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Technical Note

Complex fMRI analysis with unrestricted phase is equivalent to a magnitude-only model

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Due to phase imperfections, voxel time course measurements are complex valued. However, most fMRI studies measure activation using magnitude-only time courses. We show that magnitude-only analyses are equivalent to a complex fMRI activation model in which the phase is unrestricted, or allowed to dynamically change over time. This suggests that improvements to the magnitude-only model are possible by modeling the phase in each voxel over time.

Keywords: fMRI; Unrestricted phase; Magnitude-only model; Complex data model

Introduction

It is well known that due to phase imperfections, fMRI voxel time course measurements appear in both the real and imaginary channels (Bernstein et al., 1989; Haacke et al., 1999; Macovski, 1996). However, nearly all fMRI studies obtain a statistical measure of activation based on magnitude-only image time courses (Bandettini et al., 1993; Cox et al., 1995) by discarding phase information. We show that these magnitude-only analyses are equivalent to a complex fMRI activation model in which the phase for each voxel is completely unrestricted, that is, allowed to vary dynamically over time. Specifically, we will show that inference on task-related activation is equivalent between the dynamic phase complex fMRI model and the magnitude-only model in terms of having identical regression coefficients and likelihood ratio F statistics although they are derived with the phase included. In addition, a detailed examination shows that the maximum likelihood estimate of the variance in the unrestricted phase model is inconsistent, because the number of parameters increases with sample size. An unbiased estimate can be obtained that is identical to the unbiased variance estimate from the magnitude-only model. Therefore, the magnitude-only model results can be directly derived from a complex data model that allows for an unrestricted phase.

This unrestricted phase complex fMRI model is a generalization of the model introduced by Rowe and Logan (2004) in which the phase in each voxel was assumed to be constant over time following traditional beliefs (Nan and Nowak, 1999). This result indicates that the improved performance of the Rowe and Logan (2004) model may be due to better use of phase information by pooling across time points within each voxel. It also suggests that further improvements over the magnitude-only model, which places no restrictions on the phase, are possible by modeling the phase changes over time, for example, looking for task-related phase changes. One example of this approach is that of Menon (2002), in which the phase was used as a covariate in the magnitude-only model. This tends to minimize activation for voxels containing large blood vessels that are thought to experience task-related changes in both magnitude and phase and focus on voxels containing small vessels such as those in the capillary bed of parenchymal tissue.

Model

The complex fMRI activation model of Rowe and Logan (2004) can be written more generally as

$$\underset{2n\times 1}{y} = \underset{2n\times 2n}{\begin{pmatrix} A_1 & 0 \\ 0 & A_2 \end{pmatrix}} \underset{2n\times 2(q+1)}{\begin{pmatrix} X & 0 \\ 0 & X \end{pmatrix}} \underset{2(q+1)\times 1}{\begin{pmatrix} \beta \\ \beta \end{pmatrix}} + \underset{2n\times 1}{\eta} \tag{2.1}$$

where the observed vector of data $y = (y'_R, y'_I)$ is the vector of observed real values stacked on the vector of observed imaginary

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values and the vector of errors $\eta = (\eta'_R, \eta'_I)' \sim \mathcal{N}(0, \Sigma \otimes \Phi)$ is similarly defined. Here we specify that $\Sigma = \sigma^2 I_2$ and $\Phi = I_n$. In this expression, X is the design matrix, and β is the parameter vector. Further, A_1 and A_2 are square diagonal matrices with tth diagonal element cos θ_t and sin θ_t, respectively. Note that if $\theta_t = \theta$ for all t, then $A_1 = \cos\theta I_n$, $A_2 = \sin\theta I_n$, and this becomes the constant phase complex model proposed by Rowe and Logan (2004). If there is a single constant column in X, then it can be shown that this reduces to a constant magnitude and different phase temporal fMRI model that is analogous to a previously presented constant magnitude different phase spatial MRI model (Sijbers and van Dekker, 2004).

This model generalization allows for unrestricted temporal changes in the phase. This implies that one can test hypotheses regarding task-related changes in the magnitude of the complex voxel time courses while accounting for unrestricted temporal changes in the phase, expressed as H_0:$C\beta = 0$. For example, with a model with β_0 representing an intercept, β_1 representing a linear drift over time, and β_2 representing a contrast effect of a stimulus. Then to test whether the coefficient for the reference function or stimulus is 0, set $C = (0, 0, 1)$, so that the hypothesis is H_0:$\beta_2 = 0$.

