DETECTION OF BRAIN ACTIVATION FROM MAGNITUDE FMRI DATA USING A GENERALIZED LIKELIHOOD RATIO TEST

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ABSTRACT

Functional magnetic resonance imaging (fMRI) measures the hemodynamic response in the brain that signals neural activity. The purpose is to detect those regions in the brain that show significant neural activity upon stimulus presentation. Most statistical fMRI tests used for this purpose rely on the assumption that the noise disturbing the data is Gaussian distributed. However, the majority of fMRI studies employ magnitude image reconstructions that are known to be Rician distributed, and hence corrupted by non-Gaussian distributed noise. In this work, we propose a Generalized Likelihood Ratio Test (GLRT) for magnitude MRI data that exploits the knowledge of the Rician distribution. The performance of the proposed GLRT is evaluated by means of Monte Carlo simulations.

1. INTRODUCTION

Functional magnetic resonance (fMRI) studies intend to answer neuroscience questions by statistically analyzing a set of acquired images. Thereby, the aim is to determine those regions in the brain image in which the signal changes upon stimulus presentation. Although MR data are intrinsically complex valued, most tests are commonly applied to magnitude MR images, because these images have the advantage to be immune to incidental phase variations due to various sources [1]. A consequence of transforming the complex valued images into magnitude images is a change of the probability density function (PDF) of the data under concern. Whereas complex data are Gaussian distributed, magnitude data are Rician distributed [2]. Nevertheless, tests applied to magnitude data generally rely on the assumption of Gaussian distributed data. If the signal-to-noise ratio (SNR) of the data is high, this may be a valid assumption since the Rician PDF tends to a Gaussian PDF at increasing levels of the SNR. However, at low SNR, the Rician PDF significantly deviates from a Gaussian PDF. In this paper, we propose a Generalized Likelihood Ratio Test (GLRT) for magnitude fMRI data that fully exploits the knowledge of the Rician PDF.

The organization of this paper is as follows. Section 2 briefly reviews the general theory for the construction of a GLRT. In section 3, two GLRTs for magnitude data are described. The first GLRT is known as the General Linear Model Test (GLMT) [3]. It is based on the assumption of Gaussian distributed data. The second GLRT is newly proposed in this paper. It is based on the Rician PDF of the magnitude data. Section 4 describes the simulation experiments that have been conducted so as to assess the performance of the tests. Finally, conclusions are drawn in section 5.

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2. THE GENERALIZED LIKELIHOOD RATIO TEST

Let $\underline{\boldsymbol{m}} = (\underline{m}_1, ..., \underline{m}_N)^T$ be a random sample vector with joint PDF $p_{\underline{\boldsymbol{m}}}(\boldsymbol{x};\boldsymbol{\theta})$, in which $\boldsymbol{\theta} = (\theta_1, ..., \theta_k)^T$ denotes the vector of unknown parameters and $\boldsymbol{x} = (x_1, ..., x_N)^T$ represents the vector of variables corresponding to the random sample vector $\underline{\boldsymbol{m}}$. In this paper, random variables are underlined, small bold characters denote vectors, and capital bold characters denote matrices. The superscript T denotes matrix transposition. Suppose that we wish to test the composite null hypothesis H_0:

$$H_0 : \theta_1 = \theta_1^0, \cdots, \theta_r = \theta_r^0, \theta_{r+1}, \cdots, \theta_k \tag{1}$$

where $\theta_1^0, ..., \theta_r^0$ are known and $\theta_{r+1}, ..., \theta_k$ are left unspecified, against the alternative composite hypothesis H_1 under which all parameters $\theta_1, ..., \theta_k$ are left unspecified.

