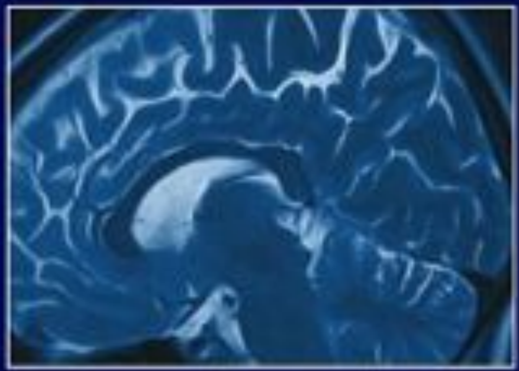

The Waisman Laboratory for Brain Imaging and Behavior

University of Wisconsin SCHOOL OF MEDICINE AND PUBLIC HEALTH

Structural Brain Network Modeling with DTI

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Brian Avants
Hyekyung Lee
Jamie Hanson
Nagesh Adluru
Moo Chung
Seung-Goo Kim
Richard Davidson
James Gee

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 epsilion-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

Press Release • July 16, 2009

NIH Launches the Human Connectome Project to Unravel the Brain's Connections

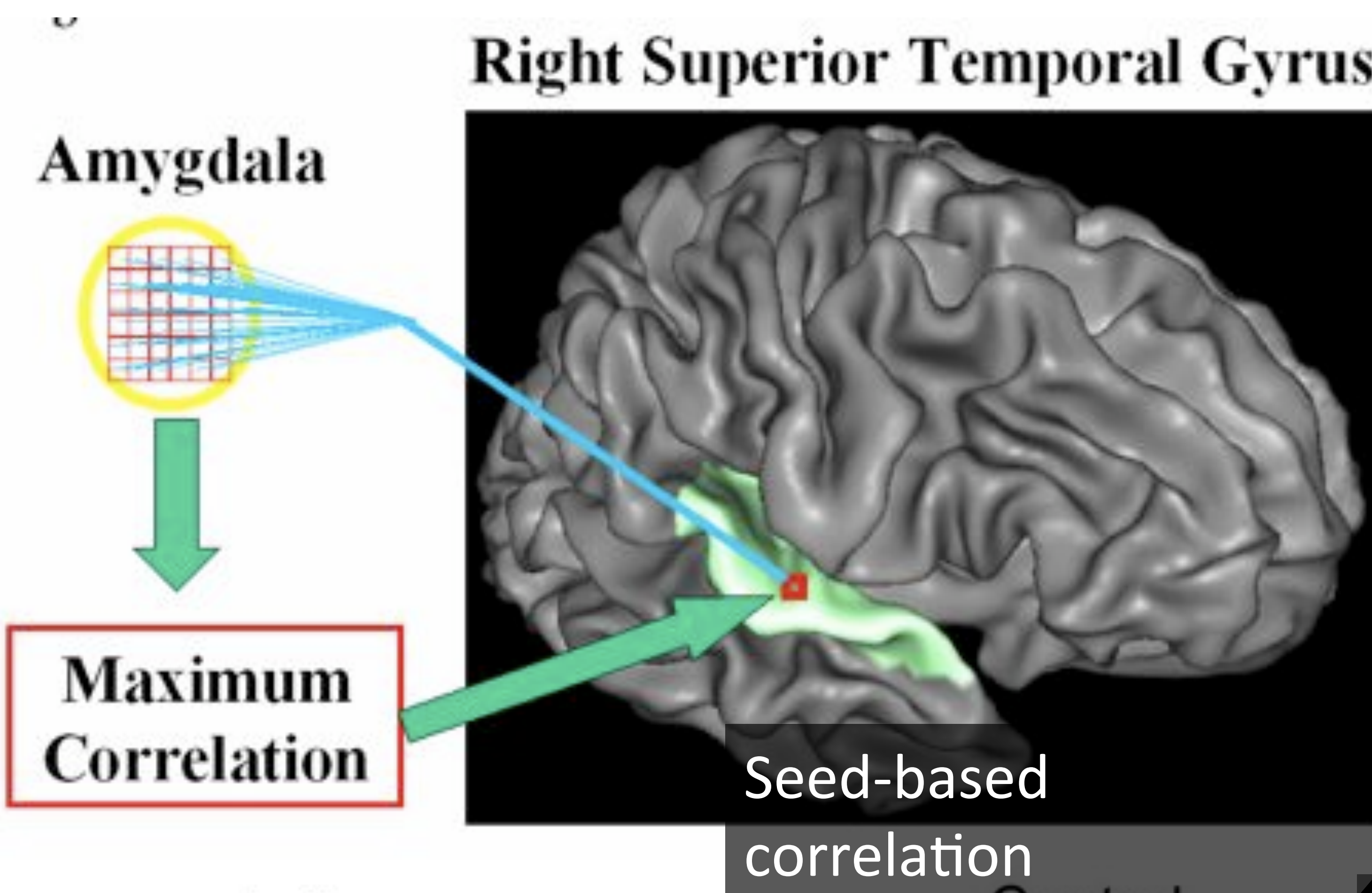
The National Institutes of Health Blueprint for Neuroscience Research is launching a $30 million project that will use cutting-edge brain imaging technologies to map the circuitry of the healthy adult human brain. By systematically collecting brain imaging data from hundreds of subjects, the Human Connectome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

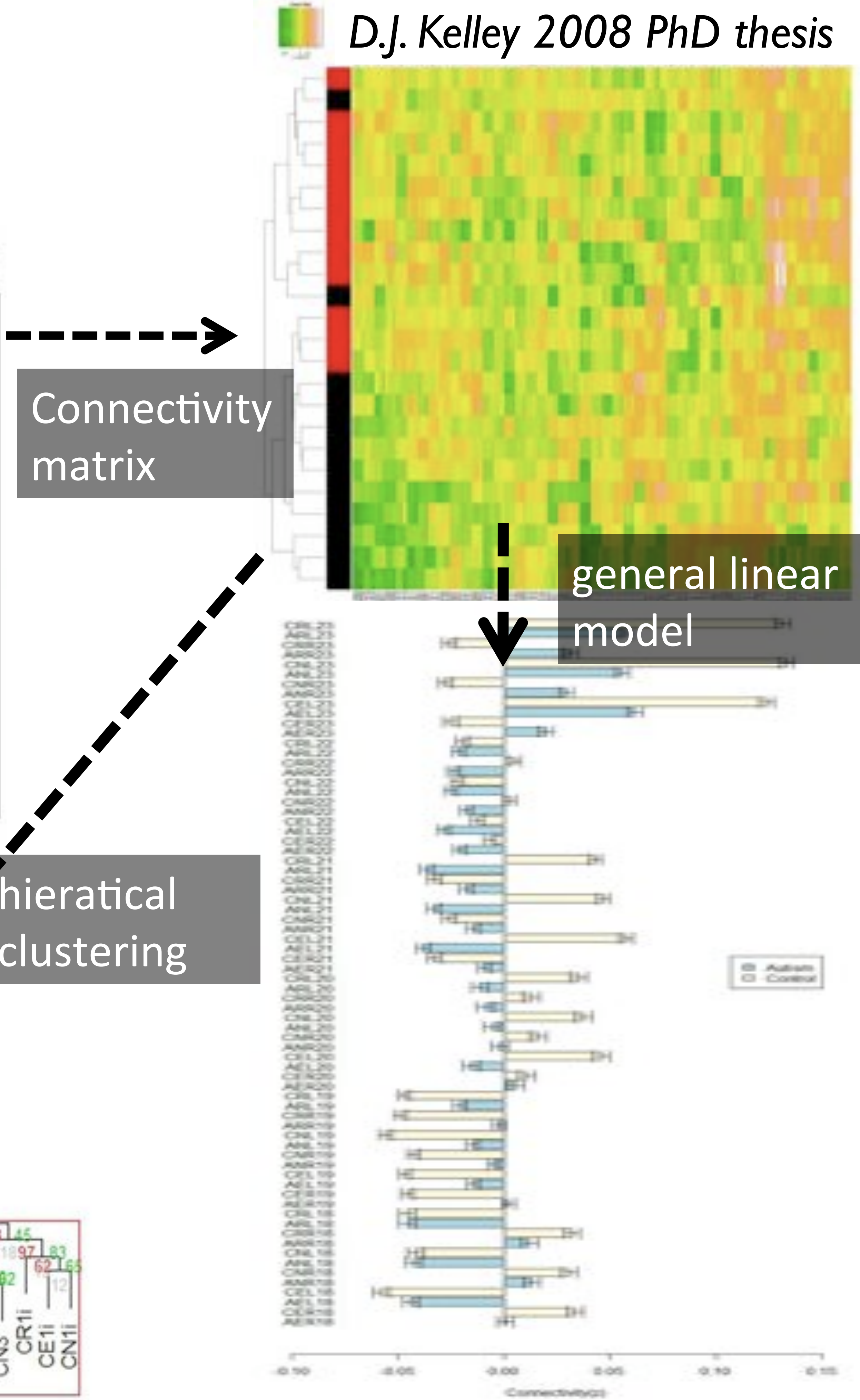
www.humanconnectomeproject.org

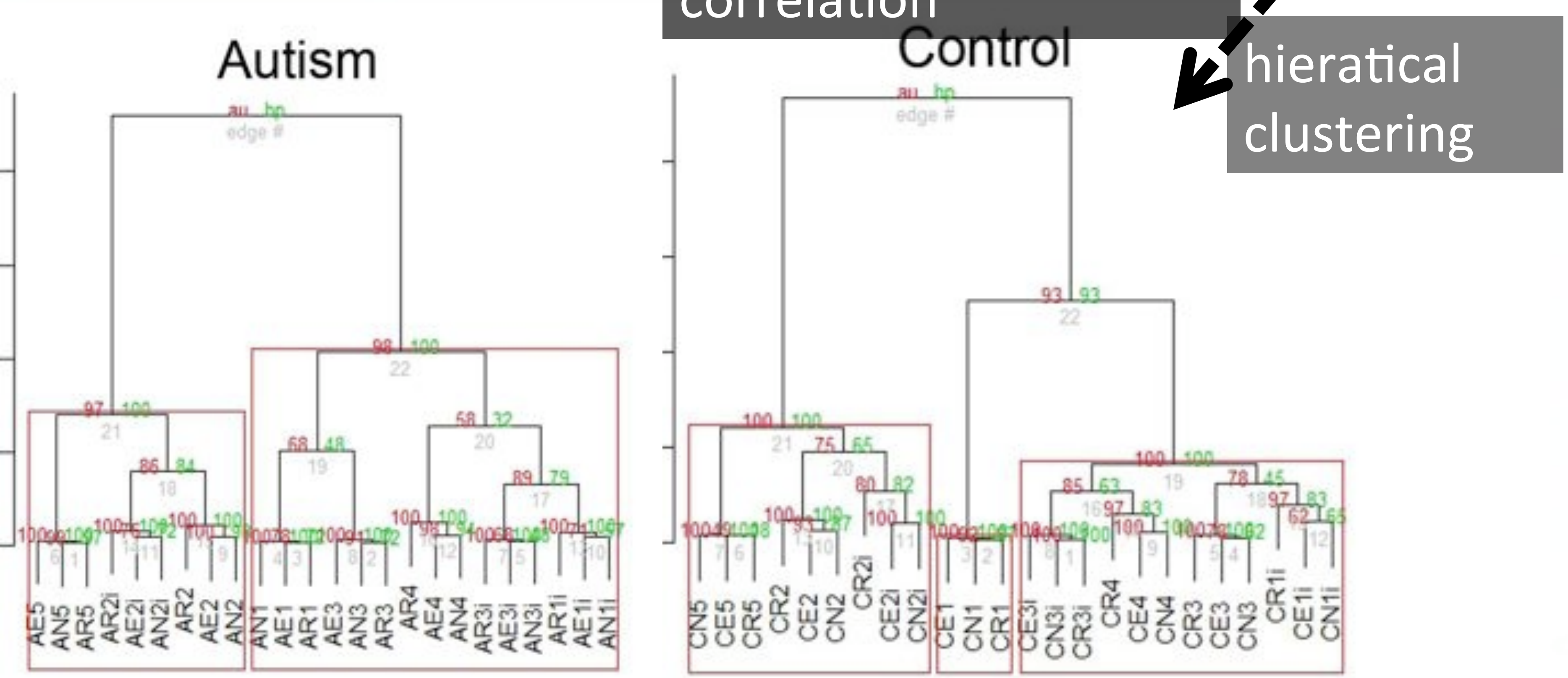
Connectome

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





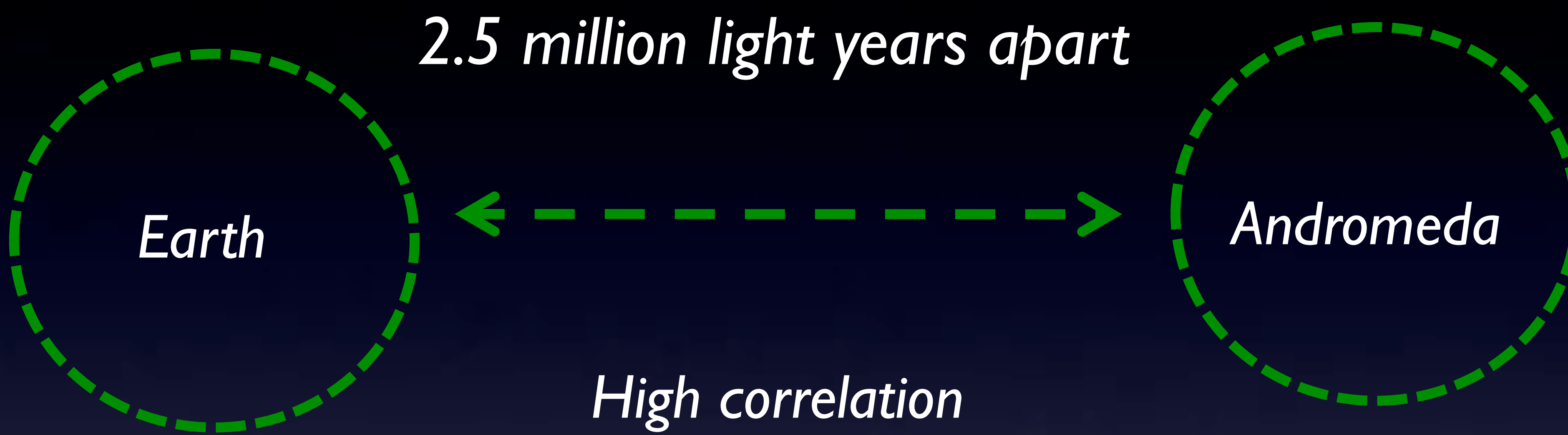


What is wrong with traditional functional connectivity studies?

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 ?



High correlation

↓

Connected ?

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

COMMENTARY

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.

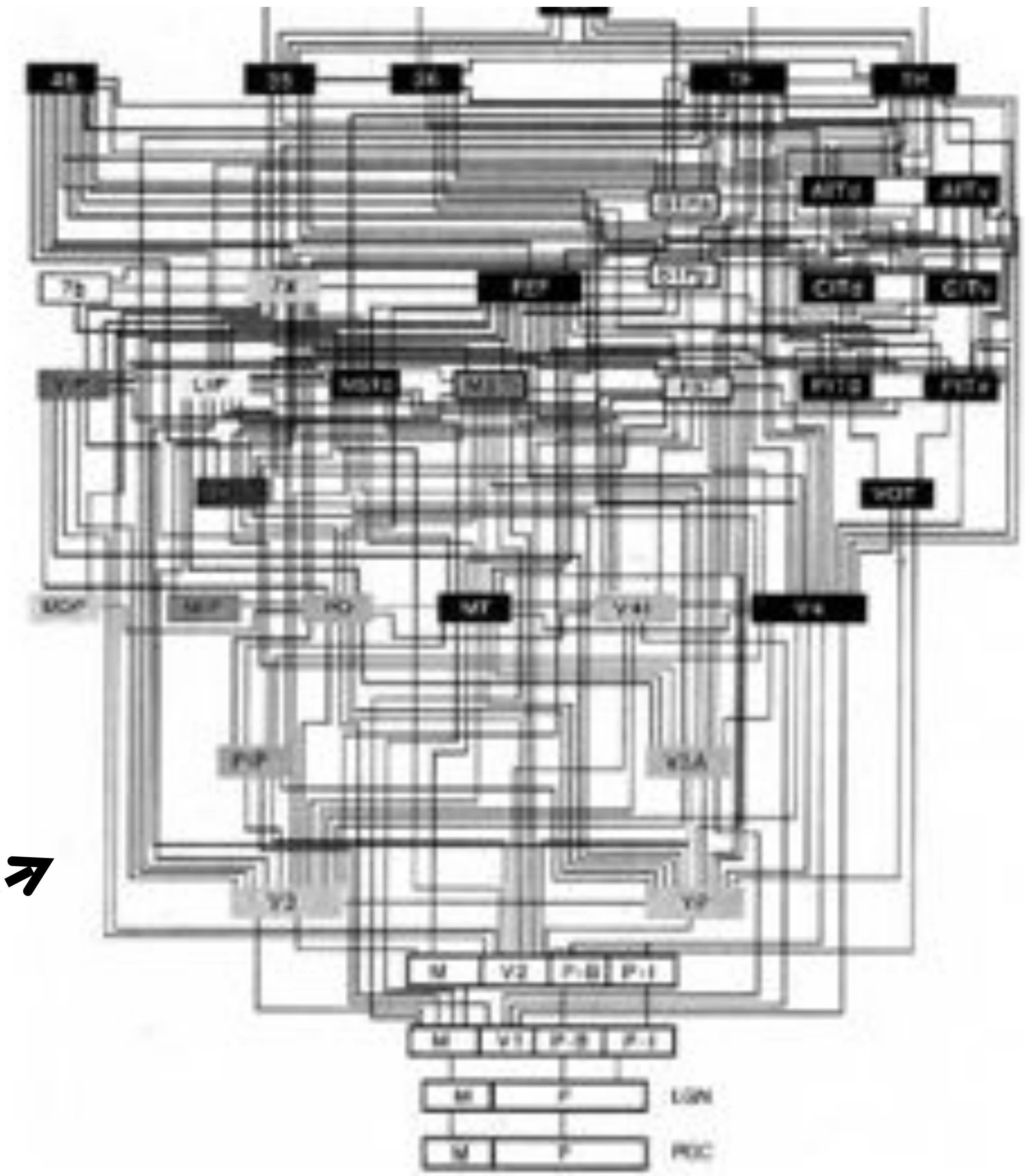
OVER the past 20 years there have been great advances in understanding the neuroanatomy of the macaque monkey, especially its cerebral cortex. We have learned much about the functional parcellation of the monkey's cortex from both anatomical and physiological studies. We know, for example, that rather

Most of 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

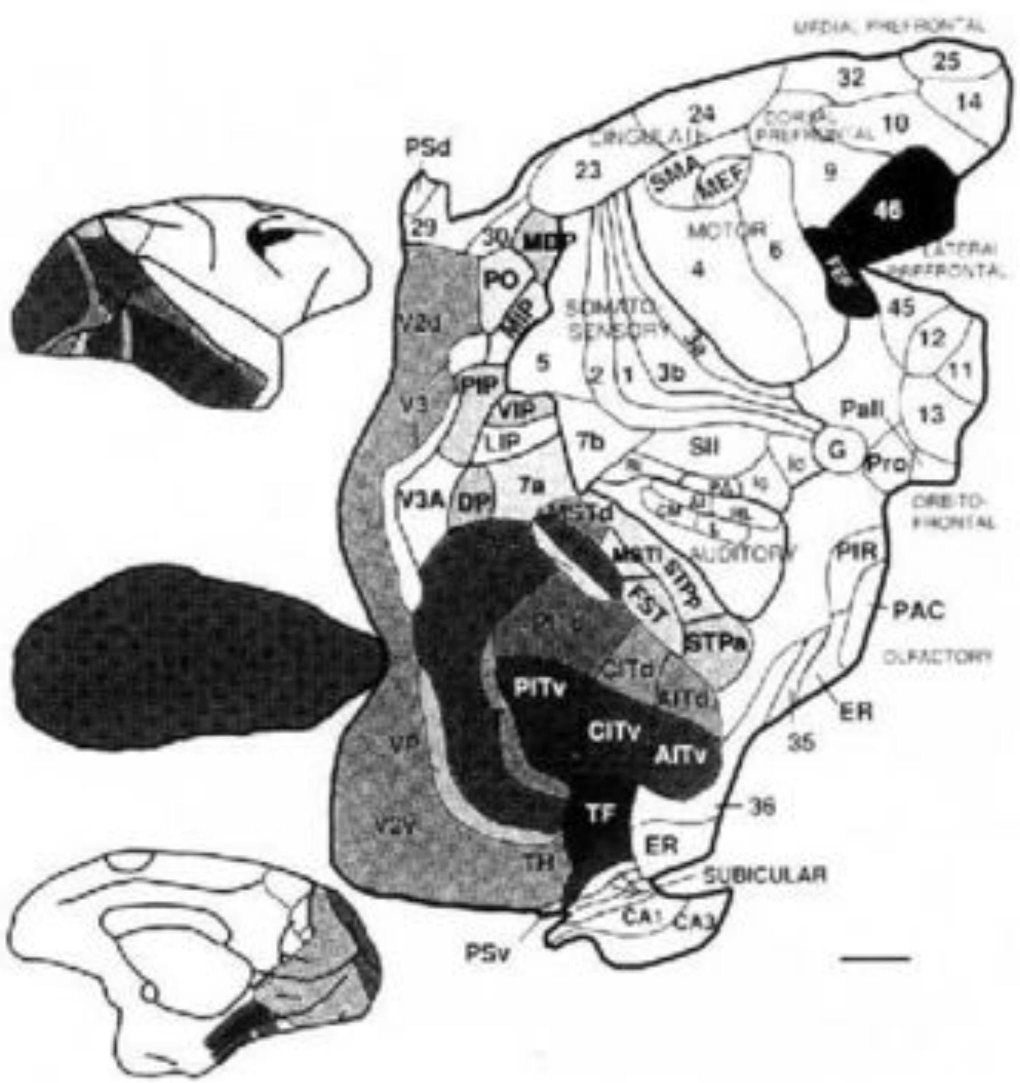
that for the macaque shown in Fig. 1? And what does the human equivalent of the connectional map of Fig. 2 look like? The shameful answer is that we do not have such detailed maps because, for obvious reasons, most of the experimental methods used on the macaque brain cannot be used on humans.

Crick, F and Jones, E. 1993. Nature 362:109-110

Connectional map of visual area



Macaque cortical map



What we can say about the neuroanatomy of the human brain?

Outdated technique

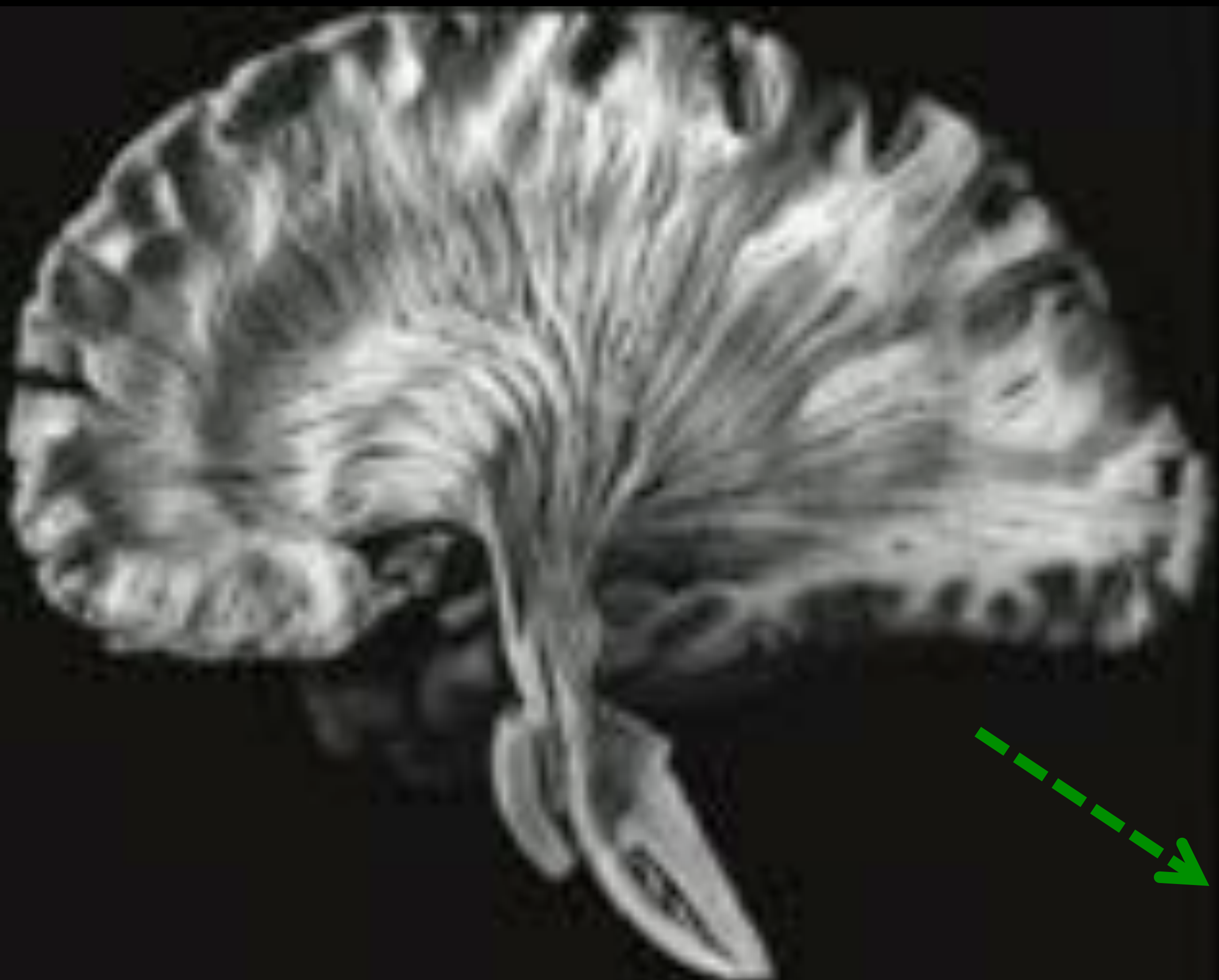
Another new method that at last permits the tracing of connections in fixed postmortem material is the use of lipid stains such as the carbocyanine dye diI[10] or one of its relatives. This spreads along axons by a diffusion process so that, in general, it is a slow method: to go 10 times as far takes 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

New technique

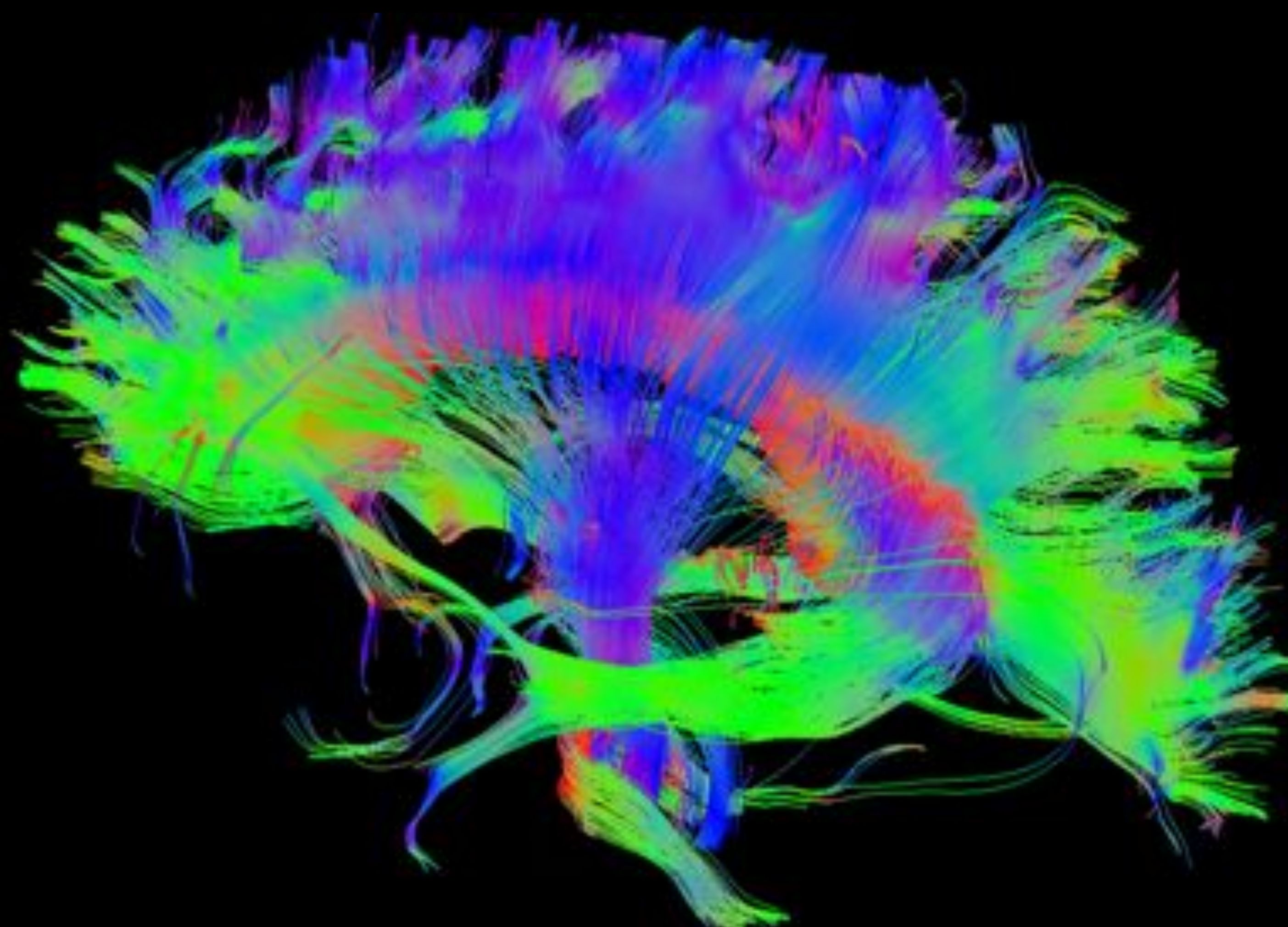
Diffusion Tensor Imaging (DTI)

DTI Preprocessing

Whole Brain Tractography



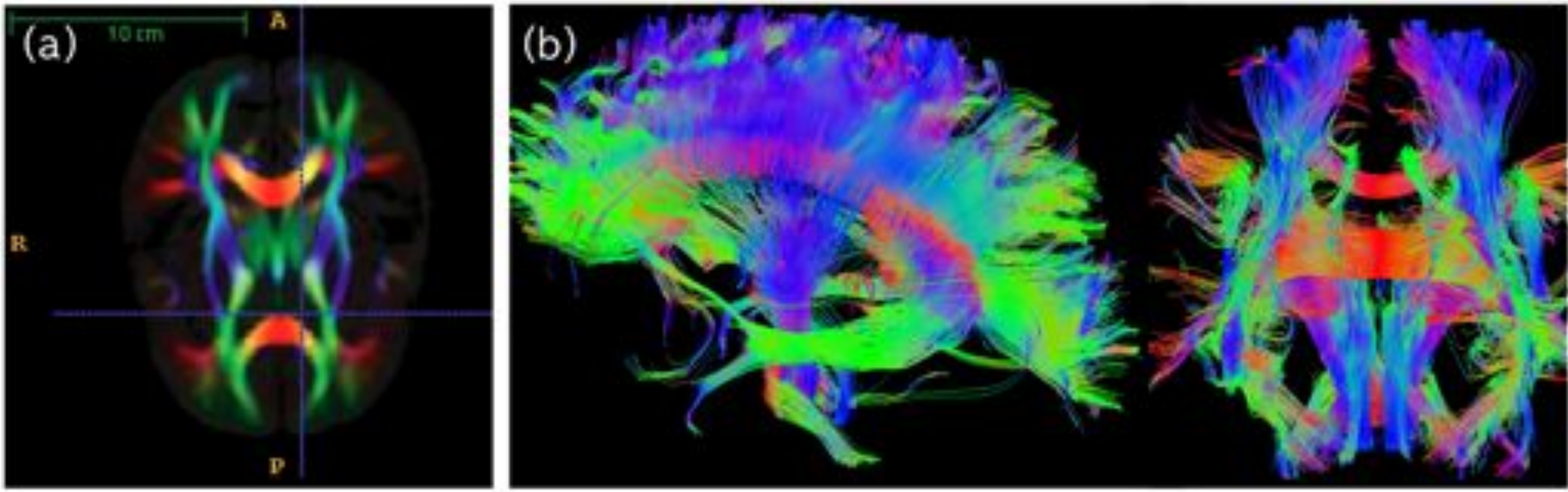
Postmortem



Reconstructed
0.5 million tracts

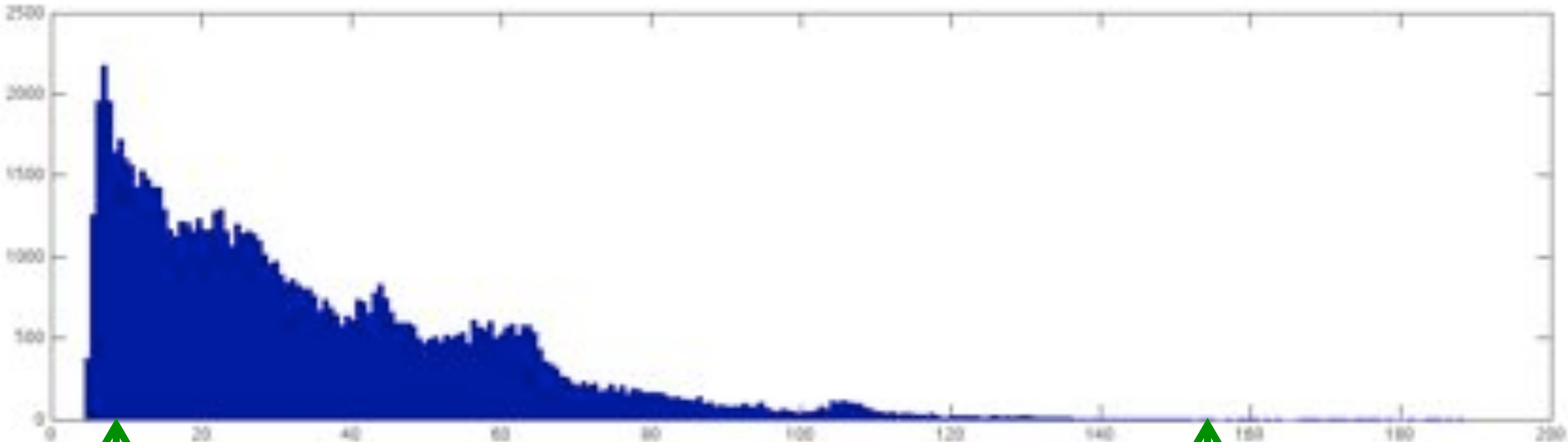
Tractography is done using the second order Runge-Kutta algorithm with TEND

CAMINO tractography based on TEND algorithm



Is the tractography done properly?

