# A NOVEL APPROACH FOR ASSESSING RELIABILITY OF ICA FOR FMRI ANALYSIS

Wei Du<sup>1</sup>, Sai Ma<sup>1</sup>, Geng-Shen Fu<sup>1</sup>, Vince D. Calhoun<sup>2</sup> and Tülay Adalı<sup>1</sup>

<sup>1</sup>University of Maryland, Baltimore County, Dept. of CSEE, Baltimore, MD 21250 <sup>2</sup>The Mind Research Network and University of New Mexico, Dept. of ECE, Albuquerque, NM 87131

# ABSTRACT

Independent component analysis (ICA) has proven quite useful for the analysis of functional magnetic resonance imaging (fMRI) data. However, stability of ICA decompositions is an issue in ICA of fMRI analysis primarily due to the noisy nature of fMRI data and the iterative nature of algorithms. In this work, we present an approach that utilizes an objective criterion and that is particularly suitable for image analysis to select the best of multiple ICA runs to use for further analysis and inference. In addition, a growing number of studies are focusing on the decomposition of single subject data and/or using high ICA model order, which both require an effective way to align components obtained from different ICA runs. In this paper, while presenting a method that provides superior performance in selecting the best run and interpreting the statistical reliability of ICA estimates, we also address the component sorting issue. Both simulated and real fMRI results show that our method selects more useful ICA runs than those selected by the widely used ICASSO software and that it is a more objective and better motivated approach to evaluate results and hence a promising tool for ICA analysis of fMRI data.

*Index Terms*— Independent Component Analysis, EBM, SimTB, assignment problem, ICASSO, fMRI

# 1. INTRODUCTION

Independent component analysis (ICA), as a data-driven method, has proven very useful for analysis of functional magnetic resonance imaging (fMRI) data [1,2]. Several types of ICA algorithms have been developed and successfully applied to fMRI analysis. Most of these algorithms are iterative in nature and thus one important issue is the stability of the decomposition achieved using ICA. The estimation of spatial maps for two ICA runs with identical input data might be different due to local minima produced by the noisy nature of fMRI data and the iterative nature of ICA algorithms [3]. This unknown estimation reliability is induced by the finite sample size of data and the non-unique ICA solution derived from the locally optimal point of the cost function. One approach to address this issue is to determine an objective way to assess and select the best run to use for further analysis and inference.

A widely used approach for resolving the problem is to make use of ICASSO [4], an explorative visualization method for investigating the relations between estimates. ICASSO runs an ICA algorithm several times and clusters estimated components from all runs based on the absolute value of the correlation between estimates, and then selects the centrotype of each cluster as the best estimate. ICASSO is incorporated in the widely used group ICA of fMRI toolbox (GIFT) software that implements both single subject and group ICA analysis for fMRI data [5]. However, the direct use of centrotypes can lead to loss of information, since more than one type of component may be grouped into the same cluster, but only one type of component can be selected as the centrotype, especially when the ICA model order is high. To address this issue, [6] proposed a method based on ICASSO to select the most stable run instead of centrotypes from multiple runs. However, ICASSO can result in different runs selected for different components, which breaks the connection with the ICA mixing model. In addition, both approaches require subjective thresholds to define a reliable cluster or run. As more studies nowadays are using high ICA model order, for example, 50 to 70 or higher, and a growing number of studies are focusing on the study of a single subject, which require an effective way to align components obtained from different ICA runs, new solutions to the run selection problem are needed.

In this work, we propose a novel approach to investigate the stability of ICA algorithms. Our method not only addresses the component sorting issue but we provide evidence to show it provides superior performance in selecting the best run and interpreting the statistical reliability of estimated components. In Section 2, we give an introduction of the ICA algorithm and present the approach that uses assignment problem and minimum spanning tree (MST) to solve the component sorting issue. We propose our approach of selecting the best ICA run in this section. Then, we introduce the generation of multi-subject fMRI-like datasets using a recently developed simulation toolbox [7], real fMRI data, and several approaches to evaluate the efficiency of the proposed method in Section 3. Next, we present experimental results in Section 4 and then present the conclusions in the last section.

