TRS-TMS: an EEGLAB plugin for the reconstruction of onsets in EEG-TMS datasets

Sara Petrichella, Luca Vollero, Florinda Ferreri, Vincenzo Di Lazzaro, Giulio Iannello

***Abstract*—The analysis of EEG evoked potentials strongly relies on the correct alignment of different segments of the recorded EEG activity. The alignment of segments is needed in order to extract event related waves hidden in the background EEG activity. Commonly, the information on onsets is provided by the acquisition system. However, wrong configuration of the recording system or human errors during the acquisition or storage of data may make this information unavailable. Usually, these errors are discovered during the datasets analysis stage, and this stage can take place even several months after the acquisition of datasets. Unluckily, changes on patients status and the expensiveness of EEG registrations make unfeasible to repeat the acquisitions. In this paper we present and evaluate two mechanisms that we included in an EEGLAB plugin for the automatic reconstruction of onsets in EEG-TMS recordings. The methods of the TMS Triggers Reconstruction Software (TRS-TMS) plugin are discussed and evaluated obtaining guidelines for their correct configuration in the routine usage.**

***Index Terms*—TRS-TMS, EEGLAB, EEG-TMS, Onsets Reconstruction**

I. Introduction

The study of evoked potentials strongly relies on the correct alignment of different segments of the EEG activity. These segments are time locked to an external event whose impact on measured electrical activity is of interest and has to be analyzed. The alignment of segments is needed in order to extract Event Related Potentials (ERP), i.e. small waves hidden in the ongoing measured EEG signal, from the background activity, i.e. the electrical activity that does not show any dependence on the stimulus [10]. The onsets, i.e. the time latencies of stimuli, are usually logged by the acquisition system used in the recording of the EEG activity. Hence, when everything works well and the onsets are correctly recorded, the alignment of EEG segments is not a problem. Unfortunately, the wrong configuration of the acquisition system or human errors during the acquisition or the storage of data may make this information unavailable. Changes in subject status and the cost of acquisition sessions are factors that make unfeasible data recovery through registration rerun. In this context the availability of tools that allows for onsets reconstruction may represent a precious help.

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In this paper we present, describe and evaluate two mechanisms that we implemented in the TMS Triggers Reconstruction Software (TRS-TMS) plugin of the EEGLAB toolbox [1] of MATLAB® for the automatic reconstruction of onsets in EEG-TMS acquisitions. EEGLAB is an open-source interactive software for processing continuous and event-related EEG, MEG and other electrophysiological data. The TMS is a noninvasive method that uses electromagnetic induction to induce weak electric currents in specific or general parts of the brain. The ability to select the brain region to stimulate makes the TMS a technique of great interest in the study of brain's functioning and interconnections [9]. The methods of the TRS-TMS plugin are based on the detection of the TMS artifacts caused by the TMS stimulus. These artifacts are used by both methods as features to track onsets. In the paper we describe, tune and evaluate the two mechanisms available in the plugin with the goal of obtaining insights on their performance and guidelines for their correct configuration in the routine usage.

II. Related Work

At the best of our knowledge there are no published papers in the field of automatic detection of TMS onsets in continuos EEG registrations. This state of the art, hence, focuses on research activities that inspired us in the definition and implementation of plugin mechanisms. In particular, we focus on solutions that detect spiky activities within a background signal as the identification of Sharp Transients (ST) in EEG signals and the detection of QRS complexes in ECG recordings.

Sharp Transient (ST) waveforms in the EEG may be related with seizures, e.g. epilepsy, of focal origin. ST waveforms are distinct from the background EEG activity and exhibit pointed peaks. Several papers propose solution for the automatic detection of ST waveforms. In [5], a multimodal detector is presented based on the analysis of multiple signals (EEG, EKG, EOG, EMG). Candidate ST waves are obtained by scanning the EEG for waves having well formed sharp shape attributes as amplitude jumps, high slope, short duration, and sharpness of the individual waveforms. In [8] a simplified arithmetic detector for EEG Sharp Transients is presented. The detector consists of three stages: (i) a first order difference filter that emphasizes the principal frequency components of STs, (ii) a product operator between the differentiated signal and a slightly delayed version of the differentiated signal, and (iii) a threshold operator with the aim of identifying the occurrence of a ST wave. In [2] a system for the automatic detection of epileptiform activities has been designed. The signal is segmented into halfwaves and a features extraction process is carried out. Parameters of the waves and the constituent halfwaves as the duration, the slope, the sharpness and the amplitude are computed and compared with threshold values.

