Application of Kalman filter to remove TMS-induced artifacts from EEG recordings

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***Abstract*— Transcranial magnetic stimulation (TMS) is a technique in which a pulsed magnetic field created by a coil positioned next to the scalp is used to locally depolarize neurons in brain cortex. TMS can be combined with electroencephalography (EEG) to visualize regional brain activity in response to direct cortical stimulation, making it a promising tool for studying brain function. A technical drawback of EEG/TMS coregistrations is that the TMS impulse generates high amplitude and long-lasting artifacts that corrupt the EEG trace.**

In this paper an off-line Kalman filter approach to remove TMS-induced artifacts from EEG recordings is proposed. The Kalman filter is applied to the linear system arising from the combination of the dynamic models describing EEG and TMS signals generation. Time-varying covariance matrices suitably tuned on the physical parameters of the problem allow us to model the non-stationary components of the EEG/TMS signal, (neglected by conventional stationary filters). Experimental results show that the proposed approach guarantees an efficient deletion of TMS-induced artifacts while preserving the integrity of EEG signals around TMS impulses.

***Index Terms*— Kalman filtering, Identification, Biomedical signal processing, EEG, Transcranial magnetic stimulation**

I. INTRODUCTION

Thanks to some recent technological advances, neuroscience became one of the leading research areas, attracting scientists not only from the medical area but also from engineering, physics, biology and psychology. Today, a large number of problems in neuroscience could benefit of tools commonly exploited in these different fields. Electroencephalographic signals processing, for instance, revealed an appealing test bed for filtering strategies developed in the control engineering area (see e.g., [2], [5], [6], [15], [25], just restricting to the literature dealing with Kalman filtering).

Electroencephalography (EEG) is the neurophysiologic measurement of brain electrical activity recorded by electrodes placed on the scalp. EEG is frequently used in experimentation because the process is noninvasive to the research subject who does not need to make any specific action during the recording. A peculiar feature of EEG over other existing techniques is its excellent temporal resolution: in fact changes in brain electrical activity with a time scale of milliseconds can be easily detected.

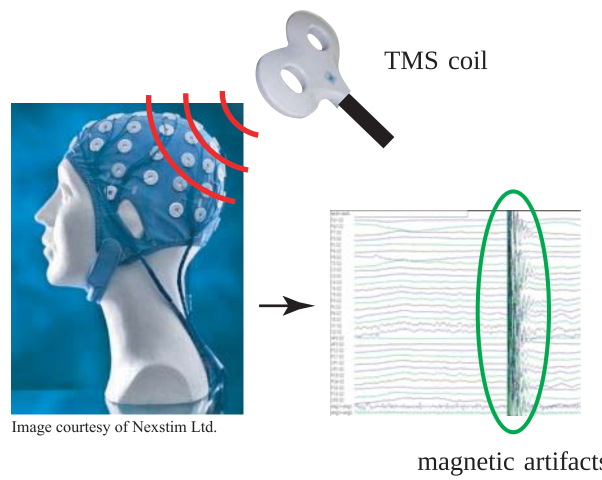

Fig. 1. TMS induces high amplitude artifacts on the EEG trace.

Recently a new powerful tool to investigate brain function has been introduced in neuroscience: the *transcranial magnetic stimulation* (TMS). TMS allows noninvasive brain stimulation using rapidly time-varying magnetic fields generated by a coil positioned in contact with the scalp [7], [13]. Besides the investigation of corticospinal motor pathways after stimulation of the motor cortex [13], [23], TMS of non-motor areas offered the unique opportunity to study several cognitive functions in a causal manner [21], [29]. TMS has been combined with several functional imaging techniques: PET (Positron Emission Tomography) [18], SPECT (Single Photon Emission Computed Tomography) [16], fMRI (Functional Magnetic Resonance Imaging) [3]. Nonetheless, TMS interleaved with EEG provides, together with high temporal resolution, unique information about the characteristics of cortical reactivity and connectivity [8], [9].

A technical drawback of EEG/TMS coregistrations is that the TMS impulse induces high amplitude and long-lasting artifacts on the EEG trace (see Fig. 1). The term "artifact" denotes any potential, not generated by the brain, that affects the EEG signals and thus modifies, twists or deletes the normal cerebral electric signal. The magnetic field generated by TMS usually saturates the EEG electrodes for 20-30 ms and even with special amplifiers designed to work with MRI, the electrodes can not correctly record the cerebral activity in this period of time.

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To solve this problem two coarse *on-line* strategies have been proposed in the literature. The first one uses sample-and-hold circuits to keep constant the output of the amplifiers during the impulse [8]. The amplifiers return to their normal operation after the impulse. The second method turns off the amplifiers 10 ms after the impulse. Besides the high costs due to the complex circuits, these methods cut off the EEG trace during TMS stimulation and therefore the information of the signal around the impulse is irremediably lost [17], [20].

