ORIGINAL ARTICLE

Transcranial Magnetic Stimulation Evoked Electroencephalography Potential Denoising with Hampel Filter

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ABSTRACT

Introduction: Transcranial Magnetic Stimulation (TMS), when combined with electroencephalography (EEG), enables the study of immediate neuronal responses, including cortico-cortical activity. However, TMS-evoked potentials (TEPs) are often obscured by high-frequency artifacts generated by direct interference with EEG electrodes. These artifacts can persist up to 40 milliseconds post-stimulation, contaminating neural signals and hindering accurate interpretation. This study aims to remove TMS artifacts using a Hampel filter without relying on an external sample-and-hold circuit, to obtain a continuous, artifact-free EEG signal. **Materials and methods:** TMS was delivered to ten healthy participants using a butterfly coil over the left frontotemporal region at 70% of the motor threshold. EEG data were recorded using a Mobita wireless amplifier and a 16-channel EEG cap. A three-stage filtering pipeline was applied: Hampel filtering to suppress impulsive TMS artifacts, wavelet denoising to eliminate broadband noise, and Butterworth filtering to isolate the EEG frequency band of interest. **Results:** Raw EEG signals were heavily contaminated by TMS artifacts that conventional filters failed to remove. The Hampel filter significantly reduced these artifacts, enabling effective wavelet and Butterworth filtering. The residual-based signal-to-noise ratio (SNR) improved markedly from 0 dB to 53 dB after processing. The cleaned EEG data revealed distinct TMS-evoked potentials previously masked by noise. **Conclusion:** The combination of Hampel filtering, wavelet denoising, and Butterworth filtering effectively removes TMS artifacts and enhances EEG signal quality. This approach allows for more accurate analysis of TEPs, supporting improved understanding of brain responses to TMS.
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INTRODUCTION

Electroencephalography (EEG) and transcranial magnetic stimulation (TMS) are two widely used techniques in neuroscience research. EEG measures the electrical activity of the brain, while TMS is a non-invasive method of stimulating specific regions of the brain using magnetic fields. Both techniques have their own strengths and limitations, and researchers often use them in combination to gain a more comprehensive understanding of brain function. Combining TMS with electroencephalography (EEG) allows for the investigation of immediate and direct neuronal responses to TMS, including cortico-cortically mediated activity.

One challenge in using EEG and TMS together is the presence of noise in the EEG signal that can be caused by the TMS pulse itself [1]. This noise can interfere with the accurate interpretation of the EEG data and may lead to erroneous conclusions. TMS-evoked potentials (TEPs) are significantly impacted by large, high-frequency magnetic artifacts generated by direct interference with the EEG electrodes. These artifacts, characterized by high amplitude and frequency, persist for up to 40 milliseconds post-stimulation. Conventional filtering methods with limited sampling rates introduce ripple artifacts beyond this window, contaminating the underlying neural signals.

Due to the typically low amplitude of evoked potentials (less than a millivolt), it is crucial to minimize noise interference, as even small disturbances can significantly affect the signal. Signal averaging is one method used to reduce noise by calculating the average of repeated responses, taking advantage of the fact that evoked potentials are time-locked to the stimulus while noise is random. However, if the TMS artefact is not eliminated beforehand, the averaged responses will be contaminated with the unwanted magnetic noise.

Many studies used a circuit within the EEG amplifier to sample-and-hold the signal during the TMS application [2–4]. This can reduce the TMS artefact, but the EEG signal will be lost throughout the TMS application. One common denoising technique is the use of independent component analysis (ICA)[5–7]. ICA is a signal processing method that separates a multivariate signal into independent components, each representing a different source of activity. However, the use of ICA still it cannot eliminate the artefact without using the sample-and-hold circuit.

Hampel filter is a robust statistical technique used for signal denoising, particularly effective in identifying and correcting outliers in time series data. Recent studies underscore the Hampel filter's efficacy in mitigating impulsive noise across various signal processing applications. For instance, Ghaleb et al. [8] introduced a two-stage algorithm combining weighted adaptive noise cancelling with a recursive Hampel filter to effectively reduce motion artifacts in ECG signals, demonstrating significant improvements in signal clarity during physical activities.

