AN ENTROPY BASED METHOD FOR ACTIVATION DETECTION OF FUNCTIONAL MRI DATA USING INDEPENDENT COMPONENT ANALYSIS

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ABSTRACT

Independent Component Analysis (ICA) can be used to decompose functional Magnetic Resonance Imaging (fMRI) data into a set of statistically independent images which are likely to be the sources of fMRI data. After applying ICA, a set of independent components are produced, and then, a "meaningful" subset from these components must be identified, because a large majority of components are non-interesting. So, interpreting the components is an important and also difficult task. In this paper, we propose a criterion based on the entropy of time courses to automatically select the components of interest. This method does not require to know the stimulus pattern of the experiment.

Index Terms— fMRI, ICA, Entropy, Activation detection

1. INTRODUCTION

Functional Magnetic Resonance Imaging (fMRI) is one of the imaging techniques that are used to study human brain function and neurological disease diagnosis [1]. Popular techniques in fMRI utilize the blood oxygenation level dependent (BOLD) contrast, which is based on the differing magnetic properties of oxygenated (diamagnetic) and deoxygenated (paramagnetic) blood [1]. In fact, when brain neurons are activated due to the neural activity, a localized change in blood flow and oxygenation is resulted. As a result of this change, MR decay parameter is changed. Advantages of fMRI over other functional imaging modalities such as Electro Encephalography (EEG), Magneto Encephalography (MEG) and Positron Emission Tomography (PET) include: being non-invasive, having better spatial resolution than other modalities and acquiring images in short time [2].

In order to analyze fMRI data, *hypothesis-driven* or *data-driven* methods can be used [3]. In univariate hypothesis-driven methods, simple approaches are used to produce maps of task-related activations with estimates of their level of significance. In contrast, multivariate data-driven techniques compute suitable statistical models in order to separate "meaningful" activation [3].

Among data-driven techniques, Independent Component Analysis (ICA) provides a powerful method for the exploratory analysis of fMRI data. ICA can be used to decompose an image sequence into a set of images or decompose it into a corresponding set of time-varying image amplitudes. *Spatial* ICA (sICA) finds a set of mutually independent component (IC) images and a corresponding set of unconstrained time courses, whereas *temporal* ICA (tICA) finds a set of IC time courses and a corresponding set of unconstrained images [4]. In general, fMRI data can be categorized into *signals of interest* and *signals not of interest*. The signals of interest include task-related, function related, and transiently task-related. The signals not of interest include physiology-related, motion-related, and scanner related [2].

Result of researches show [4] that the measured fMRI data is a mixture of a few interest and non-interest sources, and by analyzing this data by ICA, it can be decomposed into a set of statistically independent, non-Gaussian signals or images which are likely to be the sources of fMRI data.

In this work, we first use ICA on fMRI data for detecting active regions in brain, without *a priori* knowledge of neural stimulus. We use spatial ICA to find a set of mutually independent component (IC) images and a corresponding set of unconstrained time courses. Then, a "meaningful" subset from the component set must be identified, because a large majority of components are non-interesting. Many criteria such as correlation method [4] and oscillating index [5] have already been used for determining the "meaningful" component maps. In this paper, we propose a criterion based on the estimation of the entropies of time courses corresponding to component maps, to select automatically the components of interest. Up to our best knowledge, entropy criterion has not already been used in determining "meaningful" components after applying ICA for analyzing fMRI data, and we show the results of this proposed method in Section 5. It should also be noted that the correlation method can only be used for

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datasets for which the stimulus pattern of the experiment is known *a priori*, however. our method does not require this *a priori* information.

The paper is organized as follows. Basics of using ICA for fMRI is discussed in Section 2. In Section 3, we explain our proposed method for determining the components of interest. Section 4 describes the details of the simulations. Finally, in Section 5, we present the results of applying the proposed method to an fMRI dataset.

