33rd Annual International Conference of the IEEE EMBS
Boston, Massachusetts USA, August 30 - September 3, 2011

A Sparse Based Approach for Detecting Activations in fMRI

Blanca Guillen, Jose L. Paredes, Rubén Medina

Abstract— **In this paper, we propose a simple approach for detecting activated voxels in fMRI data by exploiting the inherent sparsity property of the BOLD signal. The proposed approach addresses the solution of the inverse problem induced by the General Linear Model through an l_0-regularized Least Absolute Deviation (l_0-LAD) regression method. Under this framework, the activated voxels are detected by a two-stages process: estimation and basis selection. First, an estimate of the coefficients that minimizes the absolute deviation error is found by means of the weighted median operator. Then, a thresholding operator is applied on the estimated value in order to decide whether or not a stimulus is present in the observed BOLD signal. The threshold parameter turns out to be the regularization parameter that controls the model sparseness. The method was proven on real fMRI data leading to similar activated regions than those activated by the Statistical Parametric Mapping (SPM) software.**

I. INTRODUCTION

The medical imaging modality known as functional Magnetic Resonance Imaging (fMRI) using blood oxygen level-dependent (BOLD) contrast is a noninvasive technique widely accepted as a standard tool for localizing brain activity. During the course of an fMRI experiment, a series of brain images is acquired by repeatedly scanning the subject's brain while he/she is performing a task or is exposed to a stimulus. From this sequence of images a statistical analysis is carried out to detect which voxels are activated by the stimulation. In practice, the most widely used fMRI data analysis technique is based on the General Linear Model (GLM). Under this approach a linear model is fitted to the fMRI time series of each voxel resulting in a set of voxel-specific parameters, which are then used to form statistical parametric maps (SPMs)[1].

In recent years, there has been a growing interest in the fMRI data analysis based on sparse representation of fMRI signal, specially since Daubechies *et al.* [2] demonstrated the fact that the most influential factor for the success of Independent Component Analysis (ICA) algorithm is sparsity of the components rather than independence. Moreover, they suggest to develop decomposition methods based on the GLM where the BOLD signal, at each voxel, may be regarded as a linear superposition of a sparse set of brain activity patterns.

B. Guillen is with the Department of Mathematics, Bioengineering Group, UNET, San Cristóbal, Venezuela, and Biomedical Engineering Group, USB, Caracas, Venezuela, blancag@unet.edu.ve. J. Paredes and R. Medina are with Biomedical Engineering Research Group, Electrical Engineering Department, ULA, Mérida, Venezuela, paredesj@ula.ve.
Authors would like to thank ECOS-NORD-FONACIT under grant PI-20100000299 for their financial support.

More recently, Lee *et al.* [3] exploit the sparsity property of fMRI data to describe the BOLD signal at each voxel as a sparse combination of elements of a data-driven dictionary.

Ordinary Least Squares (OLS) has been traditionally used as the primary approach to solve the inverse problem induced by the GLM leading to a solution that is, in general, dense. Therefore, to exploit the sparsity property of fMRI data a more suitable approach to solve the inverse problem should be used. Recently, there have been proposed several approaches to solve linear regression problems where the parameter vector is known in advance to be sparse [4]. Among these techniques are methods such as Orthogonal Matching Pursuit (OMP) [5], and ℓ_0-regularized Least Absolute Deviation (ℓ_0-LAD) [6] being the later the most suitable for the application at hand since it uses a continuation kind of approach to set the regularization parameter.

In this paper, the problem of detecting activated voxels is addressed under the framework of sparse signal representation where the BOLD signal is considered sparse in a dictionary. More specifically, we propose to use the ℓ_0-LAD regression method to estimate the parameters of the GLM: $\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{e}$, where $\mathbf{y}$ is the observed fMRI signal at one voxel, $\mathbf{X}$ is the design matrix (dictionary), $\boldsymbol{\beta}$ is the set of unknown parameters and $\mathbf{e}$ is the noise vector. Under this framework, each time series is considered as a linear combination of a few elements of the design matrix and the l_0-LAD algorithm is then used to find whether or not a stimulus is present in the observed signal and its contribution to signal formation. Thus, a voxel is considered activated by the stimulus X_i if the corresponding parameter β_i survives the l_0-regularized LAD regression as one of the strongest contributor to the BOLD signal.