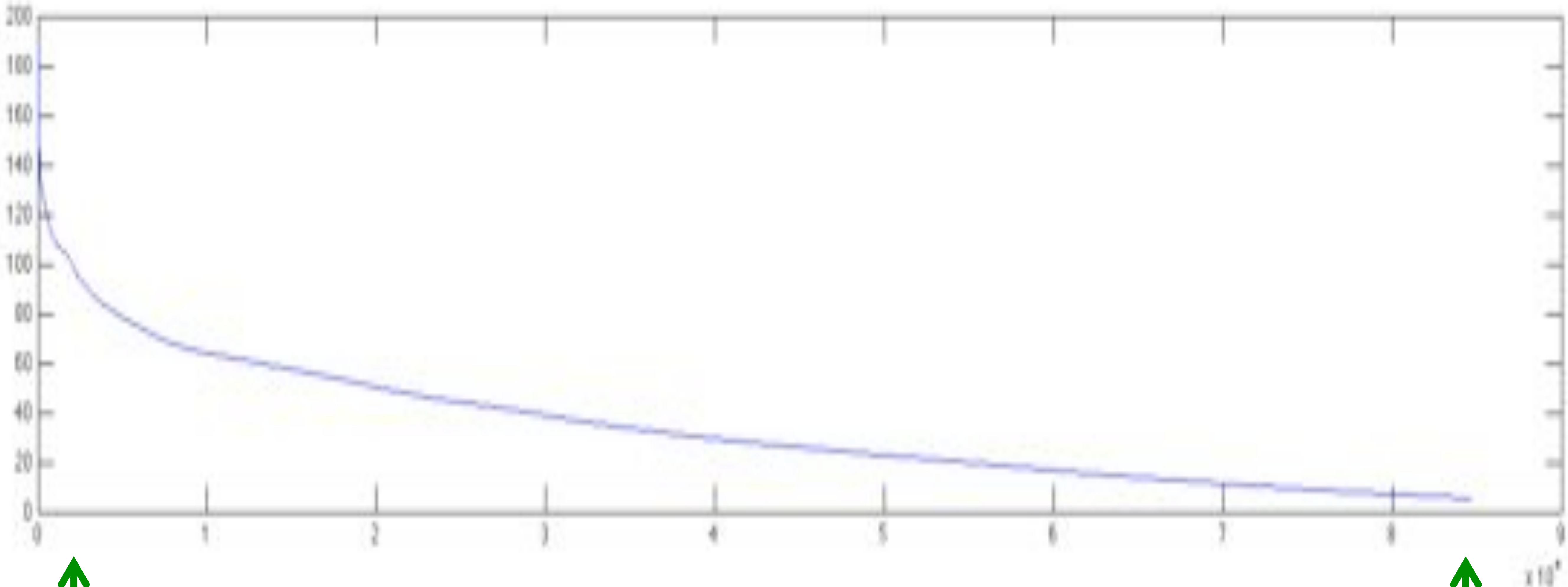
Histogram on tract length



Noise

Noise

Sorted tract length



Noise

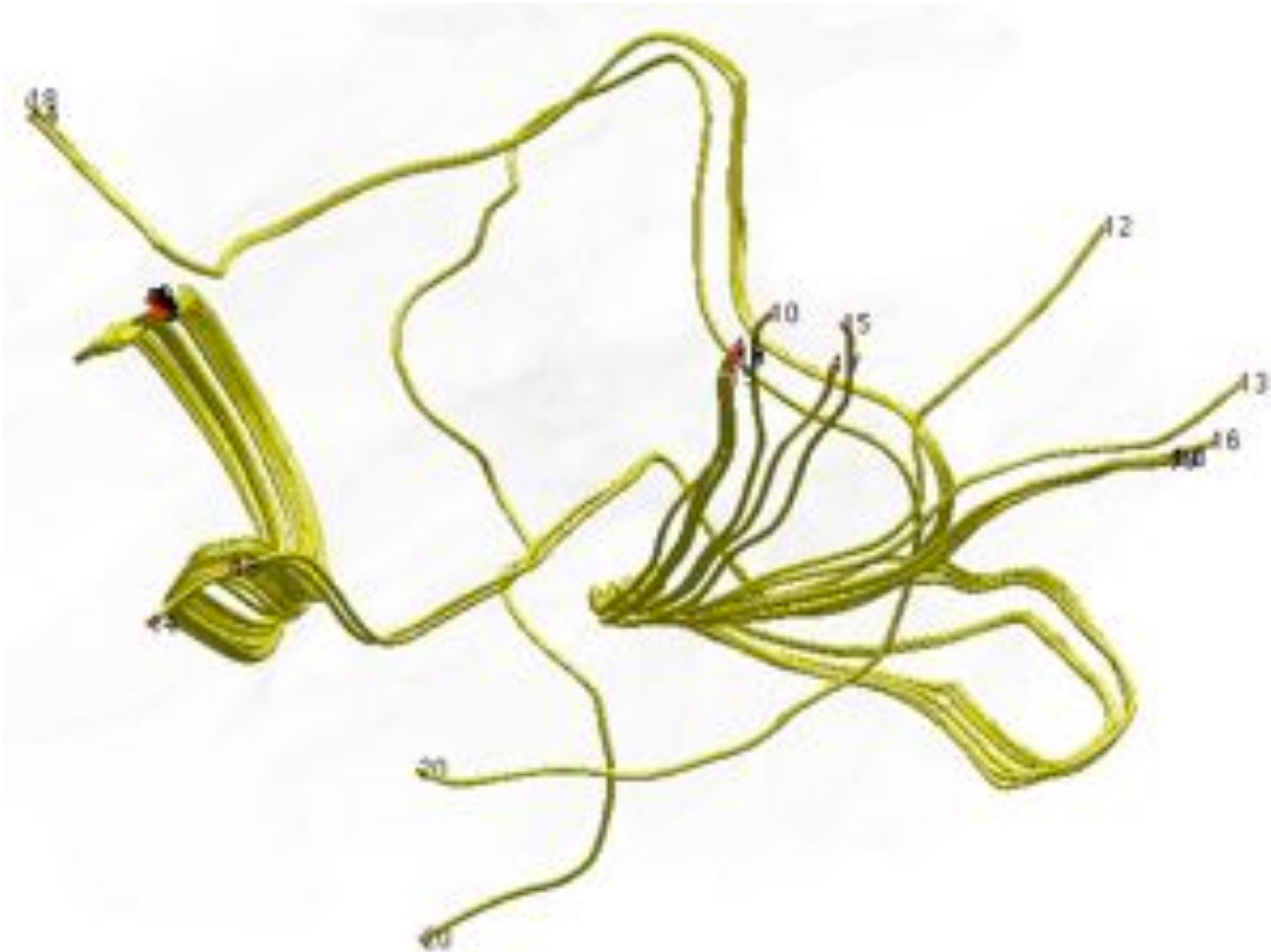
Noise

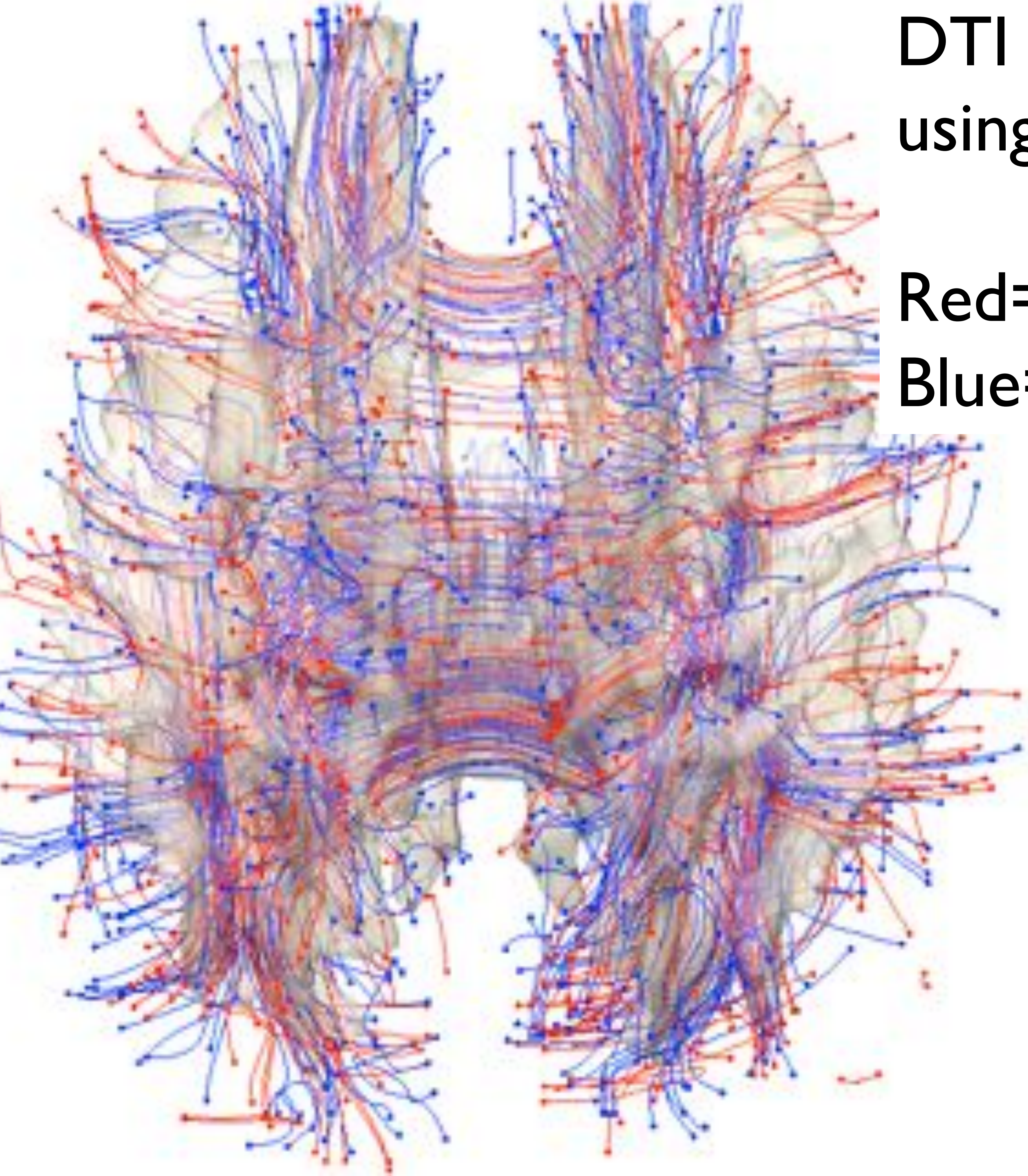
Longest tract is an outlier

Need a tract shape based filtering method possibly using the cosine representation.

Longest five tracts

Longest 20 tracts

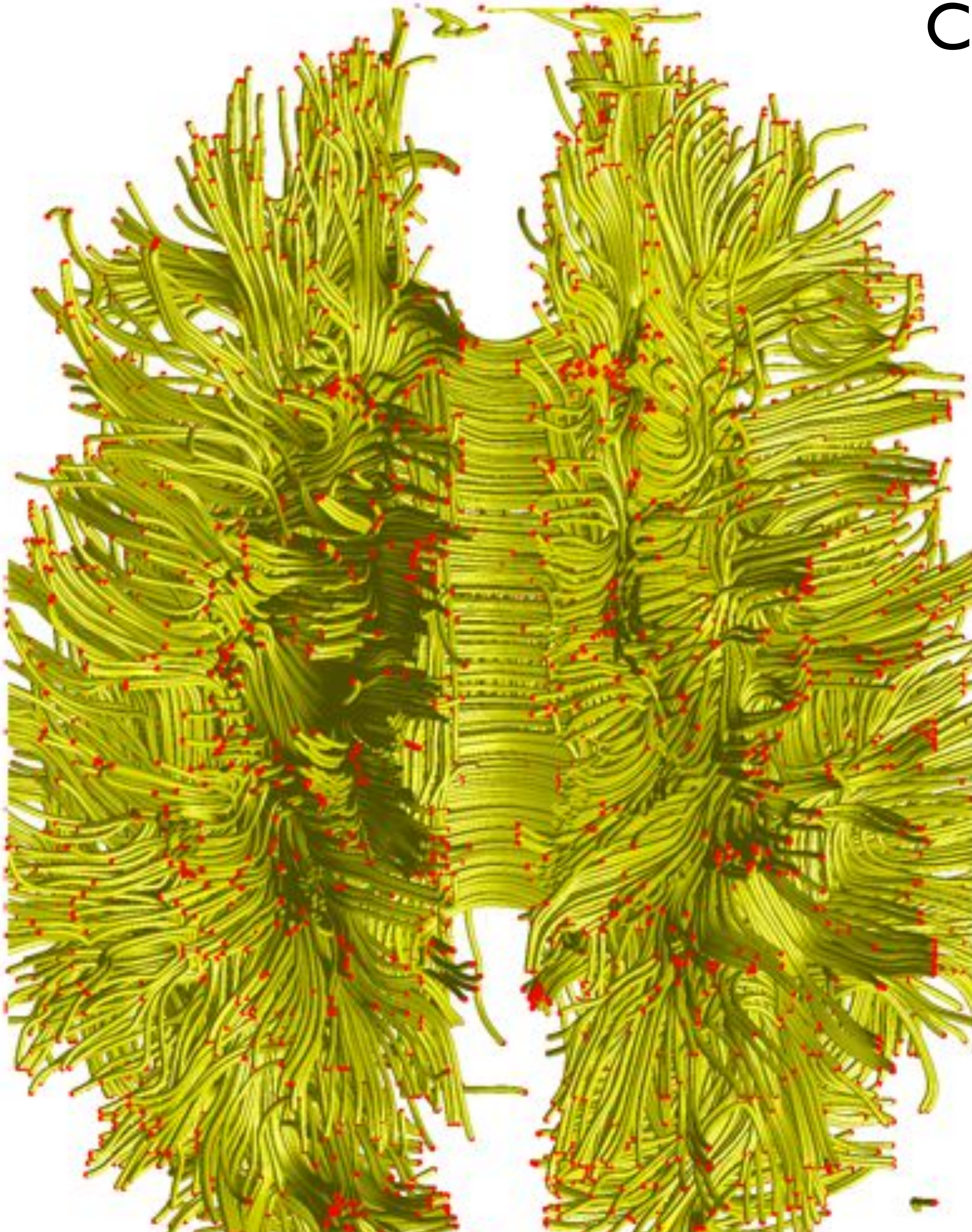




DTI alignment is done using DTI-TK package

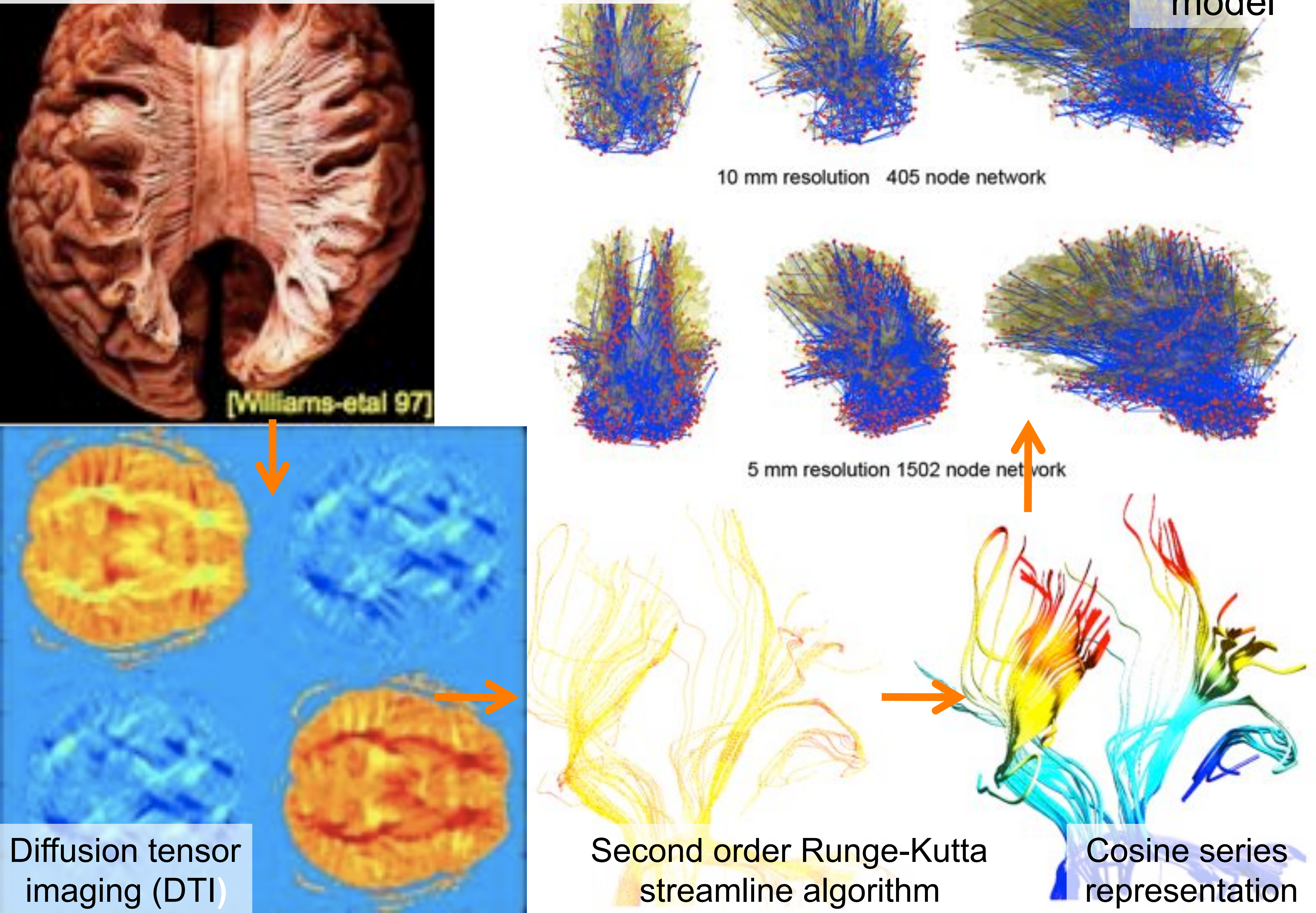
Red= subject 1
Blue= subject 2

CAMINO fiber tractograpy



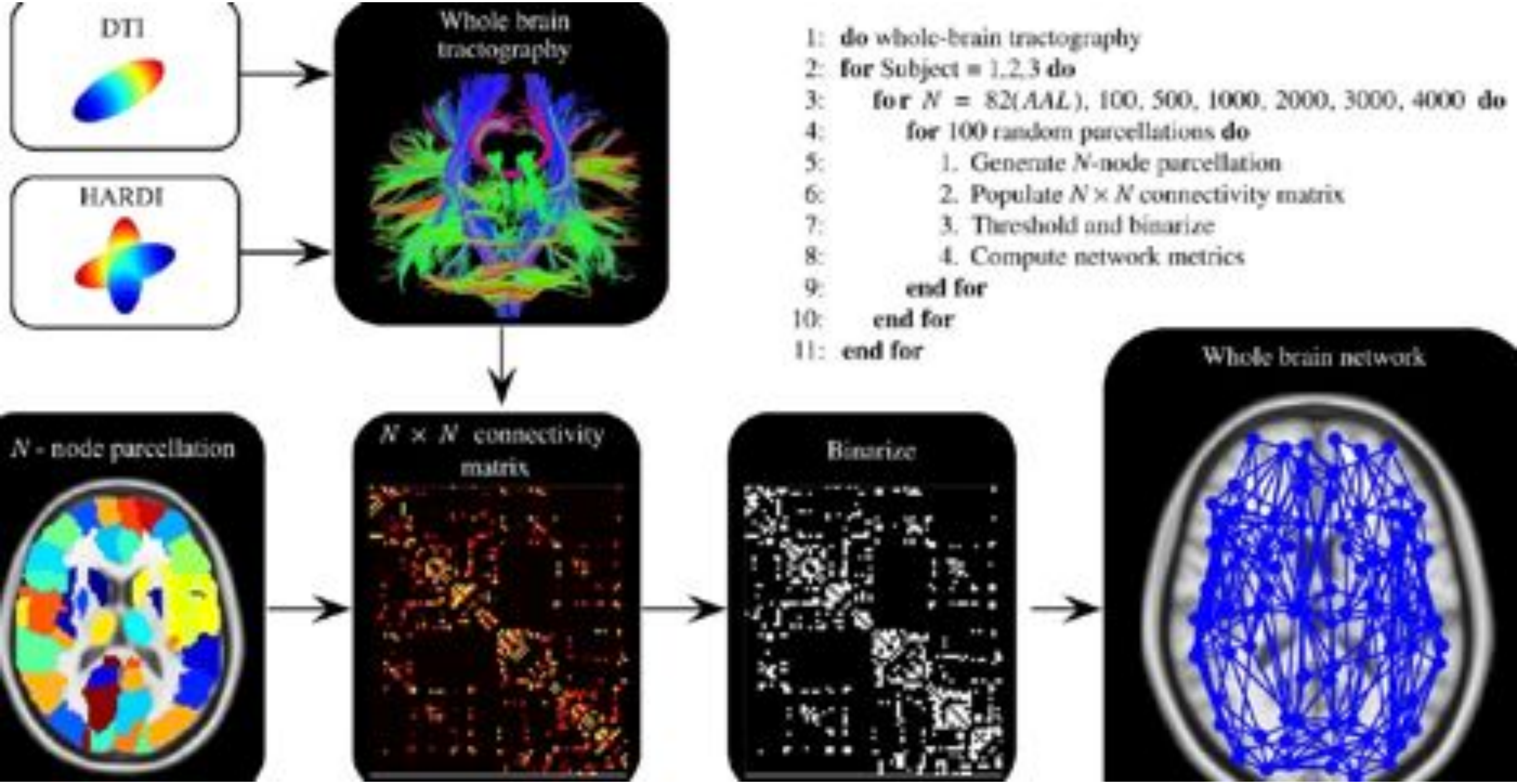
Only showing about 3000 tracts out of 90000 here

White Matter Fiber Tracts



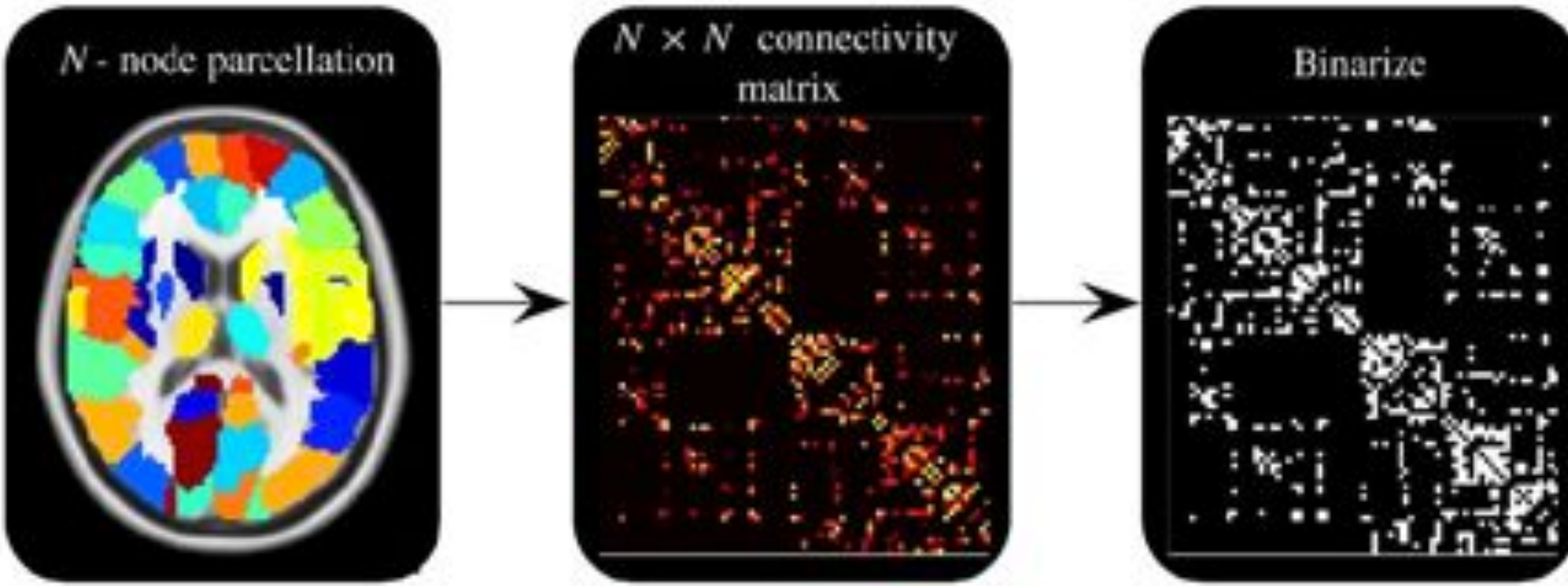
ROI-based Connectivity

Standard DTI network construction pipeline



Zalesky et al. NeuroImage 2010

Two problems with the standard method

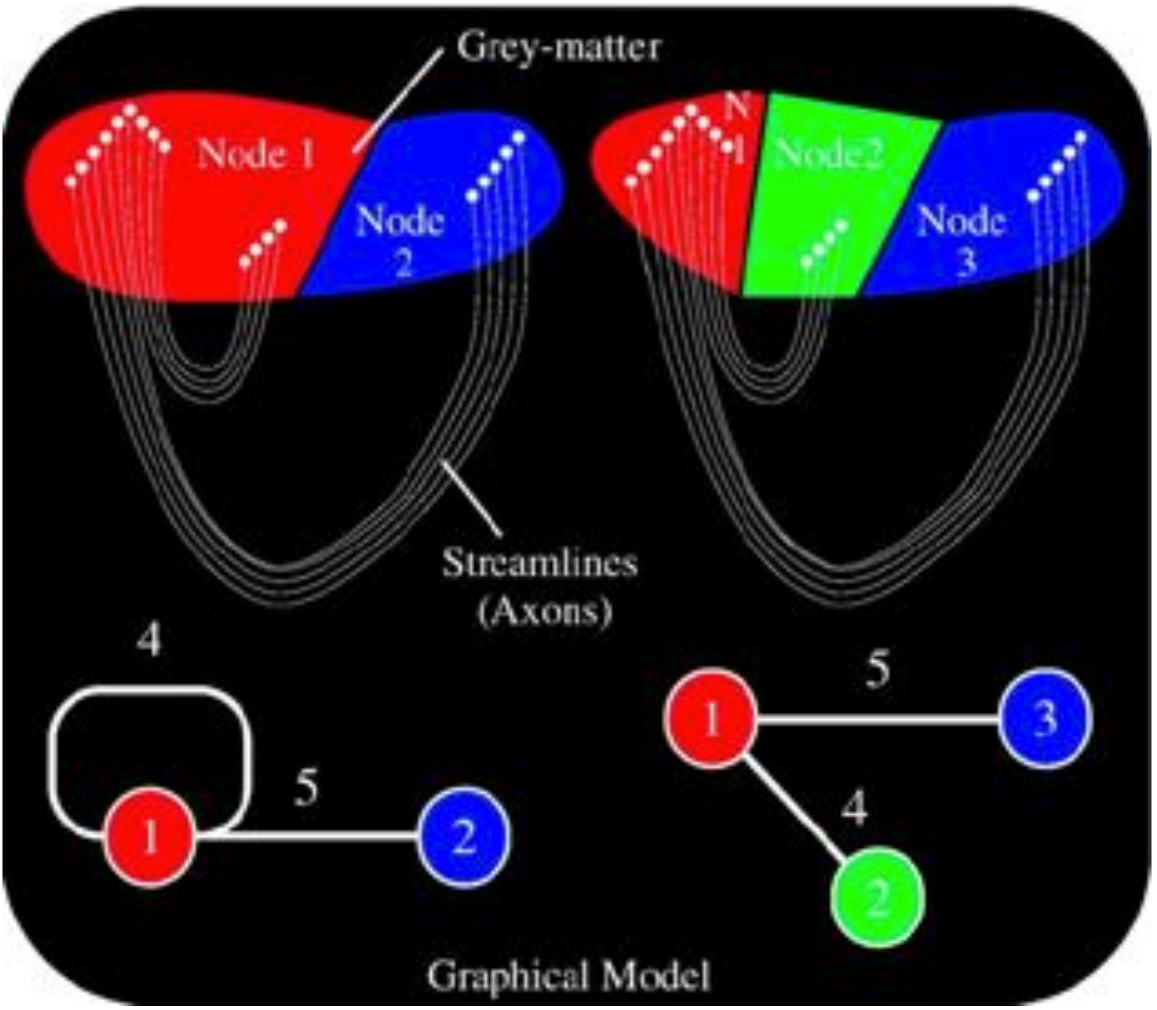


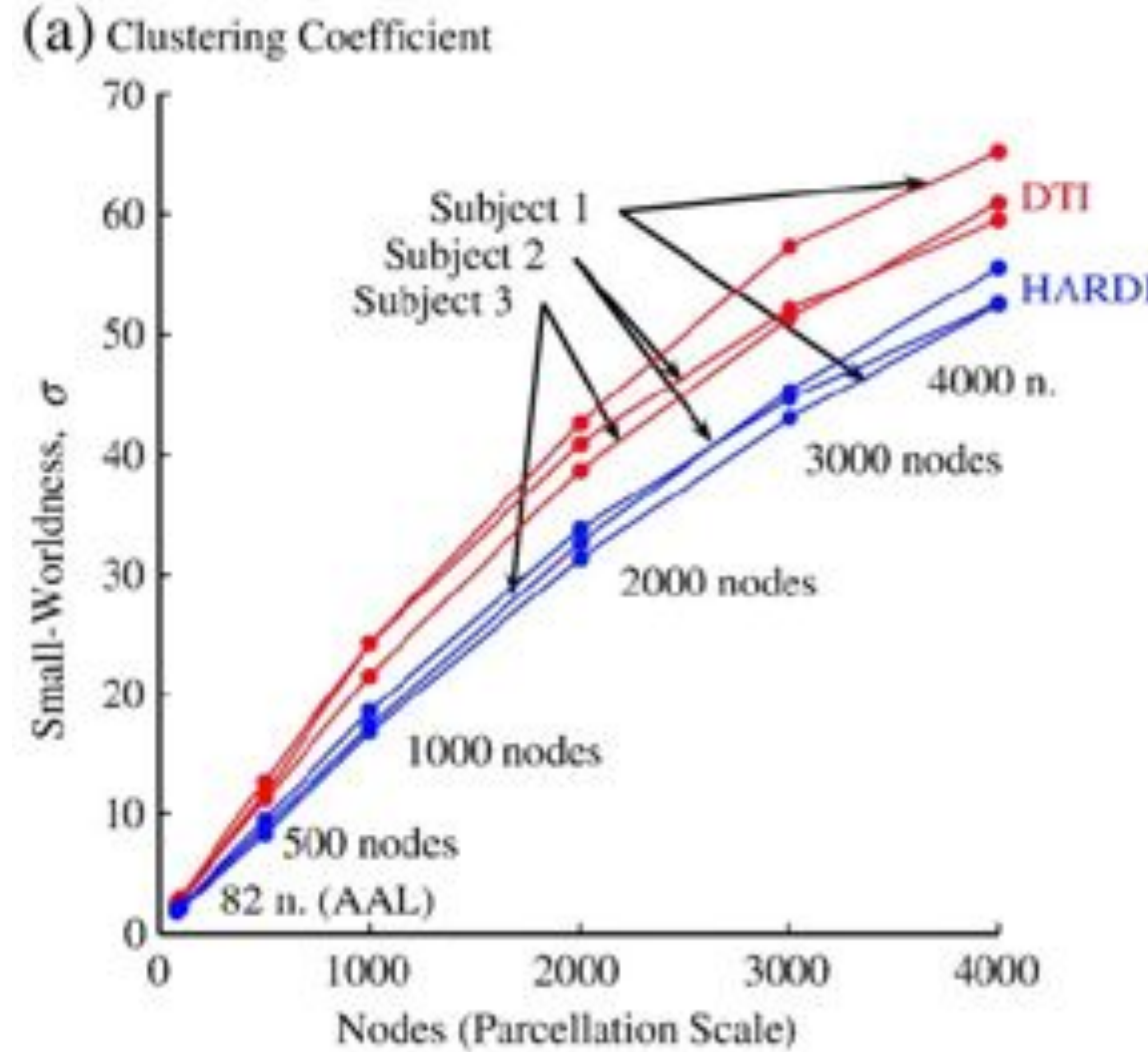
Parcellation

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

Computing the Shape of Brain Networks Using Graph Filtration and Gromov-Hausdorff Metric

Hyekyoung Lee[1,2,3], Moo K. Chung[2,6,7], Hyejin Kang[1,3], Boong-Nyun Kim[5], and Dong Soo Lee[1,3,4]

[1] Department of Nuclear Medicine,
[2] Department of Brain and Cognitive Sciences,
[3] Institute of Radiation Medicine, Medical Research Center,
[4] WCU Department of Molecular Medicine and Biopharmaceutical Sciences,
[5] Department of Neuropsychiatry, Seoul National University, College of Medicine, Seoul, Korea
[6] Department of Biostatistics and Medical Informatics,
[7] Waisman Laboratory for Brain Imaging and Behavior, University of Wisconsin, Madison, WI 53706, USA
mkchung@wisc.edu

Lee et al., 2011. Medical Image Computing and Computer Assisted Intervention (MICCAI) Lecture Notes in Computer Science (LNCS). 6892:302-309.

