Optimization of ICA for detection of weak and focal activations in fMRI

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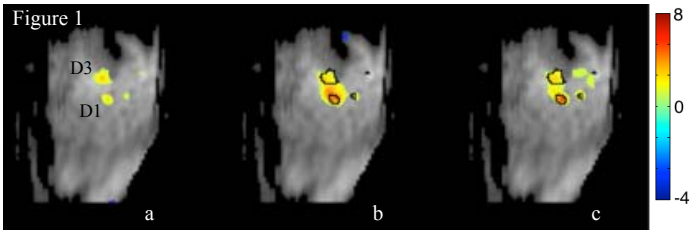
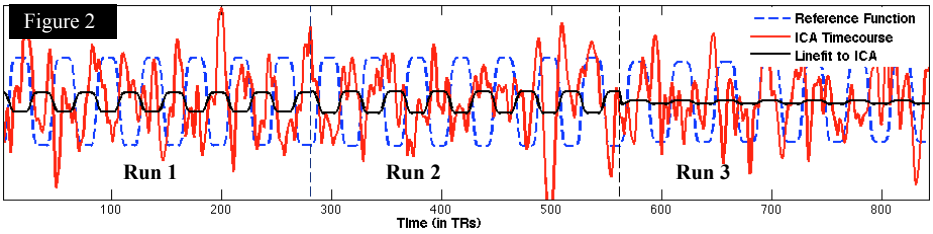
Introduction: Independent component analysis (ICA) has been successfully utilized for data driven analysis of functional MRI (fMRI) data for task-related as well as resting state studies [1, 2]. However in the setting where the signals of interest contribute only a small fraction of the total variance, i.e. very low contrast-to-noise ratio (CNR), and/or very focal response, accurate estimation of the appropriate model order is difficult, and ICA performance may suffer. In this study, we present a framework for using ICA to detect focal and weak activation patterns in low CNR fMRI data. We evaluate two model order selection criteria and demonstrate that the model order selected based upon bootstrap stability of principal components [3, 4] yields more accurate estimates of model order. We applied this approach to successfully detect focal patterns of brain activation associated with stimulation of individual digits in high-resolution data obtained from squirrel monkeys.

Methods: Imaging was performed on 9.4T Varian scanner. The monkeys (n = 2, two imaging sessions per monkey) were anesthetized and prepared for imaging as described in [5]. A bolus 12-16 mg Fe/kg dextran coated MION contrast agent with an average particle diameter of 30 nm in saline, was injected intravenously along with 0.9% saline solution to provide cerebral blood volume (CBV) weighted contrast. Piezoceramic actuators (Noliac, Kvistgaard, Denmark) delivered a vertical indentation of a 2 mm diameter probe with 0.34 mm displacement to individual distal fingerpads of digits 1 and 3 simultaneously. Seven alternating 30s blocks of baseline and vibrotactile stimulation were delivered per imaging run. Three to six runs of 2-shot, multi-slice gradient echo planar image series were acquired during the stimulation with the following parameters: TR/TE 750/10ms, in-plane resolution of 273x273 μm^2 and 300 volumes. Motion correction was performed using AFNI. All the images in the series were blurred using a 3x3 Gaussian kernel with $\sigma = 2$ pixels. Motion parameters as well as 5 principal components of the signals from the skin were regressed out of the data. Individual time-courses were low-pass filtered ($f < 0.1$ Hz). ICA was performed on each session separately using Group ICA for fMRI Toolbox (GIFT) [1] using two approaches: 1) ICA on concatenated principal components from all the runs within a session [1] (abbreviated as ICA_{concat}), and 2) ICA on the average of all runs (ICA_{avg}), as evaluated in [6]. Model order was estimated using the minimum description length criterion (MDL) [1] and bootstrap stability analysis of principal components [3, 4]. These approaches were also applied to synthetic data with 15 underlying source components and varying signal-to-noise ratios (SNRs).

Results and Discussion: The model order estimated using the MDL criterion on the real preprocessed datasets exceeded 170. ICA performed with this model order resulted in overfitting, and the individual components were found to be very sparse, with only a few voxels with high amplitude ($|z| > 2.5$). Based upon our simulations, MDL yields exaggerated estimates of the model order if temporal low-pass filtering (0-0.1 Hz) is performed on the data, even with SNRs as high as 100 (obtained by dividing standard deviation of signals generated by the linear combinations of the underlying components by the standard deviation of noise). However, the model order obtained by bootstrap stability analysis of the principal components [3] accurately predicted the true number of components (estimated model order = 14.45 ± 0.82 for 15 underlying components, based on 20 simulated datasets) for SNRs as low as 1.5. Application of the same method to real data yielded a more reasonable estimate of the number of components (9.8 ± 1.2).





Activation maps obtained using different approaches are shown in Figure 1. All the maps were scaled to z-scores prior to display, and the signs were adjusted to yield positive correlation with the stimulus time-course. As seen in Figure 1a, hypothesis driven analysis (threholded voxel-wise correlation with stimulus time-course) detects activation in area 3b of somatosensory cortex corresponding to digits 1 and 3, as expected. Some activation in area 1 is also observed. Average percentage signal change corresponding to the voxel showing the largest activation ranged between 0.35% and 0.8%. Stimulus-related activation explained 2.5-9.2% of the total variance, even after preforming all the preprocessing steps and averaging across the runs to improve effective CNR. Visual inspection suggests that the stimulus-related maps obtained using ICA_{concat} and ICA_{avg} successfully approximate the location of the activated brain areas. The stimulus-related independent components obtained from ICA_{avg} exhibit greater correlation with the hypothesis-driven activation map, in comparison with ICA_{concat} (0.63 ± 0.16 vs 0.50 ± 0.20). Additionally, the temporal profiles associated with stimulus-related independent component obtained using ICA_{avg} showed greater correlation with the stimulus time-course, as compared with that corresponding to ICA_{cocat} (0.61± 0.07 vs 0.51 ± 0.17). Figure 2 shows run-specific time-courses associated with the stimulus-related independent component obtained using ICA_{concat} (3 runs for one session, separated by vertical lines), along with the stimulus-related component of the time-courses (obtained using linear fitting). As can be seen, run-specific variations in stimulus-dependent response can be captured using ICA_{concat}.

In summary, we have presented a framework for detecting weak and focal functional changes in fMRI data using ICA. Several preprocessing steps were used to increase effective CNR. Importantly, the number of components was estimated using a completely data-driven approach, and was stable across animals and sessions. Our findings suggest that ICA can be used to detect small neuronal changes in fMRI (as small as 0.35% above the baseline) that contribute a small amount of variance towards the data (as low as 2.5%). These patterns were reproducibly detected for all monkeys and sessions. ICA_{avg} outperforms ICA_{concat} in terms of similarity of the resultant maps and time-courses with those associated with hypothesis-driven analysis for our data. One possible explanation for that could be higher effective CNR achieved due to averaging. This result is in disagreement with a previous study that reports better temporal accuracy but worse spatial accuracy associated with ICA_{avg} [6]. It should be noted that ICA_{avg} is not applicable when the temporal profiles of the patterns of interest are not coherent between the datasets to be averaged, and ICA_{concat} should be used in those cases. Future work will be focused on using this framework for analysis of resting state data.

References:

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