2. REVIEW OF BASICS OF USING ICA FOR FMRI ANALYSIS

The aim of analyzing fMRI data by ICA is to factor the data matrix into a product of a set of time courses and a set of spatial patterns [2]. Fistly, to produce the observation matrix, each image that has been acquired in each time point is converted into a one dimensional row signal vector, $\underline{x}_i (i = 1, \ldots, m)$, where i is the index of each time point, and m is the total number of time points. The length of the signal vector, v, is equal to the number of voxels per frame. The signal $\underline{x}_i$ is considered as a linear combination of the independent components, $\underline{c}_j (j = 1, \ldots, n)$, that is:

$$X_{ik} = \sum_{j=1}^{n} M_{ij} \cdot C_{jk} \quad (k = 1, \ldots, v), \tag{1}$$

where X_{ik} is the k^{th} voxel of the i^{th} observed image, M_{ij} denotes the $(i, j)^{\text{th}}$ element of the estimated mixing matrix and C_{jk} stands for the k^{th} voxel of the j^{th} estimated component. So, the entire image data can be expressed as $\mathbf{X} = \mathbf{M} \cdot \mathbf{C}$ or $\mathbf{C} = \mathbf{W} \cdot \mathbf{X}$, where $\mathbf{X}$ is the $m \times v$ measured data matrix, $\mathbf{M}$ is the $m \times n$ mixing (linear combination) matrix, and $\mathbf{C}$ is the $n \times v$ component matrix. The $n \times m$ weight matrix, $\mathbf{W}$ (also called unmixing matrix), is the pseudo-inverse of $\mathbf{M}$. Both of the weight matrix and the component matrix can be obtained by iteratively updating the elements of $\mathbf{W}$ such that the target components $\underline{c}_j$ can meet some criteria (as independent as possible to each other). The raw vector $\underline{c}_j$ is then reformed into a two dimensional image to construct the component map. Those maps are fixed over time, while the relative contribution of each map changes with a unique associated time course (column of the mixing matrix, $\mathbf{M}$).

3. ENTROPY BASED CRITERION FOR FINDING MEANINGFUL COMPONENTS

After applying ICA on fMRI data and finding a set of independent components, a "meaningful" subset of the component set must be identified, because a large majority of components are non-interesting. In this section, we propose a criterion based on an estimation of the entropies of time courses corresponding to component maps, to select automatically the components of interest.

It should be noted that the i^{th} column of the estimated mixing matrix in spatial ICA demonstrates the time course corresponding to the i^{th} component map. We note now that the time course of the components of interest change smoother than the time course of noise components, and hence, the components of interest have smaller entropies. So we propose to use entropy for detecting the "meaningful" components. Indeed, we calculate the entropy of each time course corresponding to component maps, and we choose the components with smaller entropies as the components of interest.

However, since time courses are sequences in time, calculating their entropies requires some attention. In effect, for calculating Shannon entropy of a signal, one should not neglect the dependence of successive samples. Hence, to model this dependency, we model the time samples as a first order Markov chain. To be more clear, we recall here some results from [6, Chapter 6].

According to [6], if a source is of order M, its uncertainty can be expressed as the difference of the uncertainty of $M+1$ successive symbols and that of M successive symbols. In general, the uncertainty $H(X_1, \ldots, X_n)$ of n successive symbols produced by a source is sometimes referred to as the "n-gram" uncertainty of the source (the terms "unigram" and "digram" are used for $n = 1$ and $n = 2$, respectively). Thus the uncertainty of a source of order M is the difference of its "$(M+1)$-gram" and "M-gram" uncertainties [6].

Let J_1 and J_2 denote unigram and digram respectively. Estimating J_1 is like the estimation of entropy where the sequence was independent and identically-distributed (i.i.d). That is, for estimating J_1, we calculate the probability of each symbol of the sequence as there were i.i.d, and we use the Shannon formula. Similarly, for estimating J_2, we first calculate the probability of each two adjacent points as where any pair of successive points were independent from the other pairs. In other words, if each time course is a quantized signal with μ possible levels $(a_1, a_2, \ldots, a_\mu)$, we can estimate J_1 and J_2 from:

$$J_1 = -\sum_{i=1}^{\mu} p(a_i) \log p(a_i), \tag{2}$$

$$J_2 = -\sum_{i,j=1}^{\mu} p(a_i a_j) \log p(a_i a_j), \tag{3}$$

where $p(a_i)$ is the probability of occurrence of each symbol a_i and $p(a_i a_j)$ is the probability of occurrence of each pair (a_i,a_j). Hence, modeling the time courses as Markov chains of first order, we estimate their entropies by:

$$\hat{H} = \hat{J}_2 - \hat{J}_1 \tag{4}$$

Finally, the time courses with smaller entropies are detected as active components, and the others as inactive components. The number of time courses with smaller entropies which are

chosen as active is equal to number of trials in the fMRI task (which is a priori known from the recording procedure).

