COMPARISON OF TWO DIFFERENT APPROACHES FOR BRAIN ACTIVITY DETECTION IN FMRI: SPM-MAP AND SPM-GLM

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ABSTRACT

The functional MRI (*Magnetic Resonance Imaging*), *fMRI*, is today a widespread tool to study and evaluate the brain from a functional point of view. The blood-oxygenation-level-dependent (BOLD) signal is currently used to detect the activation of brain regions with a stimulus application, e.g., visual or auditive. In a block design approach the stimuli (called *paradigm* in the *fMRI* scope) are designed to detect activated and non activated brain regions with maximized certainty. However, corrupting noise in MRI volumes acquisition, patient motion and the normal brain activity interference makes this detection a difficult task. The most used activation detection fMRI algorithm, here called *SPM-GLM* [1] uses a conventional statistical inference methodology based on the t-statistics

In this paper we propose a new Bayesian approach, by modeling the data acquisition noise as *additive white Gaussian noise* (AWGN) and the activation indicators as binary unknowns that must be estimated. Monte Carlo tests using both methods have shown that the Bayesian method, here called *SPM-MAP*, outperforms the traditional one, here called *SPM-GLM*, for almost all conditions of noise and number of paradigm epochs tested.

Index Terms— Functional MRI, Activity Detection, Bayesian

1. INTRODUCTION

The functional Magnetic Resonance imaging (fMRI) is currently the most prominent method used for functional brain imaging, and it is a big step forward in the process of answering the main question asked to all the functional imaging methods: What are the brain regions involved in mediating a specific brain function? And thought the fMRI's obvious qualities have allowed for its fast acceptance and development, its limitations are far from letting this question to become a "closed problem".

The fMRI experiments usually look for the change in blood oxygenation and blood volume resulting from altered neural activity. This signal, called blood-oxygenation-level-dependent (BOLD), results from the endogenous paramagnetic contrast property of the deoxygenated hemoglobin. Hence, increased blood volume reduces the local concentration of deoxygenated hemoglobin causing an increase in the MR signal on a T2*-weighted image [2]. It is commonly accepted, and has been empirically proved, that there is a strong correlation between neural activity and the vascular response that leads to the consequent increase of this BOLD signal [3]. This relation, know as the hemodynamic response function (HRF), is at the core of fMRI data analysis. Inferences about which brain regions are involved in the particular stimulated cognitive and sensorimotor functions are based on how well the BOLD signal correlates with this stimulation, mediated by the HRF.

Contrary to the impression one might get in a brief review of the literature, there are not many ways to analyze fMRI time-series with a diversity of statistical and conceptual approaches. In fact, with very few exceptions, every analysis is a variant of the general linear model (GLM), that expresses the observed response variable in terms of a linear combination of explanatory variables [4]. Based on this model, data analysis is usually processed in a number of steps involving image processing and statistical evaluation that, in the end, produce a functional brain map. Often methods used involve several modules for image preprocessing, spacial transformation, statistical tests and the final inferences procedures. This work focuses on the last two steps and how our Bayesian method compares with the most commonly used method, Statistical Parametric Mapping (SPM) [1] when applied to single voxel time-course data. This last method makes use of univariate statistical tests (T of F tests) at each brain voxel and subsequent statistical inferences about the observed responses using a user defined p-value threshold, for the 1D data case. This classical approach maybe a simple one with reasonable results, but it has several disadvantages that can be tackled. On this work we propose a Bayesian approach for the binary (activated or not) analysis of simulated 1D block-designed data and present the Monte Carlo results from the comparison between the presented method and the standard SPM procedure.

2. PROBLEM FORMULATION

Let us consider the voxels (volume elements) displayed in Fig. 1. Each voxel, after the application of a given paradigm, may be activated by one or more applied stimulus ($\exists_k : \beta_k = 1$) or may not be activated at all ($\forall_k : \beta_k = 0$).

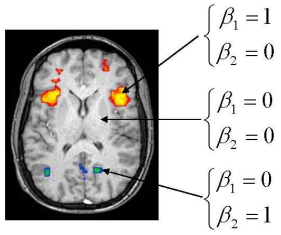

Fig. 1. Activated and non activated regions in fMRI.

