FMRI MODEL DIAGNOSTICS FOR THE DOUBLE GAMMA AND TEMPORAL DERIVATIVE

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ABSTRACT

Standard analysis techniques for Functional Magnetic Resonance Imaging (fMRI) assume a linear, time invariant model of underlying signal behaviour. These assumptions are valid for some but not all data. Hence each model characteristic should be formally tested for its validity when analysing particular data. Diagnosing model violations is a necessary step in statistical modeling but is not yet common in fMRI. In general this would be a computationally demanding task.

We present a test for the validity of the hemodynamic model comprising a Double Gamma function and its temporal derivative. Using the so-called Lagrange Multiplier method, the test only requires fitting under the statistical null hypothesis leading to simple implementation and fast computation.

The method is demonstrated with simulated and real data examples.

Index Terms— fMRI, impulse response, time derivative, model criticism

1. INTRODUCTION

The accuracy of any statistical analysis relies on using a valid model for analysis. Using an invalid model for analysing particular data can lead to false inference and misleading conclusions. So it is important to check the assumptions behind the model.

Although Functional Magnetic Resonance Imaging (fMRI) models have been developed with higher levels of complexity, it is still common practice to use a model with basic linear, time-invariant assumptions about signal and noise behaviour [1]. It has long been known that these simple model approximations are adequate for some, but not all fMRI data [2]. So there is a need for methods to quantitatively decide whether complicated models are necessary for particular fMRI data or if standard models would suffice.

The fMRI community has so far lacked such model selection and verification tools, meaning that this essential step of identifying model violations has largely been neglected.

In recent work we have introduced a framework for fMRI model diagnostics based on Lagrange Multiplier (LM) tests [3, 4]. These LM-anomaly tests are applied separately at each voxel in fMRI data to generate a spatial map of model violation. A crucial advantage of this approach is that it only requires model fitting under the statistical null hypothesis [5], leading to simple implementation and fast computation. These procedures can be easily included as part of a standard fMRI analysis.

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Here we develop an LM-anomaly test for the validity of a BOLD (Blood Oxygen Level Dependent) activation impulse response model including a Double Gamma (DG) Hemodynamic Response Function (HRF) and its temporal derivative (TD) (together referred to as the DG+TD model). This LM-anomaly test complements previous LM-anomaly tests developed in [3], for validity of a standard Double Gamma HRF, time-varying HRF and non-linear HRF models.

This paper is organised as follows. In Section 2 we summarise the LM test framework. In Section 3 we design a test for the validity of the Double Gamma HRF and its temporal derivatives as used by SPM and FSL software. In Section 4 we show a simulation and application to real fMRI data. Conclusions are offered in Section 5.

Notation: HRF = hemodynamic response function; DG+TD = Double Gamma plus temporal derivative HRF model; LM = Lagrange Multiplier; subscript $[k]$ indicates a frequency domain signal.

2. LAGRANGE MULTIPLIER TEST PROCEDURE

Given Gaussian data y having an associated log-likelihood

$$L(\theta) = -\frac{1}{2}e^T\Omega^{-1}e - \frac{1}{2}\ln|\Omega|$$

where $\theta = (\pi, \psi, \alpha)$, e is an error vector $e = y - h(\pi, \psi)$, $\Omega = \Omega(\alpha)$. Here α are noise parameters; ψ are underlying signal parameters; π relate to the anomaly at issue. We wish to test the null hypothesis $g(\pi) = 0$, e.g. $\pi - \pi_0 = 0$ where π_0 is known.

The usual approach is to construct a likelihood ratio test, but that is computationally intensive requiring model fitting under both null and alternative hypotheses. The Lagrange Multiplier test only requires fitting under the null [6].