Furthermore, research by Nagahawatte et al. [9] proposed a generalized framework for pacing artifact removal using a Hampel filter, achieving approximately 98% accuracy in outlier detection, significantly enhancing signal-to-noise ratios and reducing root mean square errors in both simulated and real datasets. These advancements highlight the Hampel filter's versatility and robustness in addressing noise-related challenges across diverse signal processing contexts. Therefore, this study is aimed to eliminate the TMS artefact to get a continuous EEG signal without interruption by using Hampel filter with no external sample-and-hold circuit.

MATERIALS AND METHODS

Materials

A cohort of ten healthy undergraduate engineering students aged between 20 and 23 years old were recruited from Universiti Teknologi Malaysia (UTM) to participate in this study. Prior to the experiment, informed consent was obtained from all participants, followed by the collection of demographic information. A standardized questionnaire was administered to gather detailed data on participants' educational background, handedness, and any relevant medical history.

To induce transcranial magnetic stimulation (TMS), a butterfly coil was precisely positioned over the left frontal-temporal region of the scalp, a brain area implicated in auditory processing. The TMS stimulation was delivered using a MagPro Compact stimulator manufactured by MagVenture, Denmark. The intensity of the magnetic field, critical for eliciting a motor evoked response (MEP), was calibrated as a percentage of the individual participant's motor threshold. To optimize the experimental conditions and minimize potential confounding effects, the stimulation intensity was set at a consistent 70% of the motor threshold for all participants. The stimulation paradigm consisted of a single TMS pulse delivered every five seconds, resulting in a stimulation frequency of 0.2 Hz. Fig. 1 provides a visual representation of the experimental setup, including the placement of the TMS coil and the recording electrodes.

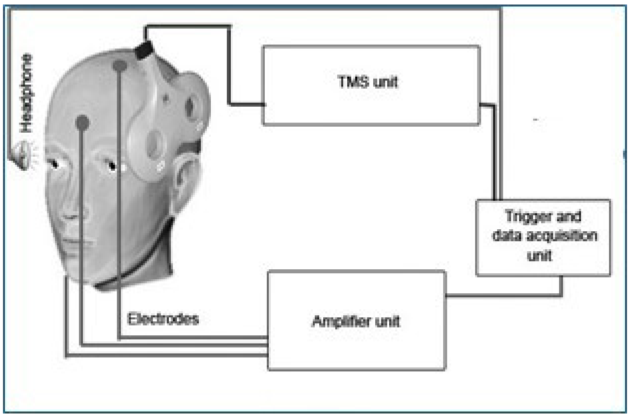

Fig. 1: Experimental setup

EEG data acquisition was conducted using a Mobita wireless EEG amplifier from TMSi, employing a 16-channel cap equipped with water-based electrodes. This system was selected for its high impedance stability and signal quality. The electrode placement adhered to the internationally recognized 10-20 system, ensuring consistent and comparable data across studies. A wrist electrode served as a reference for recording potential differences. The system's integrated amplifier provided necessary signal amplification for subsequent digitalization. Data acquisition and management were facilitated by Polybench designer software, which allowed for precise control over sampling rate, recording duration, and filtering parameters. A sampling rate of 1000 Hz was chosen to adequately capture the dynamic range of EEG signals, considering the anticipated frequency content of the brain activity under investigation.

EEG Signal Denoising

EEG signals are susceptible to noise from various sources including external devices, environmental factors, and physiological influences. As noise manifests in both time and frequency domains, a three-stage filtering approach was employed in this study. The process involved: 1) Hampel filtering to remove TMS artifacts, 2) wavelet denoising to eliminate general noise, and 3) Butterworth filtering to isolate the desired frequency band.

Hampel Filter

The initial preprocessing step involved applying the Hampel identifier to detect outliers. TMS noise, characterized by its non-conformity to the signal's statistical distribution and visual distinctiveness, can significantly distort the signal and lead to inaccurate results. The Hampel identifier, akin to the three-sigma rule, identifies outliers by calculating the mean, median, and standard deviation within a specified data window. This method's robustness against outliers is its primary advantage. The Hampel rule is defined as follows:

$$| x_i - m_i > n_\sigma \sigma_i |$$

Where,
x_i= sample number, m_i= sample local median, n_σ= given threshold, σ_i= sample standard deviation.

