

fMRI activated-voxel detection based on ICA decomposition and wavelet analysis

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Abstract—Functional magnetic resonance imaging (fMRI) is a technique for investigating activity in the brain in response to some applied stimulus during a mental process. In this paper, detection of activated voxels in a two-class block-design fMRI experiment is described. A methodology based on blind source separation using Independent Component Analysis (ICA), applied on wavelet decomposition of voxel time signals is shown to provide an adequate and robust data separation. Results obtained from simulated as well as experimental fMRI data obtained from the public repository of the fMRI Data Center, are presented.

Index Terms— fMRI, Brain, ICA, wavelet.

I. INTRODUCTION

Functional magneto-resonance imaging (fMRI) is a technique based on blood oxygen-level dependent phenomenon (BOLD) in the brain, which provides indication of brain activity in response to some defined stimulus. fMRI measures signal changes in the brain that are due to changing neural activity. The object of the analysis is finding the activation voxels in a three-dimensional representation of the brain, which correspond to some stimulus in a time axis, and use this information to classify the fMRI images from different stimuli. There are two classic paradigms which can be used to design an fMRI experiment: Block-design, and event-related design. In a block-design experiment the stimuli are applied consecutively in a previously defined order, alternating the defined task (experimental blocks), with rest periods (control blocks). This experimental configuration generates a group of a specific number of three-dimensional volumes in a time line, so each voxel in the three-dimensional representation of the brain generates a time series when is analyzed across the time axis. This time series is correlated with a theoretical model derived from the experimental setup in order to detect the activation voxels corresponding to the

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specific stimulus. Voxels with a high correlation with the reference time signal are then considered and marked as activated voxels.

Several approaches aiming to the detection of activated voxels in fMRI experiments have been reported [1]-[11]. The majority of these approaches are based on General Linear Model (GLM). A potential problem with these analysis methods [5]-[11], [22] is that they require an accurate estimate of the fMRI signal that should result of the task. Such approaches are known as hypothesis driven analysis.

Data driven analysis provide a complementary approach to testing each voxel's time course. When a data driven analysis is conducted, the researcher explores the structure of the data in the hope that task-related activation will emerge. The main benefit of using a data-driven approach to determine the underlying structure of the data is that often the expected time course of brain activation is difficult to specify a priori, or simply the temporal model is not available. Two popular data-driven techniques include ICA [1]-[3], [12]-[17] and clustering [13]. ICA has shown to be useful for fMRI analysis due in part to its ability to reveal dynamics for which a temporal model is not available.

The main goal of this work is to present a robust and noise tolerant methodology based on wavelet and Independent Component Analysis techniques, so that brain activation can be accurately detected.

II. INDEPENDENT COMPONENT ANALYSIS OF FMRI DATA

Independent Component Analysis (ICA), an approach to the problem known as Blind Source Separation (BSS), is a widely used method for separation of mixed signals [13]. The signals are assumed to be the result of linear combinations of the independent sources, as expressed in (1):

$$x_i(t) = a_{i1}s_1(t) + a_{i2}s_2(t) + \dots + a_{in}s_n(t) \quad (1)$$

or in a matrix form:

$$\mathbf{x} = \mathbf{A}\mathbf{s} \quad (2)$$

Where \mathbf{A} is a matrix containing mixing parameters and \mathbf{s} the source signals. The goal of ICA is to calculate the original source signals from the mixture by estimating an unmixing matrix \mathbf{U} that gives:

$$\mathbf{s} = \mathbf{U}\mathbf{x} \quad (3)$$

This method is called blind, because little information is available, i.e. both the mixing matrix \mathbf{A} and the matrix

containing the sources s are unknown. The unmixing matrix \mathbf{U} is found by optimizing a cost function. Several different cost functions can be used for performing ICA, e.g. kurtosis, negentropy, etc.; therefore, different methods exist to estimate \mathbf{U} . For that purpose the source signals are assumed to be non-gaussian and statistically independent. The requirement of non-gaussianity stems from the fact that ICA relies on higher order statistics to separate the variables, and higher order statistics of Gaussian signals are zero [13].

ICA can be used in two complementary ways to decompose an image sequence into a set of images and a corresponding set of time varying image amplitudes Spatial ICA (sICA) [1] finds a set of mutually independent component IC images and a corresponding dual set of unconstrained time courses whereas temporal ICA (tICA)[15] finds a set of IC time courses and a corresponding dual set of unconstrained images.