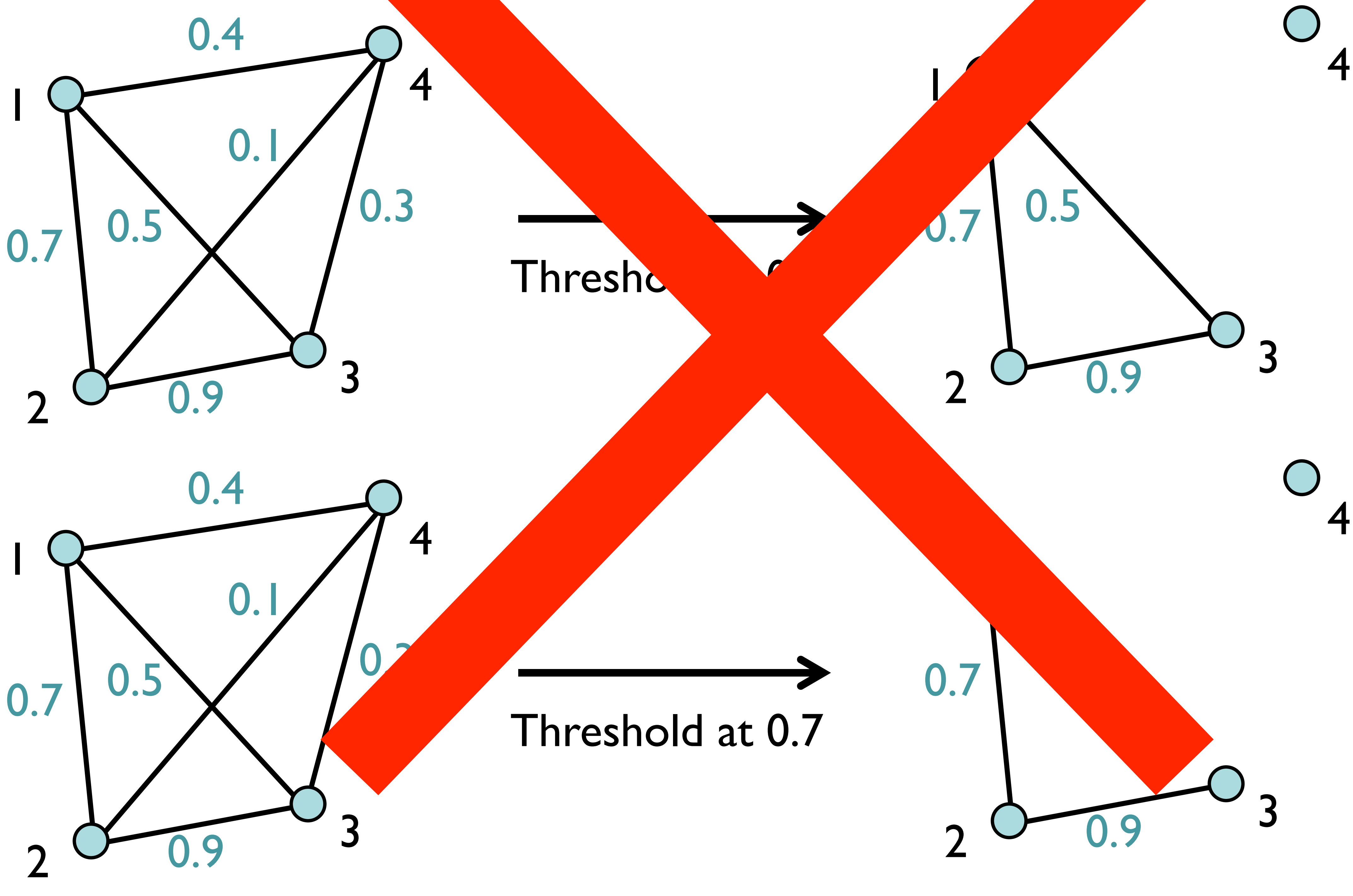
The method has been presented in the following medical imaging conferences

- 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%)

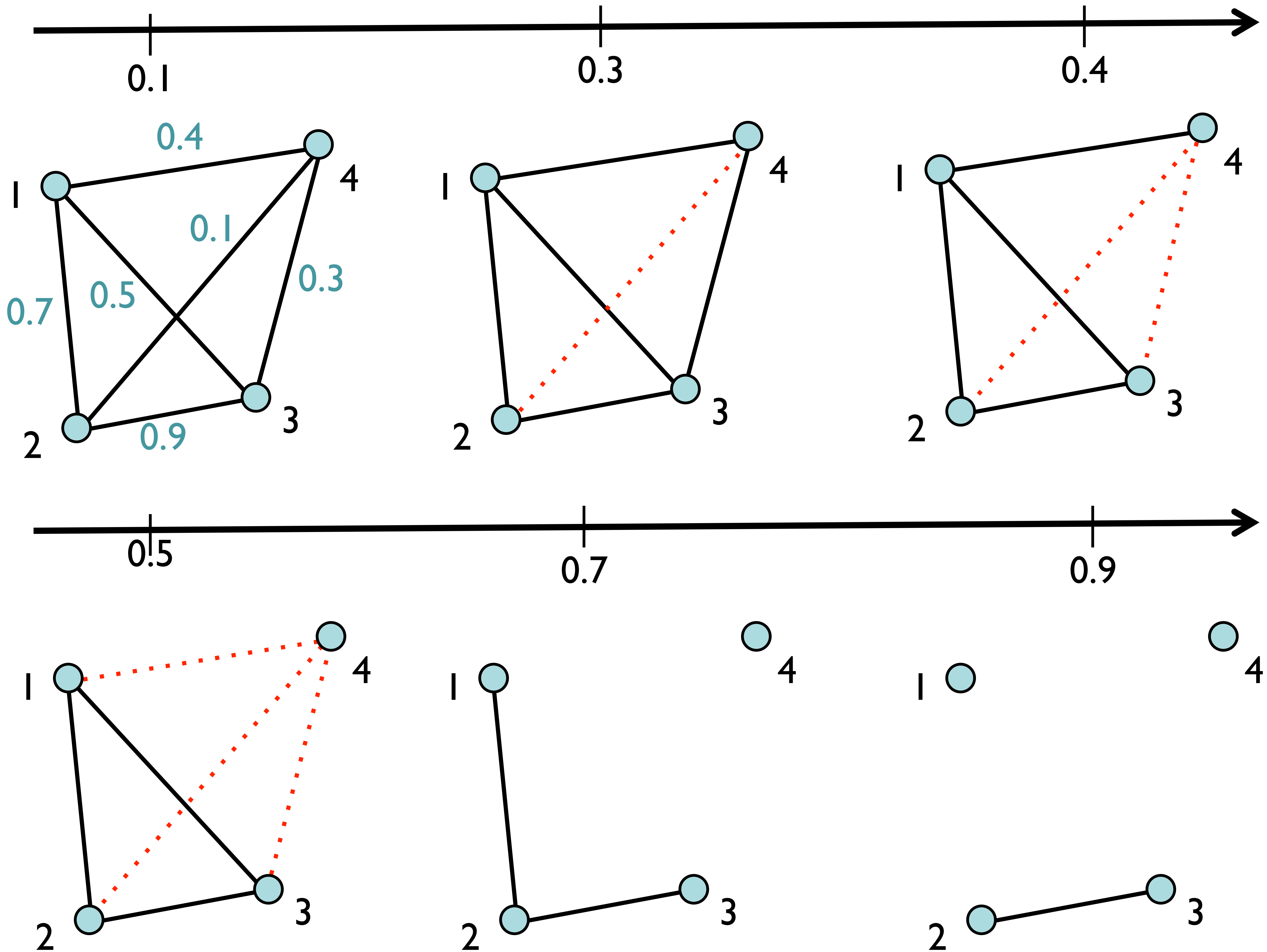
What is wrong with arbitrary thresholding?

Edge weight ρ_{ij} between node *i* and *j*

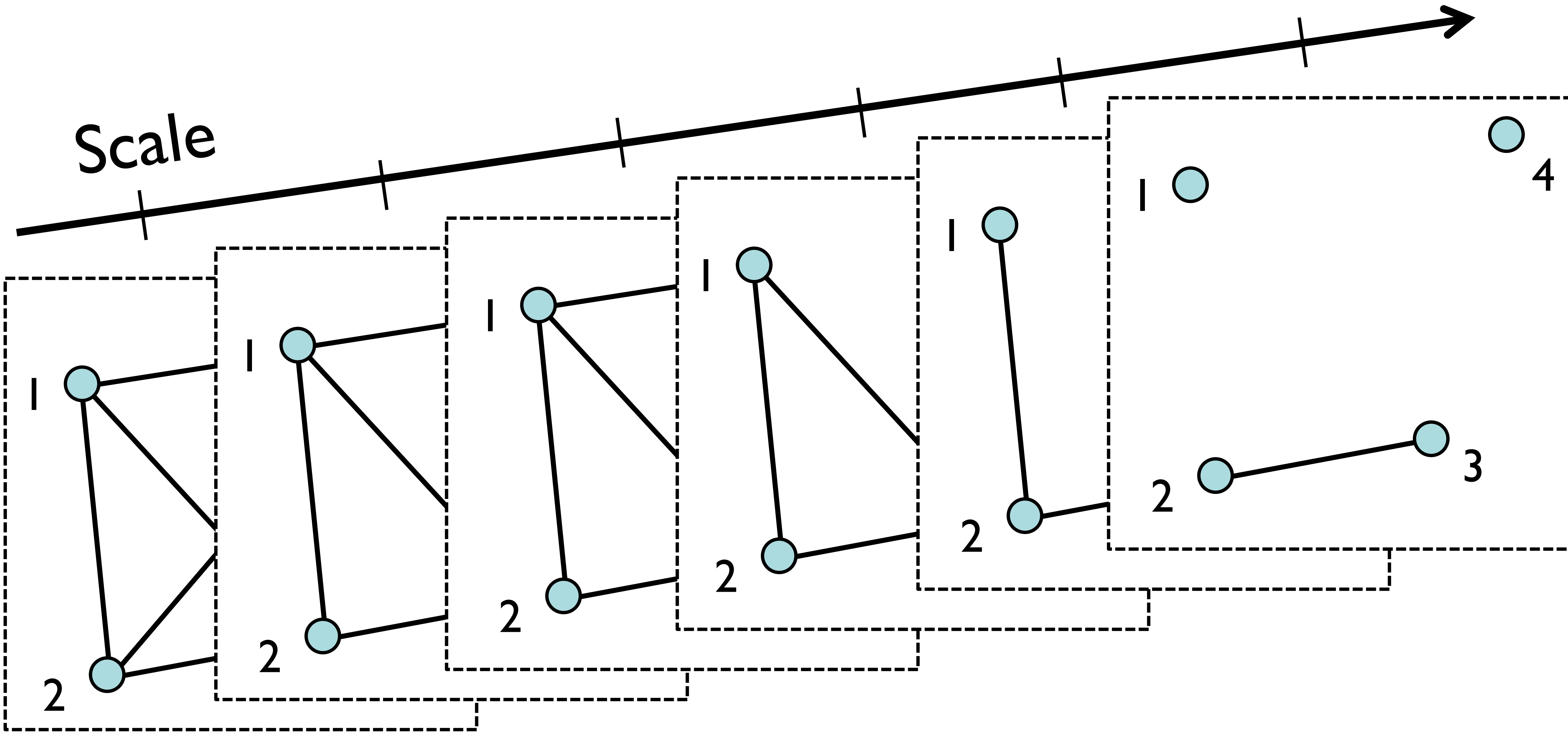
→ Connectivity mat... $\rho = (\rho_{ij})$



Decomposition of weighted graph



Network & graph filtration



Need scale invariant persistent topological features

Parcellation Free Network Construction

Epsilon-neighbor network construction

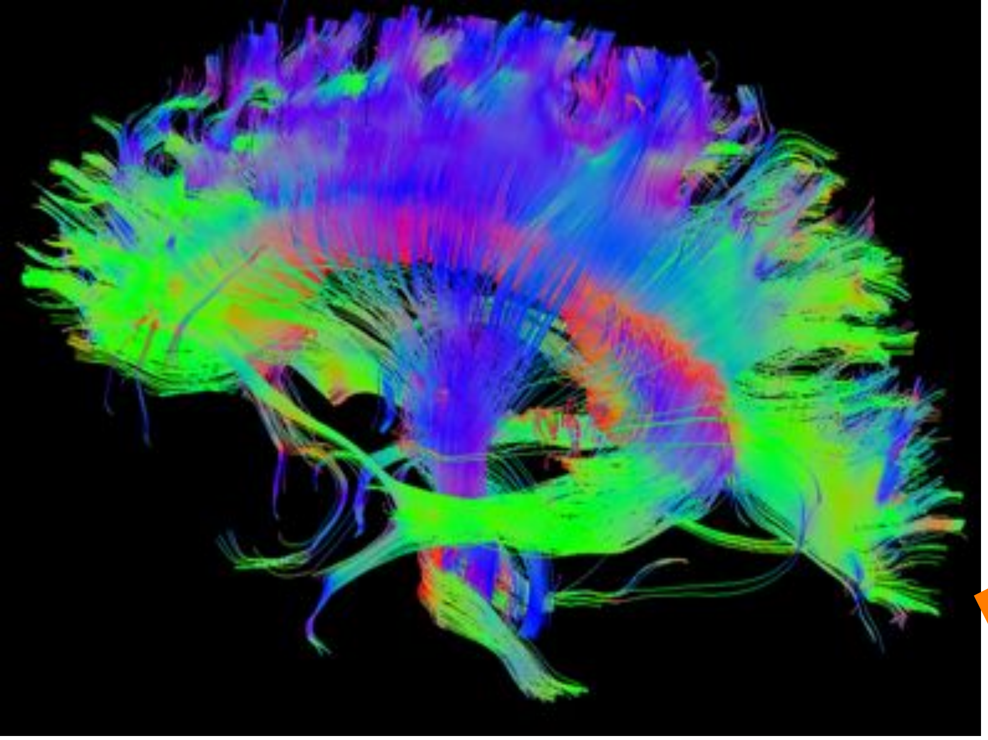
Scalable Brain Network Construction on White Matter Fibers

Moo K. Chung[1,3,6*], Nagesh Adluru[3], Kim M. Dalton[3],
Andrew L. Alexander[2,3,5], Richard J. Davidson[3,4,5]

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

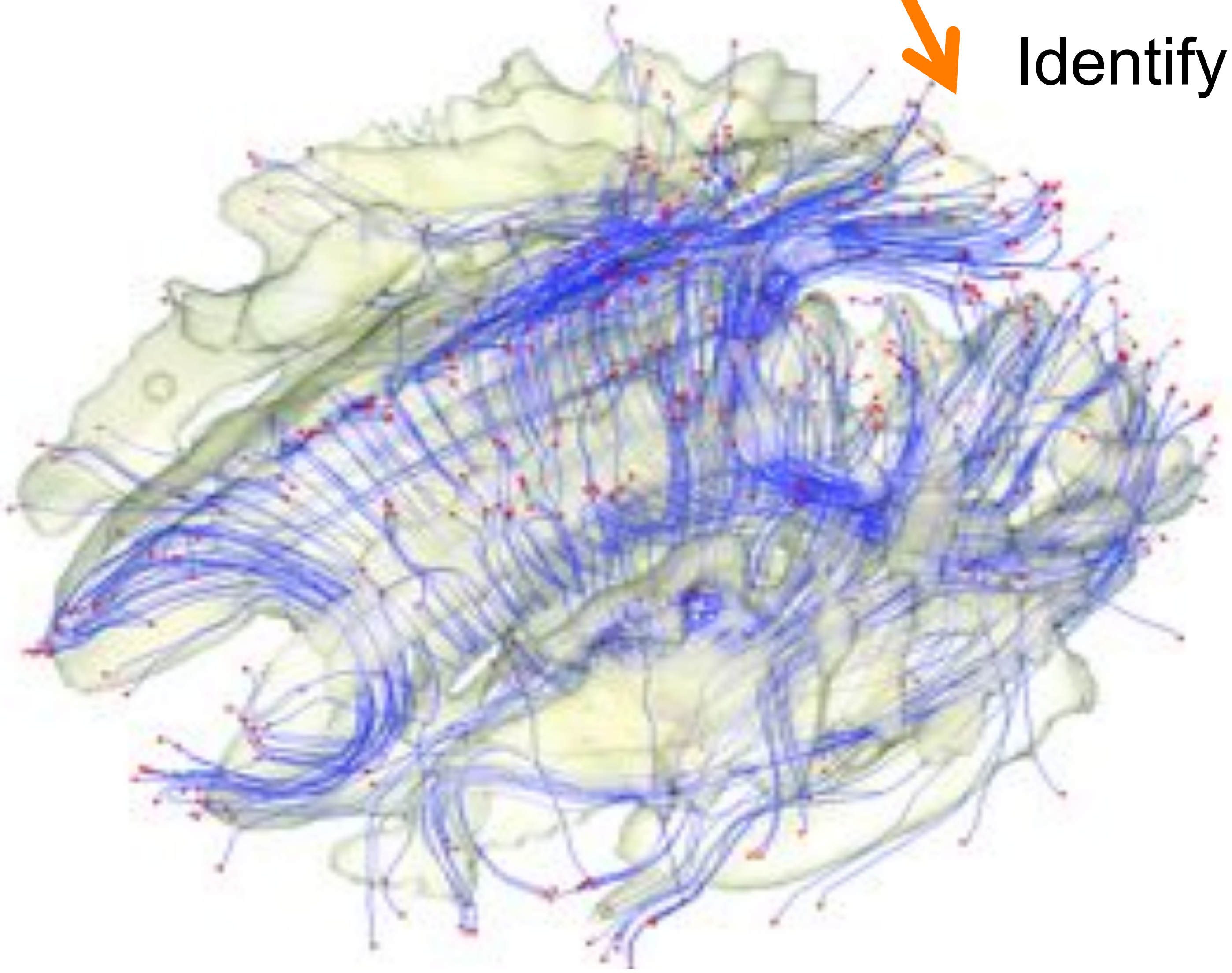
Chung et al. 2011 SPIE 7962 79624G-1

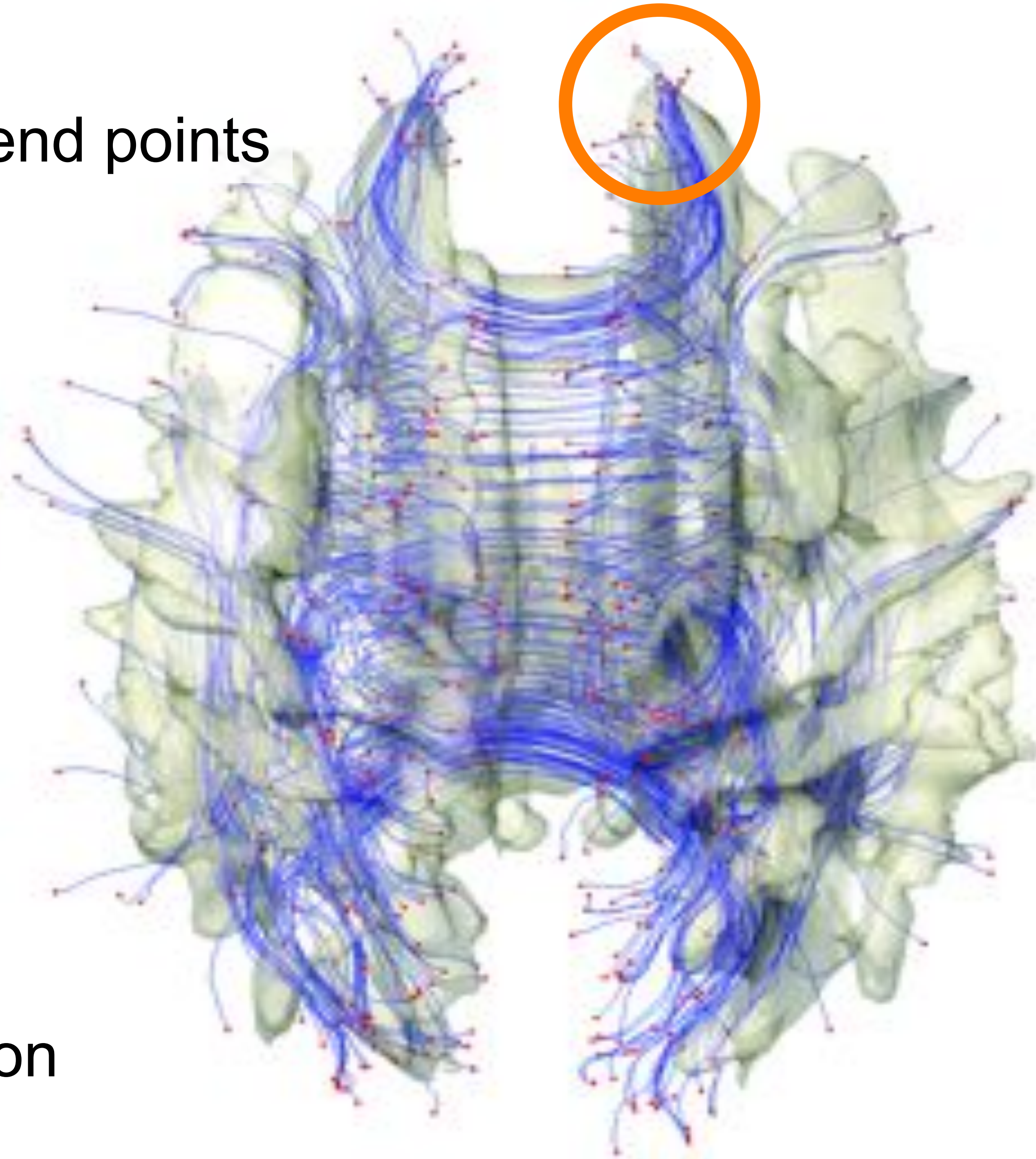
ε-neighbor network construction



Identify end points

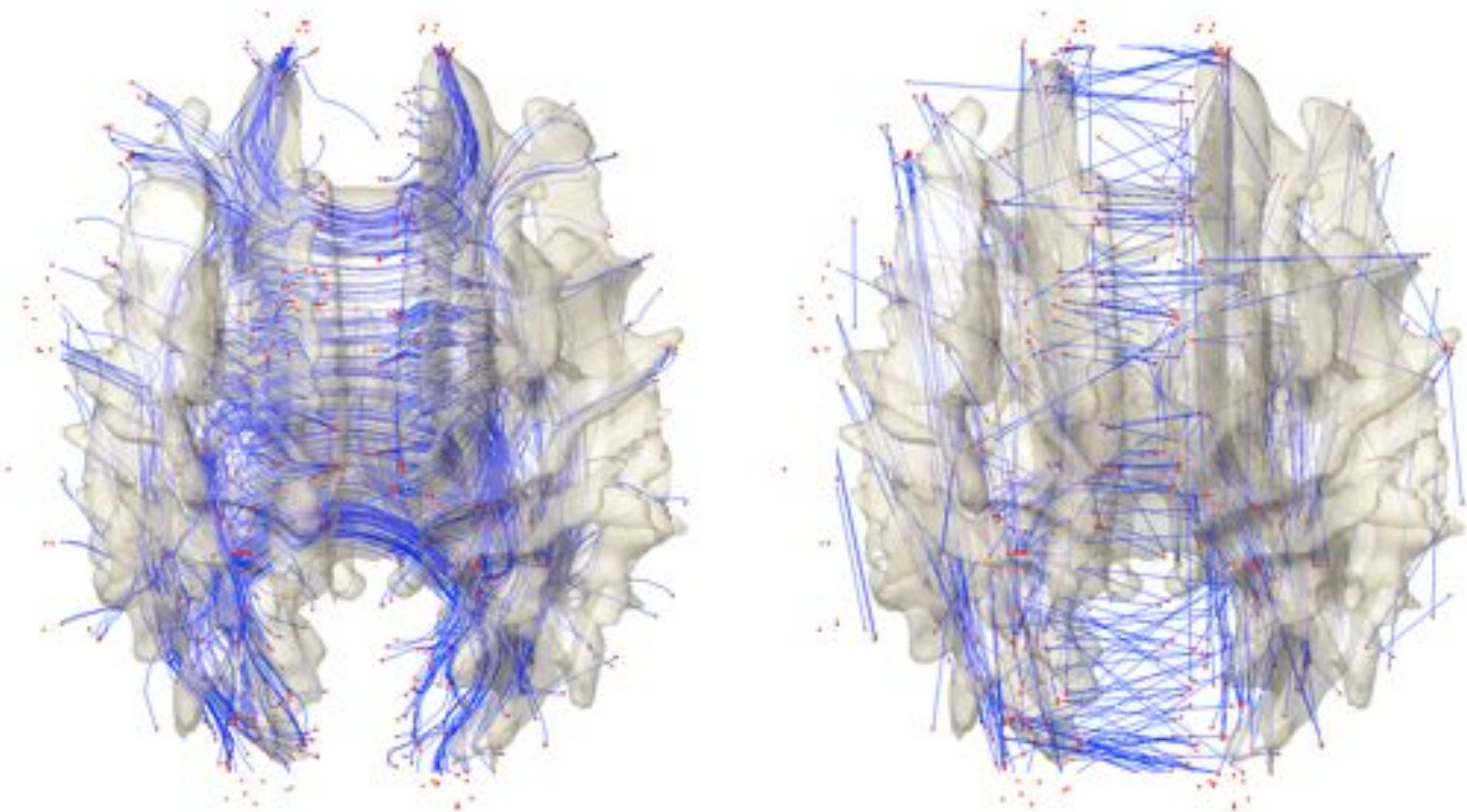
All points in the ε-neighbor are identified as a single node in a graph





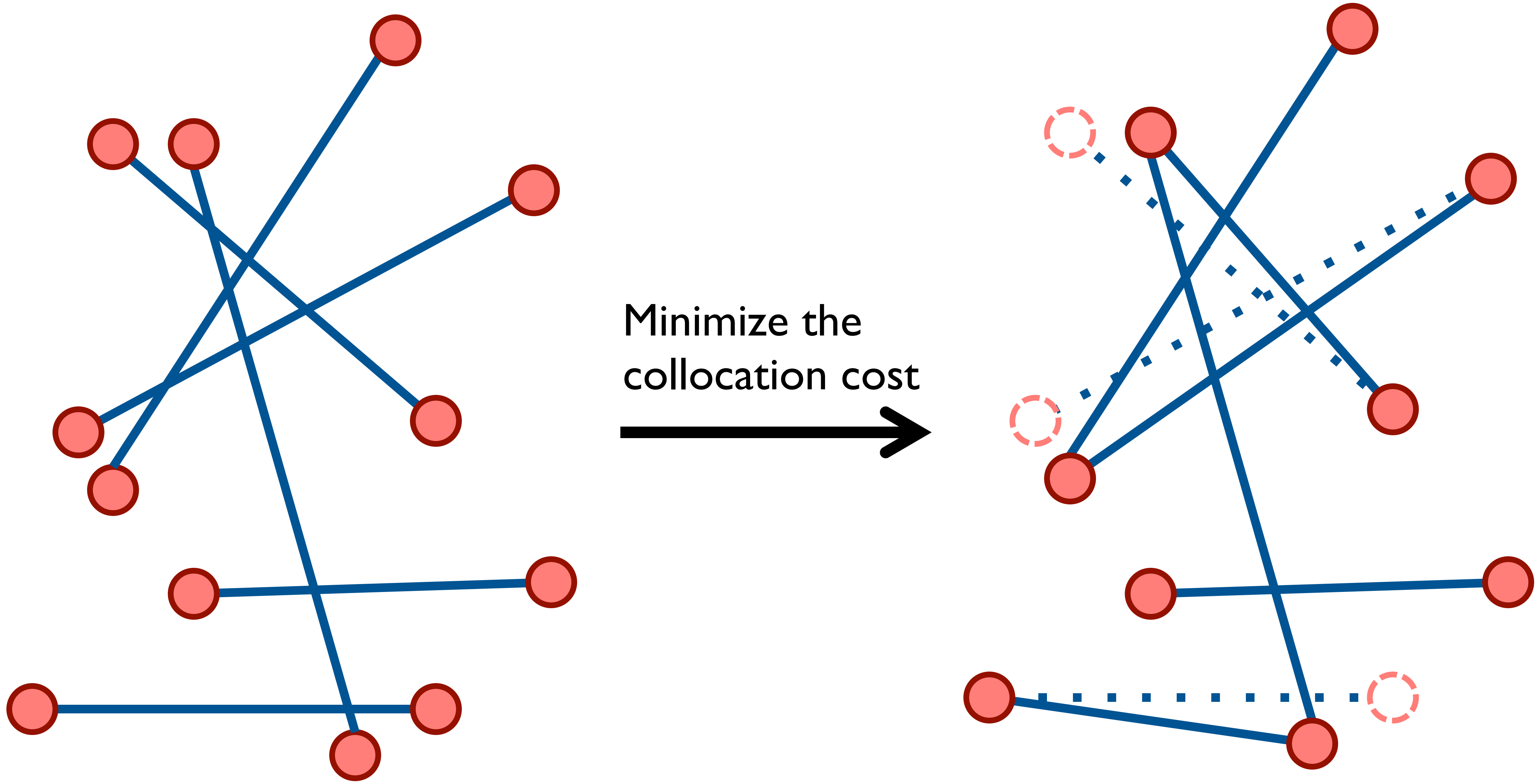
The first data-driven DTI network construction framework without any parcellation.

Needle representation



Needle collocation problem

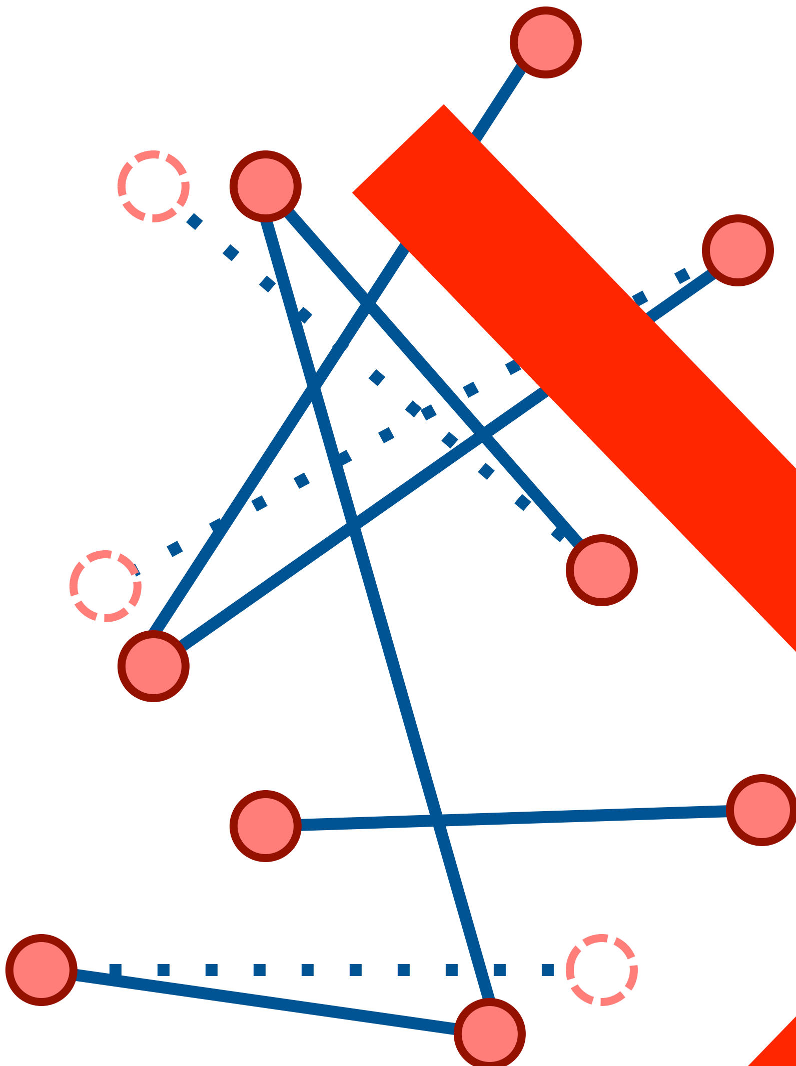
Given a collection of *n* needles, connect them into a smallest possible disjoint components that minimizes a length-related cost function.



6 disjoint needles

2 disjoint components

Algebraic formulation?



Original needl... $G=\{V,E\}$

V: vertex s...

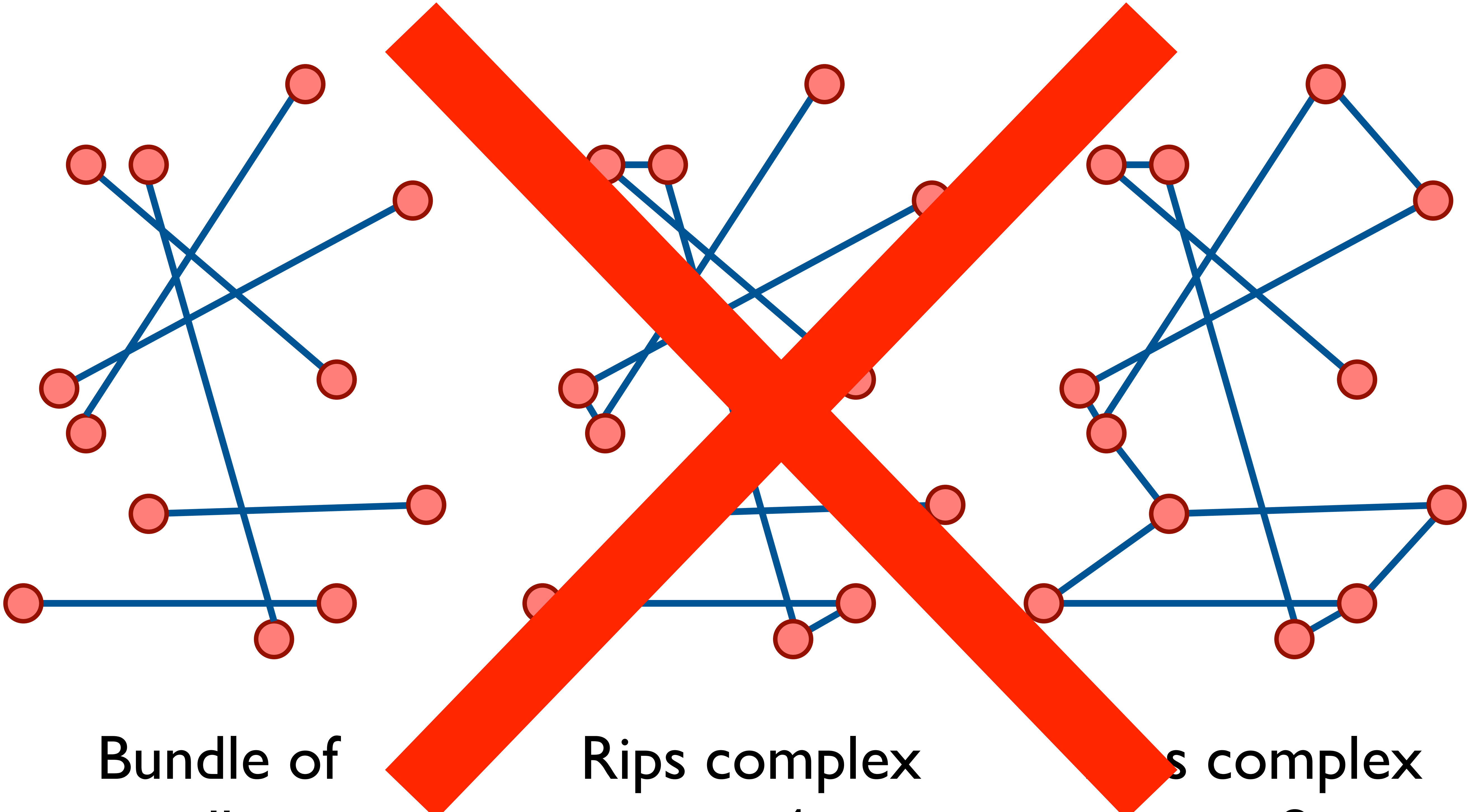
E: edge s...

Co...ted needles: $G_0=\{V_0,E_0\}$

Sparse graph regr...on:

$$\min_{E_0,V_0} f(E_0) + \lambda N(V_0) = \min_{E_0,V_0} \sum_{(i,j)\in E_0} c_{ij} + \lambda N(V_0)$$

Topological construct: Rips complex?



