

Generalized likelihood ratio tests for complex fMRI data

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ABSTRACT

Functional magnetic resonance imaging (fMRI) intends to detect significant neural activity by means of statistical data processing. Commonly used statistical tests include the Student-t test, analysis of variance, and the generalized linear model test. A key assumption underlying these methods is that the data are Gaussian distributed. Moreover, although MR data are intrinsically complex valued, fMRI data analysis is usually performed on single valued magnitude data. Whereas complex MRI data are Gaussian distributed, magnitude data are Rician distributed.

In this paper, we describe five Generalized Likelihood Ratio Tests (GLRTs) that fully exploit the knowledge of the distribution of the data: one is based on Rician distributed magnitude data and two are based on Gaussian distributed complex valued data. By means of Monte Carlo simulations, the performance of the GLRTs is compared with the classical statistical tests.

Keywords: functional magnetic resonance imaging, Statistical Parameter Maps, Magnitude Data, Complex data, Generalized Likelihood Ratio Test

1. INTRODUCTION

Functional activation detection using magnetic resonance imaging (MRI) is a rapidly growing field that has emerged in only the past decade. Functional MRI (fMRI) is the use of an MR imaging system to detect regional changes in cerebral metabolism or in blood flow, volume or oxygenation in response to task activation. The most popular technique utilizes blood oxygenation level dependent (BOLD) contrast, which is based on the differing magnetic properties of oxygenated (diamagnetic) and deoxygenated (paramagnetic) blood. These magnetic susceptibility differences lead to small, but detectable changes in susceptibility-weighted MR image intensity. However, relatively low image signal-to-noise ratio (SNR) of the BOLD effect makes detection of the activation-related signal changes difficult. Fortunately, rapid image acquisition techniques can be used to generate data sets with hundreds of images for each slice location, which can be statistically analyzed to determine foci of brain activity. The aim of the analysis is to determine those regions in the brain image in which the signal changes upon stimulus presentation. The resulting statistical parameter maps (SPM) denote the spatial locations in the brain images that show significant neural activation.

Construction of SPMs is an important issue in fMRI. In the past, many statistical tests have been proposed for this purpose (see^{1,2} for an overview). Currently, the most popular analysis methods used to obtain the activation map include the Student-*t* test, analysis of variance (ANOVA), and the general linear model test (GLMT).³ These tests share two important characteristics:

- **Data probability density function** Although MR data are intrinsically complex valued and Gaussian distributed, most tests are commonly applied to a series of *magnitude* MR images, because these images have the advantage to be immune to incidental phase variations due to various sources.⁴ 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. Indeed, whereas the complex data are Gaussian distributed,

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magnitude MR data are known to be Rician distributed.^{5,6} Nevertheless, the Student-*t* test, ANOVA, and the GLMT all rely on the assumption that the data under concern are Gaussian distributed. 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 distribution significantly deviates from a Gaussian distribution. Not incorporating the Rician PDF is therefore expected to lead to suboptimal test characteristics.

- **Single valued processing** Statistical signal processing commonly applied to fMRI data is, as explained above, generally performed on magnitude, and thus single-valued, data. This is because only the behavior of the magnitude signal component in the activation time course is of interest (i.e., in fMRI, one is usually not interested in estimation of the phase components within this time course). The magnitude signal component, however, is of course also present in the original, complex valued data. So one could have developed statistical tests based on complex valued data as well. The advantage of complex MR data is that these are Gaussian distributed, which allows derivation of closed-form expressions when developing these tests. The disadvantage is that one has to deal with the phase components as well.

The purpose of this paper is to develop and compare five Generalized Likelihood Ratio Tests (GLRTs):

- a GLRT for magnitude data with known noise variance
- a GLRT for complex data with constant phase and known noise variance
- a GLRT for complex data with constant phase and unknown noise variance
- a GLRT for complex data with random phases and known noise variance
- a GLRT for complex data with random phases and unknown noise variance

The tests will be compared with standard statistical tests. Unfortunately, quantitative comparisons of these methods based on experimental data are difficult given the absence of ground truth, little knowledge about human brain activation patterns, and the indirect role fMRI plays in capturing brain activation. Therefore, in this paper, we will conduct a number of Monte Carlo simulation experiments in which the ground truth is known. Also, for the sake of simplicity, we will only consider a square wave activation function. However, the results proposed can easily be extended to more complex reference functions.

The organization of this paper is as follows. Section 2 briefly reviews three commonly used statistical tests: the Student-*t* test, ANOVA, and the GLMT. Next, in Section 3, a GLRT for magnitude data with known noise variance is derived. In Section 4, the GLRTs for complex data with constant and random phases and with known and unknown noise variance are derived. Section 5 describes the simulation experiments that have been conducted so as to assess the performance of the proposed tests. The results of the simulation experiments are described in section 6. Finally, conclusions are drawn in section 7.