III. TIME-FREQUENCY ANALYSIS

A. Wavelet sub-band coding

The Discrete Wavelet Transform (DWT) is a transformation that can be used to analyze the temporal and spectral properties of non-stationary signals. The DWT is defined in (4):

$$W(j, k) = \sum_j \sum_k f(x) 2^{-j/2} \psi(2^{-j} x - k) \quad (4)$$

The set of functions $\psi_{j,k}(n)$ is referred to as the family of wavelets derived from $\psi(n)$, which is a time function with finite energy and fast decay called the mother wavelet. The basis of the wavelet space corresponds then, to the orthonormal functions obtained from the mother wavelet after scale and translation operations. The definition indicates the projection of the input signal into the wavelet space through the inner product, then, the function $f(x)$ can be represented in the form shown in (5) [20]:

$$f(x) = \sum_{j,k} d_j(k) \psi_{j,k} \quad (5)$$

Where $d_j(k)$ are the wavelet coefficients at level j . The coefficients at different levels can be obtained through the projection of the signal into the wavelets family as:

$$\langle f, \psi_{j,k} \rangle = \sum_l d_l \langle f, \psi_{j,k+l} \rangle \quad (6)$$

$$\langle f, \psi_{j,k} \rangle = \frac{1}{\sqrt{2}} \sum_l c_l \langle f, \psi_{j-1,2k+l} \rangle \quad (7)$$

The DWT analysis can be performed using a fast, pyramidal algorithm described in terms of multi-rate filter banks. Each sub-band contains half the samples of the neighboring higher frequency sub-band. In the pyramidal algorithm the signal is analyzed at different frequency bands with different resolution by decomposing the signal into a coarse approximation and detail information. The coarse approximation is then further decomposed using the same wavelet decomposition step. This is achieved by successive high-pass and low-pass filtering of the time signal, and a down-sampling by two as defined by the following equations:

$$a_j(k) = \sum_m h_{lp}(m-2k) a_{j+1}(m) \quad (8)$$

$$d_j(k) = \sum_m g_{hp}(m-2k) a_{j+1}(m) \quad (9)$$

Signals $a_j(k)$ and $d_j(k)$ are known as approximation and detail coefficients, respectively. This process may be executed iteratively forming a wavelet decomposition tree up to any desired resolution level.

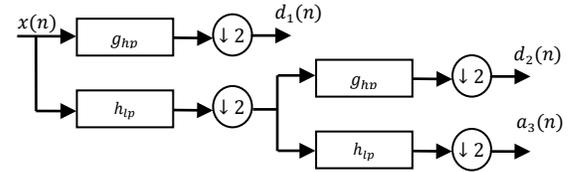


Fig.1 Two-level discrete wavelet decomposition using filter banks

IV. DESCRIPTION OF THE PROPOSED METHOD

Based on the above analysis, the Wavelet-ICA algorithm for solving the fMRI problem is described as follows.

Algorithm:

Step 1: Rearrange the fMRI data to a format so that wavelet analysis can be applied. Each row of matrix \mathbf{A} contains a different volume of the fMRI experiment.

Step 2: The wavelet analysis decomposition is carried out up to an adequate level so that is possible to preserve most of the energy with only a few coefficients and at the same time, the data are filtered of noise added during fMRI experiment.

Step 3: ICA is applied on the decomposed fMRI data in order to find a set of IC time courses that corresponds to a true task stimuli in the experiment.

Step 4: A correlation analysis is conducted. The voxel's time series is correlated with each independent component.

$$r = \frac{1}{n-1} \frac{\sum (x - x^T)(y - y^T)}{\sigma_x \sigma_y} \quad (10)$$

Step 5: Voxels with high correlation coefficient are displayed as active voxels.

The corresponding block diagram of this procedure is showed in Fig.2

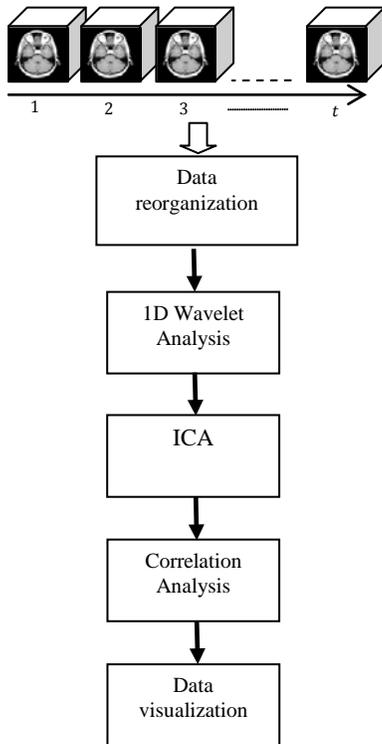


Fig.2 Block diagram of methodology

V. EXPERIMENTAL RESULTS

The proposed methodology was initially tested using a simulated fMRI sequence, artificially constructed. Further, real fMRI data taken from a public database available to the international community for research purposes, was used [24].