Next, suppose that we have a set of observations $\boldsymbol{m} = (m_1, ..., m_N)^T$, and that we substitute these observations for the corresponding variables $\boldsymbol{x}$ in the joint PDF of the random sample $\underline{\boldsymbol{m}}$. The resulting function is a function of the unknown parameter vector $\boldsymbol{\theta}$ only. By regarding these parameters as variables, the so called likelihood function $L(\boldsymbol{\theta};\boldsymbol{m})$ is obtained. Then the generalized likelihood ratio (GLR) λ is defined as follows [4]:

$$\lambda \equiv \lambda(\boldsymbol{m}) = \frac{\sup\limits_{\theta_1,\cdots,\theta_k} L(\theta_1, \cdots, \theta_k; \boldsymbol{m})}{\sup\limits_{\theta_{r+1},\cdots,\theta_k} L\left(\theta_1^0, \cdots, \theta_r^0, \theta_{r+1}, \cdots, \theta_k; \boldsymbol{m}\right)} \tag{2}$$

Note that λ is a function of the observations $\boldsymbol{m}$ only. If these observations are replaced by their corresponding random variables $\underline{\boldsymbol{m}}$, then we write $\underline{\lambda}$ for λ, that is, $\underline{\lambda} = \lambda(\underline{\boldsymbol{m}})$. Note that the denominator of $\underline{\lambda}$ is the likelihood function evaluated at the Maximum Likelihood (ML) estimator under H_0, whereas the numerator of $\underline{\lambda}$ is the likelihood function evaluated at the ML estimator under H_1. The generalized likelihood ratio test principle now states that H_0 is to be rejected if and only if the sample value λ of $\underline{\lambda}$ satisfies the inequality $\lambda \geq \lambda_0$ where λ_0 is some user specified threshold. The false alarm rate P_F is given by the probability that the test will decide H_1 when H_0 is true. The *detection rate* P_D is given by the probability that the test will decide H_1 when H_1 is true. It can be shown that, asymptotically, the test statistic $2\ln\underline{\lambda}$ possesses a χ_r^2 distribution, i.e., a chi-square distribution with r degrees of freedom, when H_0 is true [5]. This allows one to determine the proper threshold needed to achieve a desired P_F. Furthermore, a test has the so-called constant false-alarm rate (CFAR) property if the threshold required to maintain a constant P_F can be found independent of the SNR. As follows from above, GLRTs will have the CFAR property at least asymptotically. Whether or not a GLRT has the CFAR property for a finite number of observations can be found out by means of simulations. For more details on the GLRT, see [5].

3. GENERALIZED LIKELIHOOD RATIO TESTS FOR MAGNITUDE FMRI DATA

In this section, it will be shown how the theory described in the previous section can be applied to construct GLRTs for functional magnitude MR data. We considered the problem of testing whether the response of a magnitude MR data set $\boldsymbol{m}$ of sample size N to a known reference function $\boldsymbol{r} = (r_1, ..., r_N)^T$ is significant. The noiseless magnitude data set was assumed to be described by the $N \times 1$ deterministic signal vector:

$$\boldsymbol{z} = a\mathbf{1} + b\boldsymbol{r} \tag{3}$$

with $\mathbf{1}$ an $N \times 1$ vector of ones. Hence, $\boldsymbol{z}$ is a constant baseline on which a reference function $\boldsymbol{r}$ with amplitude b is superimposed. In the absence of activity, b equals zero, such that $\boldsymbol{z} \equiv a\mathbf{1}$. The hypothesis that $b = 0$ (H_0) is tested against the hypothesis that $b \neq 0$ (H_1). Two GLRTs will be considered. For both tests, it will be assumed that the deterministic signal can be described by the linear model (3). The first GLRT is based on the approximation that the data can be assumed to be disturbed by independent, zero mean, Gaussian distributed noise with variance σ^2. In the literature, this test is known as the General Linear Model Test (GLMT) [3]. The GLMT is commonly used in practice. To the authors' knowledge, it shows the best performance of all existing tests applied to magnitude data. Nevertheless, it is to be expected that the performance of the test will suffer from the inaccuracy of the Gaussian approximation (especially for low SNR, where the SNR is defined as a/σ). The second GLRT, which is the test that is proposed in this paper, exploits the knowledge of the Rician distribution of the magnitude data and is therefore expected to perform better.

