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Online EEG artifact removal for BCI applications by adaptive spatial filtering

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Abstract

Objective. The performance of brain–computer interfaces (BCIs) based on electroencephalography (EEG) data strongly depends on the effective attenuation of artifacts that are mixed in the recordings. To address this problem, we have developed a novel online EEG artifact removal method for BCI applications, which combines blind source separation (BSS) and regression (REG) analysis. **Approach.** The BSS-REG method relies on the availability of a calibration dataset of limited duration for the initialization of a spatial filter using BSS. Online artifact removal is implemented by dynamically adjusting the spatial filter in the actual experiment, based on a linear regression technique. **Main results.** Our results showed that the BSS-REG method is capable of attenuating different kinds of artifacts, including ocular and muscular, while preserving true neural activity. Thanks to its low computational requirements, BSS-REG can be applied to low-density as well as high-density EEG data. **Significance.** We argue that BSS-REG may enable the development of novel BCI applications requiring high-density recordings, such as source-based neurofeedback and closed-loop neuromodulation.

Keywords: electroencephalography, brain–computer interface, blind source separation, independent component analysis, linear regression, online processing

(Some figures may appear in colour only in the online journal)

1. Introduction

A brain–computer interface (BCI) is a computer-based system that acquires brain signals, analyses them, and eventually translates them into commands for an electronic device to carry out a desired action (Shih *et al* 2012). BCIs are often used to assist, restore or augment human sensory-motor or cognitive functions (Krucoff *et al* 2016). BCI technology is the focus of big research endeavors involving neuroscientists, engineers and clinicians. The most widely used technique for acquiring brain signals to be used in BCIs is

electroencephalography (EEG) (Müller-Putz *et al* 2005). EEG measures changes in electrical potentials at different locations on the scalp, which are produced by the synchronized firing of thousands of neurons. It has the advantage of being relatively cheap and portable, and providing millisecond temporal resolution. All these features are particularly important for BCI applications. In recent years, high-density EEG (hdEEG) systems have become available, permitting to increase the spatial resolution of the reconstructed neural activity (He *et al* 2011). These developments have opened up the doors to the use of hdEEG as a brain imaging tool (Michel and Murray 2012). Such advances may be particularly relevant also in the context of BCI, as it may be possible to rely on real-time information about brain activity in one brain region, or about connectivity

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between two brain regions, instead of using sensor-space EEG signals.

An important impediment for a reliable use of EEG for BCI applications is the presence of artifacts, which may be observed in the EEG data but are not related to neural activity. Such artifacts may be produced by power lines, electrical equipment, or be of biological origin. Sources of biological artifacts include eye blinks, cardiac activity, muscle contractions, and head movements (Winkler *et al* 2011, Kong *et al* 2013). It is essential that EEG data are cleaned before their use in BCI system, to ensure that any control achieved is related to the participant's brain activity. By the same token, it is also important that true neural activity is not distorted. Moreover, online EEG processing is strictly required in the case of BCI applications. As such, an artifact removal solution that combines high accuracy and algorithmic efficiency needs to be sought.

Generally speaking, artifacts have overlapping frequencies with respect to the neural activity of interest. As such, temporal filtering is unlikely to be an effective solution for EEG artifact removal (Muthukumaraswamy 2013). On the other hand, spatial filtering is a computationally efficient approach, which permits to remove artifacts by exploiting information about their spatial distribution over the EEG sensors (Lagerlund *et al* 1997). Spatial filters are widely used in the field of BCI (Wu *et al* 2017), as they can be applied to each input data sample as it becomes available. To carry out spatial filtering of artefactual signals, EEG data are multiplied by a $[g \times g]$ image operator, where g is the number of recordings. Such image operator can be created following different methodological approaches. There are two main solutions that are currently in use: (i) regression techniques (REG) (He *et al* 2004, Schlogl *et al* 2007) and (ii) blind source separation (BSS) techniques (Choi *et al* 2005).

REG are based on the weighted subtraction of electrical signals representing artefactual sources, as for example electrooculography (EOG) and electromyography (EMG) signals. Removal of artefactual activities using regression method is indeed based on an assumption that there is no correlation between the true neuronal activity and EOG/EMG signals (Jervis *et al* 1988, Sadasivan and Dutt 1996). As a matter of fact, any activity common to EEG and EOG/EMG signals is attenuated, if not suppressed, by regression. Furthermore, the estimate of proper weights by regression is accurate when EOG/EMG signals have very similar waveforms as compared to the actual artifacts in the EEG data. This assumption is not always met, as the relative position of the artefactual source with respect to EEG and EOG/EMG signals is not matching.

Another group of artifact removal techniques relies on BSS. The most famous method belonging to this group is independent component analysis (ICA) (Xiaopei and Zhongfu 2005, Nolan *et al* 2010, Turnip 2014), but there are also other BSS approaches such as principal component analysis (PCA) (Turnip and Junaidi 2014) and canonical correlation analysis (CCA) (Gao *et al* 2010b). BSS methods are capable of separating signals originating from different sources (i.e. components), which are mixed in the recordings (Delorme *et al* 2012, Zeng *et al* 2013). By means of BSS, it is possible to

isolate artefactual components and remove them from the EEG data with proper weights. The main disadvantage of this methodology is that the automated classification of artefactual components is not straightforward (Mahajan and Morshed 2015), and the latter may also contain residual neural activity (Winkler *et al* 2014). Another potential limitation of BSS solutions is that they typically assume the stationarity of the sources, i.e. the weights associated with the components are fixed over the whole EEG recording (Winkler *et al* 2011, Marino *et al* 2018a). Some BSS approaches do not suffer from this limitation, as they can estimate components on short time windows (Daly *et al* 2015). However, they are computationally very expensive, and therefore less suited for BCI applications.

