Tools to parcellate the brain and its relation to function: Part II

Resting State Functional Connectivity Subdivision with Supervised Learning

OHBM Course Teaching Materials Handout

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June 8, 2014
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Overview

• Resting-state network mapping
  – Seed-based correlation mapping
  – Independent component analysis

• Review: Extant unsupervised RSN definition

• Supervised vs. unsupervised learning

• Supervised RSN definition: setting up the problem
  – Input space, output space; choosing a model/algorithm

• Evaluating performance
  – Regression vs. classification

• Practical tricks for brain imaging
  – Methodological optimization tool
Seed-based Correlation Mapping

- Definition: Spatial map of brain regions correlated with mean timecourse of region of interest

- Motivation: Regions that correspond to similar brain functions have spontaneously correlated signals

Biswal et al., 1995
Seed-based Correlation Mapping
(Spatial) Independent Component Analysis

1. Resting-state data is composed of a superposition of fixed spatial maps, each evolving with some timecourse.
2. Components can be spatially overlapping – a given region can belong to multiple networks.
Overview

• Resting-state network mapping
• Literature review of unsupervised RSN definition
  – Seed definition
  – Clustering
  – Graph theory
• Supervised vs. unsupervised learning
• Supervised RSN definition: setting up the problem
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“Unsupervised” RSN Mapping

• Seed-based mapping heavily biased by choices of seed region
  – Independence from priors by systematic seeding of entire brain

Yeo et al., J Neurophysiol (2011)
Functional Connectivity Gradients

Wig et al., 2013 (NeuroImage)
See also Cohen et al. 2008 (NeuroImage)

Assignment of Parcels to Networks

Poster XXX:
"Generation and evaluation of cortical area parcellations from functional connectivity boundary maps“
Gordon et al.
Clustering Approaches

7 Clusters

17 Clusters

Yeo et al., J Neurophysiol (2011)
Clustering Approaches

Fuzzy C-means:
Each voxel yields one correlation map
Values below indicate distances to cluster centers

Lee et al., PLoS One (2012)
<table>
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<td>Clustered FC Maps</td>
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</table>
RSNs are Hierarchically Organized

- Agglomerative ICA results:
  - RSNs(23) ∈ Modules (5) ∈ Systems(2)

Doucet et al., J Neurophysiol (2011)
Graph Theoretic Approaches

The areal graph

Subgraphs replicate across cohorts

Main cohort

Replication cohort

Areal ROIs

10% Tie density

264

10% Tie density

2%

Subgraphs change hierarchically over thresholds

Spheres: areal, main cohort

Surfaces: modified voxelwise, replication cohort

weaker correlations

stronger correlations

Power et al., Neuron (2011)
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Why use supervised learning

• Different unsupervised methods recover the same RSN at different hierarchical levels
  – Superclass: Desired RSN may be agglomerated with other components
  – Subclass: Only fragments of desired RSN are returned
    → Inconsistent/unpredictable results across individuals

• Supervised methods can guarantee a recovered RSN represents the same entity across individuals
Supervised vs. Unsupervised Methods

• Benefits of unsupervised learning
  – Discovers new structure in data
  – Unbiased

• Benefits of supervised learning
  – Avoids assignment problem: (meaning of “default mode network” is consistent across groups, subjects, runs, etc.)
  – Increased SNR for modeled components
Supervised vs. Unsupervised Methods

- Complimentary, not competing approaches
  - Unsupervised methods discover meaningful components in the data
  - Supervised methods can optimally extract these known components from new datasets
Supervised vs. Unsupervised Approaches

Example application:
Automated postal mail sorting

Unsupervised Learning:
(e.g. cluster analysis, ICA)

Supervised Learning
• discriminant analysis (LDA/QDA)
• neural networks
• support vector machines

Discovery:
“These are the characters of the decimal system”

Classification:
This image represents the number “2”
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Setting up the problem

Input Space (X):
Array of pixels

Output Space (Y):

<table>
<thead>
<tr>
<th>Class</th>
<th>Desired Value</th>
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<tr>
<td>“1”</td>
<td>0</td>
</tr>
<tr>
<td>“2”</td>
<td>1</td>
</tr>
<tr>
<td>“3”</td>
<td>0</td>
</tr>
<tr>
<td>“4”</td>
<td>0</td>
</tr>
<tr>
<td>…</td>
<td>0</td>
</tr>
</tbody>
</table>

\[ Y \approx f(X, \theta) \]
Setting up the problem

Input Space (X): Array of voxels

Output Space (Y):

