An Independent Component Analysis Based Tool for Exploring Functional Connections in the Brain

Sara Rolfe
10/23/17
Functional Magnetic Resonance Imaging (fMRI)

- Non-invasive imaging technique
- Patient performs a mental task during scan
- Measures brain activity associated with task
**MRI vs. fMROI**

<table>
<thead>
<tr>
<th>MRI</th>
<th>fMRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>One 3D volume</td>
<td>Series of 3D volumes</td>
</tr>
<tr>
<td>High spatial resolution</td>
<td>Low spatial resolution</td>
</tr>
<tr>
<td>Study brain anatomy</td>
<td>Study brain function, using blood flow</td>
</tr>
</tbody>
</table>

- MRI: Magnetic Resonance Imaging
- fMRI: Functional Magnetic Resonance Imaging

**Images:**
- MRI scan of a brain
- fMRI scan showing changes over time

**Diagram Notes:**
- Time direction indicated by the arrow pointing from left to right.
Blood Oxygen Level Dependent (BOLD) Signal

Delivery of oxygen to activated neurons  Hemodynamic Response Function
BOLD Signal

Experimental Design

Regions of activity associated with task vector

TASK

CONTROL

time
BOLD Signal

Experimental Design

TASK

CONTROL

time

Regions of activity associated with task vector
Project Motivation

- Structural Informatics Group at University of Washington
- Study relationship between fMRI, Cortical Stimulation Mapping (CSM), and other brain data
  - Surgical planning
  - Mapping language regions in the brain
Functional Connectivity

- Correlations between spatially remote neural events
- Signals in two regions covary
Finding Functional Networks

• Language regions are expected to be functionally connected

• Identifying functional networks in fMRI
  – help researchers locate language regions
  – identify other interesting networks

• **Need a tool to locate and compare functional networks**
Queries

1. Starting with SUR, CSM, or fMRI data, select an (x, y, z) coordinate of interest in the brain. Get the raw data fMRI time series of the voxel at that location. Use signal similarity measures to find correlated voxels within the subject’s brain.

2. Starting with one subject’s voxel correlations, find SPM-generated statistical activation images from that patient with similar spatial patterns of activation.

3. Starting with one subject’s voxel correlations, search for other subjects who have a similar correlation pattern for a voxel in the same region.

4. For a given subject’s statistical activation image and given location, find other subjects who have greater than or equal activation values at that location, by searching the SPM images showing statistically significant activations.

5. For a given subject’s statistical activation image, find other subjects who have similar spatial patterns of activation, by searching the SPM images showing statistically significant activations.

6. For a given subject’s statistical activation image, find signal-similarity-generated correlation patterns from that subject with similar spatial patterns of activation.
Main Tasks Involved in Answering Queries

- **Voxel similarity measurement** – finding voxels with similar behavior during the scan.

- **Spatial map similarity measurement** – finding volume images with similar activation patterns
User Interface

PATIENT: SELECT PATIENT ID.  

SPM RESULTS: SELECT SCAN RESULTS  

Query Type:
- Within-patient IC Search
  Find IC volumes from the selected patient’s scan using ROI SELECT or VOLUME SELECT
- Cross-patient IC Search
  Find similar IC volumes across patients using VOLUME SELECT
- Within-patient SPM Search
  Find similar SPM volumes in one patient using VOLUME SELECT
- Cross-patient SPM Search
  Find similar SPM volumes across patients using VOLUME SELECT to find similar patterns or ROI SELECT to find similar regions

ROI SELECT  
VOLUME SELECT  
RESET

Volume 1  
Volume 2  
Volume 3

Volume 4  
Volume 5  
Volume 6

Details

See Next Matches
User Interface

Query Type:

- **Within-patient IC Search**
  Find IC volumes from the selected patient's scan using ROI SELECT or VOLUME SELECT

- **Cross-patient IC Search**
  Find similar IC volumes across patients using VOLUME SELECT

- **Within-patient SPM Search**
  Find similar SPM volumes in one patient using VOLUME SELECT

- **Cross-patient SPM Search**
  Find similar SPM volumes across patients using VOLUME SELECT to find similar patterns or ROI SELECT to find similar regions
Blind Source Separation

Cocktail Party Problem

Given \( n \) signals that are a linear mixture of source \( n \) signals, can we estimate the original signals?
Principal Component Analysis (PCA)

- Represents data as a linear combination of orthogonal components
- Each component accounts for the largest amount of variability possible given orthogonality constraint
- Widely used to explain variance in a dataset
Independent Component Analysis (ICA)

• Represents data as a linear combination of statistically independent components
• Minimize mutual information of components
ICA versus PCA

• PCA requires bases to be decorrelated
• ICA requires bases to be statistically independent
• This allows ICA bases can be very similar, if still independent
ICA – A Data Driven Method

• Statistically independent components indicate that the signal changes have separate sources