4. DETAILS OF SIMULATIONS

Before applying ICA for analyzing fMRI data, the number of independent components (ICs), n, must be determined. The exact number of ICs is always unknown in practice, but it should not be more than the number of measured signals ($n \leq m$). We estimated the number of ICs by using the MDL criterion. For our case, MDL has the form as [7]:

$$\mathrm{MDL}(k) = -0.5(m-k) \times v \times \ln \frac{\prod_{i=k+1}^{m} \lambda_i^{\frac{1}{(m-k)}}}{(\frac{1}{m-k}) \sum_{i=k+1}^{m} \lambda_i} + 0.5[1 + m.k - \tfrac{k}{2}(k-1)] \times \ln v \quad (5)$$

where k is the number of ICs (sources), m is the total number of scans, v is the number of voxels per frame, and λ_i denotes the i^{th} largest eigenvalue of the covariance matrix, $\mathbf{X}\mathbf{X}^T$. The estimation of the number of ICs is determined as the value of $k \in \{1, \ldots, m\}$ for which $\mathrm{MDL}(k)$ is minimized. Then, after determining the optimum number of ICs, ICA will be used with this number of components, and a set of independent spatial components will be produced. We employ FastICA and infomax algorithms in our work. After obtaining the components, in order to determine the "meaningful" components, we use the entropy criterion which was illustrated in Section 3.

5. RESULTS AND COMPARISON

For evaluation of the proposed method, we used a real fMRI dataset[1]. This dataset contains two trials which are repeated periodically. Each period included 55 seconds which stimulus is elongated for 15 seconds and rest mode is elongated for 40 seconds. This pattern is repeated 4 times in an imaging process. The task starts with trial 1, and trial 2 has the same pattern of trial 1, but it occurs with 20 seconds latency. 119 scans (time points) were acquired during the imaging process [8]. Results of analyzing this dataset by SPM software[2] are available at the address of the data set. Since for analyzing data by SPM, *a priori* knowledge about stimulus pattern of the experiment and the Hemodynamic Response Function (HRF) signal are needed, the results obtained by SPM can be used as a reference for comparing the results of our proposed method. By applying MDL criterion, the number of components reduced from 119 to 80 components. After applying ICA for fMRI data, 80 components and 80 corresponding time courses were achieved. We estimated the entropies of all time courses and selected two of them with smaller entropies. Figure 1 shows the detected active component maps by SPM and the proposed method. Figures 2 and 3 show the time course corresponding to active component maps. In these figures, we have also plotted the reference functions of trial 1 and trial 2. Reference functions were obtained by analyzing data by SPM and we used them to compare the estimated time courses by our method with the original reference functions. It can be seen that the estimated time courses correlate strongly with the reference functions of the two trials.

To find and display voxels contributing significantly to the "active" component map (find active regions), the map values were scored to z-scores [4]. This solved the amplitude ambiguity problem of ICA components, because images with zero mean and unit variance were achieved. Voxels whose absolute z-scores are greater than a threshold can be considered to be "active" voxels for that component. We set a primitive threshold (difference of maximum and minimum value of z-scores divided by two). We swept the threshold in a range from 0.7 to 1.4 times of a primitive threshold and plot receiver operating characteristic (ROC) curve for that range. ROC curve plots true-positive rate (TPR) versus false positive rate (FPR). When applying ROC curve to fMRI, TPR implies the ratio of the number of detected voxels as activated among truly activated voxels to the total number of truly activated brain voxels and FPR indicates the ratio of the number of detected voxels as activated among truly non-activated brain voxels to the total number of truly non-activated brain voxels. In this paper, we use active regions which were obtained by SPM as truly activated brain voxels. Figure 4 shows ROC curve for the detected active components. It also shows the comparison of performance two ICA algorithms. As it is clear from this figure, active regions can be detected accurately. The higher area under the ROC curve shows the better performance.

