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Activation Detection in Functional MRI Using Model-Free Technique Based On CCA-ICA Analysis

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Abstract— **The model-based approach for detecting the fMRI activations involves assumptions about the hemodynamic response function. If such assumptions are incorrect or incomplete, this may result in biased estimates of the true response, posing a significant obstacle to the practicality of the technique. In this work, a simple yet robust model-free technique is proposed for detecting the fMRI activations. The idea of the proposed model is to convert one of the model-based fMRI tools, namely canonical correlation analysis (CCA), to model–free with help of independent component analysis (ICA). In particular, ICA provides accurate reference functions for CCA instead of the harmonics originally used. This combination enables the elimination of the limitations of both techniques and provides a model-free approach for data analysis. Results from both numerical simulations and real fMRI data sets confirm the practicality and robustness of the proposed method.**

Keywords: Functional magnetic resonance imaging, independent component analysis, canonical correlation analysis.

I. Introduction

Functional magnetic resonance imaging (fMRI) is an exciting relatively new medical imaging technique that is providing much new information about the function of the human brain. The technique hinges upon the sensitivity of the magnetization decay rates to changes in physiological conditions. For example, the effective decay rate of the longitudinal magnetization is sensitive to increases in the inflow of blood during activation or sensory stimulation. The resulting signal change has been measured [1] in order to quantify cerebral blood flow (CBF) rates. Another example is the decay rate, which has a blood oxygenation level dependence (BOLD) [2]. The fMRI measurements are physiologically filtered versions of the actual neural activity, disturbed by electronic noise and other physical and physiological artifacts. Although blood oxygenation level dependent (BOLD) fMRI has considerable advantages over other functional imaging modalities. On a 1.5 T scanner, the BOLD signal change due to the experimental stimulation of the brain is approximate 1%-5%. In addition, various sources of noise and artifacts such as subject motion, scanner calibration drifts, and physiological processes such as vascular flow, heart rate, and vessel motion significantly confound the fMRI signal. Therefore, the analysis method should be insensitive to these interfering signals so that activations can be accurately detected. A variety of analysis methods have been developed for detecting brain activations in fMRI. Principal component analysis (PCA) [4], independent component analysis (ICA) [5], model-based fMRI signal analysis methods (e.g., [6]-[7]) assume a specific model for the fMRI signal with a specified noise structure. However, the structure of noise in fMRI is not well understood and remains a contentious subject [8]. The validity of the statistical models depends on the extent to which the data satisfies the underlying assumptions. If we assume that images are acquired during an fMRI experiment, then the data at each pixel can be represented by a discrete-time sequence of length. Each measured sequence can be thought of as containing three components: 1) a hemodynamic response signal component which arises due to the experimentally controlled activation-baseline pattern; 2) a nuisance component representing effects of no interest such as the average signal intensity, physiological biorhythms, and systematic drifts in the signal level; and 3) noise. One can think of the signal component as the response of a system whose input is the activation-baseline pattern. A widely used method for detecting activated pixels in fMRI is the cross-correlation method [9].

In this method, one computes the cross correlation between the measured time series and a reference signal which represents an estimate of the response signal component. Those pixels that show high correlations are declared to be activated. The suggestion is to select the reference signal to be formed as a periodic function by replicating this time-averaged cycle throughout the time course. As noted, the reference signals obtained using the latter may not present all kind of data. In addition, it may be difficult to represent activated pixels whose time sequences are event related fMRI. Besides, the data are in general very noisy, and much statistical research has been devoted to studying how the weak activation signals may be extracted with optimal sensitivity. Thus, the use of model-free analysis in fMRI is inherently attractive because it does not rely on imposed assumptions about experimental conditions.

II. Theory

A. Independent Component Analysis

Independent Component Analysis is a signal processing technique, created to separate a number of statistically "independent" sources that have been mixed linearly without further knowledge of their distributions or dynamics.

ICA assumes there are N statistically independent inputs that have been mixed linearly in N output channels. Knowledge of joint distributions and statistical independence of latent variables is assumed [10]. There are two types of ICA that can be calculated: spatial ICA, in which the spatial components are constrained to be independent and temporal ICA, in which the time courses of modulation are constrained to be independent. That latter is considered here.

