Structural Brain Network Modeling with DTI

Moo K. Chung
Waisman Laboratory for Brain Imaging and Behavior
Department of Biostatistics and Medical Informatics
University of Wisconsin-Madison

www.stat.wisc.edu/~mchung
Waisman Laboratory for Brain Imaging and Behavior, Madison
http://brainimaging.waisman.wisc.edu
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Jamie Hanson, Nagesh Adluru, Andrew L. Alexander, Seth Pollack, Richard J. Davidson
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Janet E. Lainhart
University of Utah, Salt Lake City
Abstract

Diffusion tensor imaging offers a unique opportunity to characterize the trajectories of white matter fiber bundles noninvasively in the brain. Whole brain tractography studies routinely generate up to half million tracts per brain. The tracts serve as edges in an extremely large 3D graph with up to 1 million nodes. Currently there is no agreed-upon method for constructing the brain structural network graphs out of large number of fiber tracts. In this talk, we present a novel scalable iterative framework called the epsilon-neighbor construction, which automatically identify nodes and establish edges. Computational issues and methods are illustrated with various case studies. The lecture material will be available through

http://brainimaging.waisman.wisc.edu/~chung/DTI/
Diffusion tensor imaging
NIH Launches the Human Connectome Project to Unravel the Brain’s Connections

The National Institutes of Health Blueprint for Neuroscience Research is launching a $30 million project that will use cutting-edge brain imaging technologies to map the circuitry of the healthy adult human brain. By systematically collecting brain imaging data from hundreds of subjects, the Human Connectome Project (HCP) will yield insight into how brain connections underlie brain function, and will open up new lines of inquiry for human neuroscience.

www.humanconnectomeproject.org
In 2005, Dr. Olaf Sporns at Indiana University and Dr. Patric Hagmann at Lausanne University Hospital independently and simultaneously suggested the term "connectome" to refer to a *map of the neural connections within the brain.*
functional (fMRI) connectivity study on face fixation in autism
What is wrong with traditional functional connectivity studies?

Where is the physical evidence of connection?
---Lack of underlying biological mechanism

What do we really need?
---Anatomical basis of connections
But can we trust functional connectivity studies?

Earth | 2.5 million light years apart | Andromeda

High correlation

Are they physically connected?
Spooky action at a distance
EPR (Einstein-Podolsky-Rosen paradox)
Backwardness of human neuroanatomy

Francis Crick and Edward Jones

To interpret the activity of living human brains, their neuroanatomy must be known in detail. New techniques to do this are urgently needed, since most of the methods now used on monkeys cannot be used on humans.

Over the past 20 years there have been great advances in understanding the neuroanatomy of the macaque monkey, especially its cerebral cortex. We have learned much about the functional parcellation of the monkey’s cortex from both anatomical and physiological studies. We know, for example, that rather than the MRI scans used, although of high resolution, are static; they show structure but not activity. Such a scan can picture, for example, exactly how the cerebral cortex is folded in a particular individual but not what part is functionally active. The spatial resolution of classical MRI is now 1 mm or less so that what does the human equivalent of the connectional map of Fig. 2 look like? The shameful answer is that we do not have such detailed maps because, for obvious reasons, most of the experimental methods used on the macaque brain cannot be used on humans.

What we can say about the neuroanatomy of the human brain?
Another new method that at last permits the tracing of connections in fixed postmortem material is the use of lipid stains such as the carbocyanine dye dil$^{10}$ or one of its relatives. This spreads along axons by a diffusion process so that, in general, it is a slow method: to go 10 times as far takes 100 times as long. It could take many months to spread through the full extent of a long pathway, so there are time limitations on using it to establish the longer connections. Nevertheless, the method is now...
DTI Preprocessing
Whole Brain Tractography

Postmortem

Tractography is done using the second order Runge-Kutta algorithm with TEND

Reconstructed
0.5 million tracts
CAMINO tractography based on TEND algorithm
Is the tractography done properly?

Histogram on tract length

Noise

Noise
Sorted tract length

Noise

Noise
Longest tract is an outlier

Need a tract shape based filtering method possibly using the cosine representation.
Longest five tracts
Longest 20 tracts
DTI alignment is done using DTI-TK package

Red = subject 1
Blue = subject 2
CAMINO fiber tractography

Only showing about 3000 tracts out of 90000 here
White Matter Fiber Tracts

Diffusion tensor imaging (DTI)

3D graph model

Second order Runge-Kutta streamline algorithm

Cosine series representation
ROI-based Connectivity
Standard DTI network construction pipeline

1: do whole-brain tractography
2: for Subject = 1, 2, 3 do
3: for N = 82(AAL), 100, 500, 1000, 2000, 3000, 4000 do
4: for 100 random parcellations do
5: 1. Generate N-node parcellation
6: 2. Populate N x N connectivity matrix
7: 3. Threshold and binarize
8: 4. Compute network metrics
9: end for
10: end for
11: end for

Zalesky et al. NeuroImage 2010
Two problems with the standard method

Parcellation
70-100 regions

Arbitrary thresholding
What is wrong with the standard network construction?