3.1 The General Linear Model Test

In the derivation of this test, it has been assumed that the magnitude data can be described as follows:

$$\underline{\boldsymbol{m}} = \boldsymbol{z} + \underline{\boldsymbol{e}} \tag{4}$$

with $\underline{\boldsymbol{e}}$ an $N \times 1$ vector of which the components are zero mean, Gaussian distributed noise with variance σ^2. Under this assumption, the likelihood function of the data is given by

$$L(\boldsymbol{z};\boldsymbol{m}) = \left(\frac{1}{2\pi\sigma^2}\right)^{\frac{N}{2}} e^{-\frac{1}{2\sigma^2}\|\boldsymbol{m}-\boldsymbol{z}\|^2} \tag{5}$$

Since the data are assumed to be Gaussian distributed, the ML estimator is equal to the least-squares estimator [6]. Moreover, the parameters enter the model in Eq. (3) linearly. Therefore, closed form expressions for the ML estimators of the unspecified parameters can easily be derived.

- Under H_0, in which $\boldsymbol{z} = a\mathbf{1}$, the ML estimators $\underline{\widehat{a}}_0$ and $\underline{\widehat{\sigma_0^2}}$ of the unspecified parameters a and σ^2, respectively, are given by:

$$\underline{\widehat{a}}_0 = \frac{1}{N}\underline{\boldsymbol{m}}^T.\mathbf{1} \tag{6}$$

$$\underline{\widehat{\sigma_0^2}} = \frac{1}{N}\|\underline{\boldsymbol{m}} - \underline{\widehat{a}}_0\mathbf{1}\|^2 \tag{7}$$

- Under H_1, in which $\boldsymbol{z} = a\mathbf{1} + b\boldsymbol{r}$, the ML estimators $\underline{\widehat{a}}_1$, $\underline{\widehat{b}}$ and $\underline{\widehat{\sigma_1^2}}$ of the unspecified parameters a, b, and σ^2, respectively, are given by:

$$\begin{pmatrix}\underline{\widehat{a}}_1\\ \underline{\widehat{b}}\end{pmatrix} = (\boldsymbol{X}^T\boldsymbol{X})^{-1}\boldsymbol{X}^T\underline{\boldsymbol{m}} \tag{8}$$

$$\underline{\widehat{\sigma_1^2}} = \frac{1}{N}\|\underline{\boldsymbol{m}} - \underline{\widehat{a}}_1 - \underline{\widehat{b}}\boldsymbol{r}\|^2 \tag{9}$$

with $\boldsymbol{X}$ an $N \times 2$ matrix given by: $\boldsymbol{X} = (\mathbf{1}\ \boldsymbol{r})$.

From Eq. (2) and (5) and using the ML estimators given in Eqs. (6-9), a closed form expression for the GLR can be obtained:

$$\underline{\lambda} = \left(\frac{\underline{\widehat{\sigma_0^2}}}{\underline{\widehat{\sigma_1^2}}}\right)^{N/2} \tag{10}$$

It can be shown that under the assumption of Gaussian distributed data the test statistic

$$(N-2)(\underline{\lambda}^{2/N} - 1) \tag{11}$$

will possess an $F_{1,N-2}$ distribution, that is, an F-distribution with 1 and $N-2$ degrees of freedom, under H_0 [7]. This allows one to select a proper threshold so as to achieve a desired false alarm rate. For $P_F = \alpha$, the threshold is given by $F_{1,N-2,1-\alpha}$, that is, the $(1-\alpha)^{\text{th}}$ quantile of the $F_{1,N-2}$ distribution. The q^{th} quantile of the distribution of a continuous random variable $\underline{x}$ is defined as the smallest number η satisfying $Q_{\underline{x}}(\eta) = q$, with $Q_{\underline{x}}(x)$ the cumulative distribution function of $\underline{x}$ [4]. The test will thus reject H_0 if and only if the test statistic described by Eq. (11) exceeds this threshold.