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B. WN criterion

The WN criterion was met if the mean power across all frequency bins of the power spectrum was greater than the standard deviation of the power across all those frequency bins. If for any given component, the WN criterion was met, then its power spectrum was considered essentially the spectrum of white noise and that component was scored as a relevant contributor to the overall noise content of the MR signal.

C. Canonical correlation analysis

Canonical correlation analysis (CCA) is a well-known tool in statistical analysis. CCA is a way of measuring the linear relationship between two multidimensional variables. It finds two bases, one for each variable, that are optimal with respect to correlations and, at the same time, it finds the corresponding correlations [11]. Given two multidimensional random vectors, CCA finds the optimal linear combination such that X and Y correlate the most.

III. METHODS

Assume that an fMRI experiment has been performed in which a number of image slices are acquired at N subsequent time points. In each pixel in each image slice we obtain a time series of length N. In activated region of the brain there should be a small signal increase during task performance due to BOLD effect. We are searching for pixels whose time series has a component that follows the paradigm. However, due to the low signal-to-noise ratio we will instead consider a region of pixels to make use of the spatial relationships between pixels. This region becomes our multidimensional x-variable, in this work, a 3×3 region is chosen leading to a nine-dimensional x-variable, the measured time series will be referred to as $x(t) = [x_1(t),\ldots\ldots, x_9(t)]^T$. Since it is not well known what the hemodynamic response in an activated region is, therefore Instead of using a modeled signal subspace as other technique [11] chose the $y(t)$ variable as a basis-function of Fourier-series expansion of a square-wave in contrast to the other technique [11], we extract the reference signal $y(t)$ directly from the outcome of ICA of a true activation selected from the real data itself without any assumption about the neuronal response. The practical implementation steps are described later. The algorithm and all supporting routines were written in Matlab (Math Works, Natick, MA). This approach was investigated by applying it to simulated fMRI datasets, for event related fMRI. In the simulation studies, the performance of the present approach was measured to make its results easier to evaluate. In the experimental studies, the present approach was applied to activated time courses from experimental data obtained to illustrate its practical utility.

The computer simulations were performed whereby a computer generated ER-fMRI activation signal was added to an actual baseline data set. The generated activation was generated using a signal of the form as per equation (1):

$$X(t) = (1 - \exp(-t/T1))^3 \cdot \exp(-t/T2), \quad (1)$$

where T1 and T2 are constants that can be adjusted to obtain the desired shape and t represents the sampling times (i.e., the image number within an epoch), the number of epochs was 5 and the length of each epoch was 100 as shown in Fig. 1. Spatial pattern of activity activations were added to the dataset in the regions as shown in Fig. 2, with different contrasts, from left to right and different pattern, from top to bottom.

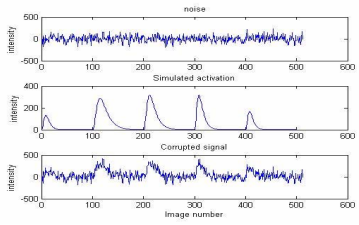

Fig. 1. Simulated activation time course

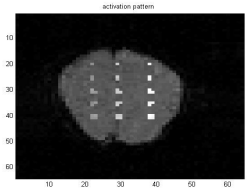

Fig. 2. Spatial pattern of activity activations were added to the dataset in the regions shown in this figure, with different contrasts, from left to right and different pattern from top to bottom.

New Postprocessing functions were added to the FastICA package [12] as shown in Fig. 3. The practical implementation steps needed to implement the new technique are as follows:

Step 1. Select the region of interest for selecting a good real reference activation time course.

Step 2. Compute the mean power for the recalled data across all frequency bins of the power spectrum.

Step 3. Compute the standard deviation of the power for the recalled data across all those frequency bins of the power spectrum.

Step 4. The power spectrum of each pixel was evaluated with white noise (WN) criterion by dividing the standard deviation over the mean as a ratio.

