An fMRI Activation Method Using Complex Data

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SYNOPSIS:

In functional magnetic resonance imaging, voxel time courses after "image reconstruction" are complex valued as a result of phase errors due to magnetic field inhomogeneities. Nearly all fMRI studies derive functional "activation" based on magnitude time courses [1,2]. Here we propose to directly model the entire complex or bivariate data rather than just the magnitude data. A nonlinear model is used to model activation on the complex signal, and a likelihood ratio test is derived to test for activation at each voxel. We investigate the performance of the model on a simulated dataset.

INTRODUCTION:

After Fourier or non-Fourier image reconstruction, each voxel contains a time course of real and imaginary components of the measured Proton Spin Density (PSD). Magnitude images are produced by taking the square root of the sum of squares of the real and imaginary parts of the measured PSD in each voxel at each time point. Nearly all fMRI studies obtain a statistical measure of functional activation based on magnitude image time courses. When this is done, phase information in the data is discarded. Previous models for complex activation have been proposed [3,4]. We reparameterize and extend the model proposed by Nan and Nowak (1999) to a multiparameter baseline and signal model, including formulating the hypothesis test in terms of contrasts and estimating the phase angle directly.

MODEL:

Neglecting the voxel location and focusing on a particular voxel, the complex valued image measured over time in a given voxel is denoted (y_{Rt},y_{It}). A nonlinear multiple regression model is introduced individually for each voxel that includes a phase error in which at time t, the measured proton spin density is given by

$$y_t = [x_t \beta \cos\theta + \eta_{Rt}] + i[x_t \beta \sin\theta + \eta_{It}]$$

where $(\eta_{Rt},\eta_{It})' \sim N(0, \Sigma)$, $\Sigma=\sigma^2 I_2$. The complex model can be written in matrix notation as

$$\underset{2n\times 1}{y} = \underset{2n\times 2(q+1)}{\begin{pmatrix} X & 0 \\ 0 & X \end{pmatrix}} \underset{2(q+1)\times 1}{\begin{pmatrix} \beta\cos\theta \\ \beta\sin\theta \end{pmatrix}} + \underset{2n\times 1}{\eta}$$

where it is specified that the 2nx 1 vector $y=(y_R',y_I')'$ is the n×1 vector of observed real components stacked on the n×1 vector of observed complex components, X is the n×(q+1) design matrix, β is the (q+1) ×1 vector of regression coefficients, θ is the 1×1 phase angle, and the 2n× 1 vector $\eta=(\eta_R',\eta_I')'$ is the n×1 vector of real component errors stacked on the n×1 vector of complex component errors. This model is a generalization of previous models [5,6] that restricted q=1, did not estimate θ, or use contrasts. The maximum likelihood estimates of the model parameters are given by:

$$\hat\theta = \frac{1}{2}\tan^{-1}\left[\frac{2\hat\beta_R(X'X)\hat\beta_I}{\hat\beta_R(X'X)\hat\beta_R - \hat\beta_I(X'X)\hat\beta_I}\right]$$

$$\hat\beta_c = \hat\alpha_1\hat\beta_R + \hat\alpha_2\hat\beta_I = \cos(\hat\theta)\hat\beta_R + \sin(\hat\theta)\hat\beta_I$$

$$\hat\sigma^2 = \frac{1}{2n}\left[y - \begin{pmatrix} X & 0 \\ 0 & X \end{pmatrix}\begin{pmatrix} \hat\beta\cos\hat\theta \\ \hat\beta\sin\hat\theta \end{pmatrix}\right]'\left[y - \begin{pmatrix} X & 0 \\ 0 & X \end{pmatrix}\begin{pmatrix} \hat\beta\cos\hat\theta \\ \hat\beta\sin\hat\theta \end{pmatrix}\right]$$

Where $\hat\beta_R = (X'X)^{-1}X'y_R$ and $\hat\beta_I = (X'X)^{-1}X'y_I$.

Note that the maximum likelihood estimates of β can be shown to be a linear combination of the estimates using only the real data y_R or only the imaginary data y_I, with α "weights" dependent on the phase angle.

Functional activation can be assessed by testing a null hypothesis in terms of contrasts such as H_0: C β=0. For example, a question of interest may be, "Is the coefficient for the reference function zero?" This can be evaluated with the choice C=(0,...,0,1), $\beta'=(\beta_0, \beta_1,\ldots, \beta_q)$, and γ =0 where the β_q coefficient corresponds to the reference function. Then the generalized likelihood ratio statistic for the complex activation model is given by

$$-2\log\lambda_C = 2n\log\left(\frac{\tilde\sigma^2}{\hat\sigma^2}\right).$$

where $\hat\sigma^2$ is the unconstrained ML estimate of σ^2 and $\tilde\sigma^2$ is the ML estimate under the constrained null hypothesis (see [5] for details). This statistic has an asymptotic χ^2 distribution with degrees of freedom equal to the rank of C.

