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Technical Note

Signal quality and Bayesian signal processing in neurofeedback based on real-time fMRI

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A B S T R A C T

Real-time fMRI allows analysis and visualization of the brain activity online, i.e. within one repetition time. It can be used in neurofeedback applications where subjects attempt to control an activation level in a specified region of interest (ROI) of their brain. The signal derived from the ROI is contaminated with noise and artifacts, namely with physiological noise from breathing and heart beat, scanner drift, motion-related artifacts and measurement noise. We developed a Bayesian approach to reduce noise and to remove artifacts in real-time using a modified Kalman filter. The system performs several signal processing operations: subtraction of constant and low-frequency signal components, spike removal and signal smoothing. Quantitative feedback signal quality analysis was used to estimate the quality of the neurofeedback time series and performance of the applied signal processing on different ROIs. The signal-to-noise ratio (SNR) across the entire time series and the group event-related SNR (eSNR) were significantly higher for the processed time series in comparison to the raw data. Applied signal processing improved the t-statistic increasing the significance of blood oxygen level-dependent (BOLD) signal changes. Accordingly, the contrast-to-noise ratio (CNR) of the feedback time series was improved as well. In addition, the data revealed increase of localized self-control across feedback sessions.

The new signal processing approach provided reliable neurofeedback, performed precise artifacts removal, reduced noise, and required minimal manual adjustments of parameters. Advanced and fast online signal processing algorithms considerably increased the quality as well as the information content of the control signal which in turn resulted in higher contingency in the neurofeedback loop.

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Introduction

Scientific interest in real-time fMRI-based neurofeedback has grown over the last decade (Birbaumer et al., 2009; Bray et al., 2007; Johnston et al., 2010; LaConte, 2010; Lee et al., 2009; Rota et al., 2009; Weiskopf et al., 2003; Yoo et al., 2008). Clinical applications were suggested to therapeutically apply circumscribed neural effects of fMRI neurofeedback training, and it was piloted with patients suffering from neurofunctional symptoms such as pain (deCharms et al., 2005) and tinnitus (Haller et al., 2010). To achieve efficient learning of self-control, the neurofeedback system must provide a contingent feedback, i.e. subjects performing the neurofeedback training must be able to recognize the relation between the localized neural activity and the feedback signal (Bagarinao et al., 2006; Cox et al., 1995; Weiskopf et al., 2003). It remains a challenge to achieve a sufficient quality of the feedback data which suffer from poor signal-to-noise ratio (Diedrichsen and Shadmehr, 2005; Hinds et al., 2010). So far there are little data on quality measures of fMRI neurofeedback systems and signal processing strategies have not been systematically evaluated. Particularly, artifacts and sudden signal changes need to be considered since they may lead to learning of nuisance signals.

The Blood Oxygen Level-Dependent (BOLD) response typically has a maximum of about 5% of the image intensity, but in neurofeedback studies even average signal changes below 1% across a region of interest (ROI) need to be considered (Boynton et al., 1996; Caria et al., 2007; Friston and Ashburner, 1994). In addition to unsystematic noise, different types of artifacts considerably reduce the feedback signal quality (Weiskopf et al., 2004). Any signal change which can be consciously or non-consciously controlled by the subject may be learned and therefore signal changes that arise from non-neural origin need to be limited.

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fMRI encompasses additive Gaussian noise and non-linear components. The Gaussian component can be well characterized by its statistics and is optimally addressed by averaging and linear filters in the temporal and spatial dimensions (Worsley and Friston, 1995). In contrast the non-linear artifacts tend to show a heavy-tail distribution, i.e. high proportion of the events emerges outside the double standard deviation range (Diedrichsen and Shadmehr, 2005). In general, the most common sources of fMRI artifacts are inhomogeneities of the static magnetic field, head movement, respiration and heart beat (Diedrichsen and Shadmehr, 2005; Friston et al., 1996; Hornak, 2010; Uludag et al., 2005; Weiskopf et al., 2004). The signal fluctuations may be due to the spin-history effects (Friston et al., 1996), scanner artifacts from electrostatic discharges (Brown and Semelka, 2010) as well as motion-by-susceptibility interaction during head movement (Wu et al., 1997), irregular respiratory activity (Gelderen et al., 2007), eye movement, heart beat, and swallowing (Beauchamp, 2003; Birn et al., 1998). Some of these non-linear artifacts are often observed as spikes, i.e. abrupt changes of signal intensity across a short time period.

Movement artifacts can be reduced with an inbuilt MR scanner motion correction package (Thesen et al., 2000) and with real-time motion correction algorithms (e.g. Mathiak and Posse, 2001). To further suppress motion artifacts, motion covariates may be included in the general linear model (GLM; Worsley and Friston, 1995; Goebel, 2001; Weiskopf et al., 2003). However, the motion artifacts can not be completely removed (deCharms et al., 2004; Grootoonk et al., 2000). Moreover, the motion correction can add noise and artifacts to the feedback signal even if the image alignment is improved (Mathiak and Posse, 2001). Particularly, abrupt movement within one volume acquisition may appear as a spike in the data. Respiration leads to shifts in the resonance frequency (Glover et. al., 2000) and thus can modulate the feedback signal. Online distortion correction based on the dynamic off-resonance effects (Weiskopf et al., 2005) may reduce such respiration artifacts. The acquired feedback time series can alternatively be processed offline with the standard signal filtering algorithms in order to achieve improved t-statistics (Weiskopf et al., 2004). However, the noise reduction approaches based on temporal or spatial characteristics usually fail to remove the non-linear spike-like noise and thus result in blurring of the spike patterns rather than a removal. Then when a standard low-pass filter is applied the local spike is blurred across a longer time interval. Therefore, spike correction needs to be performed before temporal averaging and typically requires dedicated algorithms (e.g. Chavez et al., 2009; Cui et al., 2009; Zhang et al., 2001).