The detection of QRS complexes in ECG recordings is a well established research field. Several papers review common approaches and problems that arise when dealing with this problem [4], [6]. Standard approaches are based on a band pass filtering of the signal, in order to remove baseline wander and noise, a sharp waves emphasizing filter and a threshold detector. Recently new approaches have been proposed that improve the accuracy of the detection process through innovative feature extraction techniques. Relevant to the present work is the approach of [7], [11] in which the authors propose a preprocessor ending with a Shannon energy envelope (SEE) estimator and, then, a peaks finding logic based on the Hilbert transform.

III. Signal Model of a Continuous EEG-TMS signal

A continuous EEG-TMS signal, $\mathrm{s}[n]$, can be described by the following model:

$$\mathrm{s}[n] = \sum_{k=1}^{\mathrm{N}_o} \mathrm{t}[n-n_k] + \sum_{k=1}^{\mathrm{N}_o} \mathrm{e}_k[n-n_k] + \eta[n] \tag{1}$$

where $\mathrm{t}[n]$ is the TMS stimulus artifact, $\mathrm{e}_k[n]$ is the ERP activity elicited by the k^{th} stimulus, $\eta[n]$ is the sum of the background EEG activity and the acquisition noise, and we will refer it as noise in the following. N_o is the number of stimulation onsets and n_k with $k \in \{1, 2, \ldots, \mathrm{N}_o\}$ is the onset of the k^{th} stimulus.

Based on real signal characteristics, the following hypotheses can be made on signal components:

- $\mathrm{t}[n]$ is a fast varying signal having either or both polarity, high amplitude and small time support. The signal's time support spans in the range of $0.5-1\,\mathrm{ms}$ based on the quality of the stimulation/acquisition system. The spike of the $\mathrm{t}[n]$ signal saturates or it is close to saturate the acquisition sensor. This signal can be characterized by its shape and its maximum instantaneous power $\mathrm{P_t} = \mathbb{E}\left\{\mathrm{t}^2[0]\right\}$.
- $\mathrm{e}_k[n]$ is a non-stationary causal process having power quickly decaying to zero. The vanishing time of the ERP process is a function of subject sensibility to stimulation. Common ERP vanishing times span the range $0.3-0.8\,\mathrm{s}$ [3]. The ERP component model, hence, assumes that $\mathbb{P}\{\mathrm{e}_k[n]=0\} = 1$ if $n<0$ or $n>\mathrm{M}$, and $\mathrm{M}+1$ is the vanishing time expressed in number of samples. The average ERP power of the signal in the vanishing window, assuming that the distribution of $\mathrm{e}_k[n]$ does not depend on k, can be computed as:

$$\mathrm{P_{ERP}} = \frac{1}{\mathrm{M}} \sum_{n=0}^{\mathrm{M}} \mathbb{E}\left\{\mathrm{e}_k^2[n]\right\}$$

- $\eta[n]$ is a white gaussian noise having zero mean and constant power: $\mathrm{P_{noise}} = \sigma_\eta^2 = \mathbb{E}\left\{\eta^2[n]\right\}$. The background EEG signal is independent of both the ERP and the TMS stimulus signal.

In order to fully simulate the acquisition system we consider also the saturation effect that the high dynamic of the signal may produce in the acquisition sensor. Hence, the measured signal on which the onset reconstruction has to take place is a saturated version of $\mathrm{s}[n]$, namely:

$$\tilde{\mathrm{s}}[n] = \begin{cases} s_{\min} & \text{if } \mathrm{s}[n] < s_{\min} \\ \mathrm{s}[n] & \text{if } \mathrm{s}[n] \in [s_{\min},\, s_{\max}] \\ s_{\max} & \text{if } \mathrm{s}[n] > s_{\max} \end{cases}$$

IV. Onsets Reconstruction Methods

The goal of a onsets reconstruction method is the automatic extraction of $n_k \;\forall k \in \{1, 2, \ldots, \mathrm{N}_o\}$ of Eq. 1. In order to address this task we analyze in the following the two approaches that we implemented in the TRS-TMS plugin. The former is based on a trivial maxima detection with heuristic suppression of false positive onsets, and the latter is based on the method proposed in [7] in the context of QRS complexes detection, that we adapted for TMS onsets reconstruction.