Bundle of needles

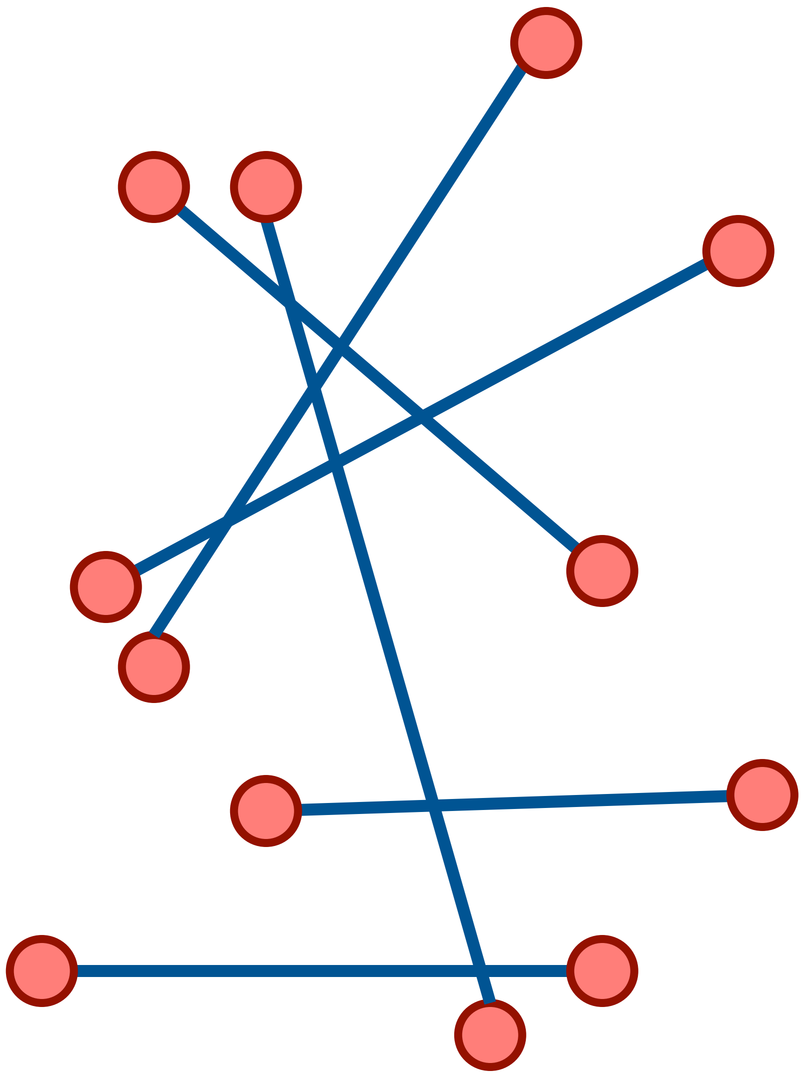
Rips complex with ε=1

s complex with ε=3

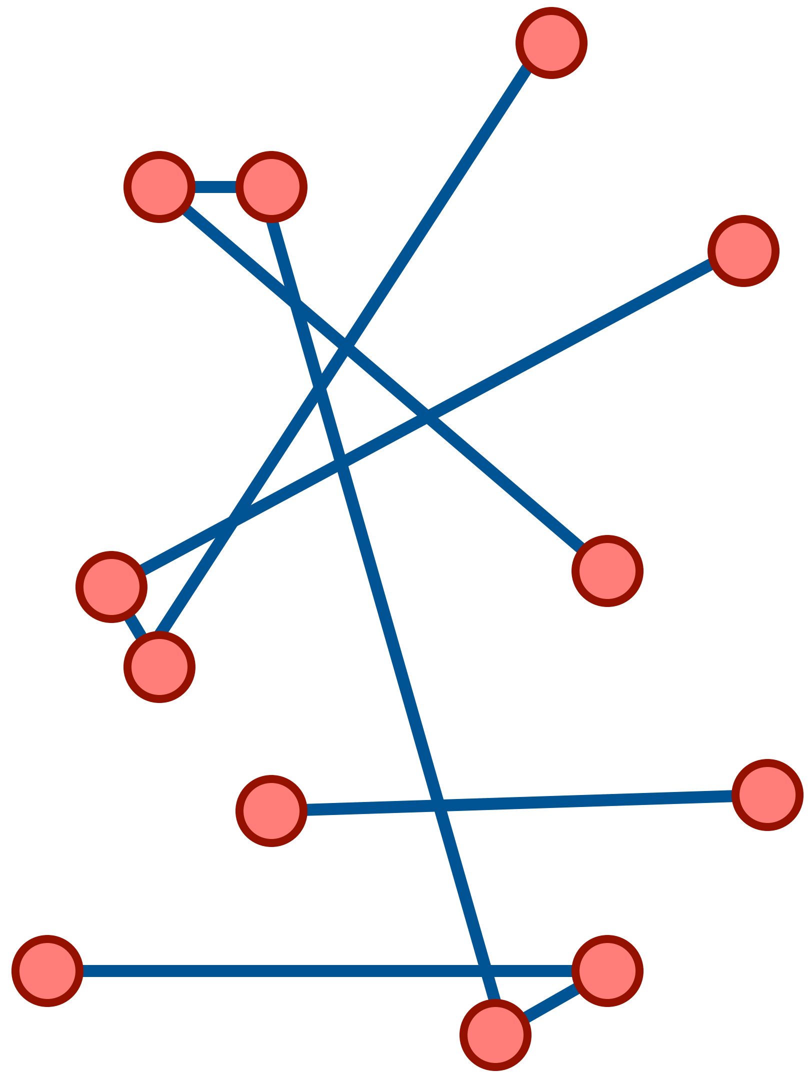
MATLAB DEMO

Rips complex

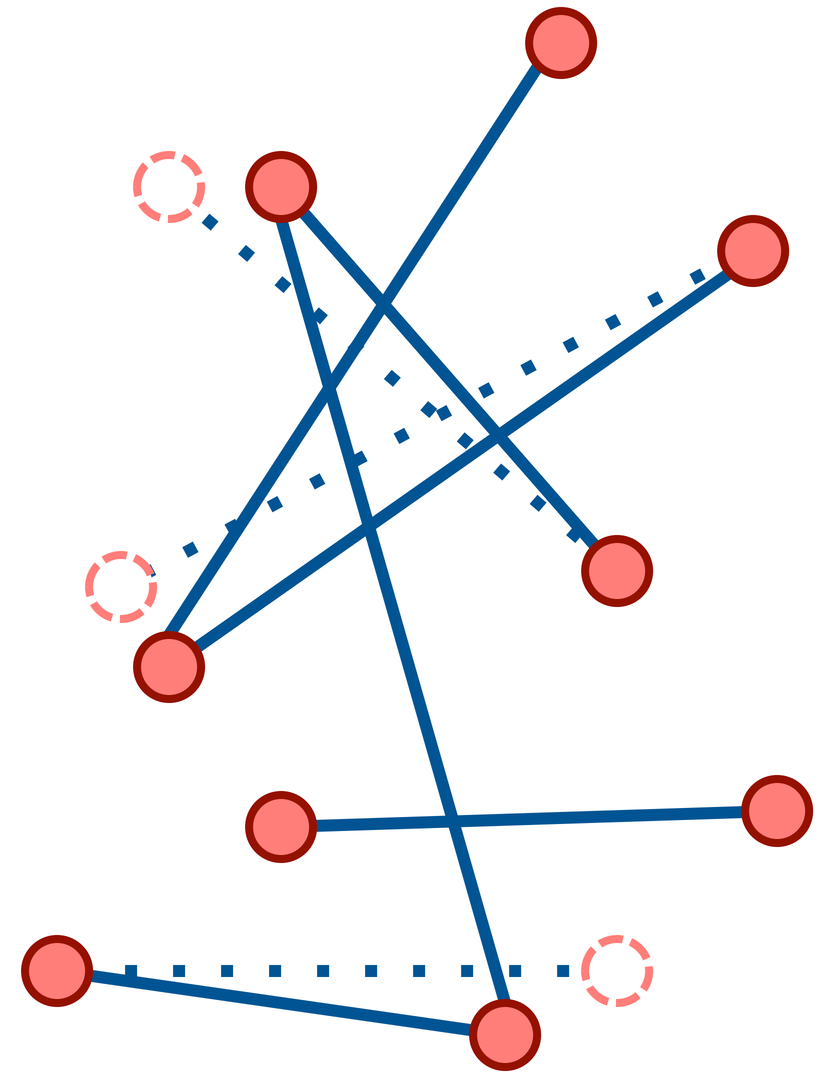
ε-neighbor network construction



Bundle of needles

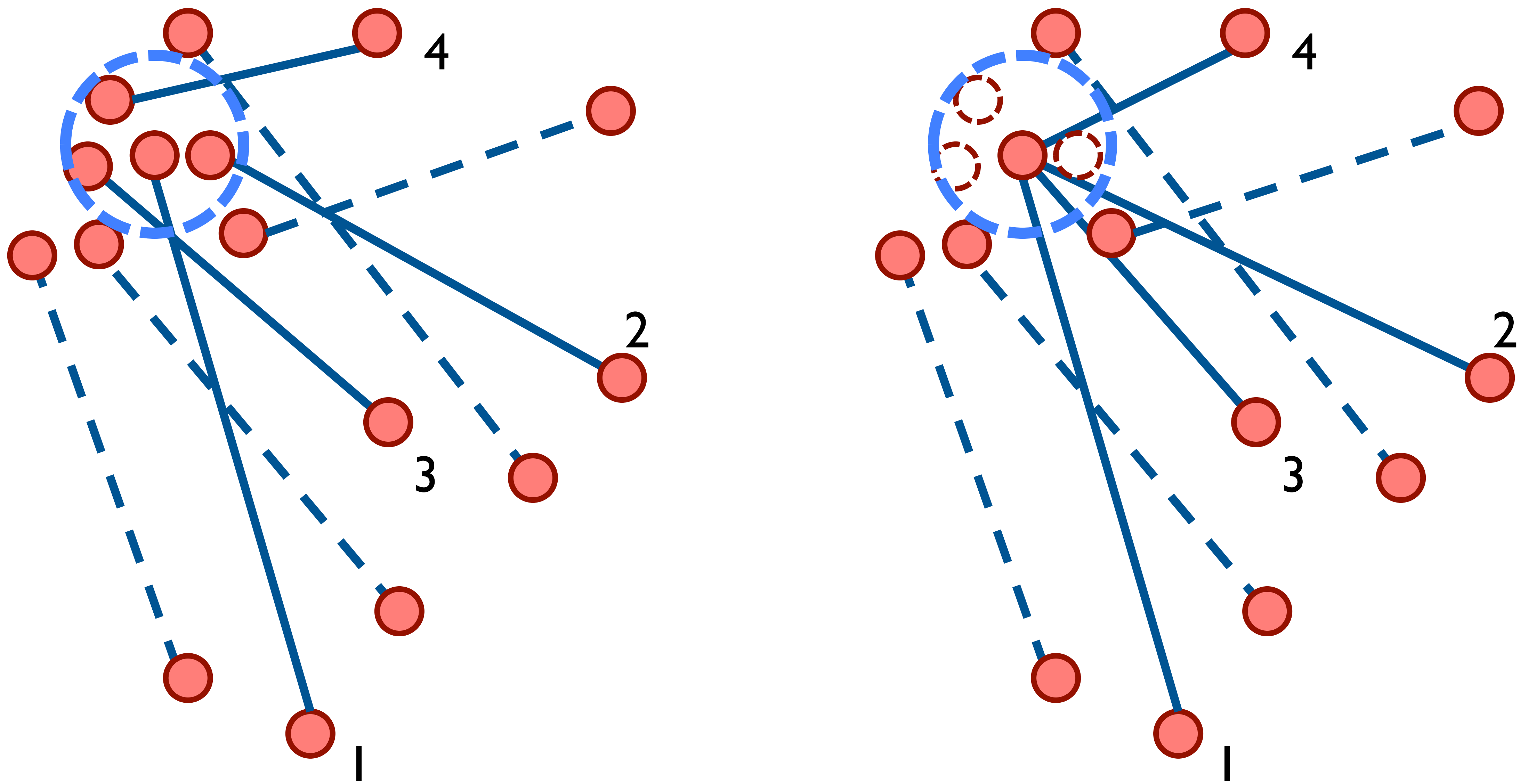


Rips complex with ε=1



ε-neighbor simplification

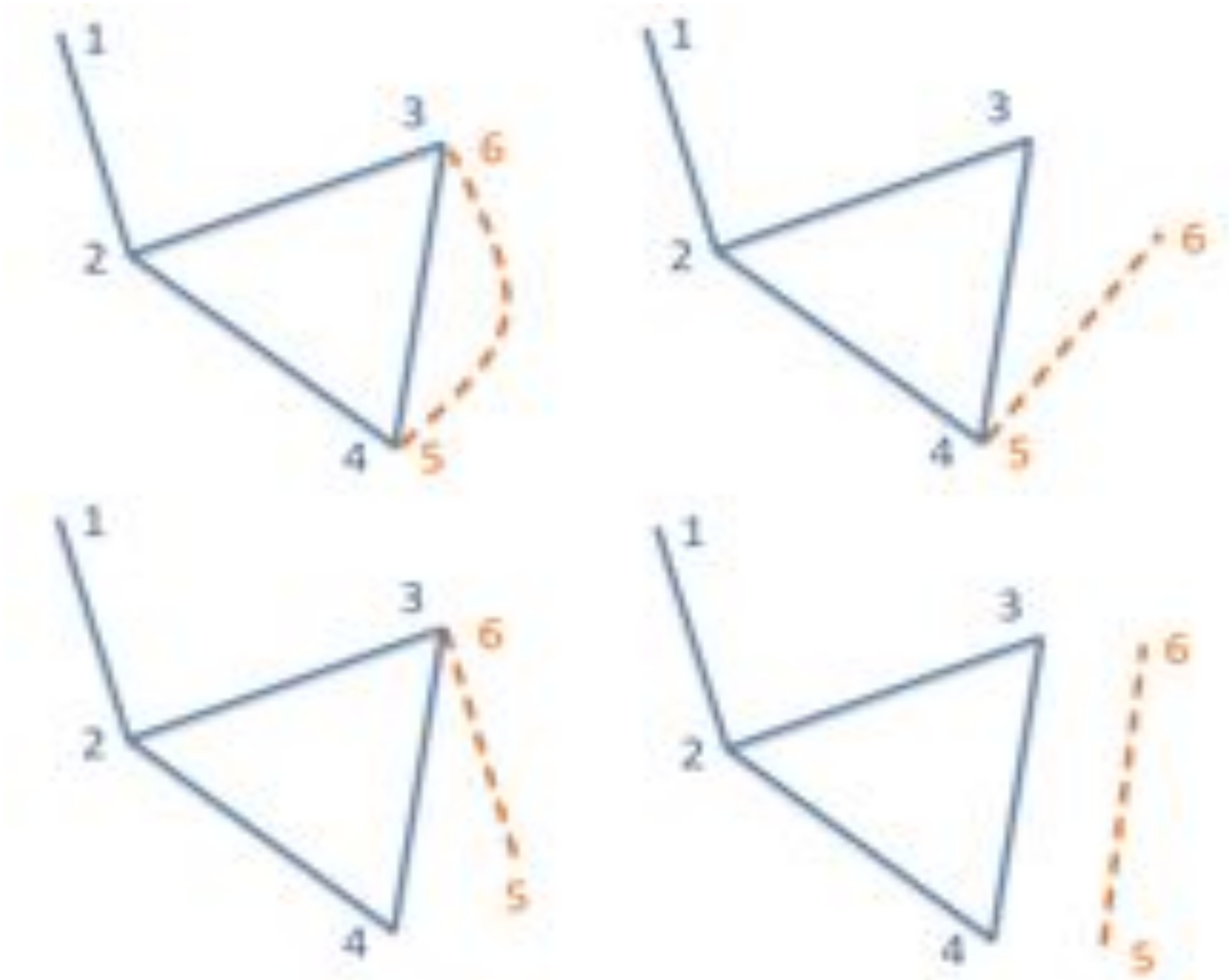
ε-neighbor graph simplification



Tract length:

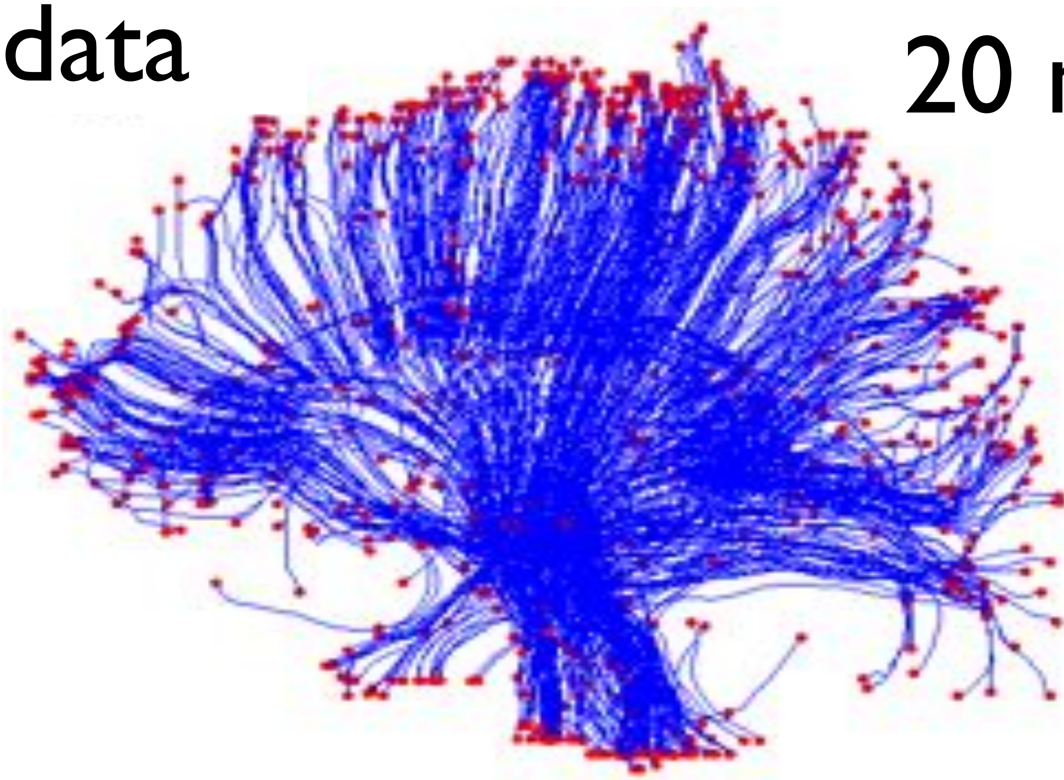
$$\rho_1 > \rho_2 > \rho_3 > \rho_4$$

Iterative epsilon network construction

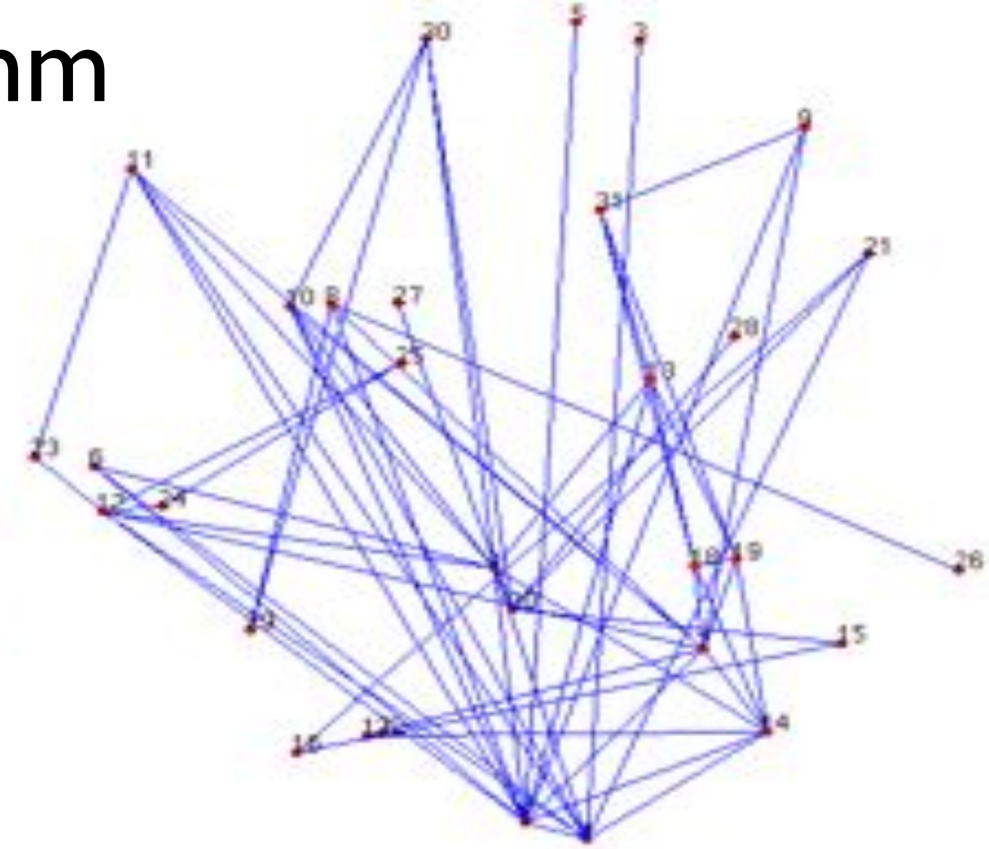


ε-neighbor graphs with different ε

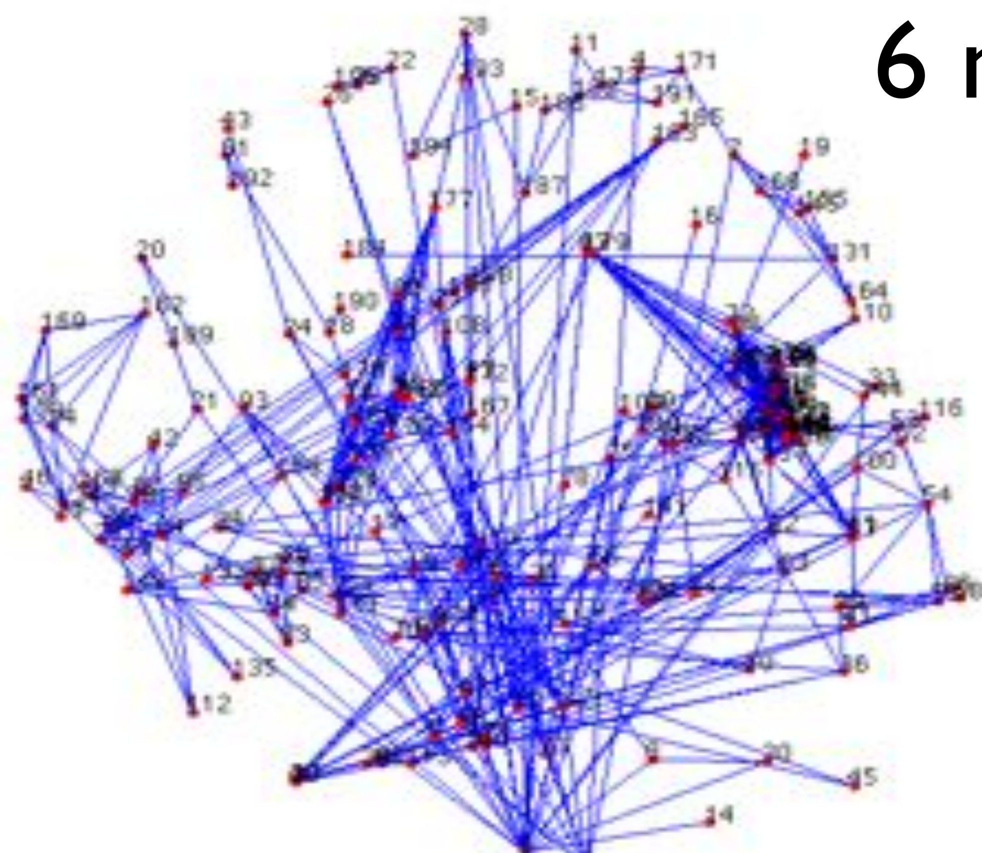
original data



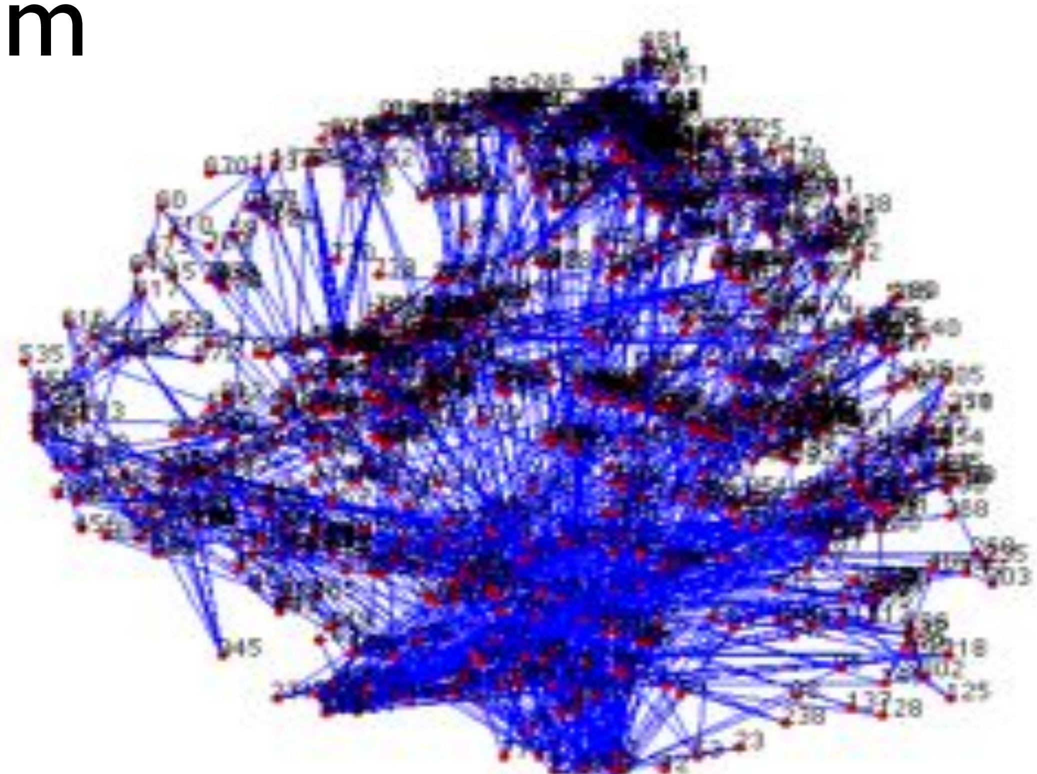
20 mm



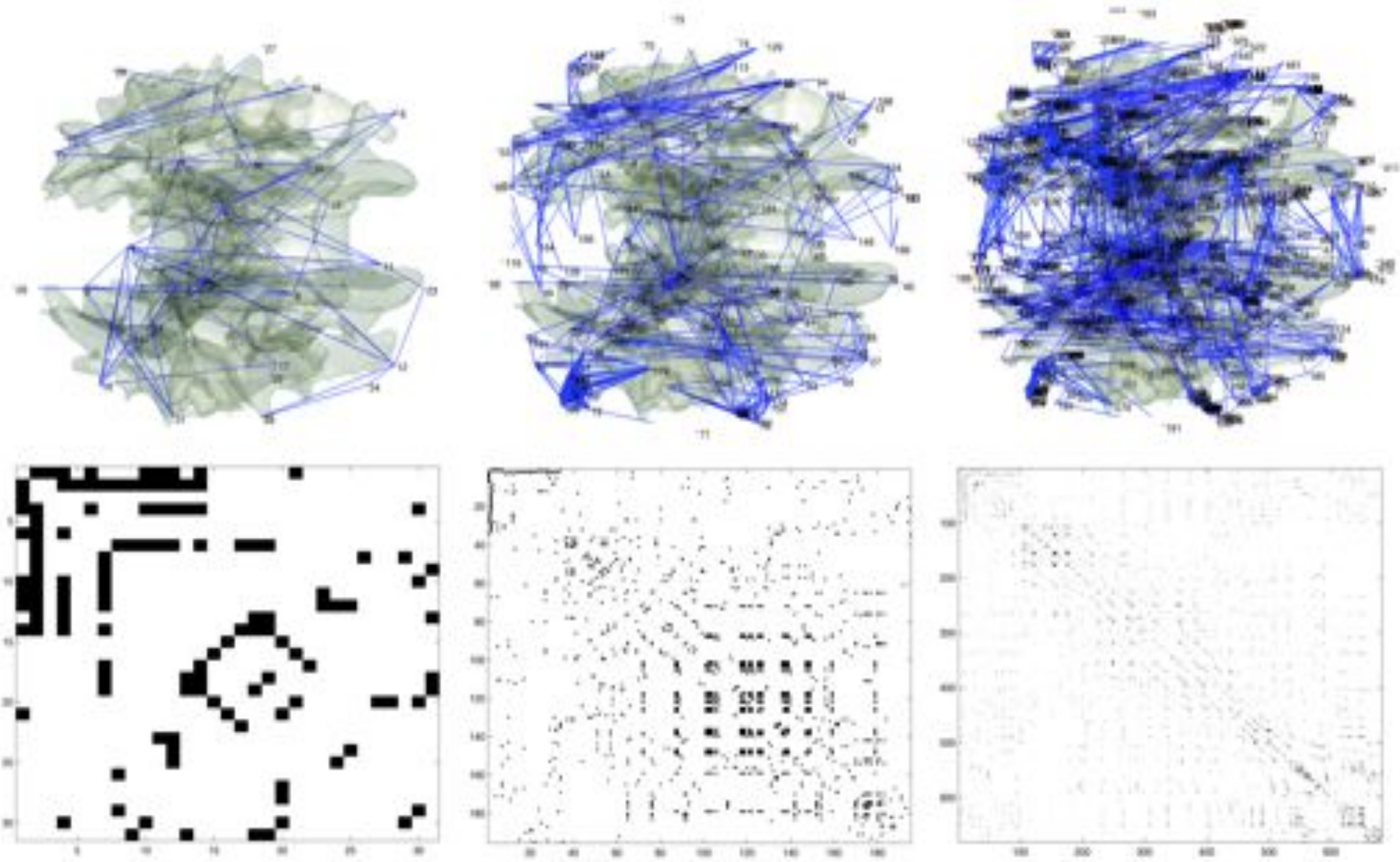
10 mm



6 mm



Adjacency matrix



MATLAB DEMO

Epsilon Neighbor method

/adjacency.matrix/matlab/DEMO.2011.07.09.IMSchina.m

Application

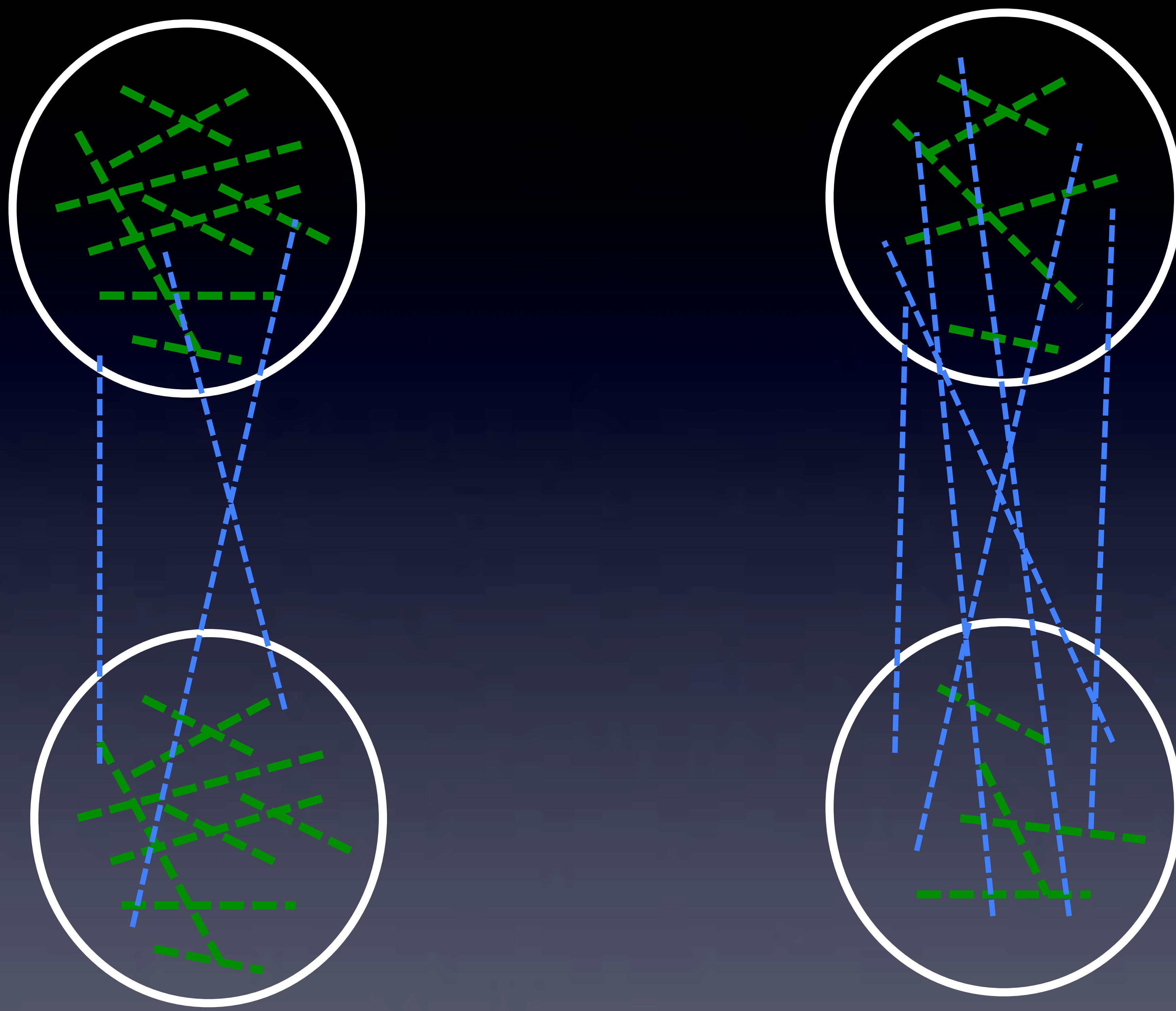
Dataset

Autistic children (n=17)
Control subjects (n=14)

Matched for age, handedness, IQ and head size

Abnormal connectivity in autism?

