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

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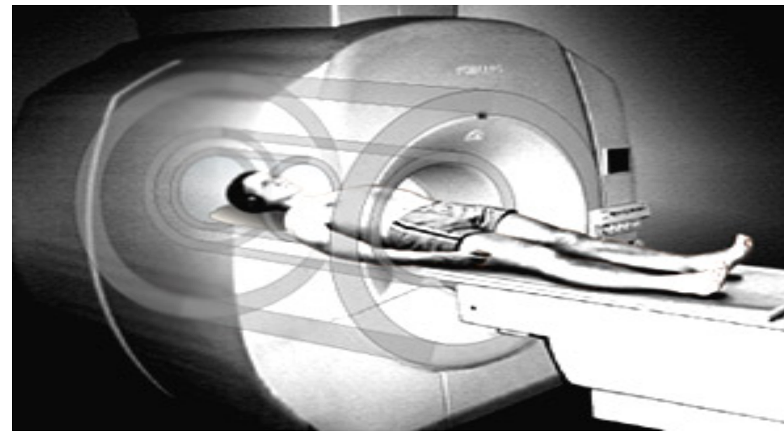
10/23/17

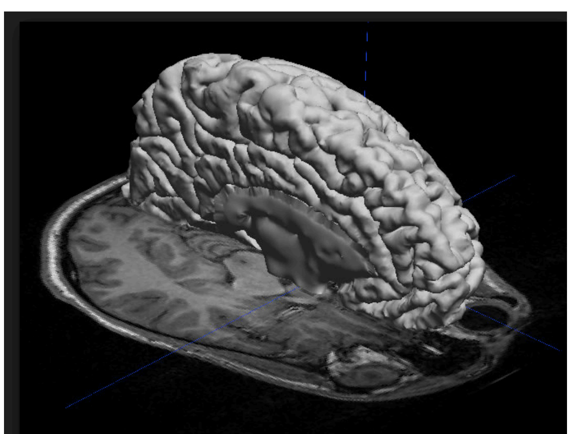
Functional Magnetic Resonance Imaging (fMRI)

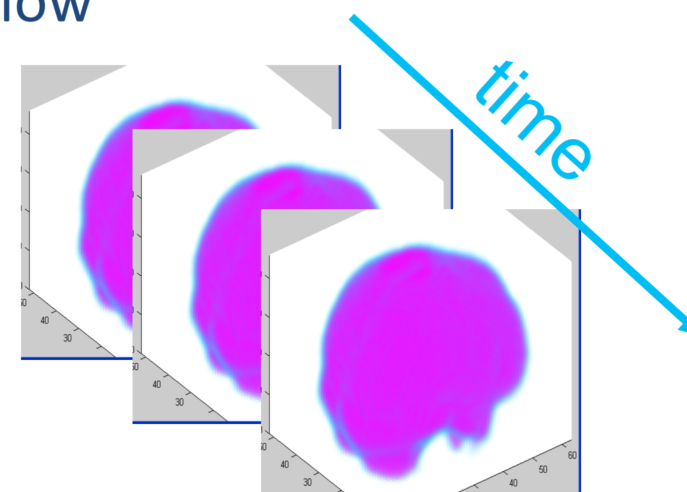
- Non-invasive imaging technique
- Patient performs a mental task during scan
- Measures brain activity associated with task



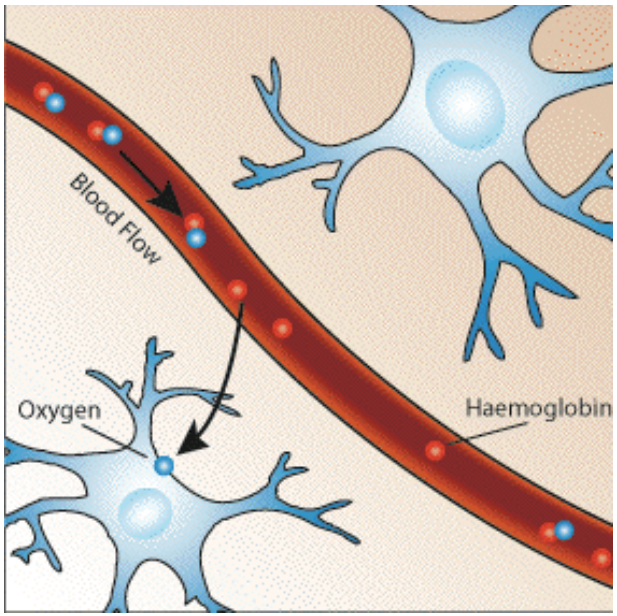
MRI vs. fMRI

MRI	fMRI
One 3D volume	Series of 3D volumes
High spatial resolution	Low spatial resolution
Study brain anatomy	Study brain function, using blood flow