The procedure is as follows,

1. Fit the model under the null obtaining $\tilde{\theta} = \arg\min_{g(\pi)=0} L(\theta)$ and the residual $\tilde{e} = y - h\left(\tilde{\pi}, \tilde{\psi}\right)$
2. Compute the pseudo regressors $\tilde{X} = \frac{\partial h^T}{\partial \tilde{\psi}}$, $\tilde{Z} = \frac{\partial h^T}{\partial \tilde{\pi}}$
3. Assuming stationary noise with spectrum $F_k = F_k(\alpha)$ the test statistic in the frequency domain is

$$V = \left(\sum \frac{\tilde{e}_{[k]}\tilde{z}^H_{[k]}}{\tilde{F}_{[k]}}\right) Q^{-1} \left(\sum \frac{\tilde{z}_{[k]}\tilde{e}^H_{[k]}}{\tilde{F}_{[k]}}\right) \quad (1)$$

$$Q = \left(\sum \frac{\tilde{z}_{[k]}\tilde{z}^H_{[k]}}{\tilde{F}_{[k]}}\right) - \left(\sum \frac{\tilde{z}_{[k]}\tilde{x}^H_{[k]}}{\tilde{F}_{[k]}}\right)\left(\sum \frac{\tilde{x}_{[k]}\tilde{x}^H_{[k]}}{\tilde{F}_{[k]}}\right)^{-1}\left(\sum \frac{\tilde{x}_{[k]}\tilde{z}^H_{[k]}}{\tilde{F}_{[k]}}\right)$$

where subscript $[k]$ indicates a frequency domain signal. The test statistic is distributed as χ^2_{p-r}.

The test is applied at each fMRI data voxel then subjected to an appropriate threshold using the Bonferroni method to correct for multiple comparisons, giving a spatial map of model violation.

3. TESTING THE DOUBLE GAMMA AND DERIVATIVE

In this work we use the standard linear time-invariant model for fMRI with time-stationary and spatially independent noise, but spatially varying noise variance, represented at each voxel as

$$\begin{aligned} y_t &= \mu_t + v_t \\ &= m_t + s_t + v_t \end{aligned}$$

where m_t is temporal drift, v_t is auto-regressive (AR(1) + white) noise, and signal $s_t = h_t * u_t$ is the convolution between the HRF and input stimulus pattern.

In our previous work we developed a test for the validity of the linear fMRI model with a Double Gamma HRF [3]. Here we design an LM-anomaly test for the validity of a linear fMRI model which includes the Double Gamma HRF and its Temporal Derivative as regressors. This combination has been asserted to provide an adequate basis to span the subspace of BOLD activation signals in fMRI data [7], though its validity is rarely checked for individual fMRI data. The derivative term is included to ostensibly provide additional flexibility in modeling the shape and latency of the BOLD signal represented by the Double Gamma function [7].

In particular we test the validity of the DG+TD HRF models used in SPM (*www.fil.ion.ucl.ac.uk/spm/*) and FSL [8] software. The basic Double Gamma function is essentially identical in both, however the definitions of the temporal derivative vary slightly. FSL software uses an accurate numerical estimate of the analytic temporal derivative, allowing close approximation via the analytic form of the temporal derivative. SPM software approximates the temporal derivative by the difference between the Double Gamma function and a 1-second delayed version of the same. This is different enough to require separate modeling for an LM-diagnostic test. So we design two structurally similar tests for these cases.

To set up the hypothesis testing problem we need a non-parametric framework. We could use a finite impulse response (FIR) model but we have found the Laguerre basis system for causal functions to require far fewer parameters than FIR when used with fMRI [3, 9].

We first show in Section 3.1 that the DG+TD model can be represented by a finite sum of weighted continuous Laguerre polynomials, each scaled individually with particular coefficients. Then in Section 3.2 we develop the test of whether the coefficients for a full non-parametric Laguerre basis set differ from those particular Laguerre coefficients for the DG+TD model.

