Brain & Cognitive Sciences

University of Wisconsin
SCHOOL OF MEDICINE AND PUBLIC HEALTH

Introduction to Brain Network Modeling

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Seoul National University

Abstract

Diffusion tensor imaging offers a unique opportunity to characterize the structural connectivity of the human brain non-invasively by tracing white matter fiber tracts. Whole brain tractography studies routinely generate up to half million tracts per brain, which serves as edges in an extremely large 3D graph with up to half million edges. Currently there is no agreed-upon method for constructing the brain structural network graphs out of large number of white matter tracts. In this paper, we review basics of structural brain network modeling and discuss various challenges.

Outline

fMRI connectivity
DTI connectivity
PET connectivity

in autism

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

The NIH Human Connectome Project | Harvard/MGH-UCLA Consortium | WU-Minn Consortium | Neuroscience Blueprint

Human Connectome Project

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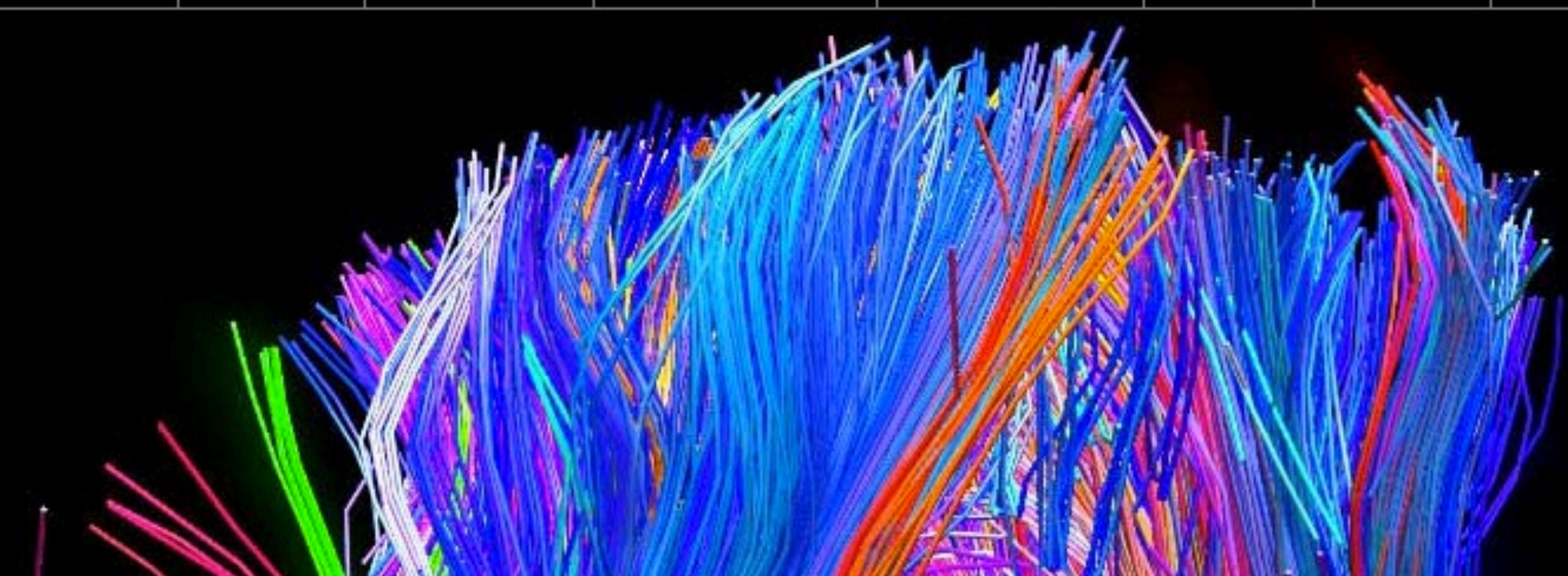
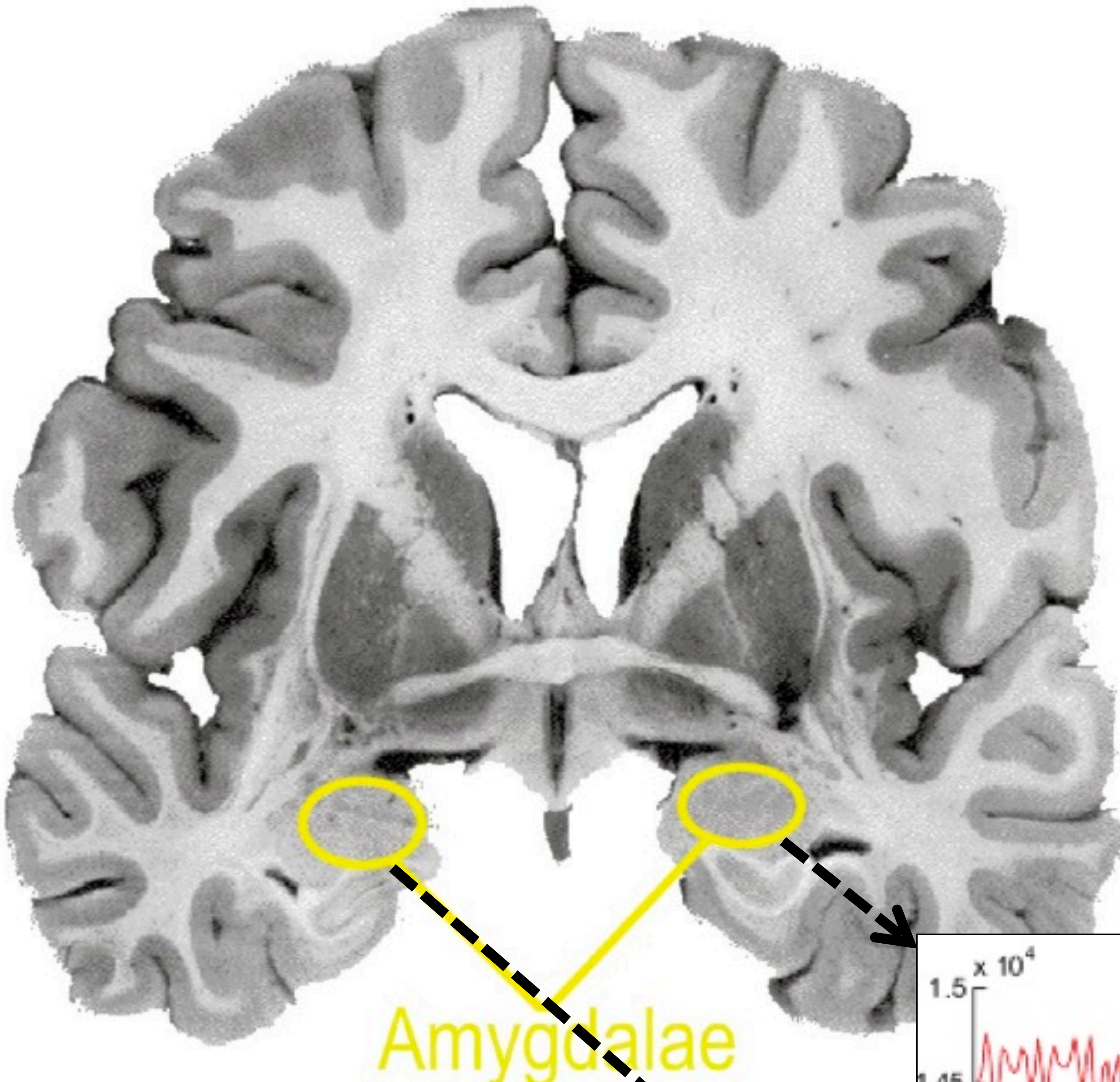