• Allows separation of small and large signal changes

• Doesn’t make assumptions about the patient response to stimuli
Model for Spatial ICA

\[ X = M \ast C \]

- \( X \) = T\times V\ matrix of observations
- \( M \) = square mixing matrix
- \( C \) = T\times V\ matrix of T independent component maps
Model in Matrix Form

\[
\begin{bmatrix}
  x_{11} & x_{12} & x_{13} & \ldots & x_{iV} \\
  x_{21} & x_{22} & x_{23} & \ldots & x_{2V} \\
  \vdots & \vdots & \vdots & \ddots & \vdots \\
  x_{T1} & x_{T2} & x_{T3} & \ldots & x_{TV}
\end{bmatrix}
\begin{bmatrix}
  m_{11} & m_{12} & \ldots & m_{1T} \\
  m_{21} & m_{22} & \ldots & m_{2T} \\
  \vdots & \vdots & \ddots & \vdots \\
  m_{T1} & m_{T2} & \ldots & m_{TT}
\end{bmatrix}
\begin{bmatrix}
  c_{11} & c_{12} & c_{13} & \ldots & c_{1V} \\
  c_{21} & c_{22} & c_{23} & \ldots & c_{2V} \\
  \vdots & \vdots & \vdots & \ddots & \vdots \\
  c_{T1} & c_{T2} & c_{T3} & \ldots & c_{TV}
\end{bmatrix}
\]
Here the column vector $[m_{11} \ldots m_{T1}]$ specifies the weights of the IC map 1 at each time point.
A Conceptual Example
Independent Components

Raw Data from fMRI
3-D Spatial Map Similarity Measurement

- Need to find similar IC and SPM results maps across patients
  - Identify activation clusters
  - Compare clusters across maps
Preprocessing Steps

- Preprocessing
  - Threshold applied to find activated voxels based on standard deviations from mean voxel value
  - Binary labeling
  - Each voxel is weighted by:
    \[ x_i = e^n \]

where \( n \) is the number of activated neighbors
Modified K-Means Clustering

• Weighted average of activated voxel locations used to find new bin location
• Incorporates a priori information about bin center locations
Novel Cluster Feature Vector

- Bin center location
- Bin size
- Average distance to bin center
- Average bin weight
- Weighted variance of distances to bin center
Extracting Feature Weights

- Elements in feature vectors have different scales and distributions
- Need to be normalized before distances can be calculated
- Each feature weighted by:

\[ w_k = \frac{1}{\text{mean}(F_k)} \text{std}\left( \frac{F_k}{\text{mean}(F_k)} \right) \]

where \( F_k \) is the set of all values for feature \( k \)
Feature Distance Measure

- Distance between two clusters:

\[ d_{ik} = \min_n(\text{abs}(f_{ik} - f_{jn})) \]

- Distance between two spatial maps:

\[
    m_{ij} = \frac{1}{\text{abs}(n_i - n_j)} \sum_k d_{ik} \cdot \text{binsize}_k \cdot \text{averagebinweight}_k, \\
    \text{Dist}_{ij} = \frac{m_{ij} + m_{ji}}{2},
\]

where \text{binsize}_k and \text{averagebinweight}_k are two values from the feature vector.
Query 1

• Given a user defined ROI, find maps of correlated voxels from one patient’s fMRI scan

• ICA used to find statistically correlated spatial maps contributing to the ROI
Query 1: Algorithm

Select ROI from patient’s structural MRI

For each IC map from patient’s scan, find average value in ROI

If average value is greater than the threshold, assign a ranking to that IC map
Sample Results: Query 1

Query

First match
Query 3

• Given an IC map from query 1, find similar IC maps from other patients.

• Uses specialized clustering method to find clusters and extract features

• Calculates distance between feature vectors
Query 3: Algorithm

Compare the query IC map to each IC map for each patient in the database.

For each cluster in the query map, find the cluster in the IC map with the minimum feature vector distance.
Query 3: Algorithm

Assign the match a rank if the cluster distance is below the threshold.

Sum cluster rankings to get IC map rank.
Repeat distance measure starting from second IC map. Average both IC rankings to get final distance measure.
Sample Results: Query 3

- Start with IC map selected using any of the queries
Sample Results: Query 3
Sample Results: Query 3, Detail Browser

Details from query IC map

Details from first match
Evaluation of Results

• A thorough evaluation is difficult in the absence of a ground truth
• Can check relationship between independent component maps and SPM maps
• ICA expected to provide more information, but should be able to replicate SPM results
Replicating SPM Results

SPM results map

Within patient query for similar IC maps
Replicating SPM Results

SPM results mapped onto patient’s structural image.

Independent component mapped onto patient’s structural image.

Time-course shows structure of experiment task.
Exploring Functional Connections in the Brain

ICA voxel similarity measure

Detecting and describing activation clusters

Activation cluster similarity measure

Workflows to address six user query types

Graphical user interface to execute queries

System to explore functional connectivity