TMS ARTIFACT REMOVAL FROM NEUROPHYSIOLICAL RECORDINGS USING A NOVEL ITERATIVE ADAPTIVE FILTERING

Milad Lankarany¹, Student Member, IEEE, Ajay Venkateswaran², Wei Ping Zhu¹, Senior Member, IEEE, M. N. S. Swamy¹, Fellow, IEEE, and Amir Shmuel²

¹Concordia University, Montreal, Quebec, Canada ² McGill University and Montreal Neurological Institute, Montreal, Quebec, Canada

ABSTRACT

A novel iterative adaptive filtering approach is proposed to remove the Transcranial Magnetic Stimulation (TMS) induced artifact from multi-channel recordings of neural responses to sensory stimuli. For each specific channel, the average of all trials is considered as the input to the adaptive filter whose coefficients are calculated by minimizing the mean square error between the voltage trace of that trial and the filter output. The residues of all trials serve as an initial estimate of the neural response. Once this estimate is calculated, the input of the adaptive filter is modified by subtracting the mean residue. It is shown that the modified input provides a better estimate of the mean TMS artifact, which serves the input of the adaptive filer, in the next iteration. Therefore, new filter coefficients are estimated in the next iteration, for each single trial, and the procedure continues till no considerable changes in the residues occur. We report a quantitative verification of the accuracy of our method by generating a controlled simulation. Furthermore, applying the algorithm to experimental data confirms the accuracy of our approach and its usefulness for extracting neurophysiological responses occurring in temporal proximity to TMS pulses.

Index Terms— Transcranial Magnetic Stimulation, TMS Artifact Removal, Neurophysiological recordings, Adaptive Filtering

1. INTRODUCTION

Transcranial magnetic stimulation (TMS) is a technique that locally depolarizes neurons in the brain using rapidly time varying magnetic fields generated by a coil positioned in close proximity to the head [1]. TMS has been and is vastly used to study brain function and the relationship between brain and behavior. It is currently being used to treat depression, and thought to have potential for therapy of other psychiatric disease, e.g. schizophrenia. In order to understand the neurophysiological mechanisms underlying TMS, it needs to be combined with neurophysiological recordings of Local-Field Potentials (LFPs) and action potentials. However, this is difficult, due to artifacts caused by the changing magnetic fields that induce currents in the recording electrodes, connecting wires and pre-amplifiers inherent to any neurophysiological recordings system.

TMS causes high amplitude and long lasting artifacts which interferes with neurophysiological recordings. Two strategies have been proposed for solving this problem, including real-time/online and offline strategies. Real-time methods include two techniques. The first uses sample and hold circuits to keep constant the output of the amplifiers during the TMS stimulation and relax it for the rest of time [2]. The second turns off the amplifiers for 10ms centered on the TMS stimulation. The main problem of such techniques is that the neurophysiological data cannot be recorded in proximity to the TMS pulses. In addition, designing complex electrical circuits for this strategy is expensive [3]. The alternatives to online methods are offline approaches based on signal processing techniques. [4] and [5] proposed a simple method to remove TMS artifact from EEG recordings by subtracting the mean artifact. This is an ineffective solution since the artifact is statistically nonstationary. Therefore, adaptive filtering approaches, which can properly track the TMS variations, are the candidates to come up with this problem. [1] proposed an offline Kalman filter approach, using time-varying covariance matrices, to remove TMS-induced artifacts from EEG recordings. In this paper, we propose an offline iterative adaptive filtering approach to remove TMS artifact from neurophysiological recordings of LFPs.

This paper is organized as follows, In Section 2, the problem of the TMS induced artifact in neurophysioligical data is stated. Our proposed algorithm for solving such a problem is then described in Section 3. Finally, in Section 4, the simulation and experimental study are carried out, demonstrating the accuracy and robustness of our proposed algorithm.

Notation: Bold lower case letters stand for real column vectors.