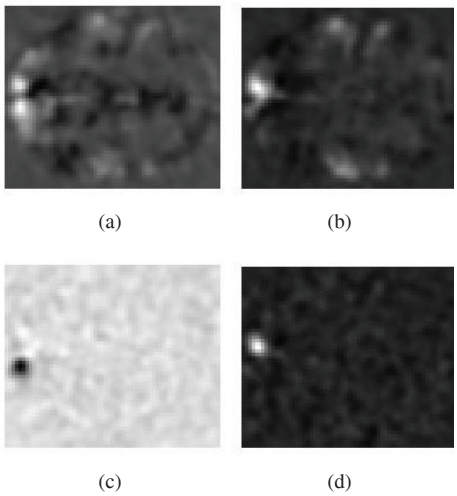

Fig. 1. (a), (b): First and second active component maps estimated by SPM software. (c), (d): First and second active component maps estimated by proposed method.

[1] www.ece.unm.edu/∼vcalhoun/courses/fMRI Spring09/fmricourse.htm

[2] http://www.fil.ion.ucl.ac.uk/spm

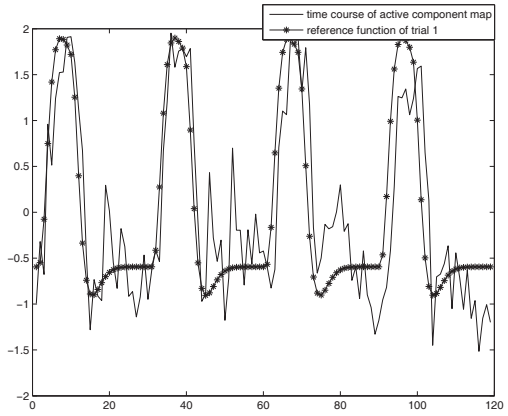

Fig. 2. Time course corresponding to the first detected active component and reference function of trial 1.

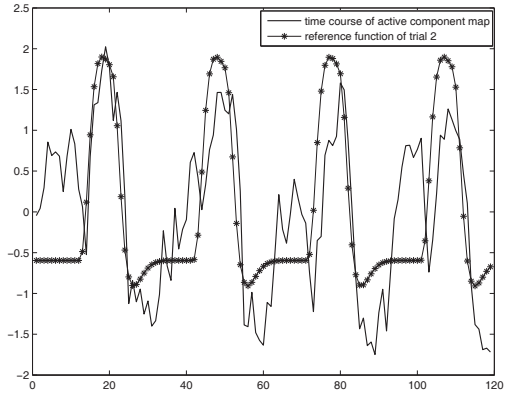

Fig. 3. Time course corresponding to the second detected active component and reference function of trial 2.

6. CONCLUSIONS

ICA has the capability to separate the fMRI data into interest and non-interest sources (image maps or time course signals) which present qualitative information about the active regions. After applying ICA, in order to automatically select the components of interest, a criterion based on the entropies of time courses was proposed. ROC curve showed that this method can detect the active regions of "meaningful" components accurately and consistent with our expectation. Further work can include the use of this proposed method for more real fMRI datasets and evaluate the results. It is also of interest to examine other ICA algorithms and compare their results.

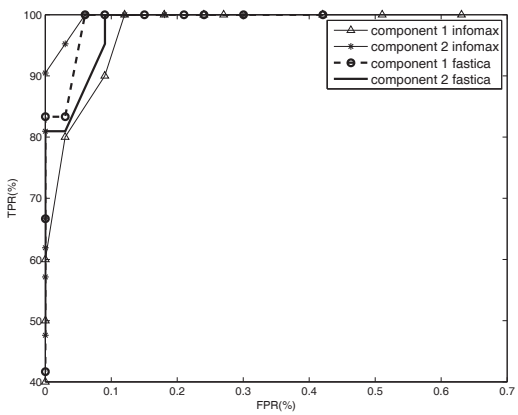

Fig. 4. ROC curve for the detected active components.

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