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Identification and Attenuation of Physiological Noise in fMRI Using Kernel Techniques

Xiaomu Song, Senior Member, IEEE, Nan-Kuei Chen, Pooja Gaur

Abstract— **Functional magnetic resonance imaging (fMRI) techniques enable noninvasive studies of brain functional activity under task and resting states. However, the analysis of brain activity could be significantly affected by the cardiac- and respiration-induced physiological noise in fMRI data. In most multi-slice fMRI experiments, the temporal sampling rates are not high enough to critically sample the physiological noise, and the noise is aliased into frequency bands where useful brain functional signal exists, compromising the analysis. Most existing approaches cannot distinguish between the aliased noise and signal if they overlap in the frequency domain. In this work, we further developed a kernel principal component analysis based physiological removal method based on our previous work. Specifically, two kernel functions were evaluated based on a newly proposed criterion that can measure the capability of a kernel to separate the aliased physiological noise from fMRI signal. In addition, a mutual information based criterion was designed to select principal components for noise removal. The method was evaluated by human experimental fMRI studies, and the results demonstrate that the proposed method can effectively identify and attenuate the aliased physiological noise in fMRI data.**

I. INTRODUCTION

Cardiac and respiration-induced physiological noise is one of the major noise sources that affect blood oxygenation level dependent (BOLD) functional magnetic resonance imaging (fMRI) data analysis. Particularly, with increased magnetic field strength, the physiological noise becomes more dominant than the thermal noise. Moreover, in most multi-slice experiments, the fMRI temporal sampling rate is not sufficient to critically sample the physiological noise. Consequently, the noise is aliased into lower frequency bands and overlapped with BOLD signal. The existence of the aliased noise could significantly affect the fMRI data analysis, especially for functional network studies under resting state, where a small "seed" region is usually selected first and the average temporal profile of this region is used to detect functionally connected regions via correlation analysis. If the aliased physiological noise exists in the seed region, then it is quite obscure if the correlated regions are functionally connected to the functional signal in the seed region, or to the noise. Therefore, it is necessary to remove physiological noise prior to the detection of functional networks.

Various techniques have been developed to attenuate physiological noise in fMRI data, such as the gating and/or synchronization techniques [1], [2], navigator echo methods [3], and retrospective correction methods [4], [5]. These methods have been shown to be effective in fMRI studies. However, none of them can distinguish frequency-overlapping signal and noise. In order to reduce the noise aliasing, Frank et al. developed a method that treats the respiration-induced noise as a global effect, and sampled for each slice in a volume [6]. The corresponding sampling rate is the number of slices per volume divided by repetition time (TR), making global effects critically sampled. This method is computationally complex and limited to global fluctuations. The digital filtering method has been applied to attenuate the aliased physiological noise [7]. However, they are not effective if BOLD activation and physiological noise overlap in the frequency domain, which is true for most multi-slice fMRI experiments.

Recently, nonlinear discriminant analysis techniques, such as kernel principal component analysis (KPCA) [8], have been applied to fMRI data analysis [9]. KPCA does not employ projections in the frequency domain and may therefore distinguish frequency-overlapping signal and noise. In addition, KPCA can capture high order dependencies among multiple voxels, providing a more accurate and complete characterization of data structure than linear methods. KPCA has been applied to remove Gaussian noise that is primarily characterized by the least significant principal components (PC). These PCs are excluded from the reconstruction to obtain the cleaned data [10]. This approach is not appropriate to physiological noise removal because the intensity of physiological noise is comparable to BOLD signal, and may be characterized by the most significant PCs. If these PCs are excluded from the reconstruction, important brain activity information will be lost. Therefore, alternative approaches should be considered. In our previous work [11], a KPCA-based physiological noise removal method was proposed to reduce physiological noise by filtering PCs contaminated by the noise. In this work, we further developed this method by evaluating the noise separation performance of different kernel functions, and implementing a new approach to identify the noise contaminated PCs. The method was evaluated on human fMRI data acquired from both task-based and resting state experiments.

The remainder of the paper is organized as follows. In Section II, we review the basic concepts of KPCA. Section III describes the proposed methods. Section IV is the experimental study and results. Finally, we conclude this work in Section V.

