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Closed-loop application and artefact correction for tACS-EEG

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Introduction

Simultaneous transcranial electrical stimulation (tES) and electroencephalography (EEG) paved the way for a better understanding of tES-induced effects, local and network effects and the functional role of brain oscillations. Individual and brain-state dependent brain stimulation gained enormous interested in recent years as it allows researchers to interfere with the participant's ongoing brain activity with high temporal and spectral precision using EEG (*Zrenner et al., 2016*; *Berényi et al., 2012*). The application of brain state triggered non-invasive brain stimulation is called closed-loop stimulation, which has been shown recently for TMS (*Zrenner et al., 2016*; *Bergmann et al., 2016*) and for tES (*Brittain et al., 2013*). As the distortions of tES are several orders of magnitude higher than the physiological EEG and are therefore impeding EEG analyses, methods for artefact correction are necessary, which still remain a challenging task. Here, we present a system for closed-loop applications of tES-EEG and demonstrate the performance of two online artefact correction methods.

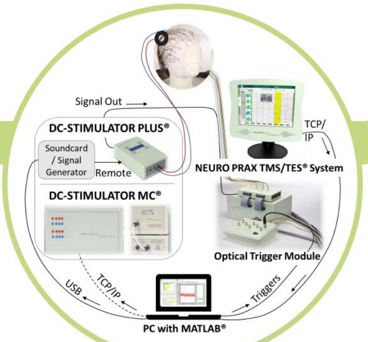

Figure 1: Diagram of the components and connections for the closed-loop application. For stimulation, the single or multi-channel device (DC-STIMULATOR PLUS / MC) can be used.

Materials & Methods

The closed-loop application is based on a spectral power dependant individual alpha detection which controls a transcranial alternating current stimulation (tACS) during eyes-open and eyes-closed condition. The EEG was recorded using neuroConn's NEURO PRAX® TMS/TES system and was sent online to a laptop computer via TCP/IP connection (either raw or corrected data), which performed the alpha detection using a customized script in MATLAB® (The Mathworks, Natick, USA). The analogue stimulation signal was sent out by means of the integrated laptop soundcard and was fed into the remote input of the DC-STIMULATOR PLUS. Furthermore, it is possible to send the analogue signal to the stimulator by a digital signal generator via USB, here we used the Rigol DG1062Z (Rigol Technologies Inc., Beijing, P.R. China). For starting neuroConn's tACS artefact correction on the NEURO PRAX® TMS/TES system, triggers were controlled by the client PC and converted to optical triggers by using neuroConn's Optical Trigger Module. The tACS signal for artefact correction was recorded with the EEG amplifier as well, using the SIGNAL OUT BOX. In another closed-loop implementation with some minor setup changes, we used the DC-STIMULATOR MC with the POWER SUPPLY EXTENSION and ACTIVE SYNC. This multi-channel stimulator was controlled remotely by the MATLAB® client via TCP/IP.

For evaluating the performance of the two built-in artefact correction methods ('sinusoidal' and 'regression') of the NEURO PRAX® TES system by Falk Schlegelmilch (*Schlegelmilch et al., 2013*), tACS-EEG recordings were compared to a baseline EEG with no tACS. High quality EEG (4000 sps, 24 bit) was recorded at 17 positions (reference electrode on M2), with the ground electrode between the stimulation electrodes for best EEG quality (FC1 in this case), using the NEURO PRAX® TMS/TES system. TACS was delivered by the DC-STIMULATOR MC with the POWER SUPPLY EXTENSION for a separation from the powerline and ACTIVE SYNC for clock synchronization. For stimulation, rubber electrodes were positioned at C4 (circular shape) and CP5 (rectangular shape). To investigate the robustness of the tACS artefact correction methods, different stimulation frequencies (1, 10 and 20 Hz) were used at an intensity of 0.5 mA. EEG data post-processing comprised re-referencing to M2, DC-offset removal, Notch filtering at 50 Hz and lowpass filtering at 30 Hz. Power spectral density was calculated by using the Welch method (Hann window) by averaging ten segments of 10 s, resulting in a spectral resolution of 0.1 Hz. The volunteer's alpha peak frequency was calculated and topographic distribution maps at this frequency were generated using the open source toolbox EEGLAB (http://sccn.ucsd.edu/eeglab).

Results

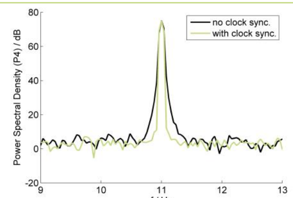

Figure 2: Clock synchronization (ACTIVE SYNC) between the EEG recording system and the stimulator decreases the spectral leakage of the tACS frequency (here 11 Hz) and enables better artefact removal.

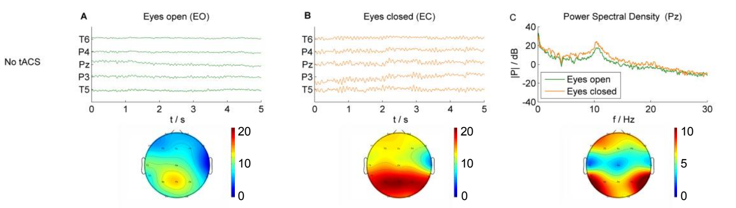

Figure 3: Time course of five EEG channels for conditions EO (left), EC (center) and their power spectral density at channel Pz (right). The topography plots show the activity (in dB) at the volunteer's alpha peak frequency of 11 Hz for EO (left), EC (center) and the difference between both conditions (right).