3.1. Laguerre Expansion of HRF Models

3.1.1. Double Gamma Function

The common Double Gamma function

$$h_\tau = A\left(\frac{\tau^{(\alpha_1-1)}\beta_1^{\alpha_1}e^{-\beta_1\tau}}{\Gamma(\alpha_1)} - c\frac{\tau^{(\alpha_2-1)}\beta_2^{\alpha_2}e^{-\beta_2\tau}}{\Gamma(\alpha_2)}\right)$$

can be expanded as $h_\tau = \sum_{j=0}^{\infty} q_j^{(\alpha)} L_j^{(\alpha)}(\tau)\, w^{(\alpha)}(\tau)$, for jth order continuous Laguerre polynomial. $L_j^{(\alpha)}(\tau)$ in turn is orthogonal with respect to a weighting function $w^{(\alpha)}(\tau)$ as

$$\int_0^\infty L_j^{(\alpha)}(\tau)\, L_n^{(\alpha)}(\tau)\, w^{(\alpha)}(\tau)\, \partial\tau = \frac{\Gamma(n+\alpha+1)}{n!}\delta_{j,n}$$

and $q_j^{(\alpha)}$ are scaling coefficients. In the cases here h_τ is known so we find $q_j^{(\alpha)}$ as

$$q_j^{(\alpha)} = \int_0^\infty \frac{L_n^{(\alpha)}(\tau)\, h(\tau)}{\binom{j+\alpha}{j}\Gamma(\alpha+1)}\partial\tau \tag{2}$$

For the Double Gamma function specified in SPM and FSL, $[\alpha_1, \alpha_2, \beta_1, \beta_2, c] = [6, 16, 1, 1, \frac{1}{6}]$ so we choose, e.g. $\alpha = 4$, $h_\tau = \tau^4 e^{-\tau}\left(\frac{\tau}{\Gamma(6)} - \frac{\tau^{11}}{6\Gamma(16)}\right)$. Then the polynomial coefficients are obtained using a monomial expansion

$$\tau^n = n!\sum_{i=0}^{n}(-1)^i\binom{n+\alpha}{n-i}L_i^{(\alpha)}(\tau) \tag{3}$$

and substituting into (2), as

$$\begin{aligned} q_m^{(4)} &= \frac{(-1)^m\binom{5}{1-m}\Gamma(5+m)}{\Gamma(6)\binom{m+4}{m}\Gamma(5)}\delta_{m,a} \\ &\quad -\frac{11!\,(-1)^m\binom{15}{11-m}\Gamma(5+m)}{6\Gamma(16)\binom{m+4}{m}\Gamma(5)\,m!}\delta_{m,b} \end{aligned}$$

for $0 \le a \le 1$, $0 \le b \le 11$; $q_m^{(4)} = 0$ for $m > 11$. An equivalent derivation for $\alpha = 0$ follows the same procedure.

3.1.2. FSL Double Gamma Temporal Derivative

The analytic temporal derivative of the Double Gamma HRF is

$$\begin{aligned} \frac{\partial h}{\partial\tau} &= \left(\tau^{\alpha_1-2}e^{-\beta_1\tau}\right)\left(\frac{\beta_1^{\alpha_1}}{\Gamma(\alpha_1)}\right)\left((\alpha_1-1)\tau^0 - \beta_1\tau^1\right) \\ &\quad -\left(\tau^{\alpha_2-2}e^{-\beta_2\tau}\right)\left(\frac{c\beta_2^{\alpha_2}}{\Gamma(\alpha_2)}\right)\left((\alpha_2-1)\tau^0 - \beta_2\tau^1\right) \end{aligned}$$

via the product rule. Substituting the parameter values for the FSL DG function gives

$$\frac{\partial h}{\partial\tau} = \left(\tau^4 e^{-\tau}\right)\left(\frac{5\tau^0 - \tau^1}{\Gamma(6)} - \frac{15\tau^{10} - \tau^{11}}{6\Gamma(16)}\right)$$