II. THE GENERAL LINEAR MODEL APPROACH

Consider the general linear model approach that models the acquired time series as a linear combination of several regressor variables (predictors) plus an error term for each voxel in an fMRI imaging system. More precisely, the GLM for the observed response variable $\mathbf{y}_j$ at voxel j, $j = 1, \ldots, N$, is given by:

$$\mathbf{y}_j = \mathbf{X}\boldsymbol{\beta}_j + \mathbf{e}_j \tag{1}$$

where, $\mathbf{y}_j \in R^M$, with M the number of scans, $\mathbf{X} \in R^{M\times L}$ denotes the design matrix, $\boldsymbol{\beta}_j \in R^L$ represents the signal strength at the j-th voxel, and $\mathbf{e}_j \in R^M$ is the noise vector at the j-th voxel. The entries of the noise vector are usually assumed to be independent and identically distributed with zero mean and variance σ^2. In the fMRI literature, there exist two different approaches to define the design matrix $\mathbf{X}$. In a first

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approach, each column-vector of the design matrix is defined by a stimulus/task function convolved with a hemodynamic response function (HRF), i.e. the predicted task related BOLD response [7]. The second approach constructs the design matrix not only with the expected task-related BOLD response, as described above, but also nuisance components that model the confounding effects are added as column-vector to the design matrix. This later approach has been found to be more convenient for the proposed approach. The simplest version of the GLM assumes that both the stimulus function and the hemodynamic response function are known in advanced. The stimulus is assumed to be equivalent to the experimental paradigm, while the HRF is modeled using a canonical HRF, typically either a gamma function or the difference between two gamma functions [7]. The predicted BOLD response is thus modeled by convolving the stimulus with the modeled HRF.

By exploiting the linear model, it is possible to assess effects of interest that are spanned by one or more columns of $\mathbf{X}$ using a contrast, that is, a linear combination of parameter estimates: $c_1\hat{\beta}_{1j} + c_2\hat{\beta}_{2j} + \ldots + c_L\hat{\beta}_{Lj}$ where the vector $\mathbf{c} = [c_1, c_2, ..., c_L]^T$ is referred to as the contrast vector. Hypothesis testing is performed on a voxel-by-voxel basis by testing individual model parameters using a t-test and subsets of parameters using a partial F-test. Having repeated this procedure for each voxel, the results are assembled into an image termed the statistical parametric map (SPM), whose voxel measurements correspond to the test statistic calculated at that particular voxel [7].

III. ACTIVE VOXEL DETECTION BY EXPLOITING SPARSITY

A. Motivation

For illustrative purposes and to gain some inside about the performance of OLS, ℓ_0-LS (using OMP) and ℓ_0-LAD in solving (1) when the parameter vector is sparse, the synthetic BOLD signal depicted in Fig. 1 is analyzed. In this example, we model the fMRI time series $\mathbf{z}$ of a particular voxel as a sparse superposition of various stimuli and additive noise. That is, $\mathbf{z} = \mathbf{X}\mathbf{a} + \boldsymbol{\eta}$, where $\mathbf{a}$ is a 3-sparse vector, i.e. only 3 components of the L-dimensional vector have nonzero values. Thus, the voxel related to the observed time series $\mathbf{z}$ is activated just by three stimuli. From the observed time series, we are interested in determining which stimuli in the design matrix $\mathbf{X}$ activate the corresponding voxel and the contributions of those stimuli. In order to generate synthetic data as close as possible to a real experiment, the design matrix $\mathbf{X} \in R^{500\times 13}$ is constructed from all 13 transformed/convolved task functions obtained from Pittsburgh Brain Activity Interpretation Competition 2007 (PBAIC 2007) [8]. Furthermore, the noise vector $\boldsymbol{\eta}$ is a scaled version of a time series extracted from a non activated voxel in the fMRI dataset provided by [8]. The scaling factor depends on the desired signal to noise ratio that for illustrative purpose it has been set to 9 dB. As can be seen in Fig. 1, OLS generates spurious components in the estimation of $\mathbf{a}$. While OMP fails to detect the right support of the sparse signal since the stimulus 10 is considered as part of the signal in place of stimulus 7. This is probably caused by the similarity between stimuli 7 and 10. These spurious can be wrongly interpreted as a presence of a stimulus/task function in the BOLD signal where, indeed, it is not present. In turn, this may lead, inevitably, to increase false-positives. On the other hand, l_0-LAD yields the right support of the activated stimulus and a relative good approximation of their contribution to $\mathbf{z}$.