The Human Connectome Project

Navigate the brain in a way that was never before possible; fly through major brain pathways, compare essential circuits, zoom into a region to explore the cells that comprise it, and the functions that depend on it.

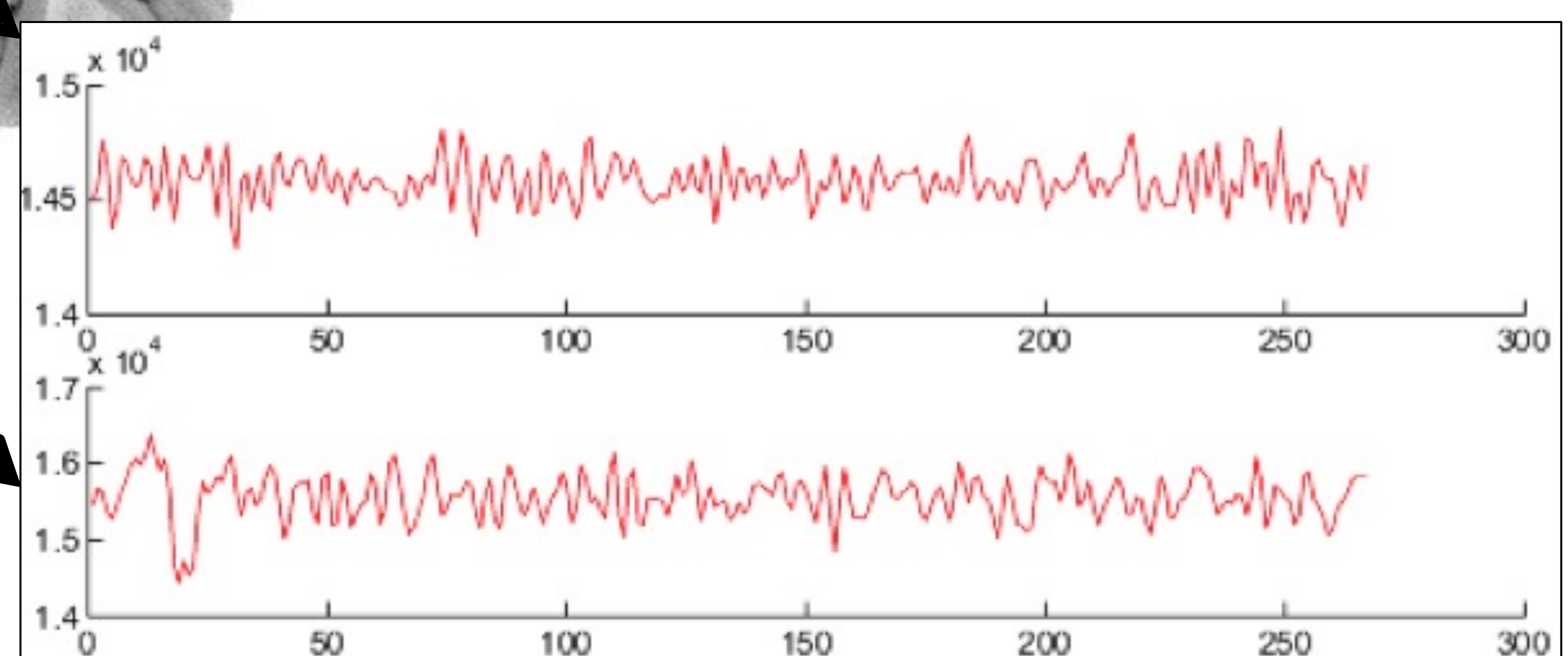
The Human Connectome Project aims to provide an unparalleled compilation of neural data, an interface to graphically navigate this data and the opportunity to

Functional magnetic resonance imaging (fMRI)



Specialized MRI scan used to measure the hemodynamic response (change in blood flow) in the brain.