In the first case, a 48-volumes sequence was constructed, by defining a theoretical experiment according to the task-rest disposition described in Fig.3, where each block corresponds to 6 volumes.

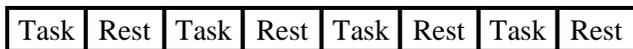


Fig.3 fMRI block design experiment

In the volumes corresponding to the task, a 3-D sphere with a radius of n pixels was introduced as a theoretical voxel-activated region Fig., with a contrast level of 2%, and additive Gaussian noise with zero mean and several values of variances from 1×10^{-6} to 1.8×10^{-4} . Above $\sigma^2 = 0.6 \times 10^{-4}$, the amount of noise masks the time signals, which makes the system practically unable to detect any activated voxels. Fig. shows

an example of a simulated voxel time signal immerse in Gaussian noise with different variance values. Fig. shows the number and percentage of activated voxels detected correctly, using the variances values of the Gaussian noise indicated.

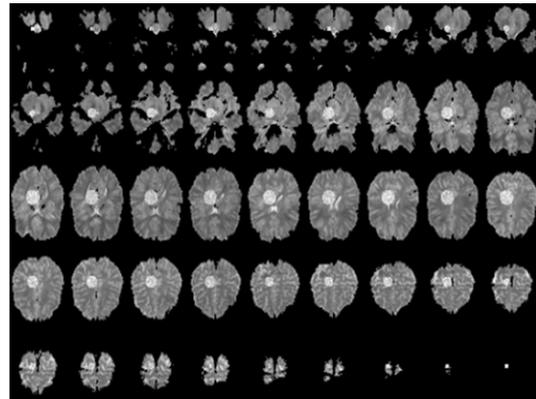


Fig.4 Volume with simulated voxel-activated region]

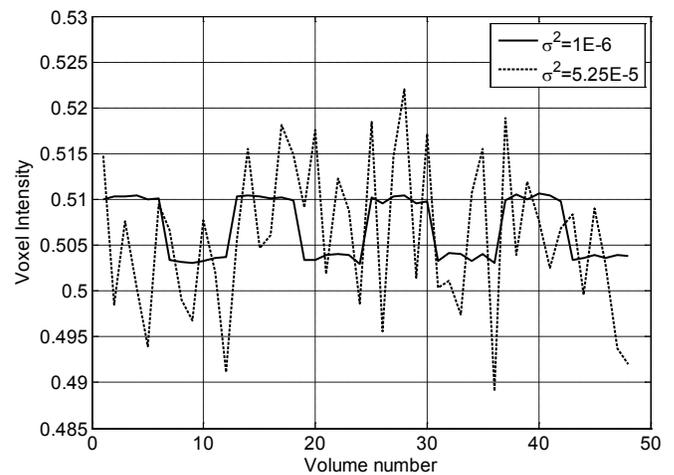


Fig.5 A voxel time signal immerse in Gaussian noise with two different variance values

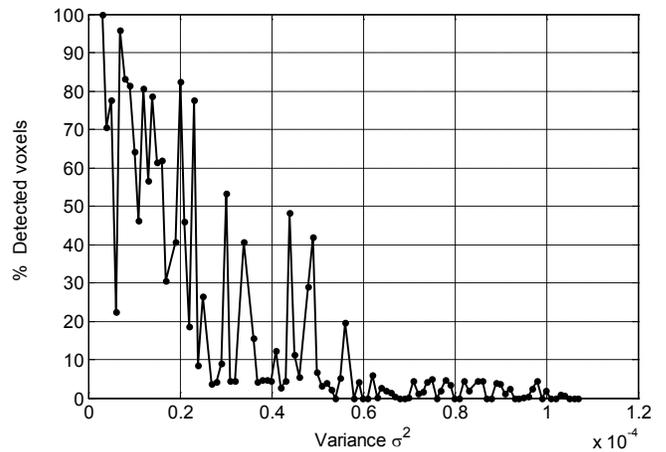


Fig.6 Percent of voxels detected correctly when Gaussian noise is added with different values of variances.

The proposed methodology was then applied to real fMRI data, using the public repository of the fMRI Data Center, University of California [24]. This database allows the access to several fMRI experiments and peer-reviewed fMRI studies, publically available to the international community for research purposes. The used experiment [23] is a block-design stimuli experiment consisting of exposing the subject to the visual exam of gray-level images representing some animals and common objects easy to recognize, in blocks of six trials each. The subject is asked to pronounce in a microphone the name of the animal or object showed in the screen. The 4D fMRI data is then formed by 96 volumes with a resolution of 64x51x45 voxels in each volume.