Online signal processing algorithms may rely on signal values acquired across the entire time series or from a sliding window, e.g. standard temporal band-pass filters or a low-pass Butterworth filter (Butterworth, 1930). The moving average algorithm (Roberts, 1959) is well suited to online application but fails in the removal of nonlinear and spike-like noise (Cui et al., 2009).

The challenge of online non-linear spike-noise identification is that given the current time point and the previous signal an algorithm should first check whether the current point is a spike and correct it if necessary. An additional requirement to such approaches could be the integration of a low-pass filter to suppress the high-frequency noise. In that case, a Bayesian approach appears promising (Grewal and Andrews, 2008; Vaseghi, 2006). The current point can be calculated using the Bayesian methods from the current measurement and the previous state through a filtering operation, e.g. by application of a Kalman filter (Kalman, 1960). Typically, the feedback is presented to the participant with a delay that depends on the time involved for image acquisition and processing which can be reduced to about 1 s (Sitaram et al., 2007; Weiskopf et al., 2007).

Quality assessment of fMRI data is particularly important for clinical and multicenter studies (Simmons et al., 1999; Stöcker et al., 2005). Real-time fMRI quality assurance was proposed for monitoring the experimental process (Cox et al., 1995; Voyvodic, 1999; Weiskopf et al., 2007). Neurofeedback signal quality can be measured with the standard quality measures like signal-to-noise ratio (SNR), event-related signal-to-noise ratio (eSNR) and contrast-to-noise ratio (CNR; see Geissler et al., 2007; Cui et al., 2009).

The expected frequency range of the BOLD signal reported is approximately 0.01–0.12 Hz (Kannurpatti et al., 2008; Robinson et al., 2006; Uludag et al., 2005), and the neurofeedback contingency can constrain the feedback signal to this physiological range to reduce the chances of attributing noise as neural signals. Application of the non-linear filtering method achieved by modification of the Kalman filter increases the functionality and flexibility of the signal processing approach. Furthermore, in contrast to the classical low-pass filter, the Kalman filter can be modified to remove spikes directly.

We investigate 1) quality assessment parameters of the real-time fMRI feedback signal in four different neuropsychological paradigms and 2) the effect of the non-linear Kalman filter on these parameters. The novel online filter was applied in real-time neurofeedback experiments to remove the low-frequency feedback signal drift with an exponential moving average (EMA) algorithm (Cui et al., 2009; Roberts, 1959) and the high-frequency noise and large signal outliers with a modified Kalman filter. Finally, the processed feedback signal was normalized to the relative displayed range. Raw signals were stored and processed offline for the comparison of raw and filtered signal properties. We tested the effectiveness of removal of non-linear and spike-like noise with respect to the quality measure SNR, eSNR, and CNR as well as the experimental statistics.

Methods

Real-time signal processing

The proposed online signal processing encompasses four consecutive operations: (1) signal drift removal, (2) spikes detection and correction, (3) high frequency noise removal, and (4) signal normalization. Operations 2 and 3 are composite and performed within one estimator, i.e. the modified Kalman filter.

EMA as high-pass filter

Online BOLD signal drift removal was achieved with the exponential moving average (EMA) algorithm and computed first. The EMA method proved to be an effective tool for real-time neuroimaging applications (e.g. in fNIRS, see Cui et al., 2009). This recursive filter applies weighting factors which decrease exponentially and can compute the low and high frequency components of the input signal independently (formulas see Appendix A). Performance of the EMA filter depends on the value of the smoothing factor α which can be chosen between 0 and 1. Setting $\alpha = 0.98$ yields a high-pass filter with time-constant $\tau = 49$ s and a sampling interval $TR = 1$ s. The cut-off frequency of such a filter is $f_C = (2 \cdot \pi \cdot \tau)^{-1} = 0.003$Hz and thus well-below the required BOLD frequency range.

The linear Kalman filter

Spike detection and high-frequency noise rejection were achieved using a non-linear modification of the Kalman filtering algorithm and performed as a second online computation step. In its linear form, a Kalman filter (formulas see Appendix A) is an adaptive estimation algorithm which is based on the principle that the desired signal can be extracted from the observation input through a filtering operation (Grewal and Andrews, 2008; Kalman, 1960; Vaseghi, 2006).

Modification and initialization of the Kalman filter

We extended the linear Kalman filter to remove outliers from the BOLD signal by implementing a non-linear modification. The update term $K_m(y_m - H \cdot x_m^-)$ (see Eq. (1.8), Appendix A) reflects the

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