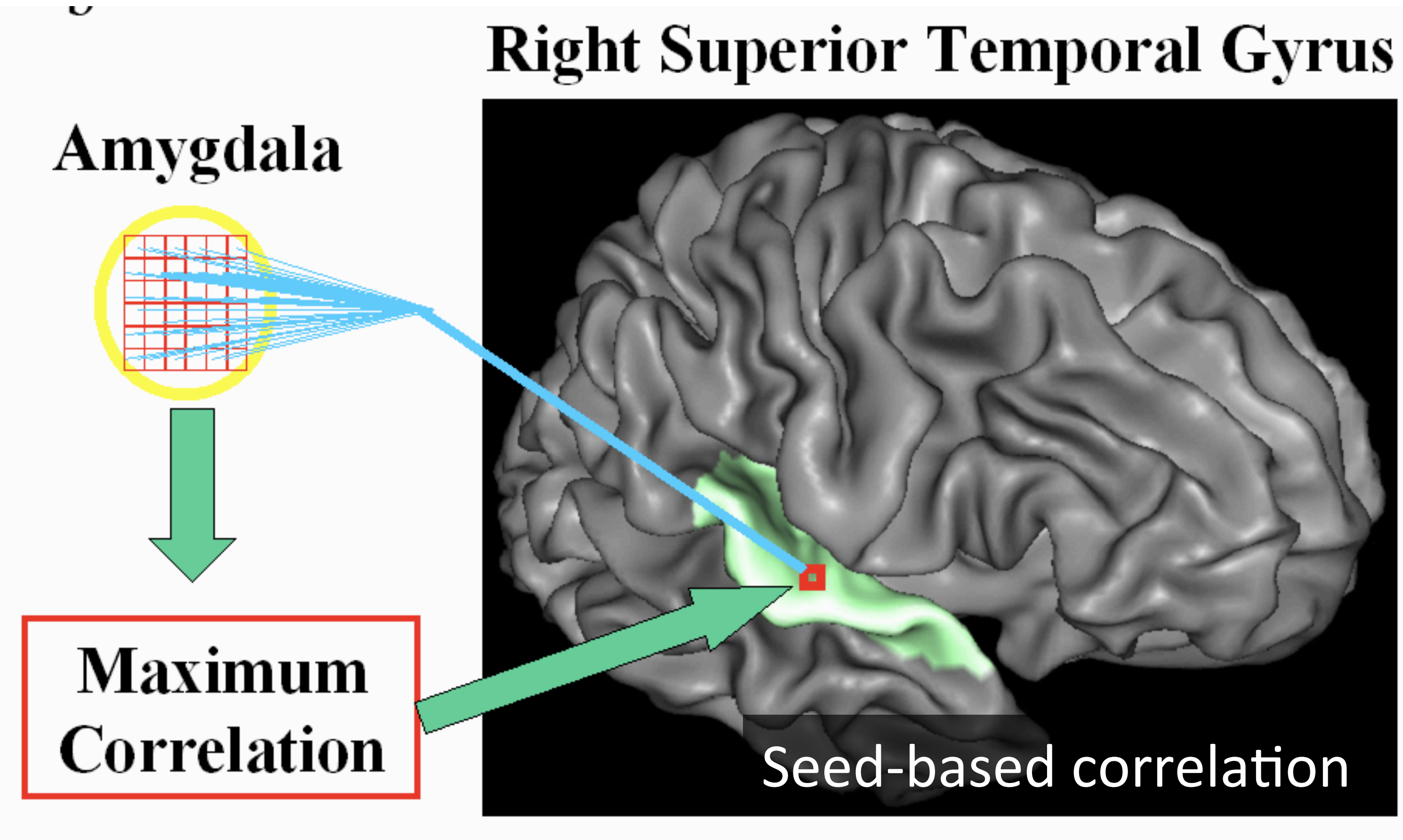
fMRI gives time series data at about 4-8mm image resolution.