Arbitrary parcellation (node) + thresholding (links) → drastic change in graph measures
Threshold Free Network Construction
Graph filtration: threshold-free method

The method has been presented in the following medical imaging conferences:

- Oral presentation in MICCAI 2011 (top 34 out of 819 papers = 4%)
- Oral presentation in OHBM Connectivity session in 2011 (< 1%)
- Oral presentation in OHBM Connectivity session in 2012 (< 1%)
What is wrong with arbitrary thresholding?

Edge weight $\rho_{ij}$ between node $i$ and $j$ → Connectivity matrix $\rho = (\rho_{ij})$

Threshold at 0.5

Threshold at 0.7
Decomposition of weighted graph
Network & graph filtration

Scale

Need scale invariant persistent topological features
Parcellation Free Network Construction
Scalable Brain Network Construction on White Matter Fibers

Moo K. Chung¹,³,⁶*, Nagesh Adluru³, Kim M. Dalton³,
Andrew L. Alexander²,³,⁵, Richard J. Davidson³,⁴,⁵

¹Department of Biostatistics and Medical Informatics, ²Department of Medical Physics,
³Waisman Laboratory for Brain Imaging and Behavior
⁴Department of Psychology, ⁵Department of Psychiatry, University of Wisconsin, Madison
⁶Department of Brain and Cognitive Sciences, Seoul National University, Korea

Chung et al. 2011 SPIE 7962 79624G-1
The first data-driven DTI network construction framework without any parcellation.

ε-neighbor network construction

All points in the ε-neighbor are identified as a single node in a graph.

Identify end points
Needle representation
Needle collocation problem

Given a collection of \( n \) needles, connect them into a smallest possible disjoint components that minimizes a length-related cost function.

Minimize the collocation cost

6 disjoint needles

2 disjoint components
Algebraic formulation?

Original needles: $G=\{V,E\}$
- $V$: vertex set
- $E$: edge set

Collocated needles: $G_0=\{V_0,E_0\}$

Sparse graph regression:

$$\min_{E_0,V_0} f(E_0) + \lambda N(V_0) = \min_{E_0,V_0} \sum_{(i,j) \in E_0} c_{ij} + \lambda N(V_0)$$
Topological construct: Rips complex?

- Bundle of needles
- Rips complex with $\varepsilon=1$
- Rips complex with $\varepsilon=3$
MATLAB DEMO

Rips complex
ε-neighbor network construction

- Bundle of needles
- Rips complex with $\varepsilon=1$
- ε-neighbor simplification
Tract length:

\[ \rho_1 > \rho_2 > \rho_3 > \rho_4 \]
Iterative epsilon network construction
\( \varepsilon \)-neighbor graphs with different \( \varepsilon \)

Original data

20 mm

10 mm

6 mm
Adjacency matrix
MATLAB DEMO

Epsilon Neighbor method
Application
**Dataset**

*Autistic children (n=17)*

*Control subjects (n=14)*

Matched for age, handedness, IQ and head size

*Abnormal connectivity in autism?*
Connectivity hypothesis in autism

Local overconnectivity
global underconnectivity

Normal controls
Node degree for a single subject

control #001

autism #120
Local inference on degree

Superimposition of every subjects

Control  Autism
pvalues = 0.024, 0.015 and 0.080 for degrees 1, 2 and 3.
Autism

Control
Connected component

largest connected component
Filtration on $\varepsilon$-neighbor graphs

$\varepsilon$-neighbor graph at the $i$-th iteration $G_i$

$G_1 \subset G_2 \subset G_3 \subset \cdots$

The size of the largest connected component:

$\#G_1 < \#G_2 < \#G_3 < \cdots$
Filtration on $\varepsilon$-neighbor networks
Number of edges and nodes in filtration
Network filtration difference

The brain network in control subjects merges to a single component faster than other populations.
In average 96% of all nodes are connected to each other. We believe 100% of all nodes are supposed to be connected. 4% is a processing noise caused by weak connections.
Disconnected components

Control=blue
Autism=red

# of nodes in the largest connected component
control: 644 ± 66
autism: 610 ± 66
pvalue = 0.01
Electronic Circuit Model

Parcellation and thresholding free technique
The purpose of a myelin sheath is to increase the speed at which neuronal impulses propagate along the myelinated fiber.