An alternative to on-line strategies is represented by *off-line* approaches. In this case the artifacts are removed only after the complete acquisition of the EEG/TMS coregistration. Off-line artifact suppression strategies are still in their infancy. In [28], [4] the authors propose to remove TMS-induced artifacts by simply subtracting the mean artifact. This strategy is indeed effective to remove physiological artifacts but residual electrical artifacts are not expected to be completely eliminated. In [1], [19] the authors use least mean square algorithms to remove fMRI-induced artifacts from EEG signals. Nonetheless TMS-induced artifacts are more energetic and less uniform than fMRI-induced artifacts and therefore poor performances are expected if these algorithms are applied to TMS.

In this paper we propose an off-line Kalman filter approach to remove TMS-induced artifacts from EEG recordings. The Kalman filter is applied to the linear system arising from the combination of the dynamic models, identified from data, describing EEG and TMS signals generation. The keystone of the approach is the use of time-varying covariance matrices suitably tuned on the physical parameters of the problem that allow one to model the non-stationary components of the EEG/TMS signal (neglected by conventional stationary filtering). The approach guarantees an efficient deletion of TMS-induced artifacts while preserving the integrity of EEG signals around TMS impulses. Experimental results show that the proposed strategy achieves a significant performance improvement over the existing off-line strategies (Wiener filter). A preliminary version of the present work appeared in [14].

The rest of the paper is organized as follows. In Sect. II some basic data structures are defined and the preprocessing phase is briefly motivated. In Sect. III the models for EEG and TMS are introduced and the Kalman filter is designed. In Sect. IV real data experiments prove the effectiveness of the proposed approach. In Sect. V the main contributions of the paper are summarized and future research directions are highlighted.

Notation: The following notation will be used in the paper: $\mathbb{R}^+$ is the set of all positive real numbers. Bold lower case and capital letters stand for real column vectors and real matrices, respectively. diag$\{\mathbf{A}, \mathbf{B}\}$ denotes a block diagonal matrix with square matrices $\mathbf{A}$ and $\mathbf{B}$ on the diagonal. $\mathbf{0}_{m\times n}$ and $\mathbf{I}_n$ denote the $m \times n$ matrix of zeros and the identity matrix of order n.

II. PRELIMINARIES

Through the paper we will refer to the following data structures. The basic structural unit is the *record*. A record corresponds to some tens of seconds EEG/TMS coregistration on multiple channels and it is divided into M *data sets* of S *samples*. Each data set is supposed to contain a single TMS-impulse or stimulus having regular time spacing.

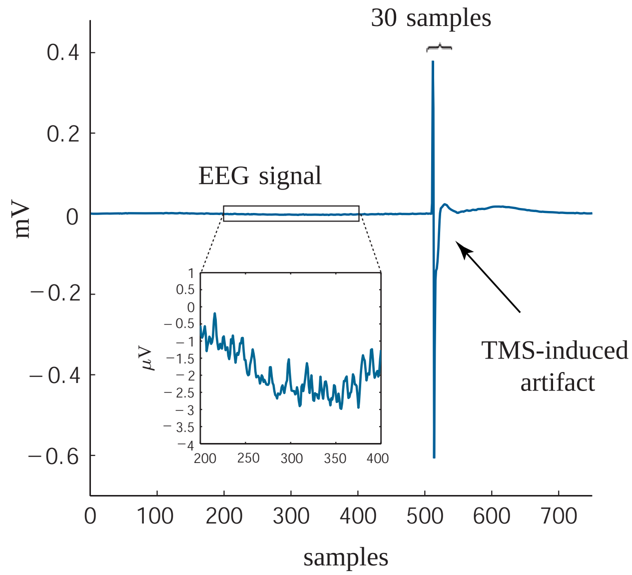


Fig. 2. A data set containing a TMS-induced artifact.

Fig. 2 shows a typical data set of 750 samples. Up to sample 510 the EEG/TMS trace includes only the EEG signal. At sample 510 a TMS-impulse induces an artifact on the trace. The duration of the impulse is about 30 samples.

Note that in spite of the electric shielding of EEG electrodes, power lines usually induce sinusoidal oscillations on the EEG signal due to the 50 Hz carrier. In order to avoid distorted results, these oscillations must be removed (e.g. by using standard Fourier series techniques) in a preprocessing phase preceding the application of the Kalman filter. Notice that since scarce EEG activity is present at 50 Hz, the carrier can be removed without significant loss of information. Hereafter $s(t)$ will denote the signal including the TMS-induced artifact and the EEG signal, with the 50 Hz carrier suppressed.