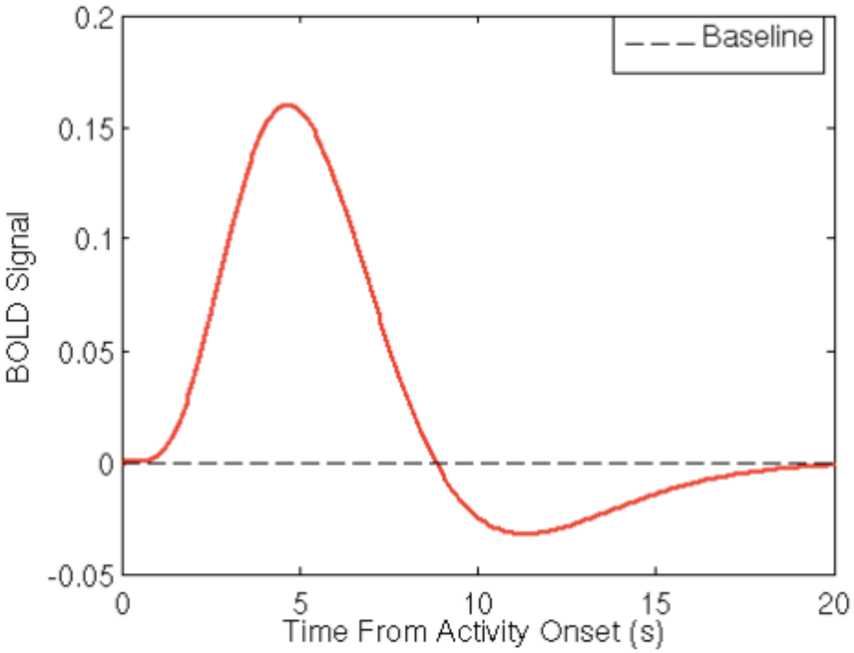




Blood Oxygen Level Dependent (BOLD) Signal



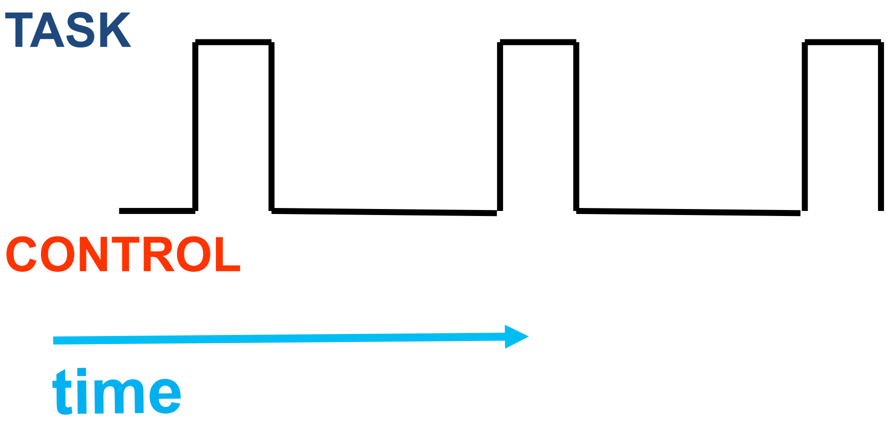
Delivery of oxygen to activated neurons



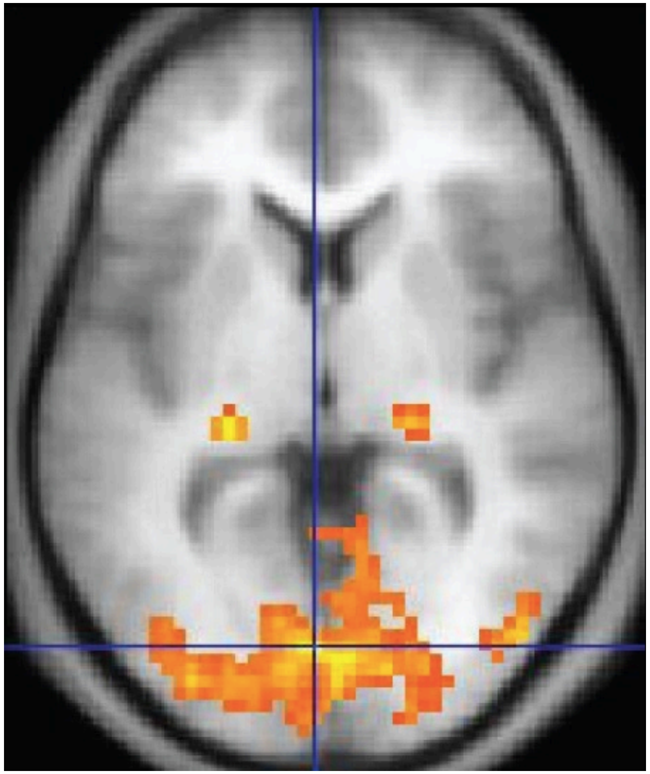
Hemodynamic Response Function

BOLD Signal

Experimental Design

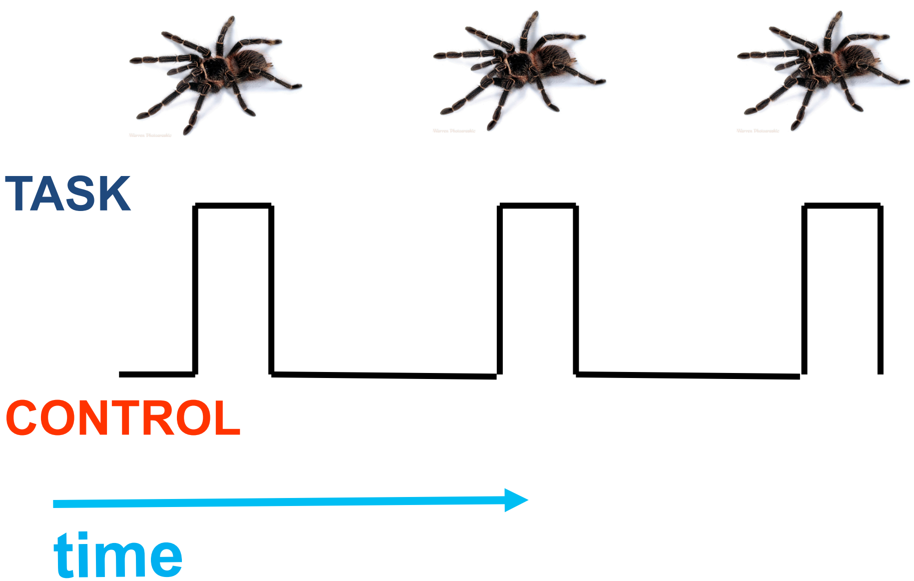


Regions of activity associated with task vector

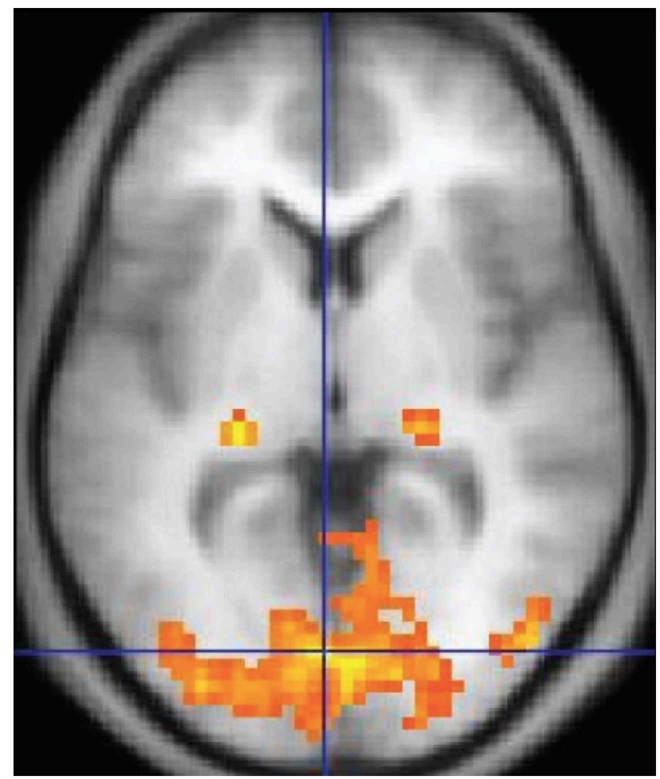


BOLD Signal

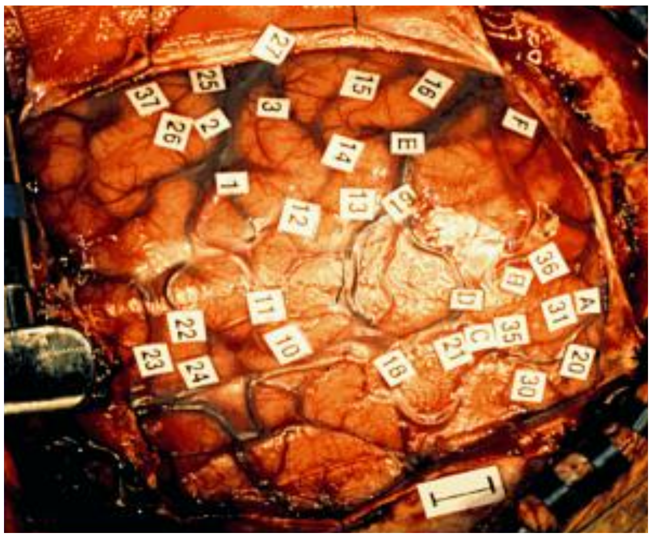
Experimental Design



Regions of activity associated with task vector



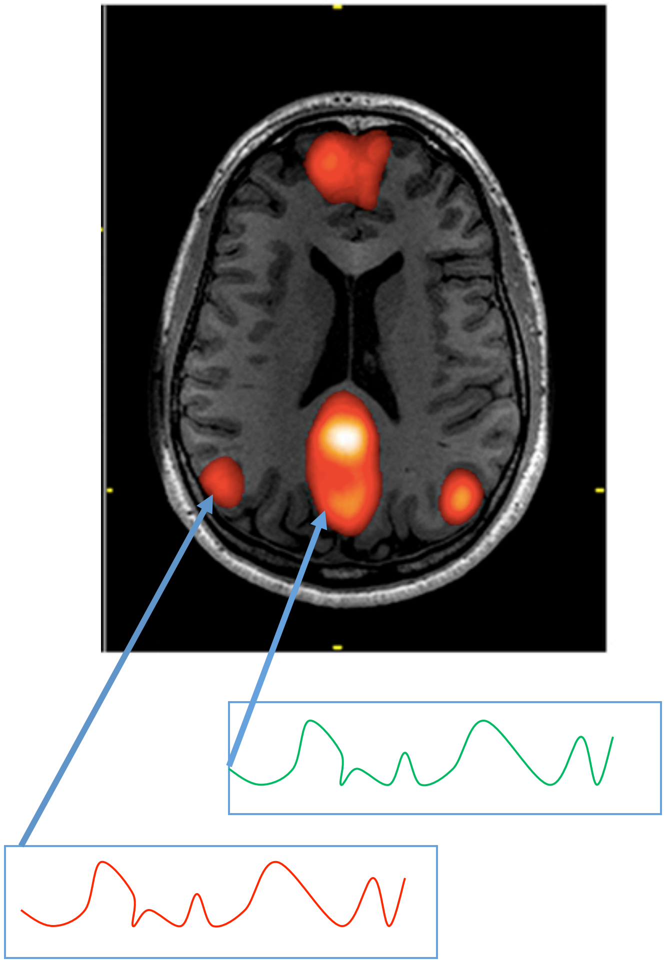
Project Motivation



- 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**

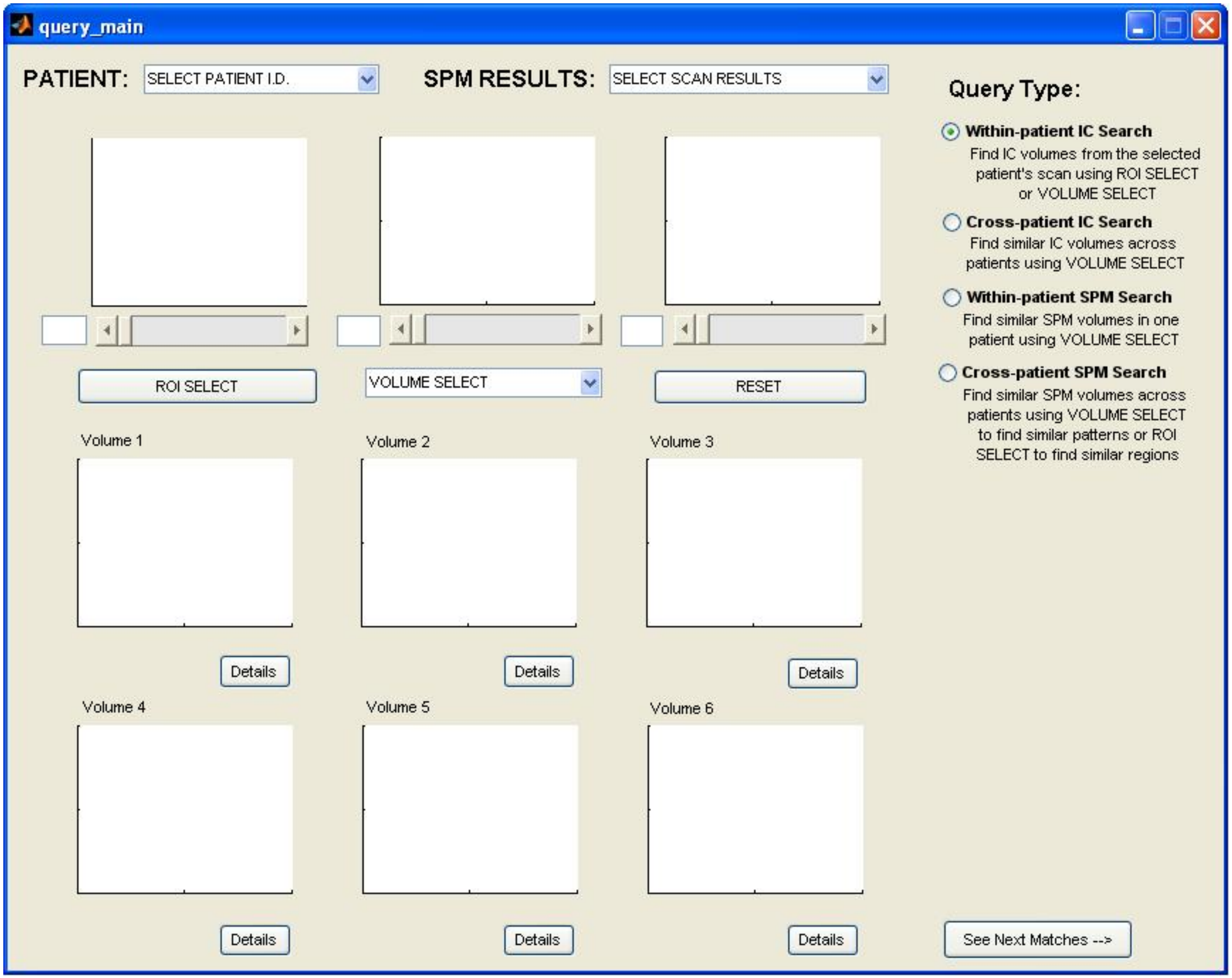
Queries

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.

