Research on Brain Networks at ICSI

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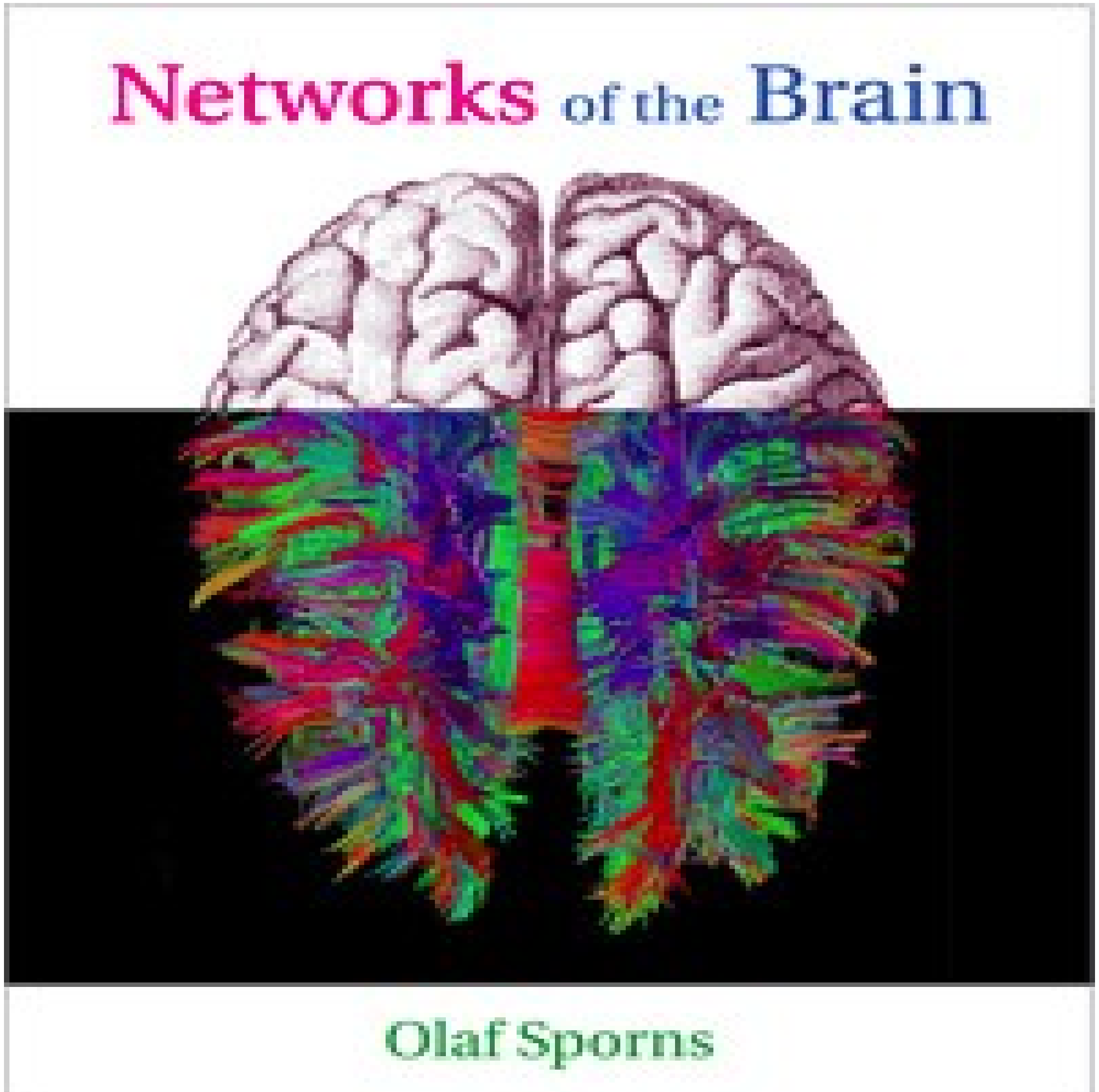
- Note: some slides have been redacted that were in the talk as they come from work that is under review.