2. COMMON METHODS FOR FMRI DETECTION

In this section, we will review three commonly used tests applied to fMRI data. Thereby, it is assumed that we want to test for each voxel the null hypothesis H_0 that activation is absent against the alternative hypothesis H_1 that activation is present. The performance of each test can be characterized by two parameters:

Probability of false alarm (P_f) The probability that the test will decide H_1 when H_0 is true.

Probability of detection (P_d) The probability that the test will decide H_1 when H_1 is true.

Furthermore, a test has the so-called constant false-alarm rate (CFAR) property if the threshold required to achieve a constant false alarm rate can be chosen independent of the SNR.

In this section, we will consider the problem of testing whether the response of a magnitude MR data set $\underline{\mathbf{m}} = (\underline{m}_1, \dots, \underline{m}_N)^T$ of sample size N to a known reference function $\mathbf{r} = (r_1, \dots, r_N)^T$ is significant*. Thereby, the noiseless magnitude data set is assumed to be described by a deterministic signal vector \mathbf{z} of which the components are given by:

$$z_n = a + br_n \quad (1)$$

Hence, \mathbf{z} is a constant baseline on which a reference function \mathbf{r} with amplitude b is superimposed. In the absence of activity, b equals zero, such that $z_n = a$, for all n . We will consider the problem of testing the hypothesis that $b = 0$ (H_0) against the hypothesis that $b \neq 0$ (H_1). As a reference function, a square wave centered about zero was chosen. This allows to divide the magnitude data $\underline{\mathbf{m}}$ into an 'on'-subset $\underline{\mathbf{m}}_1$ with sample size N_1 and an 'off'-subset $\underline{\mathbf{m}}_2$ with sample size N_2 .

2.1. Student t -test

Today, the most widely used method for detecting neural activity is the Student's t -test.² It provides a statistic being a measure of the significance of the difference between the means of two distributions having the same variance. For a square reference function, the Student's t test statistic is simply given by:

$$t = \frac{\langle \underline{\mathbf{m}}_1 \rangle - \langle \underline{\mathbf{m}}_2 \rangle}{\underline{s} \sqrt{\frac{1}{N_1} + \frac{1}{N_2}}} \quad (2)$$

with $\langle \underline{\mathbf{m}}_1 \rangle$ and $\langle \underline{\mathbf{m}}_2 \rangle$, the averages of $\underline{\mathbf{m}}_1$ and $\underline{\mathbf{m}}_2$, respectively, and

$$\underline{s}^2 = \frac{\sum_i (\underline{m}_{1i} - \langle \underline{\mathbf{m}}_1 \rangle)^2 + \sum_i (\underline{m}_{2i} - \langle \underline{\mathbf{m}}_2 \rangle)^2}{N_1 + N_2 - 2} \quad (3)$$

with \underline{m}_{1i} and \underline{m}_{2i} the i^{th} element of the sample $\underline{\mathbf{m}}_1$ and the sample $\underline{\mathbf{m}}_2$, respectively. If $t > \eta_t$, with η_t a user specified threshold, then we decide H_1 , otherwise choose H_0 . It can be shown that for independent Gaussian distributed data, the Student's t test statistic follows a t -distribution when both parts have the same mean. This allows one to find the value of η_t that corresponds with a desired false alarm rate. Moreover, it can be shown that for independent Gaussian distributed data, the Student's t test has the CFAR property.

2.2. Analysis of Variance

Another well-known tool of linear statistics, often applied to fMRI time series is analysis of variance (ANOVA).^{7,8} This technique, which does not require any assumptions about the shape of the activation time course, looks at the changes in variance upon averaging.

To detect regions of activation, the ratio of the variance of the averaged data set to the variance of the unaveraged data set is calculated for each pixel in the image. For pixels in regions of purely random intensity variations, this ratio will be around $1/n$, where n is the number of cycles averaged together. Pixels in regions of activation, however, will have a significantly higher ratio than this, since the variance of both unaveraged and averaged data sets is dominated by the stimulus locked intensity variations of the fMRI response, which does not reduce upon averaging. The one-way ANOVA test statistic for $K = 2$ groups is given by:

$$\underline{F} = \frac{\underline{s}_B^2}{\underline{s}_W^2} \quad (4)$$

where

$$\underline{s}_B^2 = \frac{1}{K-1} \sum_{k=1}^K N_k (\langle \underline{\mathbf{m}}_k \rangle - \langle \underline{\mathbf{m}} \rangle)^2 \quad \text{and} \quad \underline{s}_W^2 = \frac{1}{K} \sum_{k=1}^K \left(\frac{1}{N_k-1} \sum_{i=1}^{N_k} (\underline{m}_{ki} - \langle \underline{\mathbf{m}}_k \rangle)^2 \right) \quad (5)$$

with $\langle \underline{\mathbf{m}} \rangle$ the average taken over all observations in both samples. If $\underline{F} > \eta_a$ then we decide H_1 , otherwise choose H_0 . If H_0 is true (and the data are Gaussian distributed), the ANOVA test statistic \underline{F} will have an F -distribution with 1 and $N = N_1 + N_2$ degrees of freedom. This allows one to find the value of η_a that corresponds with a desired false alarm rate.

