Paper Review: Resting State Network Estimation in Individual Subjects

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Personal Project Summary

- Problem: Correct hierarchical labeling of resting state functional MRI (rsfMRI) scan components provides valuable pre-operative and diagnostic information, however very few neuro-radiologists are capable of such labeling
- **Goal**: Automate labeling of hierarchical network topology features in healthy patients and those with brain lesions
- Method: Convolutional deep belief network training on group ICA components extracted from rsfMRI scans of healthy and unhealthy patients

Selection Motivation

- Seeks to solve the same fundamental problem as I do
 - To computationally label rsfMRI network components
- First and only successful paper at resting state specific fMRI component labeling
- Accounts for hierarchical relationship of resting state networks

Background

- Published in 2013 in the Journal of Neuroimage
- Paved the way for future endeavors in computational applications of rsfMRI data science

Summary

- Objective: to reliably classify rsfMRI scans of healthy individuals into seven pre-selected brain networks
- General workflow
 - 1. rsfMRI pre-processing and signal normalization
 - 2. Voxel-wise correlation map generation
 - 3. Principal component analysis
 - 4. Multi-layer perceptron feedforward eigenvector training



Figure 1: Hacker et al. Primary voxel-wise network architecture and data flow.

Significance

- First rsfMRI automated classification work
- High validation accuracies across individual and group studies indicate potential for clinical grade application



Figure 2: Hacker et al. Pre-selected brain network components pertaining to existing partial hierarchical topology.

- PCA pre-processing techniques gave rise to rsfMRI component-based separation
- Addresses need for hierarchical topology incorporation

Technical Methods: Data Acquisition

- Training, optimization, individual validation:
 - 48 young and healthy adults
 - Washington University School of Medicine's Neuroimaging Laboratories
 - 3T Allegra MRI scanner
- Group validation/testing:
 - 692 young and healthy adults
 - Harvard-MGH Brain Genomics Superstruct
 Project
 - Tim Trio MRI scanner

Dataset	Training	Optimization	Validation 1	Validation 2 [§]
Number of Subjects	21 (7M + 14 F)	17 (8M + 9F)	10 (4M + 6F)	692 (305M + 387F)
Age in years	27.6 (23–35)	23.1 (18–27)	$23.3\pm3~(\mathrm{SD})$	21.4 ± 2.4 (SD)
Scanner	Allegra	Allegra	Allegra	Tim Trio
Acquisition voxel size	(4 mm) ³	(4 mm) ³	(4 mm) ³	(3 mm) ³
Flip angle	90°	90°	90°	85°
Repetition Time (sec)	2.16	2.16	3.03*	3.00
Number of frames	128×6 runs	194 × 4 runs	110×9 runs	124×2 runs
Citation	(Lee et al., 2012)	(Fox and Raichle, 2007)	(Fox et al., 2005)	(Yeo et al., 2011)

Figure 3: Hacker et al. Dataset selection and parameters.

Technical Methods: Neuroimaging Preprocessing

Normalization

- Compensation for slice-dependent time shifts
- Elimination of systematic odd-even slice intensity differences due to interleaved acquisition
- Rigid body correction of head movement within and across runs
- Visualization
 - Cortical reconstruction and volume segmentation
 - Projection of component heatmaps (BOLD signals) onto grey matter

Technical Methods: Network

- 2,500 component PCA run on normalized rsfMRI scans
 - Determined by hyperparameter optimization
- Each PCA component corresponds to independent input node (perceptron) followed by 22 layer deep network
- 8 node output for multi-label classification:
 - 7 nodes correspond to preselected hierarchical network components
 - 1 node reserved for noise

Technical Methods: Testing

- Individual variability studied through validation 1 dataset (within NIL)
 - Enables for network architecture restructuring based on identified neurological cofounders
- Testing conducted at group level on separate Harvard dataset
- Standard preprocessing and PCA input applied for both testing and training

Results

- Individual validation
 - Mean accuracy: 98.8%
 - RMS error: 16.2%
- Group testing
 - Mean accuracy: 97.7%
 - RMS error: 19.5%

	Validation 1 (N=10)		Validation 2 (N=692)	
Network	Accuracy (AUC)	Error (RMS)	Accuracy (AUC)	Error (RMS)
DAN	0.973	21.1%	0.966	23.1%
VAN	0.979	17.7%	0.962	21.0%
SMN	0.994	17.5%	0.983	23.4%
VIS	0.998	12.5%	0.993	16.5%
FPC	0.989	14.8%	0.971	17.7%
LAN	0.991	14.5%	0.979	17.7%
DMN	0.991	17.5%	0.986	20.3%
Mean	0.988	16.2%	0.977	19.5%

Figure 4: Hacker et al. Reported validation accuracies.

Places for Improvement: Partial Hierarchy

- Fails to provide a viable automated solution to full hierarchical structure recognition
 - Preselected network components with known partial hierarchical topology
- Lacks automation
- Does not incorporate topological relations into classification

Places for Improvement: PCA

- PCA is incapable of differentiating independent temporal signals by which resting state components define themselves
- Number of PCA components chosen manually
 - Not necessarily standard for each network component

Places for Improvement: Regularization

- Only regularization strategy noted in the paper is early stopping
 - Requires many validation iterations
 - Low repeatability
- Network dropout preferred
 - Mitigates unforeseen vanishing/exploding gradient issues
 - High repeatability

Places for Improvement: Data Selection

- Only trains from scans within one hospital (with one scanner)
 - Inability to generalize for other hospitals and scanners
 - Each hospital has inherent bias in patient population it selects from
- Only trains and tests on healthy patients
 - Not clinically useful

Highlights: Novelty

- Easy to critique with hindsight
- Groundbreaking for rsfMRI classification at the time
- Insightful network choices and hyperparameter tuning
- Successfully identifies confounding neurological variables and achieved high validation accuracy

Highlights: Algebraic Justification

- Identifies pitfalls of linear projection in group study and chooses PCA instead
- Identifies high projected error in dual regression
- Notes that only 20 significant components could be determined with linear discriminant analysis while more than 100 resting state networks exist, thus PCA is better with 2,500

Highlights: Neurological Confounders

- Successfully recognizes the neurological confounding variables of the 7 pre-selected brain components
 - Applications pointed hyper-parameter and network tuning
- Pearson correlation testing used to indicate strength of each selected brain network component's classification contribution

Personal Takeaways

- Learned standard methodologies for rsfMRI preprocessing which I can apply in my own data processing scripts
- An improved understanding of network topologies, and the pitfalls of brain network correlations to be aware of
- Learned new methods of individual validation testing rather than exclusively group testing
- A holistic understanding of how rsfMRI volumes interact with deep networks