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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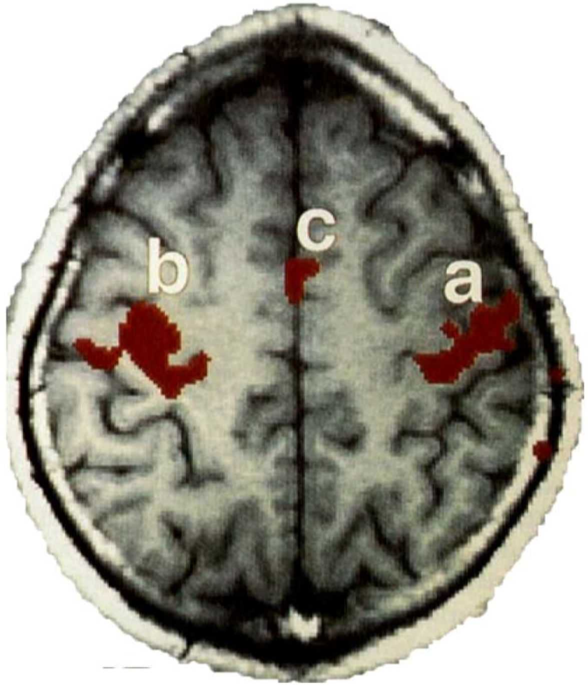
Overview

- 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

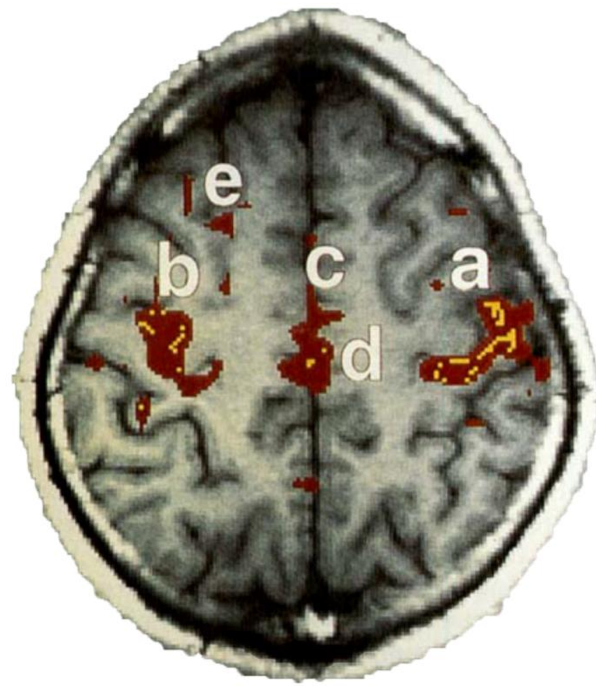
Seed-based Correlation Mapping

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

Task Response



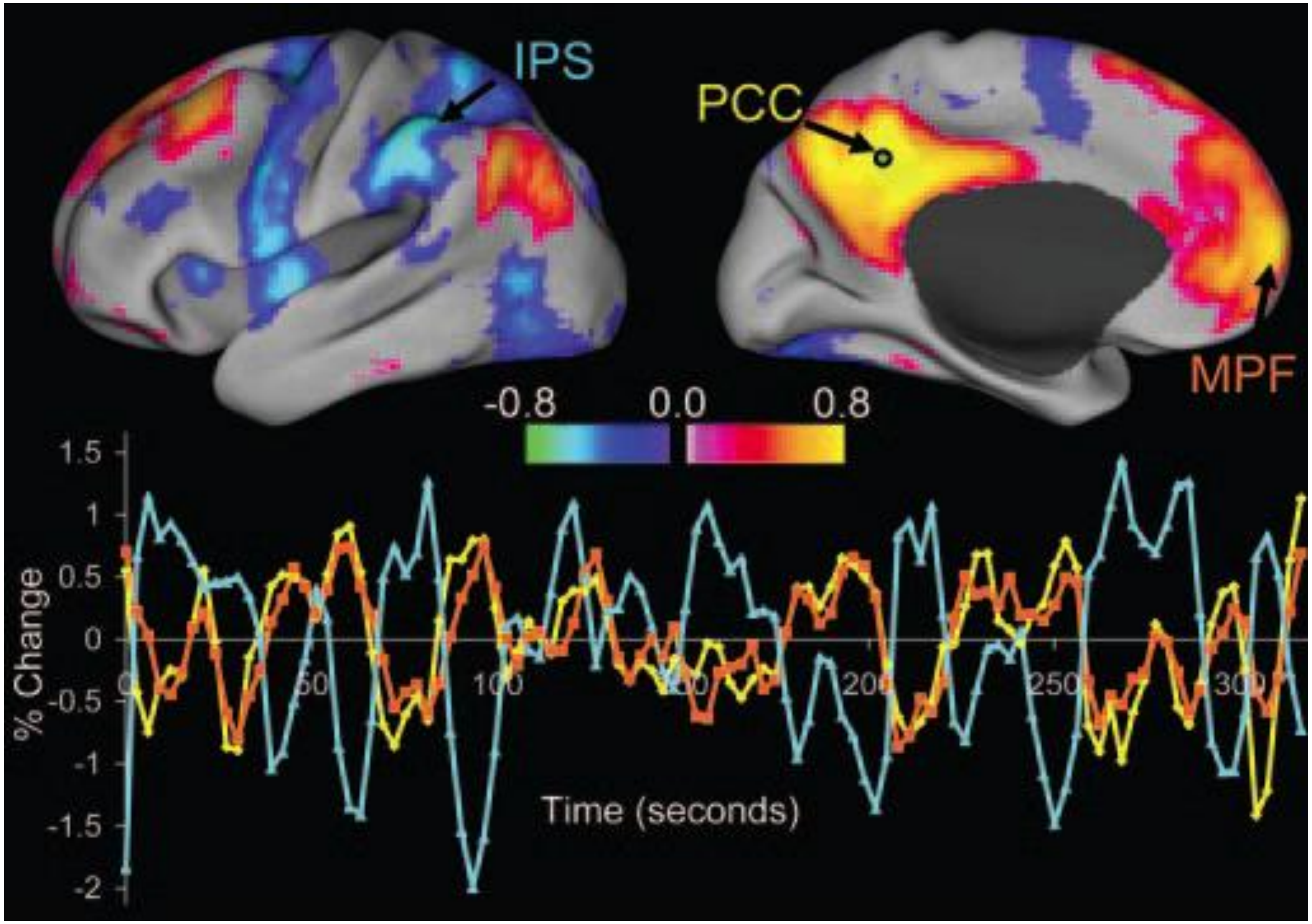
Regions Correlated with "b"



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

Biswal et al., 1995

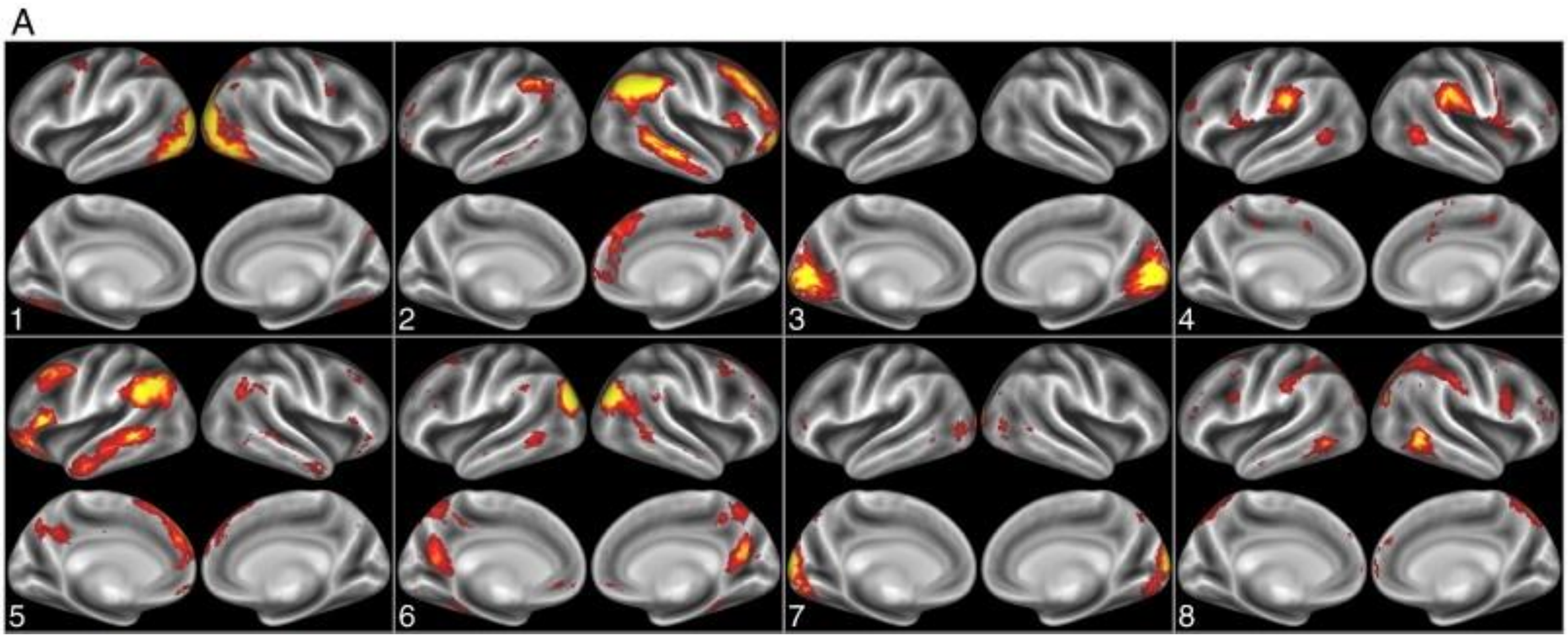
Seed-based Correlation Mapping



Fox et al., PNAS 2005

(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



Smith et al., NeuroImage (2013)