## 2. METHODS AND MATERIALS

### 2.1. Independent component analysis of fMRI

In the ICA analysis of fMRI data, we start from the ICA model as  $\mathbf{X} = \mathbf{AS}$ , where  $\mathbf{S} = [\mathbf{s}_1, \dots, \mathbf{s}_N]^T$  is an *N*-by-*V* 

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**Fig. 2**: SimTB configuration of original sources, labeled by different colors. These spatial maps are designed to represent components observed in axial slices of real fMRI data.

source matrix, N is the number of sources, V is the number of voxels and  $\mathbf{s}_i$  is the *i*th underlying component. The mixing matrix **A** is an *M*-by-N matrix where each column  $\mathbf{a}_i$  represents the time course for the *i*th source. The goal of the ICA algorithm is to determine a demixing matrix **W** such that the sources are estimated using  $\hat{\mathbf{S}} = \mathbf{W}\mathbf{X}$  under the assumption of statistical independence of spatial components.

Entropy bound minimization (EBM) algorithm is one of the most effective ICA algorithms, which minimizes the entropy bound of estimated sources and uses a line search procedure for better convergence behavior. EBM can estimate the sources that come from a wide range of distributions including sub- or super- Gaussian and it has proven useful for the analysis of fMRI data [8,9].

The group ICA analysis approach [5] reshapes 4D fMRI data such that the spatial dimension is treated as a single dimension and images from individual subjects are concatenated in time. Then principal component analysis is applied on both subject and group levels to reduce data dimension. An ICA decomposition is performed on the final matrix and individual subject maps are back-reconstructed after this step.

#### 2.2. Generalized assignment problem

Since ICA algorithms suffer a permutation ambiguity and real data never exactly follow the ICA model, some components are not estimated consistently and slightly different components may be estimated during different runs. Thus, our goal is to find the best solution of sorting or ordering the estimated components for multiple runs.

This problem arises in a number of scenarios, most typically when frequency domain ICA is used. Various methods have been developed, including imposing constrains on demixing filters [10], correlations between envelopes of band-passed signals [11], clustering estimated frequency responses [12, 13]. These methods suffer when the model order and/or data dimension are high, which are not suitable for spatial ICA. Hence, in our work, we consider this problem as a generalized assignment problem.



**Fig. 3**: Simulation results for the proposed method and ICASSO. The value in *y*-axis is the average of 100 data sets. Our method always has better performance than ICASSO for different CNR levels and/or higher ICA model order (> 8).

In a linear assignment problem (LAP) [14], given an equal number of agents and tasks, we have to assign each agent to exactly one task in such a manner that the overall cost of assignment is minimized. The optimal solution of LAP can be found by using the Hungarian algorithm [15]. It is equivalent to sorting components in the same order through best pairing them for two ICA runs. We generalize this method for an ordering from two sets to multiple sets of components, which becomes a generalized assignment problem.

We estimate N independent components (ICs) from each ICA run. Then, an N-by-N matrix  $C_{mn}$  is calculated as the input cost of LAP for sorting the mth and nth runs, where  $c_{ij} = 1 - d(\mathbf{s}_i^m, \mathbf{s}_i^n)$  is the *ij*th entry of  $\mathbf{C}_{mn}$ ,  $\mathbf{s}_i^m$  and  $\mathbf{s}_i^n$  are ICs from the *m*th and *n*th runs,  $i, j \in [1, N], m, n \in [1, K]$ and d is the correlation coefficient. The minimum cost and corresponding assignment for each pair of ICA runs are obtained by applying Hungarian algorithm. We then generate a connected, undirected graph that includes K nodes (runs) and weighted edges having the minimum costs of LAP for each pair of ICA runs as weights. Next, an MST is calculated by finding a minimum-cost subgraph connecting all nodes [16]. Finally, we reorder components in each run according to the central run in the obtained tree. The central run has the most connections with other runs and the minimum cost to the connected runs if there exists several runs having the same number of neighbors.