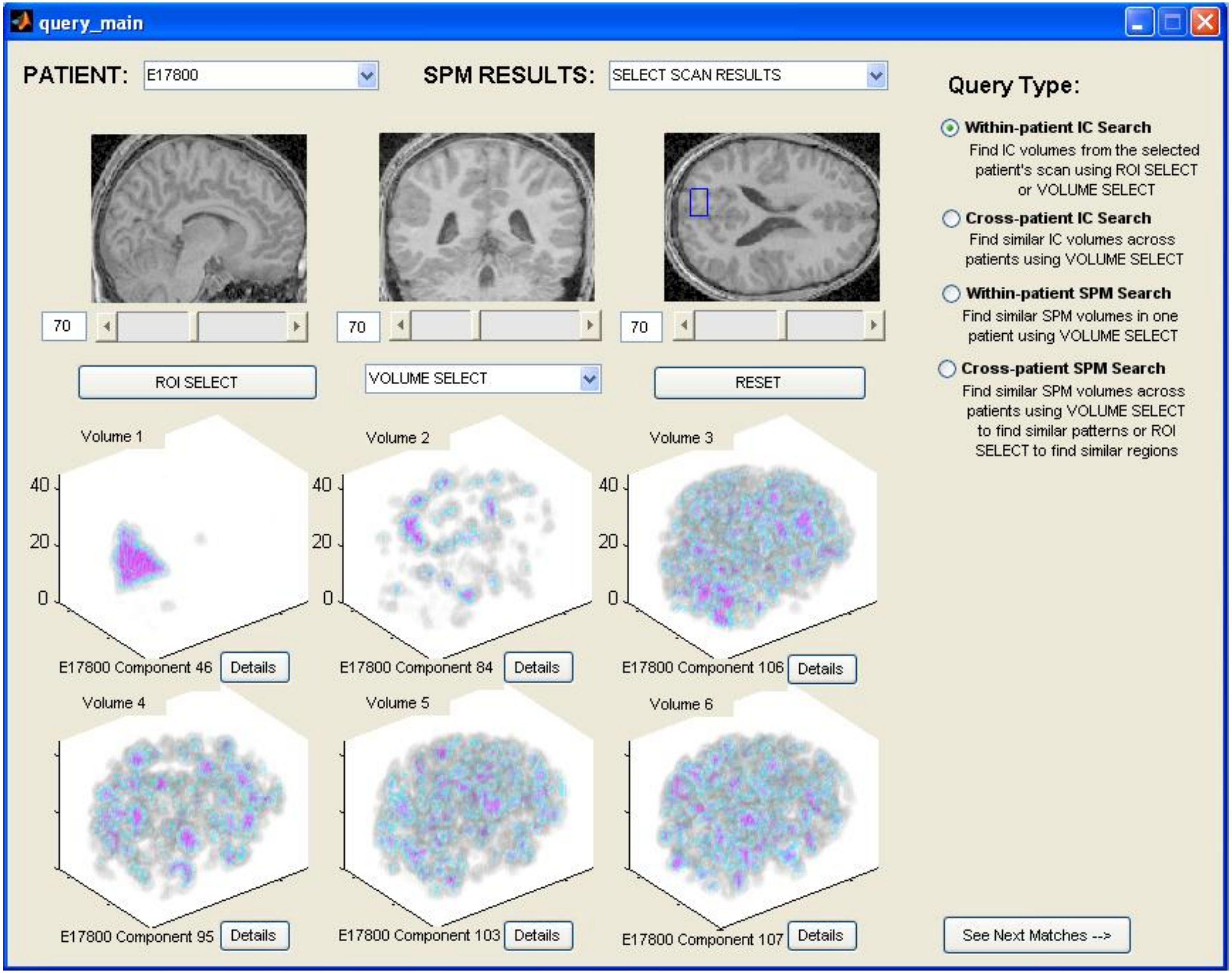
Main Tasks Involved in Answering Queries

- **Voxel similarity measurement** – finding voxels with similar behavior during the scan.
- **Spatial map similarity measurement** – finding volume images with similar activation patterns

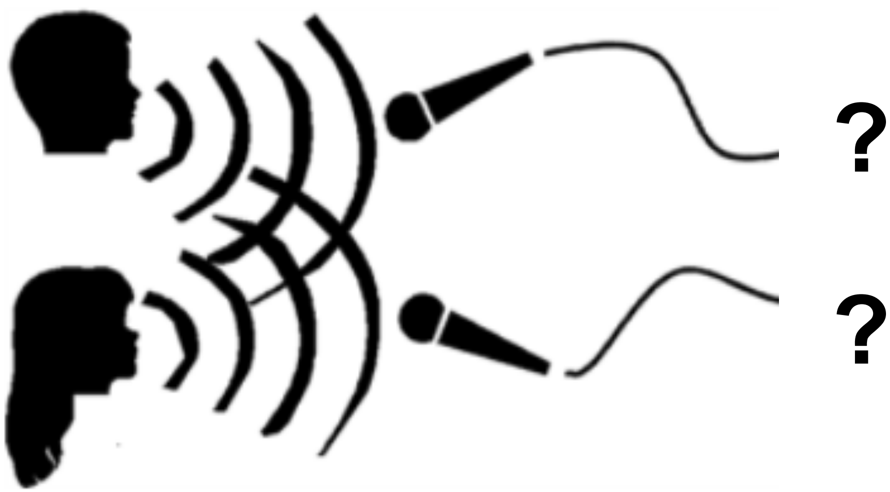
User Interface



User Interface



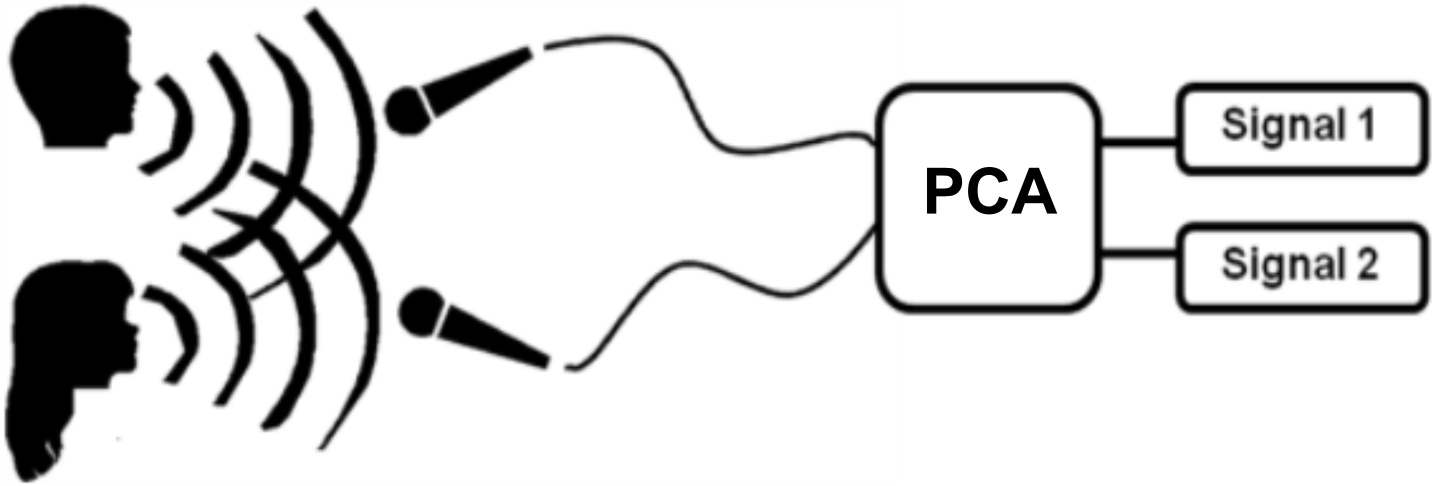
Blind Source Separation



Cocktail Party Problem

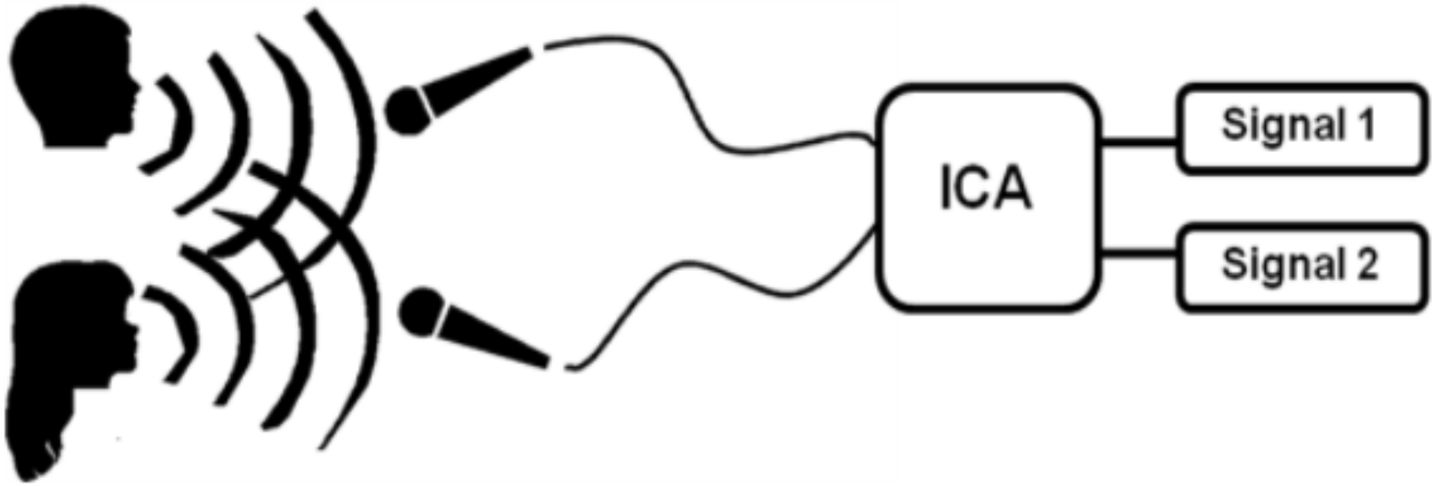
Given ***n*** signals that are a linear mixture of source ***n*** signals, can we estimate the original signals?