so using $\alpha = 4$ in (2) and (3) we get an expansion as $h(\tau) = w^{(4)}(\tau)\, q(\tau)$, $w^{(4)}(\tau) = \tau^4 e^{-\tau}$ and coefficients

$$\begin{aligned} q_m &= \frac{5}{\Gamma(6)}\delta_{m,0} - \frac{(-1)^m\binom{5}{1-m}\Gamma(5+m)}{\binom{m+4}{m}\Gamma(5)\,\Gamma(6)\,m!}\delta_{m,a} \\ &\quad -\frac{15\,(10!)\,(-1)^m\binom{14}{10-m}\Gamma(5+m)}{\binom{m+4}{m}\Gamma(5)\,6\Gamma(16)\,m!}\delta_{m,b} \\ &\quad +\frac{(11!)\,(-1)^m\binom{15}{11-m}\Gamma(5+m)}{\binom{m+4}{m}\Gamma(5)\,6\Gamma(16)\,m!}\delta_{m,c} \end{aligned}$$

for $0 \le a \le 1$, $0 \le b \le 10$ and $0 \le c \le 11$. Then $q_m = 0$ for $m > 11$ which gives a finite expansion of $\frac{\partial h}{\partial\tau}$ in terms of weighted Laguerre polynomials as required.

3.1.3. SPM Double Gamma Temporal Derivative

Since the SPM temporal derivative is expressed as a difference between 1-second delayed signals,

$$\begin{aligned} \frac{\partial h}{\partial\tau} &\approx h_\tau - h_{\tau-T} \\ &= \left(\frac{\tau^5 e^{-\tau}}{\Gamma(6)} - \frac{\tau^{15}e^{-\tau}}{6\,\Gamma(16)}\right) \\ &\quad -\left(\frac{(\tau-T)^5\,e^{-(\tau-T)}}{\Gamma(6)} - \frac{(\tau-T)^{15}\,e^{-(\tau-T)}}{6\,\Gamma(16)}\right) \end{aligned}$$

we represent this via binomial expansion with time delay $T = 1$ second as

$$h_\tau - h_{\tau-1} = \tau^0 e^{-\tau}\left(\frac{\tau^5 - \sum_{k=0}^{5}\binom{5}{k}(-1)^{5-k}\tau^k e^1}{\Gamma(6)} - \frac{\tau^{15} - \sum_{k=0}^{15}\binom{15}{k}(-1)^{15-k}\tau^k e^1}{6\,\Gamma(16)}\right)$$

Now we must use $\alpha = 0$ in (2) and (3) to expand in terms of weighted Laguerre polynomials with coefficients

$$\begin{aligned} q_m^{(0)} &= \frac{5!\,(-1)^m\binom{5}{5-m}\Gamma(m+1)}{\binom{m}{m}\Gamma(1)\,\Gamma(6)\,m!}\delta_{m,a} \\ &\quad - \frac{15!\,(-1)^m\binom{15}{15-m}\Gamma(m+1)}{\binom{m}{m}\Gamma(1)\,6\Gamma(16)\,m!}\delta_{m,b} \\ &\quad - \sum_{k=0}^{5}\frac{\binom{5}{k}(-1)^{5-k}e^1 k!\,(-1)^m\binom{k}{k-m}\Gamma(m+1)}{\binom{m}{m}\Gamma(1)\,\Gamma(6)\,m!}\delta_{m,k} \\ &\quad + \sum_{k=0}^{15}\frac{\binom{15}{k}(-1)^{15-k}e^1 k!\,(-1)^m\binom{k}{k-m}\Gamma(m+1)}{\binom{m}{m}\Gamma(1)\,6\Gamma(16)\,m!}\delta_{m,k} \end{aligned}$$

for $0 \le a \le 5$, $0 \le b \le 15$; $q_m^{(0)} = 0$ for $m > 15$. This expansion is exact for all fMRI data with TR $> T$ ($T = 1$ second here) due to the non-causal expansion of the signal $h_{\tau-T}$, and closely approximates convergence otherwise.