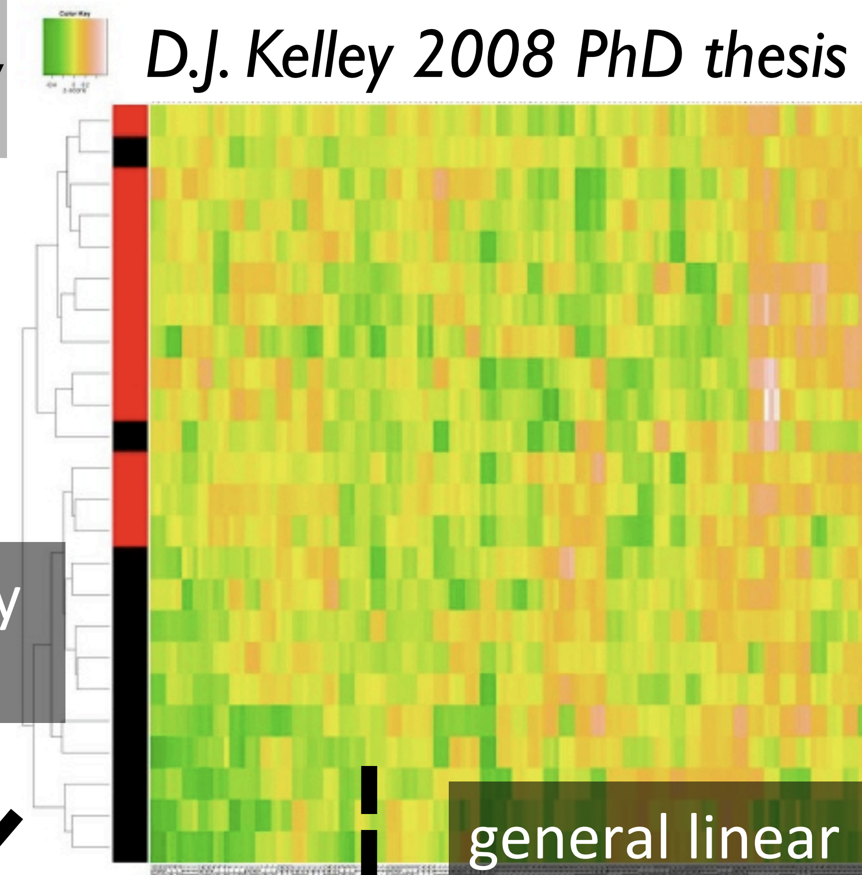


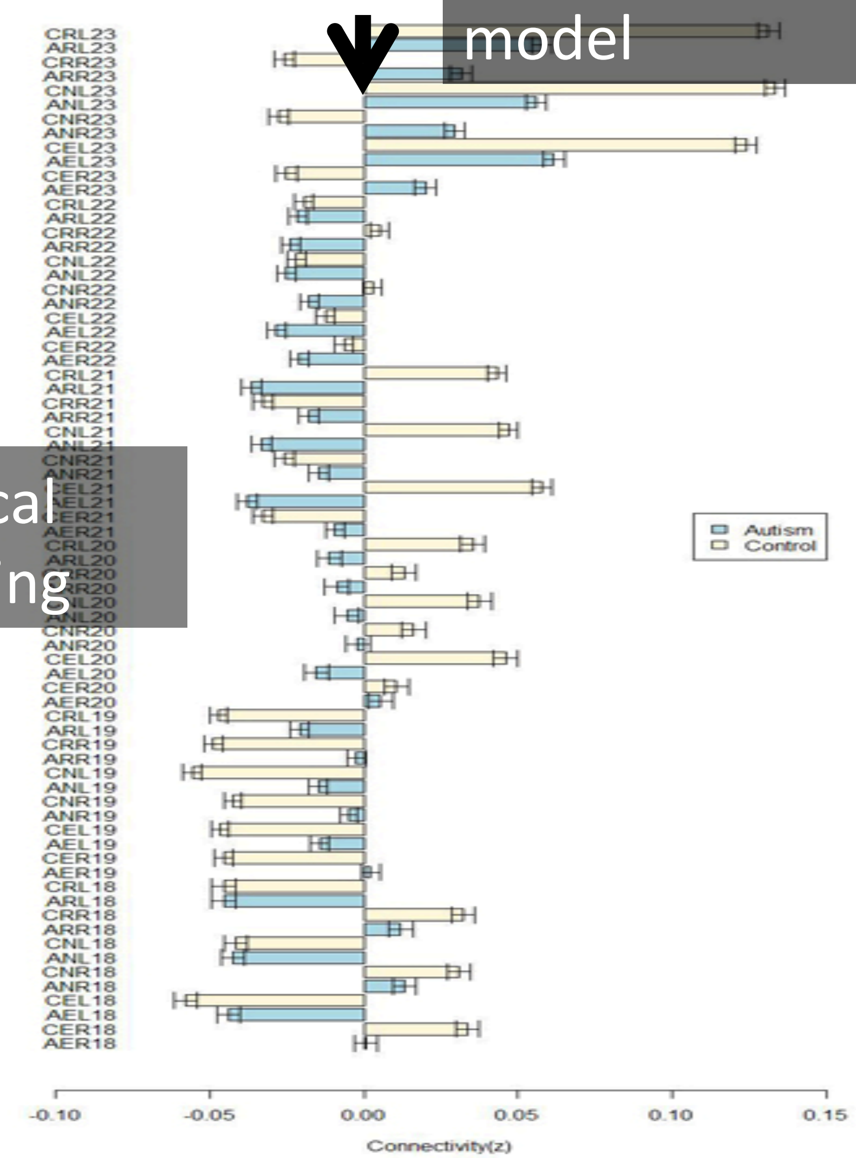
Davidson and Irwin, 1999

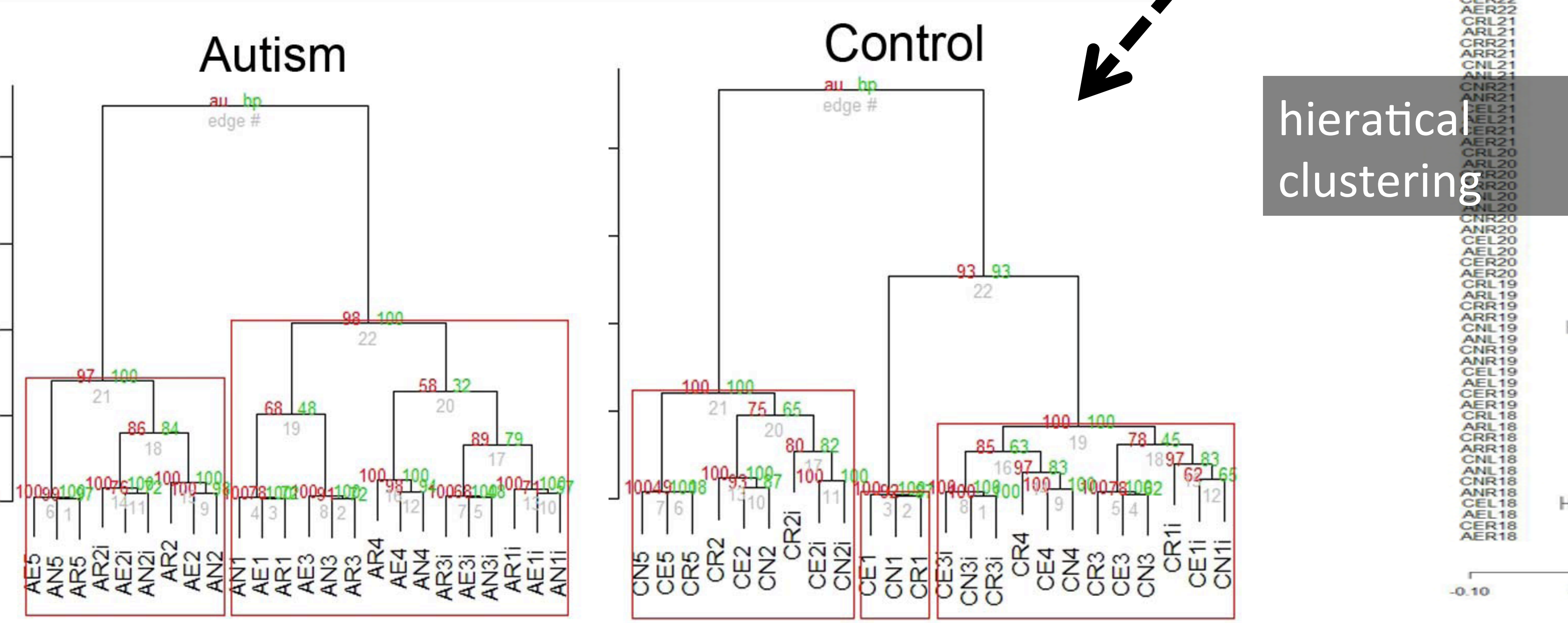
functional (fMRI) connectivity study

D.J. Kelley 2008 PhD thesis



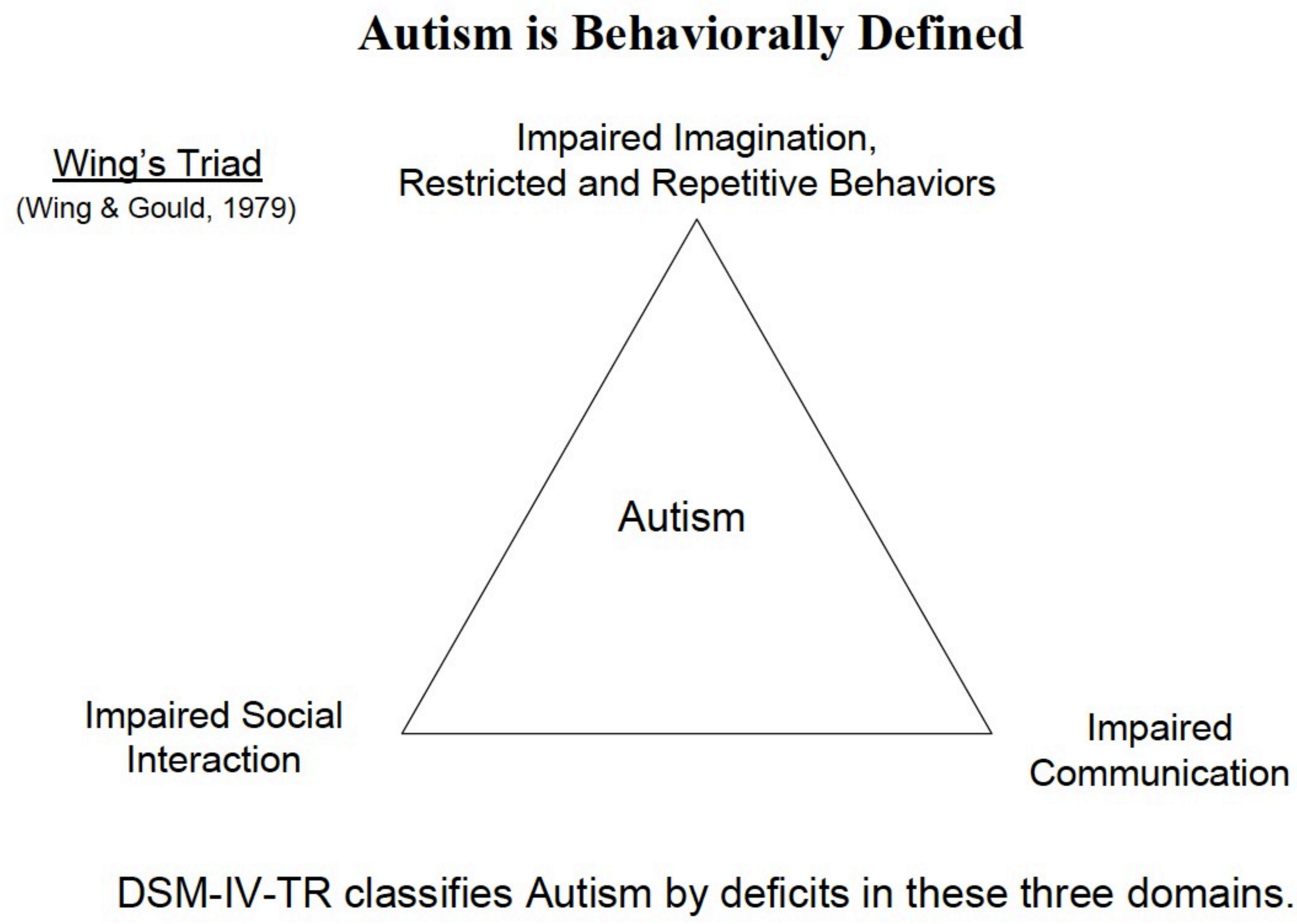


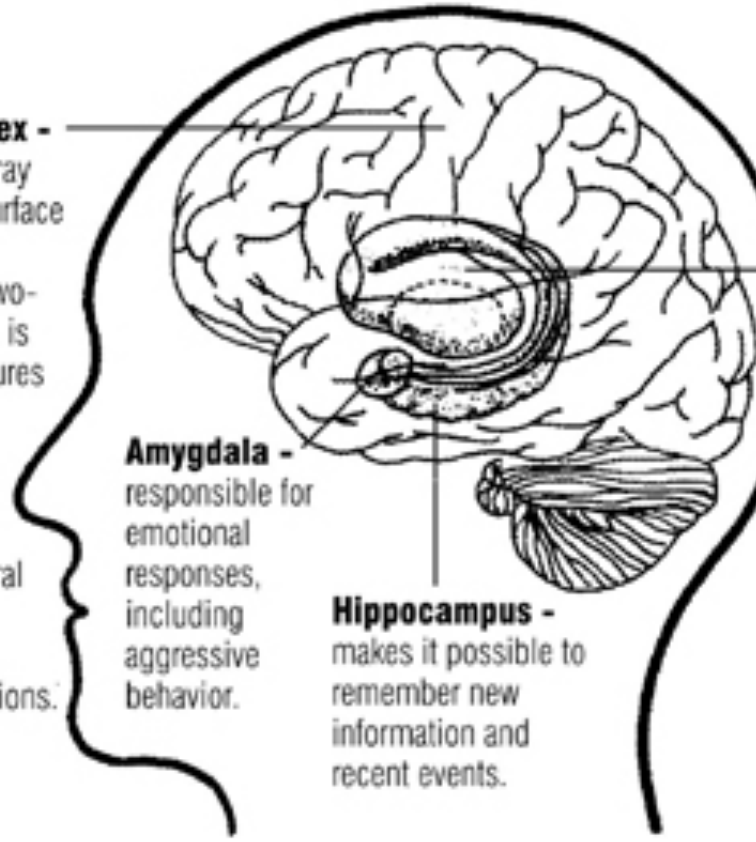