*Here, and in what follows, random variables are underlined.

2.3. Generalized linear model test

In this subsection, the generalized linear model test (GLMT) will be reviewed. In the derivation of this test, it has been assumed that the magnitude data $\underline{\mathbf{m}} = (\underline{m}_1, \dots, \underline{m}_N)^T$ can be described as follows:

$$\underline{m}_n = z_n + \underline{e}_n \quad n = 1, \dots, N \quad (6)$$

with \mathbf{z} defined by (1) and $\underline{\mathbf{e}} = (\underline{e}_1, \dots, \underline{e}_N)^T$ a vector of zero mean, Gaussian distributed noise components with variance σ^2 . Under this assumption, the likelihood function L of the data is given by

$$L(\mathbf{z}; \underline{\mathbf{m}}) = \left(\frac{1}{2\pi\sigma^2} \right)^{\frac{N}{2}} \exp \left(-\frac{1}{2\sigma^2} \sum_{n=1}^N (m_n - z_n)^2 \right) \quad (7)$$

Since the data are assumed to be Gaussian distributed, the maximum likelihood estimator (MLE) is equal to the least-squares estimator. Moreover, the parameters enter the model in Eq. (1) linearly. Therefore, closed form expressions for the MLEs of the unspecified parameters can easily be derived.

- Under H_0 , in which $z_n = a$, the MLEs $\hat{\underline{a}}_0$ and $\hat{\underline{\sigma}}_0^2$ of the unspecified parameters a and σ^2 , respectively, are given by:

$$\hat{\underline{a}}_0 = \frac{1}{N} \sum_{n=1}^N \underline{m}_n \quad (8)$$

$$\hat{\underline{\sigma}}_0^2 = \frac{1}{N} \sum_{n=1}^N (\underline{m}_n - \hat{\underline{a}}_0)^2 \quad (9)$$

- Under H_1 , in which $z = a + br_n$, the MLEs $\hat{\underline{a}}_1$, $\hat{\underline{b}}$ and $\hat{\underline{\sigma}}_1^2$ of the unspecified parameters a , b , and σ^2 , respectively, are given by:

$$\begin{pmatrix} \hat{\underline{a}}_1 \\ \hat{\underline{b}} \end{pmatrix} = (\mathbf{X}^T \mathbf{X})^{-1} \mathbf{X}^T \underline{\mathbf{m}} \quad (10)$$

$$\hat{\underline{\sigma}}_1^2 = \frac{1}{N} \sum_{n=1}^N (\underline{m}_n - \hat{\underline{a}}_1 - \hat{\underline{b}} r_n)^2 \quad (11)$$

with \mathbf{X} an $N \times 2$ matrix given by: $\mathbf{X} = (\mathbf{1} \ \mathbf{r})$ and $\mathbf{1}$ an N -dimensional vector of ones.

From Eq. (7) and using the MLEs given in Eqs. (8-11), a closed form expression for the Generalized Likelihood Ratio (GLR) can be obtained⁹:

$$\lambda = \left(\frac{\hat{\underline{\sigma}}_0^2}{\hat{\underline{\sigma}}_1^2} \right)^{N/2} \quad (12)$$

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

$$\underline{\kappa} = (N - 2) \left(\frac{\hat{\underline{\sigma}}_0^2}{\hat{\underline{\sigma}}_1^2} - 1 \right) \quad (13)$$

will possess an $F_{1,N-2}$ distribution, that is, an F -distribution with 1 and $N - 2$ degrees of freedom, under H_0 .¹⁰ This allows one to select a proper threshold so as to achieve a desired false alarm rate. For a false alarm rate α , 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} .⁹ The test will thus reject H_0 if and only if the test statistic in Eq. (13) exceeds this threshold.

Finally, it is worthwhile mentioning that, for a square wave reference function, the GLMT is equivalent to the well known unpaired two-sample Student t -test as described in subsection 2.1. Notice that due to its very nature, the use of the t -test is only justified if one can divide each time series into two samples having (a) the same variance under both H_0 and H_1 , (b) the same mean under H_0 , and (c) different means under H_1 . In the special case of a square wave reference function, these conditions are approximately met, as long as the assumption of Gaussian distributed data is accurate enough.

3. GLRT FOR MAGNITUDE FMRI DATA

In this section, a GLRT for functional magnitude MR data will be constructed, exploiting the fact that we know that magnitude data are Rician distributed. The Rician PDF of magnitude data with deterministic signal component z and noise variance σ^2 , is given by¹¹:

$$p_m(x|z) = \frac{x}{\sigma^2} e^{-\frac{x^2+z^2}{2\sigma^2}} I_0\left(\frac{zx}{\sigma^2}\right) \quad (14)$$

where I_0 is the zeroth order modified Bessel function of the first kind.