III. KALMAN FILTER DESIGN

The available signal $s(t)$ results from the combination of an electroencephalographic signal $eeg(t)$, representing the natural electric activity of the brain and of a high amplitude signal $tms(t)$, representing the artifact induced by the magnetic stimulation. Obviously $tms(t)$ is present only in correspondence of a stimulus. The signals relative to the i-th data set of a record will be denoted $s_i(t)$, $eeg_i(t)$ and $tms_i(t)$, $i = 1, 2, \ldots, M$. Signal $eeg_i(t)$ can be considered as a stationary zero mean signal [10]. On the other hand $tms_i(t)$, for its impulsive nature, is a non-stationary signal.

A pure TMS-induced artifact can be achieved by stimulating the head of a manikin. Analyzing the spectrum of this artifact (see Fig. 3), we observe that although most of signal energy is concentrated at high frequencies (300 Hz), several components are present at low frequencies (around 10 Hz). Therefore, since the EEG signals usually range from 1 Hz to 70 Hz, trivial low-pass, high-pass filters can not be exploited to separate

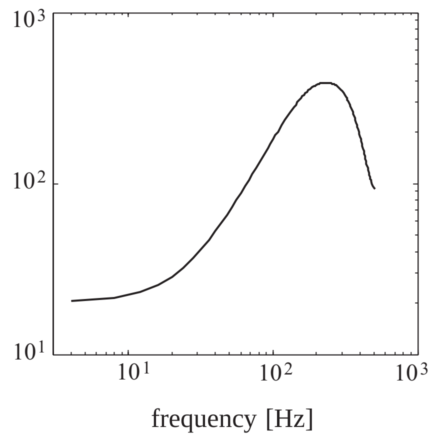


Fig. 3. Spectrum of a pure TMS-induced artifact recorded on a manikin.

EEG signals from the magnetic artifacts, since significant components of the EEG signal would be cut off.

Let us make the following assumptions:

1) $s_i(t) = eeg_i(t) + tms_i(t)$
2) $eeg_i(t)$ and $tms_i(t),\ \forall\, t,$ are uncorrelated.

Note that 1) and 2) are simplifying assumptions which most likely do not strictly hold in practice. Nevertheless, they allow us to develop a filtering procedure that will prove to be effective in removing TMS artifacts from EEG recordings. According to the first hypothesis, in the record we have,

$$\frac{1}{M}\sum_{i=1}^{M} s_i\big(t+(i-1)\,S\big) = \\ = \frac{1}{M}\Big(\sum_{i=1}^{M} eeg_i\big(t+(i-1)\,S\big) + \sum_{i=1}^{M} tms_i\big(t+(i-1)\,S\big)\Big). \tag{1}$$

Since $eeg_i(t)$ is supposed to be a zero mean signal,

$$\frac{1}{M}\sum_{i=1}^{M} eeg_i\big(t+(i-1)\,S\big) \simeq 0$$

and equation (1) approximately equals $\overline{tms}(t)$, the mean artifact. If the artifacts were purely deterministic, then $tms_i(t) = \overline{tms}(t)\ \forall\, i$, and they could be removed by the simple subtraction,

$$\widehat{eeg}_i(t) = s_i(t) - \overline{tms}(t) \tag{2}$$

where $\widehat{eeg}_i(t)$ is the EEG signal without the artifact. Nevertheless, TMS-induced artifacts are not purely deterministic and therefore (2) is not sufficient to remove the magnetic artifact from $s_i(t)$. This drove us to devise an alternative and more effective strategy.

The *Kalman filter* (see, e.g. [12]) turned out to be an appealing solution. To design this filter a state-space model describing the signals generation mechanism is necessary, therefore two dynamic systems, modelling EEG and TMS signals generation, need to be determined. For the sake of simplicity, hereafter, the subscript "i" (that refers to the data set) will be dropped.

According to the existing literature [10], for the EEG signal, AR (Autoregressive) models have been considered,

$$eeg(t) \;=\; \frac{1}{1 + a_1\, q^{-1} + \cdots + a_{N_a}\, q^{-N_a}}\; e_E(t) \tag{3}$$

i.e, signal $eeg(t)$ is supposed to be generated by a white noise $e_E(t)$ filtered by a function $1/A(q)$, where $A(q) = 1 + a_1\, q^{-1} + \cdots + a_{N_a}\, q^{-N_a}$ is a polynomial in the shift operator q, such that $q^{-1}x(t) = x(t-1)$. For the AR model order selection, several works can be found in the literature (see, e.g. [11], [26]).

