Subspaces of Spatially Varying Independent Components in fMRI

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Abstract. In contrast to the traditional hypothesis-driven methods, independent component analysis (ICA) is commonly used in functional magnetic resonance imaging (fMRI) studies to identify, in a blind manner, spatially independent elements of functional brain activity. ICA is particularly useful in studies with multi-modal stimuli or natural environments, where the brain responses are poorly predictable, and their individual elements may not be directly relatable to the given stimuli. This paper extends earlier work on analyzing the consistency of ICA estimates, by focusing on the spatial variability of the components, and presents a novel method for reliably identifying subspaces of functionally related independent components. Furthermore, two approaches are considered for refining the decomposition within the subspaces. Blind refinement is based on clustering all estimates in the subspace to reveal its internal structure. Guided refinement, incorporating the temporal dynamics of the stimulation, finds particular projections that maximally correlate with the stimuli.

1 Introduction

Functional magnetic resonance imaging (fMRI) is one of the most successful methods for studying the living human brain. Traditionally, fMRI analysis relies on artificially generated stimuli, coupled with hypothesis-driven statistical signal processing (*cf.*, [1]).

Independent component analysis (ICA) (see, *e.g.*, [2]) of fMRI data, as first proposed in [3], has recently gained considerable attention for its ability to blindly decompose the measured brain activity into spatially independent functional elements. The corresponding mixing vectors reveal the temporal dynamics of each element. However, the individual elements are often not directly relatable to a given stimulus. This is particularly true in studies using multi-modal stimuli, such as in natural environments, where the brain responses are poorly predictable. Furthermore, it has been proposed that such functional elements can participate in varying networks, to perform complex tasks [4].

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The optimization landscape of ICA is defined by structure of the data, noise, as well as the objective function used. The landscape can form elongated or branched valleys, containing many strong points, instead of singular local optima. Previous studies [5,6] have analyzed the consistency of independent components, and suggested that some components can have a characteristic variability. The goal was to provide additional insight into the components, that is not possible to attain with single run approaches. Complex valleys can also be considered as separate subspaces, where statistical independence is not necessarily the best objective for decomposition.

In this paper, we present a novel method to reliably identify subspaces formed by independent components, and illustrate two approaches to further refine the decomposition into functionally meaningful components. The subspace detection is based on analyzing the spatial variability under a similar consistent ICA as in the previous studies. The subspaces reveal connections between the individual functional elements. One refinement method uses clustering to distinguish the internal structure of the subspace. Another method is based on finding the coordinate system inside the subspace that maximally correlates with the temporal dynamics of the stimulation. The directions are found with canonical correlation analysis (CCA) [7].

Related canonical correlation approaches have been recently suggested for fMRI (see, *e.g.*, [8,9,10]). However, the goals have been to utilize several stimulation time-courses to simply rank the individual components found by ICA, or to extend the purely hypothesis-driven methods into multivariate analyses.

2 Materials and Methods

The analysis uses data from a recent fMRI study carried out by Malinen et al., at the Advanced Magnetic Imaging Centre [11]. The study combined auditory, visual, and tactile stimuli, in a continuous manner. The stimuli were presented in 6–33 s blocks, with no resting periods in between. Fig. 1 illustrates the block design of the sequence, which has a duration of 8 min 15 s.

2.1 Measured and Preprocessed fMRI Data

The recordings, thoroughly described in [11], were made with a Signa VH/i 3.0 T MRI scanner (General Electric, Milwaukee, WI, USA). Functional images were acquired using gradient echo-planar-imaging sequence (TR 3 s, TE 32 ms, matrix 64×64, 44 oblique axial slices, voxel size $3 \times 3 \times 3$ mm^3, FOV 20 cm, flip angle 90°) producing 165 volumes including 4 dummy scans, which were excluded from further analysis. Structural images were scanned with 3-D T1 spoiled gradient imaging (TR 9 ms, TE 1.9 ms, matrix 256×256, slice thickness 1.4 mm, FOV 26 cm, flip angle 15°, preparation time 300 ms, number of excitations 2).