3.2. Lagrange Multiplier test

We design the test in the frequency domain. The model is

$$\begin{aligned} y_{[k]} &= \mu_{[k]} + v_{[k]},\ k = 0, \ldots, T-1 \\ \mu_{[k]} &= d_{[k]}^T\gamma + \xi_{[k]}^T\beta \\ \beta &= (\beta_0, \ldots, \beta_q)^T \\ \xi_{[k],j} &= \text{DFT at frequency } k \text{ of} \\ &\quad \left\{L_j^{(\alpha)}(\tau)\, w(\tau) * u(\tau)\right\} \\ &\quad \text{sampled at } \tau = t\delta \\ \delta &= \text{sampling interval} = \text{TR} \end{aligned}$$

where d_k^T models baseline + drift with orthogonal monomials, $u(\tau)$ is the input stimulus pattern and convolves with weighted Laguerre polynomials to give the hemodynamic response ξ. The null hypothesis is

$$\begin{aligned} H_0:\ \beta &= \left(\varrho^T, \mathbf{0}^T\right)^T\Phi \\ \varrho &= \left[\rho^{\text{DG}}, \rho^{\text{Time}}\right]_{m\times 2} \end{aligned}$$

where ρ^{DG}, ρ^{Time} are the Laguerre polynomial coefficients for the standard Double Gamma HRF and Time-derivative as derived in Section 3.1. m is the maximum Laguerre order among the DG and TD Laguerre expansions. $\Phi = [\phi_{\text{DG}}, \phi_{\text{Time}}]^T$ are scalar amplitudes which scale the entire HRF or HRF-derivative under the null hypothesis. ϱ is an $(m \times 2)$ vector matrix and $\mathbf{0}$ is a $((q-m)\times 2)$ vector matrix of zeros.

So we fit the model under H_0:

$$\begin{aligned} y_{[k]} &= d_{[k]}^T\gamma + \xi_{[k]}^T\left(\varrho^T, \mathbf{0}^T\right)^T\Phi + v_{[k]} \\ \text{cov}\left(v_{[k]}, v_{[l]}^*\right) &= \delta_{k,l}F_{[k]}(\alpha) \\ F_{[k]}(\alpha) &= \text{AR} + \text{white noise spectrum} \end{aligned}$$

Calculate residuals of the constrained model as

$$\tilde{v}_{[k]} = y_{[k]} - d_{[k]}^T\tilde{\gamma} - \xi_{[k]}^T\left(\varrho^T, \mathbf{0}^T\right)^T\tilde{\Phi}$$

then calculate regressors as

$$\begin{aligned} X &= \left[\frac{\partial h^T}{\partial\psi}\right] = \left[\frac{\partial\mu^T}{\partial\psi}\right] = \left[\frac{\partial\mu^T}{\partial\gamma}, \frac{\partial\mu^T}{\partial\Phi}\right] \\ &= \left[\frac{\partial\mu^T}{\partial\gamma}, \frac{\partial\mu^T}{\partial\phi_{\text{DG}}}, \frac{\partial\mu^T}{\partial\phi_{\text{Time}}}\right] \\ &= \left[d_{[k]}^T, \xi_{[k]}^T\rho^{\text{DG}}, \xi_{[k]}^T\rho^{\text{Time}}\right] \\ Z &= \left[\frac{\partial h^T}{\partial\pi}\right] = \left[\frac{\partial\mu^T}{\partial\pi}\right] = \left[\frac{\partial\mu^T}{\partial\beta_0}, \ldots, \frac{\partial\mu^T}{\partial\beta_q}\right] \\ &= \left[\xi_{[k],0}^T, \ldots, \xi_{[k],q}^T\right] \end{aligned}$$

and evaluating the regressors under the null hypothesis,

$$\begin{aligned} \tilde{X} &= X|_{\pi=0} = X = \left[\tilde{x}_{[k]}^T\right] \\ \tilde{Z} &= Z|_{\pi=0} = Z = \left[\tilde{z}_{[k]}^T\right] \end{aligned}$$

Then calculate the test statistic of (1) at each voxel to form a spatial map of model violation.