Differently from the EEG, the determination of a model for TMS has not been deeply investigated in the literature. Let us first model the deterministic part $\overline{tms}(t)$. Due to the impulsive nature of the TMS artifacts, OE (Output Error) models with impulsive inputs can be considered,

$$\overline{tms}(t) = \frac{B(q)}{F(q)}\, u(t-1) \;+\; v(t) \tag{4}$$

where $u(t)$ is a unitary impulse that assumes the value 1 in correspondence of a stimulus and $v(t)$ represents the stochastic part of the OE model.

The previous AR and OE models can be utilized to build a linear state-space system describing the overall EEG/TMS signal. Consider the following state-space realization of model (3),

$$\begin{cases} \mathbf{x}_E(t+1) = \mathbf{A}_E\, \mathbf{x}_E(t) + \mathbf{G}_E\, e_E(t) \\ eeg(t) = \mathbf{C}_E\, \mathbf{x}_E(t) \end{cases} \tag{5}$$

where

$$\mathbf{A}_E = \begin{bmatrix} -a_1 & -a_2 & \cdots & -a_{N_a-1} & -a_{N_a} \\ 1 & 0 & \cdots & 0 & 0 \\ 0 & 1 & \cdots & 0 & 0 \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & \cdots & 1 & 0 \end{bmatrix},$$

$$\mathbf{G}_E = [\,1 \;\; 0 \;\; \cdots \;\; 0 \;\; 0\,]^T, \qquad \mathbf{C}_E = [\,1 \;\; 0 \;\; \cdots \;\; 0 \;\; 0\,]$$

$\mathbf{x}_E(t) \in \mathbb{R}^{N_a}$ is the EEG state vector and $e_E(t)$ is a zero-mean white noise of variance σ_E^2. Analogously, consider the following state-space realization of model (4),

$$\begin{cases} \mathbf{x}_T(t+1) = \mathbf{A}_T\, \mathbf{x}_T(t) + \mathbf{B}_T\, u(t) \\ \overline{tms}(t) = \mathbf{C}_T\, \mathbf{x}_T(t) + v(t) \end{cases} \tag{6}$$

where $\mathbf{x}_T(t) \in \mathbb{R}^{\rho}$ is the TMS state vector, $\{\mathbf{A}_T,\, \mathbf{B}_T, \mathbf{C}_T\}$ with $\mathbf{A}_T \in \mathbb{R}^{\rho\times\rho}$, $\mathbf{B}_T \in \mathbb{R}^{\rho\times 1}$, $\mathbf{C}_T \in \mathbb{R}^{1\times\rho}$ is the control canonical form of (4), $\rho = \max\{\deg(B(q)), \deg(F(q))\}$ and $v(t)$ is a zero-mean white noise of variance σ_v^2. The variances σ_E^2 and σ_v^2 of $e_E(t)$ and $v(t)$ required for Kalman filter design, are determined from the identification of the EEG and TMS models, respectively.

Collecting systems (5) and (6) together, we obtain the extended dynamic system,

$$\begin{cases} \mathbf{x}(t+1) = \mathbf{A}\, \mathbf{x}(t) + \mathbf{B}\, u(t) + \mathbf{G}\, e_E(t) \\ eeg(t) + \;\overline{tms}(t) = \mathbf{C}\, \mathbf{x}(t) + v(t) \end{cases} \tag{7}$$

where

$$\mathbf{A} = \text{diag}\{\mathbf{A}_E,\ \mathbf{A}_T\}, \quad \mathbf{B} = \begin{bmatrix} \mathbf{0}_{N_a\times 1} \\ \mathbf{B}_T \end{bmatrix}, \quad \mathbf{G} = \begin{bmatrix} \mathbf{G}_E \\ \mathbf{0}_{\rho\times 1} \end{bmatrix},$$

$$\mathbf{C} = [\mathbf{C}_E \quad \mathbf{C}_T], \qquad \mathbf{x}(t) = [\,\mathbf{x}_E(t)^T \quad \mathbf{x}_T(t)^T\,]^T.$$

Note that (7) only models the *stationary* part of signal $s(t)$. To take into account the non-stationarities of $s(t)$ we carry out two changes in model (7). Actually, the non-stationary components of signal $s(t)$ can be effectively modelled using *time-variant* covariance matrices suitably tuned on the physical parameters of the problem.