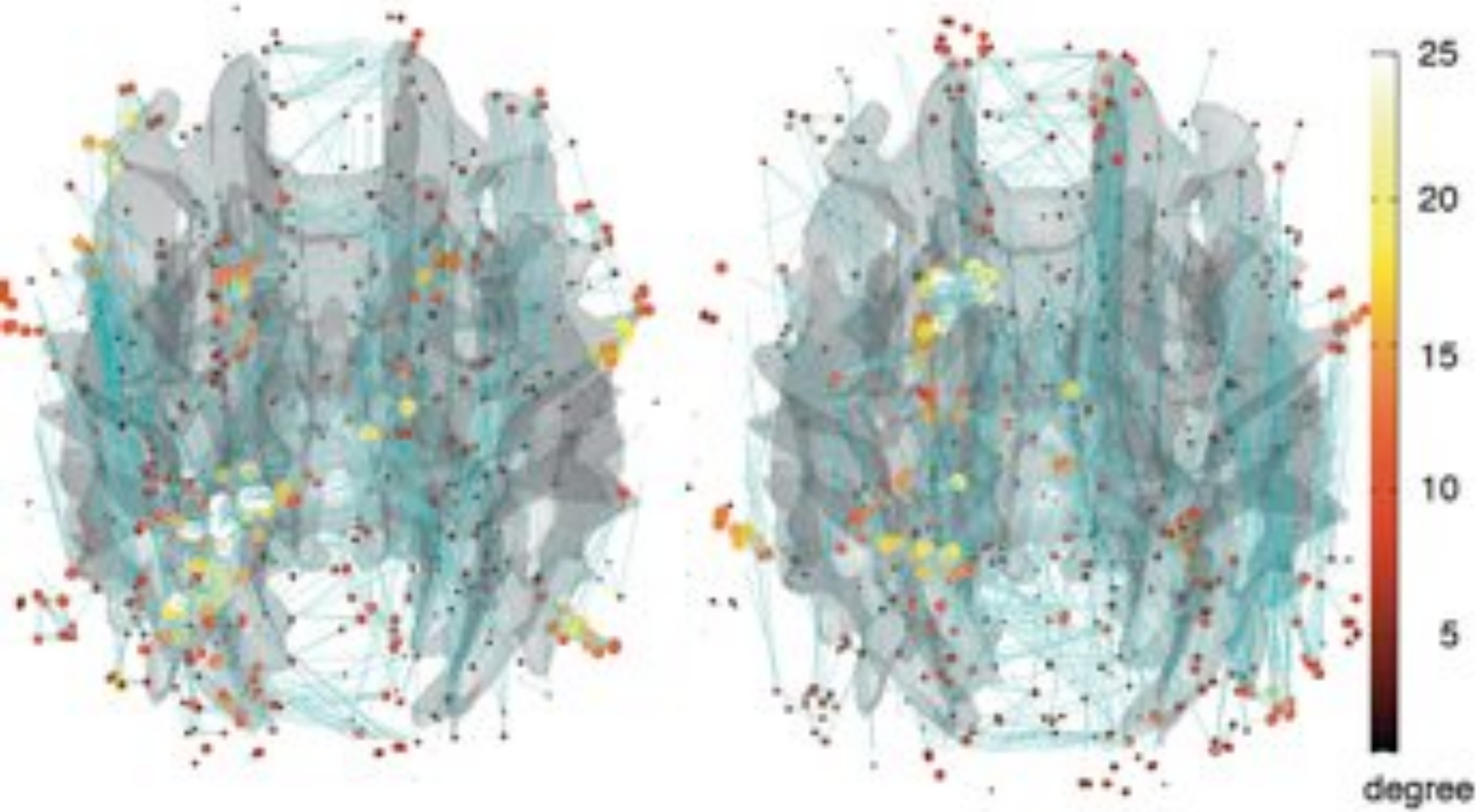
Connectivity hypothesis in autism



Local overconnectivity
global underconnectivity

Normal controls

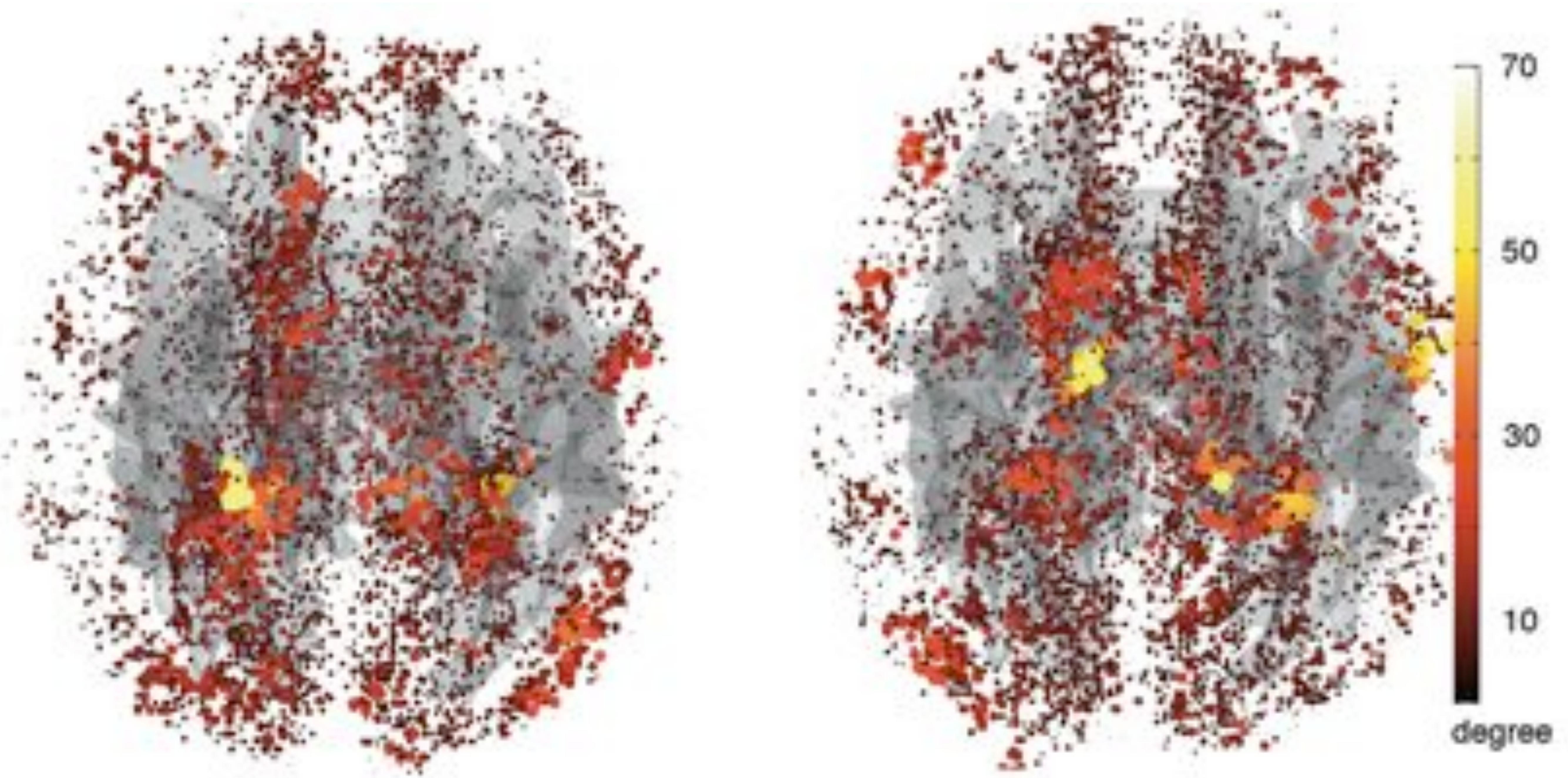
Node degree for a single subject



control #001 autism #120

Local inference on degree

Superimposition of every subjects

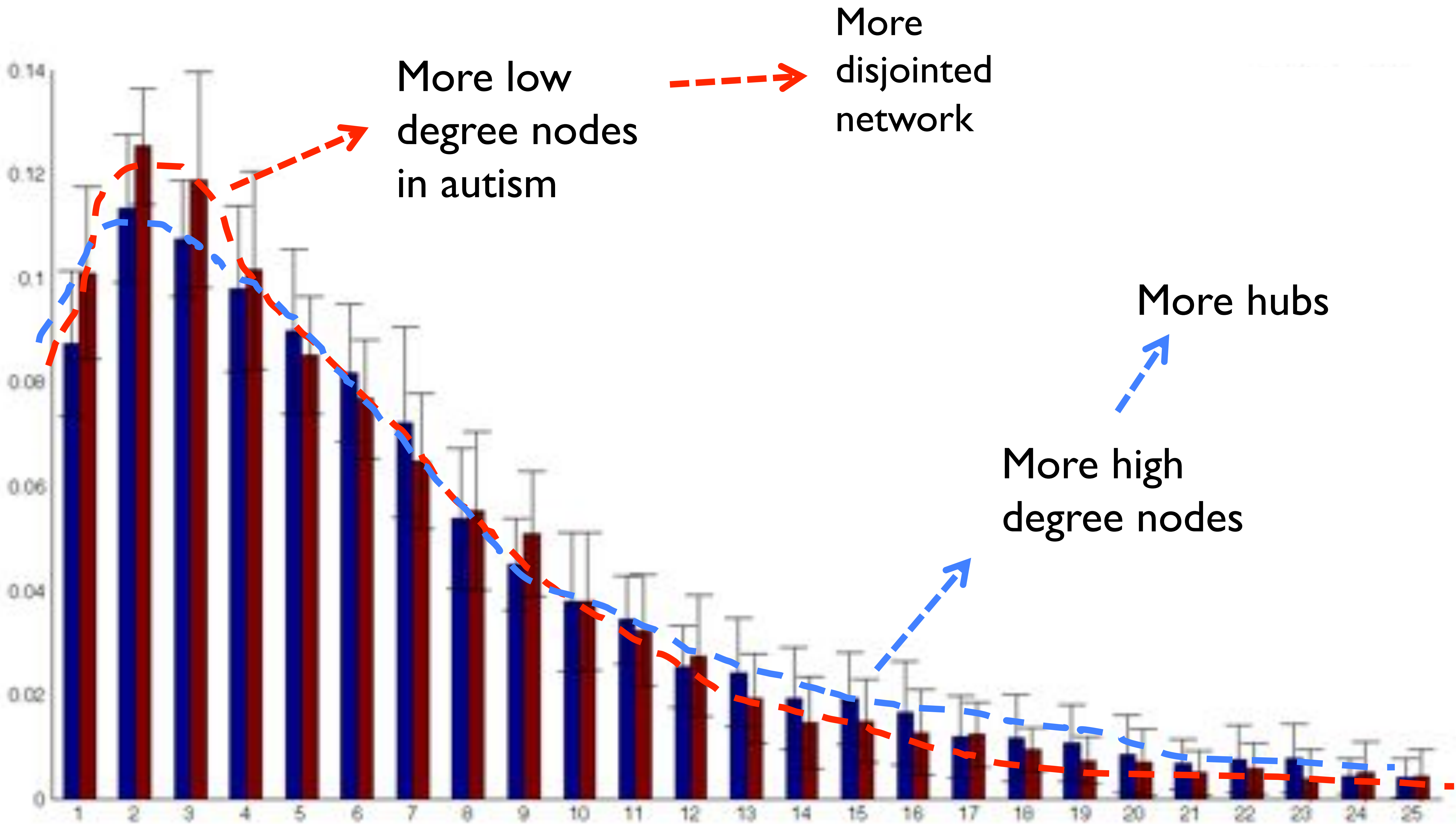


Control

Autism

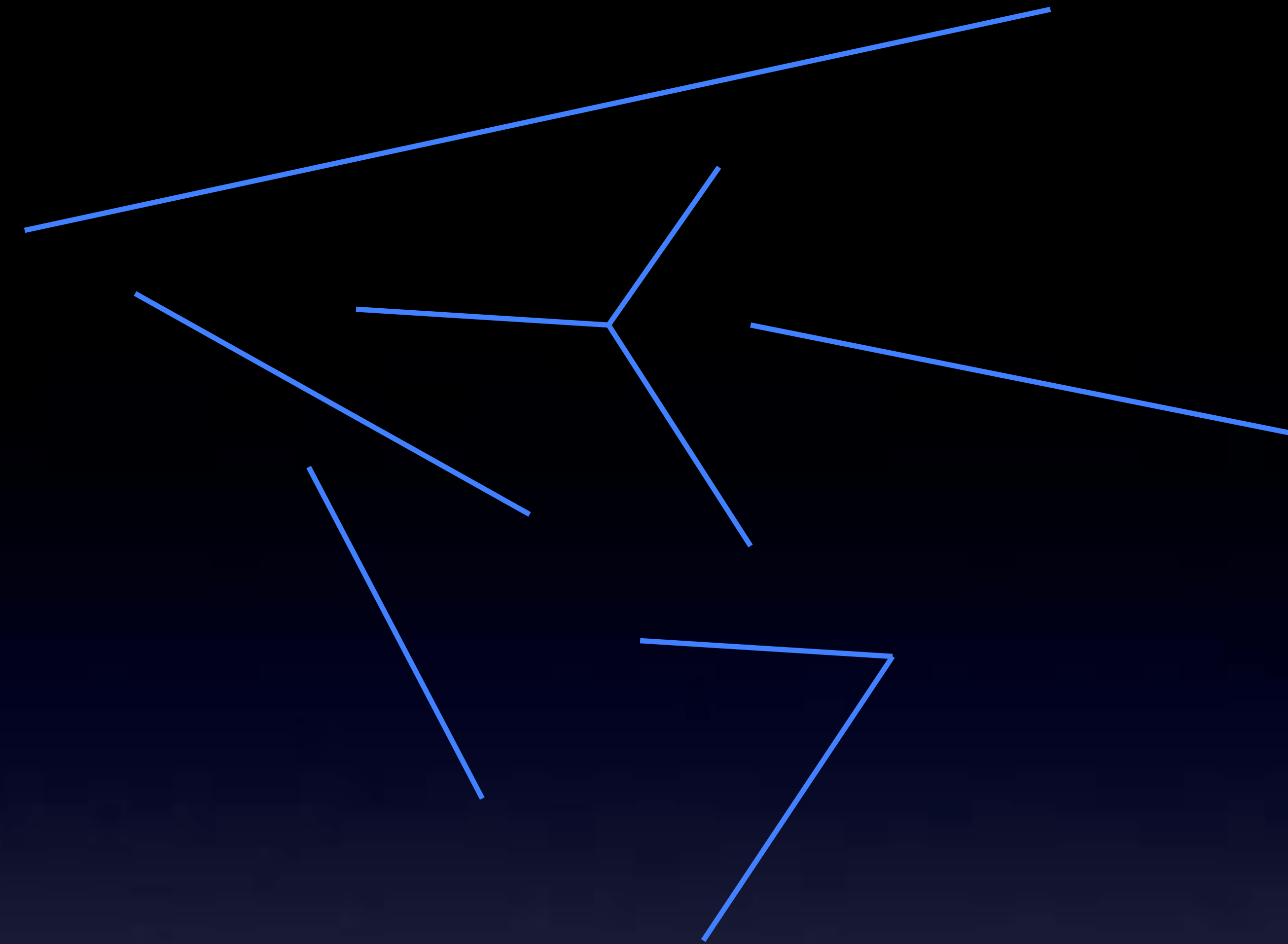
Degree distribution

red: autism
blue: control

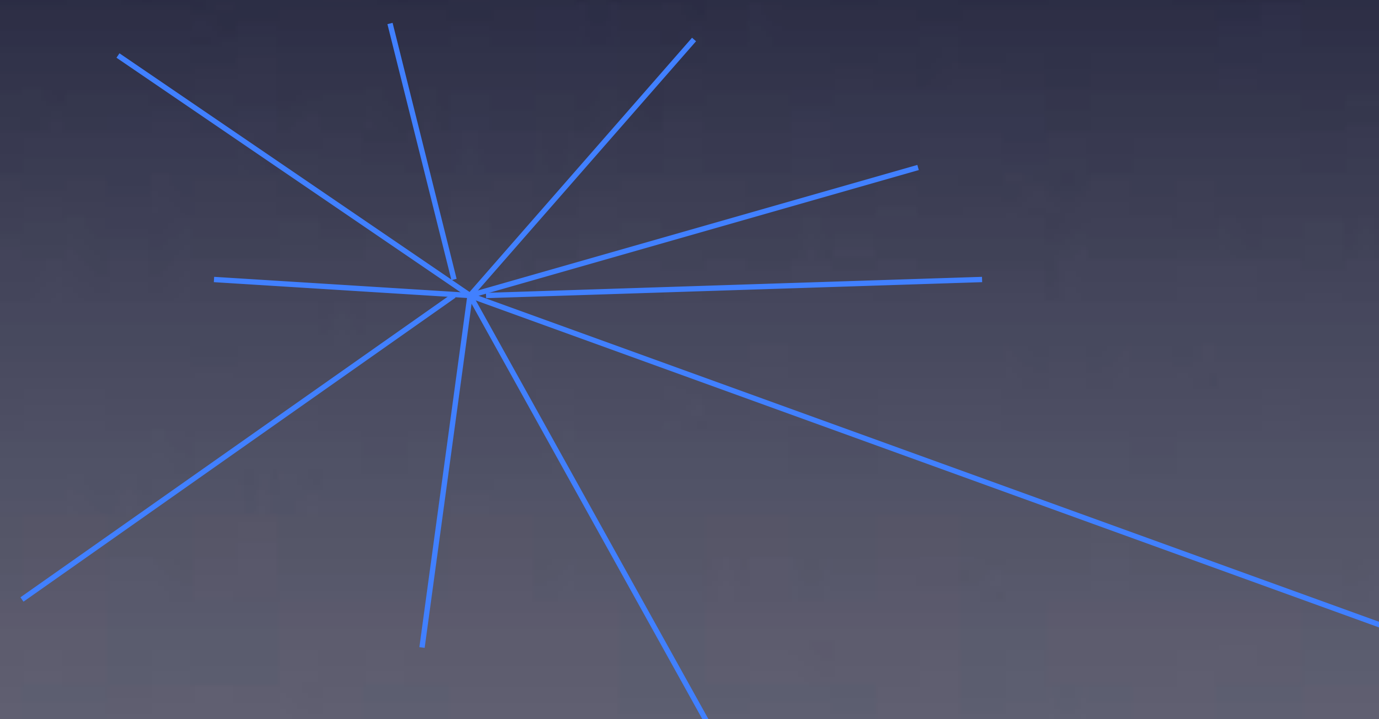


pvalues = 0.024, 0.015 and 0.080 for degrees 1, 2 and 3.

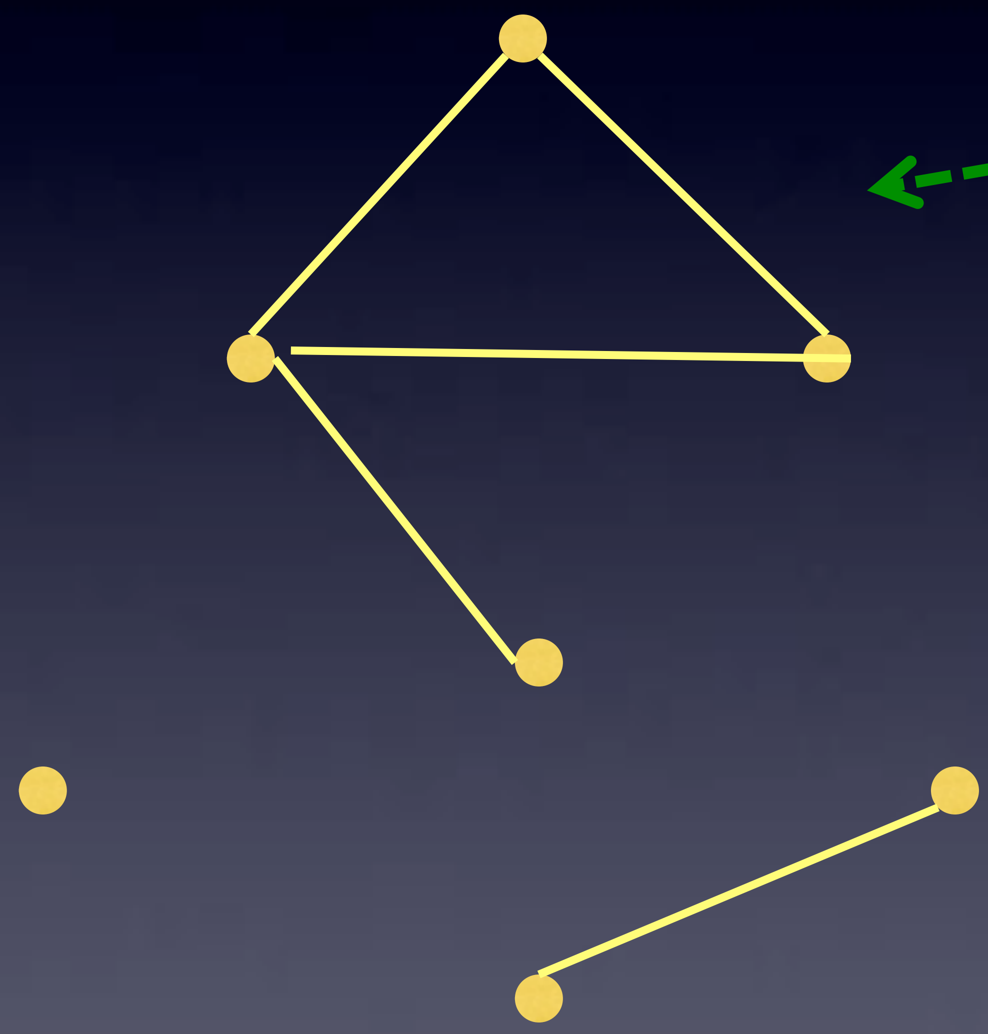
Autism



Control



Connected component



largest connected component

Filtration on ε-neighbor graphs

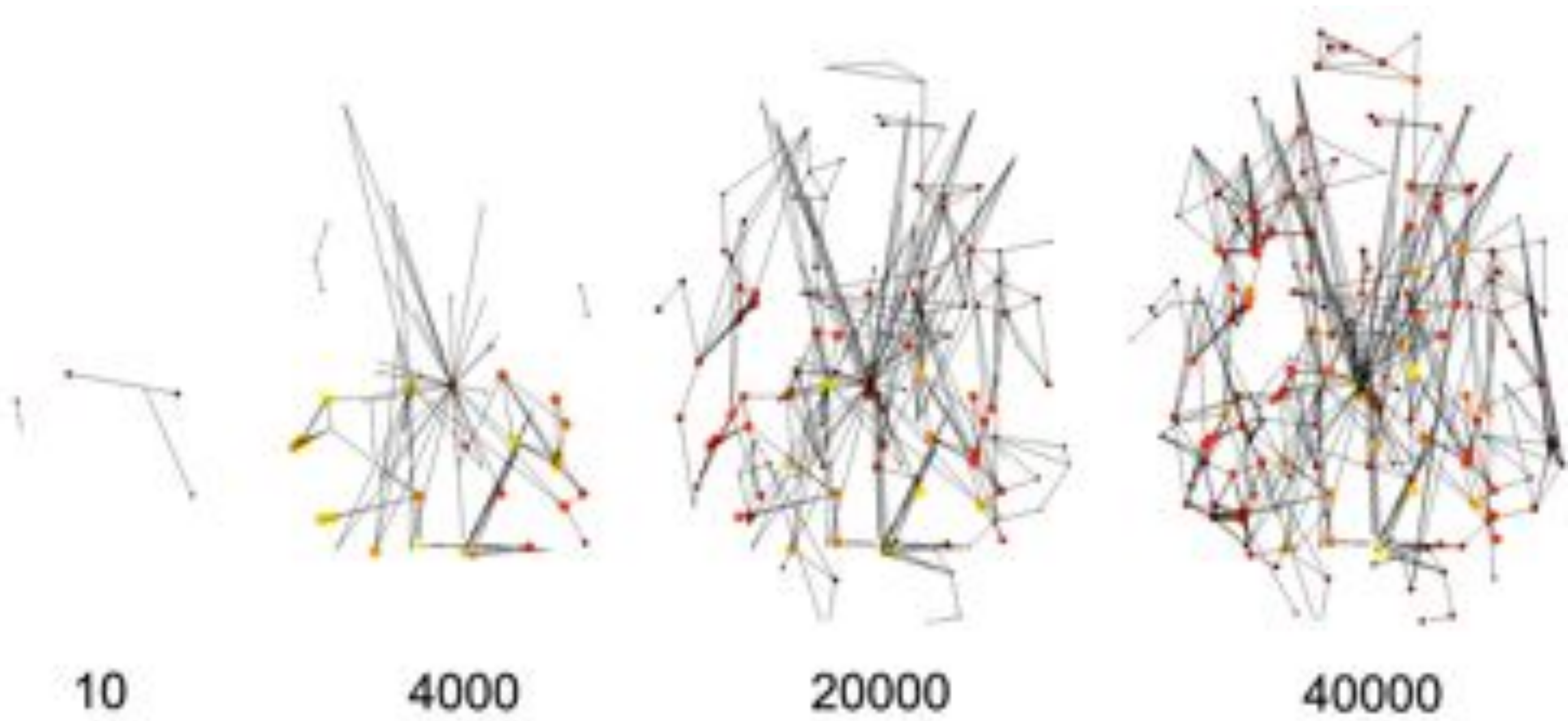
ε-neighbor graph at the *i*-th iteration $\mathcal{G}_i$

$$\mathcal{G}_1 \subset \mathcal{G}_2 \subset \mathcal{G}_3 \subset \cdots$$

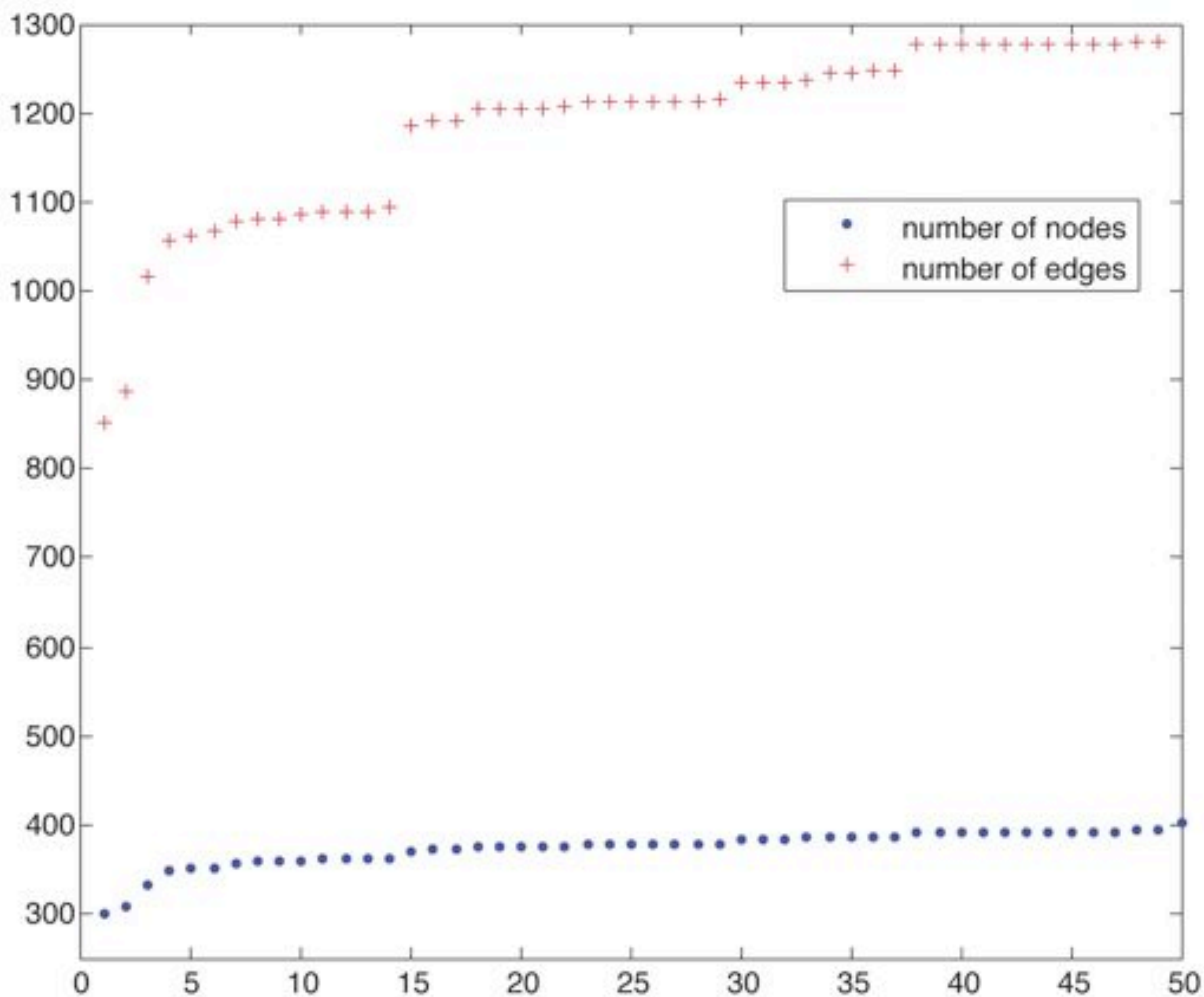
The size of the largest connected component:

$$\#\mathcal{G}_1 < \#\mathcal{G}_2 < \#\mathcal{G}_3 < \cdots$$

Filtration on ε-neighbor networks

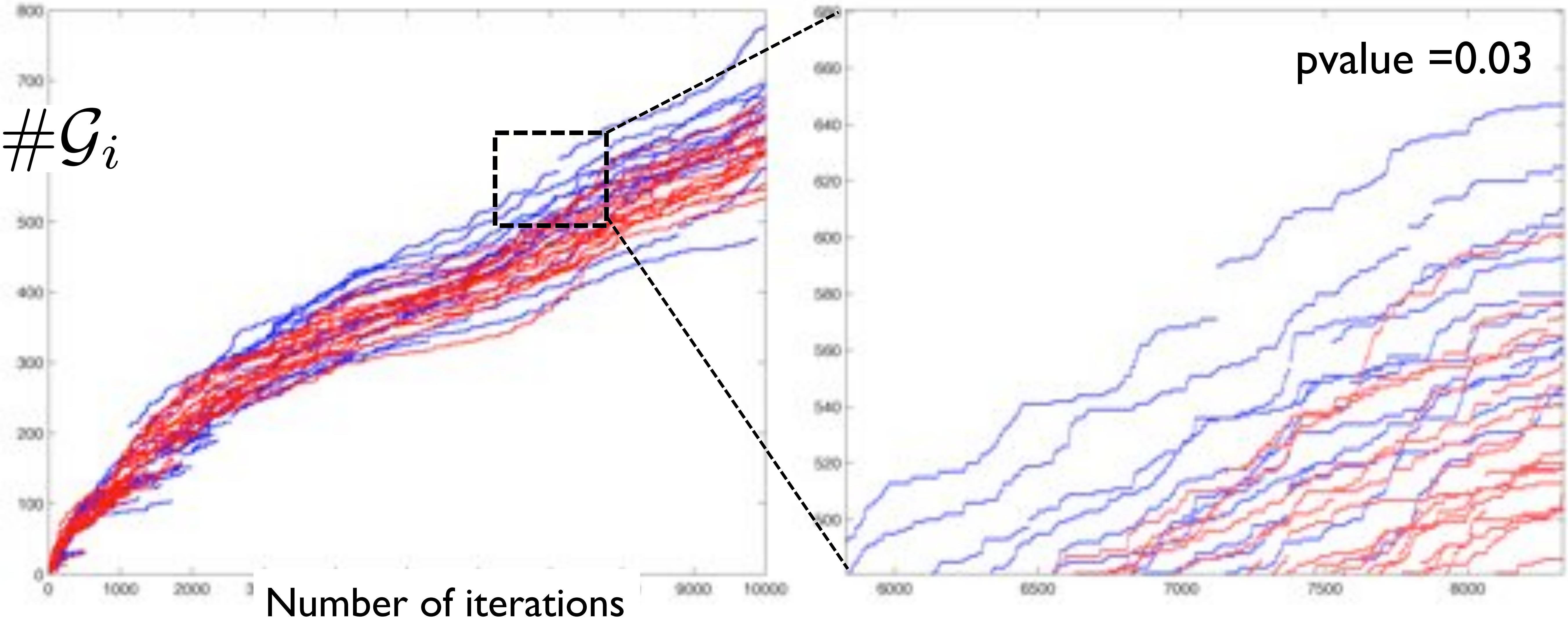


Number of edges and nodes in filtration



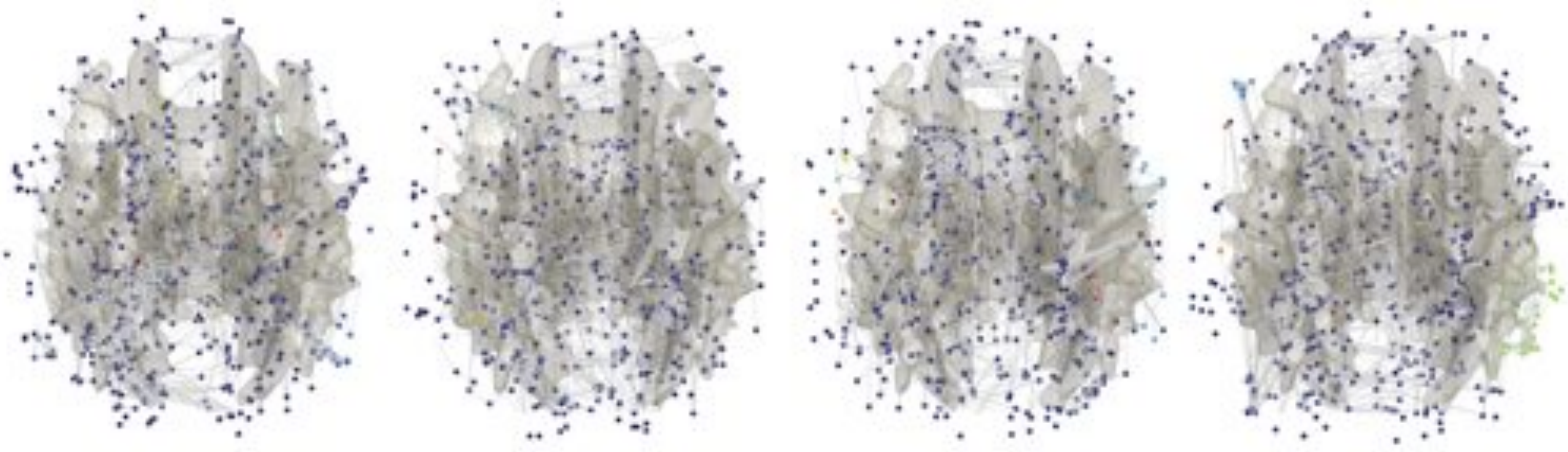
Network filtration difference

Control=blue
Autism=red



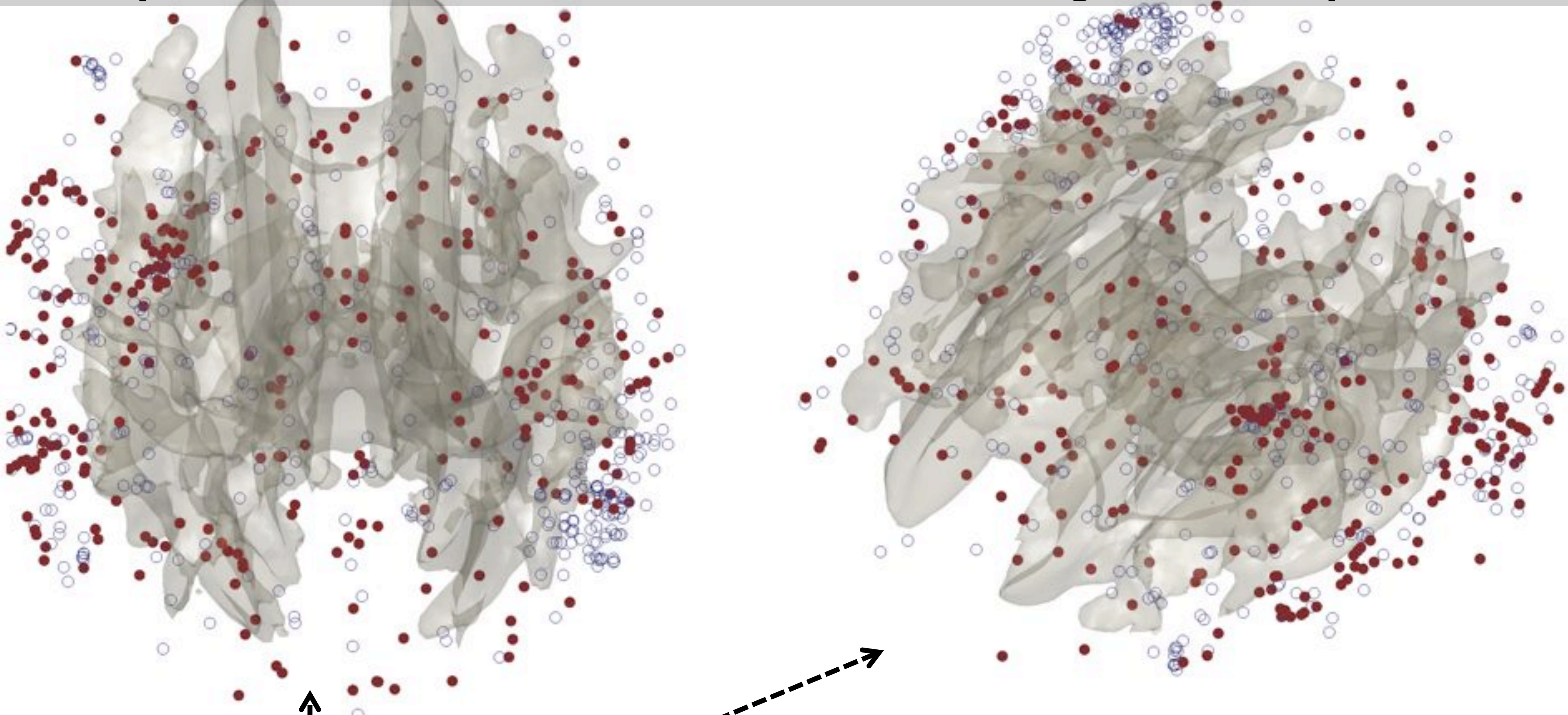
The brain network in control subjects merges to a single component faster than other populations.

Largest connected component for 4 subjects



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.

Group difference in the size of the largest component



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

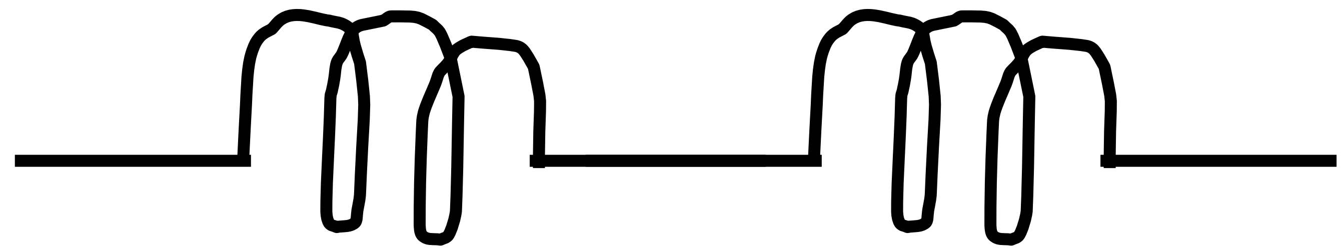
Physics of myelinated neuronal fibers

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.

