A new complex data analysis method for transition-band SSFP fMRI (BOSS fMRI)

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Introduction

Although several complex data analysis methods have been proposed [1,2], most of the fMRI data are still processed on magnitude alone. This is because the phase activation is believed to be restricted to large veins, so it is not beneficial to include the phase in GRE-fMRI [3]. In transition-band SSFP (BOSS) fMRI, however, this assumption is no longer valid: the phase activation is considered to be a primary source of the functional contrast [4], revealing as many activated voxels as the magnitude with greater activation levels compared to GRE-fMRI [5]. Moreover, this phase activation was found not only in the large veins identified in the venogram, but also in the gray matter. These findings suggest that the phase activation is beneficial to include because it also provides functionally-localized information. As a result, a complex data analysis method can provide benefits in SSFP fMRI by combining both magnitude and phase activations. Here, we propose a new complex data analysis method that incorporates a T^2–test [6] with a GLM to generate a full activation map in SSFP fMRI. This method is significantly more efficient than the previous method [2].

Theory

Hotelling's T^2-test is a generalization of the Student's t-test to a multivariate domain. It is defined as $T^2 = (\underline{\mathbf{y}}-\boldsymbol{\mu})^T(\underline{\mathbf{S}}/n)^{-1}(\underline{\mathbf{y}}-\boldsymbol{\mu})$, where n is the number of samples, $\underline{\mathbf{y}}$ is the sample mean vector, $\boldsymbol{\mu}$ is the hypothetical population mean vector and $\underline{\mathbf{S}}$ is the sample covariance matrix [5]. If a Gaussian distribution is assumed, then the T^2-statistic follows an F-distribution with 2 and n-2 degrees of freedom (# of variate = 2). A p-value can be obtained from the CDF of $F_{2,n-2}$ evaluated at $T^2(n-2)/2(n-1)$. To incorporate the hemodynamic response into this T^2-test, a GLM is utilized to estimate the mean vectors as well as the covariance matrix. The complex time-series data are decomposed into the real and imaginary axes and modeled as follows:

$$\mathbf{y}_r = \mathbf{X}\boldsymbol{\beta}_r + \boldsymbol{\varepsilon}_r = [\mathbf{x}_1 \ldots \mathbf{x}_L][\beta_{r1} \ldots \beta_{rL}]^T + \boldsymbol{\varepsilon}_r, \quad \mathbf{y}_i = \mathbf{X}\boldsymbol{\beta}_i + \boldsymbol{\varepsilon}_i = [\mathbf{x}_1 \ldots \mathbf{x}_L][\beta_{i1} \ldots \beta_{iL}]^T + \boldsymbol{\varepsilon}_i, \quad [1]$$

where $\mathbf{y} = \mathbf{y}_r + i\mathbf{y}_i$ (a complex n x 1 vector) is the time-series data of one voxel, $\mathbf{X}$ is a design matrix (a real n x m matrix) with m waveform vectors (constant = [1 1 … 1]^T, linear drift, stimulus waveform 1, …), $\boldsymbol{\beta}_r$ and $\boldsymbol{\beta}_i$ (each a real m x 1 vector) are the parameters of GLM, and $\boldsymbol{\varepsilon}_r$ and $\boldsymbol{\varepsilon}_i$ are residual errors (a real n x 1 vector each). The least square estimates of $\boldsymbol{\beta}_r$ and $\boldsymbol{\beta}_i$ are $(\mathbf{X}^T\mathbf{X})^{-1}\mathbf{X}^T\mathbf{y}_r$ and $(\mathbf{X}^T\mathbf{X})^{-1}\mathbf{X}^T\mathbf{y}_i$, respectively. The activation level or the mean difference between the two states ($\underline{\mathbf{y}}-\boldsymbol{\mu}$) becomes $\mathbf{v}^T\underline{\boldsymbol{\beta}}$ (= $\mathbf{v}^T[\underline{\boldsymbol{\beta}}_r\ \underline{\boldsymbol{\beta}}_i]$), where $\mathbf{v}$ is a contrast to a specified stimulus waveform vector, the covariance matrix of the contrast that is calculated from the residual errors and the design matrix becomes $\underline{\mathbf{S}}/n = \mathrm{COV}(\underline{\boldsymbol{\varepsilon}}_r, \underline{\boldsymbol{\varepsilon}}_i)\ \mathbf{v}^T(\mathbf{X}^T\mathbf{X})^{-1}\mathbf{v}$ where $1/n$ is embedded in $(\mathbf{X}^T\mathbf{X})^{-1}$. As a result, the T^2-value can be obtained as follows:

$$T^2 = \mathbf{v}^T\underline{\boldsymbol{\beta}}[\mathrm{COV}(\underline{\boldsymbol{\varepsilon}}_r, \underline{\boldsymbol{\varepsilon}}_i)\ \mathbf{v}^T(\mathbf{X}^T\mathbf{X})^{-1}\mathbf{v}]^{-1}\underline{\boldsymbol{\beta}}^T\mathbf{v}. \quad [2]$$