2. PROBLEM STATEMENT AND ASSUMPTIONS

For each channel, Assume sig_i denotes the voltage trace of the ith trial of the recorded signal i.e., as conventionally assumed, the combination of the corresponding TMS

artifact, *tms_i*, neural response to a sensory stimulus *neur_i*, and white noise, n_i , i.e.,

$$sig_i = neur_i + tms_i + n_i \tag{1}$$

Assuming that:

- 1- The sensory stimuli are given in different times relative to the TMS across trials, meaning that the neural responses in different trials are not aligned in time, thus they do not add in phase.
- 2- The neural signal, for each single trial, can be split into a deterministic response to the sensory stimulus, and a stochastic part i.e.,

$$neur_{i} = \begin{cases} neur_{D_{i}} & \text{to sensory stimulus} \\ neur_{S_{i}} \end{cases}$$

where *neur*_{$D_i} and$ *neur* $_{<math>S_i} denote the deterministic$ and stochastic part of the neural response,respectively. It is assumed that the deterministicparts of the neural responses, for each specificchannel, in all trials of the same stimulus aresimilar but not identical. And the stochastic partsare assumed, for the sake of simplicity, to be awhite noise.</sub></sub>

- TMS artifact is non stationary but similar for all trials.
- 4- TMS artifact and the neural response are uncorrelated.

The objective is to estimate the neural response of each channel for each trial.

3. PROPOSED METHOD

As far as the assumptions 1 and 2 hold, the average of the neural responses over all trials approaches zero if N (number of trials) approaches infinity, hence it is reasonable to expect that the mean voltage trace of all trials, \overline{sig} , for each channel, which contains the mean TMS artifact and the mean neural response can be served as the input of the adaptive filters designed for the corresponding channel's trials. The term "adaptive" is employed because the filters input adaptively tracks different trial traces of each channel. We aim to estimate filter $v_i = [v_i(1) \dots v_i(2q+1)]^T$, for ith trial, such that;

$$\min_{s.t.\mathbf{v}_i} \left\| sig_i(n) - \overline{sig}(n)^T \mathbf{v}_i \right\|_2^2$$
(2)

where, $sig_i(n) = [sig_i(n-q)...sig_i(n+q)]$ and $\overline{sig}(n) = [\overline{sig}(n-q)...\overline{sig}(n+q)].$ As shown in Fig.1, the filter's input (in the first iteration), for all trials, is $\overline{sig} = \frac{1}{N} \sum_{alli} sig_i$. The mean least square

solution for (2) is;

$$\boldsymbol{v}_i = \boldsymbol{R}_i^{-1} \boldsymbol{P}_i \tag{3}$$

where $R_i = \frac{1}{L} \sum_{n=q+1}^{L+q} \left(\overline{sig}(n) \overline{sig}(n)^T \right)$ is the autocorrelation

matrix and $P_i = \frac{1}{L} \sum_{n=q+1}^{L+q} (sig_i(n)\overline{sig}(n)^T)$ is the cross correlation

vector. *L* represents the length of each single trial (assuming that the length of all trials is same).

According to assumption 4, the residue of the i^{th} trial, res_i , would be an estimation of the *neur*_i and can be expressed as:

$$res_i(n) = sig_i(n) - \mathbf{v}_i^T sig(n)$$
(4)

By replacing (1) in (4), we will have:

$$res_i(n) = tms_i(n) + neur_i(n) - \mathbf{v}_i^T \,\overline{sig}(n) + n_i(n) \quad (5)$$

Assuming that $tms_i(n) - \mathbf{v}_i^T tms(n) \approx 0$ the residue will be: $res_i(n) = neur_i(n) - \mathbf{v}_i^T \overline{neur}(n) + n_i(n)$ (6)

As we can see, for each trial, the residue is distorted by $v_i^T \overline{neur}(n) - n_i(n)$. We propose an iterative method to reduce this distortion, for each single trial, once the residue of all trials estimated. Let us express the error between the pure neural response and the residue as follow:

$$error_i(n) = neur_i(n) - res_i(n) = \mathbf{v}_i^T neur(n) - n_i(n)$$
 (7)

The technique we use in this paper, as depicted in Fig 1, subtracts the residue of each trial from the corresponding voltage trace, sig_i , obtaining a better estimation of the TMS artifact, tms_i , averaging over all trials and using this average, tms, as the new input of the adaptive filter, in the next iteration.