First of all we introduce a stochastic component into the TMS model as an additive disturbance vector $\mathbf{e}_T(t)$ in the dynamic equation of (6). Process $\mathbf{e}_T(t)$ is a non-stationary white noise modeling the variance of the TMS artifact during the first peak of the stimulus. System (7) is thus modified as follows,

$$\begin{cases} \mathbf{x}(t+1) = \mathbf{A}\,\mathbf{x}(t) + \mathbf{B}\,u(t) + \underbrace{\begin{bmatrix} \mathbf{G}_E & \mathbf{0}_{N_a\times\,\rho} \\ \mathbf{0}_{\rho\times 1} & \mathbf{I}_\rho \end{bmatrix}}_{\mathbf{G}_M} \mathbf{e}(t) \\ eeg(t) + \overline{tms}(t) = \mathbf{C}\,\mathbf{x}(t) + v(t) \end{cases} \tag{8}$$

where $\mathbf{e}(t) = [e_E(t) \ \ \mathbf{e}_T(t)^T]^T$,

$$\text{var}\{\mathbf{e}_T(t)\} = \begin{cases} \sigma_T^2\,\mathbf{I}_\rho & \text{if } \ t_s \le t \le t_s +\ d \\ \mathbf{0}_{\rho\times\rho} & \text{otherwise.} \end{cases}$$

t_s denotes the sample at which the stimulus is generated while d is the number of samples of the first peak of the TMS. The variance σ_T^2 is a tuning parameter of the Kalman filter. To summarize, the complete covariance matrix $\mathbf{Q}(t) = \text{var}\{\mathbf{e}(t)\}$ is given by,

$$\mathbf{Q}(t) = \begin{cases} \text{diag}\{\sigma_E^2\,,\ \sigma_T^2\,\mathbf{I}_\rho\} & \text{if } \ t_s \le t \le t_s +\ d \\ \text{diag}\{\sigma_E^2\,,\ \mathbf{0}_{\rho\times\rho}\} & \text{otherwise.} \end{cases}$$

Secondly, we replace $v(t)$ by a noise $\eta(t)$ whose variance changes in time according to,

$$R(t) = \text{var}\{\eta(t)\} = \begin{cases} g(t) & \text{if } \ t_s \le t \le t_s + d_{tot} \\ 0 & \text{otherwise} \end{cases}$$

where

$$g(t) = \begin{cases} \sigma_v^2 & \text{if } \ t_s \le t \le t_s + d \\ \sigma_v^2\ e^{-\,\alpha\,(t\,-\,t_s\,-\,d)} & \text{if } \ t_s + d < t \le t_s + d_{tot}. \end{cases}$$

The idea behind this choice is that the effect of the TMS on the EEG tends to decrease after the first peak of the TMS stimulus. Such an effect has been modeled by an exponential decay. The tuning parameter $\alpha \in \mathbb{R}^+$ modulates the decay rate of the exponential while d_{tot} is the expected length (expressed in number of samples) of the TMS effect on the EEG trace.

In order to recover the EEG signal without the artifact, the Kalman filter is applied to system (8), with the measurement noise $v(t)$ replaced by $\eta(t)$:

$$\begin{aligned} \widehat{\mathbf{x}}(t+1\,|\,t) \ &= \ \mathbf{A}\,\widehat{\mathbf{x}}(t\,|\,t) + \mathbf{B}\,u(t) \\ \mathbf{P}(t+1\,|\,t) \ &= \ \mathbf{A}\,\mathbf{P}(t\,|\,t)\,\mathbf{A}^T + \mathbf{G}_M\,\mathbf{Q}(t+1)\,\mathbf{G}_M^T \end{aligned}$$

$$\begin{aligned} \widehat{\mathbf{x}}(t+1\,|\,t+1) \ &= \ \widehat{\mathbf{x}}(t+1\,|\,t) + \mathbf{K}(t+1)\,\xi(t+1) \\ \mathbf{P}(t+1\,|\,t+1) \ &= \ \mathbf{P}(t+1\,|\,t) - \mathbf{K}(t+1)\,\mathbf{C}\,\mathbf{P}(t+1\,|\,t) \end{aligned}$$

where

$$\xi(t+1) = eeg(t+1) + \overline{tms}(t+1) - \mathbf{C}\ \widehat{\mathbf{x}}(t+1\,|\,t)$$
$$\mathbf{K}(t+1) = \mathbf{P}(t+1\,|\,t)\,\mathbf{C}^T\big[\mathbf{C}\,\mathbf{P}(t+1\,|\,t)\,\mathbf{C}^T + R(t+1)\big]^{-1}.$$

At each time t, the Kalman filter delivers an estimate $\widehat{\mathbf{x}}(t\,|\,t) = [\,\widehat{\mathbf{x}}_E(t\,|\,t)^T \ \ \widehat{\mathbf{x}}_T(t\,|\,t)^T\,]^T$ of the state $\mathbf{x}(t)$. Hence, the sought estimate of the EEG signal is given by,

$$\widehat{eeg}(t) = \mathbf{C}_E\ \widehat{\mathbf{x}}_E\,(t\,|\,t), \ \ \text{for all } \ t = 1, 2, \ldots, S.$$