Overview

- Resting-state network mapping
- Literature review of unsupervised RSN definition
  - Seed definition
  - Clustering
  - Graph theory
- Supervised vs. unsupervised learning
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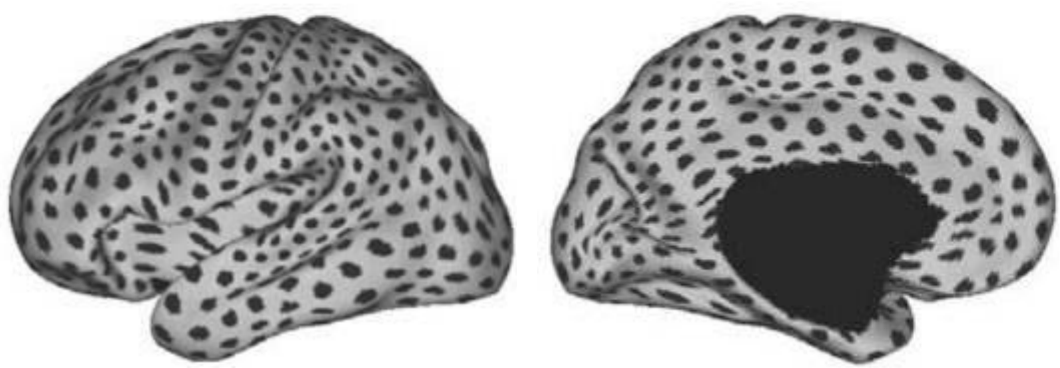
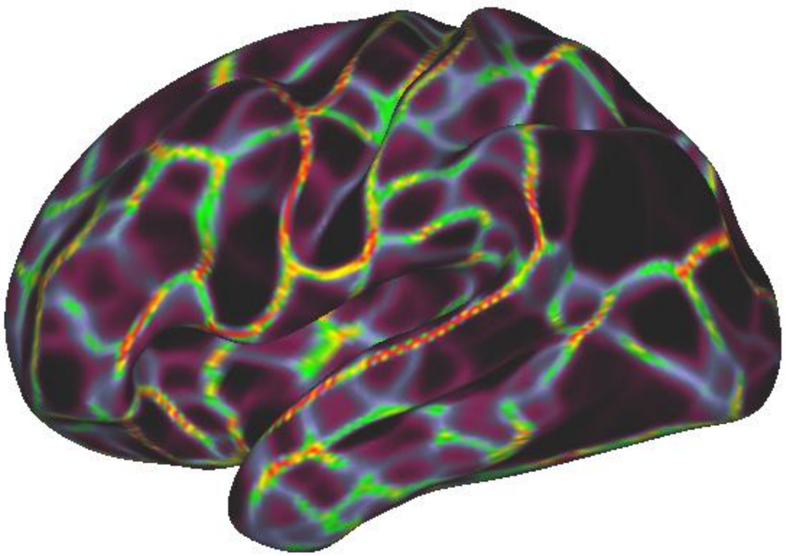
“Unsupervised” RSN Mapping

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

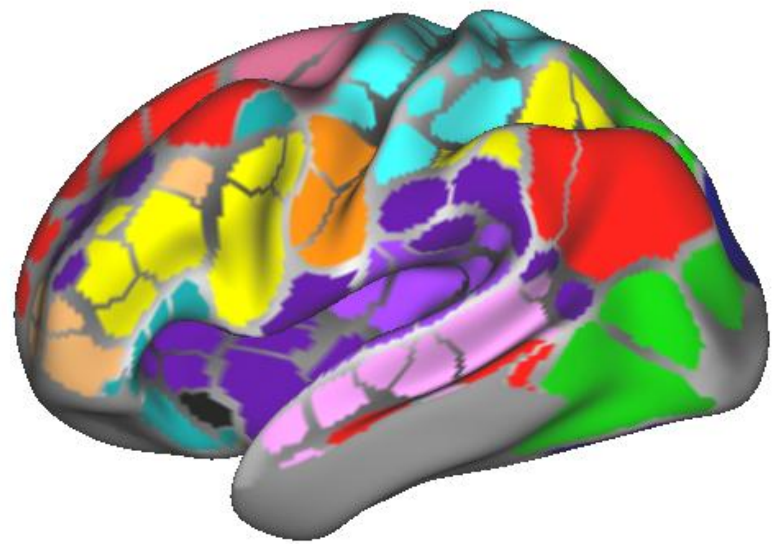


Yeo et al., J Neurophysiol (2011)

Gradient-based Approaches



Functional Connectivity Gradients



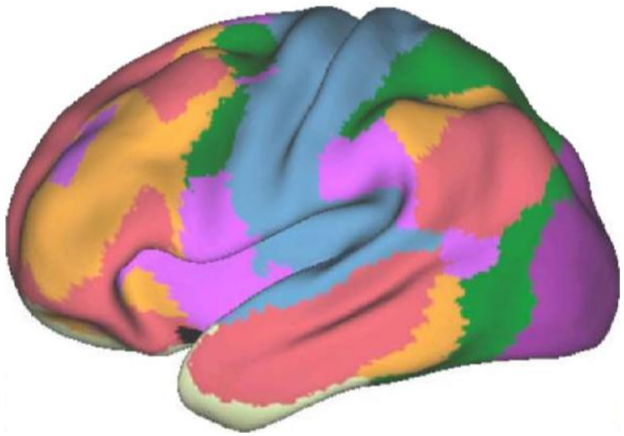
Assignment of Parcels to Networks

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

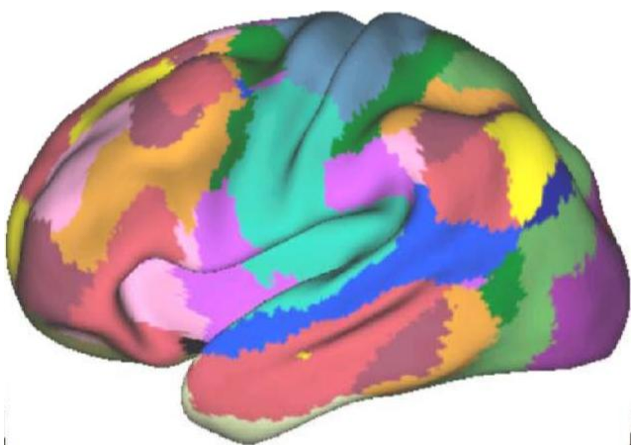
Poster XXX:
"Generation and evaluation of cortical area parcellations from functional connectivity boundary maps“
Gordon et al.