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

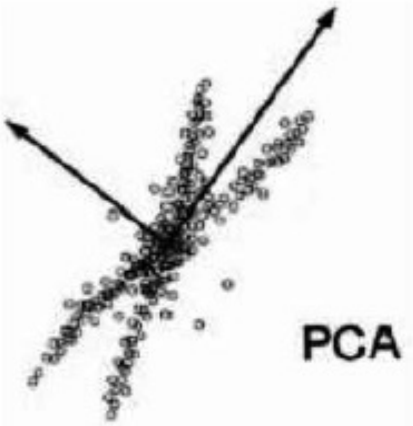
Independent Component Analysis (ICA)

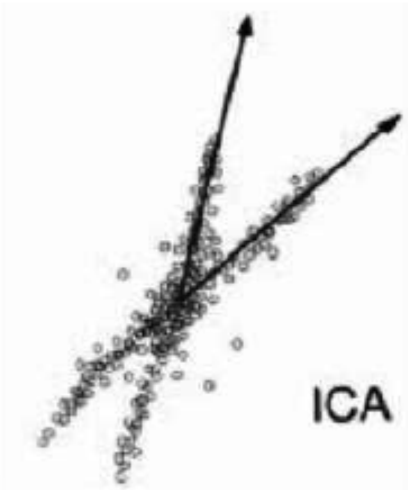


- Represents data as a linear combination of statistically independent components
- Minimize mutual information of components

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

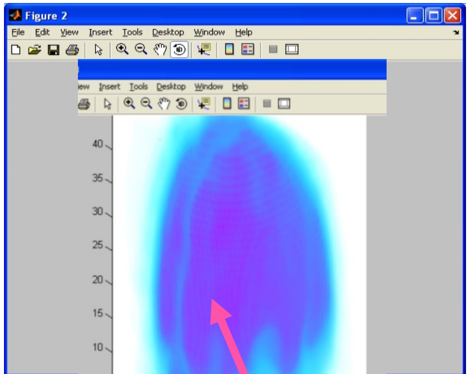
$$X = M * C$$

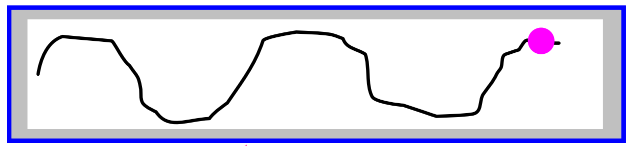
X = TxV matrix of observations

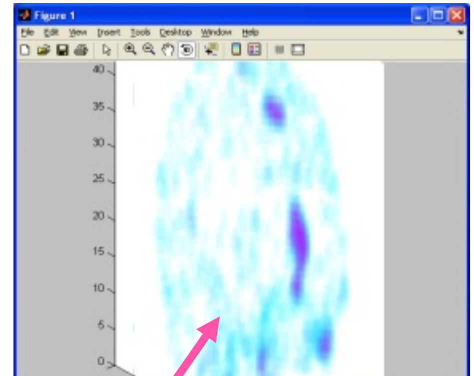
M = square mixing matrix

C = TxV matrix of T independent component maps

Model in Matrix Form







$$\begin{bmatrix} x_{11} & x_{12} & x_{13} & \cdots & x_{1V} \\ x_{21} & x_{22} & x_{23} & \cdots & x_{2V} \\ \vdots & \vdots & \vdots & & \vdots \\ x_{T1} & x_{T2} & x_{T3} & \cdots & x_{TV} \end{bmatrix} = \begin{bmatrix} m_{11} & m_{12} & \cdots & m_{1T} \\ m_{21} & m_{22} & \cdots & m_{2T} \\ \vdots & \vdots & & \vdots \\ m_{T1} & m_{T2} & \cdots & m_{TT} \end{bmatrix} * \begin{bmatrix} c_{11} & c_{12} & c_{13} & \cdots & c_{1V} \\ c_{21} & c_{22} & c_{23} & \cdots & c_{2V} \\ \vdots & \vdots & \vdots & & \vdots \\ c_{T1} & c_{T2} & c_{T3} & \cdots & c_{TV} \end{bmatrix}$$

Spatial ICA Model

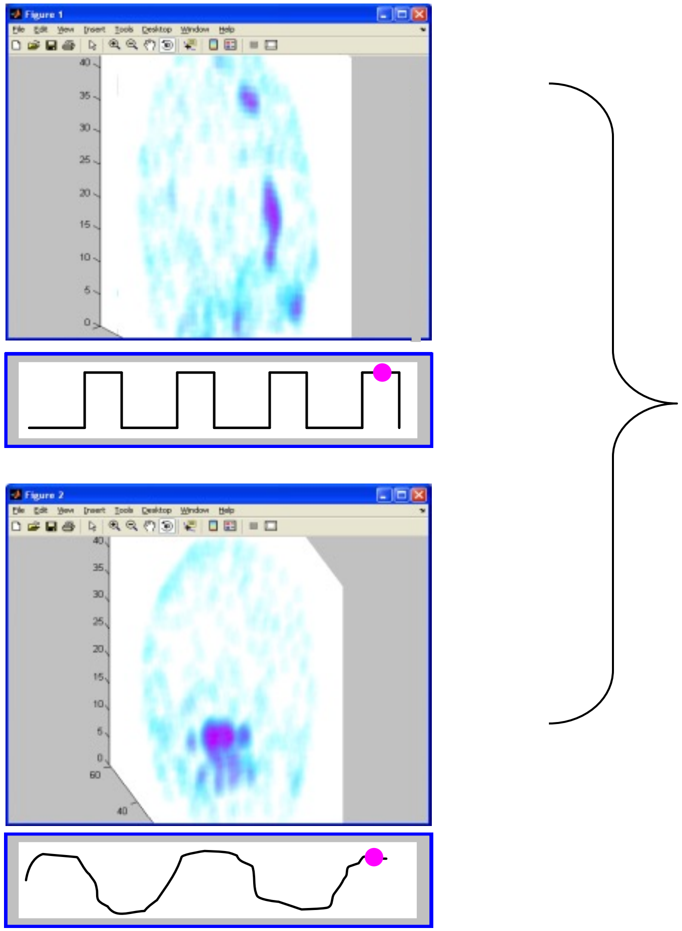
voxels →

$$X = \begin{vmatrix} m_{11}c_{11} + m_{12}c_{21} + \ldots m_{1T}c_{T1} & \cdots & m_{11}c_{1V} + m_{12}c_{2V} + \ldots m_{1T}c_{TV} \\ m_{21}c_{11} + m_{22}c_{21} + \ldots m_{2T}c_{T1} & \cdots & m_{21}c_{1V} + m_{22}c_{2V} + \ldots m_{2T}c_{TV} \\ \vdots & & \vdots \\ m_{T1}c_{11} + m_{T2}c_{21} + \ldots m_{TT}c_{T1} & \cdots & m_{T1}c_{1V} + m_{T2}c_{2V} + \ldots m_{TT}c_{TV} \end{vmatrix}$$

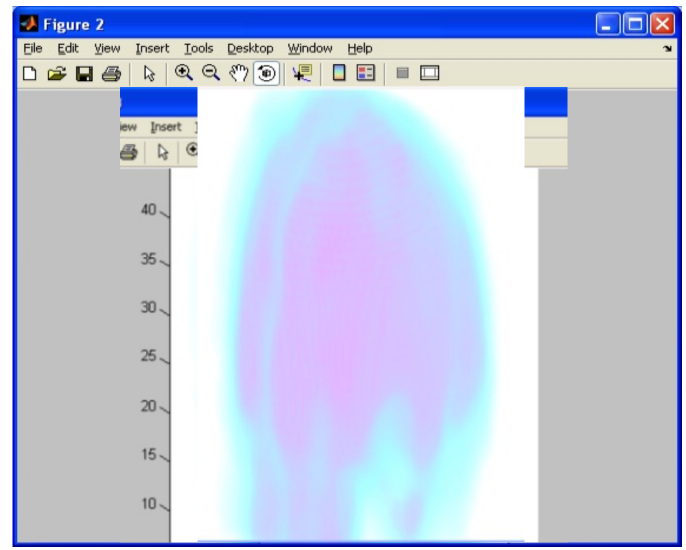
Here the column vector [m_{11} … m_{T1}] specifies the weights of the IC map 1 at each time point