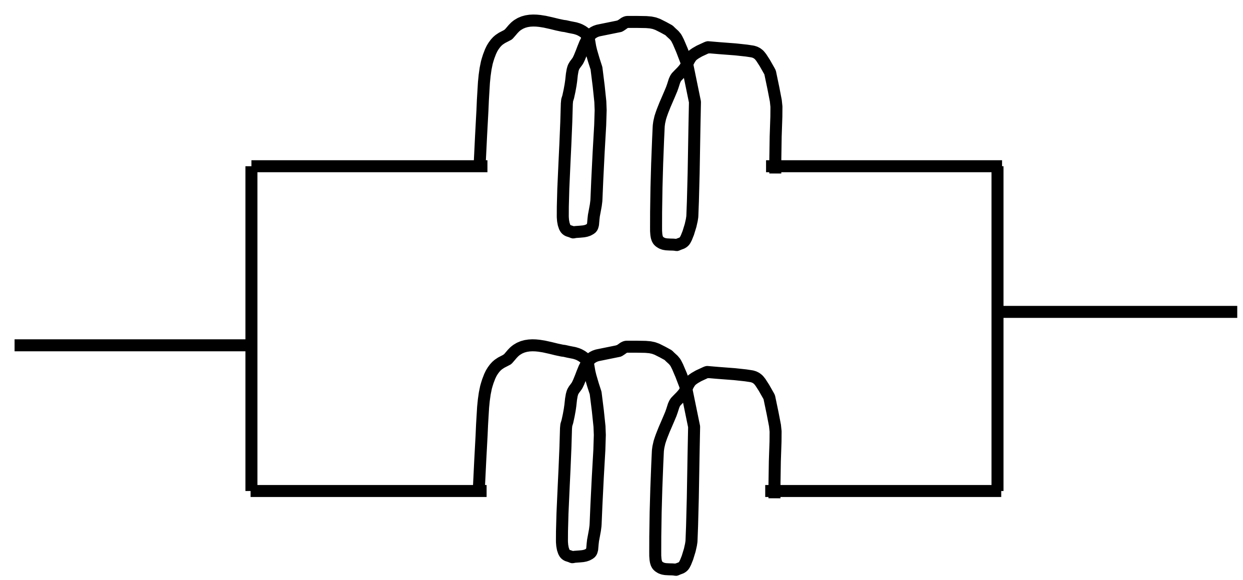
Basic circuit physics: Ohm's law

Series circuit



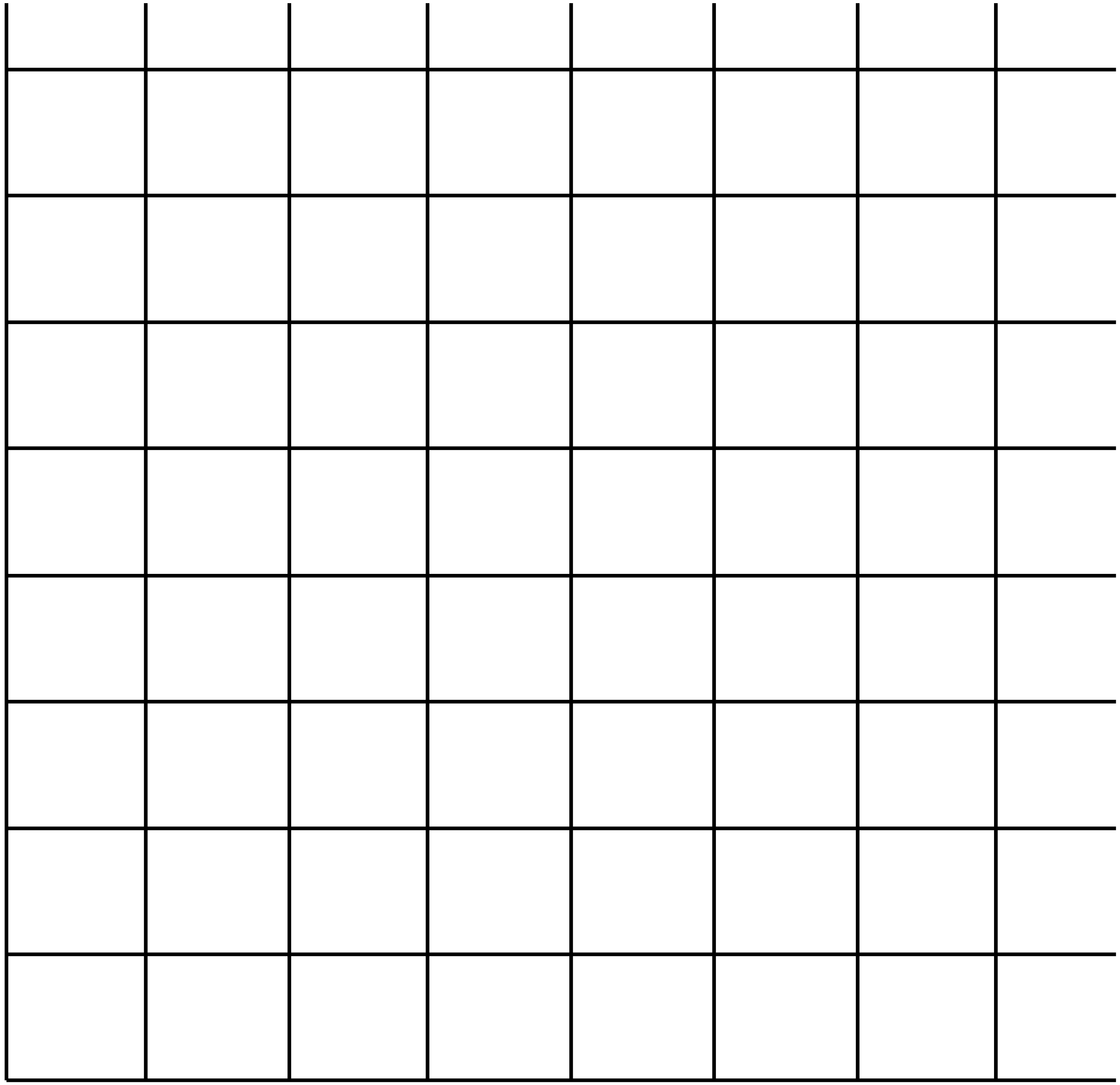
$$R = R_1 + R_2$$

Parallel circuit



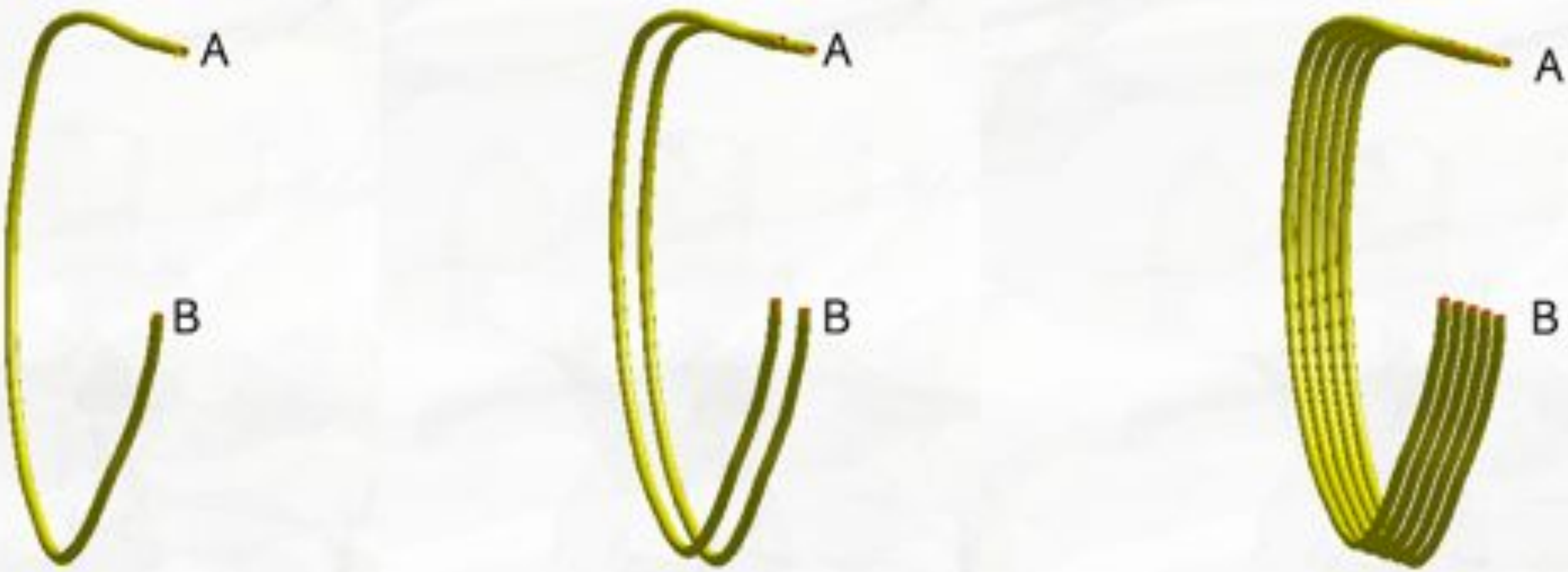
$$\frac{1}{R} = \frac{1}{R_1} + \frac{1}{R_2}$$

Infinite circuit



Compute the total resistance.

Resistance for parallel tracts



$$R = 10$$

$$\frac{1}{R} = \frac{1}{10} + \frac{1}{10}$$

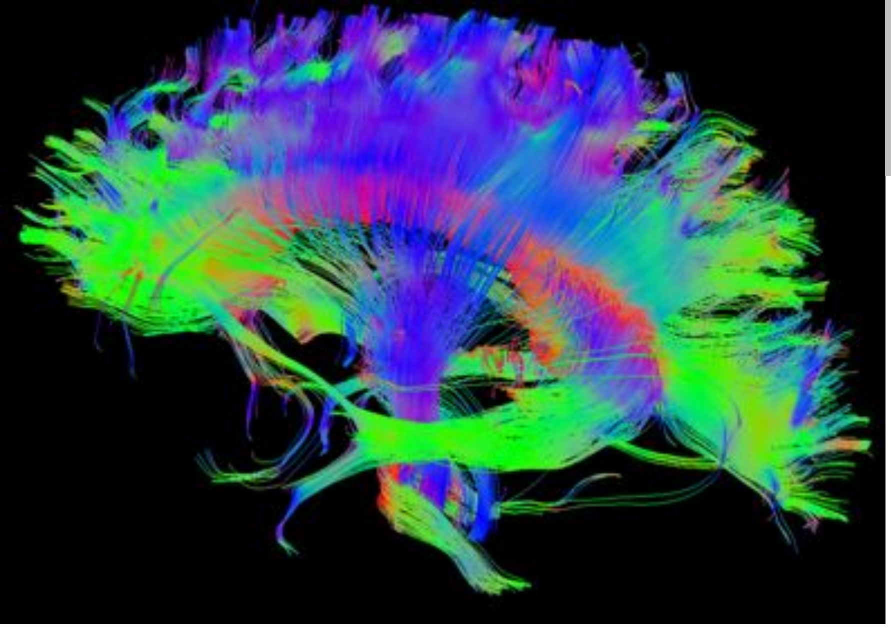
$$R = 5$$

$$\frac{1}{R} = \frac{1}{10} + \frac{1}{10} + \frac{1}{10} + \frac{1}{10} + \frac{1}{10}$$

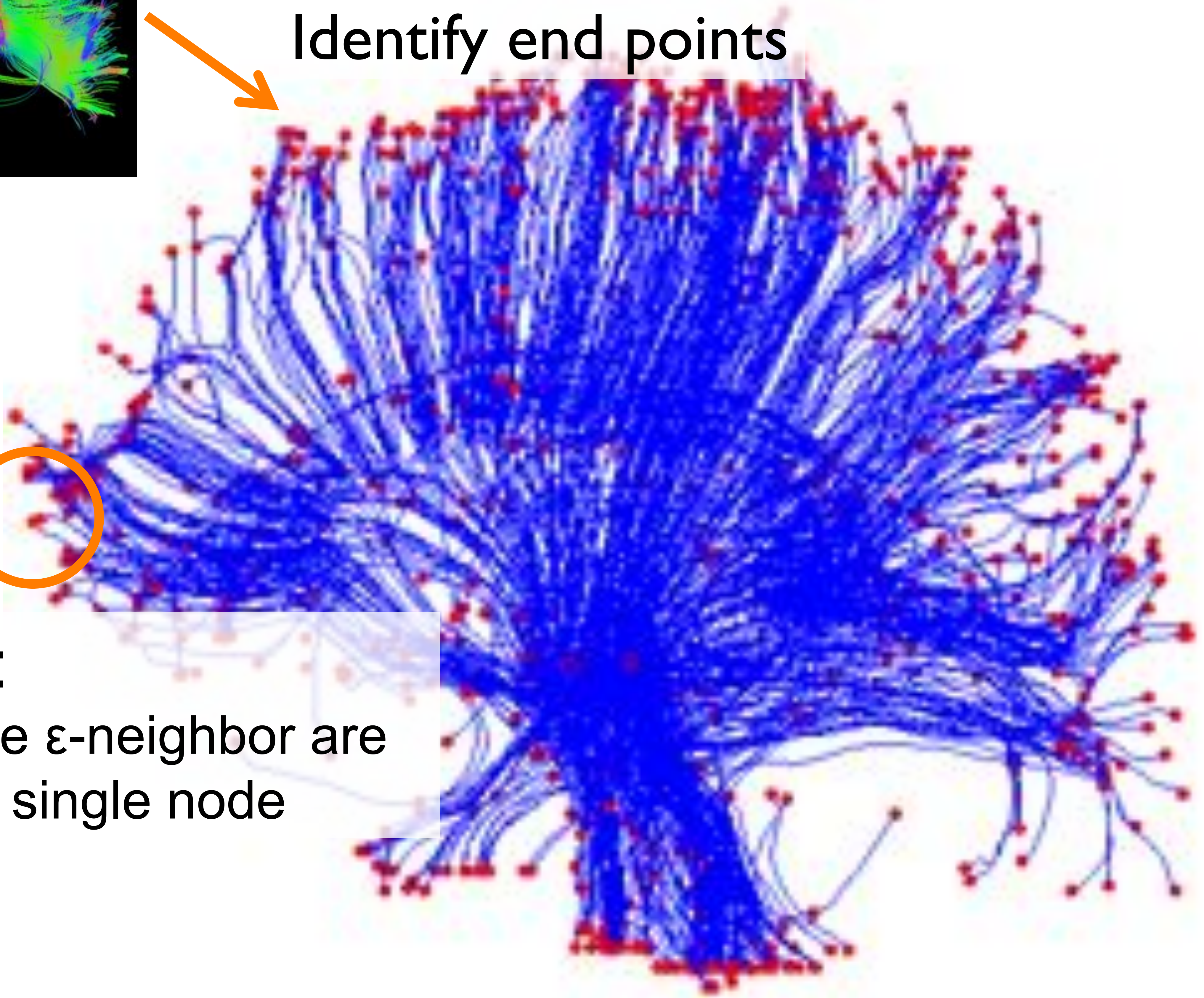
$$R = 2$$

More tracts = less resistance

Electronic circuit construction



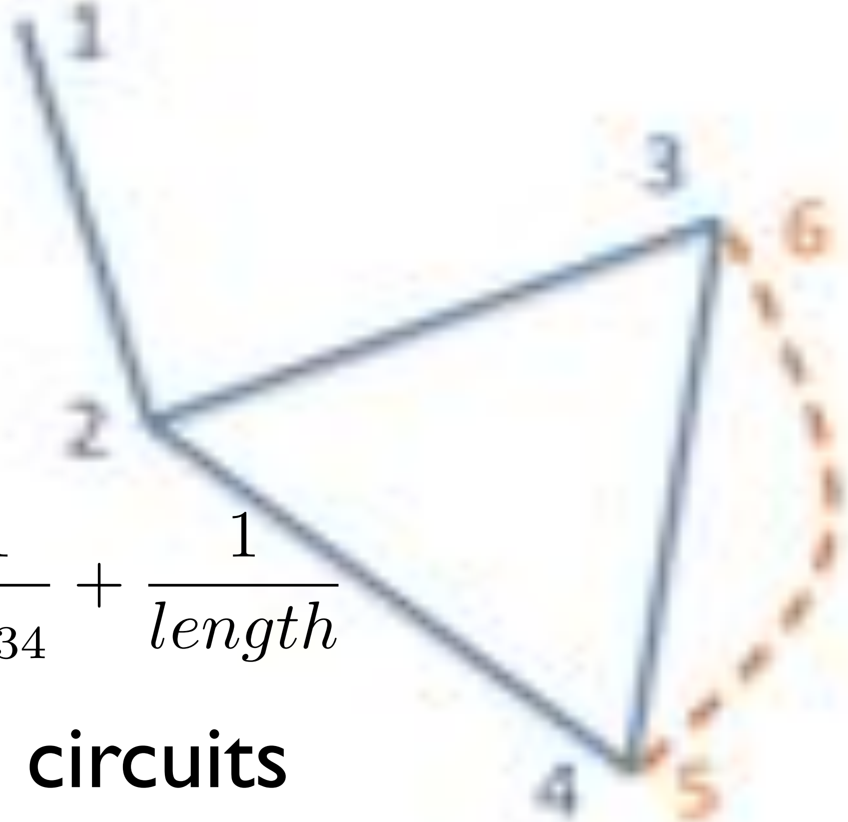
Identify end points



ε-neighbor:

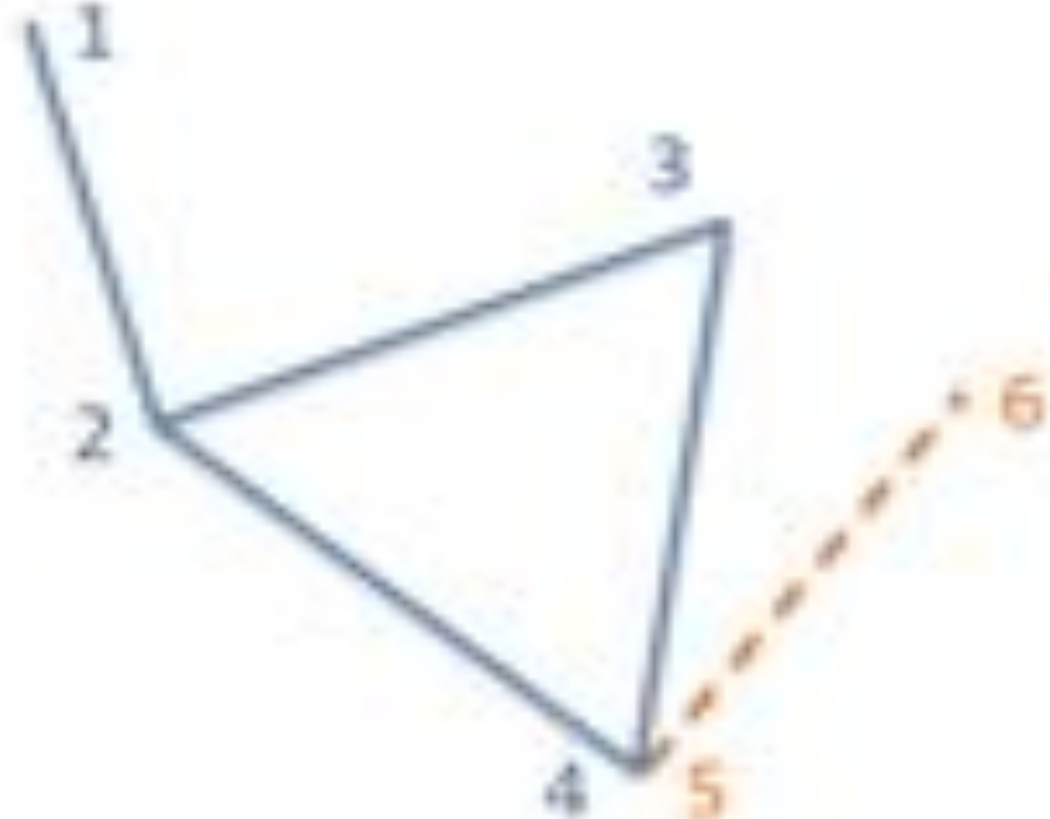
All points in the ε-neighbor are identified as a single node

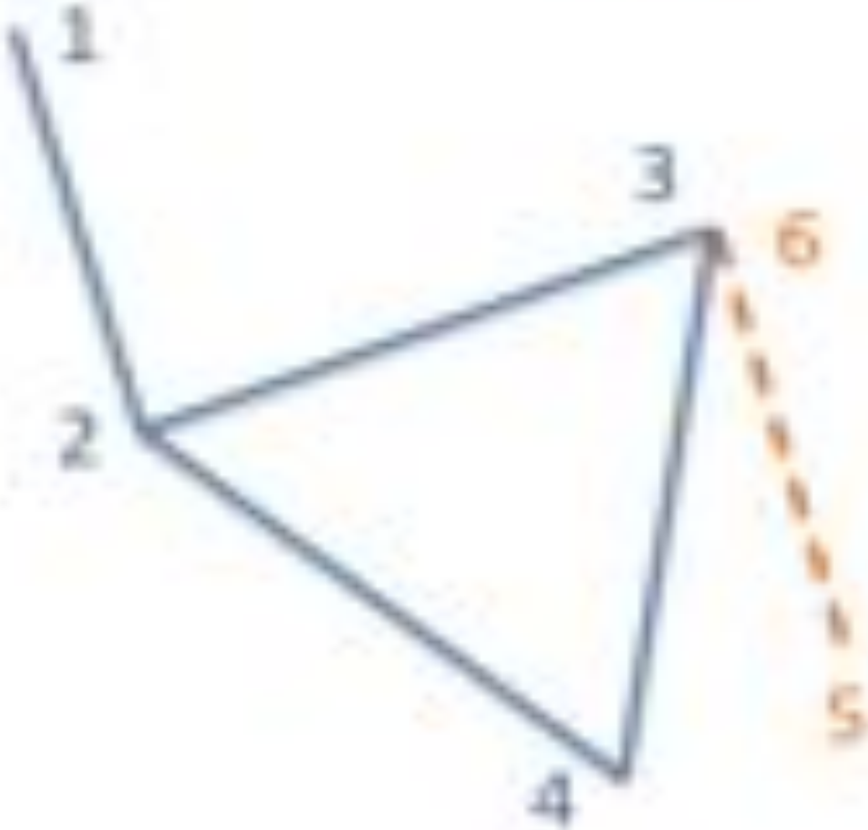
Four possible scenarios for adding a tract to the graph

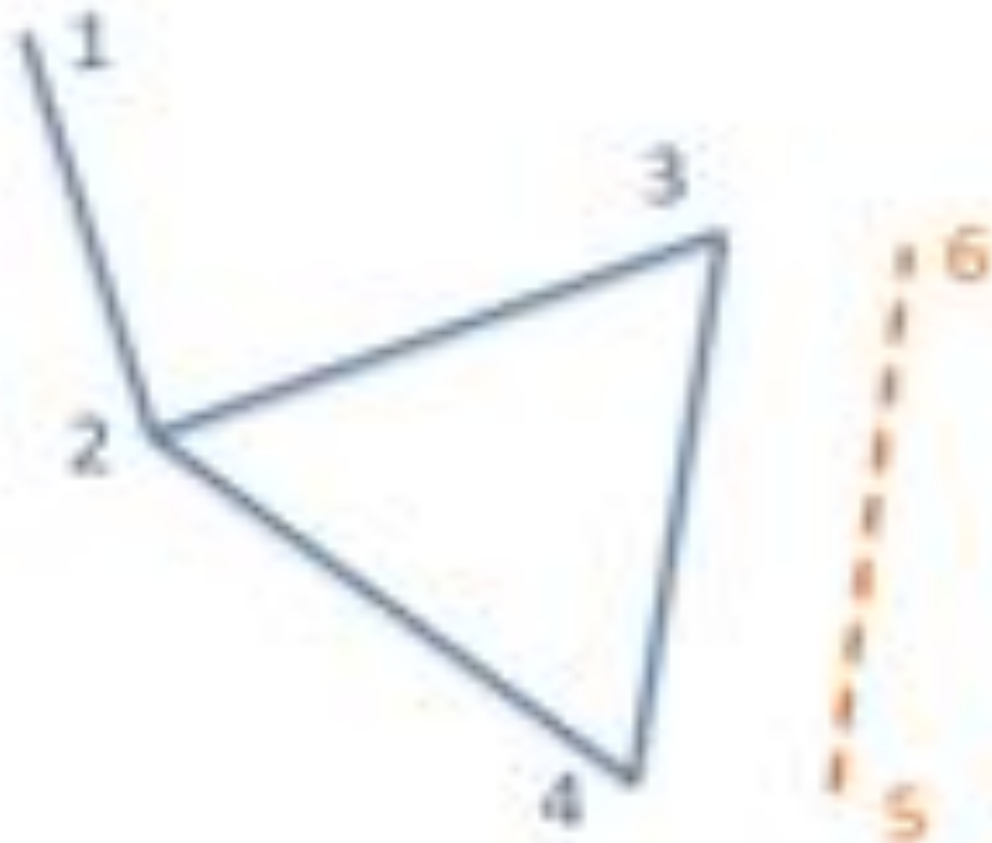


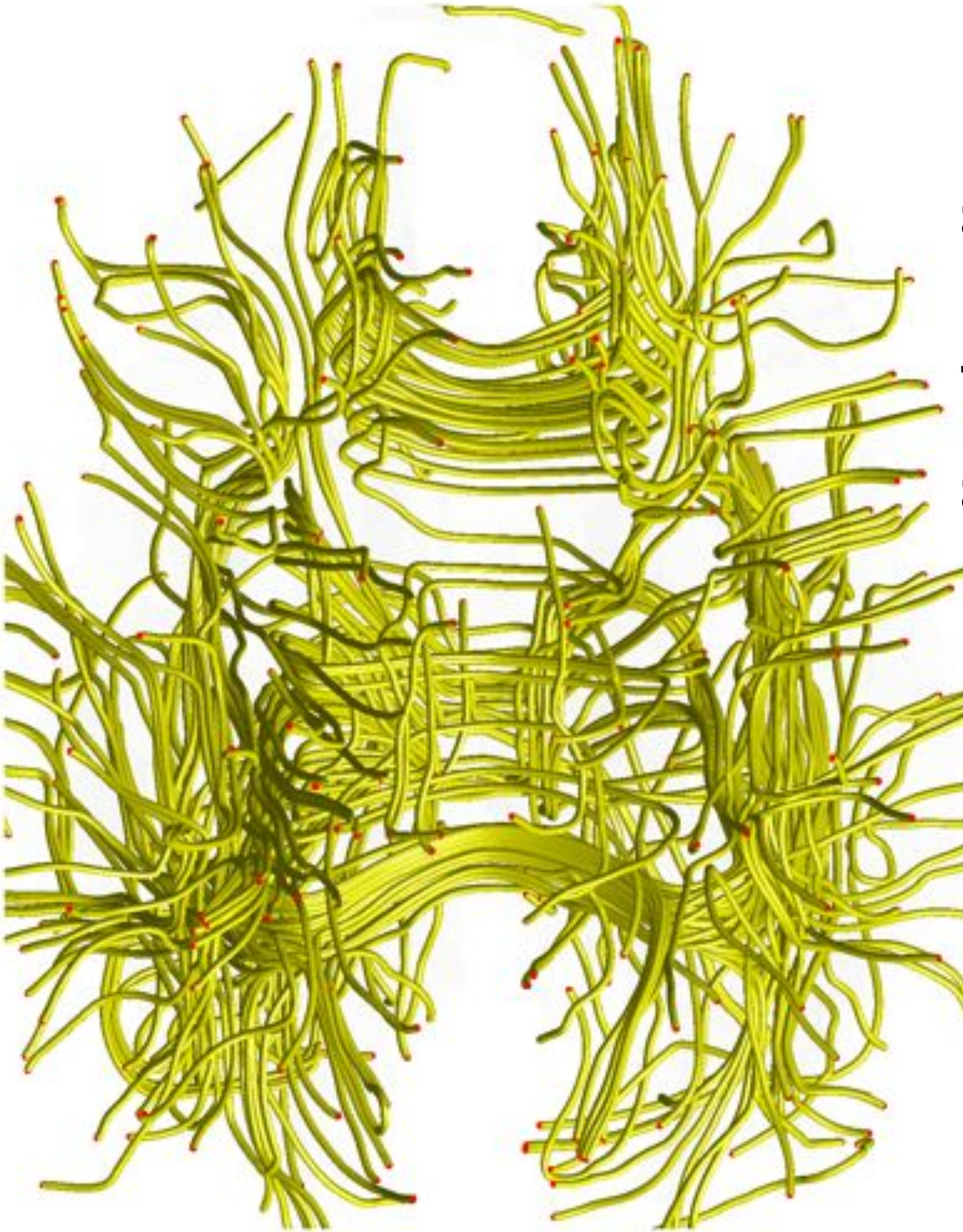
$$\frac{1}{R_{34}} \leftarrow \frac{1}{R_{34}} + \frac{1}{length}$$

Parallel circuits



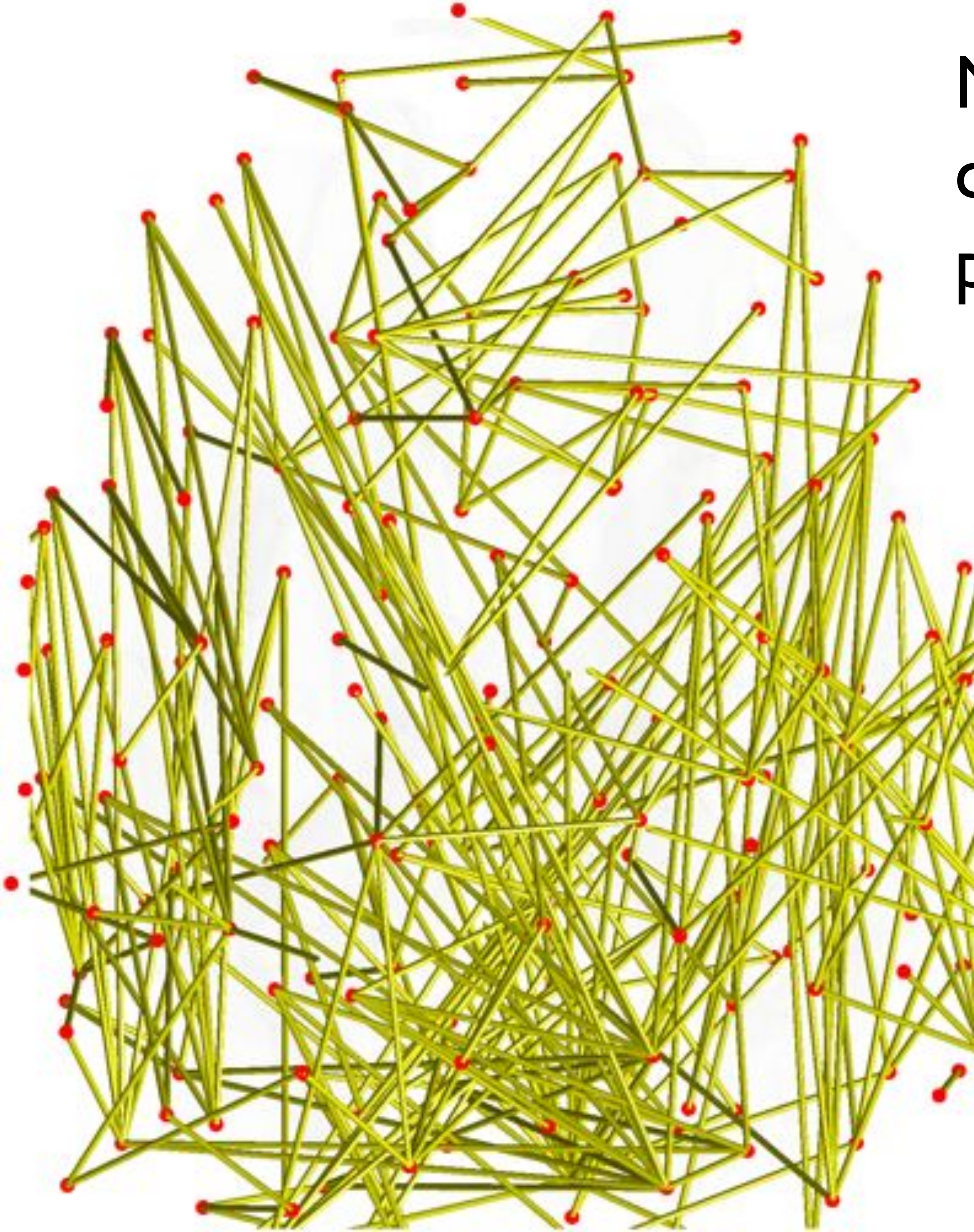




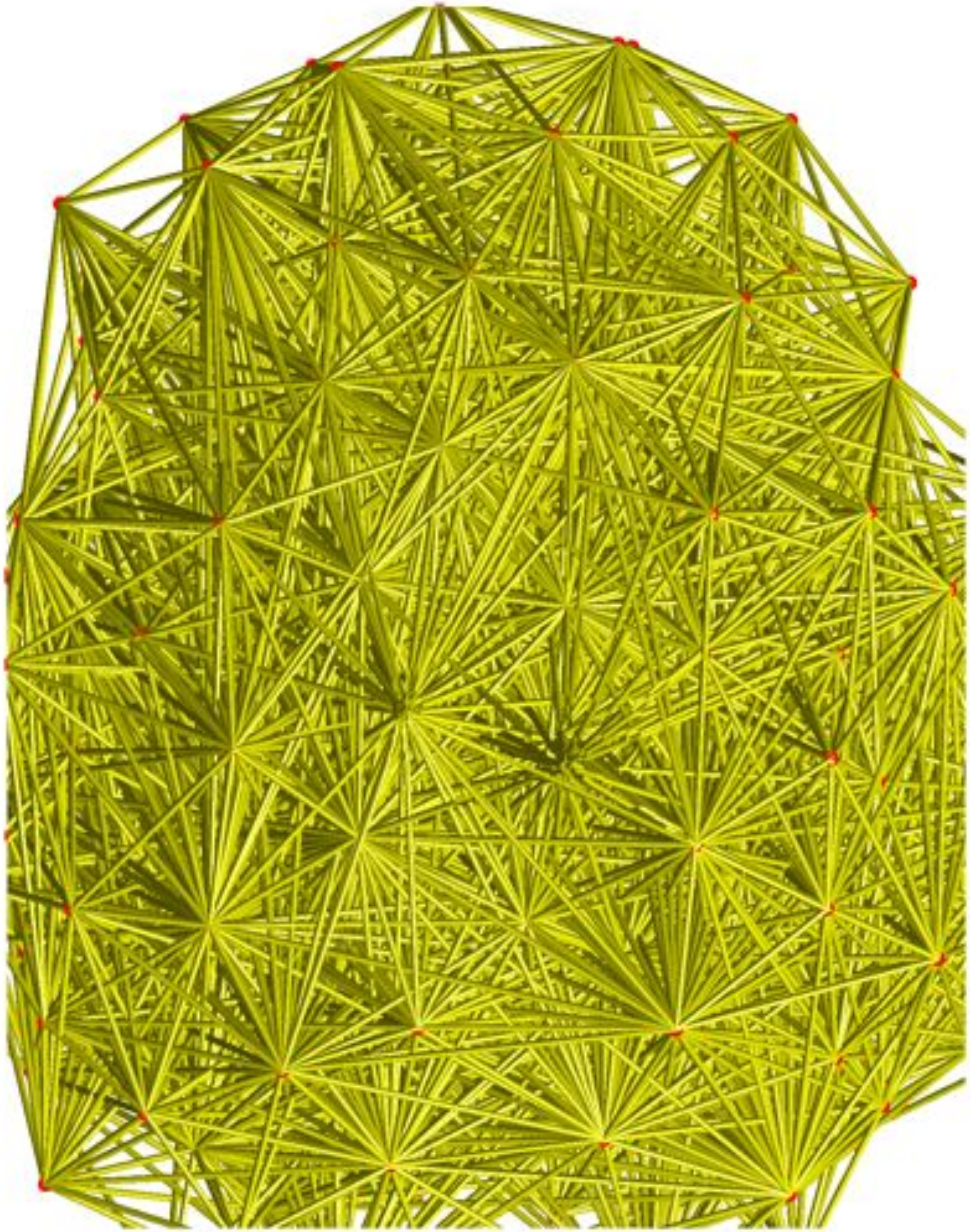


Major tracts without
parellel circuits
at epsilon=10mm.

The majority of tracts
are parallely wired.



Network constructed without parallel tracts.