A. Reconstruction Based on Maxima Detection (MAX Method)

The maxima detection method relies on the behavior of the $\mathrm{t}[n]$ signal whose shape is confined in a small time window around the corresponding onset and with a power level that makes it distinguishable along the signal. The algorithm is based on the following steps:

- The $\mathrm{s}[n]$ signal is first filtered by a proper configured band-pass filter. The goal is to remove the baseline and to reduce the noise activity.
- The filtered signal is thresholded in order to generate a set of candidates onset values. For each window composed of succeeding candidate values, the first sample of the window is marked as an effective onset candidate.
- Onset candidates are filtered out by a proximity algorithm: starting from the last onset, every candidate onset too close in time to the candidate onset preceding it is suppressed.

B. Reconstruction Based on Shannon Energy and Hilbert Transform (SaH Method)

This method is based on [7]. This paper proposes an algorithm for the detection of QRS complexes in ECG signals. The approach requires the following steps:

- The $\mathrm{s}[n]$ signal is first filtered by a proper configured band-pass filter. The goal is to remove the baseline and to reduce noise activity.
- The filtered signal is differentiated in order to emphasize fast waves in the signal: $\mathrm{d}[n] = \mathrm{s}[n] - \mathrm{s}[n-1]$
- The differentiated signal is hence rectified and normalized: $\tilde{\mathrm{d}}[n] = |\mathrm{d}[n]| / \max_n \{|\mathrm{d}[n]|\}$
- The Shannon Energy envelope is computed as:

$$\mathrm{s}_s[n] = -2\left(\tilde{\mathrm{d}}[n]\right)^2 \log\left(\tilde{\mathrm{d}}[n]\right)$$

- The Hilbert Transform of the Shannon Energy is computed in order to detect the stimuli by mean of a zero crossing algorithm.

V. Parameters Configuration

The two methods described in the previous section require the configuration of a set of parameters in order to work correctly. These parameters need an heuristic tuning that we performed on the dataset that we introduce in Section VI:

1) The Max Method relies on a band-pass filter, an amplitude threshold and a proximity threshold that we configure as follows:
   - The band-pass filter has been designed in order to preserve the energy content of the signal in the band $[0.5,\, 200]$ Hz. The chosen filter is an order 2 Butterworth filter and it is applied in both the forward and reverse directions.
   - The amplitude threshold is chosen at the 90% of the maximum of the signal.
   - The proximity threshold is chosen to be equal to $0.050\,\mathrm{s}$.
2) The SaH method relies on a band-pass filter and a zero crossing detection method:
   - The band-pass filter has been designed in order to preserve the energy content of the signal in the band $[0.5,\, 200]$ Hz. The chosen filter is an order 2 Chebyshev Type I digital filter and it is applied in both the forward and reverse directions.
   - The zero crossing algorithm has been designed in order to select, when multiple zeros are detected in the same proximity window of $0.1\,\mathrm{s}$, the zero corresponding to the maximum variability of the signal.

VI. Performance Analysis

In this section we evaluate the performance of the considered algorithms under various conditions of the dataset of analysis. In particular, we simulated different datasets using the model of Section III, where the shape of the $\mathrm{t}\,[n]$ signal has been adapted to that of a bipolar pulse following the model:

$$\mathrm{t}\,[n] = \begin{cases} s_{\max} & \text{if } n \in [0,\, 1/f_s) \\ s_{\min} & \text{if } n \in [1/f_s,\, 2/f_s) \\ 0 & \text{if } n \notin [0,\, 2/f_s) \end{cases}$$

and where f_s is the sampling frequency of the signal, that we considered in the following equal to $1000\,\mathrm{Hz}$.