According to the proposed methodology represented in Fig.2, the first step consists of a wavelet-based dimensionality reduction. For that purpose, a Haar wavelet decomposition using the sub-band coding algorithm previously described was applied to the pre-arranged fMRI data. Wavelet type and decomposition level were selected through experimentation, with the result of deciding on the Haar wavelet with seven decomposition levels. In the next stage, Independent Component Analysis was used in order to extract 3 source signals Fig.7.

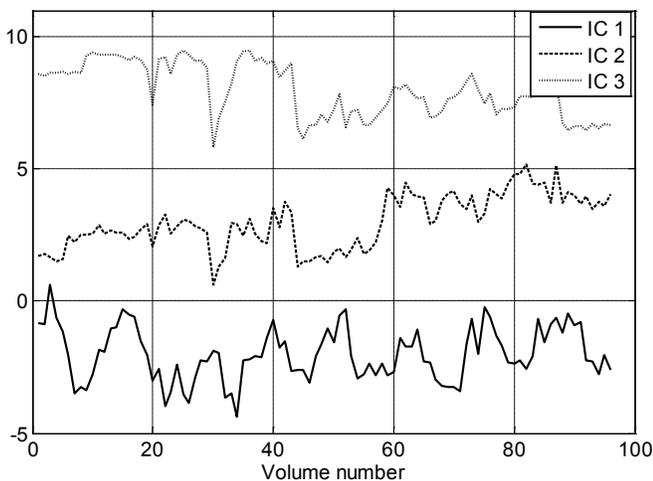


Fig.7 Three independent components extracted of our real fMRI experiment

A correlation analysis on the extracted independent component analysis with each voxel's time course allows the system to identify the activated voxels associated to the described stimuli applied during the fMRI experiment. Fig. shows the result of correlation analysis applied to the second independent component found. Voxels with coefficient value higher to 0.5 were marked as active voxels.

The color is coded according to the value of correlation analysis. Voxels with values between 0.5 and 0.6 are displayed in a dark red, values between 0.61 and 0.8 are displayed in orange and the voxels with values between 0.81 and 1 are displayed as a bright yellow.

VI. CONCLUSIONS

This work presented a methodology on fMRI data analysis based on wavelet decomposition and Independent Component Analysis. The proposed method was shown to be robust and noise tolerant on experiments using simulated fMRI sequences. Wavelet decomposition helped to reduce the computational effort related to the high-dimensionality of the processed information, by applying ICA only on the approximation wavelet coefficients. Regions of activation were identified on the fMRI images, without any a priori knowledge of the expected hemodynamic response. Experiments on the classification of the activated regions using neural networks and support vector machines are currently in progress.

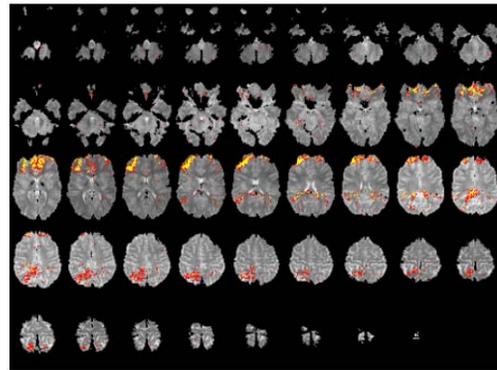


Fig.8 Activation map resulting of the correlation analysis

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VII. REFERENCES

- [1] M. McKeown, S. Makeig, G. Brown, T. Jung, S. Kindermann, A. Bell, and T. Sejnowski, "Analysis of fMRI data by blind separation into independent spatial components," *Human Brain Map.*, vol. 6, pp. 160–188, 1998.
- [2] Worsley, K. J. & Friston, K. J. "Analysis of fMRI time-series revisited – again," *Neuroimage* Vol.2, pp. 173 -181, 1995.
- [3] J.F. Cardoso, "Infomax and maximum likelihood for source separation" *IEEE letters on signal processing*, Vol.4, pp.112-114, 1997.
- [4] Filip Deleus and Marc M. Van Hulle, "A Connectivity-Based Method for Defining Regions-of-Interest in fMRI Data," *IEEE Trans. Image processing*, Vol.18, No.8, August 2009.
- [5] William F. Auffermann, Shing-Chung Ngan, Shantanu Sarkar, Essa Yacoub, and Xiaoping Hu, "Nonadditive Two-Way ANOVA for Event-Related fMRI Data Analysis," *Neuroimage*, 14: S 406-416, 2002.
- [6] Stephen Smith D.G. Leibovici, "Comparing groups of subjects in fMRI studies: a review of the GLM approach," Center for Functional Magnetic Resonance Imaging of the Brain, University of Oxford, Tech Report, 2001.
- [7] Vickers, Y. Zhang, N. De Stefano, J.M. Brady, and P.M. Matthews, "Advances in functional and structural MR image analysis and implementation as FSL," *NeuroImage*, 23(S1):208-219, 2004.
- [8] K. J. Friston and W. Penny, "Posterior probability maps and SPMs," *NeuroImage* Vol. 19, pp. 1240–1249, 2003.

