Spatial Specificity of Functional Connectivity Maps for Different Frequency Bands in Rats

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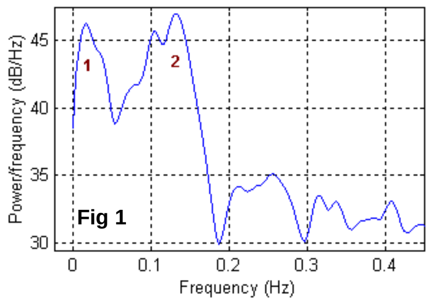
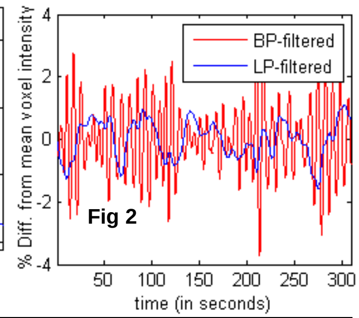
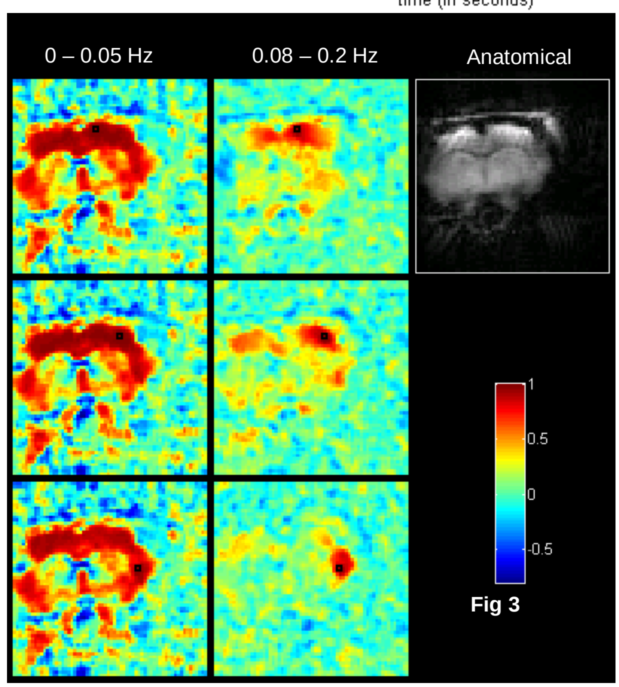
Introduction: Resting state functional connectivity and spontaneous low frequency fluctuations (LFFs) in BOLD signal [1] have gained considerable interest among the fMRI and neuroscience communities in the past few years. While functional connectivity based on BOLD fluctuations was originally observed in humans [1], recent work has shown that it can also be detected in rats and monkeys [2, 3]. Cross-correlation analysis is one of the most widely used methods for creating functional connectivity maps using LFFs. In most studies, a low pass filter with cutoff frequency of ~0.08 Hz has been used for human data, whereas a cutoff frequency of ~0.15 Hz has been used for rat data [3]. However, a lower limit to the frequencies contributing to spatially specific correlation maps has not been determined systematically to our knowledge. This work shows that multiple peaks can be observed in low-frequency range in resting state fMRI signal from rat cerebral cortex, and these peaks result in connectivity maps with different spatial specificity.

Materials and Methods: All the images were acquired on 11.7T Bruker scanner. The rats (n = 6) were anesthetized using α-chloralose and mechanically ventilated at about 1 Hz. For each rat, a series of gradient-echo EPI images was acquired of a single coronal slice covering somatosensory cortex with following parameters: TR = 100 ms, TE =15-20 ms, matrix size = 64x64, spatial resolution = 300 µm isotropic, number of repetitions = 3600. Power spectral density estimates for time series corresponding to different voxels in cerebral cortex were obtained using Welch method after discarding transient scans, detrending and de-meaning. Datasets for 3 out of 6 rats did not exhibit a clear peak in 0.11-0.17 Hz range in cerebral cortex. Individual images in the time-series were spatially blurred using a 3x3 Gaussian filter with σ = 2 pixels. Cross-correlation analysis was performed with different seed voxels after filtering the time-courses using either a low-pass (LP) filter with cutoff frequency of 0.05 Hz or a band-pass (BP) filter with f_{LOW} = 0.08 Hz and f_{HIGH} = 0.2 Hz, and performing quadratic detrending.





Results and discussion: (We discuss the results for the 3 datasets showing a clear peak in 0.11-0.17 Hz range, unless mentioned otherwise). Power spectral analysis of time-series obtained from cortex revealed low frequency peaks in following frequency ranges: below 0.05 Hz, and between 0.11 and 0.17 Hz (labeled as 1 and 2 in figure 1). Clearly, LP filter retained the lower peak (peak 1) and the BP filter retained the higher peak (peak 2). Fig 2 shows results of applying LP and BP filtering to a time-course (the two filtered time-series may have different time-lags due to potentially different group delays of the filters). Figure 3 shows connectivity maps for three different seed voxels for one dataset. Each seed voxel is marked with a black square. Clearly the correlation maps for LP filtered signal show less sensitivity to the location of seed voxel and high correlation is seen for the whole cortex and some sub-cortical areas. We observed this trend for most seeds within cortex in all the datasets. We obtained maps for the remaining three images that had only the lower frequency peak after LP filtering and observed the same trend.



The correlation maps after BP filtering seemed to be more specific as compared with those obtained after LP filtering (fig 3). High correlation was observed for bilaterally symmetric regions of the cortex for seeds in M1 and S1 (fig 3 column 2, rows 1 and 2). However, we observed unilateral correlation maps for seeds in S2 (fig 3 column 2, row 3). Correlation maps seemed to highlight specific functional areas (fig 3 column 2).

Functional connectivity studies in the simplified environment of the rat model provide valuable insights into the acquisition and interpretation of human studies. In this experiment, both the spectral resolution and the sampling rate were higher than in typical human studies, providing clear separation of the low frequency peaks and preventing aliasing of first harmonics of the cardiac or respiratory cycles. These preliminary results suggest that the two low frequency bands may contain different information, and may have different origins (neural activity, vasomotion [4], other physiological contributions). These results motivate in-depth investigation of frequency-band selection for functional connectivity studies. Future work will focus on determining the origin of these signal fluctuations in rats and extending this work to human subjects.

References: [1] Biswal, B et al. Magn. Res. Med. 1995; 34:537-541
[2] Vincent, JL et al. Nature 2007; 447:83-86
[3] Williams, K et al. Proc. ISMRM 14 (2006):Abstract 2119
[4] Kleinfeld, D et al. PNAS 1998; 95(26):15741-15746