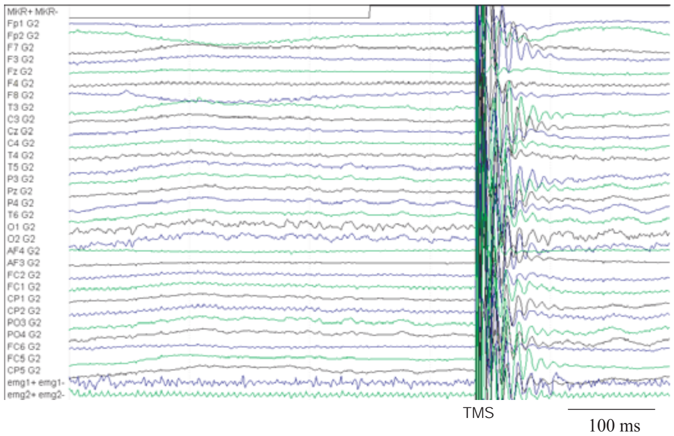
IV. EXPERIMENTAL RESULTS

A. Database, subjects and experimental equipment

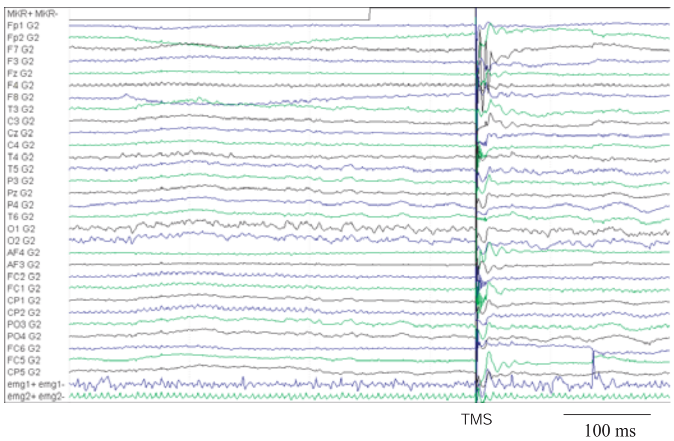
The database we used to test the effectiveness of the proposed approach consists of 7 records. A single record corresponds approximately to a 22 seconds acquisition on 32 channels. Each record is divided into 15 data sets of 1500 samples (the sampling time is 0.98 ms). Each data set contains a single TMS impulse. The database was acquired at Dipartimento di Neuroscience, Sezione di Neurologia, University of Siena. Experiments were carried out on 10 healthy volunteers (7 males) aged $22/43$ years (average 28.5 years). All subjects gave their written informed consent for the study which was approved by the local ethical committee. The experiment was well tolerated by all subjects.

Let us now turn the attention to the experimental equipment. Single-pulse TMS was generated using Magstim® *Super Rapid* biphasic stimulator and delivered through commercially available eight-shaped or circular coils (frequencies: 0.1 Hz and 10 Hz). The specifications of the equipment are: maximum discharge voltage 2 kV, maximum discharge current 7 kA, maximum magnetic field 2 T, rising time of the magnetic field 60 μs, length of the impulse 250 μs.

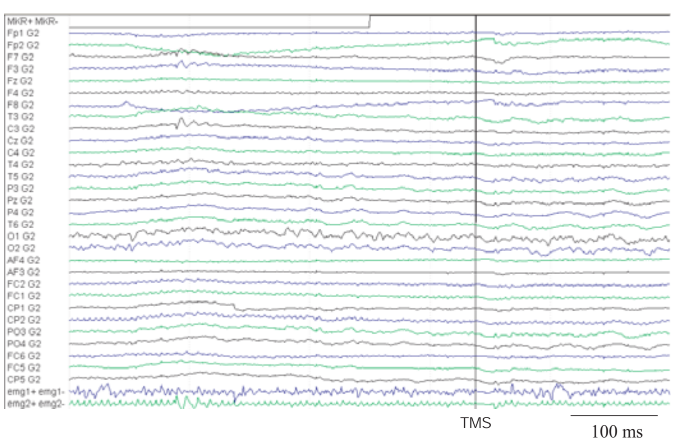
EEG recording was carried out with Micromed® equipment. To assure a good temporal precision we set the sampling frequency to 1024 Hz. The amplifier was optically connected to a PC running the *Brain-Quick System Plus* package and to a shielded cap containing the electrodes. The cap records 32 channels: 30 channels are dedicated to the electrodes disposed according to the international “10-20 EEG System”, while the last two channels are used for the electromyography of hand muscles. Before starting the EEG/TMS coregistration, the TMS threshold of each subject was determined according to standardized criteria [22]. The intensity of TMS pulses was set to 90%, 110% and 120% of the individual motor threshold. The scalp region stimulated by TMS corresponded to the position of C3 electrode, according to the standard nomenclature reported in [24].



