GENERAL LINEAR MODELS UNDER RICIAN NOISE FOR FMRI DATA

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ABSTRACT

When analyzing fMRI data to study the brain process, one faces two challenges: (i) the correct noise distribution and (ii) the brain dynamics. In general, the brain dynamics are modeled under the simplifying, but wrong assumption that the noise follows a Gaussian distribution. In this paper, we model the brain dynamics under the correct Rice distribution. We implement the hemodynamic response function into a Rice framework and apply the standard General Linear Model (GLM) which is linear-in-the-parameters and can easily be solved. Next, the statistical properties of the least squares estimator are investigated via a simulation experiment.

***Index Terms*—** Biomedical signal processing, functional magnetic resonance imaging (fMRI), hemodynamic response, Rice distribution, parameter estimation.

1. INTRODUCTION

The most popular diagnostic technique to study and visualize human brain activity is functional Magnetic Resonance Imaging (fMRI). Analyzing fMRI data remains a difficult task, mainly for two reasons. First of all, the fMRI signals to be processed are strongly disturbed by Rician noise [1], [2]. Secondly, the human brain has a memory effect and, hence, responds with a delay. When imaging the human brain to detect brain activity, the brain dynamics or so-called hemodynamics can be neglected. However, when studying and analyzing the brain process, the brain dynamics need to be taken into account [3].

The standard dynamic modeling approach to handle fMRI signals is the General Linear Model (GLM) [4], in which the fMRI signal is basically modeled as the convolution of the fMRI paradigm with a hemodynamic response function [5], disturbed by additive Gaussian noise. This approach is however only valid for high signal-to-noise ratios (SNRs), since in that case the true Rician noise distribution converges weakly to a Gaussian distribution [6]. For low SNRs, the assumption of additive Gaussian noise is no longer valid such that the true Rician noise characteristics should be taken into account.

Two upcoming fMRI trends indicate that the presence of low SNRs in fMRI will become more and more dominant. Firstly, for patient safety reasons it is desirable to reduce the magnetic field strength. Secondly, open MRI scanners which were originally designed for children, claustrophobic and obese persons will become the scanners of the future. These scanners use lower field strengths than their closed counterpart. In both trends, a reduction in field strength goes hand in hand with a reduction in image quality or SNR, for the same measurement time. This shows that the true noise distribution of fMRI signals can no longer be ignored.

In this paper, we will investigate the quality of the general linear model under Rician noise conditions. The outline is as follows: First, a brief introduction to fMRI is given. Next, the modeling framework is discussed in Section 3; the model identification in Section 4; and the simulation experiment in Section 5. Finally, conclusions are drawn in Section 6.

This work is funded by a post-doctoral fellowship of the Flemish Research Foundation (FWO-Vlaanderen).

2. FUNCTIONAL MAGNETIC RESONANCE IMAGING

2.1 Measurement principle

In fMRI measurements, typically two orthogonal measurement coils are used, decomposing the induced current in a real and an imaginary component. Due to measurement errors, physical and physiological noise sources [7], each of these two currents is disturbed by additive, Gaussian distributed noise. Hence, the induced current $x(t)$ is given by

$$x(t) \triangleq \mathcal{N}(A\cos(\omega_0 t), \sigma^2) + j\mathcal{N}(A\sin(\omega_0 t), \sigma^2) \quad (1)$$

where $\triangleq$ symbolizes the equality in distribution, ω_0 is the frequency of the applied magnetic field, A is the amplitude of the induced current, $\mathcal{N}(a,b)$ denotes a Gaussian distribution with mean a and variance b, and j indicates the imaginary unit.

An fMRI signal is in essence complex-valued, but since the phase information of $x(t)$ exhibits a time-varying behavior [8], [9], it is considered unfruitful. As a result, only the magnitude of the fMRI signal is retained for further analysis.

2.2 Rice distribution

The price paid for discarding the phase information is that the noise is no longer additive and Gaussian distributed, but instead follows a Rice distribution [1], [2].

$$y(t) = |x(t)| \triangleq \text{Rice}(A, \sigma^2) \tag{2}$$

The Rice distribution is characterized by two parameters: the amplitude A of the periodic signal and the variance σ^2 of the disturbing Gaussian noise source. It is known that for high SNRs, the Rice distribution in (2) converges to a normal distribution $\mathcal{N}(A, \sigma^2)$ [6].

The probability density function (pdf) of Rice data is given by

$$f_Y(y) = \frac{y}{\sigma^2} \exp\left(-\frac{y^2 + A^2}{2\sigma^2}\right) I_0\left(\frac{yA}{\sigma^2}\right) \tag{3}$$

with $I_0(.)$ the zero-order modified Bessel function of the first kind [11].