In this section, 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.¹²⁻¹⁴ In that case, the likelihood functions for the Rician distributed data under H_0 and H_1 are given by

$$L(a; \mathbf{m}) = \prod_{n=1}^N \frac{m_n}{\sigma^2} e^{-\frac{m_n^2+a^2}{2\sigma^2}} I_0\left(\frac{m_n a}{\sigma^2}\right) \quad (15)$$

$$L(a, b; \mathbf{m}) = \prod_{n=1}^N \frac{m_n}{\sigma^2} e^{-\frac{m_n^2+(a+br_n)^2}{2\sigma^2}} I_0\left(\frac{m_n(a+br_n)}{\sigma^2}\right) \quad (16)$$

respectively, and the GLR test statistic is given by:

$$\lambda = \frac{\sup_{a,b} L(a, b; \mathbf{m})}{\sup_a L(a; \mathbf{m})} \quad (17)$$

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

$$2 \ln \lambda = 2 \sum_{n=1}^N \ln \left[\frac{I_0\left(\frac{m_n \hat{a}_0}{\sigma^2}\right)}{I_0\left(\frac{m_n (\hat{a}_1 + \hat{b} r_n)}{\sigma^2}\right)} \right] - \frac{N \hat{a}_0^2}{\sigma^2} + \frac{1}{\sigma^2} \sum_{n=1}^N (\hat{a}_1 + \hat{b} r_n)^2 \quad (18)$$

with \hat{a}_0 and (\hat{a}_1, \hat{b}) the MLEs of the unspecified parameters under H_0 and H_1 , respectively. The MLEs can be found by maximizing the likelihood functions (15) and (16) 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 described by Eq. (18) is asymptotically distributed as a χ_1^2 random variable (i.e., a random variable with a chi-square distribution with one degree of freedom) under H_0 . 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 false alarm rate α , the threshold η can thus be chosen equal to $\chi_{1,1-\alpha}^2$, that is, the $(1-\alpha)^{\text{th}}$ quantile of the χ_1^2 distribution.

4. GLRTS FOR COMPLEX FMRI DATA

Assume we have N independent complex data points $\{(w_{r,n}, w_{i,n})\}$, of which the true (i.e., noiseless) magnitude components under H_1 are described by Eq. (1). The set of N points consists of N_1 and N_2 points with underlying true amplitude $a+b$ and $a-b$ under H_1 , respectively, which we want to estimate from these data points. In what follows, we will assume that $N_1 = N_2 = N/2$. We now derive the MLEs of a , b , and φ in case the underlying true phase values are identical and in case they are not.

4.1. Identical phase values

Let φ be the true phase of each complex data point. As the real and imaginary data are independent, the joint PDF of the complex data is simply the product of the real and imaginary PDF's. Then, from a set of complex observations $\{(w_{r,n}, w_{i,n})\}$ the likelihood function is given by:

$$L = \left(\frac{1}{2\pi\sigma^2}\right)^N \prod_{n=1}^{N_1} e^{-\frac{((a+b)\cos\varphi - w_{r1,n})^2}{2\sigma^2}} e^{-\frac{((a+b)\sin\varphi - w_{i1,n})^2}{2\sigma^2}} \prod_{n=1}^{N_2} e^{-\frac{((a-b)\cos\varphi - w_{r2,n})^2}{2\sigma^2}} e^{-\frac{((a-b)\sin\varphi - w_{i2,n})^2}{2\sigma^2}} \quad (19)$$

with $\{(w_{r1,n}, w_{i1,n})\}$ the complex data points with underlying true amplitude $a+b$ under H_1 and $\{(w_{r2,n}, w_{i2,n})\}$ the complex data points with underlying true amplitude $a-b$ under H_1 .

4.1.1. ML estimation under H_1

Under H_1 (i.e., $b \neq 0$), the MLEs of a , b , and φ are then found by maximizing (19) with respect to a , b , and φ . Taking the logarithm yields:

$$\begin{aligned} \ln L &= -N \ln(2\pi\sigma^2) - \frac{1}{2\sigma^2} \sum_{n=1}^{N_1} \left[((a+b)\cos\varphi - w_{r1,n})^2 + ((a+b)\sin\varphi - w_{i1,n})^2 \right] \\ &\quad - \frac{1}{2\sigma^2} \sum_{n=1}^{N_2} \left[((a-b)\cos\varphi - w_{r2,n})^2 + ((a-b)\sin\varphi - w_{i2,n})^2 \right] \end{aligned} \quad (20)$$