X. Song is with the Department of Electrical Engineering, Widener University, Chester, PA 19013, USA. xmsong@widener.edu

N.-K. Chen and P. Gaur are with the Brain Imaging and Analysis Center, Duke University, Durham, NC 27710, USA. nankuei.chen@duke.edu, pg46@duke.edu

II. Kernel Principal Component Analysis

KPCA is a nonlinear extension of conventional linear principal component analysis (PCA) [8]. The nonlinearity is brought in through a kernel function that implicitly projects the input data into a high dimensional feature space. A linear PCA performed in the feature space is equivalent to a nonlinear PCA in the input space.

Given n p-dimensional data samples $\mathbf{x}_i \in \mathbf{R}^p$, $i = 1, \cdots, n$, the PCs are estimated by computing eigenvalues $\lambda > 0$ and eigenvectors $\mathbf{V}$ that satisfy:

$$\lambda \mathbf{V} = \frac{1}{n} \sum_{i=1}^{n} \langle \Phi(\mathbf{x}_i) \cdot \mathbf{V} \rangle \, \Phi(\mathbf{x}_i), \tag{1}$$

where Φ is a nonlinear mapping from $\mathbf{R}^p$ to a higher dimensional feature space $\mathbf{F}$ and $\langle \cdot \rangle$ is the inner product operator. Since $\mathbf{V} = span(\Phi(\mathbf{x}_i), i = 1, \cdots, n)$, we may have $\mathbf{V} = \sum_{i=1}^{n} \alpha_i \Phi(\mathbf{x}_i)$. If we define a $n \times n$ matrix $\mathbf{K}$ with each entry as $K_{i,j} = \langle \Phi(\mathbf{x}_i) \cdot \Phi(\mathbf{x}_j) \rangle$, and replace the inner product in each entry with a kernel function $k(\mathbf{x}_i, \mathbf{x}_j)$, the previous eigen problem is represented as $\lambda \alpha = \mathbf{K} \alpha$, where $\alpha = (\alpha_1, \alpha_2, \cdots, \alpha_n)$. After computing the singular value decomposition on $\mathbf{K}$, the k^{th} PC in $\mathbf{F}$ is obtained by:

$$\left\langle \mathbf{V}^k \cdot \Phi(\mathbf{x}) \right\rangle = \sum_{i=1}^{n} \alpha_i^k \left\langle \Phi(\mathbf{x}_i) \cdot \Phi(\mathbf{x}) \right\rangle, \tag{2}$$

where $\mathbf{V}^k$ is the k^{th} eigenvector in $\mathbf{F}$. Two kernel functions, the polynomial kernel and the radial basis function (RBF) kernel, as defined in (3), were evaluated in this study.

$$\begin{aligned} \text{Polynomial kernel} \quad &: \quad k(\mathbf{x}, \mathbf{y}) = (\mathbf{x} \cdot \mathbf{y} + 1)^m, \\ \text{RBF kernel} \quad &: \quad k(\mathbf{x}, \mathbf{y}) = e^{\frac{-\|\mathbf{x}-\mathbf{y}\|^2}{2\sigma^2}}, \end{aligned} \tag{3}$$

where m is the polynomial kernel order, and σ is the RBF kernel width parameter.

III. Proposed Method

The block diagram of the proposed method is shown in Fig. 1. FMRI data is motion corrected and low-pass filtered prior to KPCA decomposition. The PCs characterizing significant physiological variations are identified, and then undergo frequency analysis to locate frequencies of aliased cardiac and respiratory cycles, as indicated by simultaneously-recorded cardiac and respiratory data. The identified PCs are filtered by digital filters designed to attenuate the power at these frequencies. Both the filtered and unfiltered PCs are used to reconstruct the denoised data for the subsequent analysis.

A. Preprocessing

The motion artifacts in fMRI data are removed by using the rigid body registration method proposed in [12], which is part of FSL tools [13]. The data acquired under resting state are low-pass filtered with a cut-off frequency of 0.1 Hz. The low-pass filter is needed to remove high-frequency signal variations from the slowly-varying signal fluctuations of interest in resting state, typically around 0.1 Hz or below. A Gaussian kernel is used to decrease the spatial noise.