Parameter estimates

As with the usual magnitude-only normal regression model and the constant phase complex nonlinear multiple regression model, we can obtain unrestricted maximum likelihood estimates of the parameters as derived in the Appendix to be

$$\hat{\theta}_t = \tan^{-1}\left(\frac{y_{It}}{y_{Rt}}\right), \quad t = 1,\ldots,n$$

$$\hat{\beta} = (X'X)^{-1}X'\left(\hat{A}_1 y_R + \hat{A}_2 y_I\right),$$

$$\hat{\sigma}^2 = \frac{1}{2n}\left[y - \begin{pmatrix}\hat{A}_1 X\hat{\beta}\\ \hat{A}_2 X\hat{\beta}\end{pmatrix}\right]'\left[y - \begin{pmatrix}\hat{A}_1 X\hat{\beta}\\ \hat{A}_2 X\hat{\beta}\end{pmatrix}\right], \tag{2.2}$$

where $\hat{A}_1$ and $\hat{A}_2$ are diagonal matrices with cos $\hat{\theta}_t$ and sin $\hat{\theta}_t$ as the tth diagonal element. Note that the estimate of the regression coefficients is a temporally "weighted" linear combination of estimates from the real and imaginary parts.

The estimated regression coefficients for the dynamic phase complex activation model can be shown to be equivalent to the usual magnitude-only ones as follows

$$\begin{aligned}\hat{\beta} &= (X'X)^{-1}X'\left(\hat{A}_1 y_R + \hat{A}_2 y_I\right)\\ &= (X'X)^{-1}X' \operatorname{vec}\left(\frac{y_{Rt}}{\sqrt{y_{Rt}^2 + y_{It}^2}} y_{Rt} + \frac{y_{It}}{\sqrt{y_{Rt}^2 + y_{It}^2}} y_{It}\right)\\ &= (X'X)^{-1}X' y_M\end{aligned} \tag{2.3}$$

where here vec(·) is used to denote an n dimensional vector whose tth element is given by its scalar argument and $y_M = \operatorname{vec}\left(\sqrt{y_{Rt}^2 + y_{It}^2}\right)$.

The maximum likelihood estimates under the constrained null hypothesis H_0:$C\beta = 0$ are similarly derived in the Appendix and given by

$$\tilde{\theta}_t = \tan^{-1}\left(\frac{y_{It}}{y_{Rt}}\right), \quad t = 1,\ldots,n$$

$$\tilde{\beta} = \Psi\hat{\beta},$$

$$\tilde{\sigma}^2 = \frac{1}{2n}\left[y - \begin{pmatrix}\tilde{A}_1 X\tilde{\beta}\\ \tilde{A}_2 X\tilde{\beta}\end{pmatrix}\right]'\left[y - \begin{pmatrix}\tilde{A}_1 X\tilde{\beta}\\ \tilde{A}_2 X\tilde{\beta}\end{pmatrix}\right]$$

$$\Psi = I_{q+1} - (X'X)^{-1}C'\left[C(X'X)^{-1}C'\right]^{-1}C, \tag{2.4}$$

where $\tilde{A}_1$ and $\tilde{A}_2$ are diagonal matrices with cos $\tilde{\theta}_t$ and sin $\tilde{\theta}_t$ as the tth diagonal element. The restricted regression coefficients can also be shown to be equivalent to the magnitude-only model because the multiplicative factor Ψ is identical in both cases.

Note that the estimate of the phase in a particular voxel at time t depends only on the complex pair (y_{Rt}, y_{It}) and is therefore unstable and not very informative. This is in contrast to the constant phase model of Rowe and Logan (2004), in which the phase information is pooled across time in voxels to estimate the constant phase. This pooling of phase information produces more stable estimates and may help explain the improved performance of the constant phase model over the magnitude-only model (or unrestricted phase complex model). It also suggests that further improvements are possible by modeling the phase changes over time, for example, by incorporating task-related phase changes.

Activation statistics

The likelihood ratio statistic in Eq. (A.3) with some algebra can be written as

$$\begin{aligned}F &= \frac{(n-q-1)}{r}\left(\lambda^{-1/n} - 1\right)\\ &= \frac{(n-q-1)}{r}\frac{\hat{\beta}'C'\left[C(X'X)^{-1}C'\right]^{-1}C\hat{\beta}}{2n\hat{\sigma}^2}.\end{aligned} \tag{2.5}$$