A Conceptual Example

Independent Components

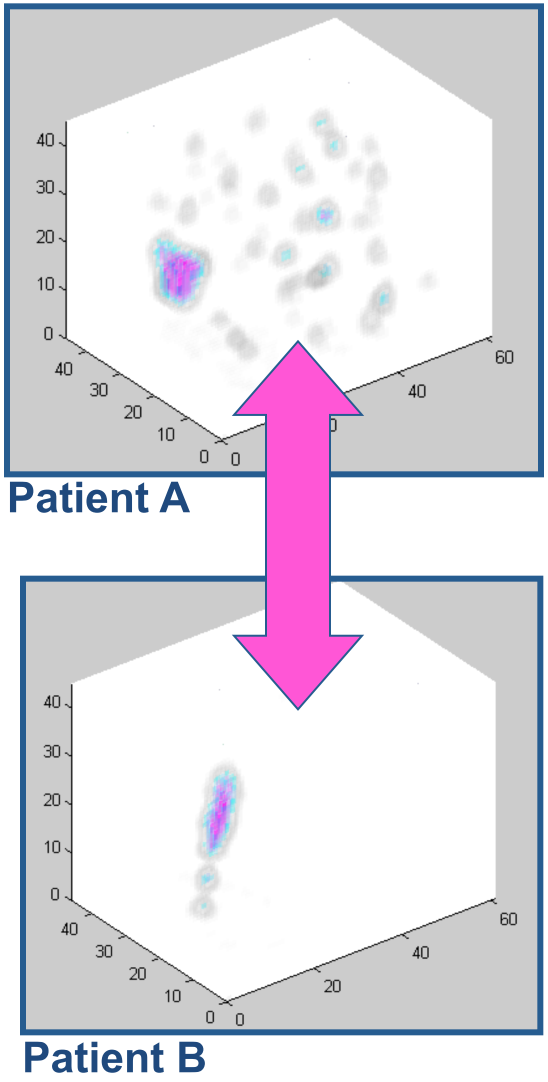


Raw Data from fMRI



3-D Spatial Map Similarity Measurement

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

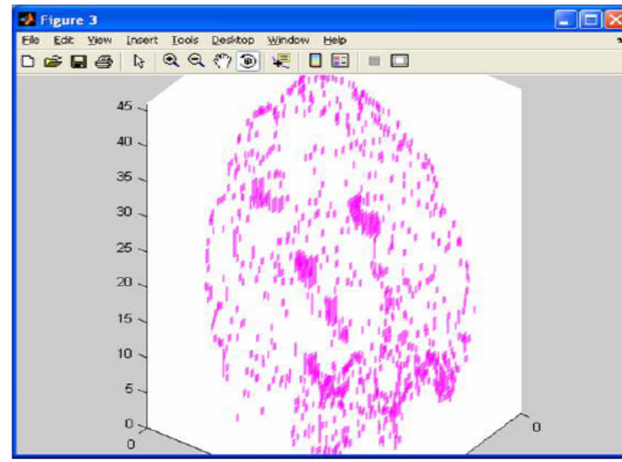


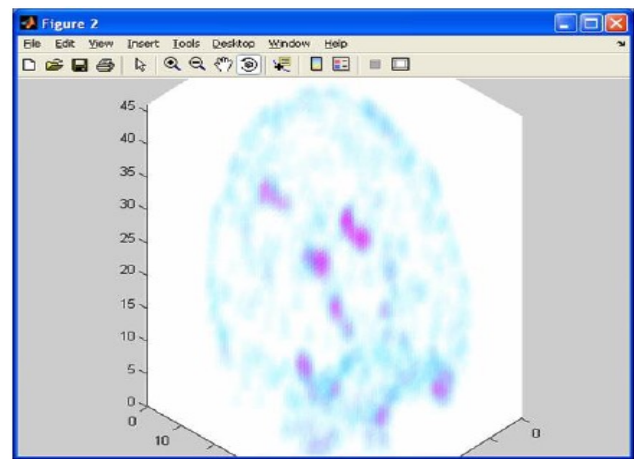
Preprocessing Steps

- Preprocessing
  - Threshold applied to find activated voxels based on standard deviations from mean voxel value
  - Binary labeling
  - Each voxel is weighted by:

$$x_i = e^n$$

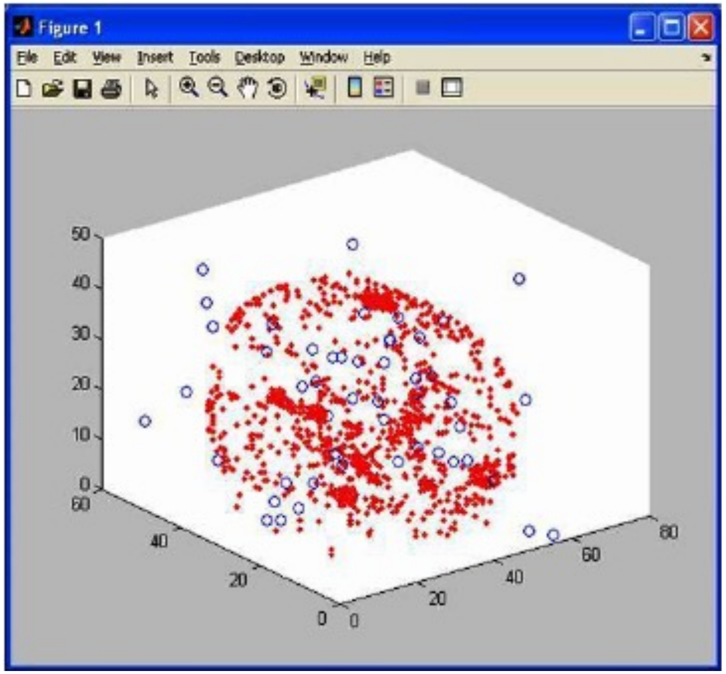
where *n* is the number of activated neighbors

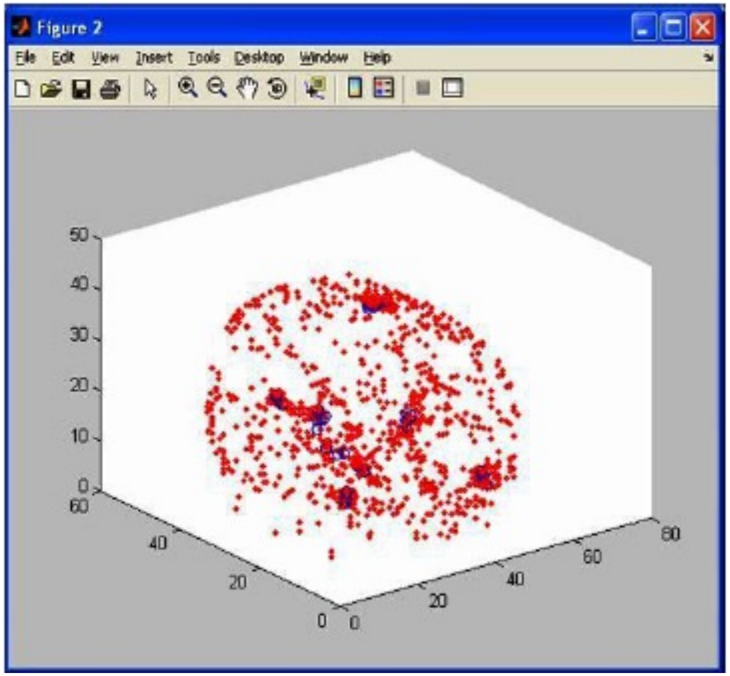




Modified K-Means Clustering

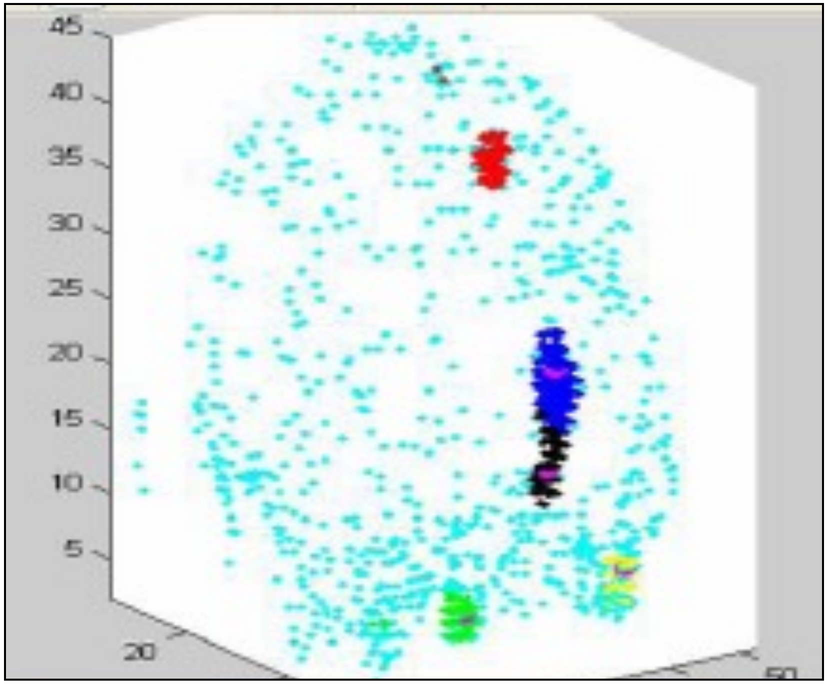
- Weighted average of activated voxel locations used to find new bin location
- Incorporates a priori information about bin center locations





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:

$$w_k = \frac{1}{mean(F_k)} std\left(\frac{F_k}{mean(F_k)}\right)$$

where F_k is the set of all values for feature k

Feature Distance Measure

- Distance between two clusters:

$$d_{ik} = \min_{n}(abs(f_{ik} - f_{jn}))$$

- Distance between two spatial maps:

$$m_{ij} = \frac{1}{abs(n_i - n_j)} \sum_{k} d_{ik} * binsize_k * averagebinweight_k,$$

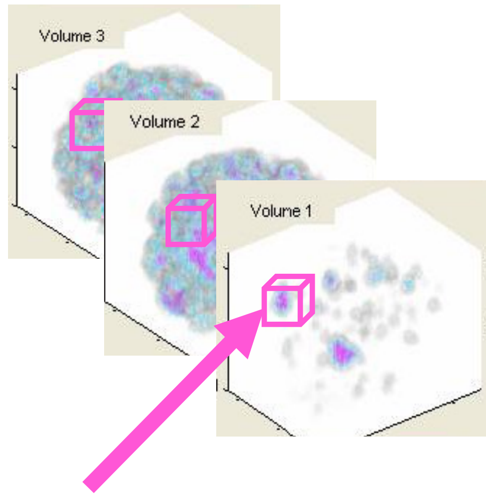
$$Dist_{ij} = \frac{m_{ij} + m_{ji}}{2},$$

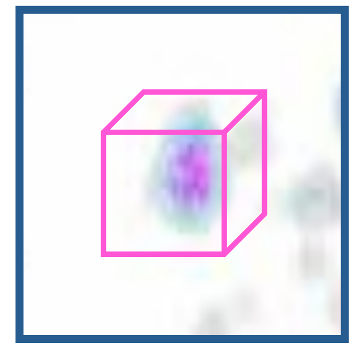
where $binsize_k$ and $averagebinweight_k$ are two values from the feature vector