In the evaluation we consider the impact that the power of the elicited ERP activity and that of the background noise have in the ability of properly detecting the onsets present in the signal. In particular, we modeled the background activity as a zero mean white gaussian noise having fixed power $\mathrm{P}_{\mathrm{noise}}$, while the ERP activity has been obtained band-pass filtering a zero mean white gaussian noise of fixed power and windowing in time the signal by an exponential decaying function. The band of the filter has been chosen in order to include activities of real ERPs as that measured in real subjects in the paper of Ferreri *et al.* [3]. In particular, we used an order 2 Butterworth low-pass filter having a $200\,\mathrm{Hz}$ cutoff frequency. The exponential time-windowing function has been chosen in order to stop the ERP activity in a $700\,\mathrm{ms}$ window after the TMS stimulus.

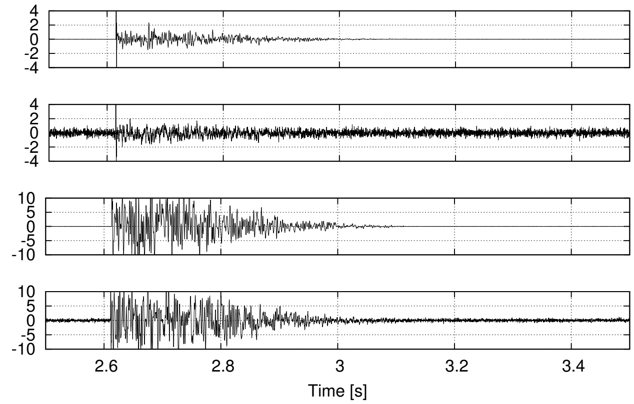

Figure 1. Simulated EEG-TMS trials, from top to bottom panel different configurations of $\left[(\mathrm{P}_{\mathrm{noise}})_{\mathrm{dB}}, (\mathrm{P}_{\mathrm{ERP}})_{\mathrm{dB}}\right]$: $(-80,\, -63)$, $(-30,\, -63)$, $(-80,\, -43)$, $(-30,\, -43)$

Being the ERP activity a non-stationary and quickly decaying process, in the following we consider the average power of such a process along its activity window:

$$\mathrm{P}_{\mathrm{ERP}} = \frac{1}{\mathrm{M}} \sum_{n=0}^{\mathrm{M}} \mathbb{E}\left\{\mathrm{e}_k^2\,[n]\right\}$$

where we assume that $\mathbb{P}\left\{\mathrm{e}_k\,[n] = 0\right\} = 1$ if $n < 0$ or $n > \mathrm{M}$, and $\mathrm{M} + 1$ is the length of the activity window expressed in number of samples. The performance evaluation is based on the sensitivity S and the positive predictivity P^+ that are defined as:

$$\mathrm{S} = \frac{\mathrm{N}_{\mathrm{TP}}}{\mathrm{N}_{\mathrm{TP}} + \mathrm{N}_{\mathrm{FN}}}$$

$$\mathrm{P}^+ = \frac{\mathrm{N}_{\mathrm{TP}}}{\mathrm{N}_{\mathrm{TP}} + \mathrm{N}_{\mathrm{FP}}}$$

Moreover, we also consider the alignment jitter that, when too big, may severely impact the extraction of the ERP waves and the clinical evaluation of results. The jitter is computed as the root value of the sum of the square errors between the true onset latencies and the estimated ones, computed over all the true positive detected onsets:

$$\Delta = \sqrt{\frac{1}{\mathrm{N}_{\mathrm{TP}}} \sum_{q=1}^{\mathrm{N}_{\mathrm{TP}}} \left(n_{k_q} - \tilde{n}_{k_q}\right)^2}$$

All the powers in the following are expressed in decibels and are referred to the power of the maximum measurable TMS activity, that we fixed equal to $s_{\max} = -s_{\min} = 10\,\mathrm{V}$.

Figure 1 shows an example of simulated signals in the case of the smallest and the greatest powers of EEG background activity ($\mathrm{P}_{\mathrm{noise}} = -80$ and $\mathrm{P}_{\mathrm{noise}} = -30$) and ERP elicited activity ($\mathrm{P}_{\mathrm{ERP}} = -63$ and $\mathrm{P}_{\mathrm{ERP}} = -43$). An expert confirmed that the simulated signals resemble that of a EEG-TMS acquisition.