Step 5. Rank the above ratio in descending order.

Step 6. Screen the region of interest. Iin our case, the motor cortex screened first then the visual cortex for the highest rank value, then a 3×3 region selected from each area which has a real activation as shown the center pixel for each area in Figs. 4 and 5 respectively.

Step 7. Perform PCA for reducing dimension and get as much signal variance possible.

Step 8. Perform ICA for the selected pixels, using the modified FastICA module [12].

Step 9. Extract the reference function needed to CCA technique from the outcome of ICA.

Step 10. Select the region of interest to be examined for a real activation, 3×3 pixel regions at a time.

Step 11. Apply the new technique for computing the correlation factor for the selected area.

Step 12. These pixels unable to pass the threshold correlation factor are classified as noise and

automatically cleared for the data sets in which noise was to be removed.

Step 13. Pixels that passed the threshold correlation factor are classified as activation and assigned an activation value corresponding to the correlation factor as shown in Figs. 6-9.

Step 14. Steps 10-13 are repeated for the rest of the pixels.

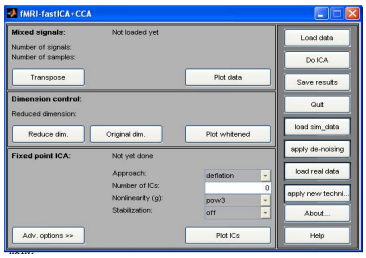

Fig.3. Postprocessing Functions added within FastICA [12]

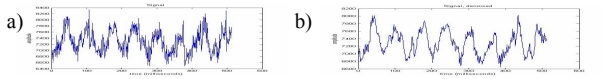

Fig. 4. Reference time course signals selected from the motor cortex area: a)original signal and b) denoised signal

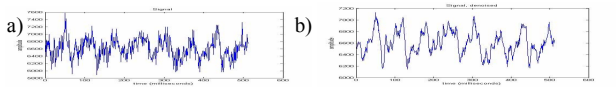

Fig. 5. Reference time course signals selected from visual cortex area: a) original signal and b) denoised signal

IV. Results and Discussion

The proposed technique for activation detection was applied to simulated and real experimental fMRI data sets and its performance compared to those of a similar time domain method. Simulated Data set for simulating an fMRI dataset was created, by adding activations, trends and noise to a base image. Also the present technique was applied to the event-related fMRI data. The data were obtained from an activation study performed on a volunteer using a Siemens 1.5T clinical scanner. In this study, an oblique slice through the motor and the visual cortices was imaged using a T2*-weighted EPI sequence (TE/TR= 60/300 ms, Flip angle=55°, FOV=22cm×22cm, slice thickness=5mm). The subject performed rapid finger movement cued by flashing LED goggles. The study consisted of 31 epochs, with 64 images per epoch where we processed 8 epochs in our case. Substantially more information is obtained using CCA compared to ordinary correlation analysis. The largest canonical correlation coefficient is a qualitative measure of how well the time series in the 3×3 neighborhood corresponded to the optimal reference signal Y, that of the CCA found in Y. A large correlation implies a high degree of similarity, and therefore an activated central pixel, a low correlation value means that it was not possible to find a signal in Y that had any similarity to the time course in the neighborhood. The largest canonical correlation coefficient (ρ), is thus the most obvious measure for distinguishing nonactivated pixels from possibly activated. At each pixel, we would like to test the hypothesis H_0: $\rho_1 = 0$ against H_1:$\rho_1 > 0$, A natural decision is to reject H_0 if the largest sample canonical correlation exceeds some threshold ($\rho \geq 0.5$ [11]). Temporal ICA was applied to process groups of pixels within a user specified region of interest of size 3×3. We found that in case of the simulated data the correlation factor for the proposed technique was 50% more than the other model based technique [11] and 80% more than the ordinary correlation technique and these results are shown clearly in Figs. 6-8, accordingly the intensity of the pixels within the selected region which has a true activation is higher in the proposed technique than the other model based [11].