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



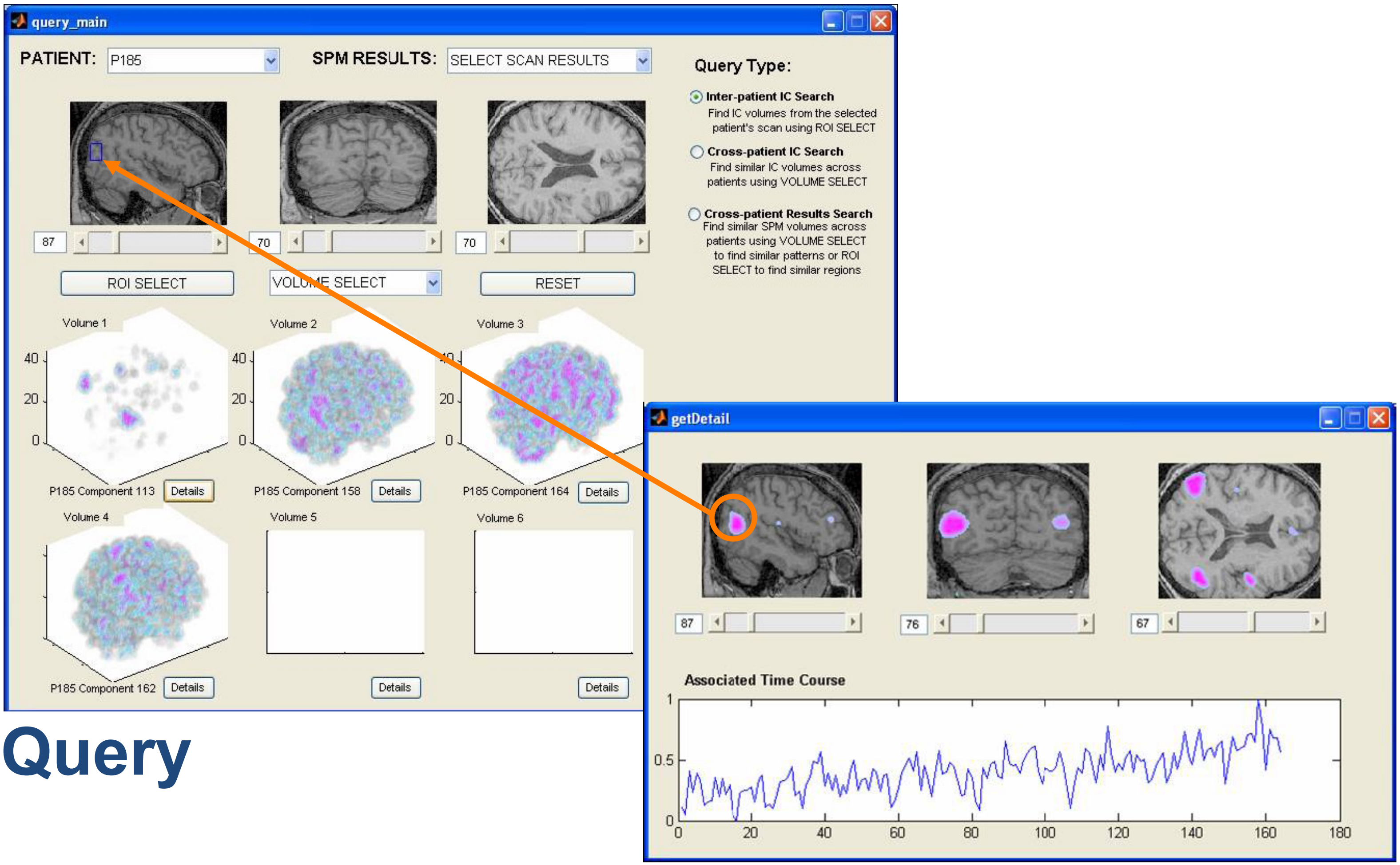


Select ROI from patient's structural MRI

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



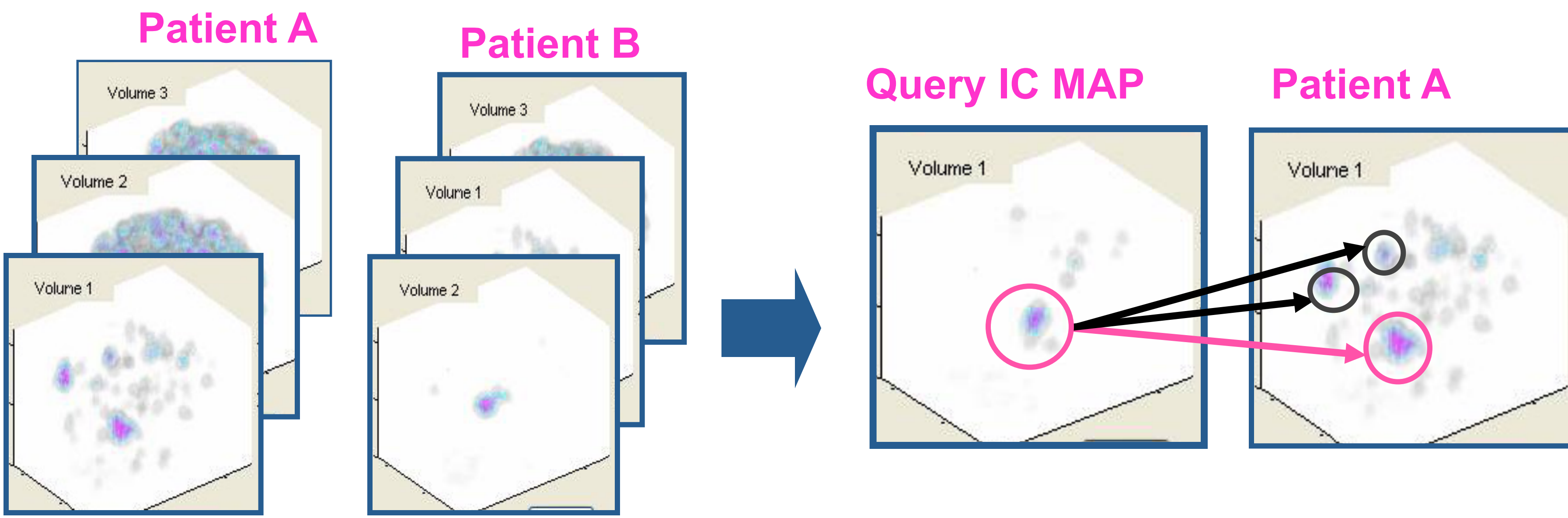
Query

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

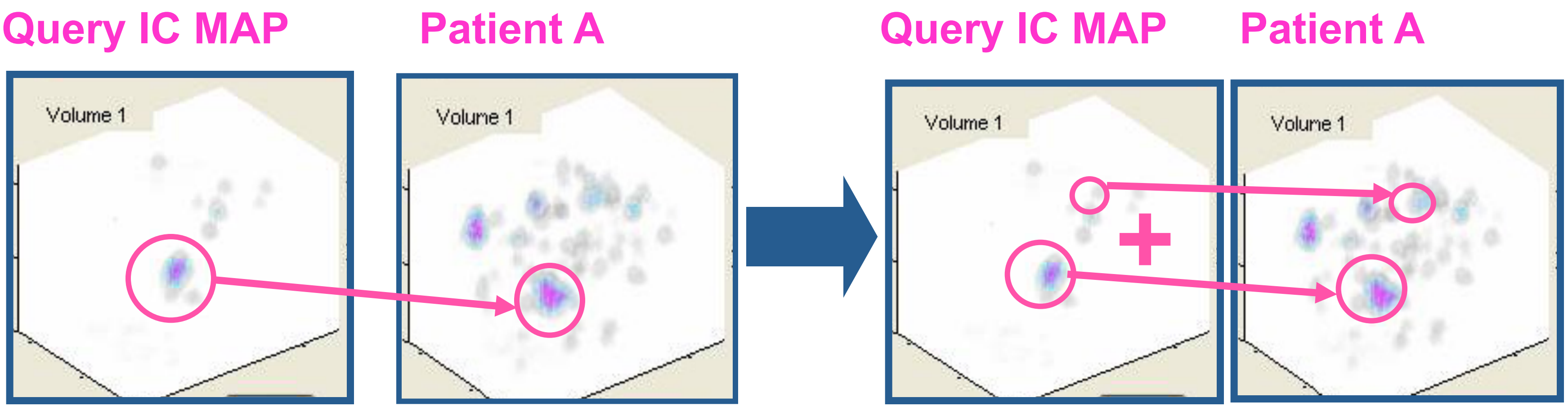
Query 3: Algorithm



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.

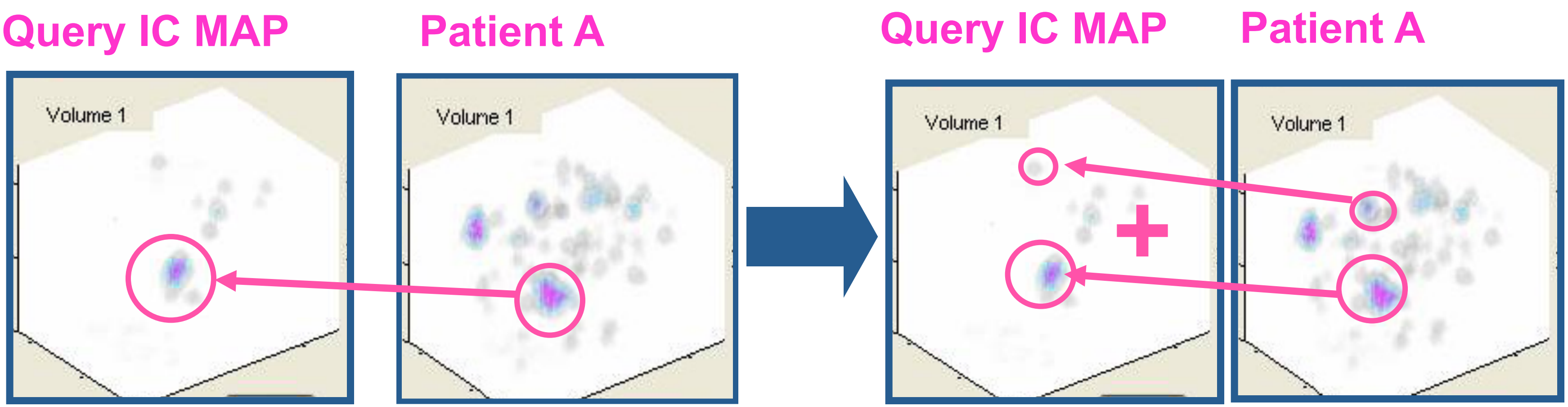
Query 3: Algorithm



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

Sum cluster rankings to get IC map rank.