A limited number of studies have attempted to combine regression and BSS techniques, tackling their major drawbacks and combining their positive features (Siew Cheok and Raveendran 2008, Gao *et al* 2010a, Klados *et al* 2011, Zhang *et al* 2015, Mannan *et al* 2016). In short, these studies proposed: (1) to decompose the EEG data by BSS; (2) select artefactual components; (3) apply regression analysis to remove true artifacts from them while preserving residual neural activity; and finally, (4) back-reconstruct the clean EEG data by recombining the non-artefactual components as well as the residuals of the artefactual components. The combination of regression and BSS techniques may hold strong potential; we identify however three potential issues with the approach described above. First, as in classical regression procedures, the method assumes the similarity between the time courses of non-cerebral electrical signals and those of the components produced by BSS. Second, the regression analysis is applied to selected components only, so it is still possible that residual artefactual contribution is present in the components that are recombined to generate the 'clean' EEG data. Third, the artifact removal is not implemented in the form of a spatial filter, which makes computations particularly heavy for hdEEG data.

In this study, we present a novel online EEG artifact removal method for BCI applications, which, by combining BSS and REG in an original way, addresses each of the three problems mentioned above. Our BSS-REG method is primarily intended as an adaptive spatial filter approach. This is meant to be particularly suitable for hdEEG due to its low computational requirements, but can be also applied to low-density EEG. In the first instance, BSS is run on a calibration dataset for the creation of a spatial filter capable of extracting artefactual signals from EEG data. This filter, while being applied to actual EEG data, is fine-tuned in a dynamic manner using regression analysis. This adaptive spatial filtering approach can be applied for the removal of a wide range of biological and non-biological artifacts. In this study, its performance is assessed by focusing on ocular artifacts, which strongly contaminate almost any EEG recording (Schlogl *et al* 2007, Zeng *et al* 2013) and have been shown to substantially affect BCI performance (Fatourechi *et al* 2007). In this case, simulated data are used to accurately quantify performance in controlled settings. A comparison with alternative methods for the online correction of ocular artifacts is conducted, both

in terms of accuracy and computational efficiency. Finally, the validation is extended to real EEG data, which are corrupted by different kinds of artifacts, such as ocular and muscular artifacts. A comparison is carried out between the results obtained using our online correction method and a previously validated offline artifact removal approach based on BSS.

2. Methods

2.1. Description of the method

The BSS-REG method relies on the availability of a calibration dataset of limited duration for the initialization of a spatial filter, which is then dynamically adjusted in the actual experiment for online artifact removal.

2.1.1. Spatial filter initialization on a calibration dataset. First of all, BSS is applied to an EEG calibration dataset for the decomposition of cerebral and artefactual signals that are present in the recordings. The number of time samples n in this EEG dataset does not need to be fixed *a priori*. However, this will inherently have an impact on the performance of data decomposition by BSS. The BSS model can be mathematically described as:

$$X(t) = A * S(t) \quad (1)$$

where $X(t) = [x_1(t), \dots, x_g(t)]$ is the matrix of g observed signals, $S(t) = [s_1(t), \dots, s_m(t)]$ the matrix of m underlying signals and $A [g \times m]$ denotes the mixing matrix (Stone 2004). It is a generative model, which means that it describes how the observed data are generated by a process of mixing the underlying signals s_i (with $i = 1, \dots, m$), also referred to as sources or components. A solution for the BSS problem is possible if the number of components is at most equal to the number of observed signals ($m \leq g$). In this case, the components can be retrieved by determining a $[m \times g]$ matrix W , named unmixing matrix, such as:

$$S(t) = W * X(t). \quad (2)$$

Notably, ICA can be used for BSS, when the components can be assumed to be statistically independent (Hyvärinen et al 2004). On the other hand, PCA and CCA rely on the assumption that these are statistically uncorrelated (less stringent criterion) (Gao et al 2010b, Turnip and Junaidi 2014). In the current implementation of BSS-REG, BSS is performed using FastICA (<http://research.ics.aalto.fi/ica/fastica>), an ICA algorithm which has shown to have fast convergence and yield accurate data decomposition (Hyvärinen et al 2004, Nolan et al 2010). However, other BSS algorithms, such as Infomax (Bell and Sejnowski 1995) and JADE (Rutledge and Jouan-Rimbaud Bouveresse 2013), PCA (Wold et al 1987, Shlens 2005, Turnip and Junaidi 2014) and CCA (Hotelling 1936), could also be alternatively used. Though, it is worth noting that the specific BSS approach to be used should be chosen depending on the specific characteristics of the artifacts to be removed (Halder et al 2007).

After BSS has been applied to the EEG calibration dataset, the underlying signals that are associated with the artifacts

need to be identified. To this end, different selection criteria can be used, depending on the specific artifact. In BSS-REG, for the identification of artefactual independent components (ICs), we use the same parameters as in Liu et al (2017): (1) correlation between the power of the IC with the vertical EOG (vEOG), horizontal EOG (hEOG) and EMG; (2) the coefficient of determination obtained by fitting the IC power spectrum with a $1/f$ function; (3) the kurtosis of the IC. The components with at least one of the three parameters outside the normal range, as defined in Liu et al (2017), are classified as artefactual. The unmixing matrix W_A for the artefactual components $S_A(t)$ is obtained by selecting the corresponding rows of the matrix W . This matrix W_A is essentially a spatial filter, which permits to obtain an estimate of (uncorrelated or independent) artefactual components $S_A(t)$, according to:

$$S_A(t) = W_A * X(t). \quad (3)$$

2.1.2. Adaptive spatial filtering for online artifact removal. During the real experiment requiring online artifact removal, EEG signals are read and stored in a buffer of k samples. The spatial filter W_A calculated on a calibration dataset is applied, for each given instant, to the EEG data $X(\tau)$ in the buffer, such that an estimate of the artefactual signals $S_A(\tau)$ can be obtained:

$$S_A(\tau) = W_A * X(\tau). \quad (4)$$

At this stage, regression analysis is used to dynamically estimate the weights B_A to be used for artifact removal. This permits to account for the non-stationarity of the artefactual contribution in the EEG signals. Different approaches can be used for estimating the weights B_A to be associated with the artefactual components (Croft and Barry 2000, Jung et al 2000b, Gomez-Herrero et al 2006), to satisfy the following equation:

$$X(\tau) = B_A * S_A(\tau) + \varepsilon(\tau) \quad (5)$$

where $\varepsilon(\tau)$ is the residual of $X(\tau)$ that cannot be explained by a linear combination of $S_A(\tau)$. In BSS-REG, we employ the ordinary least squares (OLS) regression method (Moretti et al 2003) due to its low computational complexity and numerical efficiency. Accordingly, the weights B_A are obtained as:

$$B_A = X_A(\tau) * S_A^T(\tau) * (S_A(\tau) * S_A^T(\tau))^{-1} \\ \approx X(\tau) * S_A^T(\tau) * (S_A(\tau) * S_A^T(\tau))^{-1}. \quad (6)$$

This permits us to build an adaptive spatial filter $F(\tau)$ to dynamically obtain artifact-free signals $X_c(\tau)$, such as:

$$X_c(\tau) = F(\tau) * X(\tau). \quad (7)$$

Specifically, $F(\tau)$ is defined as follows:

$$F(\tau) = I - X(\tau) * S_A^T(\tau) * (S_A(\tau) * S_A^T(\tau))^{-1} * W_A \quad (8)$$

where I is an identity matrix with dimension $[g \times g]$.