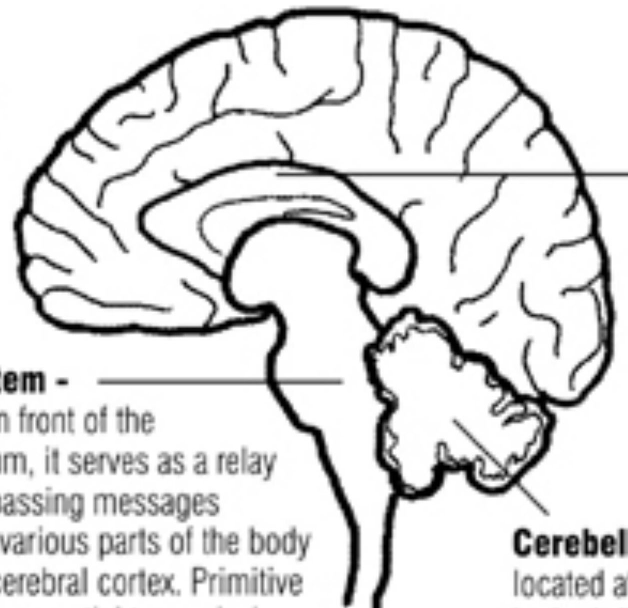
Brain connectivity study in autism

Autism (자폐증) is a developmental disorder.
About 9 per 1000 children in US.





Major Brain Structures Implicated in Autism



AUTISM

Persons with autism may possess the following characteristics in various combinations and in varying degrees of severity.