2.3 Hemodynamic response

The goal of fMRI is two-folded: (1) detecting activated brain regions and (2) characterizing the physiological process of activated brain regions, due to an external stimulus. For the second objective, the hemodynamics (i.e., the blood flow) needs to be taken into account [3]. Indeed, upon stimulus, the activated brain areas require more oxygen and glucose to function properly. This implies a change in blood flow which is known as the hemodynamic response (HDR).

A popular kernel function to describe the unknown hemodynamic response is the double-Gamma function [5], [12], since it corresponds well to the true physiological brain reaction. The double-Gamma function is represented by

$$h(t|\theta) = c_1 \frac{t^{\alpha_1 - 1}}{\Gamma(\alpha_1)} \exp(\rho_1 t) + c_2 \frac{t^{\alpha_2 - 1}}{\Gamma(\alpha_2)} \exp(\rho_2 t) \tag{4}$$

where $\Gamma(.)$ denotes the Gamma function, $c_1 \geq c_2$ and $\theta = [c_1, \alpha_1, \rho_1, c_2, \alpha_2, \rho_2] \in \mathbb{R}^6$.

Transforming (4) to the frequency domain by means of the Laplace transform gives:

$$H(s|\theta) = c_1 \frac{1}{(s - \rho_1)^{\alpha_1}} + c_2 \frac{1}{(s - \rho_2)^{\alpha_2}} \tag{5}$$

with $s \in \mathbb{C}$ the Laplace variable.

3. MODELING FRAMEWORK

3.1 Statistical model

Generally, the observed fMRI signals are modeled as the convolution of the fMRI paradigm $u(t)$ with the (unknown) hemodynamic response, disturbed by Gaussian noise $n_y(t)$. The General Linear Model describing the measurements is then given by [5]

$$y_{\text{Gauss}}(t) = h(t|\theta) * u(t) + n_y(t) \tag{6}$$

with $*$ the convolution operator. Due to the additive nature of $n_y(t)$, the GLM representation in (6) is no longer valid under Rice conditions.

In order to combine the true Rician noise distribution and the hemodynamics, we introduce the hemodynamic response in (2). This results in

$$y_{\text{Rice}}(t) \triangleq \text{Rice}(h(t|\theta) * u(t), \sigma^2) \tag{7}$$

with $h(t|\theta)$ as defined in (4).

3.2 Linear regression model for the HDR

Estimating the parameters θ is a problem that is nonlinear-in-the-parameters. To avoid this, the estimation problem is transformed into a problem that is linear-in-the-parameters by applying a linear regression model for the hemodynamic response.

The canonical values of the parameters θ in (4) are derived from experimental data and physiological knowledge. In the software package SPM, these values are $\theta_c = [11.71, 7, -1.11, -3.06, 13, -1.11]$ [13]. By implementing, θ_c into (4), the canonical HDR is obtained $h_c(t) = h(t|\theta_c)$. Since the canonical parameter values are only a 'rough' estimate of the true parameter values, they need to be corrected according to the experimental data, as described in [14]. In this paper, it is assumed that the canonical HDR approximately holds with a possible unknown dispersion ε and time delay δ. As a result, the hemodynamic response is approximated by

$$h(t|\theta) \approx h(\varepsilon(t - \delta)|\theta_c) \tag{8}$$

Next, a first order Taylor approximation is applied to (8) around the canonical parameter vector ($\varepsilon = 1, \delta = 0$):

$$\begin{aligned} h(t|\theta) \approx h(t|\theta_c) &+ \frac{\partial}{\partial \varepsilon} h(\varepsilon(t - \delta)|\theta_c)\Big|_{\substack{\varepsilon=1 \\ \delta=0}} (\varepsilon - 1) \\ &+ \frac{\partial}{\partial \delta} h(\varepsilon(t - \delta)|\theta_c)\Big|_{\substack{\varepsilon=1 \\ \delta=0}} \delta \end{aligned} \tag{9}$$

After applying the chain-rule to (9), we obtain the following result:

Proposition 1. Under assumption (8), the HDR can be approximated as

$$\begin{aligned} h(t|\theta) \approx h(t|\theta_c) &+ \frac{\partial}{\partial t} h(t|\theta_c) t(\varepsilon - 1) \\ &- \frac{\partial}{\partial t} h(t|\theta_c) \delta \end{aligned} \tag{10}$$

The first term in (10) is known as the canonical response, the second term as the dispersion derivative, and the last term as the temporal derivative [14], [15]. These different terms are illustrated in Figure 1.