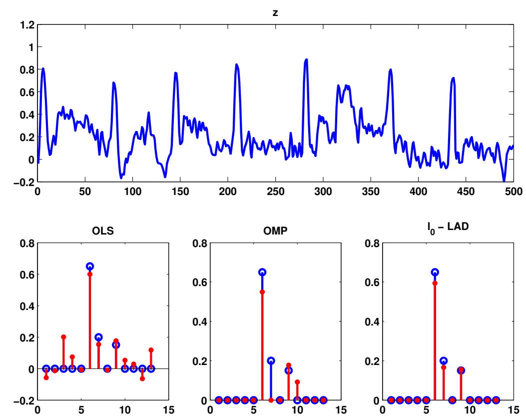


Fig. 1. Solution of the inverse problem: $\mathbf{z} = \mathbf{X}\mathbf{a} + \boldsymbol{\eta}$. Top: observed time series $\mathbf{z}$. Bottom: solutions yielded by: OLS, OMP, and ℓ_0-LAD; here $\circ$ denotes the original parameter vector and $\bullet$ denotes the estimated solution.

B. Parameter estimation by solving ℓ_0-regularized LAD

Consider the time series $\mathbf{y}$ given by the linear model:

$$\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{e} \tag{2}$$

we want to find the explanatory variables that best suit the model under a certain error criterium. That is, we want to locate the column vectors of $\mathbf{X}$ and their contribution such that the data-fitting term $\|\mathbf{X}\boldsymbol{\beta} - \mathbf{y}\|_{l_p}$ reaches a minimum subject to the constraint that $\boldsymbol{\beta}$ has a few nonzero values. Formally, we want to solve the ℓ_0-regularized ℓ_p regression problem:

$$\min_{\boldsymbol{\beta}} \|\mathbf{y} - \mathbf{X}\boldsymbol{\beta}\|_{l_p} + \tau\|\boldsymbol{\beta}\|_0 \tag{3}$$

where $\|\boldsymbol{\beta}\|_0$ denotes the ℓ_0 quasi norm that counts the number of nonzero entries in $\boldsymbol{\beta}$, $\|\cdot\|_{l_p}$ denotes the l_p-norm, and $\tau > 0$ is the regularization parameter that balances the conflicting objectives of minimizing the data-fitting term while yielding, at the same time, a sparse solution on $\boldsymbol{\beta}$ [4]. Solving this ℓ_0-regularized l_p problem is NP-hard owing to the sparsity constraint imposed by the ℓ_0-norm. In [6] an iterative algorithm has been proposed to solve this optimization problem using a coordinate descent approach where the l_1-norm is used in the data fitting term. Under this approach the solution of the l_0-LAD regression problem is achieved by reducing the L-dimensional problem given by (3) to L one-dimensional problems by supposing that all entries of the sparse vector $\boldsymbol{\beta}$ are known but one of them. Therefore, in order to estimate the n-th unknown entry of $\boldsymbol{\beta}$, the entries $\beta_j,\ j = 1, .., L,\ j \neq n$, are treated as known constants. According to this, the l_0-LAD problem reduces to the one-dimensional minimization problem:

$$\widehat{\beta}_n = \arg\min_{\beta_n} \sum_{i=1}^{M} |r_{in} - x_{in}\beta_n| + \tau|\beta_n|_0 + b \qquad (4)$$

where $b = \tau \sum_{j=1, j\neq n}^{L} |\beta_j|_0$, with $|\beta_j|_0 = 1$ if $\beta_j \neq 0$, otherwise $|\beta_j|_0 = 0$, and r_{in} denotes the i-th entry of the n-th residual column vector defined as:

$$\mathbf{r}_n = \mathbf{y} - \sum_{j=1, j\neq n}^{L} \mathbf{x}_j \beta_j \qquad (5)$$

where $\mathbf{x}_j$ denotes the j-th explanatory variable of the design matrix. Note that $\mathbf{r}_n$ is the n-th residual term that remains after subtracting from the observed fMRI signal $\mathbf{y}$ the contributions of all explanatory variables (stimuli and confounds) but the n-th one. It was shown in [6] that the solution of the optimization problem (4) can be thought of as a two-stages process: estimation and basis selection. More precisely, in a first stage, an estimation of β_n is found by solving the optimization problem (4) leading to unregularized weighted median operator as the underlying operation for parameter estimation. That is,

$$\widetilde{\beta}_n = \text{MEDIAN}\left(|x_{in}| \diamond \frac{r_{in}}{x_{in}}\right) \qquad (6)$$

where $\diamond$ denotes the operation: $W_i \diamond v_i = \overbrace{v_i, v_i, \ldots, v_i}^{W_i \text{ times}}$. The l_0-regularization induces the second stage where a hard thresholding operator is applied on the estimated value:

$$\widehat{\beta}_n = \begin{cases} \widetilde{\beta}_n, & \|\mathbf{r}_n\|_1 - \|\mathbf{r}_n - \widetilde{\beta}_n \mathbf{x}_n\|_1 > \tau \\ 0, & \text{otherwise} \end{cases} \qquad (7)$$

