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A kernel machine-based fMRI physiological noise removal method

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ABSTRACT

Functional magnetic resonance imaging (fMRI) technique with blood oxygenation level dependent (BOLD) contrast is a powerful tool for noninvasive mapping of brain function under task and resting states. The removal of cardiac- and respiration-induced physiological noise in fMRI data has been a significant challenge as fMRI studies seek to achieve higher spatial resolutions and characterize more subtle neuronal changes. The low temporal sampling rate of most multi-slice fMRI experiments often causes aliasing of physiological noise into the frequency range of BOLD activation signal. In addition, changes of heartbeat and respiration patterns also generate physiological fluctuations that have similar frequencies with BOLD activation. Most existing physiological noise-removal methods either place restrictive limitations on image acquisition or utilize filtering or regression based post-processing algorithms, which cannot distinguish the frequency-overlapping BOLD activation and the physiological noise. In this work, we address the challenge of physiological noise removal via the kernel machine technique, where a nonlinear kernel machine technique, kernel principal component analysis, is used with a specifically identified kernel function to differentiate BOLD signal from the physiological noise of the frequency. The proposed method was evaluated in human fMRI data acquired from multiple task-related and resting state fMRI experiments. A comparison study was also performed with an existing adaptive filtering method. The results indicate that the proposed method can effectively identify and reduce the physiological noise in fMRI data. The comparison study shows that the proposed method can provide comparable or better noise removal performance than the adaptive filtering approach.

1. Introduction

Advances in blood oxygenation level dependent (BOLD) functional magnetic resonance imaging (fMRI) are typically characterized by improved spatial resolution and detection of more subtle neuronal activity. However, BOLD contrast resulting from functional activation is usually small, so the advancements can depend heavily upon the signal-to-noise ratio (SNR). SNR is commonly improved by increasing the magnetic field strength [1–4], but cardiac- and respiration-induced physiological noise also increases with the field strength. Thus an increase in image SNR does not necessarily produce an equal improvement in contrast-to-noise ratio (CNR), a quantitative measure of imaging quality. Particularly, resting state studies of functional networks [5–9], which measure the baseline connectivity of functional networks, are vulnerable to reductions in CNR because they lack a clear stimulus paradigm to aid in detection and rely upon analysis of subtle, correlated signal fluctuations between brain regions.

The primary challenge to physiological noise removal is that the temporal sampling rates of most fMRI experiments are limited by the repetition time (TR), a major component governing signal intensity and image contrast, resulting in aliasing of physiological noise into frequencies of the BOLD signal. Additionally, changes of heartbeat and respiration patterns generate physiological fluctuations that have similar frequencies with the BOLD signal. Furthermore, physiological noise contaminates a wide range of frequencies whose power spectrum reflects not a purely sinusoidal variation but rather a distribution of frequencies about the peak, making them difficult to characterize in frequency domain [10].

Currently, physiological noise removal is approached either during acquisition, through gating and/or synchronization techniques [11,12] or during post-processing. Post-processing methods are desirable as they offer increased spatial and temporal specificity and place fewer limits upon the experimental design. Several post-processing approaches have been utilized previously, but each suffers from limitations. Navigator echo methods lack the specificity to localize the source of motion [13], which may lead to incomplete correction or introduce new artifacts. Retrospective correction methods [14,15], which fit a low-order Fourier series to fMRI data in either k-space or image domain based on the phase of respiration or cardiac cycle during each acquisition, have been shown to be effective [14,15]. However, these methods cannot remove the noise

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induced by changes in breathing pattern [7,8]. Other retrospective methods either require a short TR [16] or are limited to global fluctuations [17]. More importantly, none of these methods, including digital filtering and wavelet-based methods [18–20], can distinguish frequency components of the physiological noise that overlap with the BOLD activation. If the signal and noise occupy same frequency bands, then the removal of noise will also result in the attenuation of signal [21,22]. Efforts to increase the resolution and scope of BOLD-contrast fMRI, particularly in the area of characterizing resting-state functional networks, would therefore benefit greatly from new techniques better suited to separating the aliased physiological noise from the BOLD signal.

Another type of techniques, such as principal component analysis (PCA) and independent component analysis (ICA), represent a fundamentally different approach to the noise removal problem. These techniques decompose fMRI data into multiple components, and feature projections on these components share same frequency bands but could be originated from different signal and noise sources [10,23–26]. Since these feature projections are not implemented in the frequency domain, they are potentially capable of distinguishing frequency-overlapping signal and noise. In this work, we report a new fMRI physiological noise removal procedure based on the kernel principle component analysis (KPCA) [27]. KPCA is a nonlinear extension of principal component analysis (PCA) and has been used in fMRI data analysis [28–31]. Nonlinear PCA can characterize high order dependence among multiple voxels, and can provide more complete characterization of fMRI data structure than linear PCA [32,33]. KPCA provides a controllable signal-noise differentiation analysis via a kernel and its parameter. While KPCA has been successfully used to remove Gaussian noise by excluding the least significant components from reconstruction [34], the same approach is not directly applicable to the removal of physiological noise that is usually characterized by both the most and least significant components. Therefore, we further develop a KPCA-based method for physiological noise removal. This method aims to differentiate and attenuate the aliased physiological noise that could overlap with the BOLD signal. The method was compared to an adaptive filtering method [35], which is an improved version of the RETROICOR method [15], for task-related and resting state fMRI data. The results indicate that the proposed method can provide comparable or better noise removal performance than the adaptive filtering method, implying promising applications in fMRI studies.