We performed the simulation in two levels for signal to noise ratio (SNR): one set with high SNR the other with low SNR. We found that the results from the proposed technique for both level is same giving a high correlation factor in both cases while the correlation factor from the model-based technique [11] is very low in case of low SNR in this case the activation can not be detected our explanation for that with the proposed technique the reference function to be correlated with where, the area selected was extracted from a real actual data. The use of the proposed model-free analysis in fMRI is inherently attractive because it does not rely on imposed assumptions about experimental conditions but the only limitation is the way to choose a good activation to be as a reference function and therefore we added a preprocess step for screening the data with the WN criterion. The detection map from our proposed technique is coincident with the results from [13] which dealt with same data set, also we found that in case of the real data the correlation factor for The proposed technique was 25% more than the other model-based technique [11] and 80% more than the ordinary correlation which deal with data as a univeriate technique and these results are shown clearly in Fig. 8-9.

Some pixels were selected from region A and region B as shown in Figs. 9, 10 and 11. These pixels show that the proposed technique success to detect a very contaminated signals which can not be detected by the technique in [11], also pixel shown in Fig. 12 in region C shows a false detection of the other technique in [11] while our proposed technique detected as a noise, the reason behind that is the chosen sine/cosine reference function by other technique (model-based) gives an opportunity to noise by pure chance create a pixel time series in a non activated area with high correlation to some signal in chosen reference function, in contrast the proposed model-free technique does not rely on imposed assumptions.

The sensitivity of detecting the activated pixels within the interested region in visual and motor cortices that have a true activation is higher in the proposed technique. This suggests that the idea included in our proposal of converting one of the model based fMRI tools, namely canonical correlation analysis (CCA), to be a model-free with help of the outcome of ICA from actual real data make the technique more sensitive. Also this combination enables the elimination of the limitations of both techniques (CCA-ICA) and provides a robust model-free mechanism for analyzing and makes it more practical for use in clinical settings.

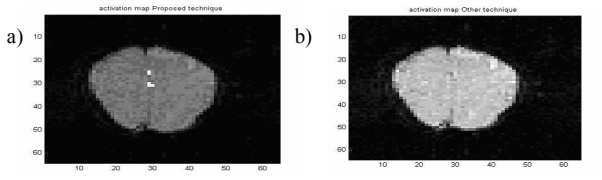

Fig. 6. Result for simulated data in case of low signal to noise ratio: a) proposed technique, and b) other technique

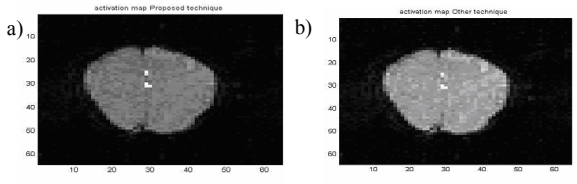

Fig. 7. Result for simulated data-case- high signal to noise ratio: a) proposed technique and b) other technique

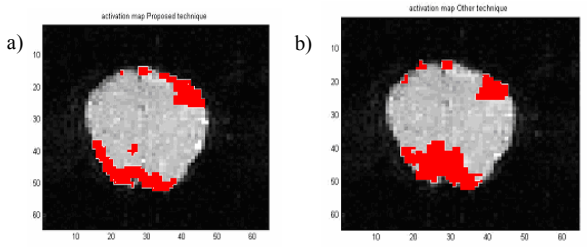

Fig. 8. Activation map for real data: a) proposed and b) other technique

V. Conclusion

A simple model-free technique is proposed for detecting the fMRI activations. This technique adds a second step to CCA (canonical correlation analysis) and the prior information about the activation paradigm which were extracted from the outcome of ICA. The new technique accounts for spatial correlations such as interactions among different regions elicited by various factors. This enables the proposed technique to provide an accurate detection method based on a robust selection of reference functions. The use of model- free analysis in fMRI is inherently attractive because it does not rely on imposed assumptions about experimental conditions.

