Dynamical statistical modeling of physiological noise for fast BOLD fMRI

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INTRODUCTION

The recent developments in fast acquisition methods for BOLD fMRI such as dynamical magnetic resonance Inverse Imaging (InI) [1,2] offer whole-brain coverage with sampling rates up to 100 milliseconds. In addition to more accurate temporal estimation of the hemodynamic responses, this allows also potentially more accurate modeling and removal of physiological noise such as cardiac and respiratory cycles, which are adequately sampled to prevent considerable aliasing. The fast sampling methods are typically used with event-related fMRI paradigms [3], and therefore accurate modeling is important for best possible separation of the stimulus related BOLD signal from the physiological noise to obtain maximal benefits from the high temporal resolution. In this work, we propose a method for physiological noise modeling and removal, which allows dynamical tracking of variations in the cardiac and respiratory frequencies during the data acquisition by using an Interacting Multiple Model (IMM) Kalman Filter (KF) approach [4].

METHODS

A quasi-periodic physiological oscillation pattern $c(t)$, such as heartbeat, can be modeled with a "stochastic harmonic oscillator" or "stochastic resonator" $d^2c(t)/dt^2 = -(2\pi j\, f_c(t))^2 c(t) + n_c(t)$, where $f_c(t)$ is the time-varying frequency and $n_c(t)$ is a white noise process. In the estimation, we treat the signals $c(t)$ and the derivatives $dc(t)/dt$ as unknowns at each voxel, which is equivalent to estimation of the unknown phases and amplitudes of the signal at the voxels. The slower "bias" components such as the BOLD signal can be modeled using a simple short-time linear model, which can be represented as Wiener velocity model $d^2b(t)/dt^2 = n_b(t)$, where $n_b(t)$ is a white noise process. This model is common in target tracking applications [4] and simply assumes that the signal $b(t)$ is smooth and low frequency dominated. If the frequency $f_c(t)$ is constant or known, the estimation problem is linear and can be effectively solved by the KF. Typically, the heartbeat and respiration frequencies vary over the data acquisition period, and the related signals can be acquired by external measurement systems. Consequently, we first estimate the time-varying frequencies from the external cardiac and respiratory measurements separately by using the IMM method as follows. The ranges of possible cardiac and respiratory frequencies are suitably discretized, such as $f_c(t) \in (40,41,\ldots,90)$ beats per minute (bpm) and $f_r(t) \in (15,16,\ldots,35)$ bpm. At each time, the signal is assumed to consist of a fundamental frequency with two additional harmonics, and a bias term. The IMM approach allows probabilistic jumps between the models with different discrete frequencies, thereby capturing the time-varying characteristics of these quantities. To obtain a benchmark data for testing the model and against which the accelerated methods could be evaluated, we collected standard EPI data with spatial coverage limited to three slices placed over calcarine sulcus. The sequence parameters were TR: 200.00 msec, TE: 30.00 msec, flip angle: 30 degrees, image matrix: 64x64, voxel size: 4 mm isotropic and the data was acquired on a Siemens 3T Tim Trio scanner using a 32 channel head coil. The visual stimulation paradigm consisted of three conditions, where either both visual hemifields were stimulated simultaneously or one hemifield stimulus was followed by the other with a lag of 200 msec. The inter-stimulus interval was 500 msec. Subject's heartbeats were recorded by using electrocardiogram and respiration was measured with a pneumatic belt around the chest.

RESULTS

The time courses of the IMM estimated frequencies demonstrate the capability of the method in following the temporal changes in the physiological signals. The estimated respiratory and cardiac frequencies varied within ranges of 24-27 and 67-72 bpm, respectively. The EPI signal time courses show drastically different noise characteristics depending on the spatial location. The more medial example voxel in **Figure 1** shows moderate cardiac and respiratory fluctuations, which are effectively cleaned by the filter. The more lateral voxel, which appears to be located on the surface of the brain, shows highly prominent respiratory oscillations. These could be due to perturbations in B0 caused by variations of bulk susceptibility or air volume in the thorax, or related to bulk movement of the head with the respiration not completely eliminated by the motion correction. For this location, the proposed method attenuated the respiratory peak at the power spectrum by a factor of ~10.

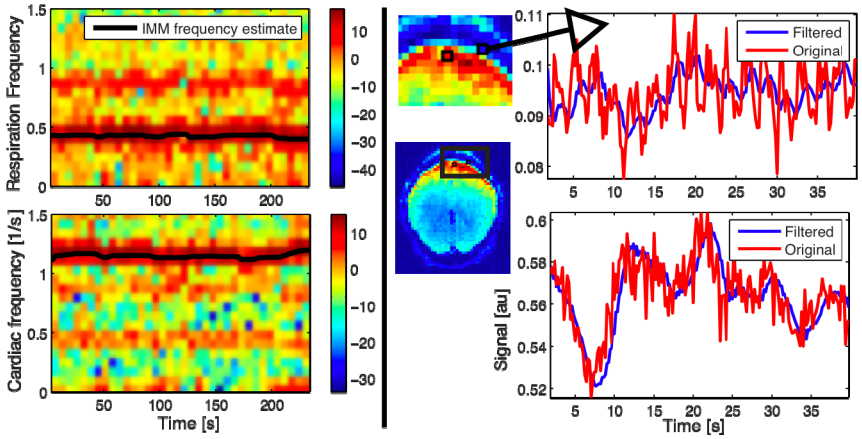

Figure 1 (Left panel) Spectrograms of the external respiration and cardiac measurements, along with the IMM time-varying frequency estimates. (Right panel) EPI slice with two example voxels marked with black squares and the corresponding original and filtered signal time courses.

DISCUSSION

Modeling of the physiological noise will most likely play an important role in analysis of rapidly sampled BOLD fMRI data. In addition to increasing the sensitivity of the event-related hemodynamic response estimation, characterization of noise will be an important factor in analysis of resting state fMRI, as the obvious confounds these signals can produce in functional connectivity studies. Moreover, in higher field strengths these effects will be even more pronounced. As the proposed filtering method yields both the amplitudes and phases of the physiological signals at each voxel, it offers a direct way to quantify phase lags between different brain areas with respect to the reference signal. Because the methodology is based on efficient tracking algorithms, is also allows for real time implementation for online applications.

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