Note that since

$$\begin{aligned}2n\hat{\sigma}^2 &= \left[y - \begin{pmatrix}\hat{A}_1 X\hat{\beta}\\ \hat{A}_2 X\hat{\beta}\end{pmatrix}\right]'\left[y - \begin{pmatrix}\hat{A}_1 X\hat{\beta}\\ \hat{A}_2 X\hat{\beta}\end{pmatrix}\right]\\ &= \sum_{t=1}^{n}\Big[y_{Rt}^2 - 2y_{Rt}\left(x'_t\hat{\beta}\right)\cos\hat{\theta}_t + \hat{\beta}x_t x'_t\hat{\beta}\cos^2\hat{\theta}_t + y_{It}^2\\ &\qquad - 2y_{It}\left(x'_t\hat{\beta}\right)\sin\hat{\theta}_t + \hat{\beta}x_t x'_t\hat{\beta}\sin^2\hat{\theta}_t\Big]\\ &= \sum_{t=1}^{n}\left[y_{Mt} - x'_t\hat{\beta}\right]^2\end{aligned} \tag{2.6}$$

equals the error sum of squares from the magnitude-only model, the F statistic and equivalent likelihood ratio statistic are identical to the one from the magnitude-only model. In either case the F statistic follows the same distribution. If the signal-to-noise ratio is large so that y_{Mt} is approximately normal, then F follows an $F_{r,n-q-1}$ distribution under the null hypothesis, where r is the full row rank of C. Otherwise, one might use the Ricean distribution (Gudbjartsson and Patz, 1995; Rice, 1944) to derive the proper distribution of the statistic denoted with the letter F. In either case, the estimates of β and the likelihood ratio test depend only on the magnitude data. A statistical map of activation statistics is produced and thesholded as in Logan and Rowe (2004).

Note from Eq. (2.6) that the maximum likelihood estimate of σ^2 from the unrestricted phase complex model is inconsistent, since it can be shown as follows that its expected value does not converge in probability or tend to its population value as the sample size tends to infinity

$$E(\hat{\sigma}^2) = \frac{1}{2n} E\left\{ \sum_{t=1}^{n} \left[y_{Mt} - x'_t \hat{\beta} \right]^2 \right\}$$

$$= \frac{1}{2n} \left\{ (n-q-1)\sigma^2 \right\}$$

$$\xrightarrow{p} \frac{\sigma^2}{2}.$$

An unbiased estimate of the variance can be obtained by simply using the unbiased estimate of the variance from the magnitude-only model.

Conclusions

A generalization of the constant phase complex activation fMRI model of Rowe and Logan (2004) was developed, where the phase angle is allowed to vary at each time point. It is shown that the estimated regression coefficients and the likelihood ratio F statistic for this unrestricted phase complex fMRI model are equivalent to those in the usual magnitude-only model. It is also seen that the maximum likelihood estimate of the variance in this model is not consistent, but that a consistent variance estimate is obtained by simply using the magnitude-only unbiased variance estimate. Therefore, inference on task-related magnitude activation that is equivalent to that of the magnitude-only model can be derived directly from the unrestricted phase complex model.

Appendix A. Estimation and generalized likelihood ratio test

In applications using multiple regression including fMRI, we often wish to test linear contrast hypothesis (for each voxel) such as

$$\begin{array}{llll} H_0: & C\beta = \gamma & \text{vs} \quad H_1: & C\beta \neq \gamma \\ & \theta_t \neq \theta_{t'} & & \theta_t \neq \theta_{t'} \\ & \sigma^2 > 0 & & \sigma^2 > 0, \end{array}$$

where C is an $r \times (q+1)$ matrix of full row rank and γ is an $r \times 1$ vector.

The likelihood ratio statistic is computed by maximizing the likelihood $p(y|\beta, \theta, \sigma^2, X)$ with respect to β, θ, and σ^2 under the null and alternative hypotheses where $\theta' = (\theta_1, \ldots, \theta_n)$. Denote the maximized values under the null hypothesis by $(\tilde{\beta}, \tilde{\theta}, \tilde{\sigma}^2)$ and those under the alternative hypothesis as $(\hat{\beta}, \hat{\theta}, \hat{\sigma}^2)$. These maximized values are then substituted into the likelihoods and the ratio taken. With the aforementioned distributional specifications, the likelihood of the model is

$$p(y|X, \beta, \theta, \sigma^2) = (2\pi\sigma^2)^{-\frac{2n}{2}} e^{-\frac{h}{2\sigma^2}} \tag{A.1}$$

where

$$h = \left[y - \begin{pmatrix} A_1 X\beta \\ A_2 X\beta \end{pmatrix} \right]' \left[y - \begin{pmatrix} A_1 X\beta \\ A_2 X\beta \end{pmatrix} \right]$$

$$= \beta'(X'X)\beta - 2\beta' X' [A'_1 y_R + A'_2 y_I] + y' y.$$

The logarithm of this likelihood can be written as

$$LL = -n\log(2\pi) - n\log\sigma^2 - \frac{1}{2\sigma^2}\beta'(X'X)\beta - \frac{1}{2\sigma^2} y' y$$

$$+ \frac{1}{\sigma^2} \sum_{t=1}^{n} y_{Rt} \cos\theta_t x'_t \beta + \frac{1}{\sigma^2} \sum_{t=1}^{n} y_{It} \sin\theta_t x'_t \beta \tag{A.2}$$

that we will use for maximization. Under the null hypothesis, the term $\psi'(C\beta - \gamma)/2$ needs to be added to the logarithm of the likelihood for the Lagrange multiplier constraint.