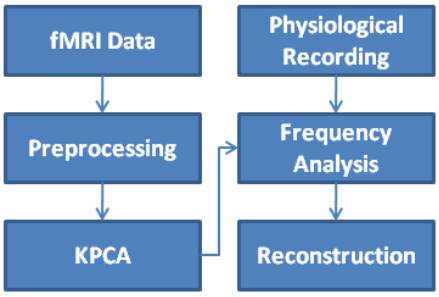


Fig. 1. Block diagram of the proposed method.

B. KPCA Decomposition

The low-pass filtered fMRI data is decomposed by KPCA with either RBF or polynomial kernel. Temporal analysis is used here to obtain temporal profiles of signal and noise. To evaluate the performance of a kernel for separating the aliased physiological noise and BOLD signal, a separation measurement S is proposed here:

$$S = \frac{1}{N} \sum_{k=1}^{N} 1 - e^{-|I_{BOLD}(k) - I_{PHYS}(k)|}, \tag{4}$$

where N is the number of PCs, I_{BOLD} is the mutual information (MI) between a PC and the experimental paradigm, and I_{PHYS} is the MI between the PC and synchronized cardiac (i.e., I_{CARD}) or respiratory (i.e., I_{RESP}) fluctuations. S values are between 0 and 1, and a S value closer to 1 means a better separation between the BOLD signal and physiological noise. This measurement is also applicable to evaluate the separation performance of a kernel for resting state fMRI data. Since there is no experimental paradigm for resting state acquisition, a different way of estimating I_{BOLD} is proposed here. First we select a seed region within a functional network we are interested in, and calculate the average time course of this region. The average time course is used as the paradigm to compute I_{BOLD}. Although it is quite possible that this seed region is contaminated by the physiological noise, this measurement can still provide a reliable evaluation of the separation performance because a kernel that can separate the BOLD signal and noise to different PCs will lead to relatively large S values.

C. Frequency Analysis and Reconstruction

The simultaneously recorded cardiac and respiratory cycles are down-sampled and synchronized to the fMRI timing. After calculating the spectra of the synchronized physiological cycles, frequencies of interest (FOI) showing peak power of the aliased cardiac and respiratory noise can be automatically detected and recorded. MI between the PCs and physiological recording and expected BOLD signal is estimated. PCs exhibiting high MI values with physiological data but low MI values with BOLD signal are ranked in terms of the power at the FOIs estimated from the synchronized physiological cycles. Finite impulse response band-stop filters are then designed to attenuate the noise components at these frequencies. This is more efficient than our previous approach where all most significant PCs are examined in the

frequency domain in order to identify the noise contaminated PCs [11]. The method proposed by Kwok et al. was used for the KPCA reconstruction [14].

D. Evaluation

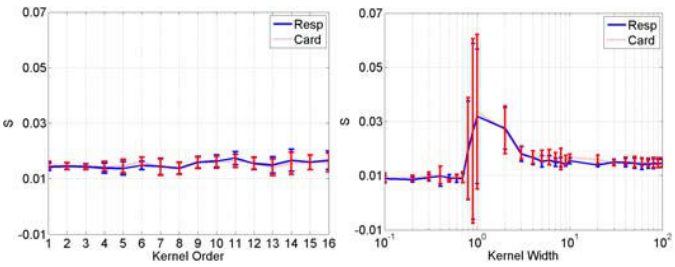
The proposed method was compared with a physiological noise removal method proposed in [15], which is an improvement of the widely used RETROICOR method [5]. For task-based fMRI data, a contrast-to-noise ratio (CNR) measurement was calculated to evaluate the denoising performance [16]. The CNR values are expected to increase or maintain at the same level after the noise removal in brain regions where BOLD activations appears during task stimulation, and to decrease in regions contaminated by the physiological noise. For resting state fMRI data, the default mode network (DMN) in human brain was identified by correlation analysis and compared between data denoised by the two methods.