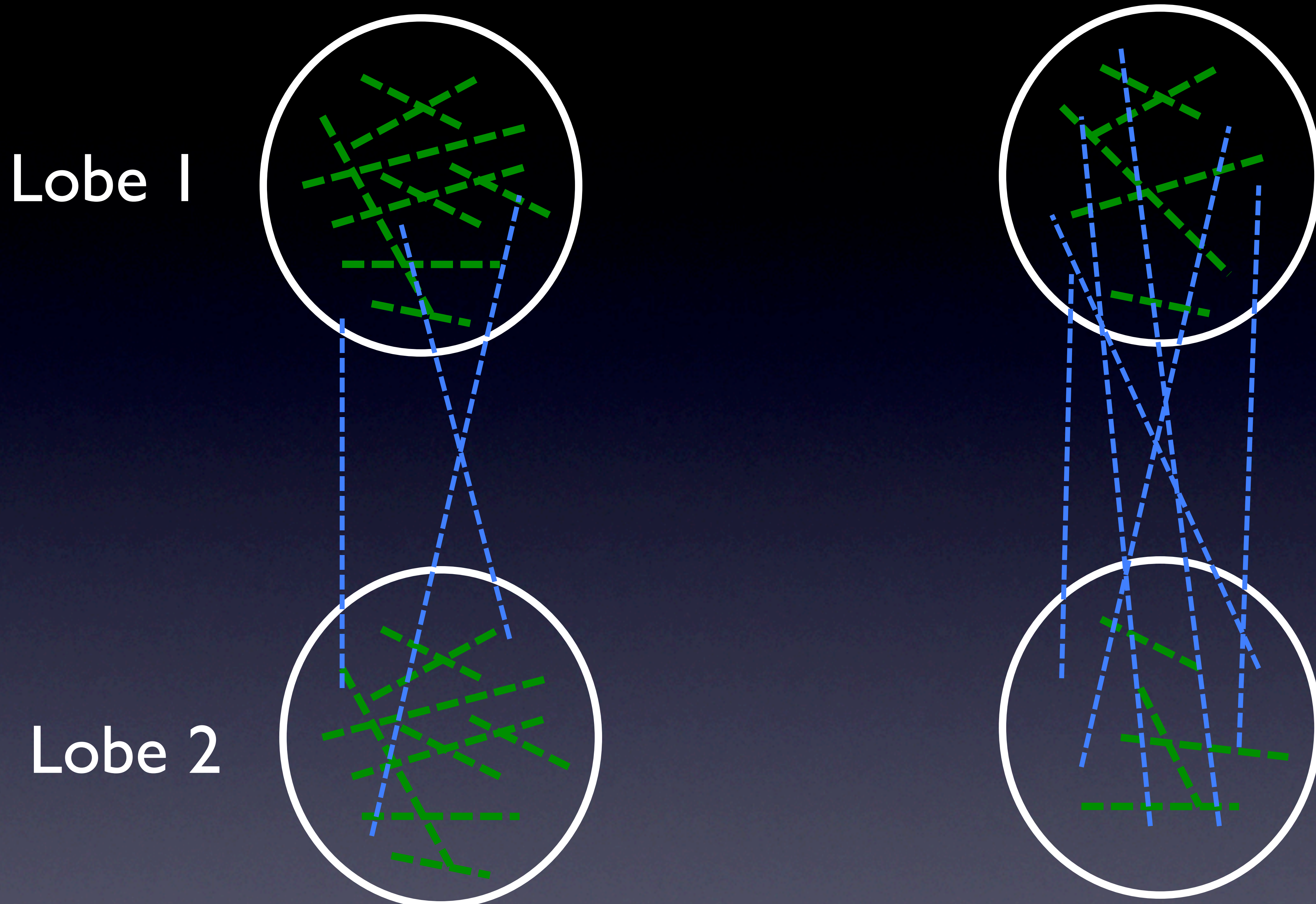
1-800-3AUTISM

Autism Society of America
7910 Woodmont Avenue, Suite 650 Bethesda, MD 20814-3015

January is National Autism Awareness Month.

Adapted from original by: Professor Rendle-Short, University of Queensland, Brisbane Children's Hospital, Australia