2.2. Validation of the method

The performance of the BSS-REG method was assessed on both simulated and real EEG data, with special focus on

ocular artifact removal. In this case, it is indeed possible to use a wide range of alternative methods as benchmark. Since BSS-REG can be used also for other kinds of artifacts in EEG recordings, we extended the validation to real datasets. The accuracy in terms of artifact removal achieved by BSS-REG was compared against that of an offline artifact removal method based on ICA (Liu *et al* 2017).

2.2.1. Real and simulated EEG data. Data used in this study were obtained from hdEEG recordings collected in 17 healthy right-handed participants (4 males and 13 females, with age ranging from 21 to 43 years). These recordings were used in our previous studies (Liu *et al* 2015, 2017). All participants reported normal or corrected-to-normal vision, had no psychiatric or neurological history, were free of psychotropic or vasoactive medication. Before undergoing the examination, they gave written informed consent to the experimental procedures, which were approved by the Institutional Ethics Committee of ETH Zurich. hdEEG signals were recorded at 1000 Hz using a 256-channel system from Electrical Geodesics (Eugene, US). The electrode at vertex (labeled as Cz in the 10/20 international system) was used as physical reference. In addition to hdEEG, we also recorded horizontal and vertical EOG (hEOG/vEOG), as well as EMG for masseter and platysma muscles, to detect head movement and swallowing, respectively.

For each participant, we recorded hdEEG signals during resting state (for 4 min) and during visual oddball tasks (for 3 min). In the resting state condition, each participant fixated a cross in the center of a screen. The visual oddball task consisted of a presentation of 80% of frequent stimuli and 20% of rare stimuli respectively (Mantini *et al* 2009). The stimuli included purple circles of 3.2° and 1.6° of visual angle for frequent and rare events respectively. They were presented on a black background for 7 ms. The task consisted of pressing a button as soon as possible after the rare event (target) appeared. The interval between stimuli was 2 s, for a total number of 90 trials (O'Connell *et al* 2012, Murphy *et al* 2014).

The collected hdEEG data were preprocessed using EEGLAB (<https://sccn.ucsd.edu/eeglab/index.php>) and built-in MATLAB functions. The preprocessing steps included: bad-channel detection and interpolation, digital filtering in the band 1–80 Hz, resampling to 200 Hz and average re-referencing. In addition, off-line artifact removal was performed by means of ICA, using the same criteria used in BSS-REG, and previously described in Liu *et al* (2017). The artifact-cleaned dataset obtained with ICA was used as a reference to evaluate the performance of the online artifact removal by BSS-REG. In addition, the same dataset was used for the generation of a new dataset, in which simulated ocular artifacts were added (figure 1). These ocular artifacts were obtained from signals reconstructed by superimposing the contribution of IC associated with EOG collected in another participant to the hdEEG recordings of the initial dataset (Romero *et al* 2008). For the definition of BSS-REG standard settings we selected seven datasets, and we then validated them using the remaining ten datasets. Both in the case of simulated and real hdEEG data, a pseudo-online test was performed by using a moving

window approach, to generate a ‘virtual’ buffer of data to be given as input to BSS-REG and other online artifact removal algorithms.

2.2.2. Analysis of BSS-REG performance. We first performed an optimization of the BSS-REG parameters and settings using the first seven datasets. Since BSS-REG relies on the creation of an initial spatial filter by performing BSS on a calibration dataset, we first compared different BSS solutions on the simulated resting-state EEG data. Specifically, we assessed the ability of the BSS-derived spatial filter to reconstruct the ocular signal that was superimposed over the EEG signals. By using resting-state EEG data, we compared the results obtained using the FastICA algorithm (our default solution) against other ICA algorithms, such as Infomax, JADE, PCA and CCA. Reconstruction performance, which was quantified in terms of temporal correlation between simulated and reconstructed ocular signals, was examined for different durations of the calibration recording (ranging between 30 s and 4 min). By using a pseudo-online test, we also assessed what size of the data buffer can lead to the best combination of artifact attenuation accuracy and computation speed required for online processing. Accuracy was quantified by means of the cosine similarity measure (CSM) (Eldeen *et al* 2017, Niknazar *et al* 2018), defined as follows:

$$\text{CSM} = \frac{\langle X_b(t), X_c(t) \rangle}{\|X_b(t)\| \cdot \|X_c(t)\|} \quad (9)$$

where $X_b(t)$ is the simulated EEG dataset before artefactual contamination and $X_c(t)$ is the reconstructed EEG dataset after artifact removal. CSM ranges between 0 and 1, and values close to 1 are associated with good reconstruction performance. Computational time was quantified using MATLAB (release 2016b) running under MacOS (with 2.5 GHz Intel Core i7 processor and 16 GB RAM). Both accuracy and computation time were evaluated using the visual oddball paradigm data for different length of the buffer size (ranging between 100 and 2000 ms).