## 2.3. Best run selection based on statistical significance

After aligning ICs from all runs, we perform one-sample Ttests for each component estimate across K runs to investigate the reliability of the estimates of the ICA algorithms. Total of N T-maps are obtained, which represent components across multiple ICA runs. The best run is selected as the run with the highest correlation between estimated components and the corresponding T-maps. In addition, when the estimation is



**Fig. 4**: Interpretation of ten runs using MST. The 4th run is selected as the reference to align components from other runs. Weights on edges are the minimum cost when aligning components of two runs.

consistent, the obtained T-maps exhibit a clear delineation of the functional area of interest whereas when the estimation is not consistent, that is not the case. Thus, the consistently estimated components are favored when selecting the best run using T-maps. The procedure is shown in Figure 1.

For a given component, the average correlation, which is between the T-map and the same components from all runs, also represents the consistency of this component estimated by an ICA algorithm. For one run, the average correlation, which is between T-maps and the corresponding estimated components from this run, denotes the reliability of this ICA run based on statistical significance. We select the run having the highest reliability as the best run to perform subsequent analysis in fMRI study.

## 3. EXPERIMENTAL DESIGN

To evaluate the efficiency of the proposed approach and compare its performance with ICASSO, we perform these methods on both simulated and real fMRI data. Group ICA is used to decompose the data for all subjects using GIFT [17]. In the subject dimension reduction step, the dimension of the data is first reduced to 40, and then the reduced data from each subject are concatenated in the temporal dimension. A group dimension reduction step is performed to reduce the dimension to a selected order. We then perform EBM 10 times with bootstrapped data and use different initial conditions at each run on this final set. The processing at this stage is maintained the same for all methods. After applying group ICA analysis to each data set, the proposed approach and ICASSO are performed to analyze the results and select the best run from ten runs.

#### 3.1. Simulation of fMRI-like data

Multi-subject fMRI-like data are generated using the simulation toolbox, SimTB [7]. This toolbox controls the generation of 2D spatial components and time courses by a selected number of parameters following the linear mixing model.

We select 27 original sources as shown in Figure 2. These spatial maps are modeled after components commonly seen in axial slices of real fMRI data and each contains  $148 \times 148$  voxels. Component time courses are simulated as the convolution of the auditory oddball (AOD) task event—which is explained in Section 3.2—with a canonical hemodynamic response function and scaled to have a peak-to-peak range of one. Each time course is 150 time points in length and the



**Fig. 5**: Reliability of components in descending order. More reliable estimates correspond to higher maximum *T*-values in their *T*-maps. The first five stable components in our method include temporal, motor and motor-temporal components, corresponding to AOD task, which is not observed using ICASSO.



**Fig. 6**: The left figure represents the relationship among ten runs. The 10th run is selected using our method. The right figure is ICASSO results showing correlation of components from all runs. More than one type of components are grouped into the same cluster.

repetition time is 2 seconds per sample. Total of 30 subjects are generated in each simulation data set. The slices of individual components across all subjects can be rotated, translated, contracted or expanded based on the distributions of relevant parameters. To emphasize the difference among multiple ICA runs in a reasonable range, we set the simulation parameters as similar to those in [18], which specifies the parameter of translation  $\mathcal{N}(0, 2)$ , rotation  $\mathcal{N}(0, 3)$ , and spread  $\mathcal{U}(0.3, 3)$ , where  $\mathcal{N}$  and  $\mathcal{U}$  denote uniform and Gaussian distributions. In addition, Gaussian noise with a variance corresponding to a standard contrast-to-noise ratio (CNR) is added to each component.

We first evaluate the performance of our proposed method for CNR values from 0.1 to 2.5 with increments of 0.2. For a given CNR, we generate 100 multi-subject data sets, where each includes 20 components randomly selected from 27 original sources. Second, to investigate the effect of ICA model orders, we fix the value of CNR to 1 and change ICA model orders from 2 to 27 with the increment of 3 in each data set. Components are randomly selected from the original sources and 100 data sets are generated for each given order.

### 3.2. Real fMRI data

The real fMRI data used in this experiment are from 28 healthy controls and 28 schizophrenia patients, all of whom provided written, informed, IRB approved consent at the

Hartford Hospital. All participants were scanned twice while performing an AOD task. Therefore, each participant has two sessions of data. The subjects were stimulated with three kinds of sounds: target (1000 Hz with a probability of 0.10), novel (nonrepeating random digital noises with a probability of 0.10), and standard (500Hz with a probability of 0.80). Preprocessing, including realignment, normalization and smoothing, was performed by SPM5 [19]. More details about the AOD paradigm and other parameters are described in [20, 21]. In the group analysis of real fMRI data, we estimate 50 components to test stability first at a higher order since the component identification becomes challenging.