To test the FSL DG+TD model, $\alpha = 4$ so ξ comprises filtered and sampled $L^{(4)}(\tau)$ polynomials ($0 \le \alpha < 4$ could also be used but would reduce the degrees of freedom of the subsequent model fit). Testing the SPM DG+TD model requires $\alpha = 0$.

4. RESULTS

Results are from real and simulated fMRI data. In all cases the test statistic has a threshold applied at the $\alpha = 0.01$ level of the χ^2_{p-r} distribution and we use the Bonferroni method to correct for simultaneous inference. We use the Bayesian Information Criterion to choose the Laguerre basis order q at each voxel.

4.1. Simulation

Simulation involved embedding block- and event-type stimulus signal in a slice of real resting-state fMRI data, 50×50 voxels. Half the voxels, chosen randomly, were embedded with a simulated HRF signal designed to be plausibly similar to a real hemodynamic response shape but which violates a BOLD activation model which uses the DG+TD HRF specification. Signal was embedded at SNR $= 1.2$, equivalent to estimates from real data.

Testing for increasing numbers of Laguerre basis functions fitted to the data (Fig. 1) gives an increasing true-positive rate as expected. Therefore the LM-anomaly test is able to detect BOLD activation signal within fMRI data which is not adequately modelled by the DG+TD basis. Results are consistent under variation of parameters.

4.2. Real Data

Single subject real data is from the same experiment as analysed in [4, 3]. Including movement parameters from preprocessing as model regressors does not affect the analyses herein. Results from testing the DG+TD HRF models from both SPM and FSL software are largely equivalent so for space considerations we only discuss the results from the SPM model analysis.

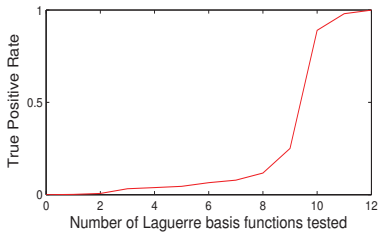
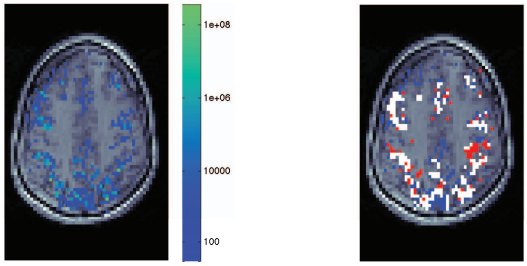


Fig. 1: Statistical power as a function of the number of basis functions tested in addition to the fitted Double Gamma plus Time Derivative Laguerre basis set.



(a) (b)

Fig. 2: Fig. (a) shows an LM-anomaly map of voxels violating the Double Gamma plus Time Derivative HRF model, with colour representing significant model violation above a threshold of $\alpha = 0.01$. Fig. (b) shows voxels detected separately by the DG+TD LM-anomaly test statistic (blue), the conventional Least-Squares activation test using DG+TD HRF specification (red) and both (white).

The LM-anomaly test statistic shows large areas of model violation for the SPM DG+TD HRF model applied to this particular data (Fig. 2a). Many of the detected anomaly voxels also overlap with those detected using a DG+TD model in a BOLD activation test (Fig. 2b).

This does not infer that every single voxel which violates the DG+TD model indicates a false positive or false negative result for the corresponding activation test, but rather indicates that the DG+TD activation test is not reliable at those voxels and we require an HRF model which can account for more complicated signals.