APPLICATION TO SIMULATED DATASET:

Data is generated to simulate a bilateral finger-tapping fMRI block design experiment with n=256 points where the true motor activation structure is known so that the proposed complex model can be compared with the usual magnitude model. A 128 x 128 slice is selected for analysis within which two 7 x 7 ROI's as lightened in Figure 1 are designated to have activation. For this slice, simulated fMRI data is constructed according to a regression model which consists of an intercept, a time trend for all voxels but also a reference function for voxels in each ROI which is related to a 8 x (16on + 16off) TR block experimental design.

Estimated complex model voxel coefficient values of (1.639005, 0.00001, 0.05870)' and variance 0.00241 were extracted from a significantly active voxel in a real fMRI bilateral finger-tapping experiment. The estimated phase was extracted for the entire image of interest. The value of β_0 was adjusted to compare the models under a lower signal to noise ratio of SNR= β_0/σ=1. Outside the ROI the regression coefficients associated with the reference function were set to 0, while inside the ROI they were set to 0.75*0.05870 times a normal hill with a variance of 2 and unit height plus .25*0.05870. This type of ROI has been successfully used before [6] and has the largest effect in the center with smaller effects toward the edge.

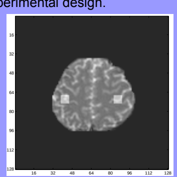

Figure 1. Anatomical with ROI.

Simulated Dataset: Estimated reference function coefficients

Figure 2 illustrates how the estimated reference function coefficients are a weighted function of the coefficients estimated from just the real or imaginary data. Figure 2A shows the combined estimate of β_2. Figure 2B shows the real "weight" (α_1=cos θ), Figure 2C shows the real data estimate of β_2, Figure 2D shows the imaginary "weight" (α_2=sin θ), and Figure 2E shows the imaginary data estimate of β_2.

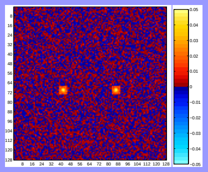

Figure 2A. Combined estimated coefficient for the reference function β_2.

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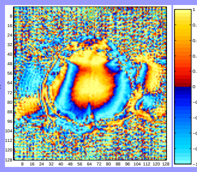

Figure 2B. Real "weight" (cos θ) .

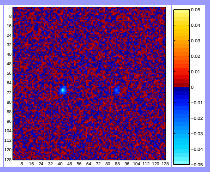

Figure 2C. Real data estimate of β_2.

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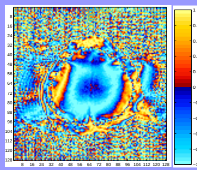

Figure 2D. Imaginary "weight" (sin θ) .

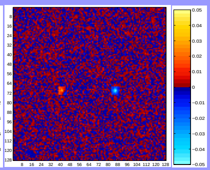

Figure 2E. Imaginary data estimate of β_2.

Simulated Dataset: Likelihood Ratio Test Results

A LR statistic for the magnitude model can be obtained in a similar fashion to the complex model (see [5] for more details), and the resulting statistic has the same asymptotic distribution as the complex LR test. The images of LR statistics for the magnitude and complex models are given in Figure 3, thresholded using the Benjamini-Hochberg procedure at a 5% false discovery rate [6, 7]. The complex model captures a larger portion of the true activation region. This is illustrated more clearly in Figure 3C, which displays the activation statistic differences.

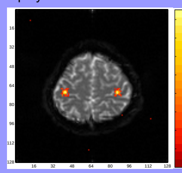

Figure 3A. Activation image using the LR test for the magnitude model.

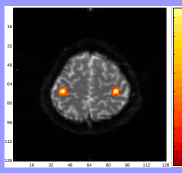

Figure 3B. Activation image using the LR test for the complex model.

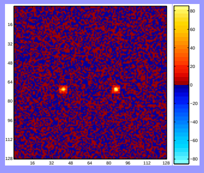

Figure 3C. Differences in activation statistics (Complex – Magnitude)

RESULTS OF ANALYSIS:

- A complex data fMRI activation model that uses phase information was presented as an alternative to the typical magnitude data model.
- Activation statistics were derived from generalized likelihood ratio tests for both models allowing for contrasts.
- Activation from both models were presented for a simulated dataset. It was found that for large signal to noise ratios, both models were comparable. However, for smaller signal to noise ratios, the complex activation model demonstrated superior power of detection over the magnitude activation model.

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