In this paper we consider the signal BOLD associated to a single voxel at a time - *time course* - with the following data observation

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model, displayed in Fig. 3,

$$y(n) = h(n) * \sum_{k=1}^{N} \beta_k p_k(n) + \eta(n) \quad (1)$$

where $\eta(n)$ is modeled as *additive white Gaussian noise* (AWGN), $h(n)$ is the hemodynamic response function of the brain tissues, $p_k(n)$ are the stimulus signals along time (see Fig. 2) and β_k are unknown binary variables to model the activation of the voxel by the k[th] stimulus. For instance, Fig. 1 shows the result of application of a two stimulus paradigm where three voxels are referenced: *i)* a voxels was activated by the first stimulus, $\beta_1 = 1$ and $\beta_2 = 0$, *ii)* a voxel was not activated, $\beta_1 = 0$ and $\beta_2 = 0$, and *iii)* a voxel was only activated by the second stimulus, $\beta_1 = 0$ and $\beta_2 = 1$.

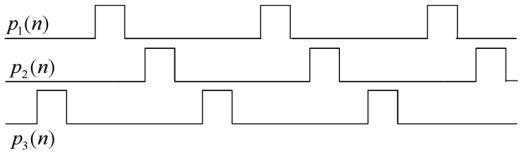

Fig. 2. Paradigm with three block-designed stimulus.

In this paper we describe a Bayesian *Statistical Parametric Mapping* algorithm (SPM) based on the *maximum a posteriori* (MAP) criterion to estimate the vector $\mathbf{b} = \{\beta_1, \beta_2, ..., \beta_N\}$, associated with each voxel, called SPM-MAP[1]. We use the observation model displayed in Fig. 3 and described by the equation (1). *Monte Carlo* tests with synthetic data are used to evaluate the performance of the algorithm and compare it with the SPM based on the *general linear model* (GLM), here called *SPM-GLM* [1], which is one of the most commonly used methods to detect activated voxels in the functional MRI scope.

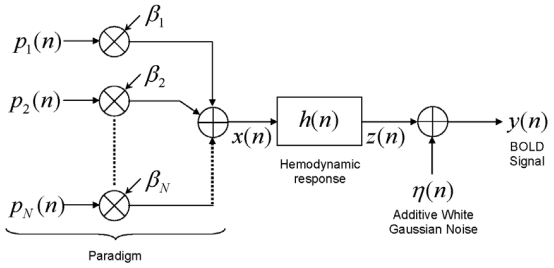

Fig. 3. BOLD signal generation model.

Let $\mathbf{x} = \{x(1), x(2), x(3), ..., x(L)\}^T$ (see Fig. 3) where L is the time-course observations length. $\mathbf{x}$ may be expressed as $x = \theta\mathbf{b}$ where

$$\theta = \begin{pmatrix} p_1(1) & p_2(1) & p_3(1) & ... & p_N(1) \\ p_1(2) & p_2(2) & p_3(2) & ... & p_N(2) \\ p_1(3) & p_2(3) & p_3(3) & ... & p_N(3) \\ \vdots & \vdots & \vdots & ... & \vdots \\ p_1(L) & p_2(L) & p_3(L) & ... & p_N(L) \end{pmatrix} \quad (2)$$

The output vector of $h(n)$ displayed in Fig. 3,

$$\mathbf{z} = \{z(1), z(2), z(3), ...z(L)\}^T, \quad (3)$$

[1]*Statistical parametric mapping is generally used to identify functionally specialized brain responses*[1]

is obtained by $z(n) = h(n) * x(n)$. Here, for sake of simplicity, $h(n)$ is assumed to be a F length finite impulse response (FIR), although infinite responses may also be considered [5]. Therefore the output signal may be expressed as $\mathbf{z} = H\mathbf{x}$ where H is the following *Toeplitz* matrix

$$H = \begin{pmatrix} h(1) & 0 & 0 & 0 & 0 & 0 \\ h(2) & h(1) & 0 & 0 & 0 & 0 \\ h(3) & h(2) & h(1) & 0 & 0 & 0 \\ ... & ... & ... & ... & ... & ... \\ 0 & ... & h(p) & h(p-1) & ... & h(1) \end{pmatrix} \quad (4)$$

The observed BOLD signal $y(n)$, $\mathbf{y} = \{y(1), y(2), ..., y(L)\}^T$ is therefore obtained as follows

$$y = \Psi\beta + n \quad (5)$$

where $\Psi = H\theta$, $\mathbf{n} = \{\eta(1), \eta(2), ..., \eta(L)\}^T$ is a vector of independent and identically distributed (i.i.d) zero mean random variables normally distributed, that is, $p(\eta(k)) = N(0, \sigma^2)$. The additive white Gaussian noise (AWGN) is usually used to model the corruption process in functional MRI although other models may also be used, e.g., Rice and Rayleigh.

