GENERAL LINEAR MODEL ESTIMATION IN FMRI USING GENETIC ALGORITHM IN THE FREQUENCY DOMAIN

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ABSTRACT

Functional magnetic resonance imaging (fMRI) has been shown to be useful in the detection of the brain activity via the relatively indirect coupling of neural activity to cerebral blood flow. This work aims to treat the parameter estimation problem of the linear model for fMRI time series which are supposed to be contaminated by fractional-integrated processes and white noise. Unlike conventional approaches such as t-test which use time domain data, a maximum likelihood (ML) method is adopted in frequency domain. However maximization of the likelihood function in this case is a highly nonlinear estimation problem. Since the genetic algorithm (GA) tends to find the globally optional without being trapped at local maxima, an estimation scheme based on the GA is therefore developed to solve the ML parameter estimation problem. Finally this method was applied to real fMRI data and better activation detection in compare with common t-test method was shown.

1. INTRODUCTION

Current tomographic technologies in medical imaging enable noninvasive studies of brain function by measuring hemodynamic changes related to changes in neuronal activity. The signal changes observed in functional magnetic resonance imaging (fMRI) are mostly based on blood oxygenation level dependent (BOLD) contrast and are usually close to the noise level [1], [2]. Consequently, statistical methods and signal averaging are frequently used to distinguish signals from noise in the data. In most fMRI setups, images are acquired during alternating task (stimulus) and control (rest) conditions.

The detection of changes in the BOLD signal is further complicated by the presence of a large number of instrumental and physiological noises that contaminate the fMRI signal Long-term physiological drifts and instrumental instability contribute to a systematic increase or decrease in the signal with time. While the exact cause for the drift of the baseline signal is not completely understood [3], this structured trend constitutes a basic hurdle to any statistical analysis of the data. This trends and physiological noise are the main source of color in the fMRI data, so before adopting any statistical method like t-test, the noise in observation must be whiten [4]. For this purpose the noise model must be known.

A careful analysis of the spectral characteristics of fMRI noise, examined in datasets acquired under resting or "null" conditions, has instead suggested that the noise may generally have 1/*f*-like properties with disproportionate power at lower frequencies [5]. In this paper this model was used for noise to show the effect of suitable whitening filter on the detection of activated area. So in first we should estimate noise model parameter for each voxel time-series separately. We maximize likelihood function for parameter estimation and problem turn into an optimization problem. There are lots of methods that deal with optimization of a function, but most of them do not reach a global solution. For this reason Genetic Algorithm method was chosen for achieving a global solution.

This paper organized as follow. In session 2, a linear model usually used in analyses is described. In session 3, a suitable model for noise is introduced. In session 4, Likelihood function was calculated in frequency domain. In session 5 a brief description of genetic algorithm was presented. Session 6 result was shown.

2. FMRI TIME-SERIES MODEL

If we assume that the hemodynamic system is a linear time-invariant system, we can write its output x(t) as:

$$x(t) = h(t) * s(t) \tag{1}$$

,where h(t) is the hemodynamic response function that was shown in figure (1) and s(t) is stimulus pattern. However fMRI measurements are contaminated by noise. If we present y(t) as the observation , we have

$$y(t) = \beta x(t) + \varepsilon(t) \tag{2}$$

where β is an unknown weight have to be estimated. This weight varies from voxel to voxel. It is obvious that if the baseline drift is not removed, any analysis based on the

model (2) will be tracking the large variation in the signal instead of the effects of the stimulus. So proper estimation of β depend on realizing noise and baseline characteristics.

In order to obtain a baseline from which one can estimate the effect of the stimulus it is thus essential to infer and remove the systematic drift, or trend, in the data. Predicting the amount, type and magnitude of drift is difficult since etiology is multifractal and poorly understood.

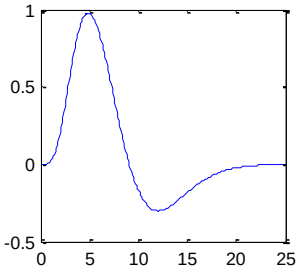

Figure 1. Hemodynamic response function

3. NOISE MODEL

Recently, fractal signals, i.e., fractionally differenced noise, have attracted much consideration in signal processing, image processing geophysical data, network traffic, and computer vision due to the wide variety of data for which they are inherently well suited. These processes provide good models for self-similarity and long-range correlation structure observed in several signal processes.

Fractal signals are increasingly important candidates for data modeling in a variety of signal processing applications. In contrast to the well-known family of autoregressive moving average (ARMA) processes, fractal signals are characterized by self-similarity and long-range correlation structure.