After defining the BSS method to be used and the method settings, we compared the performance of BSS-REG with respect to other methods using 10 additional datasets. The utility of the two-step approach implemented in BSS-REG was assessed by comparing its performance with that of BSS spatial filtering (Jung *et al* 2000a) and OLS regression (Moretti *et al* 2003), separately. Furthermore, we employed a number of commonly used approaches for online ocular artifact removal as benchmark for our method. Specifically, we used adaptive filtering (AF) (He *et al* 2004), least mean squares (LMS) (Haykin 1996), conventional recursive least squares (CRLS) (He *et al* 2004) and an adaptive algorithm based on time varying H^∞ principles (HINFTV) (Puthusserypady and Ratnarajah 2005). The first of those methods is implemented in BCILAB (<https://sccn.ucsd.edu/wiki/BCILAB>), whereas the other ones are part of the Automatic Artifact Removal toolbox (http://germangh.github.io/eeglab_plugin_aar) (Gomez-Herrero *et al* 2006). A repeated-measures one-way ANOVA and post-hoc paired

Figure 1. Illustrative example of 20s of (A) cleaned EEG signals in five representative channels; (B) simulated ocular artifact; and (C) simulated EEG signals, obtained adding the ocular artifact to the cleaned EEG signals. (A) and (B) are extracted from different subjects.

t-tests were carried out to assess significant differences across and between methods with regard to accuracy and computational efficiency.

Finally, after conducting an assessment of the performance on ocular artifact removal, we extended our investigation to other kinds of artifacts, such as muscular and movement artifacts, that are present in the EEG data. Accordingly, we used the resting state dataset for the initialization of the BSS-REG spatial filter, and applied the adaptive spatial filtering of BSS-REG to the visual oddball dataset. The reconstruction performance was assessed against that obtained on the same dataset using offline ICA processing. Both in the case of online BSS-REG and offline ICA processing, we evaluated event-related potentials (ERPs) for rare events (100ms pre-stimulus and 600ms post-stimulus time) only, as these are the ones supposedly showing the P300 response (Picton 1992, Mantini *et al* 2009, Liu *et al* 2015). We specifically quantified pre-stimulus noise level as the root mean square (RMS) in the pre-stimulus interval (Mantini *et al* 2009) and inter-trial variability defined the mean of across-trial standard deviation (Vanderperren *et al* 2010, Marino *et al* 2018b). Improvement following artifact removal was assessed by calculating the ratio between each index before and after artifact removal respectively. A paired *t*-test was used to evaluate whether there are significant differences between online BSS-REG and offline ICA processing in terms of pre-stimulus noise level and inter-trial variability, respectively.

Figure 2. Quantitative comparison of different BSS method under investigation. Comparison is performed by correlating ocular signal and reconstructed one for any BSS method across all the subjects. For each subject, the FastICA (deflation approach) method outperforms all the other methods in terms of ocular signal reconstruction as shown by the consistently higher correlation, regardless of the calibration length. Moreover, the performances of any method generally improve depending on the amount of data.

3. Results

3.1. Definition of BSS-REG standard settings

The performance of the BSS-REG approach relies in the first instance on the BSS algorithm used and on the amount of data available for the initialization of the spatial filter. Accordingly, we analyzed the accuracy and stability of different BSS

Figure 3. BSS-REG performance in a pseudo-online test. The size of the data buffer influences the reconstruction of the ocular artifact. With a longer data buffer, (A) CSM and (B) computational time both increase.

approaches for the reconstruction of the ocular artifact. As expected, the correlation between the simulated ocular signal and the reconstructed one generally increased for any BSS method under investigation (figure 2). Overall, the FastICA and Infomax algorithms showed superior performance than JADE, PCA and CCA. FastICA required more input data than Infomax to achieve a good data decomposition, and hence ocular signal reconstruction. However, when using a calibration dataset of 4 min, FastICA yielded the best reconstruction of the ocular artifact, which is likely to be acceptable in a wide range of applications. We therefore relied on this solution for adaptive spatial filtering by BSS-REG.

We then moved to the analysis of the BSS-REG performance in a pseudo-online test. As such, we examined to what extent and how the size of the data buffer influences the reconstruction of the ocular artifact. We observed that both accuracy (figure 3(A)) and computational time (figure 3(B)) increased with a longer data buffer. However, we found that a buffer of 1000 ms or more yielded a computation time above 5 ms. Since the EEG signal was sampled at 200 Hz, 5 ms is the maximum delay that could be accepted in online EEG processing. Based on these considerations, we selected 500 ms as the standard buffer size for BSS-REG. This choice yielded a CSM equal to 0.957, and a computation time equal to 2.1 ms (see figure 3).

Figure 4. Quantitative assessment of EOG artifact attenuation across methods. Comparison is performed by examining the CSM and box plots are provided. BSS-REG, ICA and OLS methods were applied for removing the EOG artifact from the EEG recordings. For each subject, the BSS-REG method outperforms the other methods in term of EOG artifact attenuation.

3.2. Analysis of BSS-REG performance on simulated EEG data

By using simulated EEG data, we could also quantify the performance of BSS-REG with respect to alternative approaches. First, we examined whether our method, in its standard settings, performs better than when using BSS and linear regression separately. As for BSS, we calculated a spatial filter on resting state EEG data by using ICA and applied it directly to the oddball paradigm EEG data. Linear regression was implemented through OLS, using the recorded EOG signals as reference signals for online artifact removal. A repeated-measures one-way ANOVA revealed significant differences among BSS-REG, ICA and OLS methods ($p < 0.0001$) (figure 4). Significant differences were found between BSS-REG and ICA ($p < 0.0001$) and between BSS-REG and OLS ($p = 0.0004$). This finding confirmed that the use of an adaptive spatial filter obtained by combining BSS and linear regression is beneficial to achieve a more accurate online artifact removal. Furthermore, the use of BSS-REG can lead to a more effective removal of ocular artifacts in comparison to AF, LMS, CRLS and HINFTV both in terms of accuracy (figure 5(A)) and computational time (figure 5(B)). A repeated-measures one-way ANOVA confirmed that there were significant differences among BSS-REG, AF, LMS, CRLS and HINFTV methods, both for accuracy and computational time ($p < 0.0001$). In terms of accuracy, paired t-tests denoted significant differences between BSS-REG and AF, CRLS and HINFTV ($p = 0.0042$, $p < 0.0001$ and $p < 0.0001$, respectively), and no significant difference between BSS-REG and LMS ($p = 0.415$). With regard to computational efficiency, paired t-tests revealed significant differences between BSS-REG and all other methods ($p < 0.0001$).

