

# Estimating the Physiological Response Functions in Resting-State BOLD: The Effect of Acquisition Speed

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**Introduction:** Variations in physiological signals such as heart beat and respiration have confounding effects on resting state BOLD signal [1] and functional connectivity calculations. Their effects on BOLD signal is typically described by response functions [2,3], estimated from fMRI series data, and generally regressed out from BOLD. Typically, resting-state fMRI scans have sampling rates of several seconds, which does not permit accurate sampling of higher-frequency noise, such as cardiac pulsation (temporal aliasing). Thus, it is unclear whether the typical resting-state fMRI temporal resolution is sufficient for accurately capturing the physiological response functions. The objective of this study is to estimate physiological response functions based on high temporal resolution fMRI data, and compare those to the responses estimated from typical fMRI acquisitions. To do so, we used simultaneous multi-slice resting-state fMRI acquisition [4] and simultaneously estimated responses to three physiological signals. We targeted the BOLD response function to cardiac rate variation (CRV), respiration volume per time (RVT) variation and end tidal CO<sub>2</sub> (PETCO<sub>2</sub>).

**Method:** 8 healthy subjects (5 male, aged between 22 and 36) were scanned using a Siemens TIM Trio 3T MRI scanner. Regular (“long TR”) resting-state fMRI images were acquired from 8 subjects using GRE-EPI sequence (TR/TE = 2000/30 ms, flip angle = 90, 26 slices, ~3.44x3.44x4.6mm<sup>3</sup>, 360 volumes). Slice accelerated single shot GE-EPI image (“short TR”) were also acquired from 6 of the subjects (TR/TE = 323/30 ms, flip angle = 40, 15 slices, ~3.44x3.44x6mm<sup>3</sup>, 2230 volumes). Processing steps for both fMRI datasets include motion correction, brain extraction, spatial smoothing (10mm FWHM), high-pass filtering (0.01 Hz), and regression of six motion parameters. The cardiac signal was recorded using a finger pulse oximeter. Respiratory-volume and PETCO<sub>2</sub> signals were recorded with a BioPac system (BioPac, Goleta, USA). Time-locked heart-beat and respiration artifacts were removed using RETROICOR [5]. Cardiac rate variation (CRV) is defined as the time interval between consecutive R waveforms [2]. RVT was calculated as the breathing depth divided by its period ((max-min)/time interval) [3]. PETCO<sub>2</sub> was computed as maxima of per-breath expired partial pressure of CO<sub>2</sub>. All the physiological signals were re-sampled to the corresponding fMRI sampling rate (2 s for long TR and 0.323 s for short TR). Voxel-wise brain responses to the three physiological signals were simultaneously estimated with the linear Gaussian model explained in [2]. Responses of all voxels inside the brain were reordered into a matrix, and the common response function was extracted by principle component analysis.

**Results:** The figure shows estimated group-average response functions for PETCO<sub>2</sub> (top), cardiac rate variation (middle), and respiratory rate variation (bottom) for long TR (left) and short TR (right). Error bars show standard error of the responses across subjects. Response functions for long TR are comparable to the ones previously reported in the literature [2,3]. Importantly, short TR and Long TR responses are very similar.

**Discussion:** We estimated BOLD response function to three physiological variables (PETCO<sub>2</sub>, CRV, and RVT) with resting-state fMRI data acquired at high and low temporal resolution. The estimated responses were found to be very similar, suggesting there is no high frequency dynamics in the responses. Moreover, despite the presence of temporal aliasing of cardiac noise in the in typical resting-state fMRI acquisitions, the estimated physiological responses seems to be insensitive to sampling rate of the data.

**References:** [1] Birn RM, Neuroimage 62 (2012) 864 – 870. [2] Chang C, et al., Neuroimage 44 (2009) 857 – 869. [3] Birn RM, et al., Neuroimage 40 (2008) 644 – 654. [4] Breuer FA, et al., Magn Reson Med 53(3), (2005) 684 – 691. [5] Glover GH, et al., Magn Reson Med. 44(1) (2000) 162 – 167.