2. Material and methods

2.1. Data acquisition

Both task and resting state fMRI data were used in this study. Task-related data were obtained from three different experiments. The first experiment was performed using a 3 Tesla GE system with an 8-channel coil at Duke University Medical Center. Four data sets were acquired from a healthy adult on a same day using T2*-weighted parallel echo planar imaging (EPI) with an acceleration factor of 2, while the subject was performing a right-hand finger-tapping motor task with a blocked-design paradigm, which consisted of four 25 sec task blocks and five 25 sec off blocks. There was a 15 sec dummy scan at the beginning of each run, which was removed before the analysis. EPI parameters included a TR of 2 sec, an echo time (TE) of 30 msec, and a flip angle of 90°. 30 axial-slices were collected for each volume with 4 mm slice thickness and 1 mm gap, FOV was 24 cm × 24 cm, and image matrix size is 120 × 120 after the sensitivity encoding reconstruction, corresponding to an in-plane resolution of 2 × 2 mm^2. The second experiment was performed using the same scanner used in the first experiment. Two fMRI data sets were collected from two subjects using a T2*-weighted EPI sequence with SENSE acceleration factor of 2 while the subjects were performing the right-hand finger-tapping motor task with a blocked-design paradigm, which consisted of five 30 sec task blocks and five 30 sec off blocks. The scan time for each run was 5 min. TR = 2 sec, TE = 25 msec. 35 axial-slices were collected in each volume with 3 mm slice thickness. FOV was 24 cm × 24 cm, and image matrix size is 64 × 64. Another three sets of task fMRI data are from the website of New York University Center for Brain Imaging (cbi.nyu.edu). The data were acquired from a subject using a 3 T Siemens Allegra scanner. The first two sets were collected using a single channel head coil, and another set was collected using a surface coil. Imaging parameters include a TR of 1.5 sec, a TE of 30 msec, and a flip angle of 75°. A visual stimulation was applied to the subject by alternatively showing a left and right circular hemifield stimulus of alternating checks at full contrast. In each set 150 volumes were acquired with 25 axial-slices in each volume. Each slice is represented by 64 × 80 3 mm isotropic voxels.

Three resting state fMRI experiments were implemented at Duke University Medical Center. In the first experiment, four data sets were collected from a subject using the same T2*-weighted parallel EPI sequence as that used in the first task related experiment while the subject was instructed to look at a crosshair. The scan time for each run was 4 min. Inversion-recovery (IR) prepared spin-echo EPI was also acquired to provide an anatomic reference with identical voxel geometry and geometric distortions as in fMRI. IR-EPI scan parameters included TR = 5 sec, TE = 24 msec, IR time = 1 sec, flip angle = 90°, slice thickness = 4 mm (with 1 mm gap), FOV = 24 cm × 24 cm, in-plane matrix size = 120 × 120 (with 2 segments), and 30 axial slices. In the second experiments, six sets of resting state fMRI data were collected from six healthy adults on different days. The imaging parameters are TR = 4 sec, TE = 35 msec. flip angle = 90°, FOV = 24 cm × 24 cm, the image matrix size is 140 × 140. 56 axial slices were acquired in each volume with a 3 mm slice thickness, and 74 volumes were collected in each data set (about 5 minutes time duration). In the third experiment, two data sets were collected from two subjects using a T2*-weighted EPI sequence with SENSE acceleration factor of 2 while the subjects were instructed to look at a crosshair. The scan time for each run was 5 min. TR = 2 sec, TE = 25 msec. 35 axial-slices were collected in each volume with a 3 mm slice thickness. FOV was 24 cm × 24 cm, and image matrix size is 64 × 64.

The cardiac and respiration cycles were simultaneously recorded using Biopac MRI-compatible transducers at a sampling rate of 100 Hz during the fMRI data acquisition. The cardiac cycles were measured by a fiber-optic finger pulse-oximeter cuff. The respiration data were collected by a stretch transducer on an elastic belly belt placed around the abdomen. All electrical connections are grounded and pass through MRI filters in the magnet room shield. Cardiac signals were amplified outside the magnet room using Biopac amplifiers. All acquired physiological signals are connected to an analog/digital data acquisition device (Measurement Computing Inc.) connected to the computer via a USB interface. The acquired physiological data were down-sampled and synchronized to the slice-acquisition timing of fMRI. The physiological data from New York University Center for Brain Imaging were obtained from their website (cbi.nyu.edu). The experiments on human subjects were compliant with the standards established by the Institutional Review Boards of Duke University.

2.2. Data analysis

A block diagram of the proposed method is shown in Fig. 1. fMRI data is first motion corrected and spatially smoothed. The pre-processed fMRI data is decomposed into multiple principal components (PC) using KPCA. The feature projections on PCs characterizing