Preprocessing of the data using SPM2 [12] included realignment, normalization and smoothing with a 6 mm (full-width half maximum) Gaussian filter. Skull stripping was also performed. For further details, see [11].

2.2 Consistent Spatial ICA

Independent component analysis is one of the most popular methods for solving the blind source separation (BSS) problem. It consists of finding solutions to the mixture $\mathbf{X} = \mathbf{AS}$, where only the observed data $\mathbf{X}$ is known. ICA assumes only statistical independence of the sources $\mathbf{S}$, and full rank of the mixing $\mathbf{A}$. In the context of fMRI, independence is considered in the spatial domain, and the mixing reveals the temporal activation patterns of the corresponding sources. The reliable ICA approach, proposed in [5], is based on multiple runs of FastICA [13] in a bootstrapping framework, *i.e.*, with resampled data and randomized initializations.

In this study, FastICA was run 100 times with *tanh* nonlinearity in *symmetric* mode. On each run, the data was whitened to 80 dimensions and 40 independent components were extracted. The estimated mixing vectors from all runs were normalized to have zero mean and unit variance, and grouped using correlation. The correlation matrix was thresholded by 0.85 and raised to a power of 4 (see [5] for further details). The parameter values were selected heuristically. Starting with a few dimensions, the dimensionality was increased until the new components were all overfits, appearing only once. Similarly, starting with a high value, the correlation was lowered as long as the most consistent components, appearing 100 times, did not split into many groups.

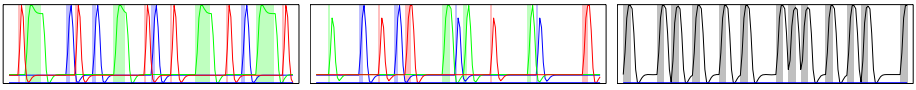
2.3 Subspace Canonical Correlation Analysis

The emergence of a subspace in ICA means that the coordinate system within the subspace can not be identified, based solely on statistical independence. Even if there is a strong relation between the subspace as a whole and the stimulation, this relation may not be readily visible as a high correlation between any given component and the stimuli.

Canonical correlation analysis seeks for covariations between two spaces. In the current work, they are the independent subspace and the stimulation design. Such relation is found through maximally correlated linear transformations of both spaces. Let $\mathbf{Y}$ be a set of columns of the mixing matrix $\mathbf{A}$, corresponding to an independent subspace, and $\mathbf{Z}$ the set of stimulation time-courses. The goal of CCA is to maximize $corr(\mathbf{W_y}^T\mathbf{Y}, \mathbf{W_z}^T\mathbf{Z})$ with respect to $\mathbf{W_y}$ and $\mathbf{W_z}$, which are the transformation projections. As a result, the coordinate system within the subspace is fixed according to maximal correlation to the stimuli, rather than independence.

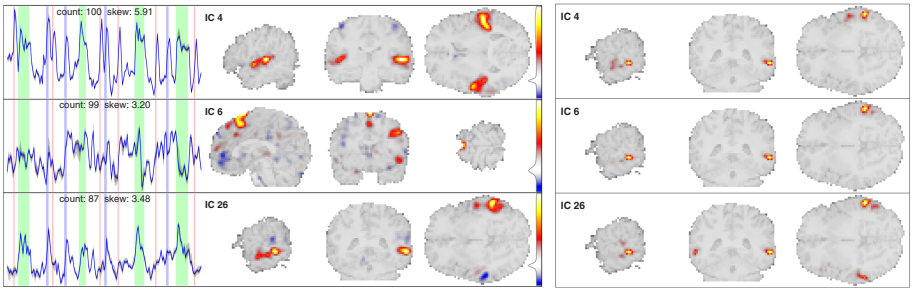
3 Results

Fig. 2 shows a set of independent components (ICs), strongly related to auditory stimulation. Each IC is consistent, appearing in all or most of the 100 runs. The mixing variability is also minimal. However, the spatial variance reveals a coincident location of variability, shared by all ICs. The variability links the ICs



