Sampling frequency* (Hz)	*Median update duration* (ms)	*Mean sample-processing duration* (ms)
126	5000	280	0.088
60	5000	37	0.018

Results presented in Fig. 3 show that there was an increase in SNR after real-time-SOUND cleaning. Median and mean relative increases in SNR over channels were 20% and 115%, respectively. The increase was especially large in frontal areas, which indicates that real-time SOUND corrected noisy frontal channels but left non-noisy parietal channels intact. The relative RMSDs demonstrated that real-time- and offline-SOUND-cleaned data were more similar than real-time-cleaned and raw data, especially in the noisiest channels. The mean relative RMSD was 36% between real-time- and offline-cleaned data and 41% between real-time-cleaned and raw data. However, the mean relative RMSD across the ten noisiest channels (based on the estimated SNR of raw data) was 63% between real-time-cleaned and raw data and only 38% between real-time- and offline-cleaned data.

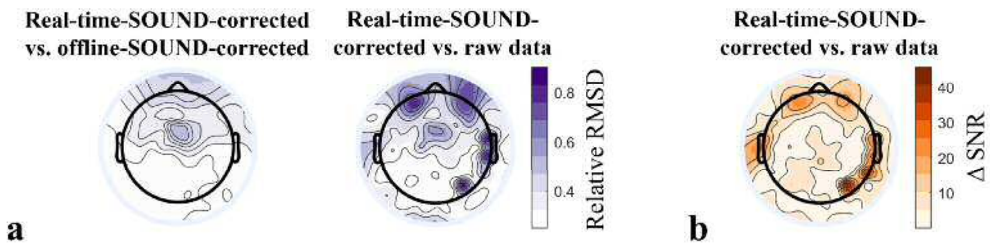

Figure 3. *Comparing real-time-SOUND-cleaned data with raw (baseline-corrected) or with offline-SOUND-cleaned EEG–TMS data. Topographies represent the median values over trials. a. Relative root-mean-square differences (RMSD) are larger between real-time-cleaned and raw data than between real-time- and offline-cleaned data, especially in noisy frontal areas. b. Signal-to-noise ratio (Δ SNR) was considerably improved in the frontal channels by real-time SOUND.*

When comparing the frequency spectra between the raw and real-time-ICA-cleaned data, ICA did not change the frequency content of pre-blink periods. However, ICA brought the blink-period spectra closer to the pre-blink-period spectra by removing large-amplitude low-frequency components. This change in the spectra suggests that real-time ICA effectively removed blink artifacts while leaving non-blink-contaminated data largely unaltered.

4. Discussion

Real-time cleaning has several advantages in addition to robust noise and artifact correction. The fast update times of the SOUND filter allow the algorithm to react promptly to sudden changes in noise signals. SOUND can also be used to monitor the noise levels of EEG data: sudden large deviations in noise might indicate temporary signal-quality issues, and the data can be ignored until the noise settles. Notably, other spatial filters, such as for rejecting muscle activity (Mutanen et al., 2016), can be easily incorporated into the developed pipeline. Effective real-time cleaning may improve discrimination accuracy of brain-computer interfaces (BCI) and in several clinical applications of EEG–TMS.

The algorithm needs further testing in different EEG–TMS scenarios. For instance, a crucial next step is to verify a possible improvement in the accuracy of a closed-loop EEG–TMS measurement. The pipeline must be implemented inside a real-time EEG-processing architecture. In such a system, spatial filtering can be a part of a linear sample-by-sample process. In turn, the SOUND update should be implemented as an asynchronous parallel process on a separate core or even a separate computer. We are currently implementing the algorithm in the EEG–TMS experimental setup proposed by Zrenner et al. (2020).

5. Summary

We developed an algorithm for real-time EEG–TMS-artifact detection and removal that can also be utilized for other streaming EEG data. The algorithm removes non-cortical noise and ocular artifacts with a runtime short enough for use in closed-loop applications. The results show that the real-time SOUND implementation detected and recovered noisy channels. The real-time ICA, trained with calibration data, removed ocular artifacts throughout the data set.

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