Overview

- A top down approach (with some background)
  - Pretty Pictures
  - Main objectives, results and roadblocks
  - Constructing brain networks
  - Analyzing brain networks
  - Applications
  - Improving analysis for brain networks

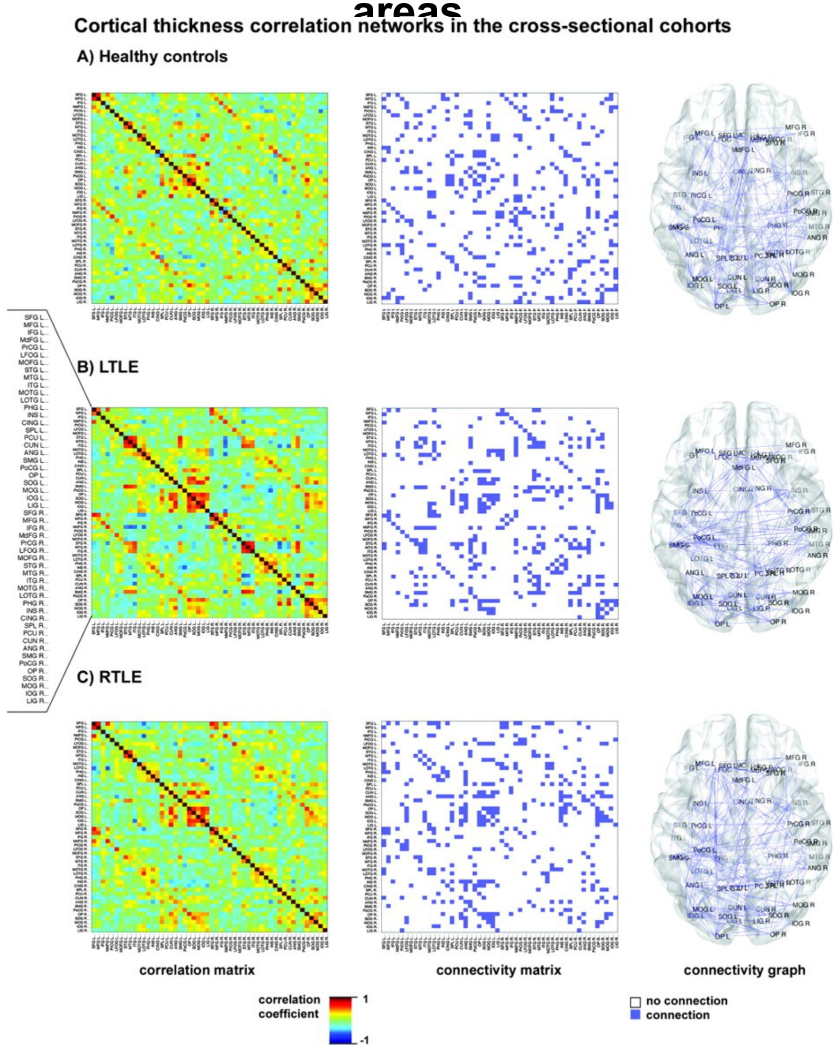
Pretty Pictures 1: Tractography (dMRI)

DMRI
(and nice introduction to this area)



Less Pretty Pictures 3: Matrix representation of cortical thickness networks

Cortical thickness correlation networks in (A) healthy controls, (B) LTLE, and (C) RTLE. The left column displays the cortical thickness correlation matrices of 52 anatomical areas



Bernhardt B C et al. Cereb. Cortex 2011;cercor.bhq291

Main Objectives

- Understand and aid in the diagnosis of brain disorders.
- Typical situation: (note sizes)
  - 30-400 patients with a disorder
  - 30-400 controls
  - Collaborators process MRI images and send us networks (or almost networks)
    - They do the supercomputing!
    - Typically about 100 nodes, experimenting with 10000 nodes.
  - We analyze the networks and try to find (statistically) significant differences between the groups

Main Results

- Understand and aid in the diagnosis of brain disorders.
  - Provide insight into the disorder
    - AZ patients have less “organized” brains (lower modularity)
    - AgCC patients have more variance in their connectivity
  - Aid in diagnosis
    - Using standard network measures we can predict conversion from MCI to AZ with ~60% confidence.
      - Not perfect, but its a start.