From (7), it can be seen that the n-th entry of $\widehat{\boldsymbol{\beta}}$ is considered relevant if $\tau < \|\mathbf{r}_n\|_1 - \|\mathbf{r}_n - \widetilde{\beta}_n \mathbf{x}_n\|_1 \leq |\widetilde{\beta}_n| \, \|\mathbf{x}_n\|_1$. This latter inequality shows that τ controls whether the $\widetilde{\beta}_n$ is significant or not based on an estimate of its magnitude. Thus, if a good estimate has been determined and τ has been properly chosen the hard thresholding stage will identify correctly the nonzero values of $\widetilde{\beta}_n$. Therefore, determining the regularization parameter is a critical step as τ governs the sparsity of $\boldsymbol{\beta}$ since it becomes the hard threshold parameter in (7). In [6], the authors follow a continuation approach which treats the regularization parameter as a tuning parameter whose value change as the iterative algorithm progresses. That is, $\tau = \alpha^k$, $0 < \alpha < 1$, and $k = 1, \ldots, K$, with K the total number of iterations. Interesting, this approach aims at detecting in order of descending signal contribution the nonzero values of the parameters vector since it starts with a large value for the regularization parameter and decreases its values as the algorithm progress. More interesting, this approach for solving (3) can be thought of as a successive cancelation of stimulus effects on the observed data. Thus, if a voxel is activated by any particular stimulus its contribution in the formation of the time series is iteratively removed to allow the identification of other stimuli in the residual signal.

IV. METHODOLOGY

A. Data

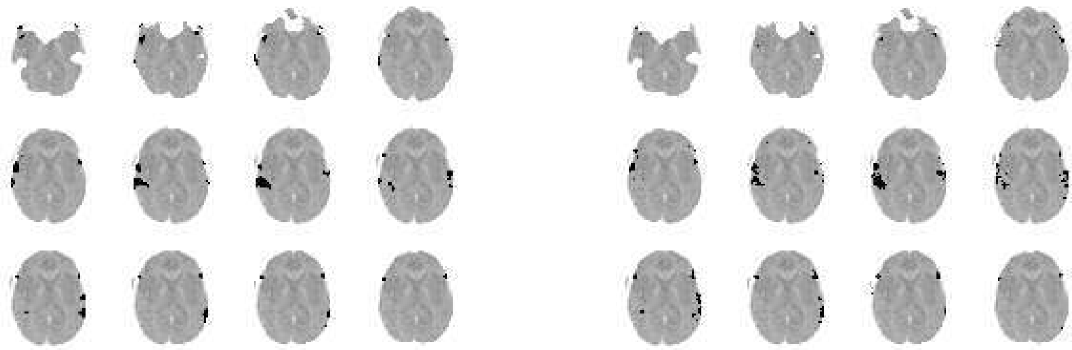
The dataset used for experimentation in this research was obtained from PBAIC 2007. Brain images databases were collected from three subjects (subject 1, subject 13 and subject 14) with a Siemens 3T Allegra scanner. The functional images were acquired by using a EpiBOLD sequence, with imaging parameters TR and TE being set to 1.75 s and 25 ms, respectively. Each subject's data consists of three runs with a time duration of approximately 20-minutes each one (704 volumes in each segment). Each volume contains $64 \times 64 \times 34$ voxels with a voxel size of $3.2 \times 3.2 \times 3.5$ mm^3. For this study, we use the preprocessed data where slice time correction, motion correction and detrending have been performed on the functional and structural data using NeuroImage (AFNI) and NeuroImage software (NIS), see [8] for further details.

During the data acquisition, the subjects were engaged in a Virtual Reality task, in which they had to perform a number of tasks, in an urban virtual reality environment. The field work included, among others, the acquisition of pictures of neighbors with piercings, the gathering of fruits and weapons, and the avoidance of a growling dog. Each run also includes 24 time series of natural stimuli or features over 704 TRs each, which had been convolved with a standard HRF. The preprocessed fMRI data were spatially smoothed with a 3D Gaussian kernel with full width at half maximum (FWHM) of twice the voxel size as suggested by [1].