Once this rule is applied, the identifier declares this sample number as an outlier and replaces it with the median value and this specified window repeated for the remaining signal.

Wavelet Denoising

The second stage involved denoising using the wavelet method, a technique renowned for its joint time-frequency analysis capabilities. This makes it an invaluable tool for signal processing. The wavelet function can be represented as follows:

$$F\,(a,b)= \int_{-\infty}^{\infty} F(x)\ \varphi^*_{(a,b)}(x)dx$$

For signal analysis, the Discrete Wavelet Transform (DWT) was applied due to its suitability for two-dimensional signals. DWT decomposes the signal into high and low-frequency components through successive filtering stages. Each stage halves the data length, adhering to the Nyquist criterion. The output from the low-pass filter is termed approximation, while that from the high-pass filter is called detail. This process can be iterated to achieve the desired level of decomposition.

Butterworth filter

The EEG signal was filtered into the desired frequency band (0.5-100Hz) using a 6th-order Butterworth passband filter. This filter was chosen due to its advantageous characteristics, including a flat passband and stopband response, which ensures minimal signal distortion within the desired frequency range. Additionally, the Butterworth filter is known for its sharp transition between the passband and stopband, providing a clear separation of the desired signal components from unwanted noise. This sharp transition is particularly beneficial in EEG signal processing, where precise frequency isolation is crucial for accurate analysis. The 6th-order configuration further enhances the filter's performance by providing a steeper cut-off frequency, effectively attenuating frequencies outside the target band and preserving the integrity of the neural signals of interest. This meticulous filtering process is essential for obtaining high-quality EEG data, free from artifacts and noise, thereby enabling more reliable and meaningful interpretation of the underlying neural activity.

Residual-based signal-to-noise ratio

Residual-based signal-to-noise ratio (SNR) provides an estimate of denoising effectiveness when the clean reference signal is unknown. It is calculated by treating the difference between the noisy input and the filtered output as residual noise. In this study, the residual SNR was used to evaluate the performance of the combined Hampel, wavelet, and Butterworth filtering approach. SNR of a filtered signal ($x_{filtered}$) from a noisy signal (x_{noisy}) can be calculated as follows:

$$SNR\ = 10\log_{10}\frac{(x_{filtered})^2}{(x_{noisy})^2}$$

where the residual noise (xnoise) is estimated to:

$$x_{noise} = x_{noisy} - x_{filtered}$$

RESULTS

The recorded EEG signal was significantly contaminated by Transcranial Magnetic Stimulation (TMS) artifacts, which could not be effectively removed using conventional filtering methods. To address this, a Hampel filter was applied to the signal, enabling subsequent analysis. Fig. 2(a) compares the original and filtered signals, clearly demonstrating the impact of TMS-induced magnetic interference on the recording electrodes.

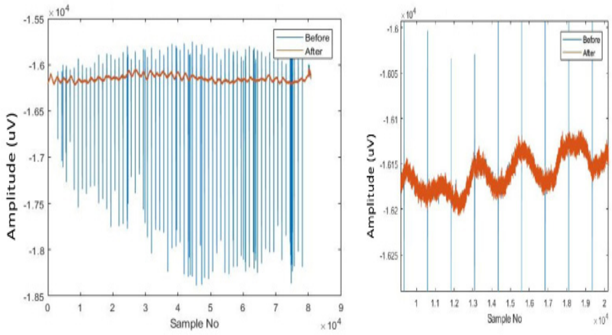

Fig. 2: (a) Difference between the original signal and the filtered signal after applying Hampel filter to the original recorded signal, (b) Zoomed signal of original signal and the filtered signal.

The Hampel filter effectively attenuates the magnetic artifacts induced in the EEG signal, enabling subsequent filtering processes. This makes it essential for mitigating the negative impact of transcranial magnetic stimulation on electroencephalography. Fig. 2(b) provides a zoomed-in view demonstrating the Hampel filter's ability to effectively remove outliers. Without this preprocessing step, the EEG data would remain contaminated by TMS artifacts, compromising the effectiveness of subsequent filtering stages.