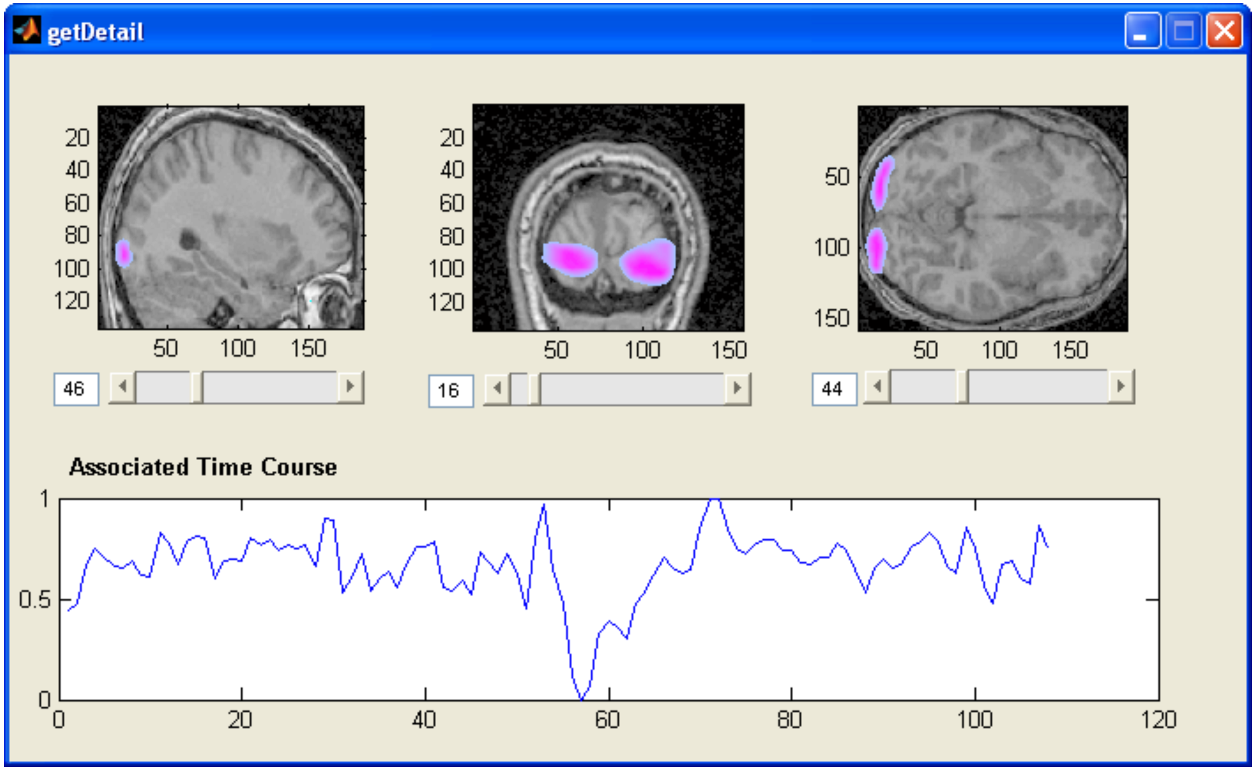
Query 3: Algorithm



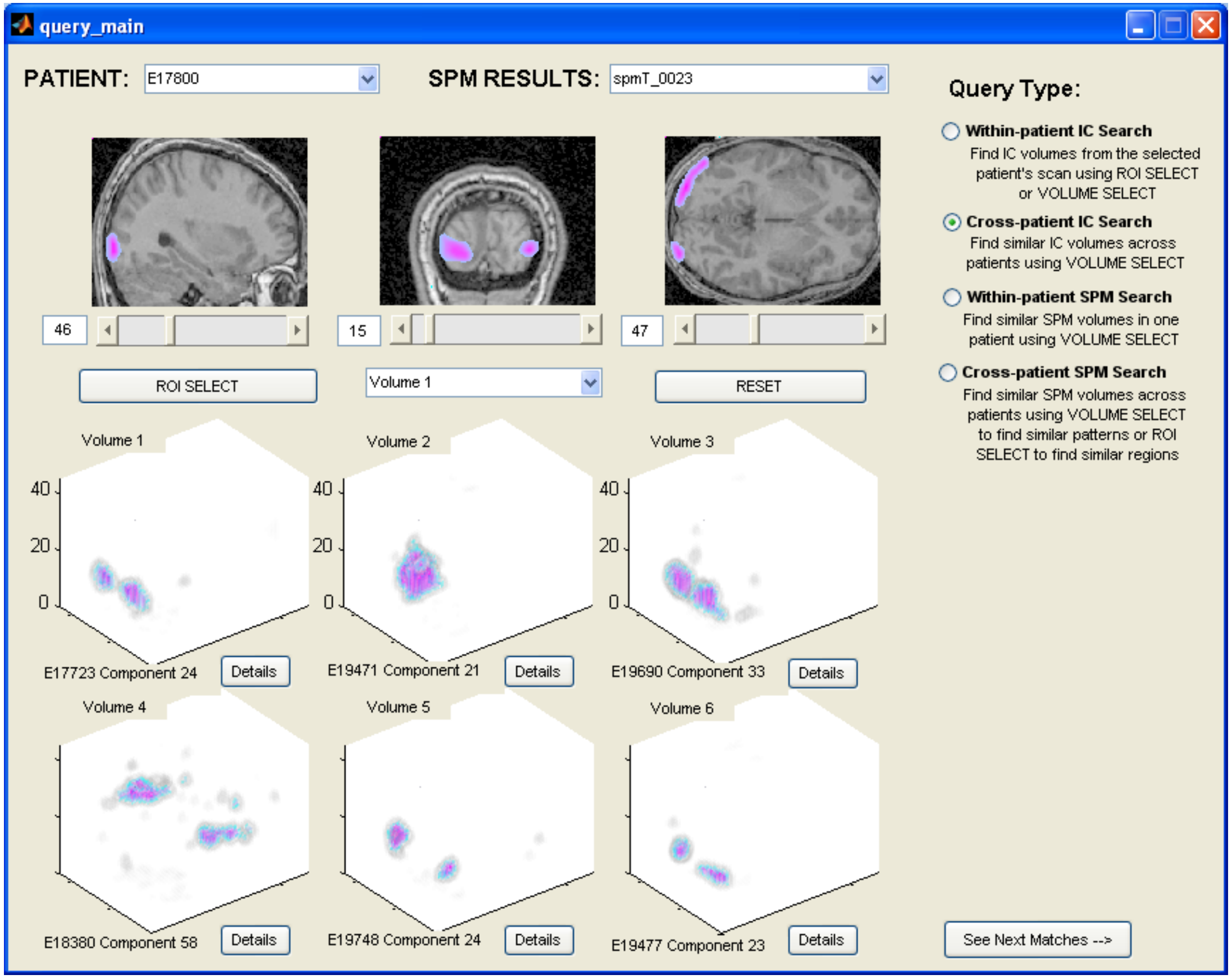
Repeat distance measure starting from second IC map. Average both IC rankings to get final distance measure.

Sample Results: Query 3

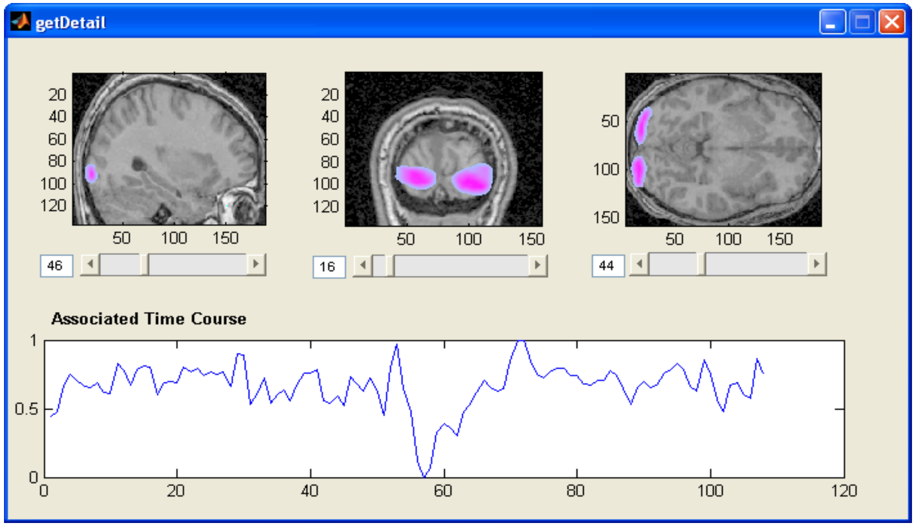
- Start with IC map selected using any of the queries