3.3. Analysis of BSS-REG performance on real EEG data

We finally evaluated whether BSS-REG can be used for the removal not only of ocular artifacts, but also muscular artifacts.

Figure 5. Quantitative assessment of EOG artifact attenuation across methods: (A) BSS-REG, AF, LMS, CRLS and HINFTV methods were applied for removing the EOG artifact from the EEG recordings. A comparison is performed by examining the CSM and box plots are provided. For each subject, the BSS-REG method outperforms the other methods in term of EOG artifact attenuation; (B) boxplots showing the computational time for each method for a single data buffer of 500 ms. The runtimes are measured over a total of 360 ‘virtual’ data buffers for each subject. The use of BSS-REG can lead to a more effective removal of ocular artifacts in comparison to the other methods, both in terms of accuracy and computational time.

Figure 6. Single-subject ERP analysis of EEG signals at the electrode Pz for rare and frequent events: (A) uncorrected; (B) corrected with offline ICA; and (C) corrected with BSS-REG. Scalp topography of ERPs associated with P300 response at 340 ms: (D) uncorrected; (E) corrected with offline ICA; and (F) corrected with BSS-REG.

To this end, we used real EEG data collected during a visual oddball paradigm (figure 6). These data were also processed by using a standard artifact removal approach based on ICA, which served as benchmark. Our ERP results showed that BSS-REG yielded a reduction of 21.04% and 26.5% in noise and inter-trial variability, respectively, with respect to unprocessed EEG data. Conversely, although there was 7.73% more noise and 10.06% more inter-trial variability with BSS-REG than offline ICA, differences between online and offline methods were on the border of significance for inter-trial variability ($p = 0.0526$) and pre-stimulus noise ($p = 0.0689$), respectively (figure 7). The topology of the scalp map at the latency of the maximum peak (between 320 and 470 ms across subjects) was largely similar (spatial and temporal correlation equal to 0.744 ± 0.1475 and 0.7978 ± 0.1447 , respectively).

4. Discussion

The BSS-REG method has been developed for online artifact removal from EEG signals, which is a very important requirement for BCI application. Our method has shown to perform better than several alternative methods for the removal of ocular artifacts. No extensive validation has been conducted on simulated data for other types of artifacts, as no specific gold-standard exists. However, we have successfully applied BSS-REG on real EEG data containing multiple artefactual sources, and have shown that the performance is comparable to those of a standard offline artifact removal approach based on ICA. What is particularly remarkable is the low computation time, which makes the BSS-REG method suitable for use not only with low-density but also high-density EEG recordings. Importantly, this feature may enable the development of more advanced BCI applications in the future.

4.1. Primary features of the BSS-REG method

The method has been specifically developed to operate in an online mode during EEG acquisitions. Like other methods (Croft and Barry 1998, Schlogl *et al* 2007, Zhang *et al* 2015), it relies on a calibration dataset for feature extraction. In BSS-REG, this is particularly important, as it ensures that a low computation time is required during the actual EEG experiment. Since BSS is used for the initialization of the spatial filter, the spatial stationarity of the artefactual sources between the calibration and the experimental phase is assumed. In other words, the demixing matrix obtained in the calibration phase is assumed to approximate the one that would be obtained by using BSS on the EEG data collected during the experiment. Our results show that this may be the case, at least for EEG data collected in the same experimental session. Furthermore, we observed that the demixing matrix that specifically relates to artefactual sources is not strongly affected by the specific task performed by the participant. A possible caveat of our approach is that the calibration dataset should contain a sufficient number of artefactual occurrences (for instance, explaining at least 1% of the total variance) for an effective initialization of the spatial filter. In this regard, it

Figure 7. Quantitative assessment of ERP analysis across ICA offline and BSS-REG. A comparison is performed by examining (A) pre-stimulus noise and (B) inter-trial variability. Inter-trial variability and pre-stimulus noise are relatively larger for BSS-REG, but there are no significant differences between methods ($p > 0.05$).

may be helpful to ask the participant to intentionally generate such artifacts (Zhang *et al* 2015).

Importantly, other studies proposed the use of ICA for online artifact removal (Halder *et al* 2007, Radüntz *et al* 2015), and some of them in combination with REG (Siew Cheok and Raveendran 2008, Klados *et al* 2011, Mannan *et al* 2016). Since we conducted our testing on hEEG data, all the techniques using ICA based on a moving window approach could not be used due to very high computation times. Indeed, the computational complexity of ICA scales at least quadratically with the number of input channels (Hyvärinen *et al* 2004). Furthermore, the number of samples required for an effective ICA decomposition is also related to the number of recordings, and this constrains its application in an online modality. One study specifically proposed the combination of ICA and REG for online removal of the ocular artifact (Mannan *et al* 2016). That approach may appear very similar to BSS-REG, but this is really not the case. Indeed, ICA is performed in

an online modality, linear regression is applied to each component using EOG signals, and the cleaned components are then back-projected over the recordings. Besides the considerations on computational complexity already made, we argue that this specific implementation may have low performance when the waveforms of EOG signals do not well match that of the ocular artifact in the EEG data.

4.2. Analysis of the method performance

To assess the performance of the BSS-REG, we first relied on a simulated dataset consisting of neural signals contaminated only by ocular artifacts. With known ground truth, we could effectively compare the mean CSM and computation time of BSS-REG with those of alternative approaches, such as AF, LMS, CRLS and HINFTV (figure 5). We also examined the performance of ICA and OLS, which allowed us to appreciate the potential advantages of using the combined (two-step) approach implemented in BSS-REG (figure 4). With the exclusion of LMS, BSS-REG outperformed all other methods in terms of artifact removal accuracy. Also, it was by large the fastest method, with a delay below 5 ms even with high-density (256-channel) EEG data (figure 3(B)).

The BSS-REG method was also assessed using actual EEG signals collected in participants during visual oddball paradigm. Through the analysis of ERP data, we could quantitatively evaluate the effectiveness in the removal of different artifacts (figure 7). The noise level and the inter-trial variability can be used to evaluate the effectiveness of artifact attenuation. On the other hand, signal preservation could be assessed by examining the main peak intensity in the ERP (figure 6). In addition to these measures, we have also presented qualitative results for actual EEG datasets. Overall, results on actual EEG datasets confirm that the BSS-REG method is suitable for online removal of different kinds of artifacts (including ocular and muscular artifacts). As expected, its accuracy was on average lower than that of widely used offline ICA method (Jung *et al* 2000a). However, the differences between the two methods were just on the border of significance.