State of MRI

MR imaging is **not typically helpful for diagnosis, outcome prediction or treatment monitoring** of many common neurodevelopmental, psychiatric and neurodegenerative disorders. Prominent examples include autism, schizophrenia, bipolar disorder, major depression, Parkinson's disease, and Alzheimer's disease. Collectively, they have much greater prevalence than those neurological diseases for which MR imaging is routinely useful, and the incidence of disorders such as autism and Alzheimer's disease continues to rise (Owen et. al. 2012)

State of MRI

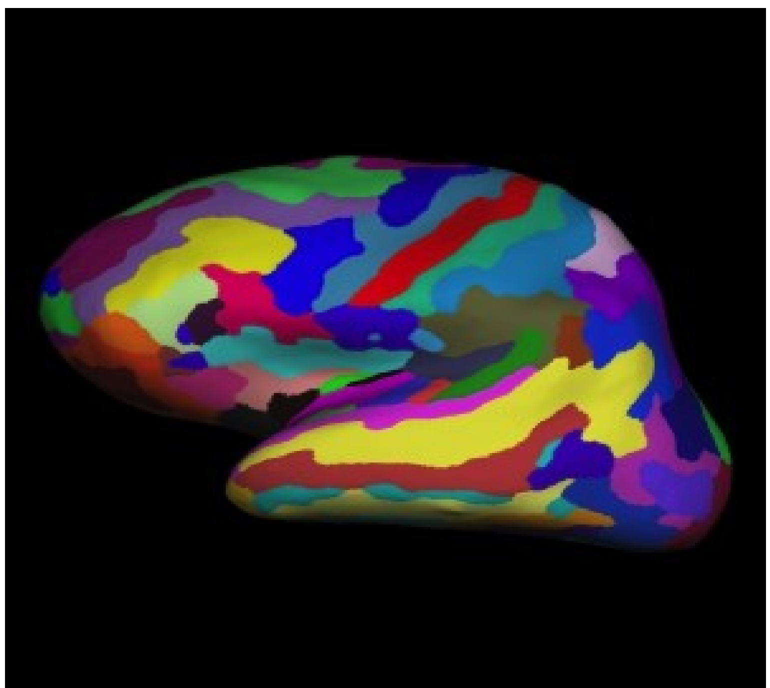
The pathophysiology of many neurodevelopmental, psychiatric and neurodegenerative diseases is **thought to be diffuse**, unlike that of more focal disorders such as stroke and brain tumors for which MR imaging has proven clinical utility. Therefore, advances in diagnosis and prognosis depend on a better understanding of the brain at a systems level. (Owen et. al. 2012)

Main Roadblocks

- Small numbers of data points – ~100
- Large numbers of attributes
  - ~100x100 = 10^4 elements in a matrix
- Need to choose a small, but powerful, set of features.
- Current: use standard network measures:
  - Diameter, clustering, modularity, centrality, etc
- Goal: find better ones.

Constructing Brain Networks

- 1) Parcellate
  - Current: use classical functional regions
  - Ideas: is geometric better?