Simulation and Experiment

Four different datasets of the complex data (no contrast, contrast in magnitude, contrast in both magnitude and phase, and contrast in phase) were simulated (10^5 voxels each) to validate the proposed complex analysis method. Each dataset was generated by Eq. [1] with n = 50, $\mathbf{X}$ = [**c h**] (**c** is a constant, **h** is ten zeros and ten ones repeat), $\beta_{r1} = \beta_{i1} = 10$, $\boldsymbol{\varepsilon}_r$ and $\boldsymbol{\varepsilon}_i$ are distributed by $N(0,1)$. The first dataset was Gaussian noise data with $\beta_{r2} = \beta_{i2} = 0$. The second, third and fourth datasets were designed to simulate a "magnitude-only" contrast ($\beta_{r2} = \beta_{i2}$), a "magnitude and phase" contrast ($\beta_{r2} = 0$), and a "phase-only" contrast ($\beta_{r2} = -\beta_{i2}$), respectively.

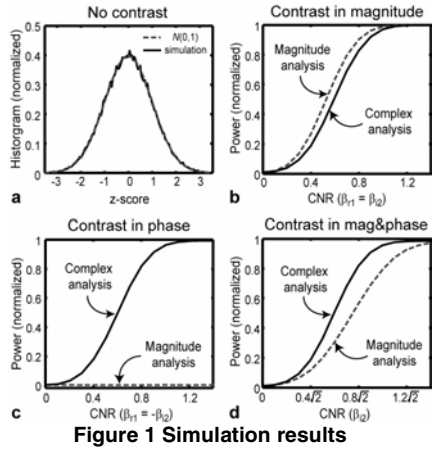

Figure 1 Simulation results

For the experiment, a 1.5 T GE EXCITE system (40 mT/m and 150 mT/m/ms) was used with a three-inch surface coil. For the transition-band SSFP fMRI studies, a 3D spiral sequence, (balanced SSFP, FOV = 16 cm^2, resolution = 1 mm^3, TR = 15 ms, flip angle = 5°, number of interleaves = 10, 16 ~ 18 slices, five subjects) was utilized to cover a volume every 3 sec. The shim was targeted to the visual cortex. The stimulus was a flashing checkerboard (15'' on/off for 2' 18''). The magnitude and phase data were processed individually to create "magnitude-only" and "phase-only" z-statistics maps using FEAT FSL ($p < 0.01$). High-pass filtering was performed to remove the baseline drift. For the complex data analysis, the functional data were decomposed into a real and imaginary time-series; then, the slow signal drift was removed by the same filter that was used previously. In each voxel, the T^2-value was calculated from Eq. [2]. The design matrix ($\mathbf{X}$) was the same as that in the magnitude and phase analyses. The p-value was calculated in each voxel from the F-distribution, and the activation maps were generated by thresholding with a one-tailed p-value 0.01 followed by converting to z-scores.

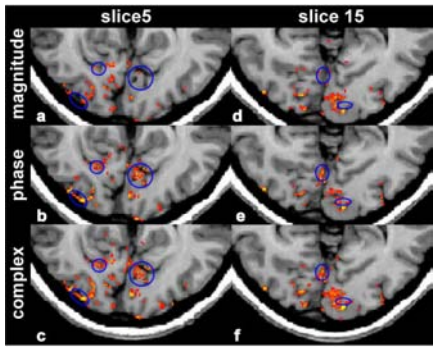

Figure 2 Experimental results

Results and Discussion

Fig. 1 shows the simulation results. When there is no activation, the null hypothesis is preserved (Fig. 1a). When the contrast is only in magnitude, the magnitude analysis performs slightly better than the complex analysis (Fig. 1b, measured in power). However, the magnitude analysis fails when the contrast is only in phase (Fig. 1c). When the contrast exists in both, the complex analysis performs better than the magnitude analysis (Fig. 1d).

The experimental results are shown in Fig. 2. The activation maps from the complex data analysis (3rd row) cover areas (circled in blue) that are missing in the magnitude data analysis results. In most of these areas, the significant activations are found in the phase activation maps, proving that the complex data analysis method includes the activated voxels from both the magnitude and phase signal changes. The complex activation maps contain, on average, 1.7 times more activated voxels than the magnitude activation maps, and 1.8 times more activated voxels than the phase.

In Fig. 3, the SNR required to detect a certain contrast level at a given P_D (=0.99) and P_{FA} (=0.01) is shown for the magnitude and the complex analysis [7]. The magnitude analysis requires an infinite SNR to detect phase activation (the red area in Fig. 3a). The required SNR difference between the two analyses indicates the superiority of the complex analysis in most contrasts, except in the dark blue areas where the contrast is primarily in the magnitude. Even in these areas, the maximum required SNR difference is only 0.69 dB. A theoretical proof that verifies the mathematical equivalence between our method and [6] is posted at www-mrsrl.stanford.edu/~jonghoyi/complex_analysis.pdf.

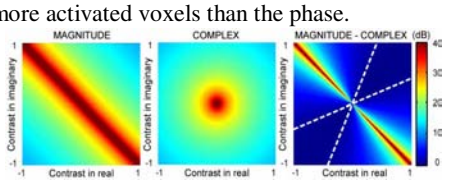

Figure 3 Required SNR

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