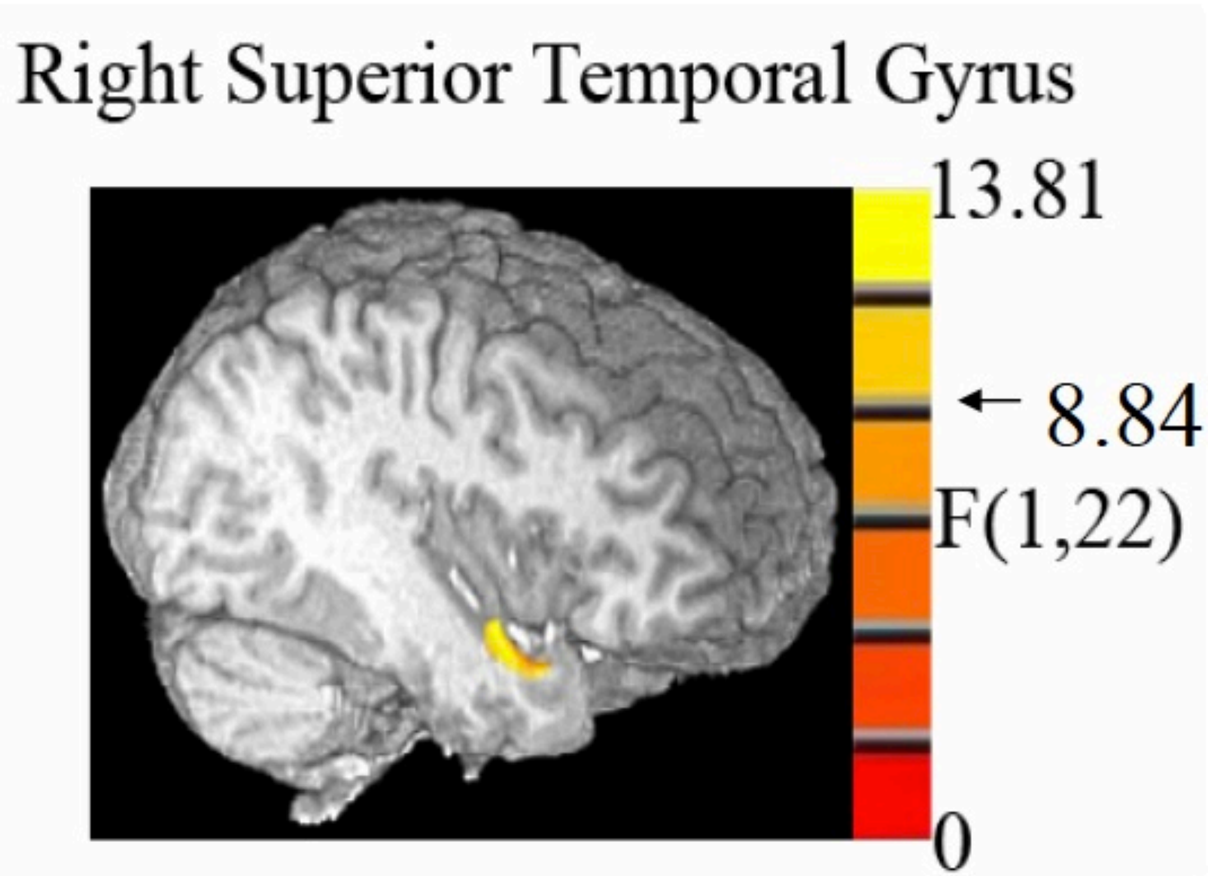
Known connectivity hypothesis in autism

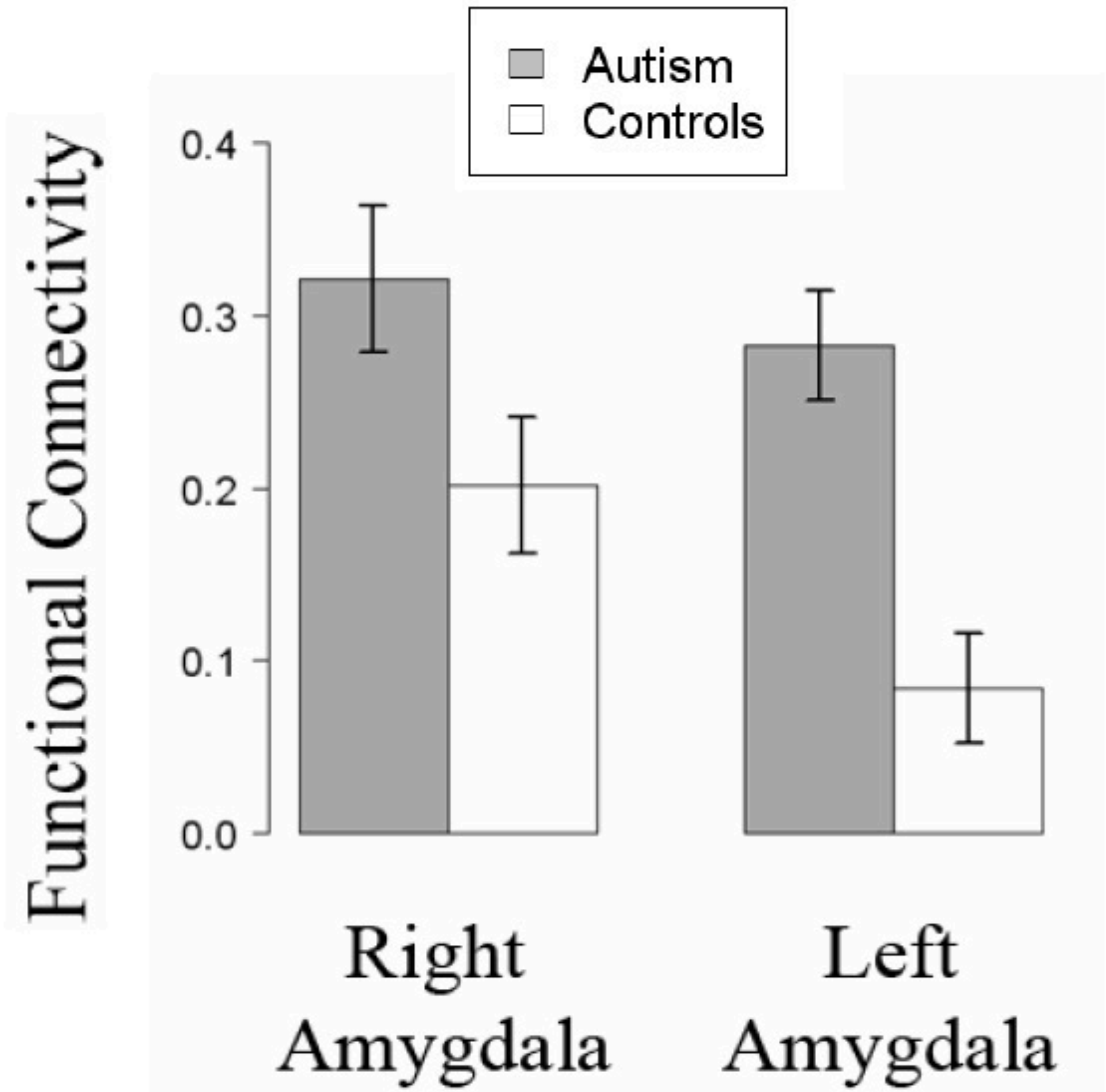


Local overconnectivity
global underconnectivity

Normal controls

Abnormal functional (fMRI) connectivity in autism





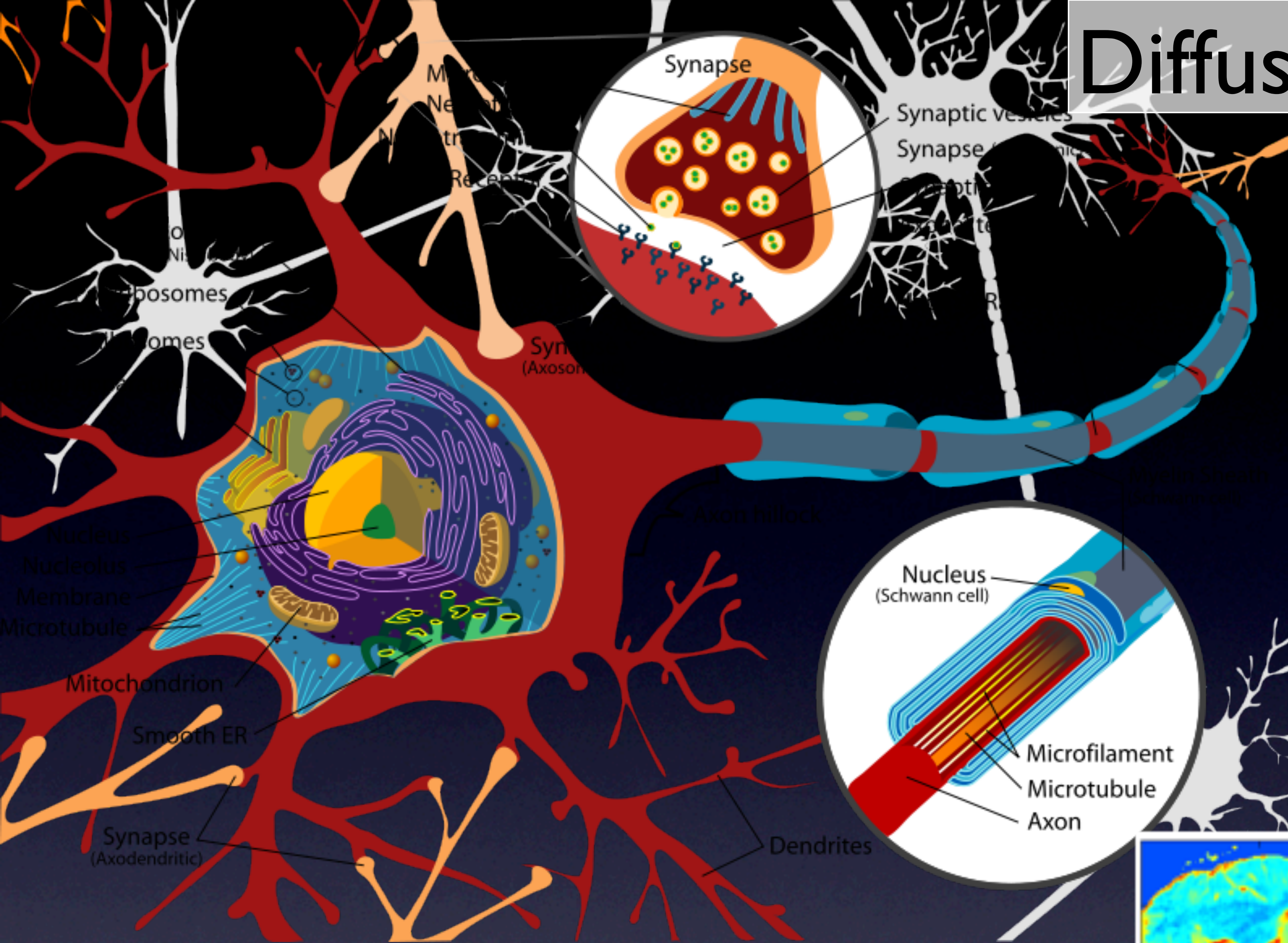