Fig. 3 illustrates the comparative effects of applying and not applying the Hampel identifier before further filtering the EEG signal. The persistence of transcranial magnetic stimulation artifacts in the signal without the Hampel filter underscores the importance of the Hampel identifier in data preprocessing.

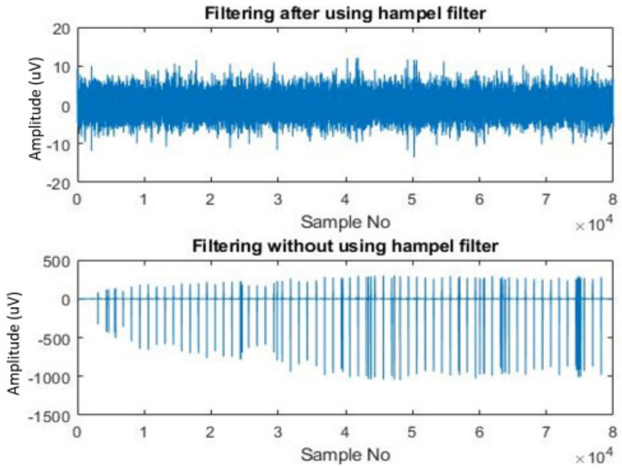

Fig. 3: Difference between filtered signal after using Hampel identifier and filtered signal without using Hampel identifier.

Following Hampel filter application, wavelet denoising using DWT was employed to further reduce signal contamination. The denoising results are depicted in Fig. 4.

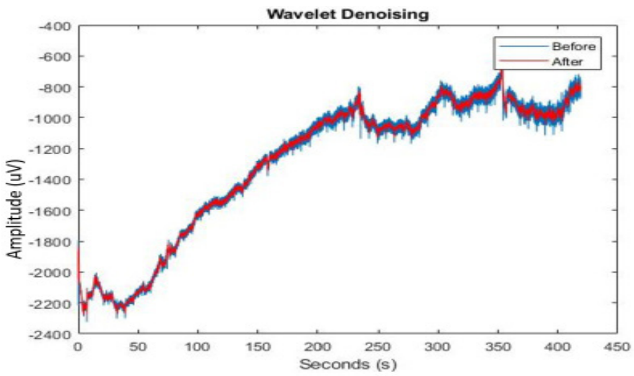

Fig. 4: EEG signal after wavelet Denoising.

As shown in Fig. 4, initial signal smoothing effectively reduced noise, but residual baseline wander persisted. To address this, a Butterworth filter was applied to eliminate unwanted low-frequency components, as illustrated in Fig. 5. The residual-based SNR for the EEG signal improved significantly after filtering, increasing from approximately 0 dB in the raw noisy signal to 53 dB in the final denoised output.

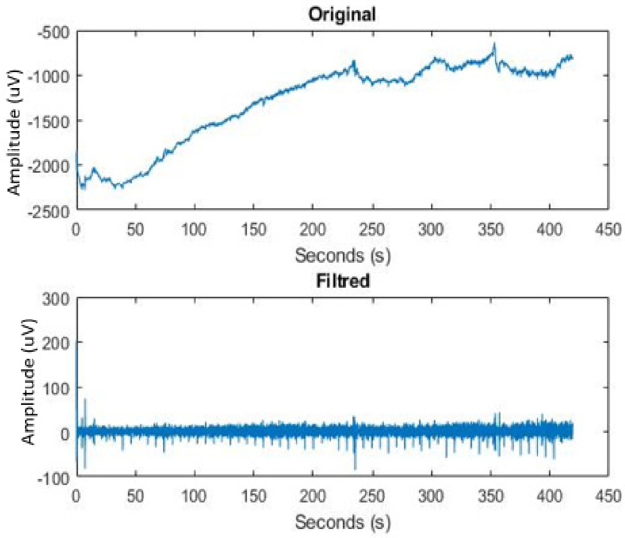

Fig. 5: EEG signal filtered with Butterworth filter to eliminate unwanted low-frequency components.

Subsequently, the signal was segmented based on TMS onset, and the resulting EEG epochs were averaged and analysed to extract evoked potentials. Fig. 6 illustrates an example of EEG signal segmentation with a 1-second interval (1000 samples per second), while Fig. 7 presents the averaged responses for different event types.