For (a, b, φ) to be a maximum, the first order derivatives of the likelihood function with respect to a , b , and φ should be zero. After some calculations, it can be shown that, in case $N_1 = N_2 = N/2$:

$$\frac{\partial \ln L}{\partial a} = -\frac{1}{\sigma^2} [Na - (W_{r1} + W_{r2})\cos\varphi - (W_{i1} + W_{i2})\sin\varphi] \quad (21)$$

$$\frac{\partial \ln L}{\partial b} = -\frac{1}{\sigma^2} [Nb - (W_{r1} - W_{r2})\cos\varphi - (W_{i1} - W_{i2})\sin\varphi] \quad (22)$$

$$\frac{\partial \ln L}{\partial \varphi} = -\frac{1}{\sigma^2} [(a+b)(W_{r1}\sin\varphi - W_{i1}\cos\varphi) + (a-b)(W_{r2}\sin\varphi - W_{i2}\cos\varphi)] \quad (23)$$

where:

$$W_{r1} = \sum_{n=1}^{N_1} w_{r1,n} \quad W_{i1} = \sum_{n=1}^{N_1} w_{i1,n} \quad W_{r2} = \sum_{n=1}^{N_2} w_{r2,n} \quad W_{i2} = \sum_{n=1}^{N_2} w_{i2,n} \quad (24)$$

Setting (21), (22), and (23) to zero and solving the resulting system yields the ML estimates of a , b and φ :

$$\hat{\varphi}_1 = \frac{1}{2} \arctan \frac{2(W_{r1}W_{i1} + W_{r2}W_{i2})}{W_{r1}^2 + W_{r2}^2 - W_{i1}^2 - W_{i2}^2} \quad (25)$$

$$\hat{a}_1 = \frac{1}{N} [(W_{r1} + W_{r2})\cos\hat{\varphi}_1 + (W_{i1} + W_{i2})\sin\hat{\varphi}_1] \quad (26)$$

$$\hat{b} = \frac{1}{N} [(W_{r1} - W_{r2})\cos\hat{\varphi}_1 + (W_{i1} - W_{i2})\sin\hat{\varphi}_1] \quad (27)$$

4.1.2. ML estimation under H_0

Under H_0 , b is zero. Hence, $\ln L$ is simply given by:

$$\ln L = -N \ln(2\pi\sigma^2) - \frac{1}{2\sigma^2} \sum_{n=1}^N \left[(a\cos\varphi - w_{r,n})^2 + (a\sin\varphi - w_{i,n})^2 \right] \quad (28)$$

Maximizing $\ln L$ with respect to (φ, a) then yields the following ML estimates of φ and a under H_0 :

$$\hat{\varphi}_0 = \arctan \frac{W_{i1} + W_{i2}}{W_{r1} + W_{r2}} \quad (29)$$

$$\hat{a}_0 = \frac{1}{N} \sqrt{(W_{r1} + W_{r2})^2 + (W_{i1} + W_{i2})^2} \quad (30)$$

4.1.3. GLRT statistics

Known σ^2 If σ^2 is known, it can be shown that the test statistic $2 \ln \lambda$, where

$$2 \ln \lambda = \frac{\underline{S}_0^2 - \underline{S}_1^2}{\sigma^2} \quad (31)$$

is asymptotically χ_1^2 distributed under H_0 , in which:

$$\begin{aligned} \underline{S}_1^2 &= \sum_{n=1}^{N/2} \left[(\hat{a}_1 + \hat{b}_1) \cos \hat{\varphi}_1 - \underline{w}_{r1,n} \right]^2 + \left[(\hat{a}_1 + \hat{b}_1) \sin \hat{\varphi}_1 - \underline{w}_{i1,n} \right]^2 \\ &\quad + \sum_{n=1}^{N/2} \left[(\hat{a}_1 - \hat{b}_1) \cos \hat{\varphi}_1 - \underline{w}_{r2,n} \right]^2 + \left[(\hat{a}_1 - \hat{b}_1) \sin \hat{\varphi}_1 - \underline{w}_{i2,n} \right]^2 \end{aligned} \quad (32)$$

$$\underline{S}_0^2 = \sum_{n=1}^N \left[\hat{a}_0 \cos \hat{\varphi}_0 - \underline{w}_{r,n} \right]^2 + \left[\hat{a}_0 \sin \hat{\varphi}_0 - \underline{w}_{i,n} \right]^2 \quad (33)$$

Unknown σ^2 If σ^2 is unknown, it can be shown that the test statistic

$$\underline{\kappa} = (2N - 3) \left(\frac{\underline{S}_0^2}{\underline{S}_1^2} - 1 \right) \quad (34)$$

is asymptotically $F_{1,2N-3}$ -distributed under H_0 .

4.2. Random phase values

Next, let φ_n be the true phase of the complex data point $(w_{r,n}, w_{i,n})$. Then, the likelihood function is given by:

$$L = \left(\frac{1}{2\pi\sigma^2} \right)^N \prod_{n=1}^{N_1} e^{-\frac{((a+b) \cos \varphi_{1,n} - w_{r1,n})^2}{2\sigma^2}} e^{-\frac{((a+b) \sin \varphi_{1,n} - w_{i1,n})^2}{2\sigma^2}} \prod_{n=1}^{N_2} e^{-\frac{((a-b) \cos \varphi_{2,n} - w_{r2,n})^2}{2\sigma^2}} e^{-\frac{((a-b) \sin \varphi_{2,n} - w_{i2,n})^2}{2\sigma^2}} \quad (35)$$

For this complex data set, we will discuss maximum likelihood (ML) estimation under H_0 and H_1 , as well as the GLRT statistic, derived from the MLEs.