3.2 GLRT based on the Rician distribution

Next, we will no longer assume that the magnitude data are Gaussian distributed. Instead we will now exploit the fact that we know that the magnitude data are Rician distributed. The Rician PDF of magnitude data with deterministic signal component z and noise variance σ^2, is given by [8]:

$$p_{\underline{m}}(x|z) = \frac{x}{\sigma^2}e^{-\frac{x^2+z^2}{2\sigma^2}} I_0\left(\frac{zx}{\sigma^2}\right) \tag{12}$$

where I_0 is the zeroth order modified Bessel function of the first kind. It will be assumed that the noise variance σ^2 is known. This is usually a valid assumption, since the noise variance can mostly be estimated independently, with high accuracy and precision, from a region of background noise, away from any image signal [9, 10]. In that case, the likelihood functions for the Rician distributed data under H_0 and H_1 are given by

$$L(a;\boldsymbol{m}) = \prod_{n=1}^{N}\frac{m_n}{\sigma^2}e^{-\frac{m_n^2+a^2}{2\sigma^2}} I_0\left(\frac{m_n a}{\sigma^2}\right) \tag{13}$$

$$L(a,b;\boldsymbol{m}) = \prod_{n=1}^{N}\frac{m_n}{\sigma^2}e^{-\frac{m_n^2+(a+br_n)^2}{2\sigma^2}} I_0\left(\frac{m_n(a+br_n)}{\sigma^2}\right) \tag{14}$$

respectively, and the likelihood ratio test statistic is given by:

$$\underline{\lambda} = \frac{\sup_{a,b} L(a,b;\underline{\boldsymbol{m}})}{\sup_{a} L(a;\underline{\boldsymbol{m}})} \tag{15}$$

The modified test statistic $2\ln\underline{\lambda}$ can then be written explicitly as:

$$2\ln\underline{\lambda} = 2\sum_{n=1}^{N}\ln\left[\frac{I_0\left(\frac{\underline{m}_n\underline{\widehat{a}}_0}{\sigma^2}\right)}{I_0\left(\frac{\underline{m}_n(\underline{\widehat{a}}_1+\underline{\widehat{b}}r_n)}{\sigma^2}\right)}\right] - \frac{N\underline{\widehat{a}}_0^2}{\sigma^2} + \frac{1}{\sigma^2}\sum_{n=1}^{N}\left(\underline{\widehat{a}}_1 + \underline{\widehat{b}}r_n\right)^2 \tag{16}$$

with $\underline{\widehat{a}}_0$ and $(\underline{\widehat{a}}_1, \underline{\widehat{b}})$ the ML estimators of the unspecified parameters under H_0 and H_1, respectively. The ML estimates can be found by maximizing the likelihood functions (13) and (14) with respect to the parameter a and the parameters a and b, respectively. Notice that the maximization of these likelihood functions is a nonlinear optimization problem for which no closed form solution exists. The solution can be found by means of iterative numerical optimization methods. The test statistic in Eq. (16) is asymptotically distributed as a χ_1^2 random variable when H_0 is true. The test will select H_1 if and only if this test statistic exceeds a user specified threshold value η. In order to achieve a desired $P_F = \alpha$, the threshold can thus be chosen equal to $\chi^2_{1,1-\alpha}$, that is, the $(1-\alpha)^{\text{th}}$ quantile of the χ_1^2 distribution.

4. SIMULATION EXPERIMENTS

Exhaustive Monte Carlo simulation experiments were set up to evaluate the performance of the GLMT and the Rician PDF based GLRT. For this purpose, numerous realizations of time series of N Rician distributed magnitude data points were generated of which the deterministic signal components are described by Eq. (3). Two reference functions were considered: a square wave and a square wave convolved with a hemodynamic response function (HRF).