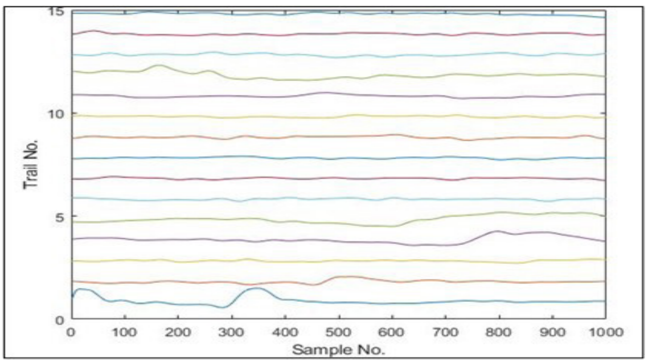

Fig. 6: EEG signal segmentation with 1 second interval.

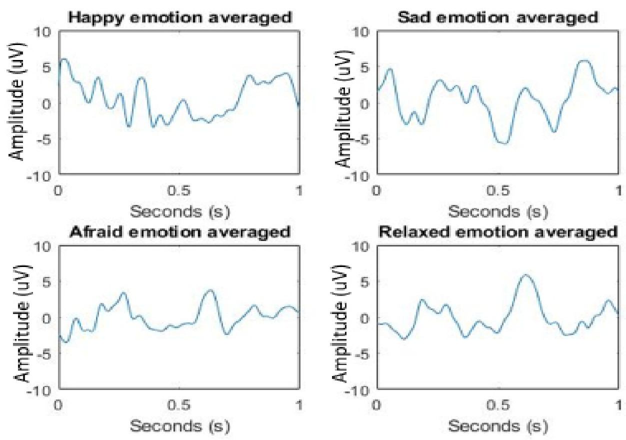

Fig. 7: Example of averaged EEG signal responses for different event.

DISCUSSION

This study addresses a significant challenge in the field of TMS-EEG research which is the contamination of EEG signals by TMS-induced artifacts. The results demonstrate the effectiveness of a three-stage filtering approach, comprising Hampel filtering, wavelet denoising, and Butterworth filtering, in mitigating these artifacts and enhancing the quality of EEG data. The Hampel filter, in particular, proved to be highly effective in attenuating the high-frequency and high-amplitude distortions caused by TMS, which conventional filtering methods failed to remove. This preprocessing step is crucial as it ensures that the subsequent filtering stages can operate on cleaner data, thereby improving the overall signal quality.

The application of wavelet denoising further reduced the noise in the EEG signals, highlighting the utility of this technique in handling the complex, non-stationary nature of EEG data. The Butterworth filter, with its sharp transition between passband and stopband, effectively isolated the desired frequency components, eliminating residual low-frequency noise. The combination of these filtering techniques allowed for the extraction of clear TMS-evoked potentials, which are essential for investigating the immediate and direct neuronal responses to TMS.

The study's findings underscore the importance of robust denoising methods in TMS-EEG research. By effectively removing TMS artifacts, the proposed filtering approach enables researchers to obtain more accurate and reliable EEG data, facilitating a deeper understanding of the neural mechanisms underlying TMS. This has significant implications for both basic neuroscience research and clinical applications, where precise measurement of neural responses is critical. The study also highlights the potential of the Hampel filter as a valuable tool in EEG preprocessing, particularly in scenarios where traditional methods fall short.

Overall, this research contributes to the advancement of TMS-EEG methodologies by providing a practical solution to a common problem, thereby enhancing the reliability and interpretability of TMS-EEG studies. Future research could build on these findings by exploring the application of this filtering approach in different experimental settings and with larger sample sizes to further validate its effectiveness.

CONCLUSION

In conclusion, the Hampel filter demonstrates its efficacy in eliminating TMS artifacts embedded within EEG signals, effectively suppressing the associated high-frequency and amplitude distortions. By mitigating these artifacts, the filter significantly enhances the quality of the EEG data, enabling the subsequent extraction of meaningful neural information. This improved data can be confidently subjected to further analysis to uncover subtle differences between event classes, thereby facilitating a deeper understanding of the underlying neural processes.

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