4.2.1. ML estimation under H_1

Under H_1 (i.e., $b \neq 0$), the MLEs for a , b , and φ_n are then found by maximizing (35) with respect to a , b , and φ_n . Taking the logarithm yields:

$$\ln L = -N \ln(2\pi\sigma^2) - \frac{1}{2\sigma^2} \sum_{n=1}^{N_1} \left[((a+b) \cos \varphi_{1,n} - w_{r1,n})^2 + ((a+b) \sin \varphi_{1,n} - w_{i1,n})^2 \right] \quad (36)$$

$$- \frac{1}{2\sigma^2} \sum_{n=1}^{N_2} \left[((a-b) \cos \varphi_{2,n} - w_{r2,n})^2 + ((a-b) \sin \varphi_{2,n} - w_{i2,n})^2 \right] \quad (37)$$

For (a, b, φ_n) to be a maximum, the first order derivatives of the likelihood function with respect to a , b , and φ_n should be zero. Solving the resulting system then leads to the following MLEs:

$$\hat{\varphi}_{1,n} = \arctan \left(\frac{w_{i,n}}{w_{r,n}} \right) \quad (38)$$

$$\hat{a}_1 = \frac{1}{N} \sum_{n=1}^N m_n \quad (39)$$

$$\hat{b} = \frac{1}{N} \left[\left(\sum_{n=1}^{N_1} m_{1,n} \right) - \left(\sum_{n=1}^{N_2} m_{2,n} \right) \right] \quad (40)$$

4.2.2. ML estimation under H_0

Under H_0 , b is zero. In that case, maximizing $\ln L$ with respect to φ and a yields:

$$\hat{\varphi}_{0,n} = \arctan\left(\frac{w_{i,n}}{w_{r,n}}\right) \quad (41)$$

$$\hat{a}_0 = \frac{1}{N} \sum_{n=1}^N m_n \quad (42)$$

4.2.3. GLRT statistic

Known σ^2 If σ^2 is known, it can be shown that the test statistic $2 \ln \lambda$, where

$$2 \ln \lambda = \frac{\underline{S}_0^2 - \underline{S}_1^2}{\sigma^2} \quad (43)$$

is asymptotically χ_1^2 -distributed under H_0 , in which:

$$\begin{aligned} \underline{S}_1^2 &= \sum_{n=1}^{N/2} \left[(\hat{a}_1 + \hat{b}_1) \cos \hat{\varphi}_{1,n} - \underline{w}_{r1,n} \right]^2 + \left[(\hat{a}_1 + \hat{b}_1) \sin \hat{\varphi}_{1,n} - \underline{w}_{i1,n} \right]^2 \\ &\quad + \sum_{n=1}^{N/2} \left[(\hat{a}_1 - \hat{b}_1) \cos \hat{\varphi}_{2,n} - \underline{w}_{r2,n} \right]^2 + \left[(\hat{a}_1 - \hat{b}_1) \sin \hat{\varphi}_{2,n} - \underline{w}_{i2,n} \right]^2 \\ &= \sum_{n=1}^{N/2} \left[(\hat{a}_1 + \hat{b}_1) - \underline{m}_{1,n} \right]^2 + \sum_{n=1}^{N/2} \left[(\hat{a}_1 - \hat{b}_1) - \underline{m}_{2,n} \right]^2 \end{aligned} \quad (44)$$

$$\underline{S}_0^2 = \sum_{n=1}^N \left[\hat{a}_0 \cos \hat{\varphi}_{0,n} - \underline{w}_{r,n} \right]^2 + \left[\hat{a}_0 \sin \hat{\varphi}_{0,n} - \underline{w}_{i,n} \right]^2 = \sum_{n=1}^N [\hat{a}_0 - \underline{m}_n]^2 \quad (45)$$

Unknown σ^2 If σ^2 is unknown, it can be shown that the test statistic

$$\underline{\kappa} = (N - 2) \left(\frac{\underline{S}_0^2}{\underline{S}_1^2} - 1 \right) \quad (46)$$

is asymptotically $F_{1,N-2}$ -distributed under H_0 . Note that this test is identical to the GLMT applied to magnitude data (cfr. subsection 2.3).

5. SIMULATION EXPERIMENTS

In case the reference function \mathbf{r} is a square wave, it can be shown that the Student- t test, the one-way ANOVA and the GLMT are equivalent. Furthermore, since the GLMT was shown to be equivalent to the GLRT for complex data with random phases unknown noise variance, it will also be excluded from the simulation tests. Therefore, in this section, the simulation experiments will be restricted to comparisons of the proposed GLRTs. During exhaustive Monte Carlo simulation experiments, numerous realizations of time series of N Rician distributed magnitude data points were generated of which the deterministic signal components are described by Eq. (1). As a reference function, a square wave was considered that fluctuated between -1 and +1 with period 20 as shown in Fig. 1. For this reference function, the CFAR property as well as the detection rates of the tests described above were evaluated.