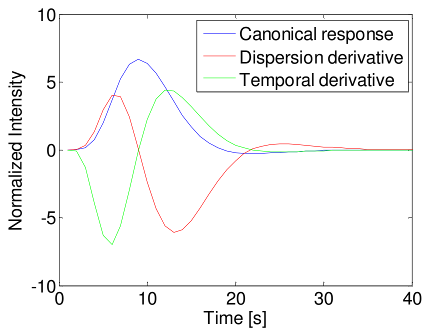

Figure 1: Illustration of the double-gamma function and its partial derivatives.

Based on Proposition 1, the following linear regression model $h_{LR}(t|\beta)$ is obtained for the unknown hemodynamic response $h(t|\theta)$:

$$h_{LR}(t|\beta) = \beta_1 h(t|\theta_c) + \beta_2 \frac{\partial}{\partial t} h(t|\theta_c)t - \beta_3 \frac{\partial}{\partial t} h(t|\theta_c) \tag{11}$$

In order not to overload the paper, we will take on the simplifying notation $h_{LR} = h_{LR}(t|\beta)$ and $h_c = h(t|\theta_c)$. In matrix notation, (11) then becomes

$$h_{LR} = \begin{bmatrix} h_c & \frac{\partial h_c}{\partial t} t & -\frac{\partial h_c}{\partial t} \end{bmatrix} \begin{bmatrix} \beta_1 \\ \beta_2 \\ \beta_3 \end{bmatrix} = R.\beta \tag{12}$$

with R the regressor matrix, and β the parameters to be estimated.

4. MODEL IDENTIFICATION

The unknown hemodynamic response in (7) can now be modeled using the linear regression model in (11). Hence, we obtain:

$$\begin{aligned} y_{\text{Rice}} &\triangleq \text{Rice}(y_0, \sigma^2) \\ &\triangleq \left| \mathcal{N}\big(y_0 \cos(\omega_0 t), \sigma^2\big) + j\mathcal{N}\big(y_0 \sin(\omega_0 t), \sigma^2\big) \right| \end{aligned} \tag{13}$$

with the noise-free fMRI signal y_0 defined as

$$y_0 = h_{LR} * u = (R * u).\beta = R_u.\beta \tag{14}$$

Since for high SNRs, the Rice distribution weakly converges to a normal distribution [6], we formulate the following property:

Proposition 2. The measured fMRI signal converges to a normal distribution

$$y_{\text{Rice}} \xrightarrow{\Delta} \mathcal{N}(y_0, \sigma^2) \ \text{ if } \ \frac{\text{range}(y_0)}{\sigma} \to \infty \tag{15}$$

The parameters β can be identified in Least Squares (LS) sense by solving the following optimization:

$$\hat{\beta}_{LS} = \underset{\beta}{\text{argmin}} |y_{\text{Rice}} - R_u.\beta|^2 \tag{16}$$

The least squares solution is then given by

$$\hat{\beta}_{LS} = ({R_u}^{\tau} R_u)^{-1} {R_u}^{\tau} y_{\text{Rice}} \tag{17}$$

with τ the transpose operator. The following holds for the Rician LS estimator.

Theorem 1. Under Rice conditions, the following properties hold for the least squares estimator:

$$\begin{aligned} \text{E}\big[\hat{\beta}_{LS}\big] &= \beta_0 + b \\ \text{cov}\big(\hat{\beta}_{LS}\big) &= \alpha \frac{({R_u}^{\tau} R_u)^{-1}}{\sigma^2} \end{aligned} \tag{18}$$

with β_0 the true parameter values, b the bias term, and the factor α representing the efficiency loss.

For high SNRs, Theorem 1 reduces to $b = 0$ and $\alpha = 1$. We will now study how the bias vanishes and the efficiency loss drops to 1 as a function of the SNR.

5. SIMULATION EXPERIMENT

In the simulation experiment, we used a block paradigm consisting of 6 periods with 40 samples per period, corresponding to 20 samples for the activation phase and 20 samples for the rest phase. The block paradigm is modeled as a block wave equaling 1 for activation and 0 for rest. The sampling frequency was set to 0.75Hz.

The goal is to estimate the parameters $\beta = [\beta_1 \ \ \beta_2 \ \ \beta_3]$ of the linear regression model (11) in the Rice framework and to compare the results with the classical Gaussian approach. First, the true parameters β were set in order to compute the noise-free fMRI signal y_0 as given in (14). For the true hemodynamic response, we used the double-gamma function as defined in (5) with parameters $\theta = \theta_c + \Delta\theta_c$.