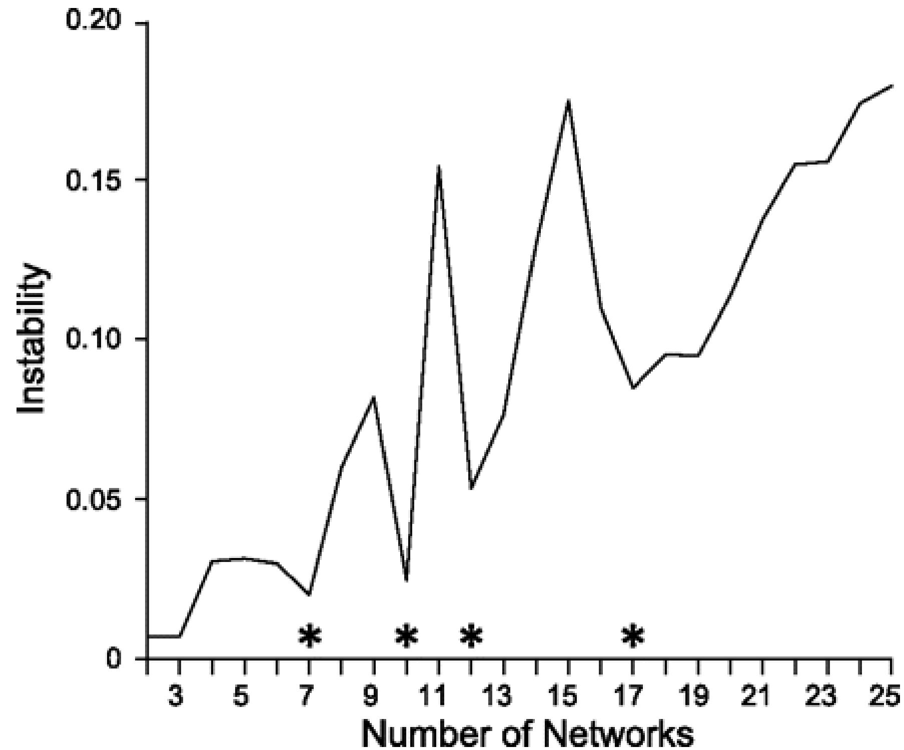
Clustering Approaches

7 Clusters



17 Clusters





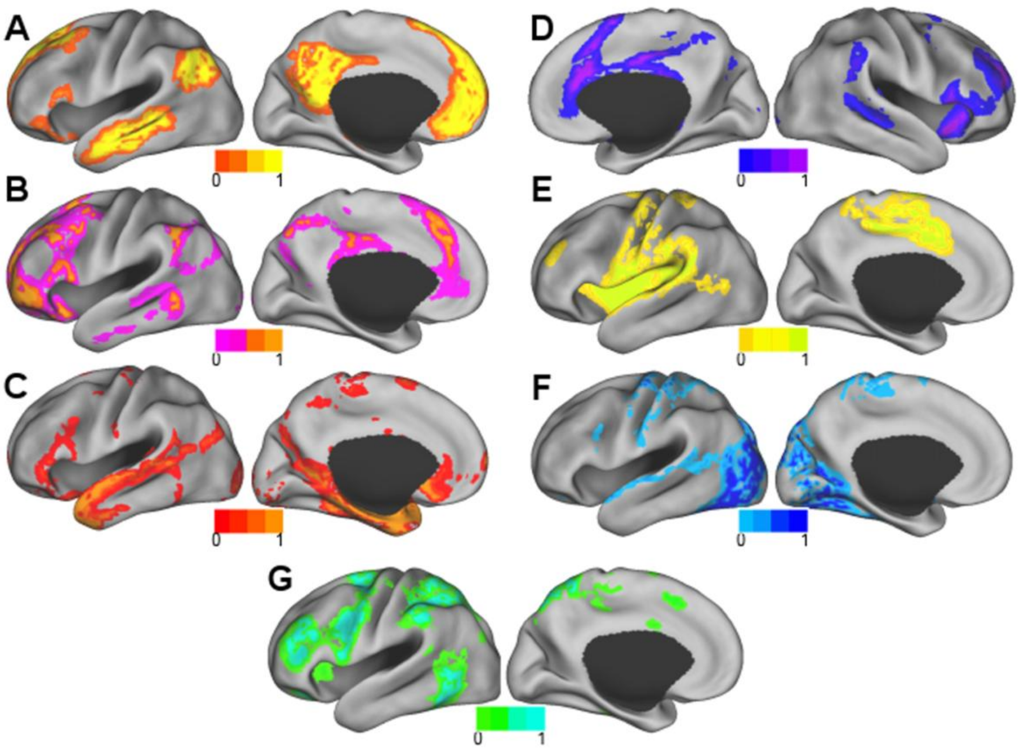
Yeo et al., J Neurophysiol (2011)

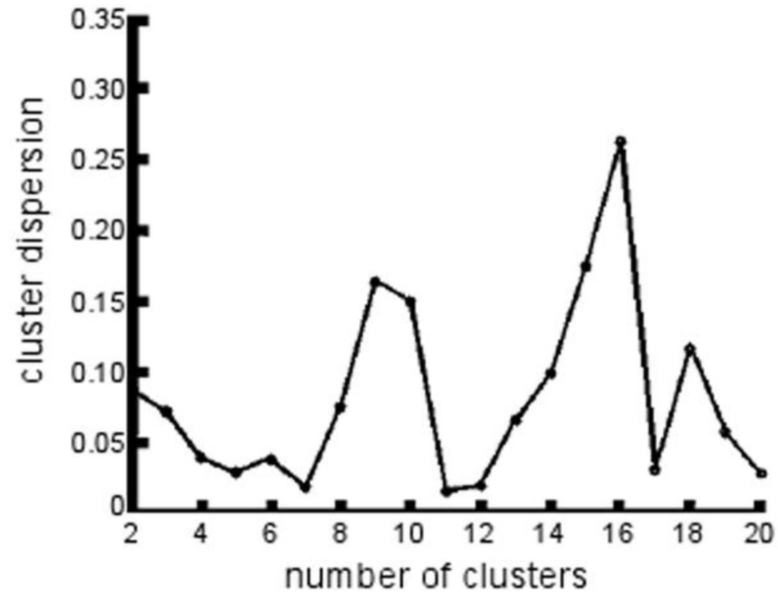
Clustering Approaches

Fuzzy C-means:

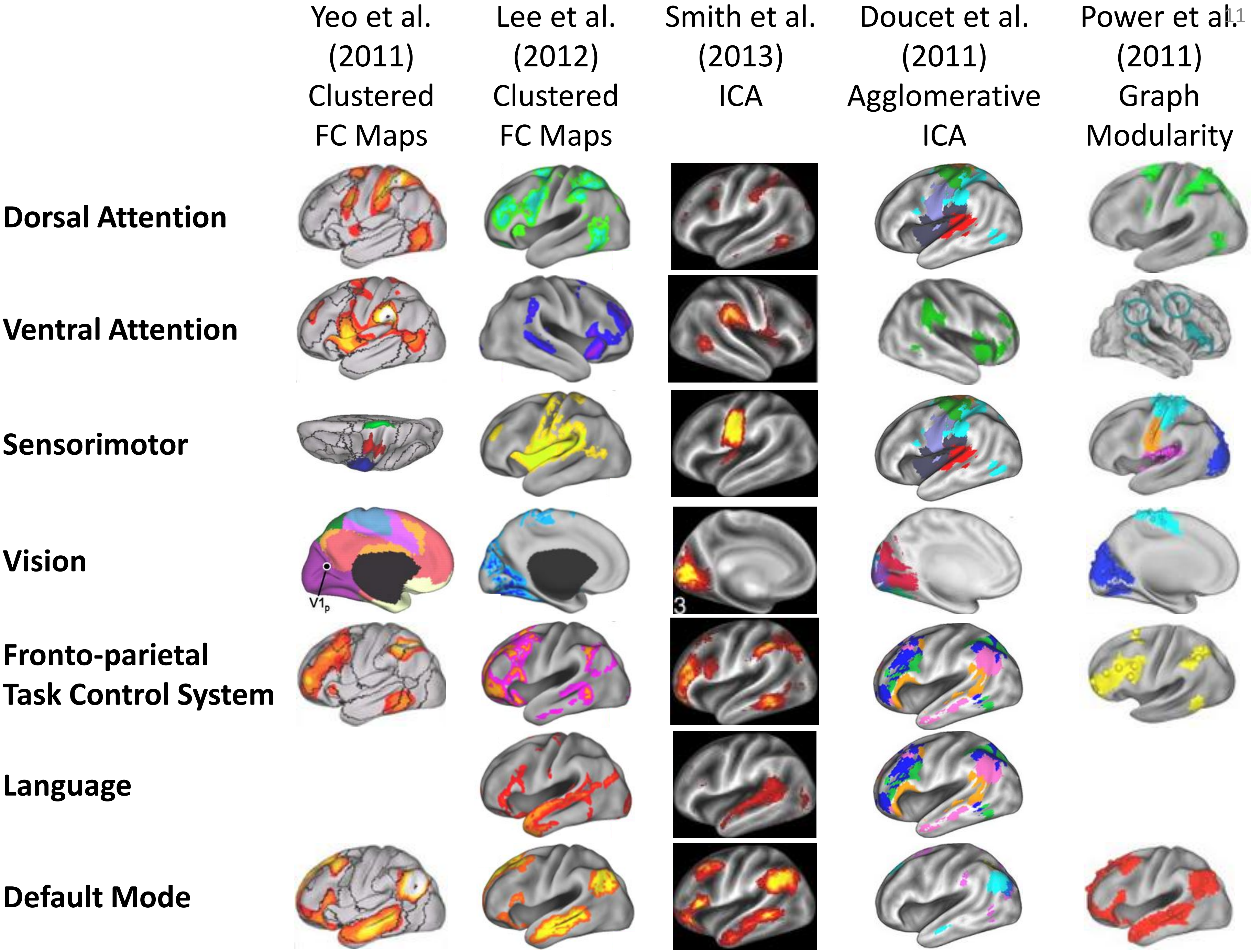
Each voxel yields one correlation map

Values below indicate distances to cluster centers



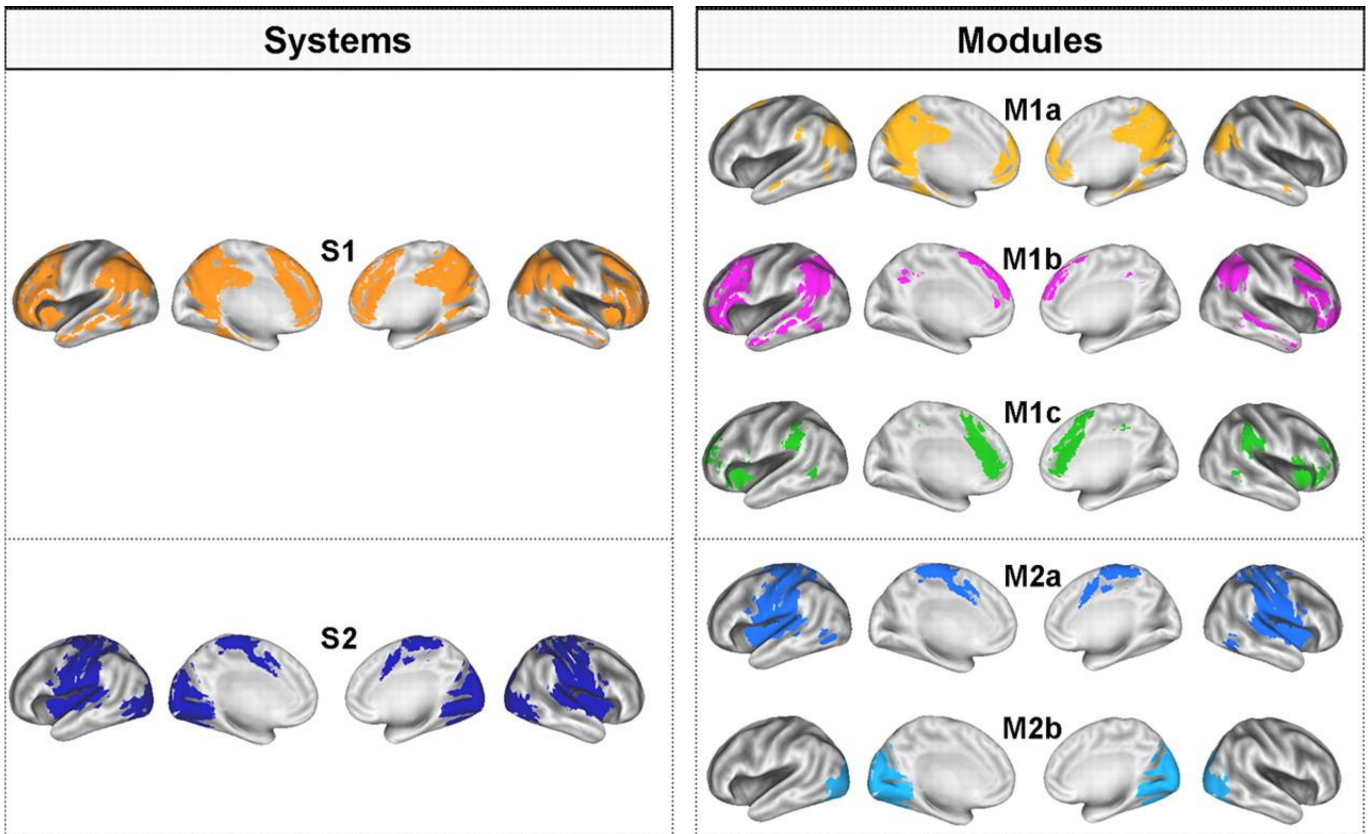


Lee et al., PLoS One (2012)


Yeo et al. (2011) Clustered FC Maps
Lee et al. (2012) Clustered FC Maps
Smith et al. (2013) ICA
Doucet et al. (2011) Agglomerative ICA
Power et al. (2011) Graph Modularity
Dorsal Attention
Ventral Attention
Sensorimotor
Vision
V1p
3
Fronto-parietal Task Control System
Language
Default Mode

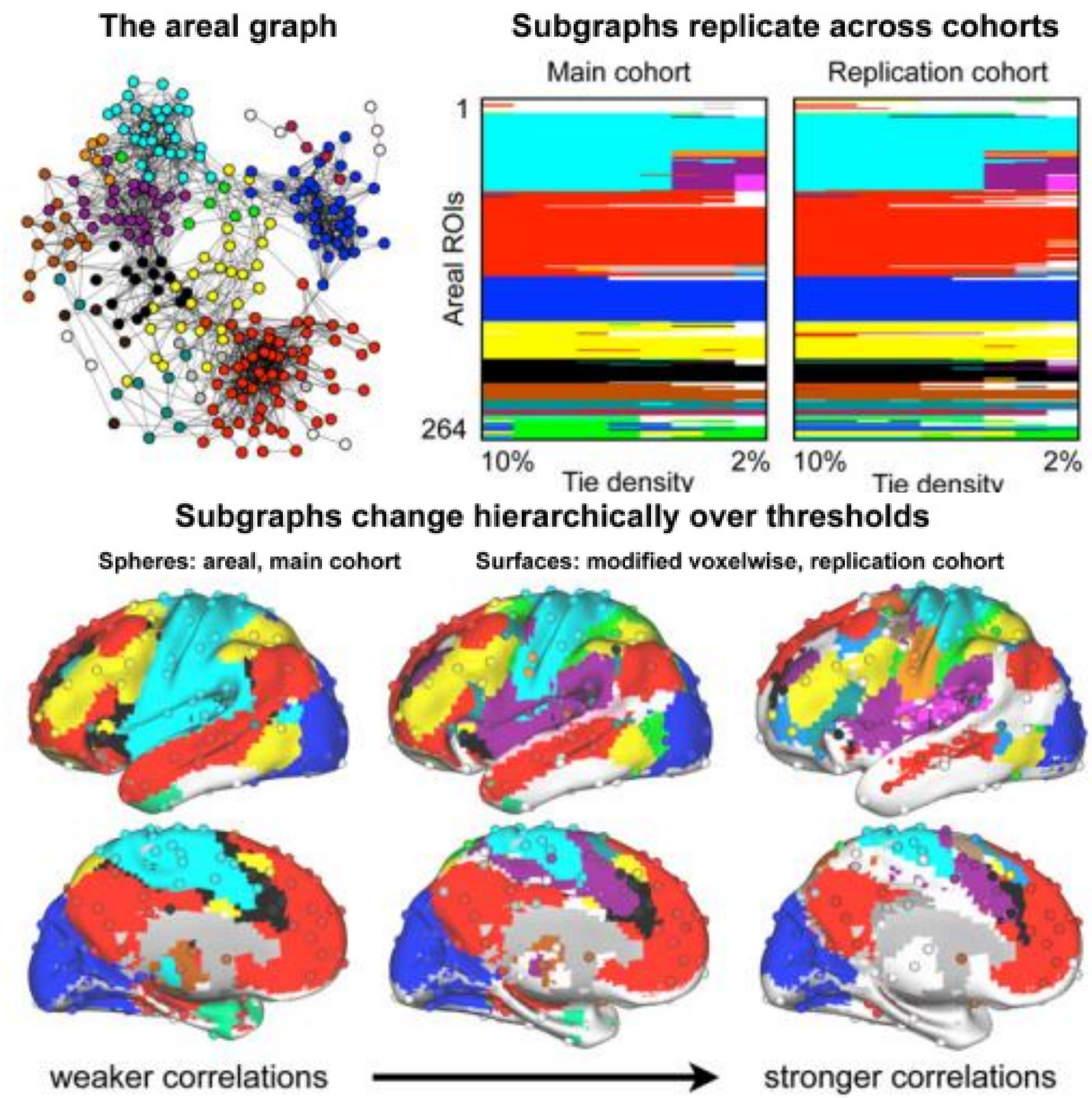
RSNs are Hierarchically Organizaed

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



Doucet et al., J Neurophysiol (2011)

Graph Theoretic Approaches



Power et al., Neuron (2011)

Overview

- Resting-state network mapping
- Literature review of unsupervised RSN definition:
- Supervised vs. unsupervised learning
- Supervised RSN definition: setting up the problem
  - Input space, output space; choosing a model/algorithm
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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

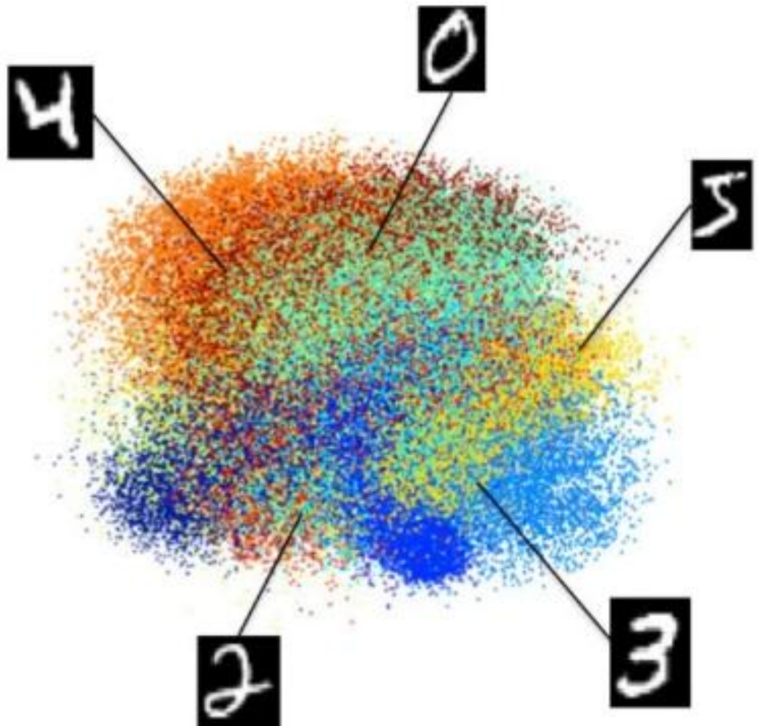
- Complimentary, not competing approaches
  - Unsupervised methods discover meaningful components in the data
  - Supervised methods can optimally extract these known components from new datasets

Supervised vs. Unsupervised Approaches

Example application:
Automated postal mail sorting

Unsupervised Learning:

(e.g. cluster analysis, ICA)

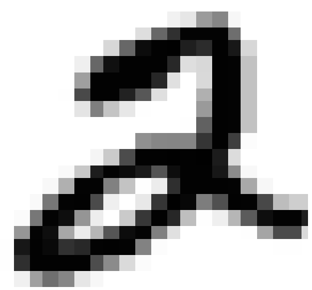


Bresson et al., 2012

Discovery:
"These are the characters of the decimal system"