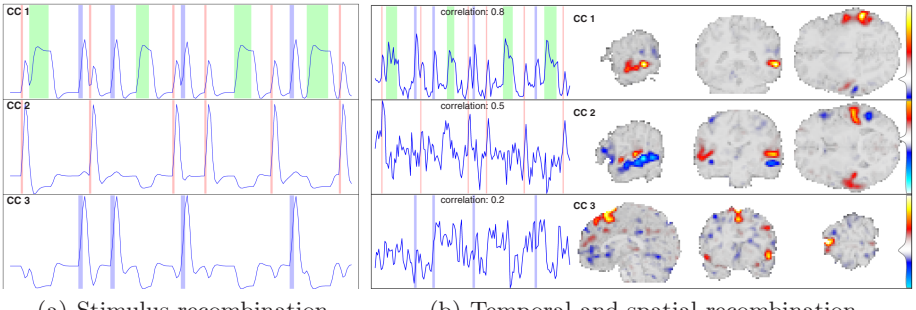
(a) Auditory stimulation (b) Visual stimulation (c) Tactile stimulation

Fig. 1. Stimulation block design with hemodynamically convolved time-courses. (a) Auditory stimulation with tone pips, spoken history text and spoken instruction text (represented by red, green and blue in the color version). (b) Visual stimulation with scenes dominated by buildings, faces and hands (represented by red, green and blue in the color version). (c) Tactile stimulation.



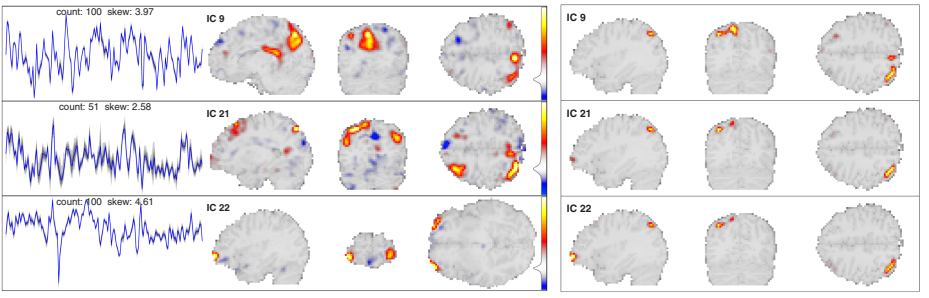
(a) Temporal and spatial mean (b) Spatial variance

Fig. 2. A set of independent components identified as a subspace through the shared variance, with strongly auditory stimulus-related time-courses. (a) The mean spatial maps and time-courses of each component. (b) The spatial variance maps of the corresponding components. A sagittal, coronal and axial slice of each volume is shown with the histogram of the mean volume. Consistency counts and skewness of the histograms are shown as text, and the reference blocks for the time-courses are from Fig. 1(a).



(a) Stimulus recombination (b) Temporal and spatial recombination

Fig. 3. A set of linear combinations that maximize the correlation between the mean time-courses of the subspace components shown in Fig. 2, and the stimulation time-courses shown in Fig. 1(a). (a) The time-courses combined from the stimulation design. (b) The spatial maps and time-courses of the corresponding, maximally correlated, combinations of the independent components. Other details as in Fig. 2.