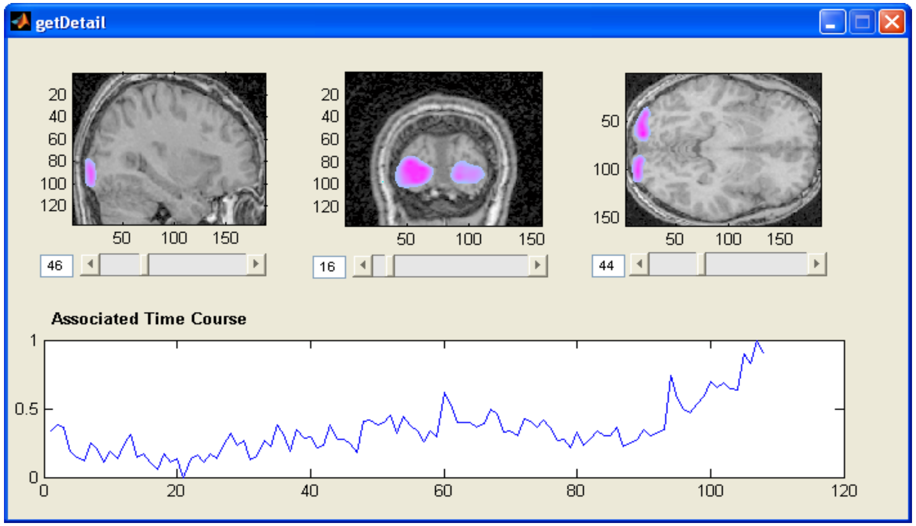
Sample Results: Query 3



Sample Results: Query 3, Detail Browser



Details from query IC map

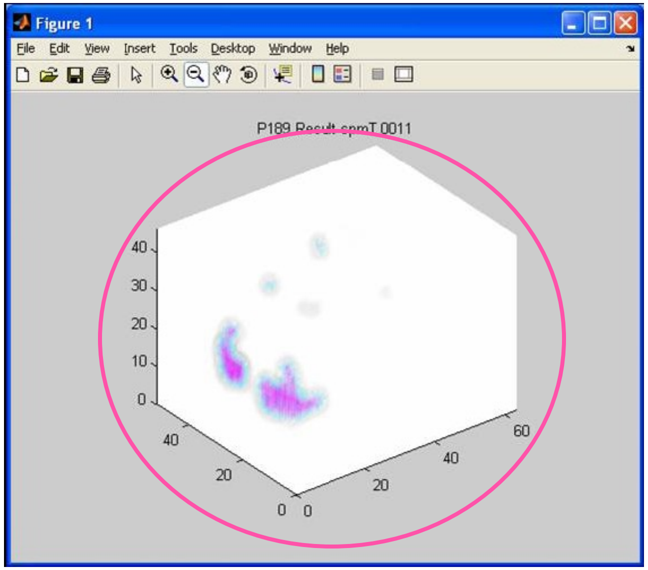


Details from first match

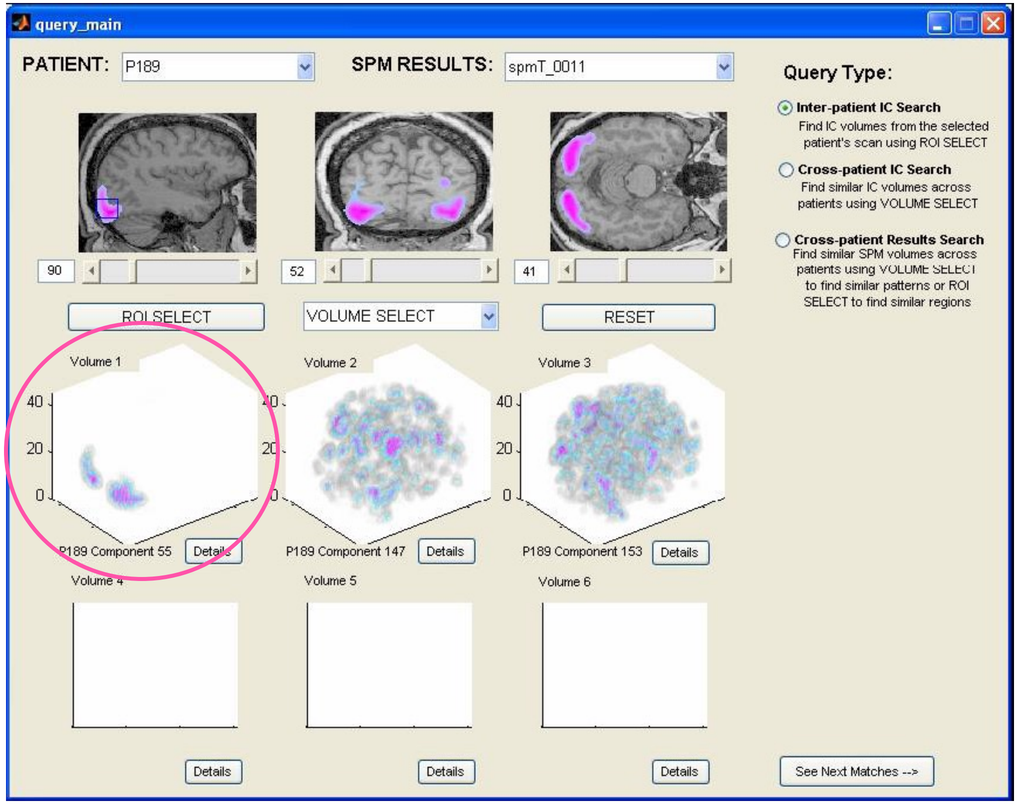
Evaluation of Results

- 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

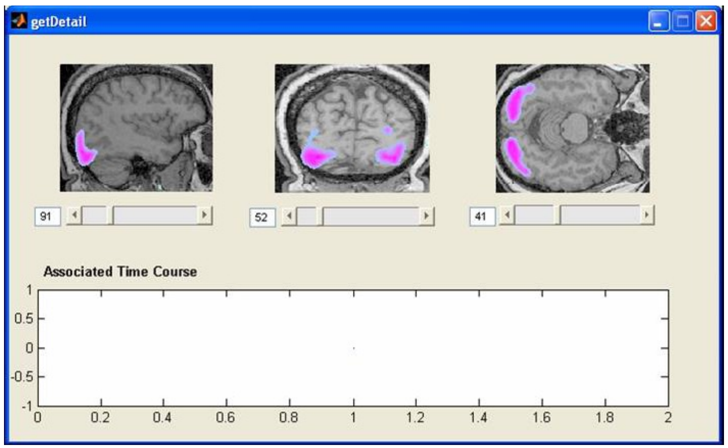


SPM results map

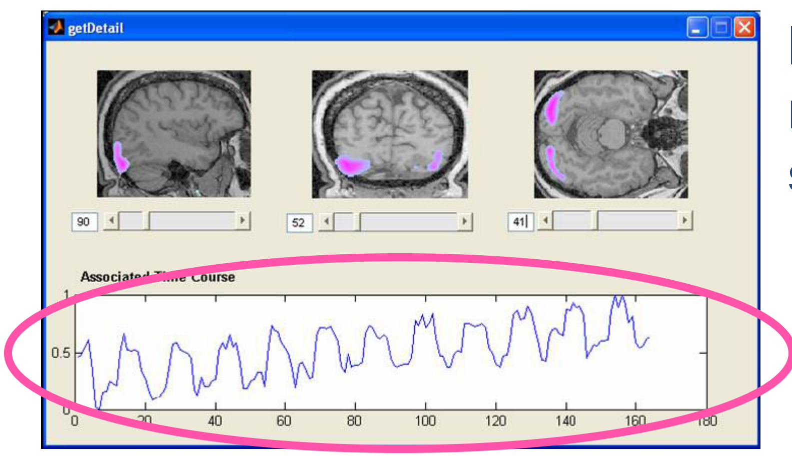


Within patient query for similar IC maps

Replicating SPM Results



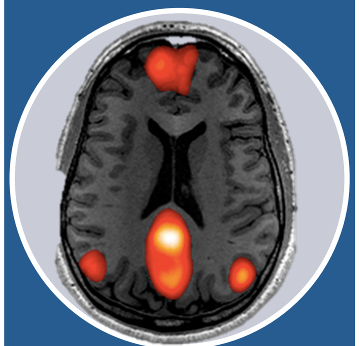
SPM results mapped onto patient's structural image



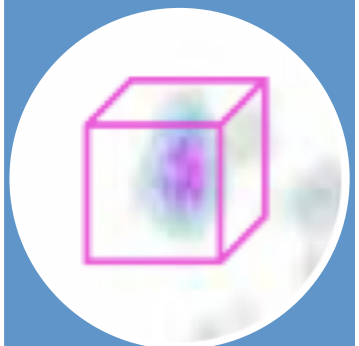
Independent component mapped onto patient's structural image

Time-course shows structure of experiment task

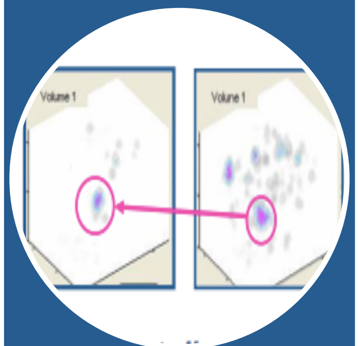
Exploring Functional Connections in the Brain



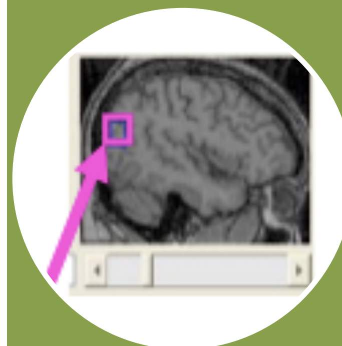
ICA voxel similarity measure



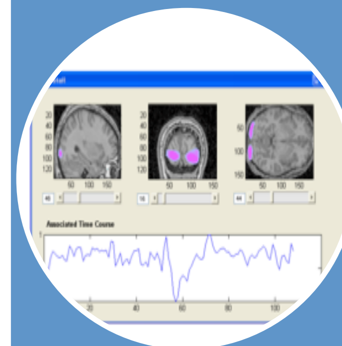
Detecting and describing activation clusters



Activation cluster similarity measure



Workflows to address six user query types



Graphical user interface to execute queries

System to explore functional connectivity