Discrete time fractal process called discrete fractionally differenced Gaussian noise (fdGn) has been defined by Granger and Joyeux [6]:

$$u(n) = (1-q^{-1})^{d} v(n) \tag{3}$$

where q^{-1} is the delay operator, v(n) is a zero-mean Gaussian white noise with variance σ^2. The relation between the fractional number and the Hurst parameter *H* in long memory process in the discrete-time case is $H = d + 0.5$. The power spectrum of u(n) can be presented as [7]:

$$S(f) = \frac{2^{-2d}\sigma^2}{(\sin(\pi f))^{2d}} \tag{4}$$

where $0 < d < 0.5$. also we have noticed that several authors [5] have argued that fMRI signal is also contaminated by a white noise in addition to the long memory noise. Therefore, in this paper we consider fMRI noise power spectrum as:

$$S_{\varepsilon}(f) = S(f) + \sigma_w^2 \tag{5}$$

where σ_w^2 is the variance of white noise w(n). We also assumed white noise and fractal noise are statistically independent.

4. LIKELIHOOD FUNCTION FOR PARAMETER ESTIMATION

By observing the spectral density $S_y(f)$ of the observation, it is found that $S_y(f)$ has a very simple structure, and it depends to the parameters d, σ, σ_w and β. Taking the N-point discrete Fourier transform of (2) yields the frequency-domain model

$$Y(k) = \beta X(k) + U(k) + W(k) \tag{5}$$

where Y(k), U(k) and W(k) denote the Fourier transform coefficients of y(n), u(n) and w(n), respectively.

In [7] log-likelihood function for fractal noise estimation was calculated. We reform it for linear model as follow:

$$L_{\varepsilon}(\beta, \sigma, d, \sigma_w) \approx \sum_{k=1}^{N/2-1} [-\log \mathrm{var}(\varepsilon(k)) - \frac{|\varepsilon(k)|^2}{\mathrm{var}(\varepsilon(k))}] \tag{6}$$

where N is the number of data points in fMRI time series and $\mathrm{var}(\varepsilon(k)) = \frac{N2^{-2d}\sigma^2}{(\sin(\pi k/N))^{2d}} + N\sigma_w^2$. Then the ML parameter estimation problem of linear model parameters in the frequency domain is to find an optimal vector $\theta^* = (\beta, d, \sigma, \sigma_w)$.

5. PARAMETER ESTIMATION VIA THE GENETIC ALGORITHM

The GA is a stochastic optimization algorithm that was originally motivated by the mechanisms of natural selection and evolution of genetics. The underlying principles of the GA were first proposed by Holland in 1962 [8], whereas the mathematical framework was

developed in the late 1960s and was presented in Holland's book [9].

5.1. Search Space

In the following, a parameter estimation algorithm is developed based on the GA to estimate the parameter vector $\theta = (\beta, d, \sigma, \sigma_w)$ of the fdG process in (2) by carrying out maximization of the log-likelihood function in (7).

By using the GA to solve the problem of maximization of the log-likelihood function $L_Y(\theta)$ in (16), the search space of the parameter vector θ must be specified properly beforehand. This is because an appropriate choice of the search space may speed up the convergence of the GA.

For this purpose before any process, we normalize each time-series using division by its standard deviation. By then the unknown parameters σ, σ_w will be limited up to 1. Also the absolute value of β is always less than 1.

5.2. Genetic Operators

The most important and basic operations for the GA for maximizing (7) are maintaining, reproduction, crossover, and mutation. A brief description of these operations is presented in the following.

• *Maintaining:* This is a process of copying the best string in this generation (with the highest fitness) to the next generation. The purpose of this operation is to ensure that the best string in the next generation is at least no worse than the best one in this generation.

• *Reproduction:* Reproduction is a process in which individual strings are copied and put in a mating pool for further genetic operations according to their fitness values.

• *Crossover:* Crossover provides a mechanism for exchanging information in two strings via probabilistic decision. Combined with reproduction, it is an effective way of exchanging information and combining portions of high-quality solutions.

• *Mutation:* Mutation is occasional alteration of each bit of a chromosome from 0 to 1 or from 1 to 0 with a small probability P_m. The purpose of mutation is to introduce occasional perturbation to the estimated parameters to ensure that all points in the search space can ultimately be reached.

6. EXPERIMENTS

6.1. Simulation

For simulation of a fMRI time-series according to described fractal noise model, we need to synthesize fBm process. There a lot of methods to produce this noise. In this paper, the noise was a synthetic fBm generated with the wavelet-based approach described in [10] (see also [11]). This new construction reproduces the theoretical properties of fBm and makes it possible to control the variance of the noise process. Fig. 2 shows a realization (with 256 times samples) of the synthetic fBm with H =0.7; the magnitude of the Fourier transform of the time–series, shown in Fig. 2(b), is a straight line in the log-log scale. We used for all our experiments.

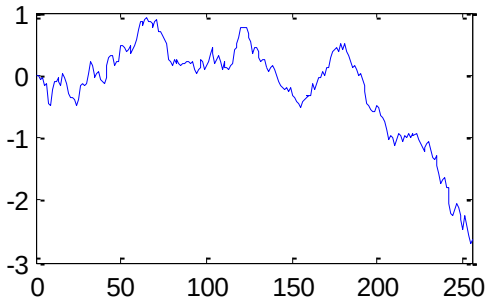

Figure 2. A realization (with 256 times samples) of the synthetic fBm with H=0.7.