Square wave The square wave reference function $s(t)$ considered fluctuates between -1 and +1 with period 20.

HRF model A more realistic reference function is obtained from a convolution of the square wave $s(t)$ with an HRF:

$$r(t) = \int_0^{+\infty} s(t-u)h(u)du \tag{17}$$

Several models for the HRF have been proposed. Here, we used the HRF proposed by Friston et al. [11]:

$$h(t) = \left(\frac{t}{c_1}\right)^{c_2} \exp\left(-\frac{t-c_1}{c_3}\right) - d\left(\frac{t}{c_1'}\right)^{2c_2} \exp\left(-\frac{t-c_1'}{c_3}\right) \tag{18}$$

where t is time in seconds, $c_1 = c_2c_3$ is the time to the peak, $c_1' = 2c_2c_3$ is the time to the under-shoot, and $c_2 = 6$, $c_3 = 0.9s$, and $d = 0.35$ [12].

For both reference functions, the CFAR property as well as the detection rates of the tests described above were evaluated.

4.1 CFAR property

First, simulation experiments have been carried out so as to find out to what extent the tests under concern have the CFAR property, that is, whether a specified false-alarm rate P_F could be achieved irrespective of the SNR. The reason for this is that tests that do not have the CFAR property are of little practical use, since the SNR is usually unknown beforehand. Although it is known that GLRTs have the CFAR property asymptotically, it remains to be seen whether this property still applies to a finite number of observations. Moreover, the GLMT is based on the assumption of Gaussian distributed data, which is an invalid assumption for magnitude data. Clearly, this may affect the CFAR property of the test. Simulation results revealed that for numbers of observations that are representative of those available in practical fMRI experiments ($N \geq 60$), both tests have the CFAR property and proper thresholds can be determined from standard tables of the $F_{1,N-2}$ distribution (GLMT) and the χ_1^2 distribution (Rician PDF based GLRT).

4.2 Detection rate

Next, simulation experiments were run in which, for a fixed false alarm rate, the detection rate P_D was determined as a function of the standard deviation of the noise. This was done for several combinations of the relative response strength $\mu = \frac{b}{a}$ and the time course length N, which corresponds to the number of images in the fMRI data set. The false alarm rates P_F were selected to be representative of those commonly used in fMRI. As long as the tests have the CFAR property, a desired $P_F = \alpha$ can easily be achieved by selecting $F_{1,N-2,1-\alpha}$ as the threshold for the GLMT and $\chi^2_{1,1-\alpha}$ as the threshold for the Rician PDF based GLRT. The detection rates obtained from 6 simulation experiments are summarized in Tables 1-6.

σ	GLMT (%)	GLRT (%)
1.0	100	100
1.4	99.75	99.85
1.8	94.09	95.51
2.2	78.75	81.44
2.6	60.50	63.72
3.0	45.13	47.95
3.4	33.11	35.49
3.8	25.32	27.11
4.2	19.14	20.52
4.6	15.03	15.96
5.0	11.92	12.67

Table 1: Detection rates obtained from 10^5 realizations for the GLMT and the Rician PDF based GLRT, for $N = 60$, $\mu = 0.1$, $a = 10$, $P_F = 0.01$ (square wave).

σ	GLMT (%)	GLRT (%)
1.5	100	100
2.0	99.57	99.67
2.5	92.68	93.66
3.0	74.07	75.97
3.5	51.90	54.00
4.0	34.48	36.39
4.5	22.89	24.17
5.0	15.59	16.58

Table 2: Detection rates obtained from 10^5 realizations for the GLMT and the Rician PDF based GLRT, for $N = 80$, $\mu = 0.25$, $a = 5$, $P_F = 0.01$ (square wave).