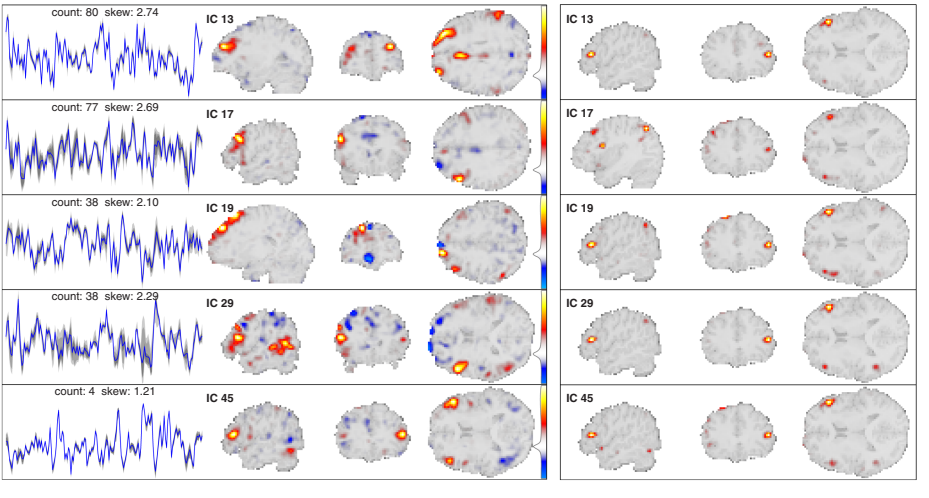


(a) Temporal and spatial mean (b) Spatial variance

Fig. 4. A set of independent components identified as a subspace through the shared variance, with weakly stimulus-related time-courses. Other details as in Fig. 2, except no reference blocks are shown.

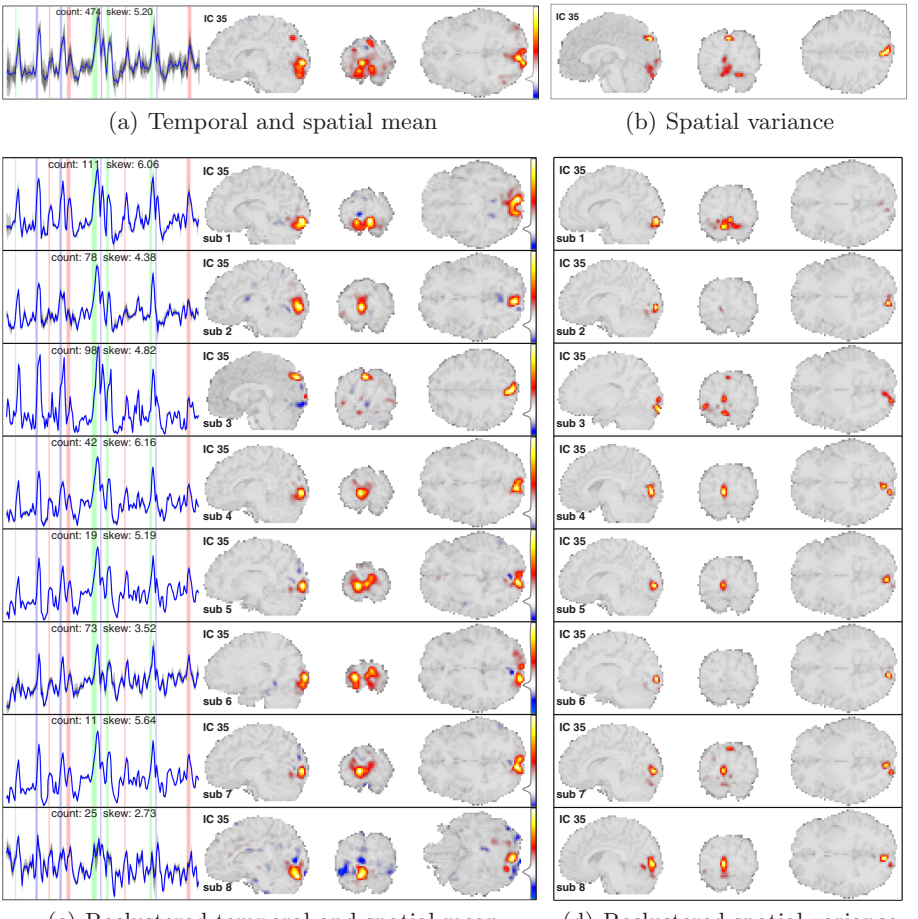
into a three dimensional subspace, even though ICA has consistently identified directions within the subspace.