A.1. Unrestricted MLEs

Maximizing this likelihood with respect to the parameters is the same as maximizing the logarithm of the likelihood with respect to the parameters and yields

$$\frac{\partial LL}{\partial \beta}\bigg|_{\beta=\hat{\beta}, \theta=\hat{\theta}, \sigma^2=\hat{\sigma}^2} = -\frac{1}{2\hat{\sigma}^2} \left[2(X'X)\hat{\beta} - 2X' \left(\hat{A}_1 y_R + \hat{A}_2 y_I \right) \right]$$

$$\frac{\partial LL}{\partial \theta_t}\bigg|_{\beta=\hat{\beta}, \theta=\hat{\theta}, \sigma^2=\hat{\sigma}^2} = -\frac{1}{\hat{\sigma}^2} \left[y_{Rt} x'_t \hat{\beta} (-1) \sin\hat{\theta}_t + y_{It} x'_t \hat{\beta} \cos\hat{\theta}_t \right]$$

$$t = 1, \ldots, n$$

$$\frac{\partial LL}{\partial \sigma^2}\bigg|_{\beta=\hat{\beta}, \theta=\hat{\theta}, \sigma^2=\hat{\sigma}^2} - \frac{2n}{2}\frac{1}{\hat{\sigma}^2} + \frac{\hat{h}}{2}\frac{1}{(\hat{\sigma}^2)^2}$$

where $\hat{h}$ is h with MLEs substituted in. By setting these derivatives equal to zero and solving, we get the MLEs under the unrestricted model given in Eq. (2.2).

A.2. Restricted MLEs

Maximizing this likelihood with respect to the parameters is the same as maximizing the logarithm of the likelihood in Eq. (A.2) with respect to the parameters with the Lagrange multiplier term $\psi'(C\beta - \gamma)/2$ added for the null hypothesis restriction and yields

$$\frac{\partial LL}{\partial \beta}\bigg|_{\beta=\tilde{\beta}, \theta=\tilde{\theta}, \psi=\tilde{\psi}, \sigma^2=\tilde{\sigma}^2}$$

$$= -\frac{1}{2\tilde{\sigma}^2} \left[2(X'X)\tilde{\beta} - 2X' \left(\tilde{A}_1 y_R + \tilde{A}_2 y_I \right) \right] + \frac{1}{2} C' \tilde{\psi}$$

$$\frac{\partial LL}{\partial \theta_t}\Big|_{\beta=\tilde{\beta},\theta=\tilde{\theta},\psi=\tilde{\psi},\sigma^2=\tilde{\sigma}^2} = -\frac{1}{\tilde{\sigma}^2}\left[y_{Rt}x'_t\tilde{\beta}(-1)\sin\tilde{\theta}_t + y_{It}x'_t\tilde{\beta}\cos\tilde{\theta}_t\right] \; t=1,\ldots,n$$

$$\frac{\partial LL}{\partial \psi}\Big|_{\beta=\tilde{\beta},\theta=\tilde{\theta},\psi=\tilde{\psi},\sigma^2=\tilde{\sigma}^2} = \frac{1}{2}\left(C\tilde{\beta}-\gamma\right)$$

$$\frac{\partial LL}{\partial \sigma^2}\Big|_{\beta=\tilde{\beta},\theta=\tilde{\theta},\psi=\tilde{\psi},\sigma^2=\tilde{\sigma}^2} = -\frac{2n}{2}\frac{1}{\tilde{\sigma}^2}+\frac{\tilde{h}}{2}\frac{1}{(\tilde{\sigma}^2)^2}$$

where $\tilde{h}$ is h with MLEs substituted in. By setting these derivatives equal to zero and solving, we get the MLEs under the restricted model given in Eq. (2.4).

Note that $\tilde{\sigma}^2 = \hat{h}/(2n)$ and $\hat{\sigma}^2 = \tilde{h}/(2n)$. Then the generalized likelihood ratio is

$$\lambda = \frac{p\left(y|\tilde{\beta},\tilde{\sigma}^2,\tilde{\theta},X\right)}{p\left(y|\hat{\beta},\hat{\sigma}^2,\hat{\theta},X\right)} = \frac{(\tilde{\sigma}^2)^{-2n/2}e^{-2\tilde{h}n/\left(2\tilde{h}\right)}}{(\hat{\sigma}^2)^{-2n/2}e^{-2\hat{h}n/\left(2\hat{h}\right)}}\;, \tag{A.3}$$

and Eq. (2.5) follows.

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