4.3 Discussion

As can be observed from the numerical results, the GLRT that is based on the Rician distribution performs significantly better than the GLMT, which is based on the assumption of Gaussian distributed data. At first sight, the fact that the proposed Rician PDF based GLRT requires the noise variance to be known may seem to be an impediment to its practical use. However, in practice, the noise variance can most times be assumed to be known as it can be estimated very precisely from a background region, where the data are governed by a Rayleigh distribution [13]. Using the ML estimator, which has been described in [14, 10], an unbiased estimate of σ^2 can easily be obtained. The standard deviation of this ML estimator is given by $\sigma^2/\sqrt{N}$, with N the number of background observations. Hence, to estimate σ^2 with a relative precision of, for instance, 1%, 10^4 background observations are required. For an experiment in which the number of images equals 100, a background area of 10×10 pixels would thus be sufficient to achieve this precision. This illustrates the relative ease with which precise knowledge of the noise variance can be obtained.

It may be possible to extend the GLRT proposed in this paper to the case of unknown noise variance. In this case, the noise variance has to be estimated simultaneously with the parameters of model (3), resulting in a slightly modified GLRT statistic. This possibility is under study and we intend to publish results on this subject in the near future.

5. CONCLUSIONS

A generalized likelihood ratio test (GLRT) for magnitude data has been proposed based on the Rician distribution that characterizes magnitude data. The proposed GLRT has been compared to the commonly used general linear model test (GLMT), which is a GLRT based on the assumption of Gaussian distributed data. It has been shown that the proposed GLRT outperforms the GLMT in the sense that it provides higher detection rates for a fixed false alarm rate.

σ	GLMT (%)	GLRT (%)
2	98.90	99.12
3	73.19	74.94
4	41.05	42.50
5	22.38	23.26
6	13.17	13.67

Table 3: Detection rates obtained from 10^5 realizations for the GLMT, and the Rician PDF based GLRT, for $N = 100$, $\mu = 0.1$, $a = 10$, $P_F = 0.01$ (square wave).

σ	GLMT (%)	GLRT (%)
1.0	100.00	100.00
1.2	99.83	99.85
1.4	98.52	98.65
1.6	94.79	95.16
1.8	88.28	88.80
2.0	79.83	80.51
2.2	71.29	71.96
2.4	62.47	63.13
2.6	54.40	55.13
2.8	47.69	48.18
3.0	41.77	42.16
3.2	36.23	36.61
3.4	32.14	32.62
3.6	28.45	28.64
3.8	25.07	25.42
4.0	22.57	22.77

Table 4: Detection rates obtained from 10^5 realizations for the GLMT and the Rician PDF based GLRT, for $N = 120$, $\mu = 0.1$, $a = 10$, $P_F = 0.025$ (HRF model).

σ	GLMT (%)	GLRT (%)
2.0	97.63	97.71
2.2	93.77	93.95
2.4	88.14	88.36
2.6	80.58	80.94
2.8	72.60	72.93
3.0	64.38	64.73
3.2	56.06	56.34
3.4	48.64	48.96
3.6	42.55	42.75
3.8	36.49	36.84
4.0	31.76	32.07

Table 5: Detection rates obtained from 10^5 realizations for the GLMT and the Rician PDF based GLRT, for $N = 240$, $\mu = 0.2$, $a = 5$, $P_F = 0.025$ (HRF model).

σ	GLMT (%)	GLRT (%)
0.8	99.98	99.98
1.0	99.09	99.24
1.2	94.80	95.24
1.4	86.32	87.02
1.6	75.66	76.54
1.8	64.87	65.67
2.0	54.90	55.49
2.2	46.74	47.34
2.4	39.40	39.81
2.6	33.81	34.23
2.8	29.14	29.60
3.0	25.28	25.61
3.2	22.07	22.40

Table 6: Detection rates obtained from 10^5 realizations for the GLMT and the Rician PDF based GLRT, for $N = 60$, $\mu = 0.2$, $a = 5$, $P_F = 0.05$ (HRF model).

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