3. ESTIMATION

The MAP estimate of $\mathbf{b}$ can be obtained by solving the following equation

$$\hat{\mathbf{b}} = \arg\min_b E(\mathbf{y}, \mathbf{b}) \quad (6)$$

where $E(\mathbf{y}, \mathbf{b})$ is an energy function defined as follows

$$E(\mathbf{y}, \mathbf{b}) = \underbrace{-\log(p(\mathbf{y}|\mathbf{x}(\mathbf{b})))}_{\text{Data fidelity term}} \underbrace{-\log(p(\mathbf{b}))}_{\text{Prior term}} \quad (7)$$

where $E_y(\mathbf{y}, \mathbf{b}) = -\log(p(\mathbf{y}|\mathbf{x}(\mathbf{b})))$ is the likelihood term and $E_b(\mathbf{b}) = -\log(p(\mathbf{b}))$ incorporates the *a priori* knowledge about the unknowns to be estimated; in this case, that β_k are binary.

Statistical independence of the observations means that

$$p(\mathbf{y}|x(\mathbf{b})) = \prod_{i=1}^{L} p(y(i)|x(\mathbf{b})). \quad (8)$$

Since the noise is assumed to be additive white and Gaussian (AWGN), $p(y(i)|x(\mathbf{b})) = \frac{1}{\sqrt{2\pi\sigma^2}} e^{-\frac{(y(i)-x(i))^2}{2\sigma_y^2}}$. The unknowns to be estimated, β_k, are also assumed to be independent, that is,

$$p(\mathbf{b}) = \prod_{i=1}^{N} p(\beta_k) \quad (9)$$

where $p(\beta_k)$ is a bi-modal distribution defined as a sum of two Gaussian distributions centered at zero and one, of σ_β^2 variance

$$p(\beta_k) = \frac{1}{2}\left[N(0, \sigma_\beta^2) + N(1, \sigma_\beta^2)\right] \quad (10)$$

because β_k are binary variable, $\beta_k \in \{0, 1\}$. In order to better approximate the binary answer σ_β should be as small as possible but numerical stability reasons prevent the adoption of too small values.

The MAP estimate is therefore the minimizer of the following energy function

$$E(\mathbf{y}, \mathbf{b}) = (\Psi\mathbf{b} - \mathbf{y})^T(\Psi\mathbf{b} - \mathbf{y}) + E_b(\mathbf{b}) + C \quad (11)$$

where C is a constant and

$$E_b(\mathbf{b}) = \sum_{k=1}^{N} \left[\frac{2\beta_k^2 - 2\beta_k + 1}{4\sigma_\beta^2} - \log\left(\cosh\left[\frac{2\beta_k - 1}{4\sigma_\beta^2} \right] \right) \right]. \quad (12)$$

The MAP estimate is obtained by finding the stationary point of $E(\mathbf{y}, \mathbf{b})$,

$$\nabla_{\mathbf{b}} E(\mathbf{y}, \mathbf{b}) = 0 \quad (13)$$

where $\nabla_{\mathbf{b}}$ is the gradient operator w.r.t. $\mathbf{b}$, which may be written as follows

$$\nabla_{\mathbf{b}} E = \Psi^T(\Psi\mathbf{b} - \mathbf{y}) + \frac{\sigma_{\mathbf{y}}^2}{\sigma_{\mathbf{b}}^2} \left[\mathbf{b} - \frac{1}{2} R(\mathbf{b}) \right] = 0 \quad (14)$$

where $R(\mathbf{b})$ is a column vector with N elements r_k

$$r_k = 1 + tanh\left[\frac{2\beta_k - 1}{4\sigma_\beta^2} \right] \quad (15)$$

The solution of (14) may be obtained by using the fixed point method which leads to the following recursion

$$\hat{\mathbf{b}}^{t+1} = (\Psi^T\Psi + \alpha I)^{-1}(\Psi^T y + \alpha R(\hat{\mathbf{b}}^t)) \quad (16)$$

where $\alpha = \sigma_y^2/2\sigma_\beta^2$ is a parameter, I is a $N \times N$ identity matrix and $\hat{\mathbf{b}}^t$ is the $\mathbf{b}$ estimate at t[th] iteration.