Supervised Learning

- discriminant analysis (LDA/QDA)
- neural networks
- support vector machines



= "2"

Classification:
This image represents the number "2"

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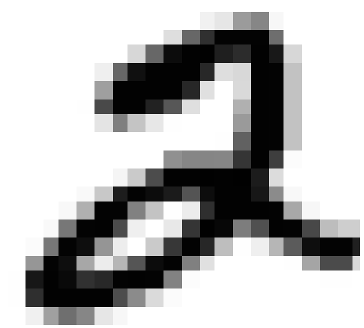
Setting up the problem

Input Space (X):
Array of pixels



$$f\left(\cdot,\theta\right)$$

Output Space (Y):

Class	Desired Value
“1”	0
“2”	1
“3”	0
“4”	0
…	0

$$Y \approx f\left(X,\theta\right)$$

Setting up the problem

Input Space (X):
Array of voxels

$$f\left(\cdot,\theta\right)$$

Output Space (Y):

Class	Desired Value
"DAN"	0
"VAN"	0
"SMN"	1
"VIS"	0
…	0

$$Y \approx f\left(X,\theta\right)$$

Training Data

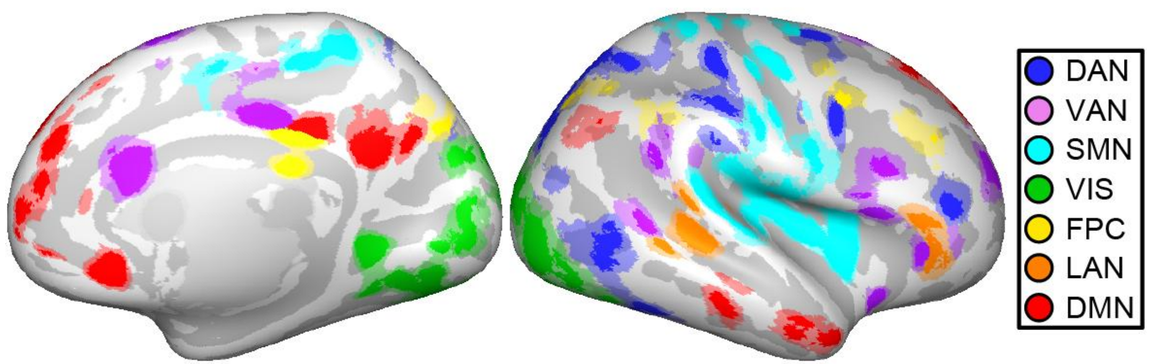
- Must represent the final data to be classified
- Goal: classify the RSN identity of every brain locus based on its correlation map
- Training data should consist of correlation maps generated from a representative sample of seed locations, each belonging to a known class (or RSN)

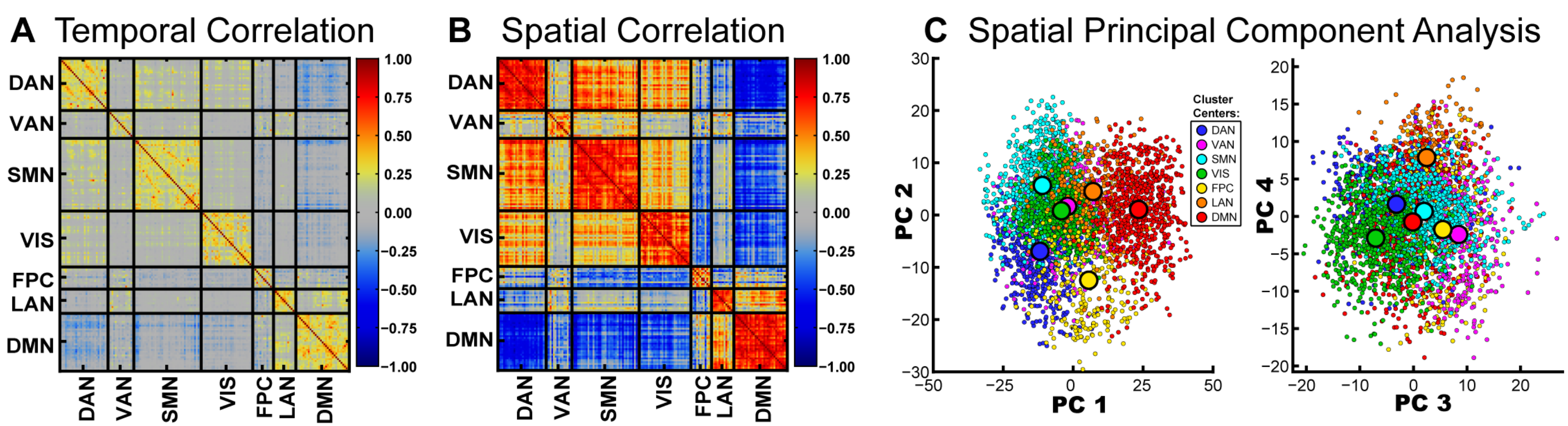
Design considerations ❗

- 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

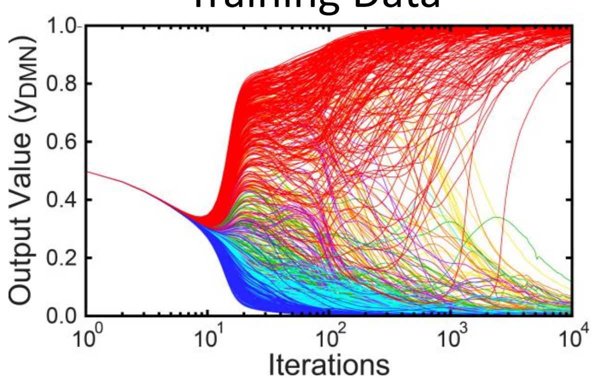
$$f\left(\cdot,\theta\right)$$

Output Space (Y):

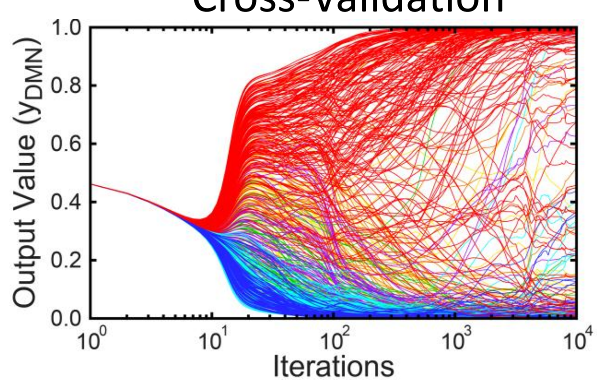
Class	Output	Desired Value
"DAN"	0.12	0
"VAN"	0.24	0
"SMN"	0.75	1
"VIS"	0.21	0
…	…	0