B. Data Analysis

The proposed approach is applied to subject 3 dataset in a voxel-by-voxel basis. For our analysis, fixation periods are extracted from the original data set leading to a total of 500 volumes to analyze in each run. Based on the structure of the design matrix two experiments are considered. First, the design matrix is constructed following the framework of Statistical Parametric Map (SPM) software (see http://www.fil.ion.ucl.ac.uk/spm/). In this case, the design matrix $\mathbf{X} \in R^{500\times 14}$ is constructed by considering thirteen convolved stimulus/task function that are part of the features set provided by PBAIC and a column vector consisting of all ones that models the whole brain activity [1]. The set of stimuli includes the following features vectors: Arousal, Dog, Faces, FruitsVegetables, Hits, Instructions, InteriorExterior, SearchFruit, SearchPeople, SearchWeapons, Valence, Velocity, and WeaponsTools. Under this approach, a temporal smoothing was applied to both data and model in order to remove low frequency variations in signal (confounds) due to artifacts such as aliased biorhythms and other drift terms [1]. This highpass filter was implemented by mean of a DCT basis set with harmonic periods up to a cutt-off of 1/128 Hz.

In the second experiment, predictors for confounds are added to the design matrix and the all-ones column vector is removed. Specifically, the thirteen DCT basis generated above for filtering purposes are incorporated to $\mathbf{X}$ leadings to a design matrix $\mathbf{X} \in R^{500\times 26}$. The model parameters



(a) SPM

(b) l_0-LAD

Fig. 2. Activation maps for the Instructions feature. Slices 9 to 20 activated by both methods numbered from top to bottom and from left to right.

are then estimated by using the iterative ℓ_0-LAD regression algorithm described above. The parameter α and the number of iterations are set to 0.95 and 100, respectively. After fitting the model, for each voxel, contrast vectors to estimate signal magnitudes in response to a single condition through $\mathbf{c}^T\boldsymbol{\beta}_j$ are used, where $\mathbf{c}$ is defined according to the stimulus task function that we are interested in. For instance, to evaluate the instructions task, all the components of the contrast vector are set to zero but the sixth one that is set to one. From $z_j = \mathbf{c}^T\boldsymbol{\beta}_j$, it is possible to generate an activation map either by using thresholding strategies or by selecting a set of voxels with the most significant z_j-values. Finally, for comparison purposes the SPM software was used considering the design matrix of experiment 1.

V. PRELIMINARY RESULTS

To illustrate the performance of the proposed method in detecting activations the results of analysis for subject 14 run 1 are selected. Figure 2 shows the activation maps for the Instructions task obtained with: 1) SPM software (Fig. 2(a)), and 2) ℓ_0-LAD regression method (Fig. 2(b)). In order to be fair in the comparison, these maps are generated by selecting the 300 most significant statistics, that is, 300 statistics z for ℓ_0-LAD regression method and 300 statistics t for SPM. Note that a more elaborate approach that exploits the statistic of non-activated voxels, as in SPM, can be used to set a threshold parameter based on a target false alarm probability.

Under this condition, both methods activated 17 slices. Although the activated slices are not exactly the same, the number of matching activated slices is high. To be more precise 14 (slices 8 to 21) for a matching percentage of 82.35% at slices level. At voxels level, however, the percentage of matching is 53.33%. Additional slices activated by SPM are 5, 6, and 7, whereas our approach actives slices 2, 3 and 22. From Fig. 2 it is possible to see that the activated regions are similar in each one of the matching activated slices, although the ℓ_0-LAD regression method tends to exhibit more isolated voxels than SPM which promotes clusterings. This behavior is likely caused by the treatment of the temporal correlation between residual errors that SPM does. SPM uses an iterative estimation scheme which allows simultaneous estimation of model parameters and autocorrelation (hyper)parameters. The autocorrelation model used by SPM is an "AR(1)+white noise" model, where AR(1) indicates an Auto Regressive model of order 1 [9]. Despite these differences, it is clear that the activated regions by ℓ_0-LAD method are consistent with those achieved by SPM. Furthermore, as expected for this kind of stimulus, the activated areas detected by both methods appear to be in the auditory cortex.

VI. CONCLUSIONS AND FUTURE WORKS

In this paper, we combine the GLM model with the l_0-LAD regression method to exploit the inherent sparsity of decomposing real fMRI signal as a sparse superposition of elements of an suitable set. The proposed approach is validated through the comparison with the SPM software by using real data obtained from the PBAIC 2007. Results demonstrate that the activated regions by our approach are similar to those activated by SPM, although the clustering patterns are slightly different and there exist more isolate activated voxels than with SPM. The obtained results are promising and constitute the starting point to elaborate a more accurate technique. An approach that jointly exploits sparsity and, at the same time, induces clustering in the solution is under consideration as a future work.

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