<table>
<thead>
<tr>
<th>Class</th>
<th>Desired Value</th>
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</thead>
<tbody>
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<td>“DAN”</td>
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<tr>
<td>“VAN”</td>
<td>0</td>
</tr>
<tr>
<td>“SMN”</td>
<td>1</td>
</tr>
<tr>
<td>“VIS”</td>
<td>0</td>
</tr>
<tr>
<td>...</td>
<td>0</td>
</tr>
</tbody>
</table>

\[ Y \approx f(X, \theta) \]
Training Data

• Must represent the final data to be classified
• Goal: classify the RSN identity of every brain locus based on its correlation map
• Training data should consist of correlation maps generated from a representative sample of seed locations, each belonging to a known class (or RSN)
Design considerations

• What RSNs to define?
  – Must be well represented in training data

• Generalizability
  – Are the subjects used in training representative?
  – Similar acquisition parameters?

• Choices in preprocessing
  – Head motion correction
  – Temporal / spatial censoring and/or blurring
  – Common signal regression?
  – Many others
Generating Training Data

Task-derived Seed Regions

Hacker et al., NeuroImage (2013)
Training

Input Space (X): Array of voxels

Output Space (Y):

<table>
<thead>
<tr>
<th>Class</th>
<th>Output</th>
<th>Desired Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>“DAN”</td>
<td>0.12</td>
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<tr>
<td>“VAN”</td>
<td>0.24</td>
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<tr>
<td>“SMN”</td>
<td>0.75</td>
<td>1</td>
</tr>
<tr>
<td>“VIS”</td>
<td>0.21</td>
<td>0</td>
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<tr>
<td>…</td>
<td>…</td>
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</tr>
</tbody>
</table>

Error Signal

Training Data

Cross-Validation
Bias-Variance Trade-off

Fixed data size

Mean Error

Model Complexity

Cross-validation error

Training error

High bias

High variance

Rickey Ho, 2012 (http://horicky.blogspot.com/)
Overfitting/Underfitting

Andrew Ng, 2011 (http://ml-class.org/)
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Evaluating Performance

Scalar RSN Estimates (Regression)

• Computed as root mean square difference between estimates and desired values:
\[ E = \| f (X, \theta) - Y \| \]

• Can be computed within each class, or overall (black line below)

Hacker et al., NeuroImage (2013)
Evaluating Performance

Categorical RSN Estimates (Classification)

- Sensitivity and specificity are computed across a range of thresholds ($T$) of $f(X, \theta)$
- The area under the resulting “receiver operating characteristic” curve is a good summary measure of accuracy

$$AUC = \int TPR(T) \cdot FPR(T) \cdot dT$$

http://www.medcalc.org/manual

Hacker et al., NeuroImage (2013)
RSN Classification Technique

• Assign each point in the brain to a known functional system based on its correlation map

Hacker et al., NeuroImage (2013)
Generalizability to Untrained Brain Regions

- Correct extrapolation to regions not in the training data (cerebellum, thalamus in this example) indicates learning of an underlying function

Hacker et al., *NeuroImage* (2013)
Generalizability to New Subjects

• Does function vary with structure across subjects?
  – Motor topography conforms to gyral morphology
  – Motor network centroid covaries with central sulcus

Hacker et al., NeuroImage (2013)
Comparison to Linear Methods

• Dual Regression
  – For a group-level maps, find associated timecourses in an individual
  – Correlate timecourse with each voxel to recover component in the individual

• Linear Discriminant Analysis
  – Project data onto vectors that maximize separation of class means (between vs. within class scatter)
Algorithm Comparison

A

Dual Regression

Linear Discriminant Analysis

Multi-layer Perceptron

B

SMN Score vs. VIS Score

SMN Score vs. LAN Score

SMN Score vs. ROI (DAN, VAN, SMN, VIS, FPC, LAN, DMN)

Hacker et al., NeuroImage (2013)
Methodological Optimization

Hacker et al., NeuroImage (2013)
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References