Error Signal

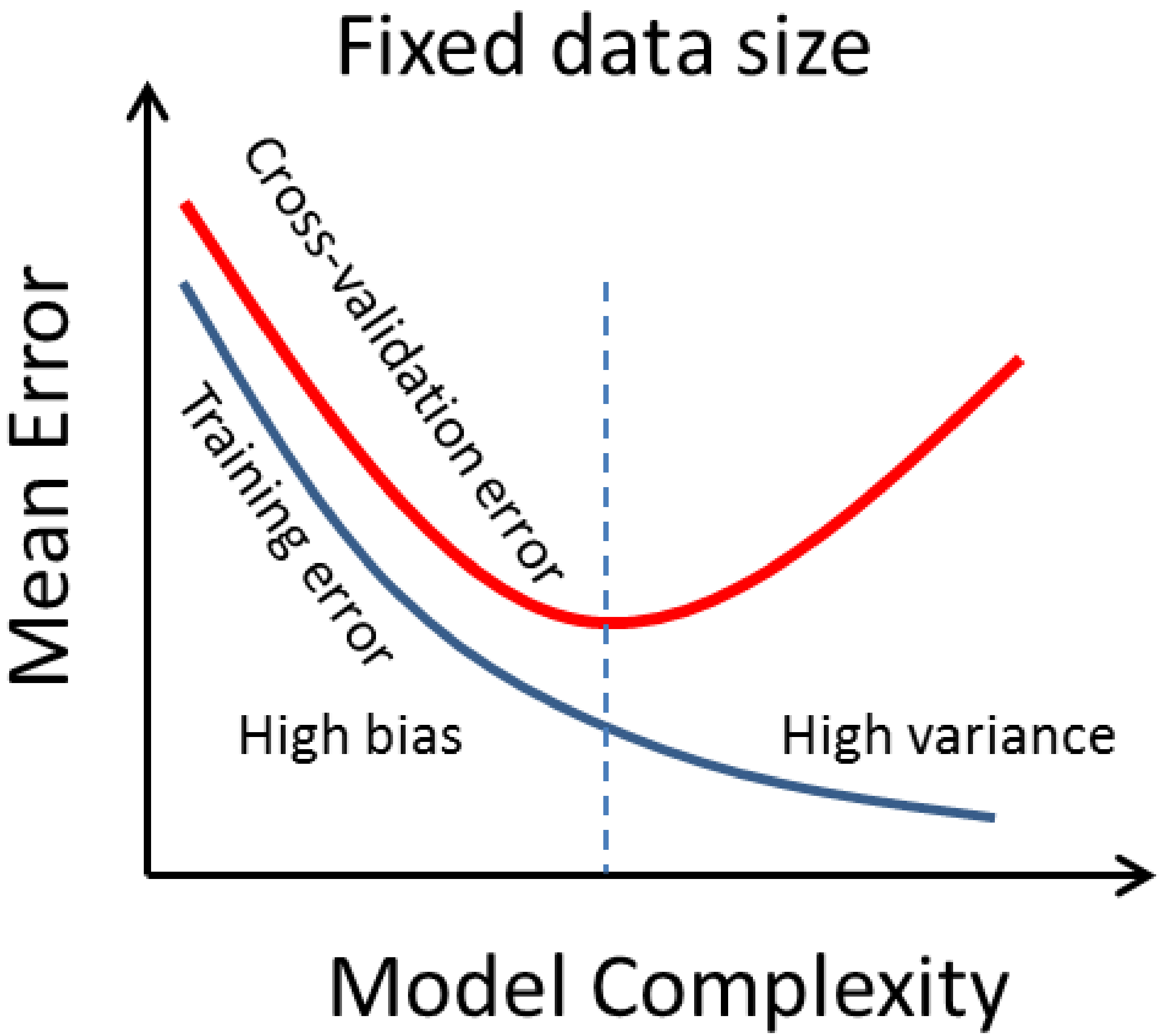
Training Data



Cross-Validation

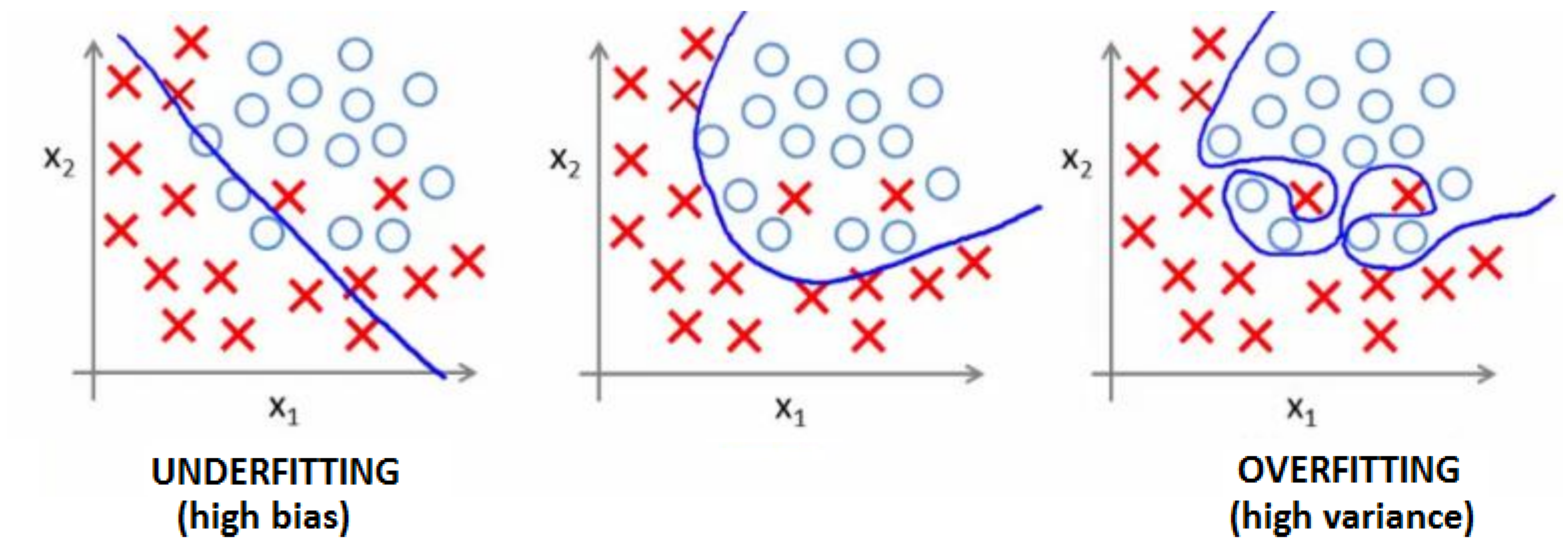


Bias-Variance Trade-off



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

Overfitting/Underfitting



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

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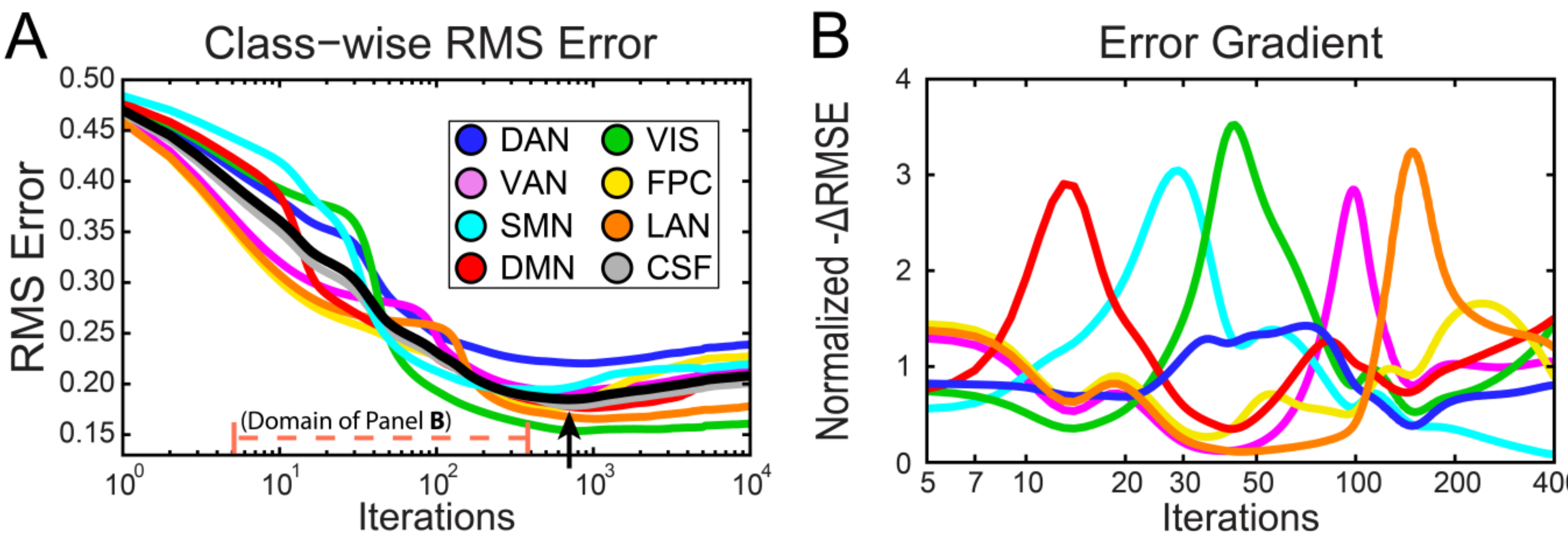
Evaluating Performance

Scalar RSN Estimates (Regression)

- Computed as root mean square difference between estimates and desired values:

$$E = \left\| f(X, \boldsymbol{\theta}) - Y \right\|$$

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



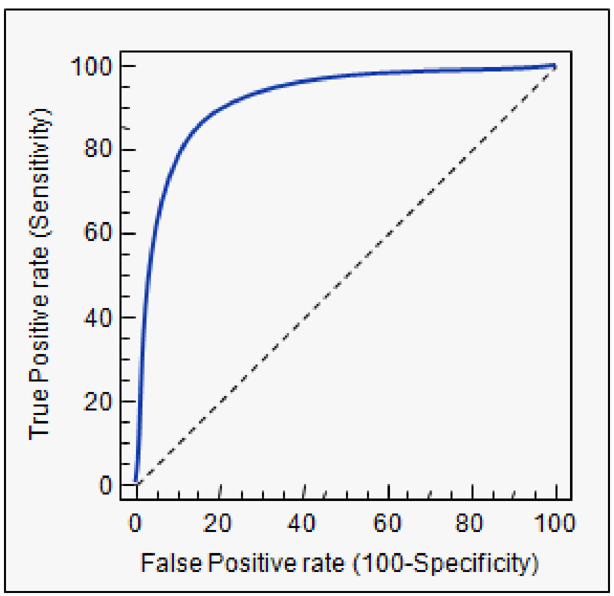
Hacker et al., NeuroImage (2013)