(a)



(b)



(c)

Fig. 4. (a) The EEG/TMS trace on the 32 channels before the filtering. The signals after the application of: (b) a Wiener filter of order 15, (c) the Kalman filter. In correspondence of the black vertical line a TMS impulse is generated.

B. Identification of EEG and TMS models

For the sake of exposition, the experimental results presented hereafter refer to one data set of a single subject. The performance of the proposed procedure does not change significantly for different data sets, records and subjects.

For the EEG signal, AR models of different orders have been estimated and compared using the Matlab® System Identification Toolbox, according to Fit (percentage of the signal correctly reproduced by the model) and residuals autocorrelation. For the identification procedure, we used 2000 samples not affected by magnetic artifacts on a single channel. An AR(3) model, with $A(q) = 1 - 1.354\, q^{-1} + 0.6846\, q^{-2} - 0.3036\, q^{-3}$ was selected for the considered data set. To test the validity of this model we carried out validation tests using data from different channels: the considered AR(3) turned out to be a reliable model for all the channels. Higher order AR models have been also employed in the TMS removal procedure, but they did not provide a significant improvement of the results.

For the TMS, OE models of different orders were identified using 5 samples before and 35 samples after the stimulus. The validation procedure was conducted on 15 stimuli. The OE(3,3) proved to be the best choice for TMS, suitably trading off accuracy of measured output reproduction and simplicity of model structure.
When validating the model using signals from other channels, we observed that differently from EEG, TMS model has only local validity (in fact in general, TMS artifacts are higher in the electrodes close to the stimulation site). However, repeating the identification procedure in the other channels, the OE(3,3) model still revealed the most suited structure.

C. Tuning of the Kalman filter and discussion of the results

From the analysis of the data, we observed that the number of samples d of the first peak of the TMS impulse is approximately equal to 4 and the effect of TMS on the EEG trace is about 30 samples long. Hence we set $d_{tot} = 30$. Moreover, after some trials we chose $\sigma_T^2 = 0.1$ and $\alpha = 0.3$. Note that the previous parameters are equal for all the 32 channels. The Kalman filter was initialized with,

$$\hat{\mathbf{x}}(0|-1) = \mathbf{0}_{6\times 1}\,, \qquad \mathbf{P}(0|-1) = \begin{bmatrix} \mathbf{I}_3 & \mathbf{0}_{3\times 3} \\ \mathbf{0}_3 & 10^{-6}\,\mathbf{I}_3 \end{bmatrix}.$$

The EEG/TMS signals in our database were processed using the Kalman filter and a stationary filter, the Wiener filter, that has been used as a benchmark. Fig. 4(a) shows the EEG/TMS signals in a reference data set before the filtering. Fig. 4(b) shows the same signals after the application of a Wiener filter of order 15. In spite of an amplitude reduction, the artifacts have not been removed. Similar results were obtained with filters of different order. A basic condition for the application of the Wiener filter is that $tms(t)$ can be modelled as a stationary signal. But since $tms(t)$ is indeed non-stationary, a satisfactory deletion of TMS-induced artifacts can not be expected. Fig. 4(c) shows the EEG/TMS signals after the application of the Kalman filter. In this case, the effect of the magnetic artifacts on the EEG recordings has been strongly reduced, while preserving the integrity of EEG signals around TMS impulses.

For a further validation of the proposed Kalman filter approach some standard tests have been considered.