IV. Experiments and Results

A. Data Acquisition

FMRI data were acquired from a healthy volunteer at a 3 Tesla system with a 8-channel coil. For task-based experiment, 4 sets of fMRI data were obtained using $T2^*$-weighted parallel echo planar imaging (EPI), while the subject was performing right finger-tapping motor task with a blocked-design paradigm, which was consisted of four 25-sec task block and five 25-sec off block. EPI parameters included TR = 2 sec, TE = 30 msec, flip angle = 90°, slice thickness = 4 mm (with 1 mm gap), FOV = 24 cm x 24 cm, in-plane matrix size = 120 x 120, and the number of axial-slice = 30. For resting state experiment, 4 sets of data were acquired using the same T2*-weighted parallel EPI sequence. The scan time for each resting state fMRI run was 4 min. Inversion-recovery prepared spin-echo EPI was also acquired to provide an anatomic reference with identical voxel geometry and geometric distortions as in fMRI. The cardiac and respiration circles were simultaneously recorded and synchronized to the fMRI timing.

B. Task-based Experiment



(a) Polynomial kernel (b) RBF kernel

Fig. 2. The mean and SD of S values calculated as a function of (a) the polynomial kernel order, and (b) the RBF kernel width by using the task-based experimental fMRI data.

The separation performance of the two kernel functions in (3) with different parameter settings was examined using the acquired task-based fMRI data. For the polynomial kernel, the kernel order values ranged from 1 to 16 with an interval of 1. For the RBF kernel, the kernel width parameter was set from 0.1 to 100, with an interval of 0.1 when $0.1 \leq \sigma < 1$, with an interval of 1 when $1 \leq \sigma < 10$, and with an interval of 10 when $10 \leq \sigma \leq 100$.

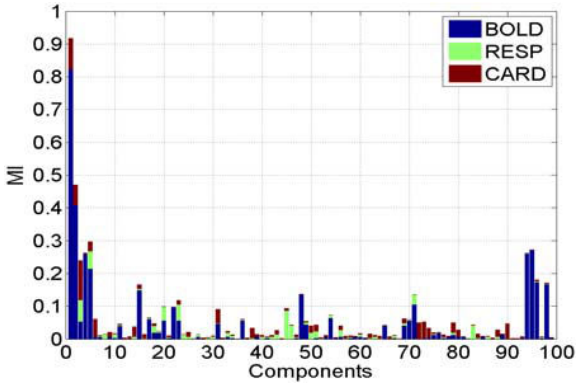
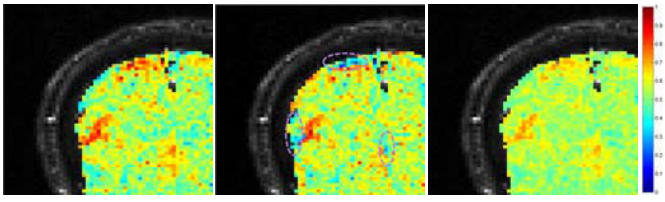


Fig. 3. A stacked bar representation of I_{BOLD} (blue), I_{RESP} (light-green), and I_{CARD} (red-brown) values of all PCs.

Fig. 2 shows the average and standard deviation (SD) of S values of the two kernels obtained from the task-based fMRI data, where the solid blue line represents the separation between BOLD signal and respiration-induced physiological noise, and the dotted red line indicates that between BOLD signal and the cardiac-induced physiological fluctuation. It was observed that there is no significant difference between S values when different kernel orders was used for the polynomial kernel, as shown in Fig. 2 (a). However, when the RBF kernel was used, there is a significant increase of S value when σ is around 1. When the σ value exceeds 10 or is close to 0.1, the S values obtained from the RBF kernel are close to those of the polynomial kernel. It was also observed that the SD of S values is relatively large when $0.8 \leq \sigma \leq 1$, implying an inconsistent noise separation performance. Therefore, we chose $sigma = 2.0$ for KPCA decomposition, and Fig. 3 illustrates the computed I_{BOLD} (blue), I_{RESP} (light-green), and I_{CARD} (red-brown) values of all obtained PCs via the stacked bars, where the length of each color bar indicates the MI value. It can be seen that most PCs with large I_{BOLD} values are associated with small I_{RESP} and I_{CARD} values, indicating a clear separation between the BOLD signal and physiological noise.