4.3. Potential applications in the field of BCI

Our validation was conducted on hdEEG recordings, which are not commonly used for BCI applications. Our recent work was focused on the use of hdEEG for accurate source reconstructions and connectivity analyses (Liu *et al* 2017). We developed a comprehensive pipeline for offline analysis of hdEEG data, which can contribute to a more widespread utilization of EEG as a brain-mapping tool (Michel and Murray 2012). In future work, our efforts will be devoted to the implementation of computationally-efficient techniques for real-time analysis of hdEEG data, aiming to estimate neural activity in the brain in an online modality. This work will be relevant to all applications that may require estimates of source-based activity rather than EEG recordings. For instance, source-based EEG neurofeedback has been recently introduced (Boe *et al*

2014, van Lutterveld *et al* 2017). This holds great promise for studies aiming at more specific, and possibly more effective, brain training than with classical EEG neurofeedback. Also, closed-loop neuromodulation techniques combining EEG with transcranial magnetic stimulation or transcranial current stimulation can be developed by controlling the phase of neural signals estimated in specific brain areas (Bergmann *et al* 2016, Zrenner *et al* 2016). Furthermore, novel BCIs can be optimized for use on activity estimated from different brain regions. This may ultimately lead to increased classification accuracy as compared to classical EEG-based BCIs, and may contribute to bridging the gap between human studies that use scalp EEG and animal studies, for which intracranial recordings are possible (Capogrosso *et al* 2016).

4.4. Limitations and future work

As many existing online artifact removal approaches, BSS-REG relies on electrical signals recorded simultaneously with EEG, such as EOG and EMG. In our method, the latter are primarily used to identify the components extracted from the calibration dataset, which need to be used for the initialization of the spatial filter. It should be noted that it may be possible to use different criteria for the identification of the artefactual components. For instance, the ocular components are characterized by high kurtosis values (Klados *et al* 2010), whereas the muscular components have very low autocorrelation values (De Vos *et al* 2010). Future studies are warranted to test the effectiveness of these approaches, and their impact on artifact removal accuracy. The impact of the specific BSS approach used should be also considered. In the present study, we showed that the FastICA algorithm has comparable performance as compared to Infomax, and that ICA-BSS generally outperforms PCA- and CCA-BSS on ocular artifacts. This assessment could be extended to other kinds of artifacts. Furthermore, recent studies are proposing the use of tensor decomposition techniques for artifact removal as a valid alternative to ICA and BSS (Triantafyllopoulos and Megalooikonomou 2014). It may be interesting to verify whether these approaches can effectively yield improved reconstruction of artefactual sources within the BSS-REG framework. Concerning online artifact removal, we opted for the use of a standard linear regression approach based on OLS. This ensures that the removal of artifacts can be implemented using a spatial filter, and therefore that computation time is kept low even for hdEEG recordings. However, alternative regression methods could be implemented and compared to OLS. Finally, it may be worth extending the validation of our approach to other EEG datasets, collected with different systems and different experimental protocols. In particular, it would be important to further validate the efficacy of the BSS-REG method during BCI operation, as for example during ERP-based BCI control. Considering the growing interest of the neuroscientific community on closed-loop neuromodulation approaches (Semprini *et al* 2018), it would be interesting to extend BSS-REG, such that it can be applied

also for the attenuation of electrical noise from transcranial alternating current stimulation.

5. Conclusions

We have introduced BSS-REG, a method for the online artifact removal of EEG signals, which is suitable not only for low-density but also high-density systems. The method requires the use of a calibration recording for the initialization of the spatial filter. This ensures a low computation time during the actual EEG experiment. BSS-REG outperforms other methods in terms of artifact removal accuracy and computational time. Furthermore, it can remove different kinds of artifacts with accuracy comparable to achieved by an offline ICA approach (Jung *et al* 2000a). We argue that BSS-REG may enable the development of novel BCI applications requiring high-density recordings, such as source-based neurofeedback and closed-loop neuromodulation.

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Competing financial interests

The authors declare no competing financial interests.