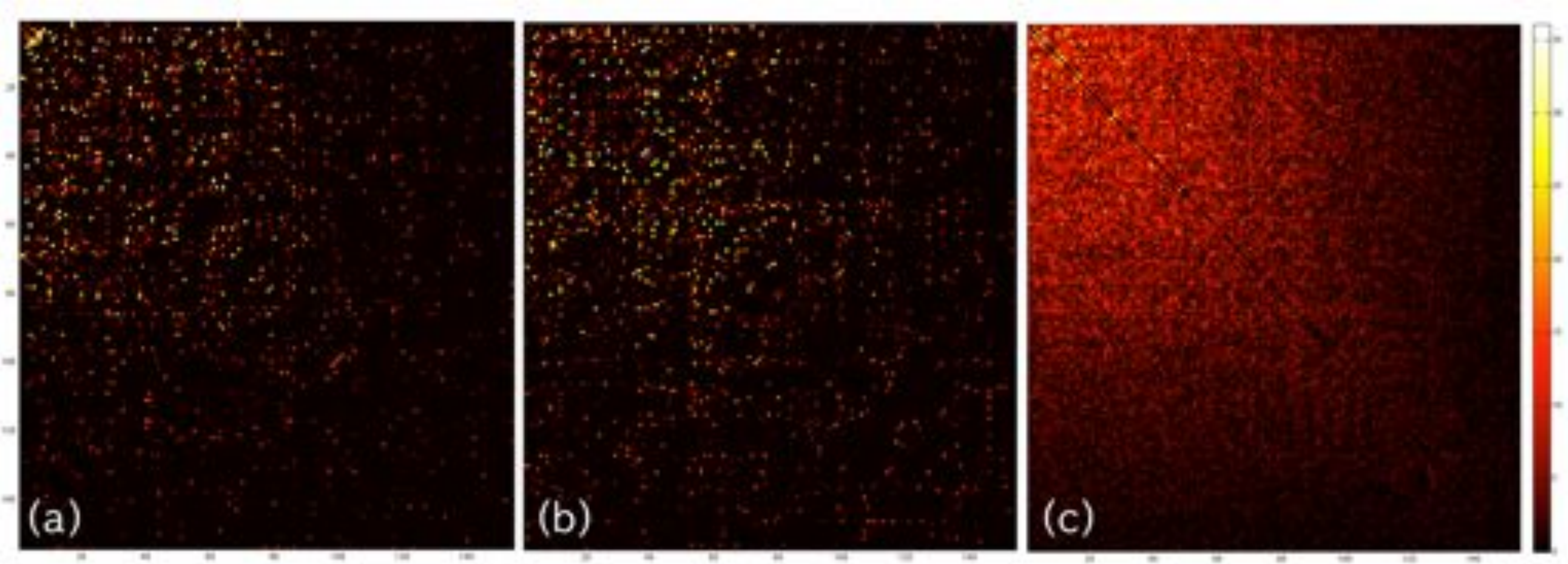
Network constructed with all the circuits

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 Kim[1] *Hyekyoung Lee*[1,2,3] *Moo K. Chung*[1,4,5,*] *Jamie L. Hanson*[5,6]
Brian B. Avants[7] *James C. Gee*[7] *Richard J. Davidson*[5,6] *Seth D. Pollak*[3,6]

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

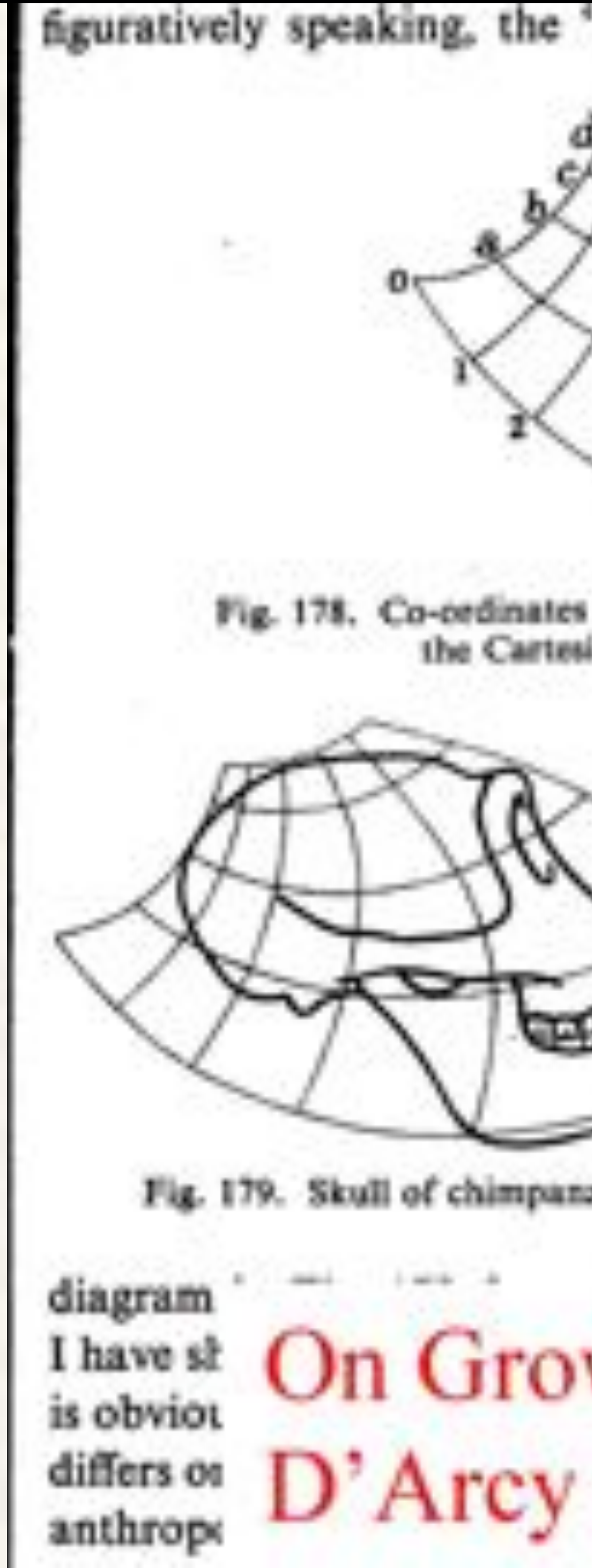
2012 IEEE International Symposium on Biomedical Imaging (ISBI)

Data Set

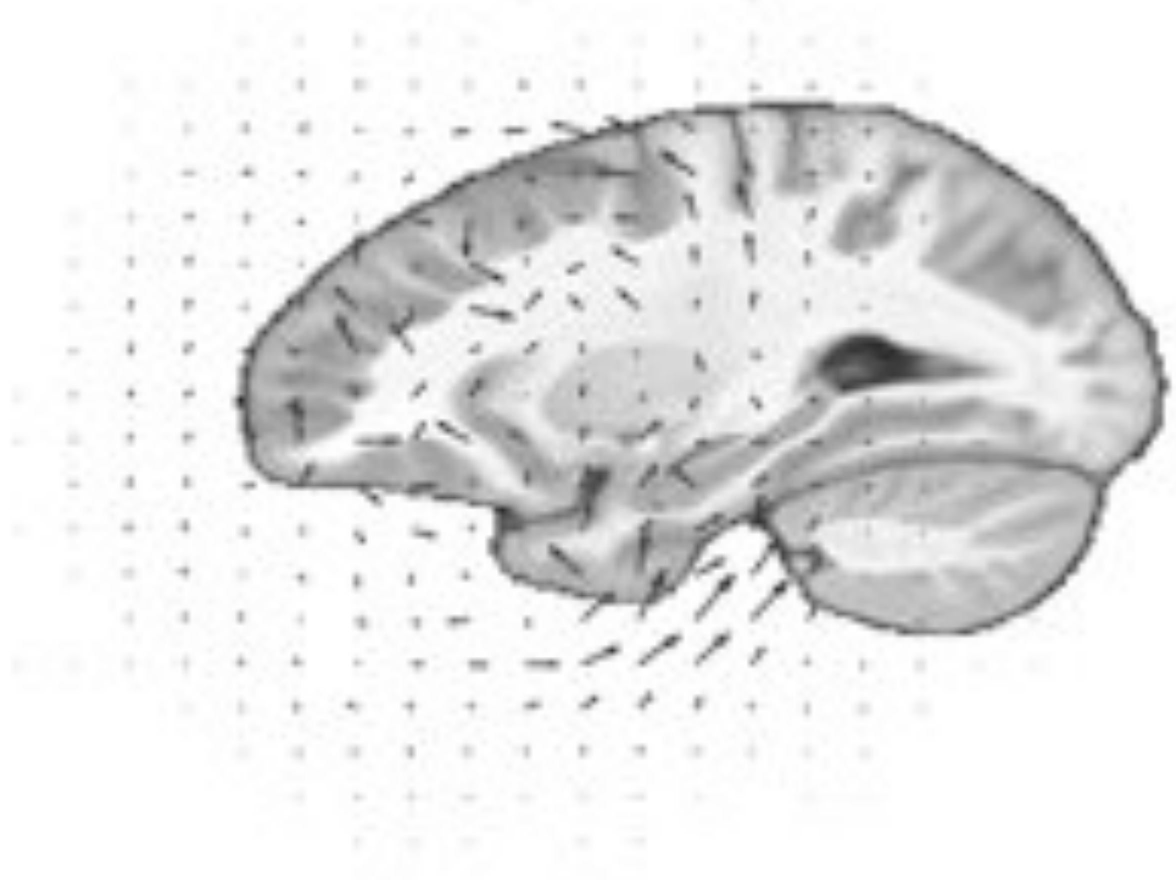
32 post-institutionalized (PI) maltreated children
33 normal controls

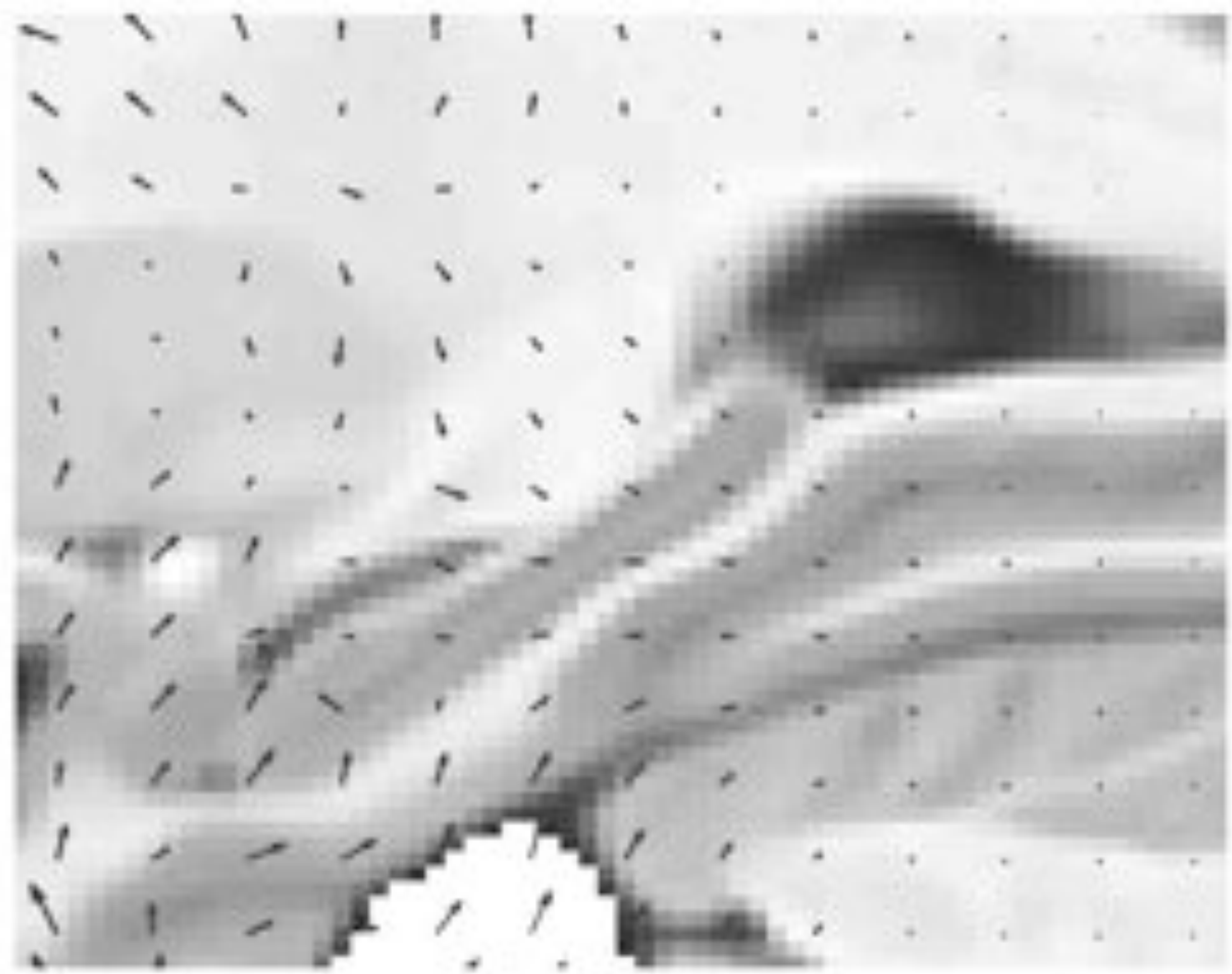
Tensor-Based Morphometry

Deformable shape model
D'Arcy Thompson 1860-1948



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

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

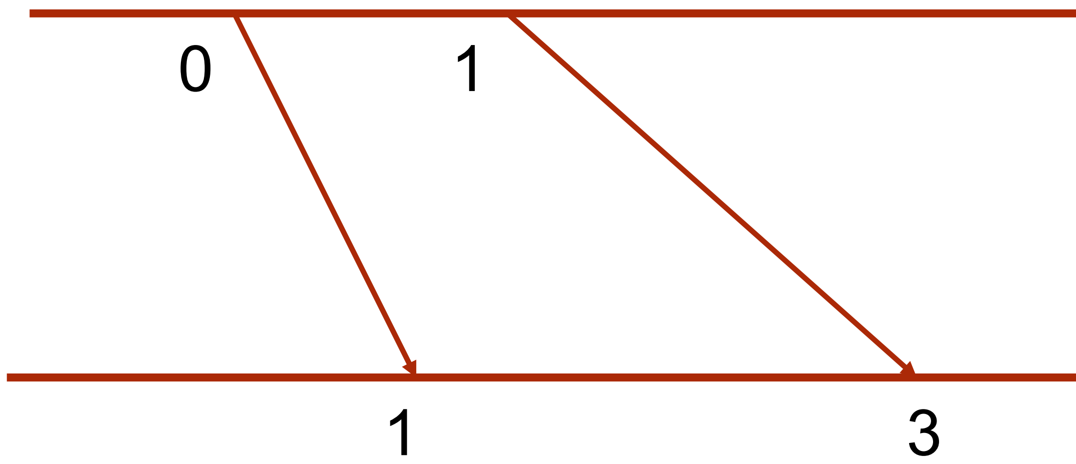
$$J(x) = \det \frac{\partial d(x)}{\partial x} = \det\left(\frac{\partial d_j}{\partial x_i}\right)$$

Examples. How to compute Jacobian determinant

- 1D:

$$x' = 2x + 1$$

$$J(x) = 2$$

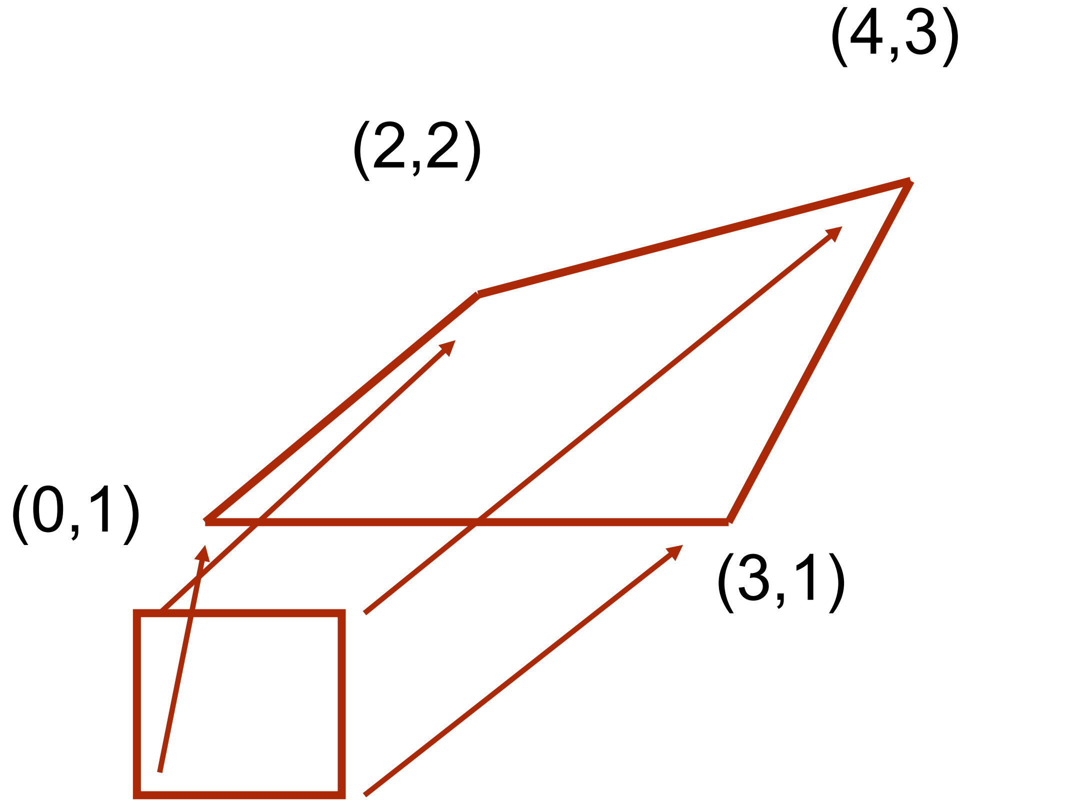


- 2D:

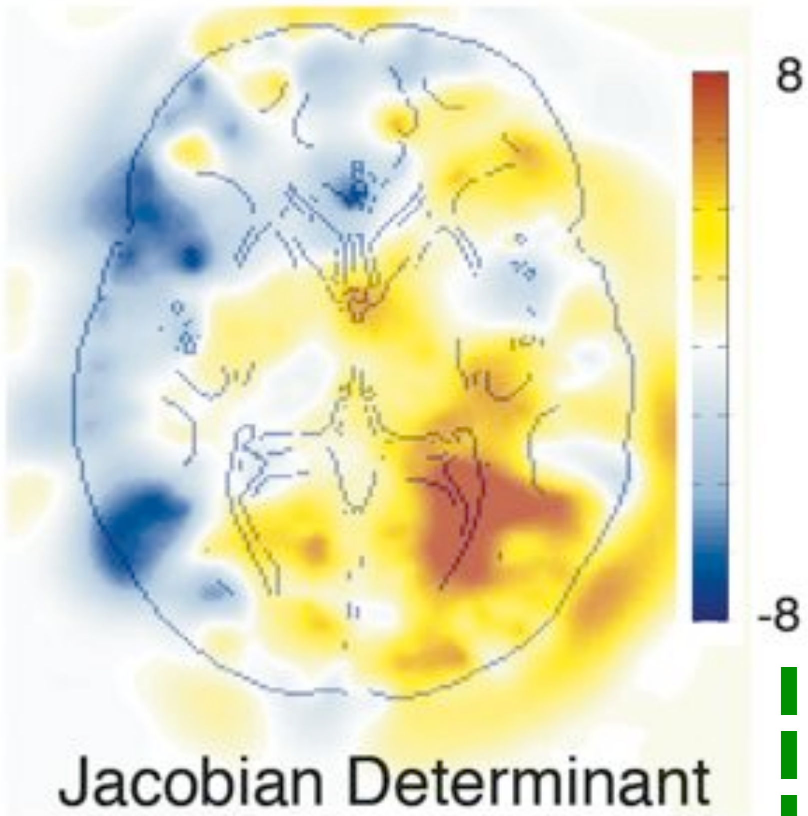
$$x' = 2x + y + 1$$

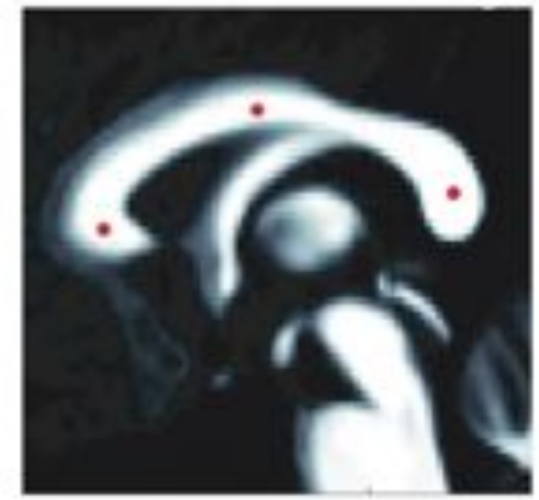
$$y' = x + 2y$$

$$J(x, y) = 4 - 1 = 3$$



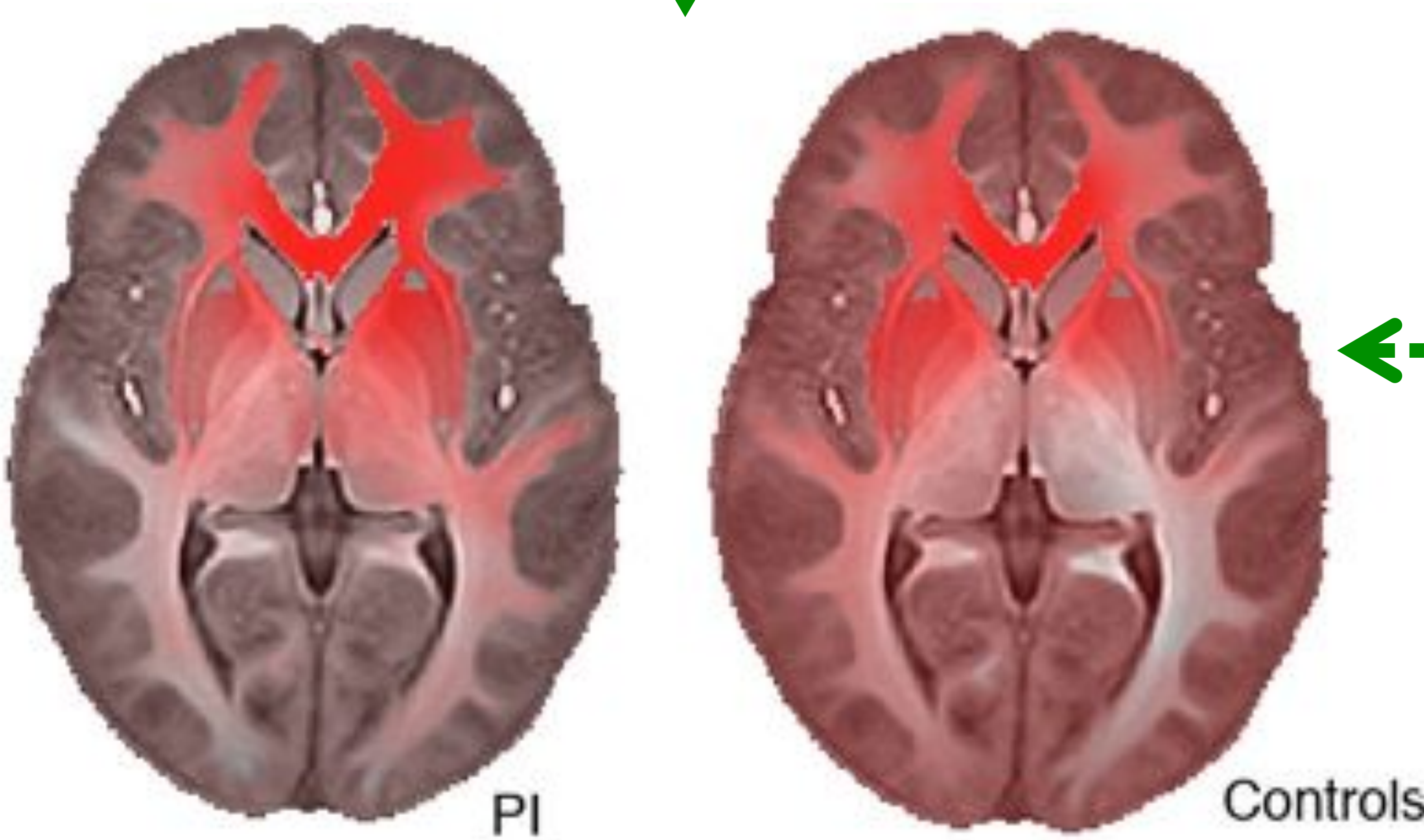
Connectivity from tensor based morphometry (TBM)

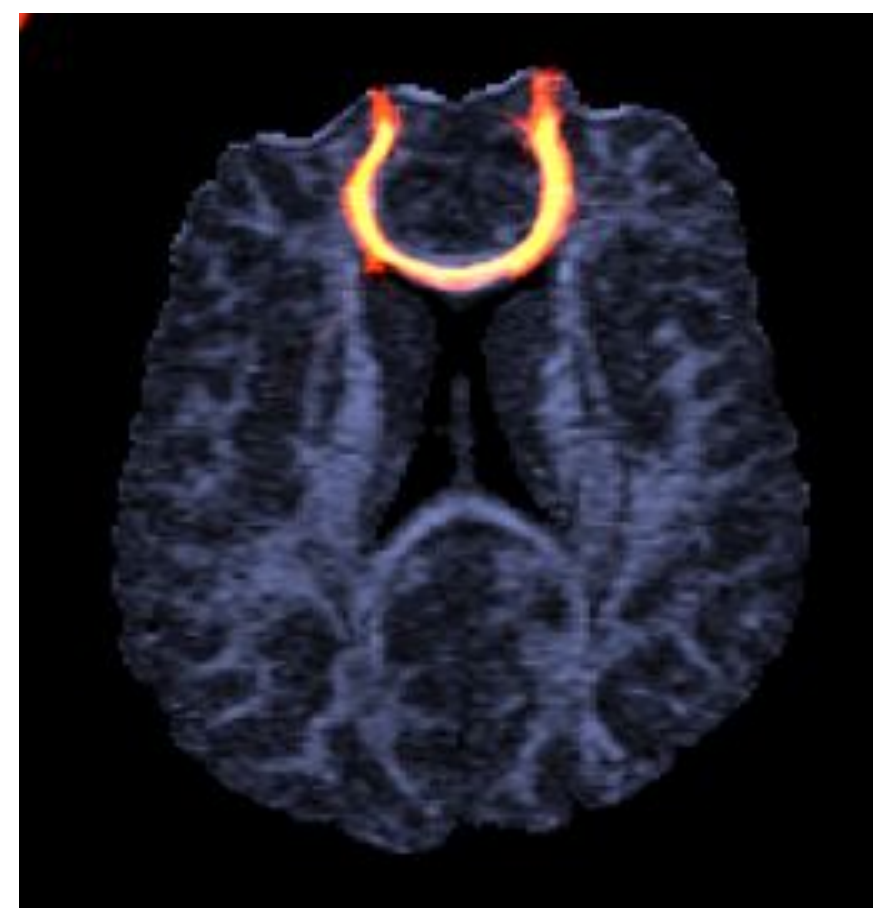



Seed voxels

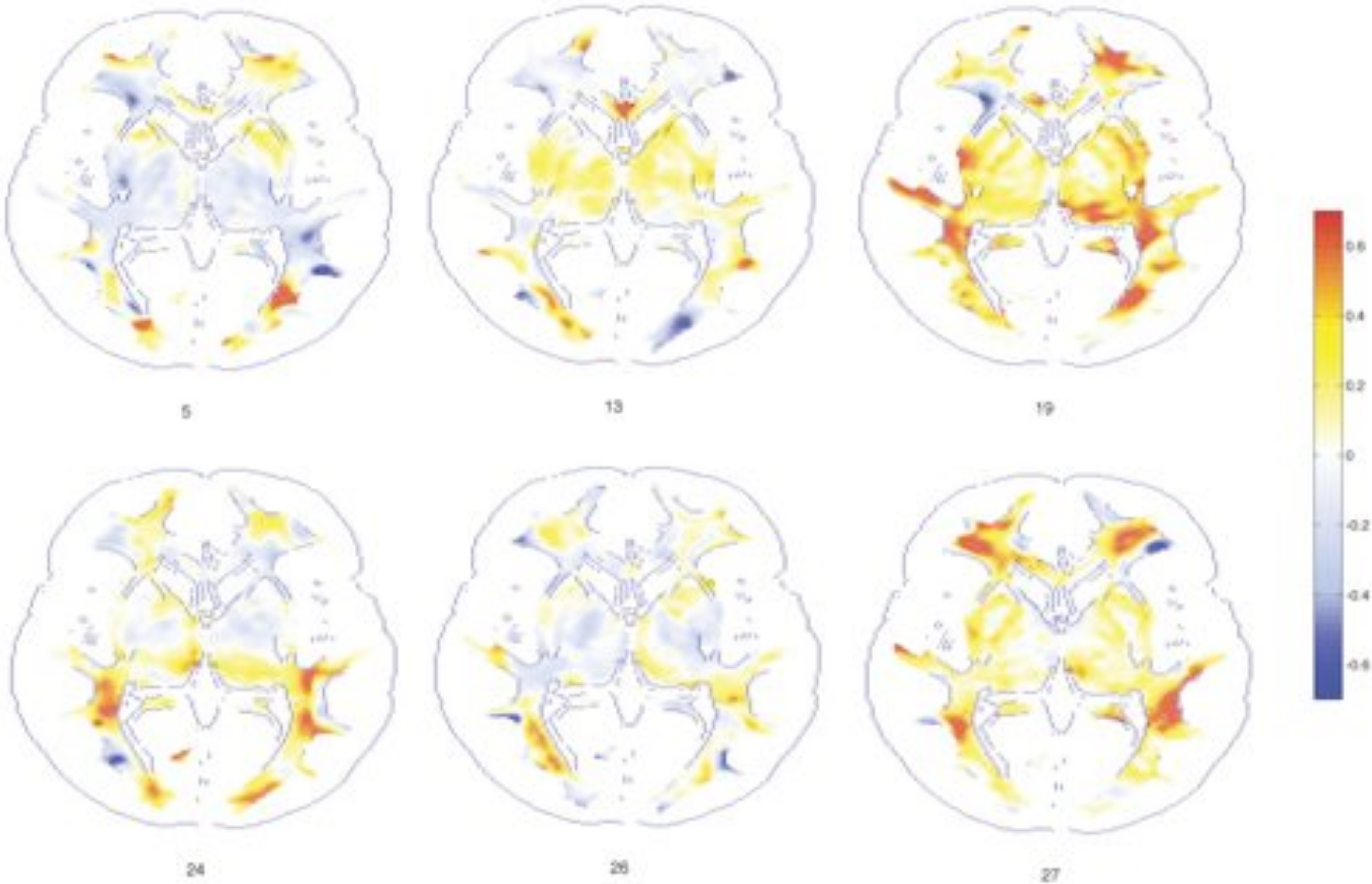
Correlation on Jacobian determinant

Probabilistic map from DTI

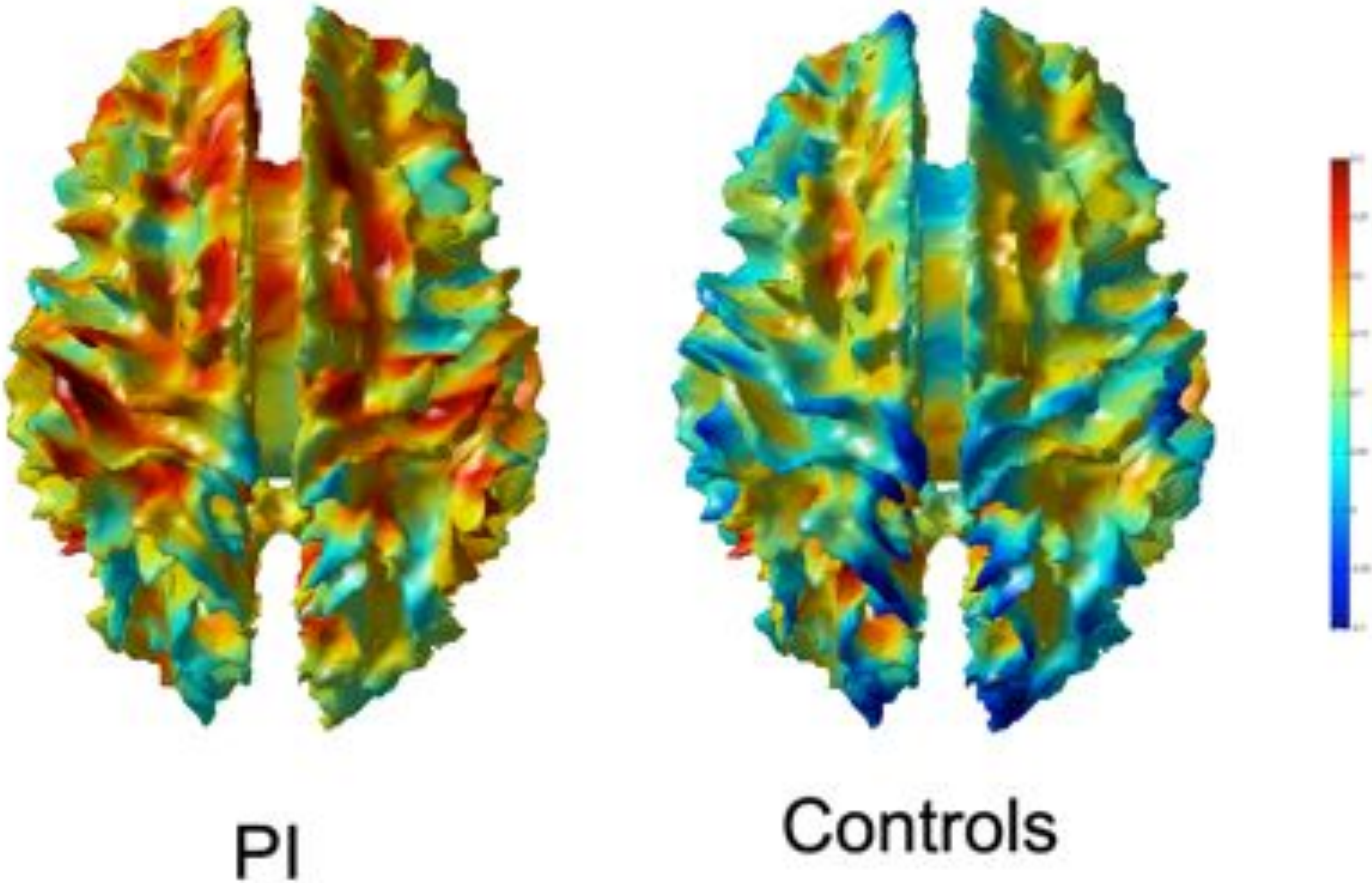



McGraw and Nadar, 2007

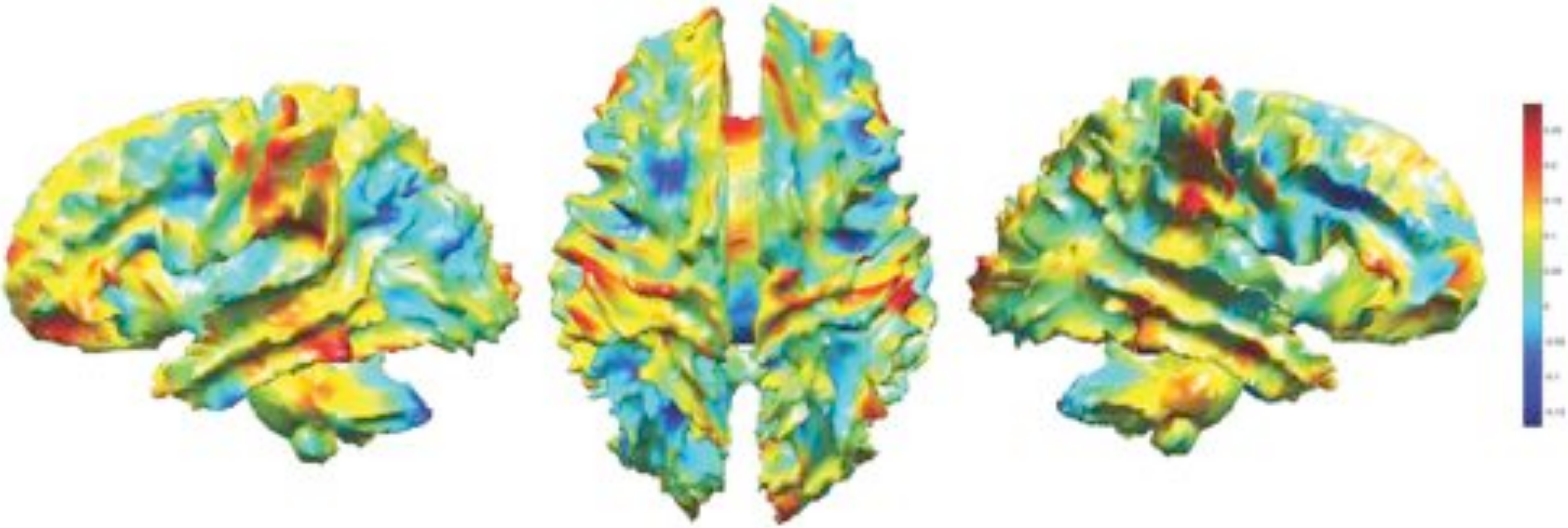
Jacobian determinant (tissue volume change) with respect to the template



