# Joint inference of functional ROIs and their interaction graph

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## Introduction:

Function-induced brain networks are commonly modeled with a graph abstraction where nodes are brain regions of interest (ROI) and edges represent their interactions. Defining the nodes is a non-trivial task. Although it is common to default to a predefined atlas for ROI definition, such approach can greatly reduce sensitivity of the network structure inference. For example, due to cross-mixing of time series when different functional units are incorrectly split between ROIs (Shirer et al. (2011); Smith et al. (2010)). Addressing this issue, data driven methods for functional ROI definition are gaining popularity in the field.

The following approach to network identification has recently become the state of the art: 1) identify a large number of functional units in the brain using a data-driven approach (commonly a high model order independent component analysis (ICA)); 2. apply a network structure inference algorithm to thus obtained ROIs. Despite the apparent improvements in network structure sensitivity brought forth by the use of functional ROIs, the identification process is still separately performed for the two steps, and hence suboptimal.

## Methods:

We extend the current research on functional brain networks by developing a method to jointly estimate the ROIs and their interaction graph. Our base models are nonnegative matrix factorization (NMF) (Lee and Seung, 1999) for data driven ROI estimation and Gaussian graphical models (GGM) (Friedman et al., 2008) for network connectivity inference. The choice mainly influenced by robustness of the two.

Starting from an fMRI dataset in the  $n \times m$  matrix, where each column is one of the m vectorized volumes with n voxels each, and specifying model order r and the sparsity level of our network connections  $\lambda$  we formulate the objective function as: (see below)

where HF, H1, Tr and H denote Frobenius, L1 norms, trace and determinant respectively, with an additional requirement of nonnegativity on W and possibly H. On the output, W contains activation maps of the ROIs with the corresponding time courses in H, while  $\Theta$  stores the symmetric connectivity matrix of the network, where zero entries mean that certain ROIs are independent conditioned on the rest of the network.

$$\frac{argmin}{W,H,\Theta} \Big( |X - WH|_F - \log |\Theta| + Tr \Big( \frac{1}{m} H\Theta H^T \Big) + \lambda |\Theta|_1 \Big)$$

### **Results:**

The new method infers a sparse graph focusing on refining only those ROIs that are engaged in interactions. Figure 1 compares performance of ICA and NMF ROI extraction and the two stage network identification with the new method on a block design visuomotor task. The new method results in 5 actively interacting ROIs, with the graph of their corresponding interactions. Active but not communicating ROIs are suppressed from the network, thus providing a data driven model order selection. The two stage NMF results end up with sparser network but denser spatial ROIs, whereas ICA results in a dense network not providing any information on what components are important.

# Conclusions:

We have developed a method for concise and efficient joint identification of network nodes and their conditional independence structure. This avoids a priori biases which occur in assuming which brain regions are relevant and then fitting the network. It avoids the need for multiple studies to identify first the regions involved, and then their interactions; and it inherently focuses on signal rather than noise, through mutually constraining ROIs and interactions.

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Figure 1: Comparing results of our new method (leftmost column) with the two-stage approaches of ICA and NMF. The 6 ROIs on the left are provided automatically as the output of our method. We display ROIs for the other two method that are most correlated with these 6. Adjacency matrices on the bottom are not matched in order and strength, the point is to show the sparsity of the new solution. See the stem plots at the bottom. Note that the highest strength edges in the ICA are between motion components.

#### Abstract Information

#### References

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