Destrieux Atlas

From freesurfer

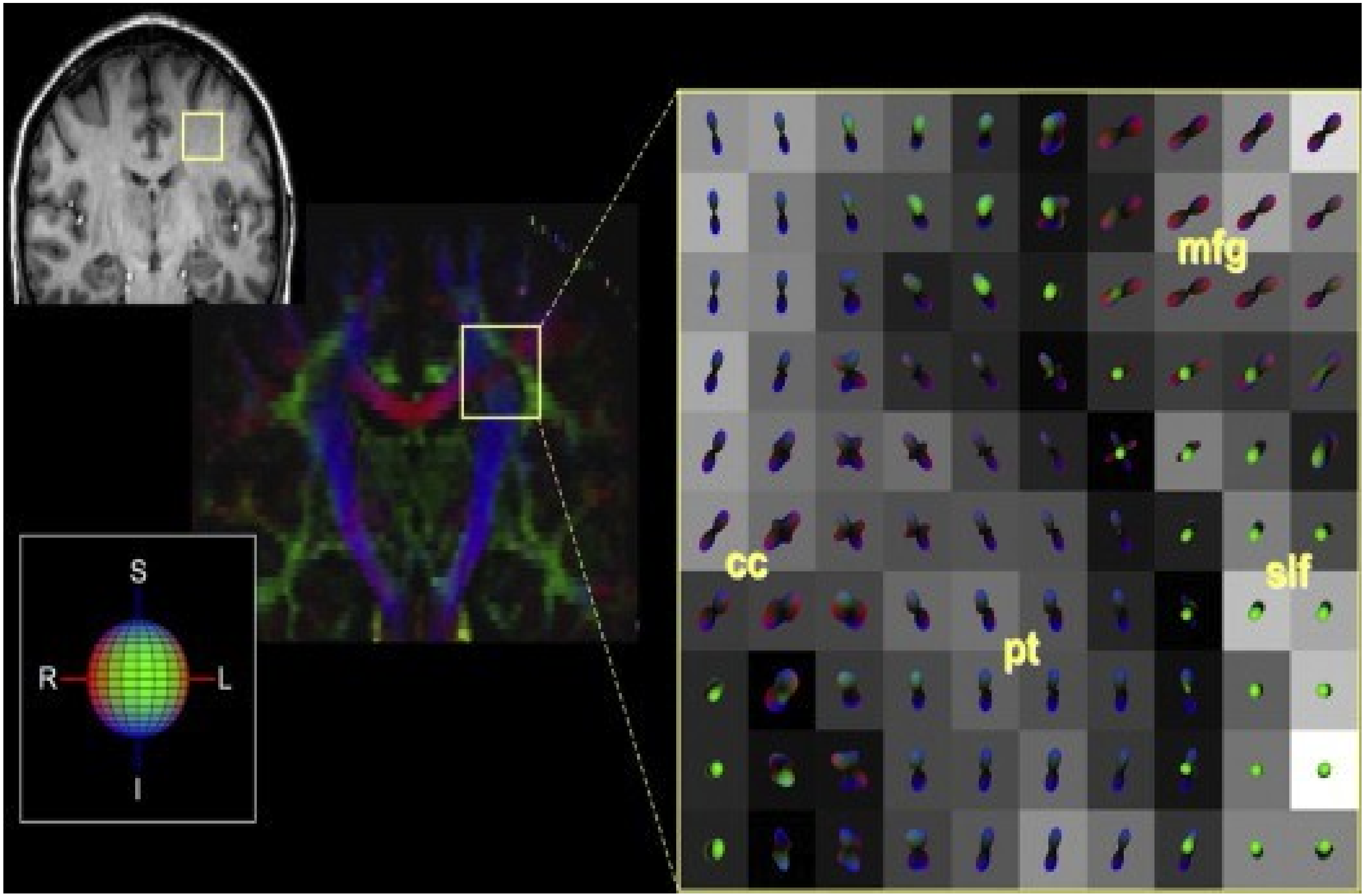
Constructing Brain Networks

- 2) Determine connections
  - From most natural to least
  - But, not necessarily most useful
  -
  - NOISE, NOISE, NOISE
    - Nature is a bit messier than engineered systems...

Constructing Brain Networks

- Structural: dMRI and tractography
  - Use dMRI to construct vector (and sometimes tensor) fields from axons.
    - Try to jiggle water molecules to find axons
  - Use randomized tractography algorithms (like DE solvers) to find the paths which connect regions of the brain.

DMRI tractography



Constructing Brain Networks

- Functional: fMRI and correlations
  - Use fMRI and compute correlations between brain regions
    - fMRI is the modern workhorse of cognitive psychology
  - Threshold the correlations to get a network
  - Use the weights in the analysis (weighted network)
    - Problems: destroys sparsity, hard to interpret, what is the scaling, doesn't always improve results.