Figure 2 shows the sensitivity performance that the two mechanisms provide fixing the background activity either at the smallest or the greater power value and for an increasing level of excitability of the subject, i.e. for an increasing

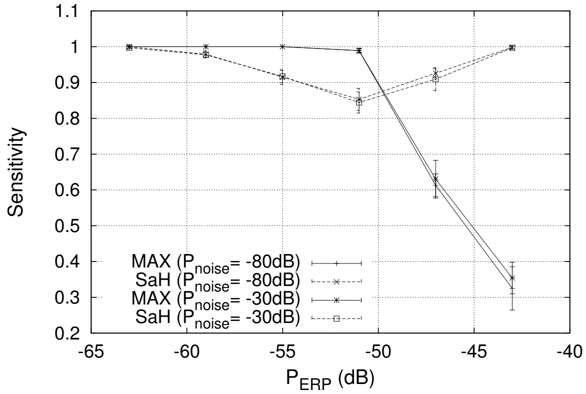

Figure 2. Sensitivity for fixed $\mathrm{P_{noise}}$.

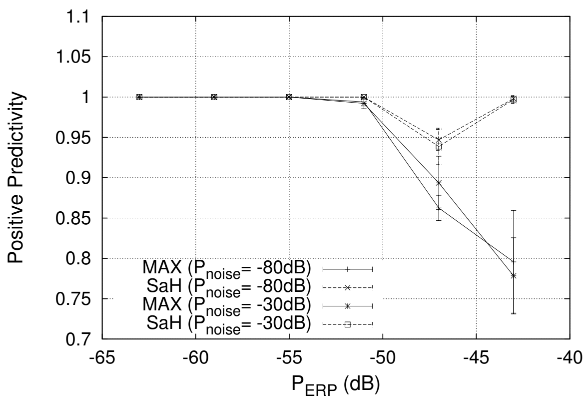

Figure 3. Positive Predictivity for fixed $\mathrm{P_{noise}}$.

power of ERP activity. Every condition has been repeated 50 times and the results show the average values and the 95% confidence intervals of the estimated figure of merit. We can observe that the performance of both mechanisms do not depend on the level of background EEG activity, while they show a marked dependency on the power of elicited ERP activity. When the ERP has a low power level both mechanisms perform pretty well, while the SaH method is better under low ERP powers while the MAX method is preferable when the ERP power increases.

Figure 3 shows the Positive Predictivity performance that the two mechanisms exhibit (average values and 95% confidence intervals of the figure of merit over 50 simulations). In all the conditions the SaH method performance are better than those of the MAX method. Hence, the SaH method is better than the MAX method when the false positives may impact in the reconstruction of evoked potentials, as in the case of repeated acquisition close in time and with high power in noise activity. Eventually, Figure 4 shows the performance of the jitter between the true offsets and the estimated ones (average values and 95% confidence intervals of the figure of merit over 50 simulations). When the power of elicited ERP is low, both methods show a low jitter. However, when the power of elicited ERP activity is high, the SaH is preferable if the waves to extract have a time support higher than $10\,\mathrm{ms}$.

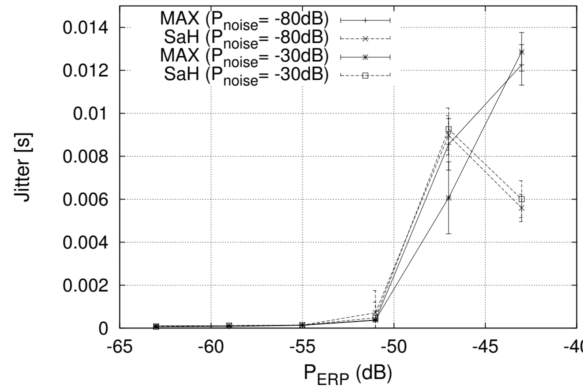

Figure 4. Jitter for fixed $\mathrm{P_{noise}}$.

VII. Conclusions

In this paper we present and evaluate two mechanisms for the onset reconstruction in EEG-TMS signals available in the TRS-TMS EEGLAB plugin that we developed. Based on a simulated model of continuous EEG-TMS recordings, we evaluated the ability of the two mechanism to correctly identifying the onset of stimuli and the jitter that the reconstruction process introduces. This evaluation constitutes a benchmark in the choice of the mechanism to adopt in a real scenario when the plugin has to be used.

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