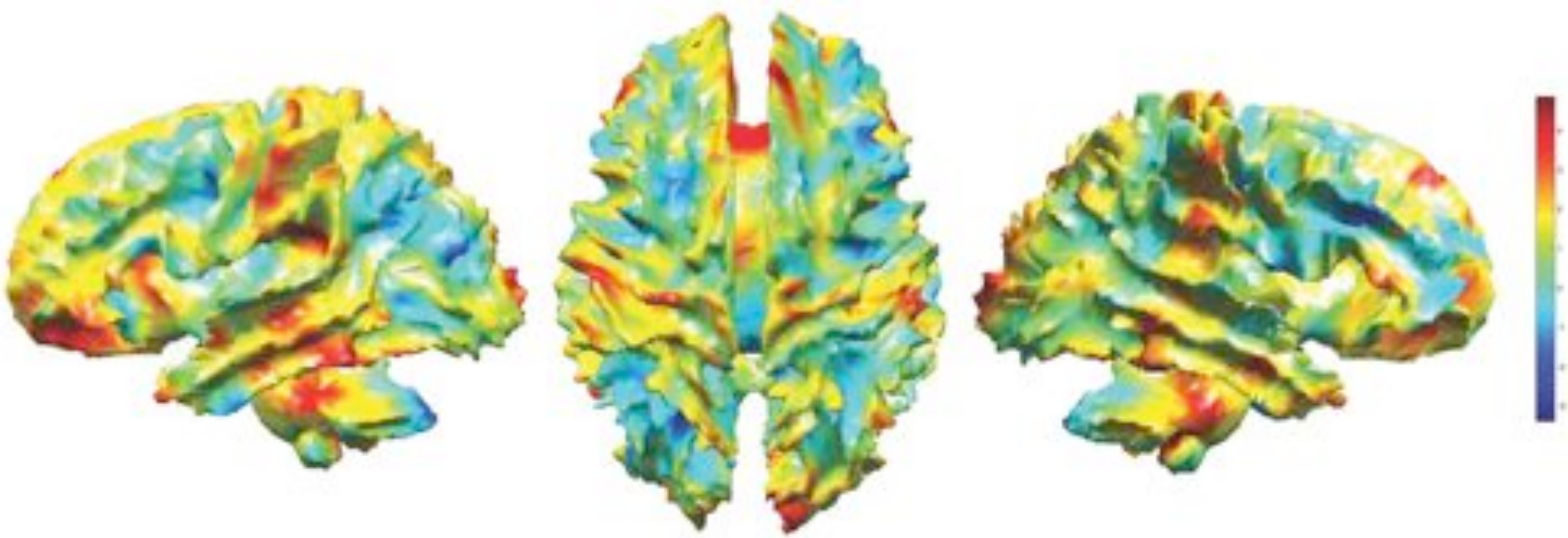
Seed-based (genu) correlation map of Jacobian determinants



T-stat map on correlation map difference (seed= genu)



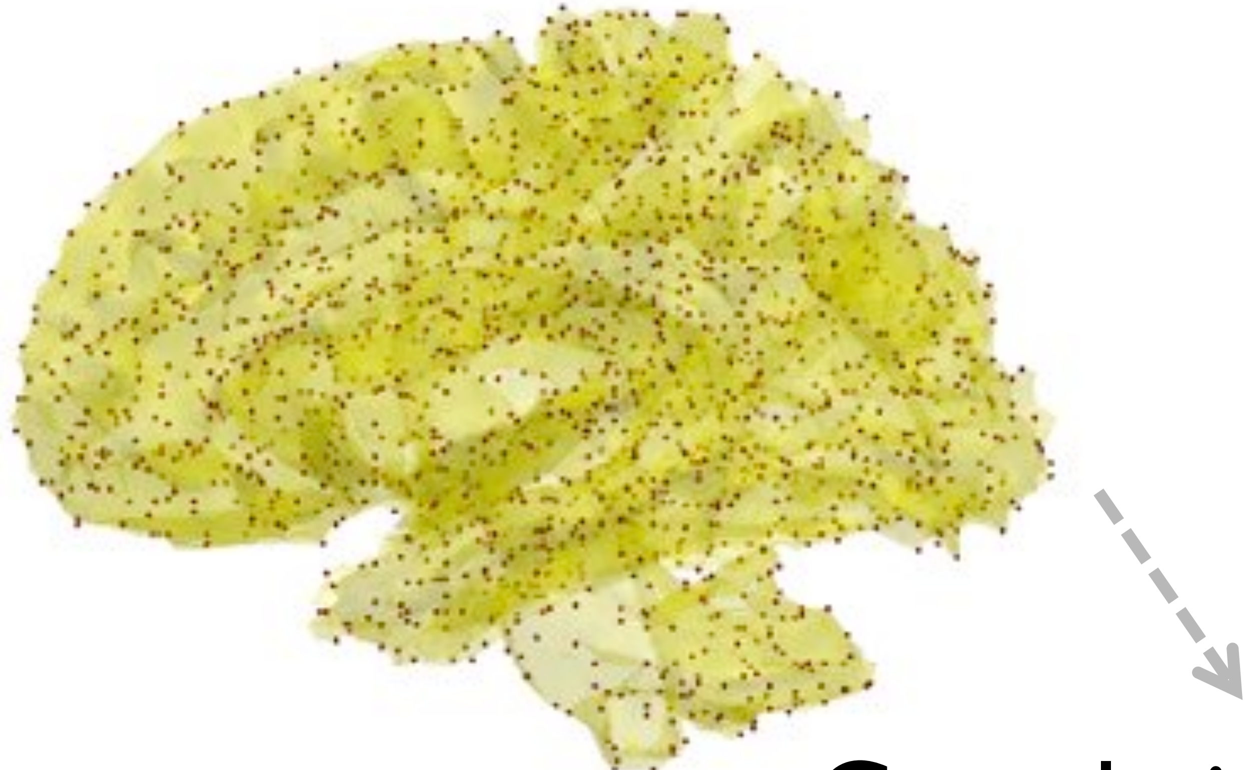
Mean difference (PI - controls)



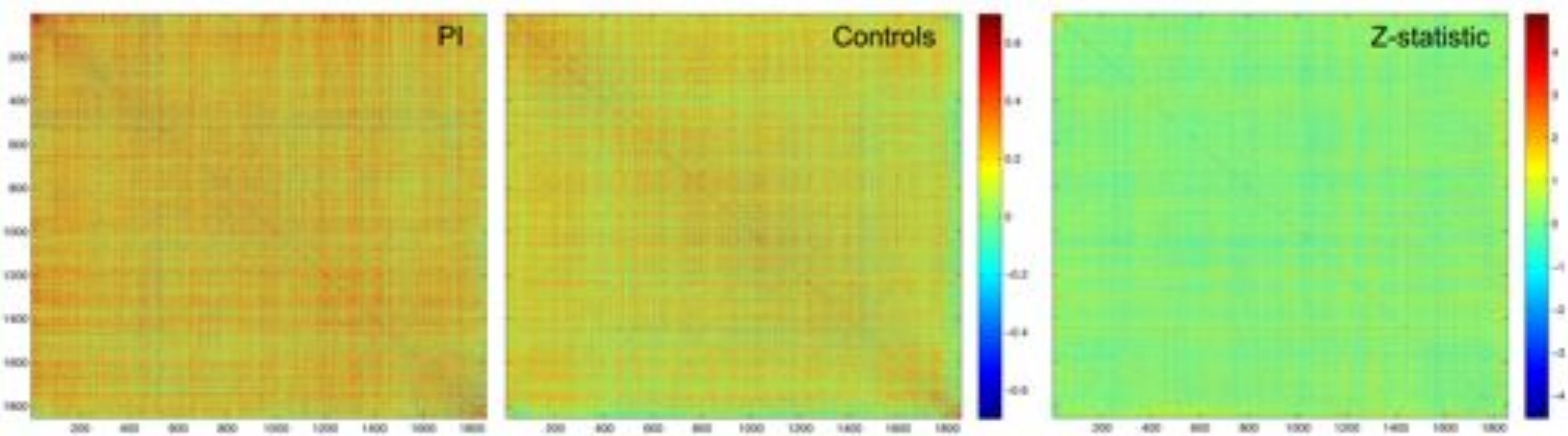
T-statistic map

1856 preselected nodes

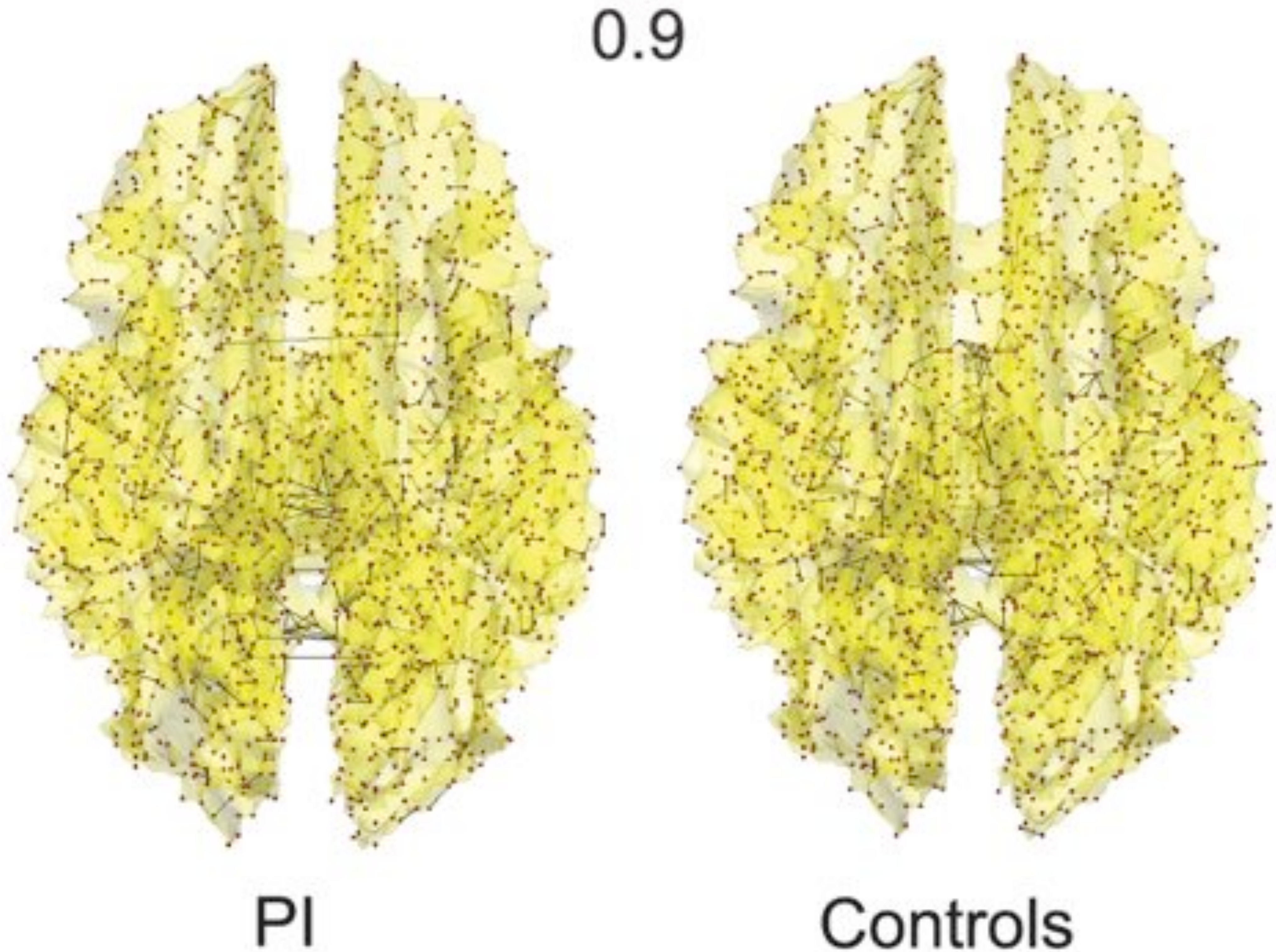
Whole brain correlation map of Jacobian determinants



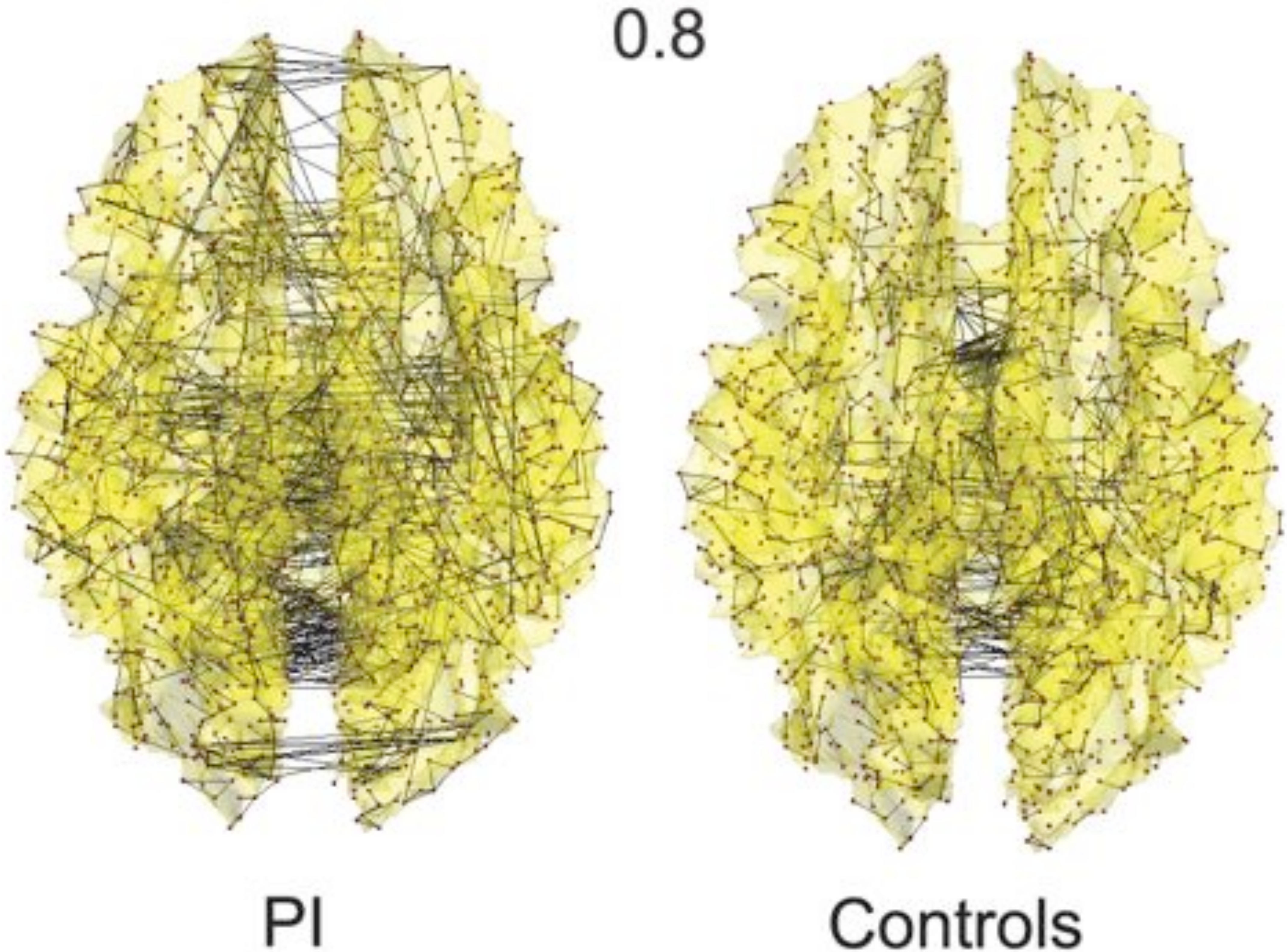
Correlation maps



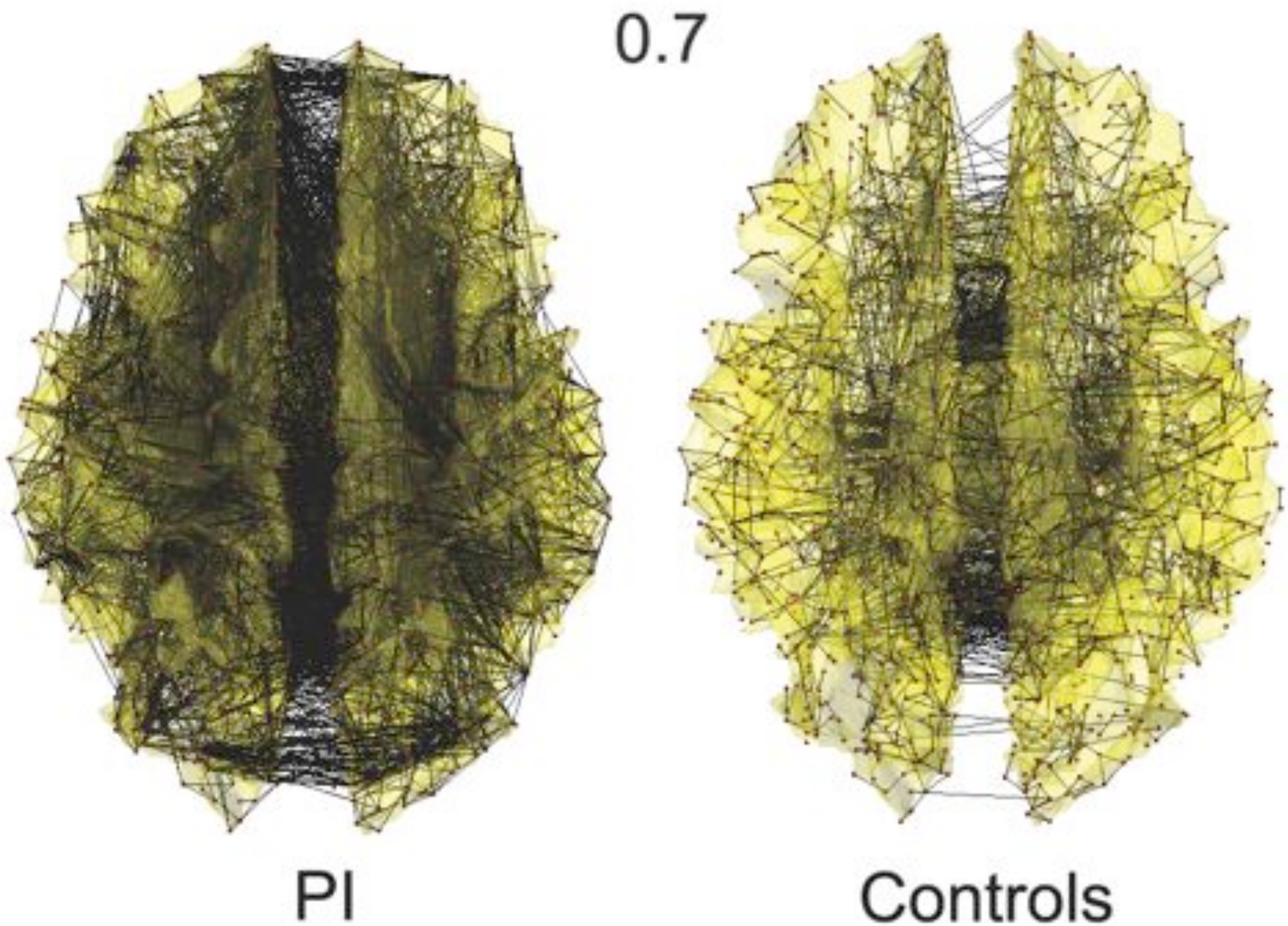
Graph representation of thresholded correlation



Graph representation of thresholded correlation

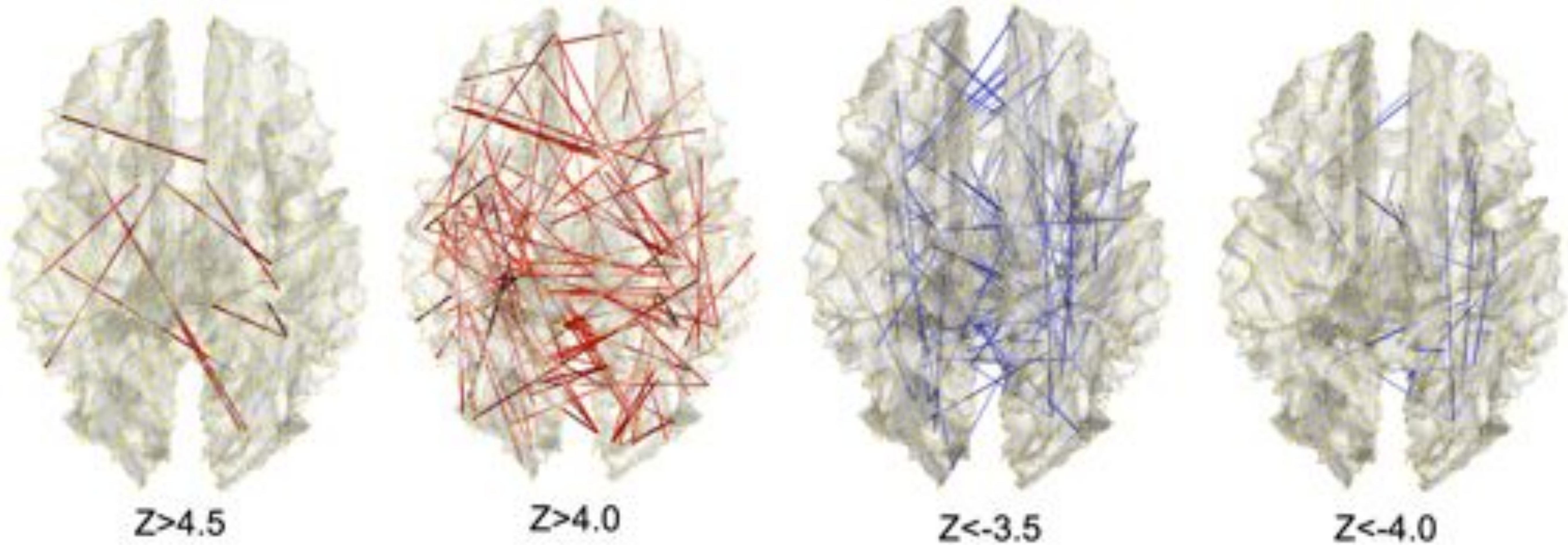


Graph representation of thresholded correlation

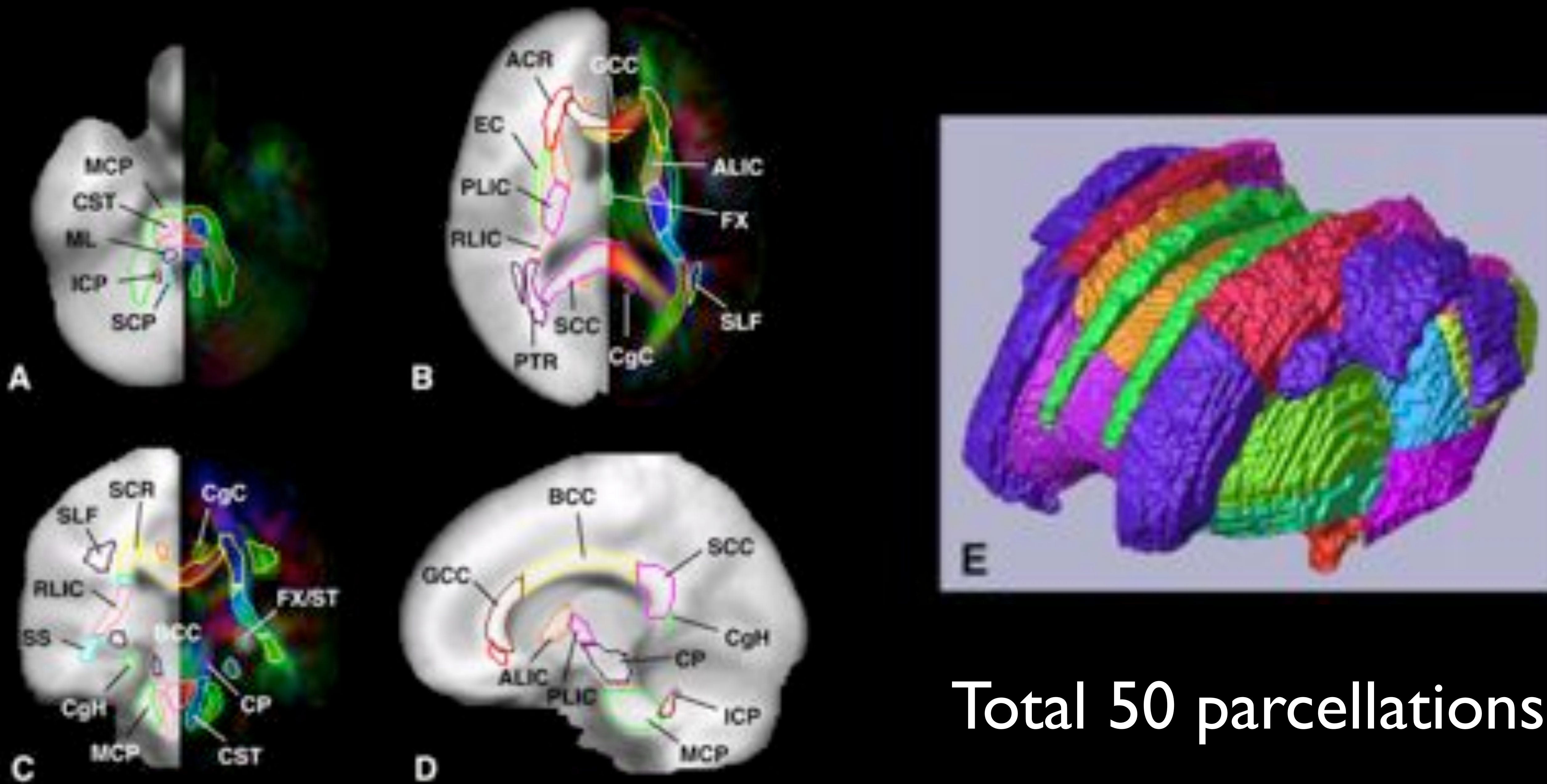


Interpretation: PI is more homogenous than the controls.

Z-statistic map of group difference (PI- controls)



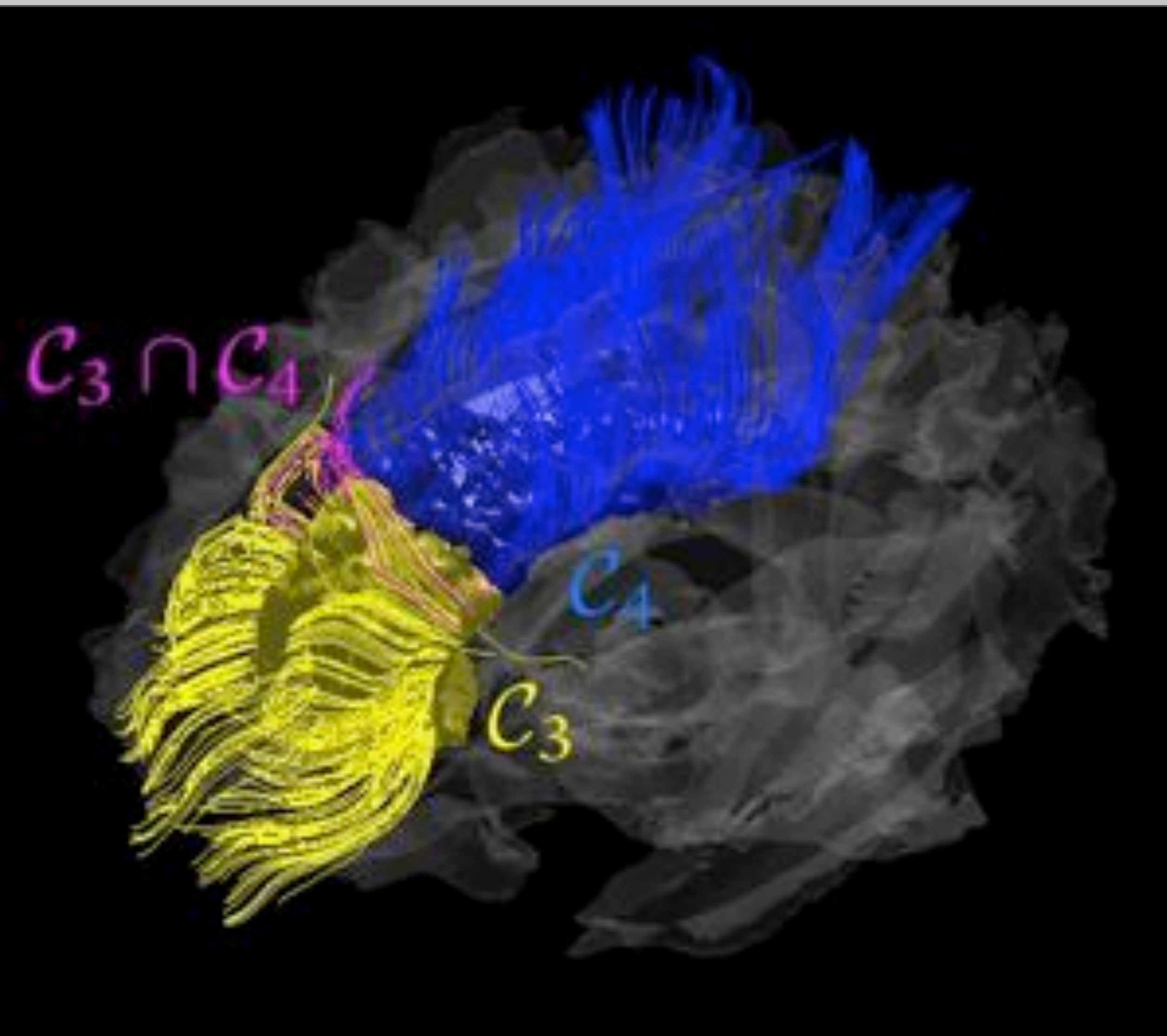
DTI-based white matter atlas (ICBM-DTI-81)

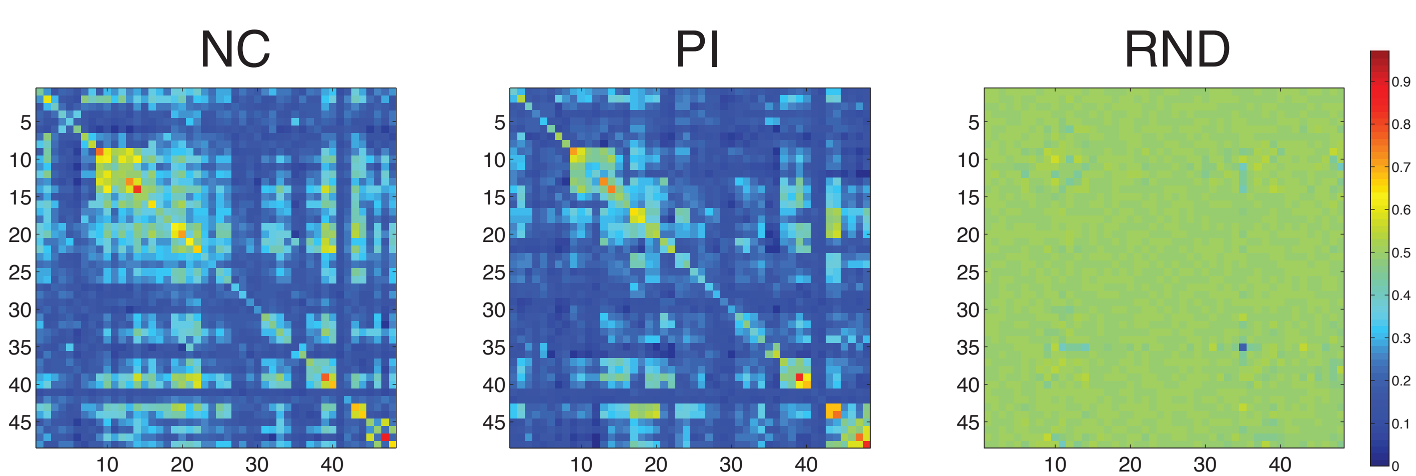


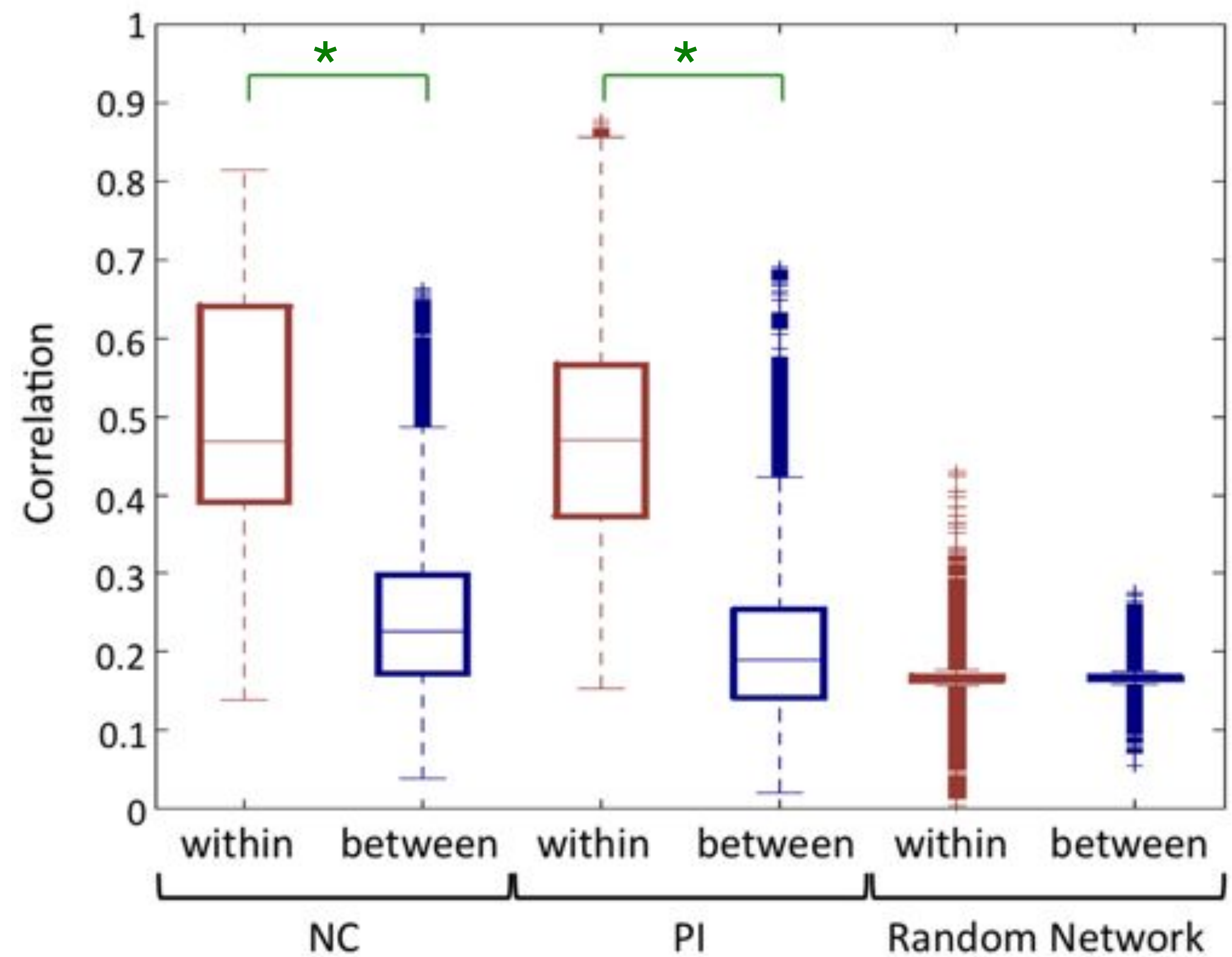
Total 50 parcellations

S. Mori et al., 2008, *NI*.

Validation against DTI white matter parcellations







pvalue < 0.001

Kim et al. 2012 ISBI

Thank you