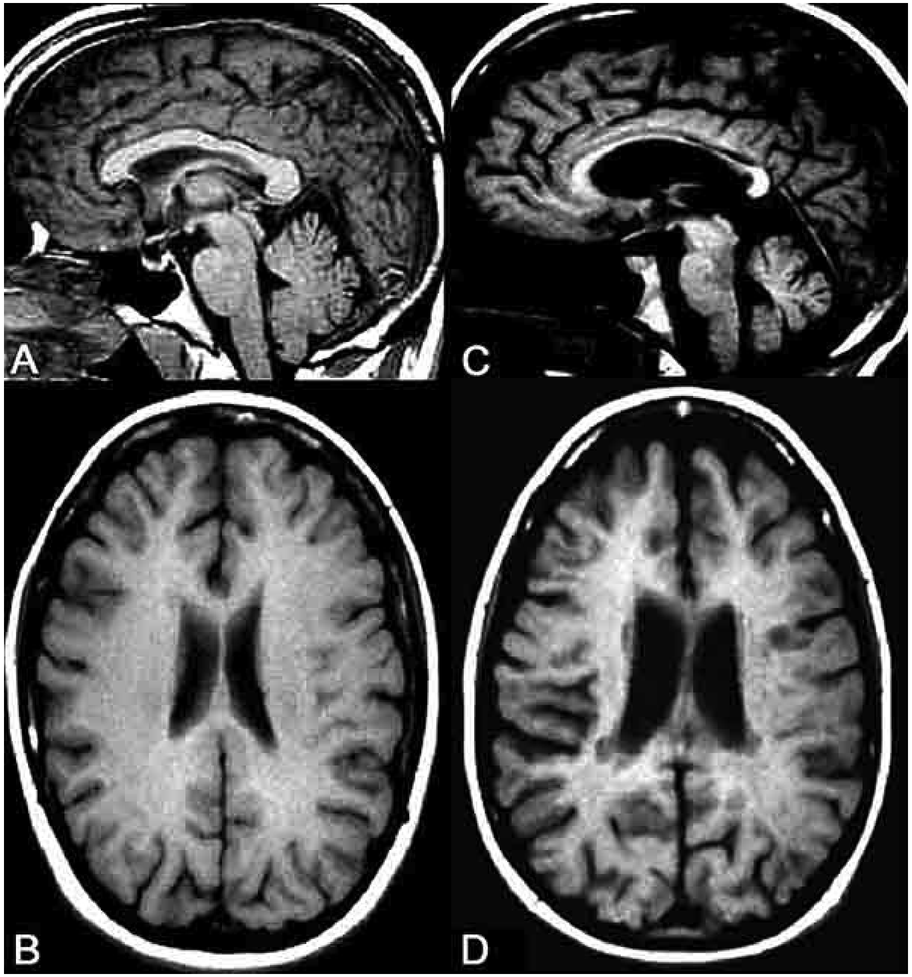
Standard fMRI Pretty Picture

A very happy brain!

Constructing Brain Networks

- Cortical Thickness: MRI and correlations
  - Use MRI to compute thickness of brain regions
    - AZ and MS patients show thinning of the cortex
  - Correlate the thickness, or rate of thinning, between regions over cohorts or over time.
  - Threshold (or not) to create network
  -
  - Much less expensive than PET scans

Cortical Thinning in MS Patient



Normal vs MS

Analyzing Brain Networks

- Recall: 10000 attributes for 100 samples
  - Brute force datamining is hopeless
- Idea: use network “measures” that people study and are “interpretable.

Network Measures

- Degree distribution – often heavy tailed
  - Gini indices.
- Diameter – largest (hop) distance between a pair of nodes.
- Clustering Coefficient – pick a node and two neighbors at random then compute the probability that the two neighbors are connected. (Are my friends friendly with each other?)
- Modularity – does the network decompose nicely into a network of subnetworks
- Centrality (or pagerank) – find “important” nodes and their statistics.

Whole Network Metrics

(average and std. *across subjects*, with thresh=500 for AgCC)

Small Worldness

- Short paths and high clustering.
- Smallworldness: clustering coefficient divided by average path length.
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- Claims: small worldness (and heavy tails in degree distribution) lead to effective computation.
  - Is it true? Does it matter?

Improvements

- Much of modern network theory was developed to study the Internet, WWW, social networks and biological networks.
  - Usually one instantiation of a very large somewhat noisy network.
- Brain nets, have many instantiations of a small very noisy network.
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- We need to “personalize” the approach.

Null Networks

- Key idea: fixed degree distributions
  - Erdos-Renyi random networks have Poisson degree distribution, while real world graphs often don't.
- Used as reference – null hypothesis
- Also used for designing meausures
  - Girvan-Newman modularity looks at the “surprising” edges.

Brain Network Imaging Analysis and Computation Lab (BNIAC) Goals

- Automate brain network analysis
  - Currently people use matlab by hand
  - Develop stable and scalable algorithms
    - Many measures are $O(n^4)$ or exponential.
- Improve brain network analysis.
  - Improve null models
  - Understand measures and their inter-correlations
  - Develop new measures
- Assist the medical researchers.

Students hosted by ICSI

- UCB Computer Science (*current)
  - Current: *Scott Wilson, *Danial Muhhammad
  - Summer 2012: Inderjit Jutla, Michael Liang, Jason Liang, Graham Tremper.
  - 2011-12: Wenson Hsieh, Moeka Tanagi.

External Collaborators

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