As well as being due to misfit of the DG+TD model, false positive or negative detection of voxels in this data could also be due to the corrupting influence of other signal characteristics, e.g. non-stationary noise or temporal delay within the activation signal. It is important that this test is applied in conjunction with other anomaly tests (such as those developed in [3]) to test the validity of all underlying model assumptions, thereby justifying an appropriate model which can be used for subsequent analysis.

Regardless, the linear DG+TD HRF model is insufficient for modeling the information within this fMRI data and a better model must be used to properly detect BOLD activation.

Analysis of multiple subject data from the fMRI Data Center repository (*www.fmridc.org*, Item: 2-2005-1198T [10]) shows violation of the DG+TD model somewhere throughout the brain volume in $353/456 \approx 77\%$ of tests, across all applicable combinations of subject, intra-subject session and input-stimulus pattern.

We suggest that data containing any DG+TD model violation is instead analysed using a more general nonparametric HRF, e.g. FIR or Laguerre basis model.

5. CONCLUSION

A common model for the hemodynamic response function in fMRI is a combination of a Double Gamma function and its temporal derivative. Using a Lagrange Multiplier hypothesis testing framework we have developed a diagnostic test for the validity of this model on particular fMRI data. The approach has the significant computational advantage of only requiring model fitting under the null, so can be easily added to standard analysis procedures.

Real and simulated data examples show that the LM-anomaly test is able to detect model violation. Analysis of multiple subject real data shows extensive failure of the Double Gamma plus Time-derivative HRF model. This test should be applied in conjunction with other LM-anomaly tests to accurately critique a proposed model for fMRI analysis.

Future work will involve extending this test to the SPM HRF model which includes the Double Gamma function, temporal and dispersion derivatives.

6. REFERENCES

[1] M. Lindquist, "The statistical analysis of fMRI data," *Statistical Science*, vol. 23, no. 4, pp. 439–464, 2008.

[2] G. Boynton, S. Engel, G. Glover, and D. Heeger, "Linear Systems Analysis of Functional Magnetic Resonance Imaging in Human V1," *Journal of Neuroscience*, vol. 16, no. 13, pp. 4207–4221, 1996.

[3] B. Cassidy, C. Long, C. Rae, and V. Solo, "Identifying fMRI model violations with lagrange multiplier tests," *submitted for publication*.

[4] V. Solo, B. Cassidy, C. Long, and C. Rae, "Time-to-onset latency in fMRI: Fast detection of delayed activation," in *Acoustics, Speech and Signal Processing (ICASSP), 2011 IEEE International Conference on*, pp. 725–728, 2011.

[5] S. Silvey, "The Lagrangian multiplier test," *The Annals of Mathematical Statistics*, pp. 389–407, 1959.

[6] A. Buse, "The likelihood ratio, Wald, and Lagrange multiplier tests: An expository note," *American Statistician*, pp. 153–157, 1982.

[7] K. Friston, P. Fletcher, O. Josephs, A. Holmes, M. Rugg, and R. Turner, "Event-related fmri: Characterizing differential responses," *Neuroimage*, vol. 7, no. 1, pp. 30–40, 1998.

[8] S. Smith, M. Jenkinson, M. Woolrich, C. Beckmann, T. Behrens, H. Johansen-Berg, P. Bannister, M. De Luca, I. Drobnjak, D. Flitney, *et al.*, "Advances in functional and structural MR image analysis and implementation as FSL," *Neuroimage*, vol. 23, pp. 208–219, 2004.

[9] M. Burock and A. Dale, "Estimation and detection of event-related fMRI signals with temporally correlated noise: A statistically efficient and unbiased approach," *Human Brain Mapping*, vol. 11, no. 4, pp. 249–260, 2000.

[10] V. Venkatraman, S. Siong, M. Chee, and D. Ansari, "Effect of language switching on arithmetic: A bilingual fmri study," *Journal of Cognitive Neuroscience*, vol. 18, no. 1, pp. 64–74, 2006.