The subspace in Fig. 2 was further analyzed with CCA using all auditory references, shown in Fig. 1(a). Fig. 3 shows the canonical components (CCs) identified within the subspace. Compared to the ICs, the CCs reveal the best stimulation-matching decomposition within the subspace. A thorough physiological interpretation of the results is out of the scope of this paper, but the



(a) Temporal and spatial mean (b) Spatial variance

Fig. 5. A set of independent components identified as a subspace through the shared variance, with transiently stimulus-related time-courses. Other details as in Fig. 2, except no reference blocks are shown.



(a) Temporal and spatial mean (b) Spatial variance

(c) Reclustered temporal and spatial mean (d) Reclustered spatial variance

Fig. 6. One independent component, identified as a subspace through overall variability, with strongly visual stimulus-related time-course. (a) The mean spatial map and time-course of the component. (b) The spatial variance map of the component. (c) The mean spatial maps and time-courses of components from reclustering within the subspace. (d) The spatial variance maps of the corresponding components. Other details as in Fig. 2, except the reference blocks are from Fig. 1(b).

decomposition appears refined. The first, and highest correlating, CC depicts a baseline of activity related to all types of auditory stimulation. The second CC reveals a clear deviation from the baseline, occurring during the tone pip stimuli. It includes two brain regions, associated with auditory processing, having opposite signs in the spatial map. The last CC appears quite scattered, containing most of the activity within the subspace that is not explained by the other two CCs, as indicated by the low correlation.

Another example of a subspace linked through spatial variance is shown in Fig. 4, which appears weakly stimulus-related. The last IC in the subspace presents a potential artifact, with a sharp peak at a single time instance.

Fig. 5 shows a more complex set of activity, also identified as a subspace by the shared spatial variance. In this case, the ICs themselves are less consistent, and have considerable mixing variability. As no single component appears in all 100 runs, ICA can not identify consistent directions within the subspace. Some of the ICs are weakly stimulus-related, so a meaningful coordinate system inside the subspace could be fixed with CCA. However, the given stimulus design is not rich enough to decompose the 5 dimensional subspace.

The last example, shown in Fig. 6, is identified as a subspace already by the consistent ICA method. The strong mixing variability, together with the count of 474 estimates suggest that ICA can separate the subspace from the other components, but roughly 5 arbitrary directions from the subspace appear on each run. Additionally, the spatial variance coincides with the component itself, rather than being shared with other ICs. To further analyze the consistency of the strongly stimulus-related subspace, the 474 estimates within the subspace were clustered again, now using a higher threshold of 0.95. Fig. 6 also shows the set of 8 most consistent directions within the subspace. The directions are not strictly independent, since the clustering does not take into account from which run the estimates are taken. The subspace directions appear functionally meaningful, representing separate brain regions of the visual processing stream, including the primary visual cortex and other areas along the occipital lobes. Again, with a richer set of stimulus references, CCA could offer further refinement.

In addition to the illustrated subspaces, several other were identified, either through the overall variability of the components or by their shared spatial variance. The complete set of 46 consistent ICs also included several that were not part of a subspace.

4 Conclusions

Analyzing the variability of independent components, under a consistent ICA framework, can reveal characteristic information related to the underlying phenomena that is otherwise not visible. As shown by the results, components can be roughly divided into 3 classes based on spatial variance: individual and consistent components, with distributed variance due to noise; consistent members of a subspace, with focal variance coincident with the variance of the other members (see Fig. 2); and unconsistent subspaces, with variances coincident with their own mean (see Fig. 6). Such subspaces can provide information on networks of related activity in a purely data-driven manner.

Directions within each subspace can be further refined either blindly by clustering them into semi-independent constituents, or by using CCA with additional data. More than just refining the subspace decomposition, CCA provides a direct link to the set of related stimuli. However, the use of CCA is limited by the richness of the stimulation design. A more supervised approach was recently

presented, with the goal of relating networks of brain activity with given complex stimulus features [4].

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