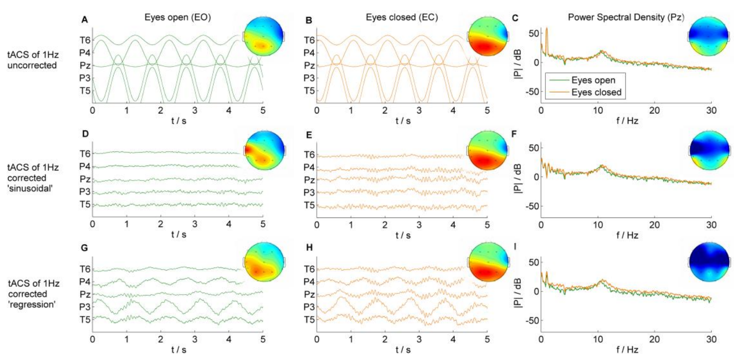

Figure 5: TACS of **1 Hz** uncorrected (1st row), 'sinusoidal' (2nd row) and 'regression' (3rd row) presented analogous to Figure 3. The 'sinusoidal' approach shows a very good correction. Influences on neighbouring frequencies, in the spectrum are very low. The 'regression' method shows residual artefacts .

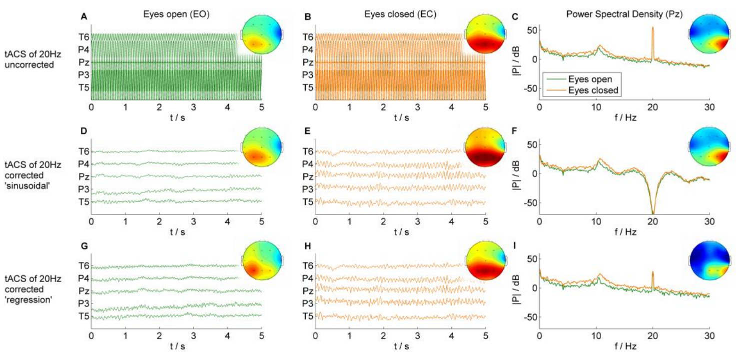

Figure 4: TACS of **20 Hz** uncorrected (1st row), 'sinusoidal' (2nd row) and 'regression' (3rd row) presented analogous to Figure 3. 'Sinusoidal' artefact correction shows a clear EEG without residual tACS artefacts, while for 'regression' method there remain slight residual artefacts. The alpha activity is not affected by both correction approaches.

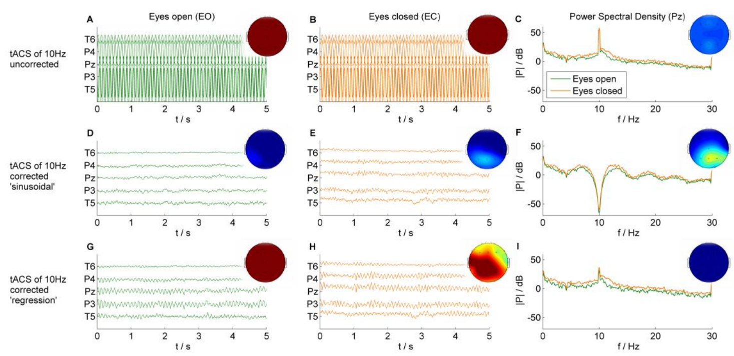

Figure 6: TACS of **10 Hz** uncorrected (1st row), 'sinusoidal' (2nd row) and 'regression' (3rd row) presented analogous to Figure 3. Time courses show clear EEG signals. The 'sinusoidal' approach shows very strong artefact elimination that even affects neighbouring frequencies, while the 'regression' method shows residual artefacts of tACS.

Conclusion

The evaluation of the performance of the two artefact correction approaches for delivered information about the advantages of each method. The 'sinusoidal' artefact correction based on a recursive discrete Fourier transformation at the stimulation frequency delivers overall good signal reconstruction. The elimination might be too strong in some cases though (e.g. 10 Hz), particularly on the neighbouring frequencies, which needs to be further investigated and improved. However, this approach shows robust results for all applied frequencies. Furthermore, the algorithm can be extended to correct for up to 21 harmonics of the stimulation frequency. When stimulating at the frequency range of interest, this approach impedes to analyse the remaining activity. In this case, the 'regression' algorithm is more beneficial, which is based on a dynamic linear regression model and does consequently not cut out the stimulation frequency. In a recent abstract by *Kohli et al. (2017)*, the performance of the **NEURO PRAX® TMS/TES** built-in algorithm ‚regression' was compared to two other methods. The recording results for tACS and ERP on a head model showed the **highest accuracy** of all applied methods. Comparing both correction approaches, they differ concerning the learning period, which is necessary only for the 'regression' method to calculate the parameters for each channel. Both algorithms benefit from their online implementation and that only a few electrodes are necessary.

In conclusion, the demonstration of **closed-loop tACS-EEG** application showed the possibilities and also challenges in setting up and performing brain-sate dependent brain stimulation. **By combining our neuroConn devices for EEG and tES stimulation and providing our expertise of more than 15 year in both fields, we are now able to support our customers in developing such closed-loop systems for neuroscientific research.**

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