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References

- Bell A J and Sejnowski T J 1995 An information-maximization approach to blind separation and blind deconvolution *Neural Comput.* **7** 1129–59
- Bergmann T O, Karabanov A, Hartwigsen G, Thielscher A and Siebner H R 2016 Combining non-invasive transcranial brain stimulation with neuroimaging and electrophysiology: current approaches and future perspectives *NeuroImage* **140** 4–19
- Boe S, Gionfriddo A, Krautner S, Tremblay A, Little G and Bardouille T 2014 Laterality of brain activity during motor imagery is modulated by the provision of source level neurofeedback *NeuroImage* **101** 159–67
- Capogrosso M 2016 A brain–spine interface alleviating gait deficits after spinal cord injury in primates *Nature* **539** 284
- Choi S, Cichocki A and Park H M 2005 Blind source separation and independent component analysis: a review *Neural Inf. Proc. Lett. Rev.* **6** 1–57
- Croft R J and Barry R J 1998 EOG correction: a new aligned-artifact average solution *Electroencephalogr. Clin. Neurophysiol.* **107** 395–401
- Croft R J and Barry R J 2000 Removal of ocular artifact from the EEG: a review *Neurophysiol. Clin. Neurophysiol.* **30** 5–19
- Daly I, Scherer R, Billinger M and Müller-Putz G 2015 FORCE: fully online and automated artifact removal for brain-computer interfacing *IEEE Trans. Neural Syst. Rehabil. Eng.* **23** 725–36
- De Vos M, Ries S, Vanderperren K, Vanrumste B, Alario F X, Van Huffel S and Burle B 2010 Removal of muscle artifacts from EEG recordings of spoken language production *Neuroinformatics* **8** 135–50
- Delorme A, Palmer J, Onton J, Oostenveld R and Makeig S 2012 Independent EEG sources are dipolar *PLoS One* **7** e30135
- Eldeen A, Seddik A and Allah A 2017 A hybrid approach for artifacts removal from EEG recordings *Int. J. Comput. Appl.* **168** 10–9
- Fatourehchi M, Bashashati A, Ward R K and Birch G E 2007 EMG and EOG artifacts in brain computer interface systems: a survey *Clin. Neurophysiol.* **118** 480–94
- Gao J, Yang Y, Sun J and Yu G 2010a Automatic removal of various artifacts from EEG signals using combined methods *J. Clin. Neurophysiol.* **27** 312–20
- Gao J, Zheng C and Wang P 2010b Online removal of muscle artifact from electroencephalogram signals based on canonical correlation analysis *Clin. EEG Neurosci.* **41** 53–9
- Gomez-Herrero G, Clercq W D, Anwar H, Kara O, Egiastian K, Huffel S V and Paesschen W V 2006 Automatic removal of ocular artifacts in the EEG without an EOG reference channel *Proc. 7th Nordic Signal Processing Symp.—NORSIG 2006* pp 130–3
- Halder S, Bensch M, Mellinger J, Bogdan M, Kübler A, Birbaumer N and Rosenstiel W 2007 Online artifact removal for brain–computer interfaces using support vector machines and blind source separation *Comput. Intell. Neurosci.* **2007** 82069
- Haykin S 1996 *Adaptive Filter Theory* 3rd edn (Englewood Cliffs, NJ: Prentice-Hall)
- He B, Yang L, Wilke C and Yuan H 2011 Electrophysiological imaging of brain activity and connectivity—challenges and opportunities *IEEE Trans. Biomed. Eng.* **58** 1918–31
- He P, Wilson G and Russell C 2004 Removal of ocular artifacts from electro-encephalogram by adaptive filtering *Med. Biol. Eng. Comput.* **42** 407–12
- Hotelling H 1936 Relations between two sets of variates *Biometrika* **28** 321–77
- Hyvärinen A, Karhunen J and Oja E 2004 *Independent Component Analysis* (New York: Wiley)
- Jervis B W, Ifeachor E C and Allen E M 1988 The removal of ocular artefacts from the electroencephalogram: a review *Med. Biol. Eng. Comput.* **26** 2–12
- Jung T P, Makeig S, Humphries C, Lee T W, McKeown M J, Iragui V and Sejnowski T J 2000a Removing electroencephalographic artifacts by blind source separation *Psychophysiology* **37** 163–78
- Jung T P, Makeig S, Westerfield M, Townsend J, Courchesne E and Sejnowski T J 2000b Removal of eye activity artifacts from visual event-related potentials in normal and clinical subjects *Clin. Neurophysiol.* **111** 1745–58
- Klados M A, Bratsas C, Frantzidis C, Papadelis C L and Bamidis P D 2010 A Kurtosis-based automatic system using naïve bayesian classifier to identify ICA components contaminated by EOG or ECG artifacts *XII Mediterranean Conf. on Medical and Biological Engineering and Computing 2010 (Chalkidiki, Greece, 27–30 May 2010)* ed P D Bamidis and N Pallikarakis (Berlin: Springer) pp 49–52
- Klados M A, Papadelis C, Braun C and Bamidis P D 2011 REG-ICA: a hybrid methodology combining Blind Source