Figure 1. Block diagram of the proposed iterative algorithm, in the k^{th} iteration, for TMS artifact removal.

Apparently, better estimation of the mean TMS artifact, as the filter's input, leads to better estimation of the neural response, as the residue. Accordingly, using (1), (6), (7), the input of the next iteration can be written as:

$$input = \frac{1}{N} \sum_{i} (sig_{i} - res_{i}) = \overline{sig} - \overline{res}$$
$$= \frac{1}{N} \sum_{i} (tms_{i} + error_{i} + n_{i}) = \overline{tms} + \overline{error} + \overline{n}$$
⁽⁸⁾

Hence, this new input contains the mean error which is negligible in comparison with the mean artifact. In other word, this technique ensures that the fit between the residue and the original neural response in each iteration is no worse than that in the previous one. Our algorithm is summarized as below;

Algorithm

Step 1) set *k*=0; (*k* represents the number of iteration)
res^[k]=0
Step 2) *k* = *k* + *1*;
input^[k] = *sig*-*res*^[k-1]
*v*_i^[k] = (*R*^[k])⁻¹*P*_i^[k],
R^[k] = *E*{*input*(*n*)^[k](*input*(*n*)^[k])^{*T*}}, *P*_i^[k] = *E*{*sig*_i(*n*)(*input*(*n*)^[k])^{*T*}}
Step 3) *res*_i^[k] = *sig*_i - *v*_i^[k] * *input*^[k]
if *k*=1, go to step 2,
else calculate
$$E = \frac{\left\|res_{i}^{[k-1]} - res_{i}^{[k-1]}\right\|_{2}^{2}}{\left\|res_{i}^{[k-1]}\right\|_{2}^{2}} \times 100\%$$

Step 4) if $E \le 5\%$, for all trials (*i*), then stop the algorithm, else go to step 2.

4. SIMULTIONS & EXPERIMENTAL RESULTS

Our dataset includes recordings of 5 channels obtained invivo from intra-cranial electrodes within the somatosensory region S1. The recording electrodes were right below the center of a 70 mm figure-of-8 TMS coil. Recordings were pursued using a multi-channel neurophysiological system (Tucker-Davis Technologies, Alachua, FL). For each channel, there are three classes of data (Fs = 24,414 Hz); 1-TMS only, 2- median nerve stimulation only, and 3- TMS combined with median nerve stimulation at different time lags between them (-250:5:250 ms). Each data set contains 100 trials, each lasting approximately 10s. In the trials in which median nerve stimulation takes place (either alone or with TMS), the median nerve stimulus pulse is right in the middle of the trial. In trials where only TMS happens, the TMS pulse is also in the middle of the trial. We perform our algorithm separately for each channel. Firstly, for the simulation case, we added the median nerve (neural) responses (data class 2) for each channel to the data with the TMS artifacts (data class 1) on a trial by trial basis, such that the onset of the TMS artifacts are triggered and the neural responses is randomly distributed between -250:5:250 ms relative to the TMS pulse, in order to satisfy the first assumption. The aim is to remove the artifact of each channel, trial by trial, and compare the result with the corresponding neural responses in trials with no interference. For each trial, the correlation coefficient MI, the quantity that gives the quality of a least squares fitting [6], between the estimated and original neural response is calculated and then averaged over all trials of each channel to indicate the mean similarity between the estimated and non-interfered neural response.