The estimated elements of $\mathbf{b}$, β_k, are real numbers and not binary. Therefore, the binary estimate of $\hat{\beta}_k$, b_k, is obtained as follows

$$b_k = \begin{cases} 0 & \hat{\beta}_k < 0.5 \\ 1 & otherwise \end{cases} \quad (17)$$

Two main differences must be stressed between the proposed *SPM-MAP* and the standard *SPM-GLM* method:

1. In the *SPM-GLM* method the whole N period signal is sometimes broken into N pieces corresponding to each paradigm period and the resulting observation pieces are averaged to reduce the noise corrupting the observations Y. The matrix θ, defined in (2), is built by using only a single paradigm period. In the proposed method, instead of braking the signal, it is dealt with as a whole signal. And the same goes for the paradigm signal. The noise reduction is performed in a Bayesian framework where a realistic observation model is used to cope with it. In the case of AWGN both methods are very similar, but if other noise models (e.g. multiplicative) are used this would no longer be true. This is because the averaging procedure is only adequate for certain noise models.
2. In the *SPM-GLM* method the estimation of each β_k is based on the well known classical t-test [6] applied to the estimated coefficients β_k. This statistical inference technique is based on the *null hypothesis* test, H_o, where the activation probability of a given voxel is computed with a certain confidence degree. This test is performed over the estimated coefficients, β_k, obtained with the *GLM*. These coefficients used to linearly combine the EVs (usually a convolution between the paradigm stimulus and the HRF model (s)) are estimated by using the MSE criterion. These real coefficients reflect the estimated "presence" amplitude of each EV in the observed data. In the *SPM-MAP* method the coefficients set are assumed to be binary and are estimated in a Bayesian framework where a prior distribution forces its values to be close of $\{0, 1\}$. Once again, our concern is to follow a realistic model where it is assumed that a given voxel was activated or not by a given stimulus. Partial voxel activation is not acceptable in this scope: it is totally activated or it is not activated at all, by a given stimulus, $p_k(n)$.

To better understand the difference between both methods, a short description of the *SPM-GLM* method is presented where the t-test is used to determine if a given voxel is or is not activated by a single EV , $p(n) * h(n)$, which means that $\mathbf{b}$ is a scalar, $\mathbf{b} = [\beta]$.

The observed BOLD signal is assumed to be obtained from the following model

$$\mathbf{y} = \beta(p(h) * h(n)\theta) + \mathbf{e} \quad (18)$$

where θ is defined in (2) but with only one stimulus,

$$\theta = \{p(1), p(2), ..., p(L)\}^T, \quad (19)$$

$h(n)$ is the canonical gamma function [1,4,7] and $\mathbf{e}$ is the residual error vector not explained by the model. The β estimation given by the GLM method, in this very simple case, is computed as follows

$$\hat{\beta} = \theta^+ Y \quad (20)$$

where $\theta^+ = (\theta^T\theta)^{-1}\theta^T$ is the so called *pseudoinverse* of θ.

The *SPM-GLM* method core, tags each voxel as activated, $b = 1$, or as inactivated, $b = 0$, by computing the probability of being activated by the stimulus with a confidence level α, that is,

$$b = \begin{cases} 1 \text{ (Active)} & \text{if} p < \alpha; \text{(reject } H_0) \\ 0 \text{ (No Active)} & Otherwise; \text{(acept } H_0) \end{cases} \quad (21)$$

where H_0 is the null hypothesis which assumes no activation with a confidence level α.

The p-value is obtained as follows

$$p = P(t \geq T) = 1 - I_{\frac{L}{L+T^2}}(L/2, 0.5) \quad (22)$$

where $I_x(a, b)$ is the *incomplete Beta-function* [6] defined as

$$I_x(a, b) = \frac{\Gamma(a+b)^x}{\Gamma(a)\Gamma(b)} \int_0^x \tau^{a-1}(a - \tau)^{b-1} d\tau \quad (23)$$

and

$$T = \hat{\beta}/\sigma_\beta \quad (24)$$

is the T estimator associated t-statistics, where $\hat{\beta}$ is the estimation value of β, and σ_β the standard deviation. t is large if the estimated value is much larger than the estimator variance and t is small if the estimated value is comparable with the corresponding estimator variance.

The estimator variance, σ_β^2, may be numerically estimated using the following expression

$$\sigma_\beta^2 = \sigma_y^2 \sum_{n=1}^{L} p^2(n) \quad (25)$$

where $p(n)$ is the n^{th} θ element and σ_y^2 is the estimated noise energy

$$\sigma_y^2 = \frac{1}{L-1} \sum_{n=1}^{L} \left[y(n) - \hat{\beta} p(n) \right]^2. \quad (26)$$

In the next section Monte Carlo simulations are presented comparing the *probability of error* (P_e), obtained with both methods, *SPM-MAP* and the *SPM-GLM* described above.