- Separation and regression techniques for the rejection of ocular artifacts *Biomed. Signal Process. Control* **6** 291–300
- Kong W, Zhou Z, Hu S, Zhang J, Babiloni F and Dai G 2013 Automatic and direct identification of blink components from scalp EEG *Sensors* **13** 10783–801
- Krucoff M O, Rahimpour S, Slutzky M W, Edgerton V R and Turner D A 2016 Enhancing nervous system recovery through neurobiologics, neural interface training, and neurorehabilitation *Frontiers Neurosci.* **10** 584
- Lagerlund T D, Sharbrough F W and Busacker N E 1997 Spatial filtering of multichannel electroencephalographic recordings through principal component analysis by singular value decomposition *J. Clin. Neurophysiol.* **14** 73–82
- Liu Q, Balsters J H, Baechinger M, van der Groen O, Wenderoth N and Mantini D 2015 Estimating a neutral reference for electroencephalographic recordings: the importance of using a high-density montage and a realistic head model *J. Neural Eng.* **12** 056012
- Liu Q, Farahibozorg S, Porcaro C, Wenderoth N and Mantini D 2017 Detecting large-scale networks in the human brain using high-density electroencephalography *Hum. Brain Mapp.* **38** 4631–43
- Mahajan R and Morshed B I 2015 Unsupervised eye blink artifact denoising of EEG data with modified multiscale sample entropy, Kurtosis, and wavelet-ICA *IEEE J. Biomed. Health Inf.* **19** 158–65
- Mannan M M, Jeong M Y and Kamran M A 2016 Hybrid ICA-regression: automatic identification and removal of ocular artifacts from electroencephalographic signals *Frontiers Hum. Neurosci.* **10** 193
- Mantini D, Corbetta M, Perrucci M G, Romani G L and Del Gratta C 2009 Large-scale brain networks account for sustained and transient activity during target detection *NeuroImage* **44** 265–74
- Marino M, Liu Q, Del Castello M, Corsi C, Wenderoth N and Mantini D 2018a Heart–Brain interactions in the MR environment: characterization of the ballistocardiogram in EEG signals collected during simultaneous fMRI *Brain Topogr.* **31** 337–45
- Marino M, Liu Q, Koudelka V, Porcaro C, Hlinka J, Wenderoth N and Mantini D 2018b Adaptive optimal basis set for BCG artifact removal in simultaneous EEG-fMRI *Sci. Rep.* **8** 8902
- Michel C M and Murray M M 2012 Towards the utilization of EEG as a brain imaging tool *NeuroImage* **61** 371–85
- Moretti D V, Babiloni F, Carducci F, Cincotti F, Remondini E, Rossini P M, Salinari S and Babiloni C 2003 Computerized processing of EEG–EOG–EMG artifacts for multi-centric studies in EEG oscillations and event-related potentials *Int. J. Psychophysiol.* **47** 199–216
- Müller-Putz G R, Scherer R, Pfurtscheller G and Rupp R 2005 EEG-based neuroprosthesis control: a step towards clinical practice *Neurosci. Lett.* **382** 169–74
- Murphy P R, O’Connell R G, O’Sullivan M, Robertson I H and Balsters J H 2014 Pupil diameter covaries with BOLD activity in human locus coeruleus *Hum. Brain Mapp.* **35** 4140–54
- Muthukumaraswamy S D 2013 High-frequency brain activity and muscle artifacts in MEG/EEG: a review and recommendations *Frontiers Hum. Neurosci.* **7** 138
- Niknazar H, Motie Nasrabadi A and Shamsollahi M B 2018 A new similarity index for nonlinear signal analysis based on local extrema patterns *Phys. Lett. A* **382** 288–99
- Nolan H, Whelan R and Reilly R B 2010 FASTER: fully automated statistical thresholding for EEG artifact rejection *J. Neurosci. Methods* **192** 152–62
- O’Connell R G, Balsters J H, Kilcullen S M, Campbell W, Bokde A W, Lai R, Upton N and Robertson I H 2012 A simultaneous ERP/fMRI investigation of the P300 aging effect *Neurobiol. Aging* **33** 2448–61
- Picton T W 1992 The P300 wave of the human event-related potential *J. Clin. Neurophysiol.* **9** 456–79
- Puthusserypady S and Ratnarajah T 2005 H/sup/spl infin// adaptive filters for eye blink artifact minimization from electroencephalogram *IEEE Signal Process. Lett.* **12** 816–9
- Radüntz T, Scouten J, Hochmuth O and Meffert B 2015 EEG artifact elimination by extraction of ICA-component features using image processing algorithms *J. Neurosci. Methods* **243** 84–93
- Romero S, Mañanas M A and Barbanj M J 2008 A comparative study of automatic techniques for ocular artifact reduction in spontaneous EEG signals based on clinical target variables: a simulation case *Comput. Biol. Med.* **38** 348–60
- Rutledge D N and Jouan-Rimbaud Bouveresse D 2013 Independent components analysis with the JADE algorithm *TRAC Trends Anal. Chem.* **50** 22–32
- Sadasivan P K and Dutt D N 1996 ANC schemes for the enhancement of EEG signals in the presence of EOG artifacts *Comput. Biomed. Res.* **29** 27–40
- Schlogl A, Keinrath C, Zimmermann D, Scherer R, Leeb R and Pfurtscheller G 2007 A fully automated correction method of EOG artifacts in EEG recordings *Clin. Neurophysiol.* **118** 98–104
- Semprini M, Laffranchi M, Sanguineti V, Avanzino L, De Icco R, De Michieli L and Chiappalone M 2018 Technological approaches for neurorehabilitation: from robotic devices to brain stimulation and beyond *Frontiers Neurol.* **9** 212
- Shih J J, Krusienski D J and Wolpaw J R 2012 Brain–computer interfaces in medicine *Mayo Clin. Proc.* **87** 268–79
- Shlens J 2005 A tutorial on principal component analysis
- Siew Cheok N and Raveendran P 2008 Removal of EOG artifacts using ICA regression method *4th Kuala Lumpur Int. Conf. on Biomedical Engineering 2008: BIOMED 2008 (Kuala Lumpur, Malaysia, 25–28 June 2008)* ed N A Abu Osman et al (Berlin: Springer) pp 226–9
- Stone J V 2004 *Independent Component Analysis: A Tutorial Introduction* (Cambridge, MA: MIT Press)
- Triantafyllopoulos D and Megalooikonomou V 2014 Eye blink artifact removal in EEG using tensor decomposition *Proc. Artificial Intelligence Applications and Innovations: AIAI 2014 Workshops: CoPA, MHDW, IIVC, and MT4BD (Rhodes, Greece, 19–21 September 2014)* ed L Iliadis et al (Berlin: Springer) pp 155–64
- Turnip A 2014 JADE-ICA algorithm for EOG artifact removal in EEG recording *2014 2nd Int. Conf. on Technology, Informatics, Management, Engineering & Environment* pp 270–4
- Turnip A and Junaidi E 2014 Removal artifacts from EEG signal using independent component analysis and principal component analysis *2014 2nd Int. Conf. on Technology, Informatics, Management, Engineering & Environment* pp 296–302
- van Lutterveld R et al 2017 Source-space EEG neurofeedback links subjective experience with brain activity during effortless awareness meditation *NeuroImage* **151** 117–27
- Vanderperren K et al 2010 Removal of BCG artifacts from EEG recordings inside the MR scanner: a comparison of methodological and validation-related aspects *NeuroImage* **50** 920–34
- Winkler I, Brandl S, Horn F, Waldburger E, Allefeld C and Tangermann M 2014 Robust artifactual independent component classification for BCI practitioners *J. Neural Eng.* **11** 35013
- Winkler I, Haufe S and Tangermann M 2011 Automatic classification of artifactual ICA-components for artifact removal in EEG signals *Behav. Brain Funct.* **7** 30

- Wold S, Esbensen K and Geladi P 1987 Principal component analysis *Chemom. Intell. Lab. Syst.* **2** 37–52
- Wu D, King J-T, Chuang C-H, Lin C-T and Jung T-P 2017 Spatial filtering for EEG-based regression problems in brain–computer interface (BCI) *IEEE Trans. Fuzzy Syst.* **26** 771–81
- Xiaopei W and Zhongfu Y 2005 Online infomax algorithm and its application to remove EEG artifacts 2005 *IEEE Engineering in Medicine and Biology 27th Annual Conf.* pp 4203–7
- Zeng H, Song A, Yan R and Qin H 2013 EOG artifact correction from EEG recording using stationary subspace analysis and empirical mode decomposition *Sensors* **13** 14839–59
- Zhang C, Tong L, Zeng Y, Jiang J, Bu H, Yan B and Li J 2015 Automatic artifact removal from electroencephalogram data based on *a priori* artifact information *Biomed Res. Int.* **2015** 720450
- Zrenner C, Belardinelli P, Muller-Dahlhaus F and Ziemann U 2016 Closed-loop neuroscience and non-invasive brain stimulation: a tale of two loops *Frontiers Cell Neurosci.* **10** 92