5.1. 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.

5.2. 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 SNR. 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. In each experiment, the false alarm rate P_f was set to 0.01, which is a representative value of the P_f values used in fMRI. As long as the tests have the CFAR property, this can easily be achieved by selecting $F_{1,N-2,0.99}$ as the threshold for the GLMT and $\chi^2_{1,0.99}$ as the threshold for the Rician PDF based GLRT.

6. RESULTS AND DISCUSSION

Results were obtained for the square reference function and for various numbers of observations. The detection rates obtained from 3 simulation experiments are shown in Tables 1-3 for $N = 60$, $N = 120$, and $N = 240$, respectively. To allow a fair comparison, for each experiment only the detection rates of tests for which the CFAR property could be verified are shown. Since simulation results revealed that the GLRT for complex data with random phases and known noise variance lacks the CFAR property, this test will not be included in the evaluation.

As can be observed from the numerical results, the GLRT based on the Rician distribution performs significantly better than the GLMT (i.e., the GLRT for complex data, random phases and unknown σ^2), which is based on the assumption of Gaussian distributed data. Furthermore, the GLRT for complex data with identical phases and unknown noise variance performs better than the GLRT for magnitude data. Finally, of course, the GLRT for complex data with identical phases scores better in case σ^2 is known.

The fact that some of the tests considered require knowledge of the noise variance might seem an impediment to their practical use. Fortunately, 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.¹⁵ Using the ML estimator, which has been described in,^{13,14} an unbiased estimate of σ^2 can easily be obtained. The standard deviation of this ML estimator is given by σ^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.

7. CONCLUSIONS

Although statistical tests are available to construct statistical parameter maps from magnitude functional MR data, there is still room for significant improvement by exploiting the knowledge of the distribution of magnitude data. An even higher detection rate can be achieved when the assumption of identical phases is valid. In that case, it is strongly advised to employ a generalized likelihood ratio test (GLRT) for complex data.

	magn.	complex, iden. φ ,	complex, iden. φ ,	complex random φ
σ	σ^2 known	σ^2 known	σ^2 unknown	σ^2 unknown
1.4	99.83	99.85	99.81	99.74
1.6	98.76	98.84	98.59	98.23
1.8	95.43	95.79	95.19	94.12
2.0	89.64	90.33	89.33	87.51
2.2	81.54	82.69	81.49	78.92
2.4	72.60	74.19	72.71	69.61
2.6	63.87	65.64	64.15	60.69
2.8	55.27	57.55	55.98	52.25
3.0	47.60	50.25	48.73	44.73
3.2	41.64	44.21	42.86	39.01
3.4	35.36	38.23	36.96	33.29
3.6	30.70	33.55	32.46	28.78
3.8	26.64	29.55	28.55	24.99
4.0	23.34	26.22	25.29	21.92

Table 1. Detection rates obtained from 10^5 realizations for the GLRT for magnitude data with known σ^2 , the GLRT for complex data with identical phases and known σ^2 , the GLRT for complex data with identical phases and unknown σ^2 , and the GLRT for complex data with random phases and unknown σ^2 , for $N = 60$, $\mu = 0.1$, $a = 10$, $P_f = 0.01$.

	magn.	complex, iden. φ ,	complex, iden. φ ,	complex random φ
σ	σ^2 known	σ^2 known	σ^2 unknown	σ^2 unknown
2.0	99.78	99.82	99.78	99.71
2.2	99.02	99.21	99.12	98.85
2.4	97.24	97.64	97.44	96.83
2.6	94.12	94.96	94.68	93.42
2.8	89.43	90.97	90.50	88.47
3.0	83.68	85.80	85.16	82.49
3.2	77.30	80.07	79.42	75.88
3.4	70.62	74.01	73.29	69.16
3.6	64.07	67.84	67.08	62.41
3.8	57.50	62.03	61.29	55.98
4.0	51.48	56.62	55.89	50.14
4.2	45.88	51.26	50.54	44.54
4.4	40.46	46.15	45.46	39.37
4.6	36.15	41.92	41.33	35.23
4.8	32.53	38.57	38.02	31.66
5.0	29.11	35.08	34.53	28.16

Table 2. Detection rates obtained from 10^5 realizations for the GLRT for magnitude data with known σ^2 , the GLRT for complex data with identical phases and known σ^2 , the GLRT for complex data with identical phases and unknown σ^2 , and the GLRT for complex data with random phases and unknown σ^2 , for $N = 120$, $\mu = 0.1$, $a = 10$, $P_f = 0.01$.