## 4. EXPERIMENTAL RESULTS

# 4.1. Simulation results

A set of mean components is calculated across true sources of 30 subjects for each generated data set. The ground truth allows us to evaluate results explicitly. First, we calculate the mutual information between the ground truth and estimated aggregated components for each run. Next, ten runs are sorted in descending order according to the average mutual information of one run. Then we assign an integer score from 10 to 1 for each run to quantify the estimation of these 10 runs. The larger score value indicates a better ICA run having larger mutual information with the ground truth.

Results are shown in Figure 3. The score in y-axis is the average of 100 data sets. Our method always has better performance than ICASSO for different CNR levels. Figure 3(b) shows that our method selects better runs than ICASSO when the number of estimated components is greater than eight. Since ICASSO uses components from all runs to perform clustering, smaller number of components yields a better performance. We also calculate the mutual information between the truth sources and selected centrotypes of original ICASSO and compare the results with both best run selection methods. Figure 3(c) shows that our method always leads to higher mutual information with true sources than both ICASSO methods while changing CNR from 0.5 to 2.5. We remove the results where CNR is smaller than 0.5, since estimates of three methods all have very low mutual information with true sources due to the low CNR. Figure 3(d) shows the average mutual information is decreasing while increasing the number of estimated components. Our method has the best performance when the order is large and similar results with ICASSO when the order is small in terms of mutual information.

### 4.2. Real fMRI data results

An MST is generated to demonstrate the relationship between ten runs, as shown in Figure 4. The proposed approach selects the 4th run as the reference to align components of other runs. Then total of 50 *T*-maps are generated across 10 runs. If an estimated independent component is stable, the ICA algorithm should produce very similar results. Thus, more reliable components correspond to higher maximum *T*-values in their *T*-maps. Figure 5 presents the reliability of components in descending order. Since experimental data are AOD task data, results show that the most significantly reliable components are task-related components including temporal, motor



**Fig. 7**: Comparison of two components selected by our method and both ICASSO methods. Components of interest have highest *Z*-values and/or larger activated regions in our method than the best run selected using ICASSO.

and motor-temporal components. The default mode network (DMN) is also constantly estimated. Most of the unreliable components tend to be artifacts that might be expected since they likely exhibit greater variability among subjects. Instead of mixing components from all runs in ICASSO, which groups more than one type of component into the same cluster, we calculate the correlation between estimated components and T-maps for each run. As shown in Figure 6, our method (left) shows correlation values in each run on one box. The central mark is the median, the edges of the box are the 25th and 75th percentiles, the whiskers extend to the most extreme data points not considered outliers, and outliers are plotted individually.

The 10th run is selected as the best in our method and the 2nd run is the best using ICASSO. In Figure 7, we compare two components selected using our method, best run of ICASSO and centrotype of ICASSO. Components of interest have highest Z-values and/or larger activated regions in our method than the best run selected using ICASSO. Other components that are not included in this paper due to the page limitation also have the same trend, such as frontoparietal, motor, visual component and so on. We also apply our method when estimating different model orders, including 20, 30 and 40. Results show similar conclusions with an order of 50.

#### 5. CONTRIBUTIONS AND CONCLUSIONS

In this paper, we propose a novel method for selecting the best ICA run out of multiple runs and show that the proposed method not only selects the best run as indicated by higher Z-value and larger activated regions in ICs, but it is also effective in interpreting estimated results, which is especially important for fMRI data analysis. We compared the performance of our method and ICASSO in terms of mutual information and best run scores by applying on multi-subject fMRI-like datasets with increasing CNR and ICA model order. Using assignment algorithm and MST, we addressed the sorting problem of different ICA runs. We also performed our method on real fMRI data and analyzed the results in several ways. Our experimental results show that the proposed method appears to select better ICA runs than ICASSO and provides a more objective and better motivated approach to evaluate results. Given this, it is a promising approach for the ICA analysis of fMRI data.

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