$$M1 = \frac{1}{N} \sum_{i=1}^{N} \frac{COV(neur_i, res_i)}{\sqrt{VAR(neur_i)VAR(res_i)}}$$

However, as the information of the neural responses in the interval between their onsets and 100ms after is of our interest, the second measurement M2 is calculated in a manner similar to M1 but in this interval. The results of M1 and M2 for all tested channels are shown in table I.

$$M2 = \frac{1}{N} \sum_{i=1}^{N} \frac{COV(neur_i(1:l_i), res_i(1:l_i))}{\sqrt{VAR(neur_i(1:l_i))VAR(res_i(1:l_i))}}$$

where l_i is the length of ith trial 100ms after the electrical stimulation. The onset of each trial is equal to the onset of the TMS artifact. The filter order is 23 (q=11) in our algorithm for both simulations and experiments. Fig 2.A shows a selected part of our simulation for channel #55. Fig 2.B shows the estimated neural response after TMS artifact removal versus the original one. One trial of the estimated and the original neural responses is magnified in Fig 2.C. The deterministic part (red window in Fig 2.C) of this neural response (100ms after onset), for both estimated and original, is depicted in Fig 2.D.



Figure 2. A, Part of the simulation; the combined TMS and neural response of channel #55. B, the original versus estimated neural response after TMS artifact removal. C, a magnified trial of part b. D, the deterministic part of the neural response, of the trial of part C.

TABLE I, Results M1 & M2 for the simulation case

Channel Similarity	#3	#22	#35	#55	#64
<i>M</i> 1	0.65	0.68	0.69	0.69	0.70
M2	0.85	0.92	0.92	0.93	0.92

Secondly, as the experimental case, our algorithm is applied to the combined TMS and neural responses: the third class of our dataset. Although, according to the recording strategy, the electrical pulses are right in the middle of trials and TMS onset varies around the middle of trials (between -250ms to 250 ms), since we segment 5s before and 5s after the TMS onsets the first assumption still holds. Since there is no original neural response to compare the accuracy of the estimated neural response after TMS artifact removal, the average of the estimated neural response, for each channel, is calculated over all trials to represent the mean neural response of each channel. This signal is then compared, in term of correlation coefficient, with the mean neural response of the corresponding channel in the absence of TMS artifact (second class of dataset). The comparisons are reported in table II. Fig 3 shows a selected part of our experimental data for channel #64, before (up) and after (middle) TMS artifact removal. The mean estimated neural response versus the mean neural response in the absence of TMS artifact is plotted for the 100 ms after electrical stimulation in Fig. 3 (bottom).



Figure 3. a selected segment of the recordings of neuron # 64, combined with TMS (up), after TMS artifact removal (middle), and the mean estimated neural response versus the mean neural response in the absence of TMS artifact (bottom).

TABLE II, Results of $\rho_1 \& \rho_2$ for the data obtained experimentally

Channel Similarity	#3	#22	#35	#55	#64
ρ_1	-0.23	0.65	0.59	0.67	0.60
ρ_2	-0.34	0.83	0.80	0.81	0.85

Where ρ_1 and ρ_2 are the correlation coefficients for the entire and 100 ms of the trial length, respectively. As can be seen in the both simulation and experimental cases, the results, in term of the mean similarity between the estimated neural response and original neural response are promising. However, it is noteworthy to remember that we expect some differences, in the experimental case, between the estimated neural responses and the clean ones (with no TMS) which might be originated from the TMS actions in the neural responses.

5. CONCLUSION

We have presented a novel iterative adaptive filtering approach for removing the TMS induced artifact from the recordings of the neural responses to the electrical stimuli. The proposed algorithm is applied to both simulation and experimental data. In simulation, the similarities between the estimated and original neural responses over all trials demonstrate encouraging results. Furthermore, experimental results confirm the accuracy of our approach especially in order to preserve the first 100 ms (after the onset) of the neural response.

6. REFERENCES

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