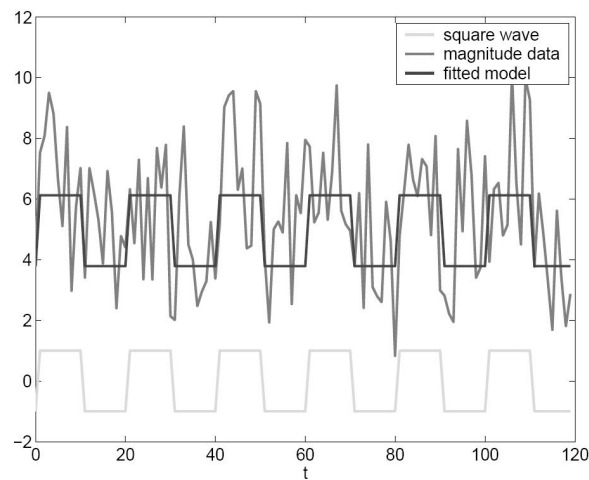


Figure 1. For $N = 120$, a square wave is shown that was fitted to the magnitude fMRI data.

σ	magn. σ^2 known	complex, iden. φ , σ^2 known	complex, iden. φ , σ^2 unknown	complex random φ σ^2 unknown
3.0	99.35	99.54	99.51	99.28
3.2	98.35	98.83	98.80	98.25
3.4	96.62	97.59	97.50	96.37
3.6	94.20	95.83	95.71	93.89
3.8	90.88	93.38	93.18	90.43
4.0	86.78	90.28	90.04	86.21
4.2	82.22	86.70	86.45	81.52
4.4	76.95	82.71	82.30	76.20
4.6	71.82	78.44	78.11	71.10
4.8	66.27	74.18	73.83	65.60
5.0	61.33	70.05	69.68	60.65
5.2	56.04	65.60	65.19	55.42
5.4	51.43	61.70	61.27	50.67
5.6	46.68	57.53	57.23	46.01
5.8	42.46	54.01	53.57	41.84
6.0	38.46	50.10	49.76	37.83

Table 3. Detection rates obtained from 10^5 realizations for the GLRT for magnitude data with known σ^2 , the GLRT for complex data with identical phases and known σ^2 , the GLRT for complex data with identical phases and unknown σ^2 , and the GLRT for complex data with random phases and unknown σ^2 , for $N = 240$, $\mu = 0.1$, $a = 10$, $P_f = 0.01$.

REFERENCES

1. K. J. Worsley, "An overview and some new developments in the statistical analysis of PET and fMRI data," *Human Brain Mapping* **5**, pp. 254–258, 1997.
2. A. S. Lukic, M. N. Wernick, and S. C. Strother, "An evaluation of methods for detecting brain activations from functional neuroimages," *Artificial Intelligence in Medicine* **25**, pp. 69–88, 2002.
3. K. J. Friston, P. Jezzard, and R. Turner, "Analysis of functional MRI time series," *Human Brain Mapping* **1**, p. 153171, 1994.
4. D. C. Noll, C. H. Meyer, J. M. Pauly, D. G. Nishimura, and A. Macovski, "A homogeneity correction for magnetic resonance imaging with time-varying gradients," *IEEE Transactions on Medical Imaging* **10**(4), pp. 629–637, 1991.
5. A. Macovski, "Noise in MRI," *Magnetic Resonance in Medicine* **36**, pp. 494–497, 1996.
6. A. H. Andersen and J. E. Kirsch, "Analysis of noise in phase contrast MR imaging," *Medical Physics* **23**(6), pp. 857–869, 1996.
7. G. A. F. Seber and C. J. Wild, *Nonlinear regression*, John Wiley and Sons, New York, 1989.
8. S. Clare, M. Humberstone, J. Hykin, L. D. Blumhardt, R. Bowtell, and P. Morris, "Detecting activations in event-related fMRI using analysis of variance," *Magnetic Resonance in Medicine* **42**(6), pp. 1117–1122, 1999.
9. A. M. Mood, F. A. Graybill, and D. C. Boes, *Introduction to the Theory of Statistics*, McGraw-Hill, Tokyo, 3rd ed., 1974.
10. L. Scharf and B. Friedlander, "Matched subspace detectors," *IEEE Transactions on Signal Processing* **42**(8), pp. 2146–2157, 1994.
11. S. O. Rice, "Mathematical analysis of random noise," *Bell System of Technology* **23**, p. 282, 1944.
12. G. McGibney and M. R. Smith, "An unbiased signal-to-noise ratio measure for magnetic resonance images," *Medical Physics* **20**(4), pp. 1077–1078, 1993.
13. J. Sijbers, A. J. den Dekker, M. Verhoye, J. Van Audekerke, and D. Van Dyck, "Estimation of noise from magnitude MR images," *Magnetic Resonance Imaging* **16**(1), pp. 87–90, 1998.
14. J. Sijbers, A. J. den Dekker, E. Raman, and D. Van Dyck, "Parameter estimation from magnitude MR images," *International Journal of Imaging Systems and Technology* **10**(2), pp. 109–114, 1999.
15. H. Gudbjartsson and S. Patz, "The Rician distribution of noisy MRI data," *Magnetic Resonance in Medicine* **34**, pp. 910–914, 1995.