Evaluating Performance

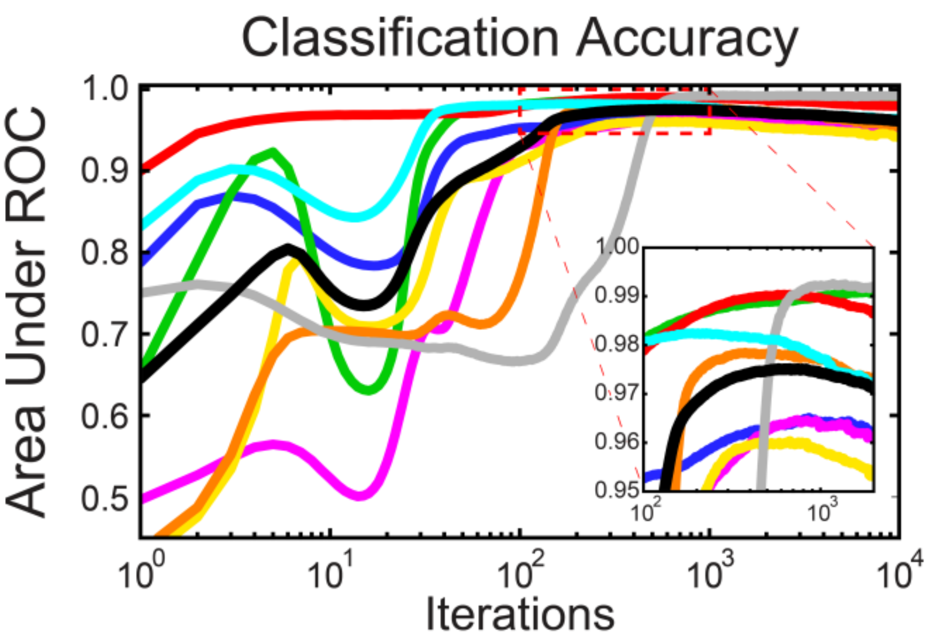
Categorical RSN Estimates (Classification)

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

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



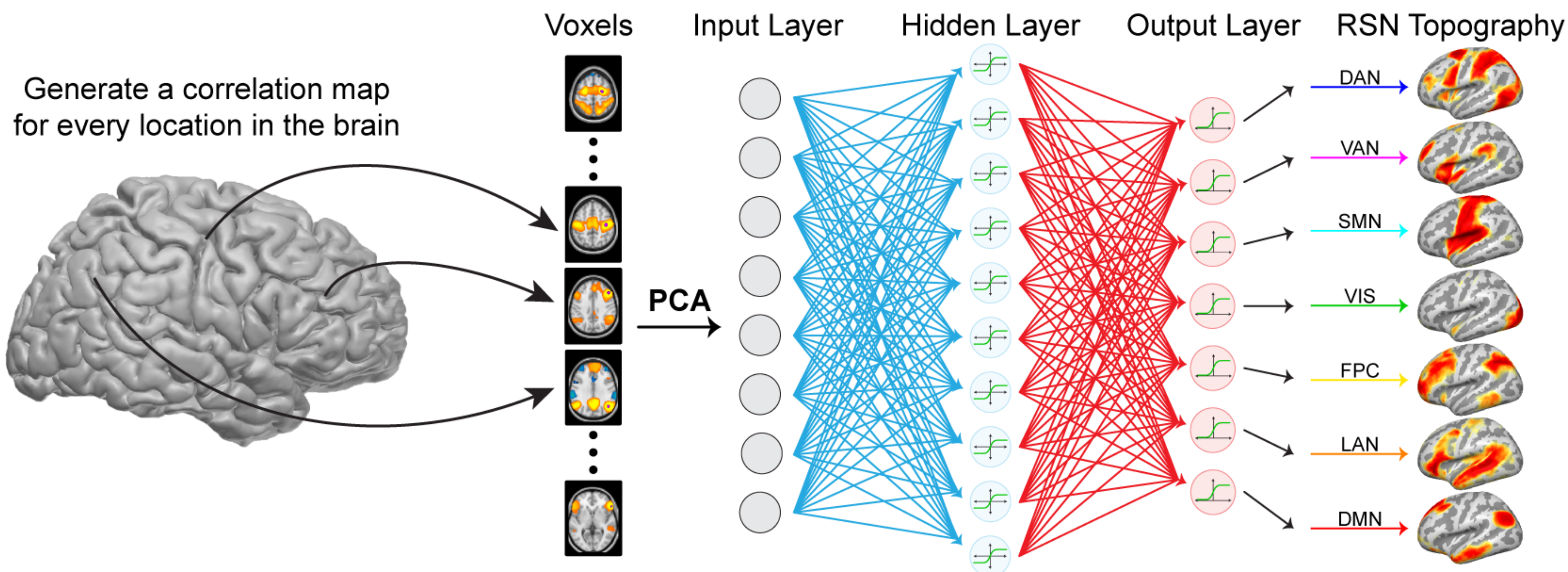
http://www.medcalc.org/manual



Hacker et al., NeuroImage (2013)

RSN Classification Technique

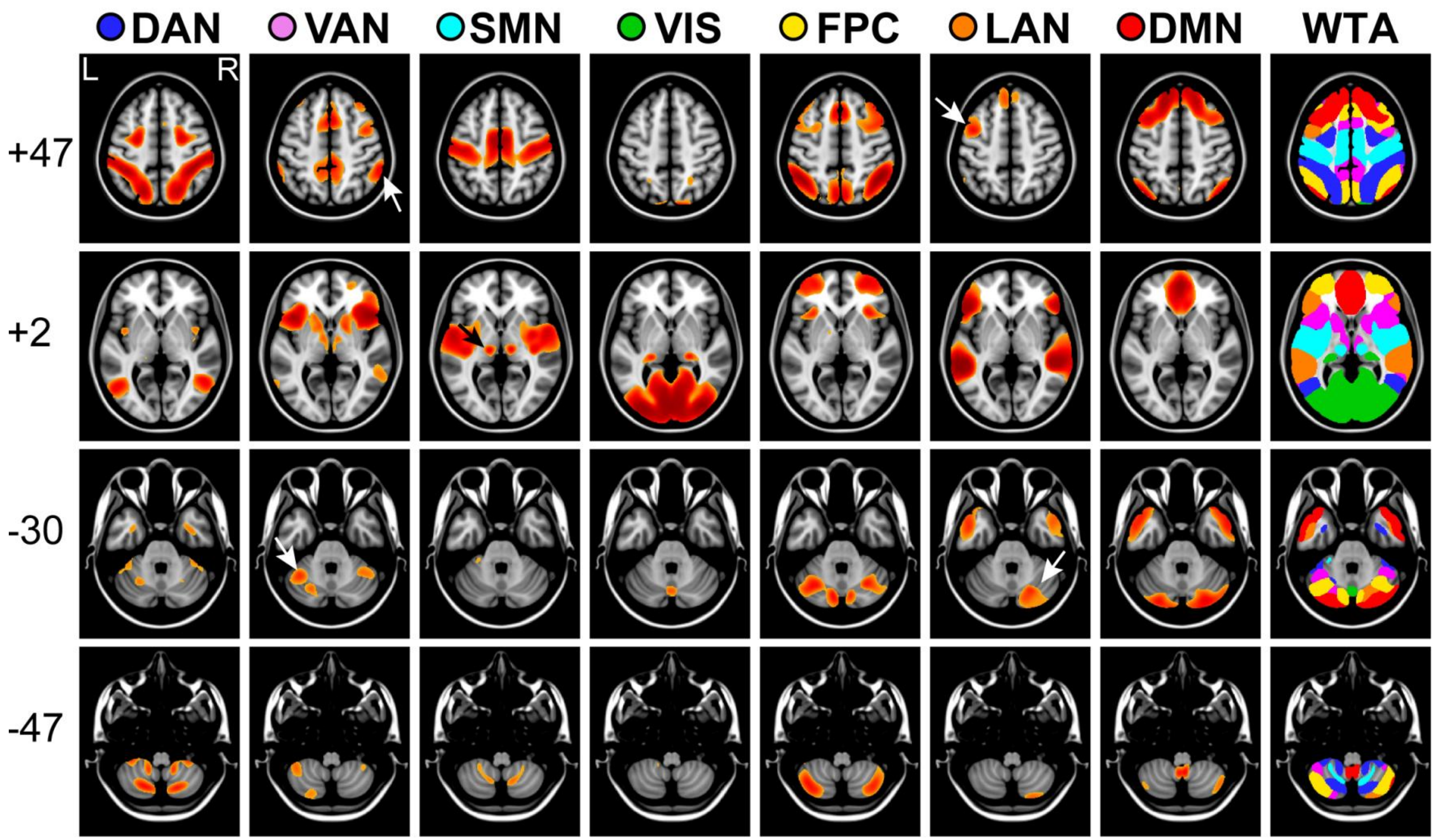
- Assign each point in the brain to a known functional system based on its correlation map



Hacker et al., NeuroImage (2013)

