Spatiotemporal Dynamics of Low Frequency Fluctuations in BOLD fMRI of Rats

W. Majeed[1], M. Magnuson[1], and S. Keilholz[1]

[1]Biomedical Engineering, Georgia Institute of Technology / Emory University, Atlanta, GA, United States

Introduction: Resting state functional connectivity and spontaneous low frequency fluctuations (LFFs) in the BOLD signal [1] have gained considerable interest among the fMRI and neuroscience communities in the past few years. Functional connectivity has been observed in humans, monkeys and rats [1, 2, 3]. To date, most analysis techniques (cross-correlation e.g. [1], independent component analysis e.g. [4], and clustering e.g. [5]) have been based on the assumption that connectivity remains unchanged over time needed to acquire the data (usually several minutes), and the spatiotemporal properties of the LFFs have not been explored in detail. This work presents some initial findings about temporal and spatial dynamics of LFFs in rat cerebral cortex.

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 microns 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 time-points, detrending and de-meaning. 3 out of 6 datasets were discarded due to absence of a peak in 0.11-0.17 Hz range in cerebral cortex. Individual time-courses were filtered using a band-pass filter with cutoff frequencies of 0.08 Hz and 0.2 Hz, after performing spatial blurring, followed by quadratic de-trending. A series of images with each image consisting of corresponding time-points in the filtered time-series was constructed, and we looked for temporally evolving spatial patterns in these images. For each filtered time-course, envelope was detected using Hilbert transformation. The envelope was divided into two 'states' (corresponding to high and low amplitudes) using k-means algorithm (k = 2) for each time-series. Average durations of high- and low-amplitude states (T_H and T_L) were calculated on voxel-by-voxel basis. Also, T_H and T_L were calculated for a simulated dataset (3600 images with matrix size = 30x30, consisting of Gaussian white noise) order to obtain the values for 'null-hypothesis' conditions.

Results and Discussion: Different patterns evolving over time were observed in the filtered images. One pattern which was consistently observed in all the datasets is displayed in fig 1. The time-labels indicate time-lag relative to the first image displayed in the figure. This pattern looks like a propagating wave, with high signal intensities starting from SII and traveling along the cortex. Intensity fluctuations were approximately 2-4%. We intend to investigate these patterns in greater details to determine if there is a neural basis for the fluctuations or if they are related to vasomotion [6].

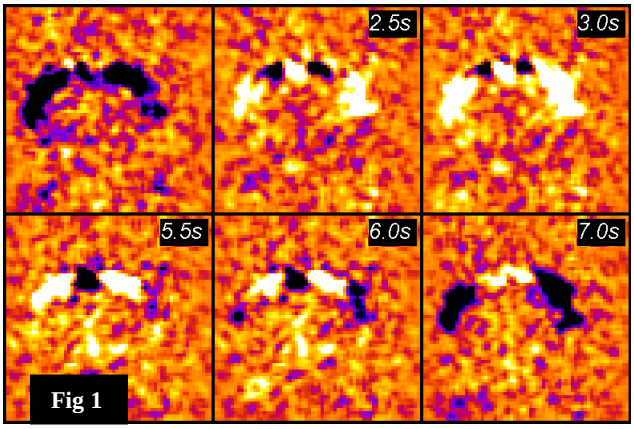

Fig 1

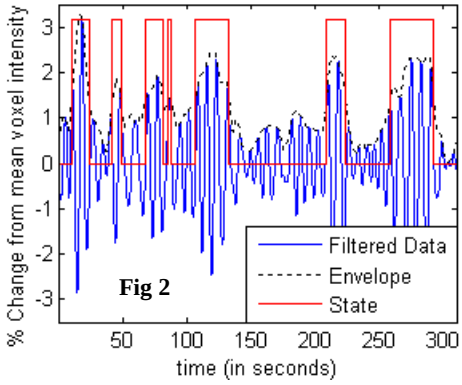

Fig 2

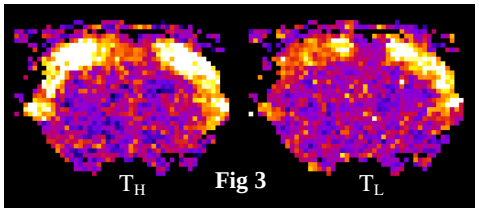

Fig 3

Fig 2 shows classification of a filtered time-series corresponding to a cortical location into low- and high-amplitude states. Filtered signal from sub-cortical areas showed more randomness and less obvious structure (data not shown). Fig 3 shows T_H and T_L maps for one dataset (with different colormaps). Clearly, cortex shows higher T_H as compared with sub-cortical areas. However, for one of the rats (referred to as rat 3) some part of caudate-putamen also showed relatively high T_H. Average T_H values obtained for the three rats were 9.9±20s, 14.2±4.5s and 10.7±1.7s for cortex, and 6.6±1.0s, 7.0±1.1s and 6.8±1s for sub-cortical area (caudate-putamen region for rat 3, showing relatively high T_H, was not included in ROI analysis). We also observed higher average T_L for cerebral cortex (fig 3), although T_L values showed greater variability as compared with T_H. Mean T_H and T_L values obtained for sub-cortical region were within one standard deviation from the values obtained for simulated data (6.42±0.96s and 10.15±2.52s respectively). These observations suggest that filtered time-courses from cortex show different temporal structure, as compared those obtained from sub-cortical area. An interesting question to address in future would be: Do these 'high amplitude states' represent neural events? A multimodality approach will be very useful in addressing such questions.

These results suggest that detailed examination of the spatiotemporal dynamics of the low frequency fluctuations may provide more insight into brain function than steady-state analysis methods. Further development of such methods and their application to human and animal data can help us to understand and interpret LFFs and resting state functional connectivity.

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