Myelin increases electrical resistance across cell membrane by a factor of 5000 and decreases capacitance by a factor of 50.
Basic circuit physics: Ohm’s law

Series circuit

\[ R = R_1 + R_2 \]

Parallel circuit

\[ \frac{1}{R} = \frac{1}{R_1} + \frac{1}{R_2} \]
Infinite circuit

Compute the total resistance.
Resistance for parallel tracts

More tracts = less resistance
Electronic circuit construction

Identify end points

$\epsilon$-neighbor:
All points in the $\epsilon$-neighbor are identified as a single node
Four possible scenarios for adding a tract to the graph

\[
\frac{1}{R_{34}} \leftarrow \frac{1}{R_{34}} + \frac{1}{\text{length}}
\]

Parallel circuits
Major tracts without parallel circuits at \( \epsilon = 10 \text{mm} \).

The majority of tracts are parallely wired.
Network constructed without parallel tracts.
Network constructed with all the circuits

Almost a complete graph

Interpretation:
1. Brain is redundantly wired.
2. Any two regions are connected.
Resistance matrix

Subject 1   Subject 2   Group average for 36 controls
Group comparison on 36 NC and 41 autistic (Utah autism data set):

Total resistance is given by summing all entries in the resistance matrix.

Group median:
Normal controls 225 (mm?)
Autism 212 (mm?)
The rank-sum test p=0.07

More resistance = more long range connections
After showing DTI based structural connectivity analysis...

Do we really need DTI?

Not necessarily!
 AGREEMENT BETWEEN THE WHITE MATTER CONNECTIVITY BASED ON THE TENSOR-BASED MORPHOMETRY AND THE VOLUMETRIC WHITE MATTER PARCELLATIONS BASED ON DIFFUSION TENSOR IMAGING

Seung-Goo Kim¹  HyeYoung Lee¹,²,³  Moo K. Chung¹,⁴,⁵,*  Jamie L. Hanson⁵,⁶
Brian B. Avants⁷  James C. Gee⁷  Richard J. Davidson⁵,⁶  Seth D. Pollak³,⁶

¹Department of Brain and Cognitive Sciences, ²Department of Nuclear Medicine,
³Institute of Radiation Medicine, Medical Research Center, Seoul National University, Korea. 
⁴Department of Biostatistics and Medical Informatics,
⁵Waisman Laboratory for Brain Imaging and Behavior,
⁶Department of Psychology, University of Wisconsin, Madison, WI, USA.
⁷Penn Image Computing and Science Laboratory, Department of Radiology, 
University of Pennsylvania, Philadelphia, PA, USA.

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Data Set

32 post-institutionalized (PI) maltreated children
33 normal controls
Tensor-Based Morphometry
Deformable shape model

D’Arcy Thompson 1860-1948

Fig. 179. Skull of chimpanzee.

Fig. 180. Skull of baboon.

On Growth and Form
Deformation vector field on the template

The deformation field match the homologous anatomy across two different images.
How to compute Jacobian determinant

\[ d_1, d_2, d_3 = d(x_1, x_2, x_3) \]

**target position** \( \quad \) **Initial position**

\[ U(x_1, x_2, x_3) = d(x_1, x_2, x_3) - (x_1, x_2, x_3) \]

**Displacement vector**

**Jacobian determinant**

\[ J(x) = \det \frac{\partial d(x)}{\partial x} = \det \left( \frac{\partial d_j}{\partial x_i} \right) \]
Examples. How to compute Jacobian determinant

- **1D:**
  \[ x' = 2x + 1 \]
  \[ J(x) = 2 \]

- **2D:**
  \[ x' = 2x + y + 1 \]
  \[ y' = x + 2y \]
  \[ J(x, y) = 4 - 1 = 3 \]
Connectivity from tensor based morphometry (TBM)

Correlation on Jacobian determinant

Probabilistic map from DTI

McGraw and Nadar, 2007
Jacobian determinant (tissue volume change) with respect to the template
Seed-based (genu) correlation map of Jacobian determinants
T-stat map on correlation map difference (seed= genu)
1856 preselected nodes

Whole brain correlation map of Jacobian determinants

Correlation maps
Graph representation of thresholded correlation
Graph representation of thresholded correlation
Graph representation of thresholded correlation

Interpretation: PI is more homogenous than the controls.
Z-statistic map of group difference (PI- controls)
DTI-based white matter atlas (ICBM-DTI-81)

Total 50 parcellations

S. Mori et al., 2008, NI.
Validation against DTI white matter parcellations

Kim et al. 2012 ISBI

pvalue < 0.001
Thank you