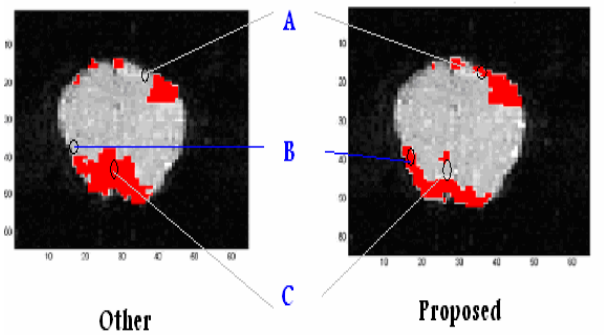

Fig. 9. Activation map for real data set, comparison between the proposed (model free) and technique in [11]

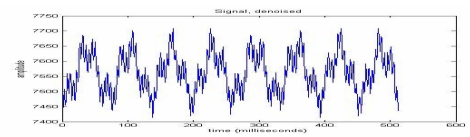

Fig. 10. Time course from a pixel chosen from area A

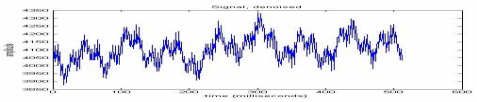

Fig. 11. Time course from a pixel chosen from area B

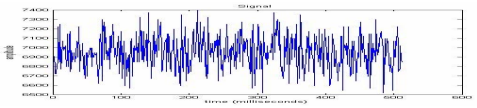

Fig. 12. Time course from a pixel chosen from area C

References

[1] D. D. Stark and W. G. Bradley, *Magnetic Resonance Imaging*, Mosby Inc., New York, 1999.

[2] M. S. Cohen and S. Y. Bookheimer, "Localization of brain function using magnetic resonance imaging," *Trends Neurosci*., vol. 17, pp.268-277, 1994.

[3] D. L. Bihan, *Diffusion and Perfusion Magnetic Resonance Imaging: Application to Functional MRI*, New York, 1995.

[4] A. H. Andersen, D. M. Gash, and M. J. Avison, "Principal component analysis of the dynamic response measured by fMRI: A generalized linear system framework," *Magn. Reson. Imag.*, vol. 17, no. 6, pp. 795-815, 1999.

[5] M. J. McKeown, S. Makeig, G.G. Brown, T.-P. Jung, S. S. Kindermann, A. J. Bell, and T. J. Sejnowski, "Analysis of fMRI data by blind separa- tion into independent spatial components," *Human Brain Mapping*, vol. 6, pp. 160-188, 1998.

[6] K. J. Friston, A. P. Holmes, K. J. Worsley, J.-P. Poline, C. D. Frith, and R. S. J. Frackowiak, "Statistical parametric maps in functional imaging: A general linear approach," *Human Brain Mapping*, vol. 2, pp. 189-210, 1995.

[7] E. Bullmore, M. Brammer, S.C.R. Williams, S. Rabe-Hesketh, N. Janot, A. David, J. Mellers, R. Howard, and P. Sham, "Statistical methods of es-timation and inference for functional MR image analysis," *Magn. Reson. Med.*, vol. 35, pp. 261-277, 1996.

[8] E. Bullmore, C. Long, J. Suckling, J. Fadili, G. Calvert, F. Zelaya, T.A. Carpenter, and M. Brammer, "Colored noise and computational inference in neurophysiological (fMRI) time series analysis: resampling methods in time and wavelet domains," *Human Brain Mapping*, vol. 12, pp. 61-78, 2001.

[9] P. A. Bandettini, A. Jesmanowicz, E. C. Wong, and J. S. Hyde, "Processing strategies for time-course data sets in functional MRI of the human brain," *Magn. Reson. Med.*, vol. 30, pp. 161-173, 1993.

[10] A. Hyvarinen, J. Karhunen, and E. Oja, *Independent Component Analysis*, John Wiley & Sons, New York, 2001.

[11] O. Friman, J. Cadefamn, 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] FastICA Package, Available: http://www.cis.hut.fi/projects/ica/fastica

[13] S. M. La Conte, S.–C. Ngan and X. Hu, "Wavelet transform-based wiener filtering of event-related fMRI data," *Magn. Reson. Med.*, vol. 44, pp.746-757, 2000.