# Characterization of an Intrinsic Low-frequency Component at around 0.025 Hz in Steady-state fMRI Signals

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**Introduction:** Spontaneous low-frequency components (SLFs) from the human brain, as detected by functional MRI (fMRI) methods, have been used to study functional connectivity within functional networks. However, it is not clear if there is a dominant frequency component that determines the functional synchrony. In this study, we propose a novel method to analyze previously published datasets from cognitive studies [1] and report that there is an intrinsic low-frequency component (IFC) at around 0.025 Hz in the SLFs. The dynamic characteristics of this IFC in the voxelwise cross-spectra are evident in that its phase delay can be modulated by different memory tasks. In addition, the standard deviation of its phase-delay distribution determines the functional synchrony. These results significantly advance our knowledge about SLF signals during different functional states. Consequently, they can be applied to many functional-connectivity studies focusing on a variety of neural networks under different conditions.

**Theory:** The regional cross-spectrum of pair-wised voxel time courses from a given region of interest (ROI) is investigated. The maximum peak of this cross-spectrum within the predefined frequency range of SLF (0.015~0.1Hz), is taken as the IFC of SLF signal $\hat{f}_c$. Then, the phase delay $\hat{\tau}_{ij}$ is calculated for each pair of voxel time courses (*i*th and *j*th voxel) upon this intrinsic frequency [2]:

$$\varphi_{ij}(f) = \tan^{-1}\left(\mathrm{Im}\left(S_{ij}(f)\right)/\mathrm{Re}\left(S_{ij}(f)\right)\right),\quad \hat{\tau}_{ij} = \frac{1}{2\pi}\left|\sum_{|f-fc|<\Delta f}\varphi_{ij}(f)\right| \Big/ \sum_{|f-fc|<\Delta f} f \qquad (1)$$

where $S_{ij}(f)$ is the voxel pair-wised cross-spectrum, $\varphi_{ij}(f)$ is the phase of $S_{ij}(f)$, and $\Delta f$ is defined as the computation range for the phase delay, which is set as 0.005Hz in our study. Then, the regional phase delay is estimated as: $\hat{\sigma}_\tau \approx \sqrt{\pi}\sum_{i>j}\hat{\tau}_{ij} \Big/ (K^2 - K)$ (2)

where K is the number of voxels in the ROI and assumed quite large, $\hat{\sigma}_\tau$ is the standard deviation of the phase-delay distribution of the intrinsic frequency $\hat{f}_c$ in the ROI, and named as the regional-phase delay. This regional-phase delay manifests the extent of functional synchrony for the ROI — the larger the regional phase delay, the less synchronized the IFC is; the smaller the regional phase delay, the more synchronized the IFC.

There is another approach to evaluate regional functional synchrony $\hat{\sigma}_\theta$ by using the phase-shift index (PSI) [1, 3]. If the detected IFC $\hat{f}_c$ is a dominant component in the SLF signal, the following relation will hold: $\hat{\sigma}_\theta \approx 2\pi \hat{f}_c \cdot \hat{\sigma}_\tau$ (3)

**Materials and Methods**: Our method and hypothesis have been published with previous fMRI data [1], which evaluated functional synchrony by using the phase-shift index with two steady-state cognitive tasks (each lasting 6 min): 1) discriminating indoor/outdoor pictures (Task A) and 2) judging which side of a picture was larger (a vertical red line separated a picture into two parts with an unequal width) (Task B). By using a block-design scan the activated parahippocampal gyrus was indicated as the ROI (Task A vs. Task B). Two sets of fMRI experiment data were investigated. The first set is of 2-sec TR with nine young, healthy subjects at a Bruker 3T scanner, which is quoted as Long-TR data. The second set is of 0.5-sec TR with eight young, healthy subjects at a GE 3T scanner, quoted as Short-TR data. Informed consents were obtained from all subjects for this IRB-approved study. More details from the experiment can be found in the original paper [1]. To evaluate the functional-synchrony measurement, all the voxel time courses in the ROI were interpolated to sampling frequency 2Hz for Long-TR data. Then, both sets of data were filtered by using a band-pass filter 0.015~0.1Hz. The cross-spectrums were computed by using the Welch method. Then, the IFC, regional-phase delays and regional-phase-shift indices were obtained.

**Results and Discussion**: For all the steady-state fMRI scans (two scans for each subject: Tasks A and B), the detected IFC appears consistently around 0.025Hz. Figure 1 shows spectra for the Long-TR and Short-TR from representative subjects. The phase delays at this IFC are significantly different between the two tasks, while the selection of TR remains irrelevant. Further, the phase delays, IFC and the phase-shift indices are matched very well in Eq.(3). The functional synchrony measurements are listed in Table 1. In Short-TR datasets, the corresponding phase delays at the aliased cardiac pulsation peak from the unfiltered voxel time courses are as follows: 0.23±0.04 seconds for Task A and 0.23±0.03 seconds for Task B. The Experiment Results help us to reach four conclusions: 1) An IFC existed around 0.025Hz in SLF signal; 2) The phase delay of the IFC can be modulated by different cognitive tasks; 3) The close match of the phase delay, the IFC and the phase shift demonstrates that the IFC is a dominant factor in determining the functional synchrony; 4) It is unlikely that cardiac pulsation interferes with the functional-synchrony analysis in the Long-TR case.

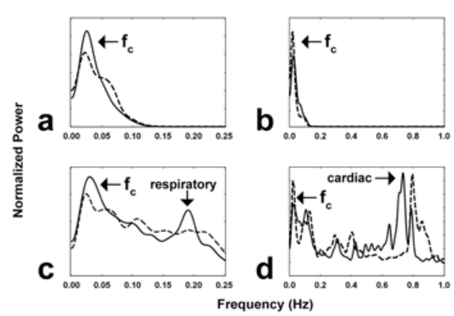


Fig 1a. regional cross-spectrum for a representative Long-TR subject;
Fig 1b. regional cross-spectrum for a representative Short TR subject;
Fig 1c. original regional spectrum for the Long-TR subject;
Fig 1d. original regional spectrum for the Shoft-TR subject.

Table 1. Measurements of functional synchrony (* denotes that there is statistical difference between two tasks)

| | Long TR | | | | Short TR | | | |
|---|---|---|---|---|---|---|---|---|
| | $\hat{f}_c$ (Hz) | $\hat{\sigma}_\tau$ (seconds) | $\hat{\sigma}_\theta$ (degree) | $2\pi\hat{f}_c \cdot \hat{\sigma}_\tau$ (degree) | $\hat{f}_c$ (Hz) | $\hat{\sigma}_\tau$ (seconds) | $\hat{\sigma}_\theta$ (degree) | $2\pi\hat{f}_c \cdot \hat{\sigma}_\tau$ (degree) |
| Task A | 0.027±0.003* | 3.53±0.61* | 32.63±5.00* | 34.46±5.89* | 0.026±0.004 | 4.10±1.91* | 31.28±10.83* | 36.70±13.17* |
| Task B | 0.023±0.001* | 5.82±0.88* | 49.56±6.00* | 49.85±7.93* | 0.023±0.002 | 6.41±1.76* | 45.88±10.24* | 52.41±9.00* |

**References**: 1. Xu G et al. MRM 2006;56:41–50. 2. Sun F et al. NeuroImage 2005;28:227-237. 3. Xu Y et al. ISMRM 2004;12:498.

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