We simulated 10000 fMRI time series. In this data we added activation to 1000 time series with different bold contrasts and the remains used for false alarm rate accuracy research. Then we used our proposed method and t-test for activation detection. The results of t-test and Genetic Algorithm are shown below (figure 3).

Genetic Algorithm was run in 250 generations for each time series. We set the $Pm = 0.1$ in all estimation. The resulted activation regions are shown in figure 3(b), where as the activation regions detected by t-test are illustrated in figure 3(c). These figures show that the proposed method detected more activated voxels. In figure 4, measured false positive rate versus expected false rate is plotted. For purposed algorithm, measured false alarm rate is approximately is the same everywhere.

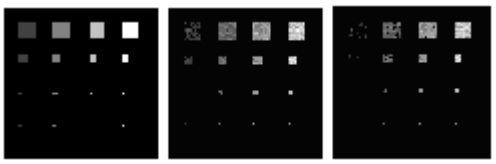

Figure 3. a) Spatial pattern of active regions (with different Bold Contrasts) in the simulated data, b) Activation area detected by proposed method. c) Activation area detected by t-test method.

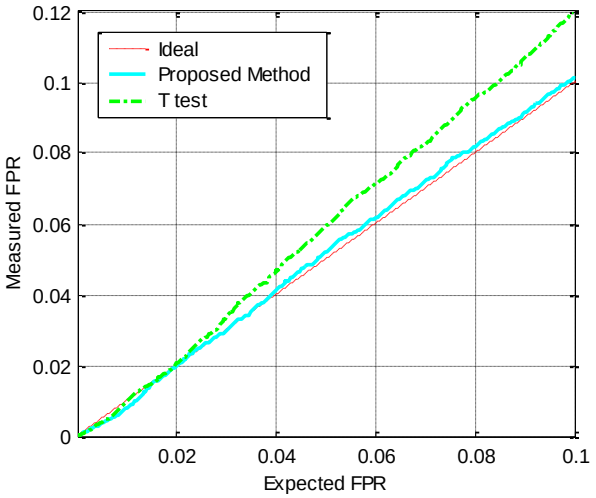

Figure 4. Measured false positive rate versus expected false rate

6.2. Real Data

For evaluation of our method we used Block-design real fMRI data. Functional images were acquired from a normal volunteer using a single-shot gradient echo EPI sequence (TR=3 sec, TE=50 ms, FOV=250×250×100 mm^3, matrix size=64×64×20) on a 1.5 Tesla Siemens Vision MRI scanner. The subject performed a finger to thumb opposition task. The task consisted of 4 periods of 84 seconds, where each period contained 30 seconds of left hand finger opposition, 12 seconds of rest, followed by 30 seconds of right hand finger opposition, and another 12 seconds of rest. A 3D high-resolution anatomical image volume was also acquired from the subject using an MP-RAGE sequence. This data was processed by purposed method and t-test. Results were presented using AFNI. AFNI runs under Linux operating system and was produced by Dr. Cox.

Both methods detect three active area motor cortex, cerebrum and supplementary motor area (Figure 5). Detected activated areas using purposed method are wider than using t-test method. These results show that proper noise model can help better activation detection. Figures 5(a) and 5(d) are coronal profiles. Supplementary motor area and motor cortex area were shown to be activated.

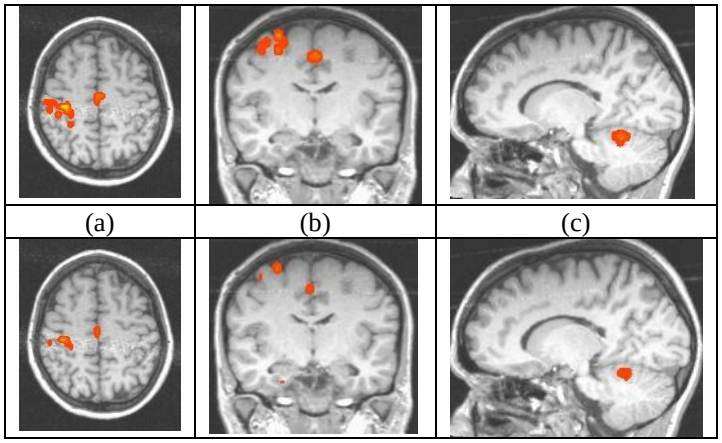

Figure 5. Activation area in experimental fMRI. The activated areas were shown in color. The first row shows activated areas achieved by purposed method. The second row shows activated areas achieved by t-test statistic. a, d) axial section. Two active areas motor cortex and supplementary motor area was detected in this section. b, e) coronal section. Two active areas motor cortex and supplementary motor area was detected in this section. c ,f)) sagital section. one active area cerebrum was detected in this section.

7. REFERENCES

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