The noisy fMRI signal is obtained in the Rice framework by applying (13), and in the Gaussian framework by adding normally distributed noise to y_0. In Figure 2, an example of simulated fMRI signals are shown (for an SNR equal to 1), together with the block paradigm (black). The noise-free signal is given in blue, and the noisy signal is plotted in red and green for respectively, the Rice and Gaussian framework.

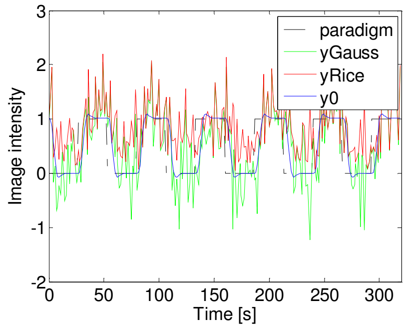

Figure 2: Simulated fMRI signals with a block paradigm: noise-free signal (blue), noisy signal in the Gaussian framework (green) and in the Rice framework (red).

Since the SNR (defined as y_0/σ) influences the signal's distribution, we explore different SNRs by varying the standard deviation (std) from 0.1 to 20. For each SNR, we performed a Monte Carlo simulation of 10000 runs in which we computed the least squares estimator and studied its statistical properties. In Figure 3, the root mean square error (RMSE) and the bias for parameter β_1 are shown for both the Rice (red) and the Gaussian (green) framework. The results for the other parameters are similar.

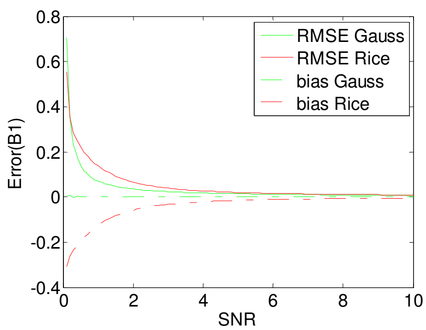

Figure 3: The RMSE (full line) and the bias (dash-dotted line) of parameter β_1 of the linear regression model: (red) Rice and (green) Gaussian framework.

It can be seen that for high SNRs the bias in the Rice framework converges to the bias of the Gaussian framework which is zero. Hence, asymptotically there is a good fit of the parameters of the linear regression model in (11) used to describe the hemodynamic response.

The bias of the different model parameters is plotted on a log-log scale in Figure 4. It follows that for a sufficiently high SNR the bias decreases almost linearly.

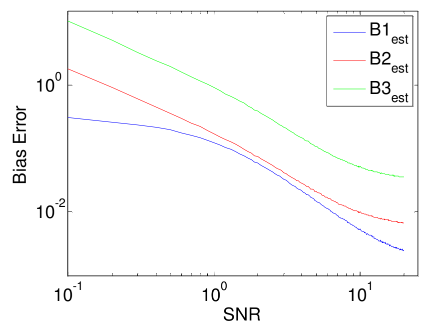

Figure 4: Bias of the estimated parameters in the Rice framework: $\widehat{\beta}_1$ (blue), $\widehat{\beta}_2$ (red) and $\widehat{\beta}_3$ (green).

In Figure 5, one realization of the model output is plotted together with the noise-free signal, for an SNR equal to 1 and 5. For SNR=1, the true shape is captured by the model, but there exists an overestimation. For SNR=5, we observe a very good fit between the modeled signal in the Rice framework and the true brain response.

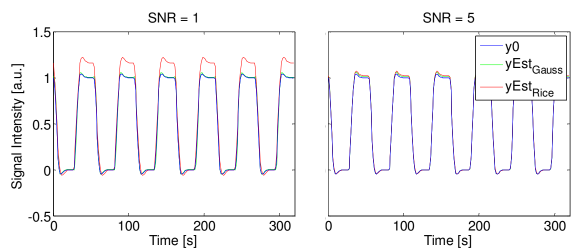

Figure 5: Model output: noise-free (blue), in the Rice framework (red) and in the Gaussian framework (green).

6. CONCLUSION

In this paper, the impact of Rice distributed data on the existing GLM framework was investigated. This study revealed that asymptotically, for high SNRs, the least squares estimator of the GLM is not influenced by the Rice distribution. As a result, the presented GLM approach is successful for modeling the brain dynamics. However, for fMRI signal detection this approach overestimates the SNR, which implies the need for a low SNR correction for the LS estimator in order to compensate for the Rician noise characteristics.

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