4. EXPERIMENTAL RESULTS

To access the effectiveness of the proposed *SPM-MAP* method against the presented *SPM-GML*, synthetic 1D-block-designed single stimulus data, with several AWGN noise levels (σ) and several stimulus epochs (periods in a block design paradigm approach), N, are used in Monte Carlo simulations. In these, the *error probability* (P_e), was obtained for each method as follows

$$P_e(\sigma, N) = \frac{1}{R} \sum_{i=1}^{R} |\hat{b}_i - b_i| \tag{27}$$

where $R = 250$ is the number of data repetitions used in the Monte Carlo tests. The HRF function is assumed to be known and was selected from the PBH model estimation on real data [5].

The resulting P_e differences between *SPM-MAP* and *SPM-GLM*, i.e: $\Delta P_e = P_{e(SPM-MAP)} - P_{e(SPM-GLM)}$, was computed for each experiment, and the average results for the different noise levels and epochs are displayed in Fig.4 and in table 1. Notice that in table 1, σ values that resulted in all null P_e are not displayed.

Although the performance of both algorithms decreases, as expected, with the amount of noise and with the decrease in epochs number, the ΔP_e obtained is negative for most of the (N, σ) data pairs tested, which means that the *SPM-MAP* outperforms the *SPM-GLM* method for almost every configuration tested. This is confirmed by Table 1, where the summation of ΔP_e, $\sum_{i,j} \Delta P_e(N_i, \sigma_j) = -0.46$, is negative. The number of negative values of ΔP_e, $\#(\Delta P_e < 0) = 23$ and the number of positive values of ΔP_e, $\#(\Delta P_e > 0) = 6$, which confirms that the *SPM-MAP* surpasses the traditional *SPM-GLM* method. Still it is obvious that both methods present high accuracy in these tests due to the exact knowledge of both the HRF and noise distribution.

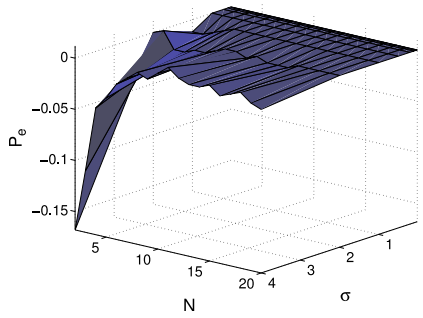

Fig. 4. Difference of probability errors, $\Delta P_e = P_{e(SPM-MAP)} - P_{e(SPM-GLM)}$, between the *SPM-MAP* and the *SPM-GLM* methods for two different views. N is the number of epochs and σ is noise standard deviation level.

5. CONCLUSIONS

In this paper a new Bayesian method for detection of brain activated regions in the scope of functional MRI is proposed where the noisy observations are modeled with additive white Gaussian noise (AWGN) and the activation indicators are modeled by binary variables that are estimated. The prior associated with the binary indicators is a bimodal Gaussian distribution around the 0 and 1 values to cope with the uncertainty related with the noise.

The proposed method is compared with the one proposed in [1] that uses a classical statistical inference methodology based on the *t*-test method. Monte Carlo tests on synthetic-1D-block-designed data with both methods have shown that the proposed Bayesian method, called *SPM-MAP*, outperforms the classical one based on the *general linear model* (GLM), here called *SPM-GLM*. The performance evaluation was based on the computation of the *error probability*, $P_e(N, \sigma)$, for each method which proved to be smaller for the proposed *SPM-MAP* method than the corresponding ones obtained with the *SPM-GLM* method, for almost every tested conditions: different noise levels, σ_j and number of paradigm epochs, N_i, in a block design framework.

$N \backslash \sigma$	1	2	4
2	-0.012	0	-0.168
3	-0.012	0.004	-0.108
4	-0.008	-0.012	-0.044
5	-0.004	-0.012	-0.032
6	0	-0.008	-0.016
7	0	-0.008	-0.008
8	0	-0.004	0
9	0	0	-0.004
10	0	0	0.004
11	0	-0.004	0.012
12	0	0	0.004
13	0	-0.004	0
14	0	-0.004	0
15	0	-0.004	0.004
16	0	0	-0.004
17	0	0	0
18	0	0	0.004
19	0	0	-0.004
20	0	0	-0.008

Table 1. $\Delta P_e = P_{e(SPM-MAP)} - P_{e(SPM-GLM)}$ for $2 \leq N \leq 20$ and $\sigma = \{1, 2, 4\}$. For all other tested values of $\sigma = 0.01, 0.02, 0.05, 0.1, 0.2, 0.5$.

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