Generalizability to Untrained Brain Regions

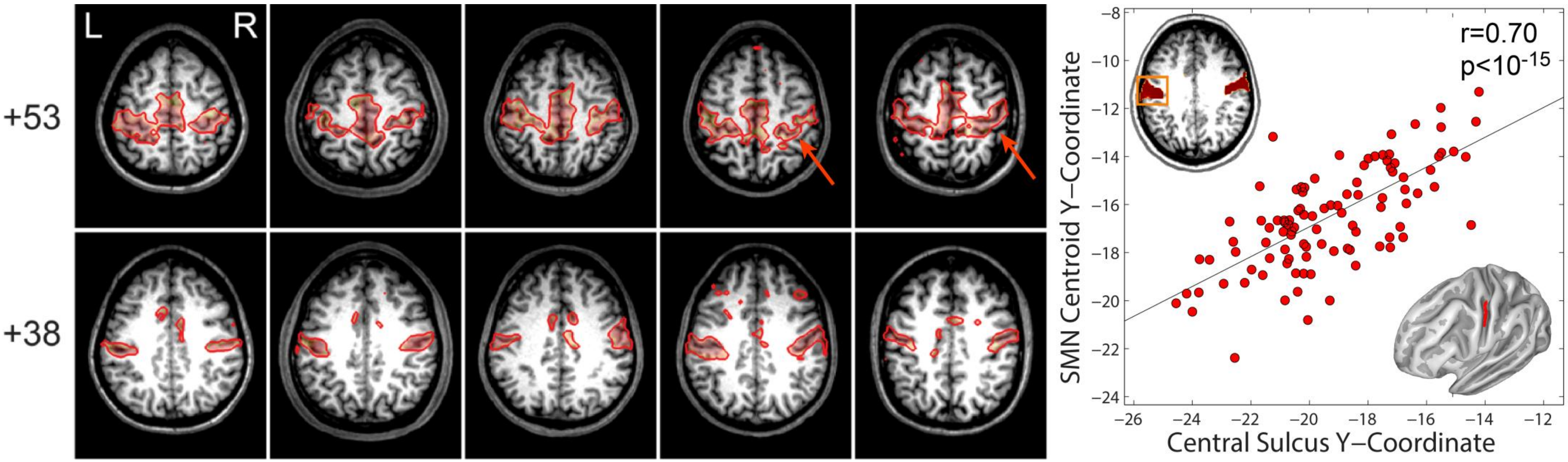
- Correct extrapolation to regions not in the training data (cerebellum, thalamus in this example) indicates learning of an underlying function



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

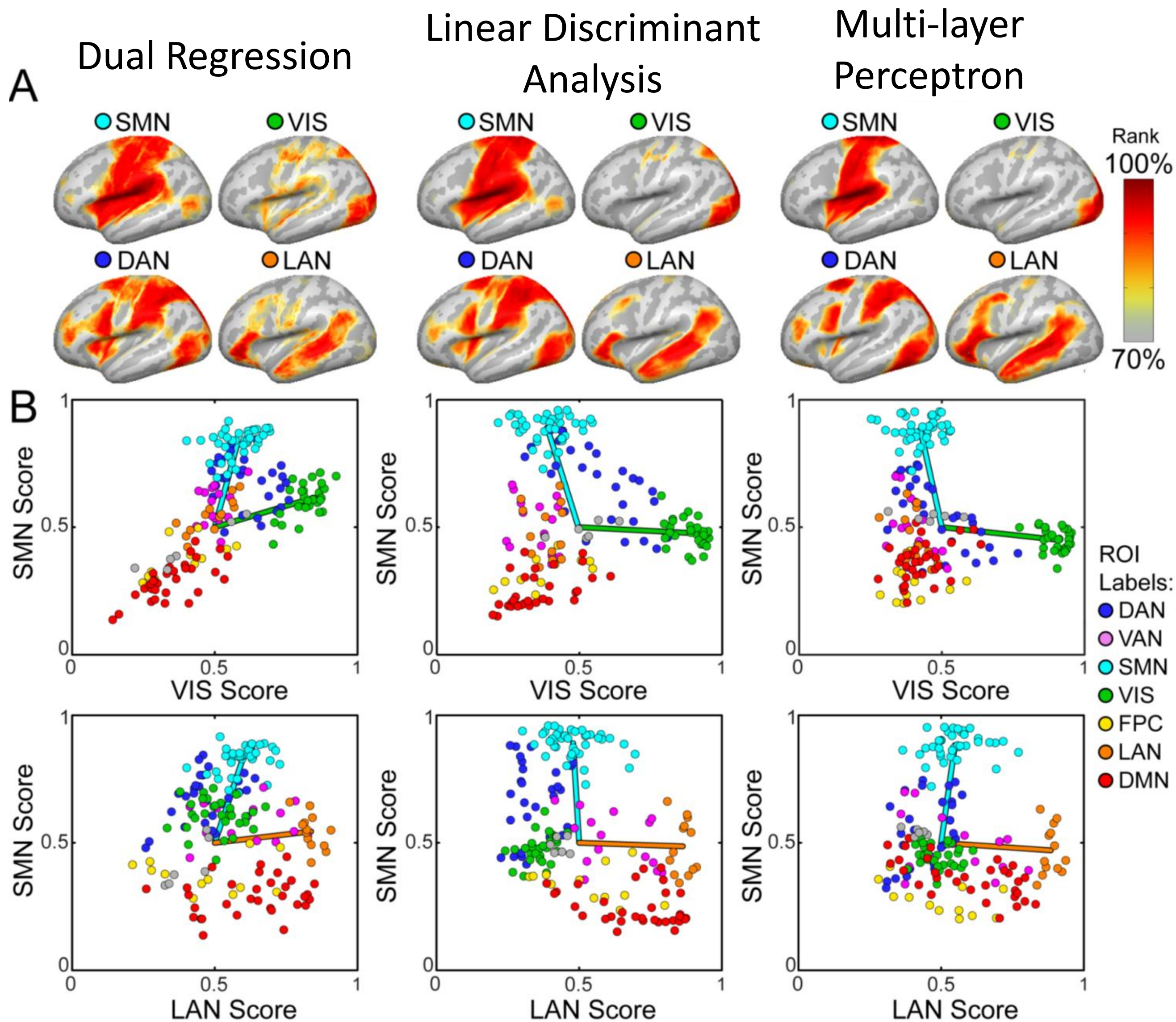


Hacker et al., NeuroImage (2013)

Comparison to Linear Methods

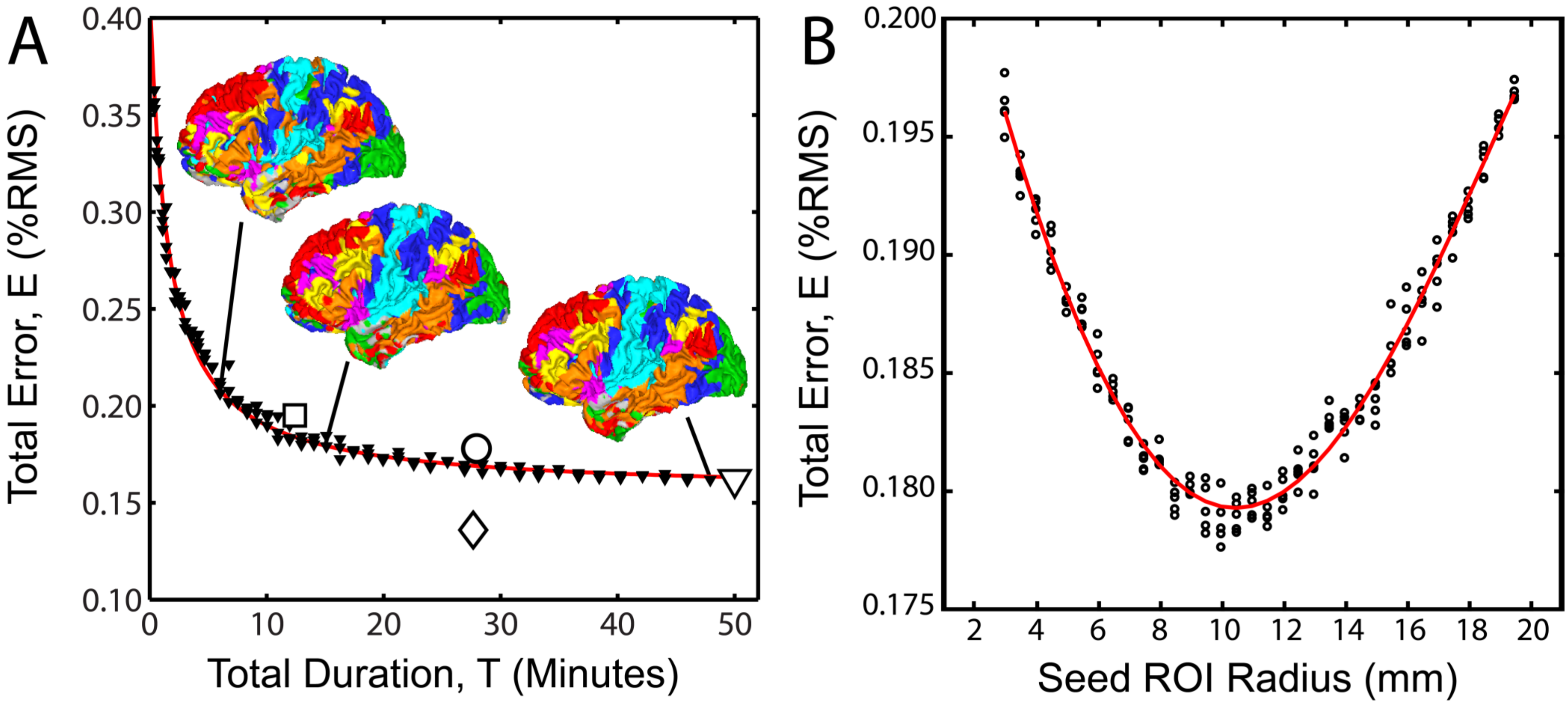
- Dual Regression
  - For a group-level maps, find associated timecourses in an individual
  - Correlate timecourse with each voxel to recover component in the individual
- Linear Discriminant Analysis
  - Project data onto vectors that maximize separation of class means (between vs. within class scatter)

Algorithm Comparison



Hacker et al., NeuroImage (2013)

Methodological Optimization



Hacker et al., NeuroImage (2013)

Acknowledgements

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