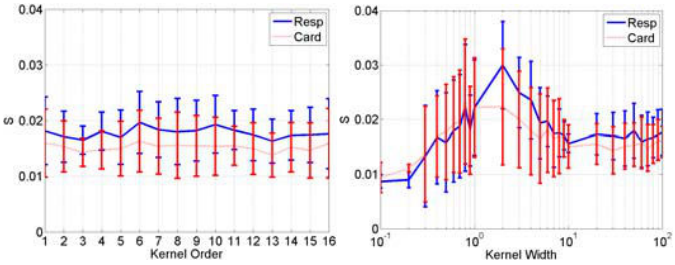
(a) (b) (c)

Fig. 4. CNR maps calculated from (a) the original data, (b) the data denoised by the KPCA-based method, and (c) the data denoised using the improved RETROICOR method. Encircled regions in (b) indicate where physiological noise is attenuated by the KPCA-based method.

Fig. 4 shows a comparison of the normalized (between 0 and 1) CNR values for one run of the task-based experiment. Fig. 4 (a) was obtained from the original data, (b)

was calculated from the data denoised by the KPCA-based method, and (c) was from the data denoised by the improved RETROICOR method. Note the change of CNR values in the three encircled regions in (b) that are affected by the physiological fluctuation, indicating a successful attenuation of the physiological noise that cannot be identified by the improved RETROICOR method.

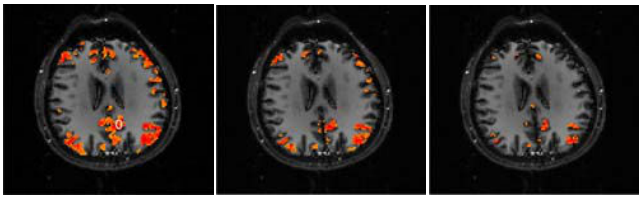
C. Resting State Experiment



(a) Polynomial kernel (b) RBF kernel

Fig. 5. The mean and SD of S values calculated as a function of (a) the polynomial kernel order, and (b) the RBF kernel width by using the resting state experimental fMRI data.

A seed region was manually defined in the posterior cingulate cortex (PCC). The average time course of this seed region was used as a "paradigm" for BOLD signal, based on which I_{BOLD} in (4) can be calculated. Fig. 5 shows the average and SD of S values of the two kernels estimated from the resting state fMRI data. Most of S values calculated from the two kernels are at a similar level, but we may see an apparent increase from the RBF kernel when $\sigma \approx 2$. Therefore, we chose the RBF kernel with $\sigma = 2$ for the resting state physiological noise removal.



(a) (b) (c)

Fig. 6. Part of the correlated DMN regions obtained from (a) the original data, (b) the data denoised by the proposed KPCA-based method, and (c) the data denoised using the improved RETROICOR method. The encircled region in (a) is the seed region.

Using the same seed, correlation analysis was performed at a significance level of 0.01 with the Bonferroni correction. Fig. 6 shows the correlation maps obtained from (a) the original data, (b) the data denoised by the KPCA-based method, and (c) the data processed by the improved RETROICOR method. The encircled region in Fig. 6 (a) is the seed region. Figs. 6 (b) and (c) show that both the KPCA-based and improved RETROICOR methods can reduce correlation in regions close to the brain boundary where effects from respiration are more evident, while the correlated regions in the ventromedial prefrontal cortex (vmPFC) is better preserved by the proposed method. These results, along with those from the task-based experiments, indicate that the proposed method can provide reasonable and effective attenuation of the cardiac and respiration-induced physiological noise, facilitating the analysis of brain activity.

V. Conclusions

We addressed the issue of physiological noise removal in fMRI data by using kernel machine techniques. Two kernel functions were evaluated in terms of their performance to differentiate the aliased physiological noise in fMRI data. Experimental results indicate that the RBF kernel outperforms the polynomial kernel when its width parameter is properly set. Based on the RBF kernel, an improved KPCA-based physiological noise removal method was developed and compared with an existing method by using the task-based and resting state fMRI data acquired from a human subject. The results show that the proposed method can provide comparable or better physiological noise removal performance than the existing method.

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