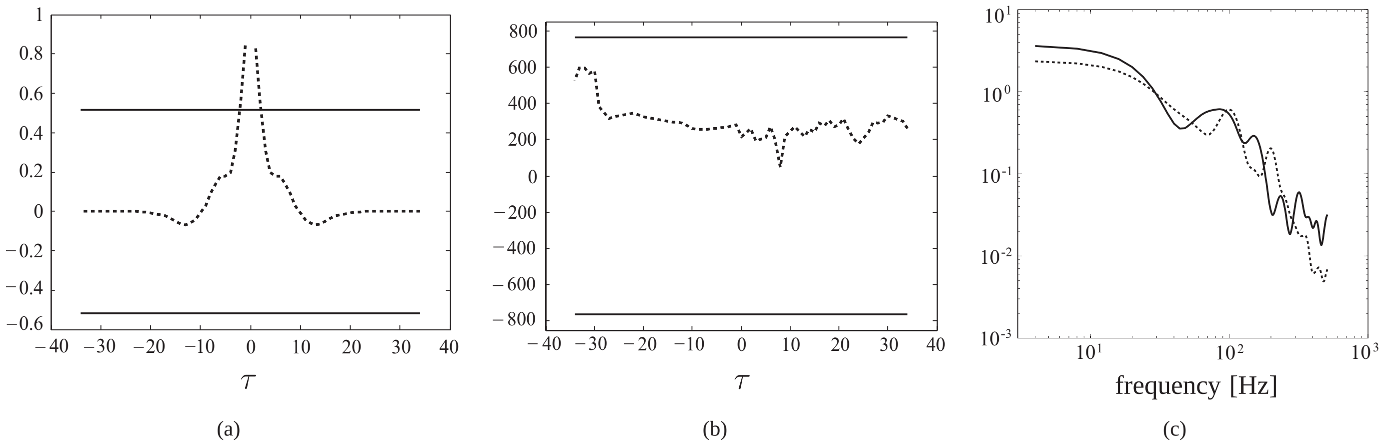


Fig. 5. Validation of the Kalman filter. (a) $\hat{R}^N_\xi(\tau)/\hat{R}^N_\xi(0)$ and the 99% confidence region ($N = 1500$, $H = 35$); (b) $\hat{R}^N_{\xi,\widehat{eeg}}(\tau)$ and the 99% confidence region ($N = 1500$, $H = 35$); (c) Spectrum of $\widehat{eeg}(t)$ (solid) and $eeg(t)$ (dash). $\widehat{eeg}(t)$ has been computed using 80 samples (including the artifact) on a single channel.

First, statistical tests on the Kalman filter residuals $\xi(t)$ have been performed. It has been observed that $\hat{R}^N_\xi(\tau)/\hat{R}^N_\xi(0)$, $\tau = 0, 1, \ldots, H$, where $\hat{R}^N_\xi(\tau)$ is the sample autocorrelation of the residuals computed on N samples, is always inside the 99% confidence region, except for $\tau = 1$ (see Fig. 5(a)). It has also been noticed that $\hat{R}^N_{\xi,\widehat{eeg}}(\tau)$ (the sample cross-correlation between $\xi(t)$ and $\widehat{eeg}(t)$) keeps always inside the 99% confidence region, thus showing that there is no evidence in the data that $\xi(t)$ and $\widehat{eeg}(t)$ are correlated (see Fig. 5(b)). Second, a frequency analysis has been conducted. The spectra of $eeg(t)$ and $\widehat{eeg}(t)$ proved to be similar for each channel (see Fig. 5(c)). Therefore we can infer that $\widehat{eeg}(t)$ has the characteristics of an electroencephalographic signal.

The proposed Kalman filter approach proved to be computationally efficient. Processing the EEG/TMS trace reported in Fig. 5(a) takes about 32 seconds on a laptop equipped with Pentium IV, 3 GHz processor and 512MB RAM. However, if the code is translated from Matlab to a lower level programming language, we are allowed to expect a 30% computation time reduction.

V. CONCLUSIONS AND FUTURE WORK

In this paper an off-line Kalman filter approach to remove TMS-induced artifacts from EEG recordings is proposed. Current results show that an effective procedure to screen out the artifacts is the following. First, identify from data two models describing EEG and TMS signals generation and collect them in an extended state-space system. According to the existing literature we chose an AR model for EEG. An OE model for TMS is proposed in the paper. Second, apply the Kalman filter, with time-variant covariance matrices suitably tuned on real data, to the extended system. Such peculiar covariance matrices allow us to model the non-stationary components of the EEG/TMS signal, neglected by conventional off-line filtering approaches.

The Kalman filter has been tailored to the specific application of TMS-induced artifacts removal, by suitably tuning the covariance matrices $\mathbf{Q}$ and R in order to cope with the impulsive nature of TMS artifacts. Therefore other artifacts that can be encountered in the EEG/TMS research may not be suppressed by the proposed strategy. However, future developments may address the tuning of the Kalman filter on these artifacts as well.

Although the obtained results are promising, still investigations are needed to validate the reliability of the estimated EEG signal. In particular, more accurate models of the interaction between TMS and EEG (e.g., with coupling nonlinear terms) should be addressed. Another objective of future research concerns an in-depth analysis of the stochastic component of the TMS, thus yielding more effective representations of the non-stationary behavior of the TMS signal. Finally, it would be interesting to analyze other estimation algorithms, like the Kalman smoother (see, e.g. [27]) or nonlinear non-stationary filters, in case of nonlinear models accounting for EEG/TMS joint dynamics.

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