- [9] M.W. Woolrich, S. Jbabdi, B. Patenaude, M. Chappell, S. Makni, T. Behrens, C. Beckmann, M. Jenkinson, S.M. Smith, "Bayesian analysis of neuroimaging data in FSL," *NeuroImage*, 45:S173-186, 2009.
- [10] William D. Penny, Nelson J. Trujillo-Barreto, and Karl J. Friston, "Bayesian fMRI time series analysis with spatial priors," *Neuroimage* Vol. 24, pp. 350-362, 2004.
- [11] O. Friman, J. Cedefamn, P. Lundberg, M. Borga, and H. Knutsson, "Detection of neural activity in functional mri using canonical correlation analysis," *Magn. Reson. Med.*, vol. 45, pp. 323-330, 2001.
- [12] Martin J. McKeown, Scott Makeig, Greg G. Brown, Tzyy-Ping Jung, Sandra S. Kindermann, Anthony J. Bell, and Terrence J. Sejnowski, "Analysis of fMRI Data by Blind Separation into Independent Spatial Components," Meeting of the American Academy of Neurology, 1997.
- [13] Aapo Hyvarinen, Juha Karhunen, Erkki Oja. *Independent Component Analysis*, John Wiley & Sons, 2001.
- [14] Bell AJ, Sejnowski TJ, "An information-maximization approach to blind separation and blind deconvolution," *Neural Comput.* Vol. 7, pp. 1129-1159, 1995.
- [15] Martin J McKeown, Lars Kai Hansen, Terrence J. Sejnowski, "Independent component analysis of functional MRI: what is signal and what is noise?," *Neurobiology*, Vol.13, pp. 620-629, 2003.
- [16] Biswal BB, Ulmer JL, "Blind source separation of multiple signal sources of fMRI data sets using independent component analysis," *J. Comput Assist Tomogr* 1999;23:265-71.
- [17] Hammeke TA, Yetkin FZ, Mueller WM, Morris GL III, and Amar Kachenoura, Laurent Albera, Lotfi Senhadji, and Pierre Comon, "ICA: A Potential Tool for BCI Systems," *IEEE signal Processing Magazine*, pp. 57-68, January 2008.
- [18] John L. Semmlow, *Biosignal and Medical Image Processing*, Second Edition, CRC Press, Taylor and Francis Group, New York, 2008.
- [19] M.B. Priestley, "Wavelets and time-dependent spectral analysis," *Journal of Time Series Analysis*, Vol.17, No. 1, pp. 85- 103, 2008.
- [20] Mark A. Pinsky, *Introduction to Fourier analysis and Wavelets, Graduate Studies in Mathematics*, Vol. 102, American Mathematical Society, 2009.
- [21] Saleem Zaroubi, Gadi Goelman, "Complex denoising of MR data via wavelet analysis: Application for functional MRI," *Magnetic Resonance Imaging*, 18 pp. 59-68, 2000.
- [22] S.M. Smith, M. Jenkinson, M.W. Woolrich, C.F. Beckmann, T.E.J. Behrens, H. Johansen-Berg, P.R. Bannister, M. De Luca, I. Drobnjak, D.E. Flitney, R. Niazy, J. Saunders, J. Doug Greve, "Statistics Review for fMRI Data Analysis," *HST.583: Functional Magnetic Resonance Imaging*, pp. 10-11.
- [23] Irene P. Kan, Joseph W. Kable, Amanda Van Scoyoc, Anjan Chatterjee, and Sharon L. Thompson-Schill, "Fractionating the Left Frontal Response to Tools: Dissociable Effects of Motor Experience and Lexical Competition," *Journal of Cognitive Neuroscience* 18:2, pp. 267-277, 2006.
- [24] The fMRI Data Center, <http://www.fmridc.org/fmridc>

VIII. BIOGRAPHY



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