t(22)=2.06,p=0.052 t(22)=4.425,p=0.0021

What is wrong with functional connectivity studies?

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

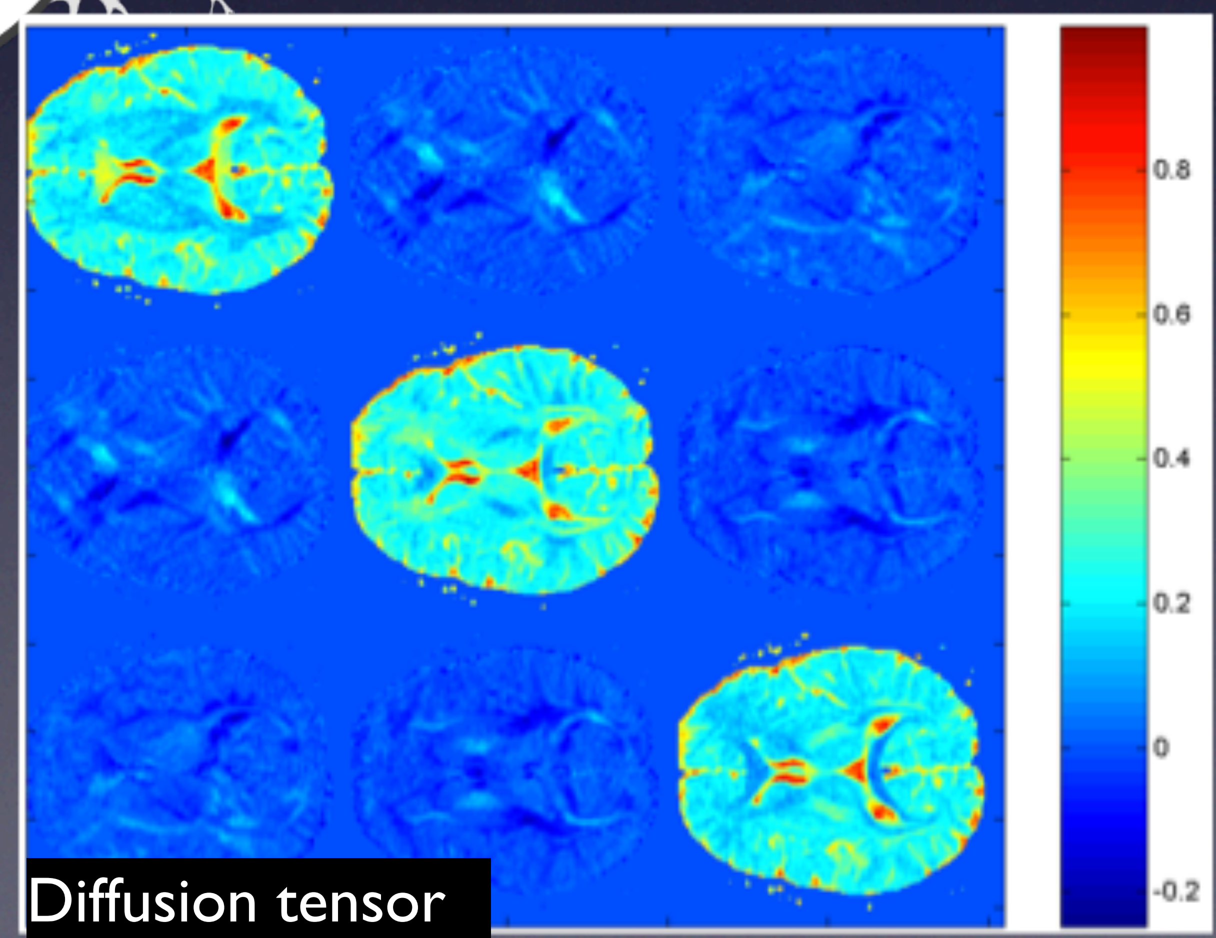
What do we really need?
-- Anatomical basis of connections

Diffusion Tensor Imaging

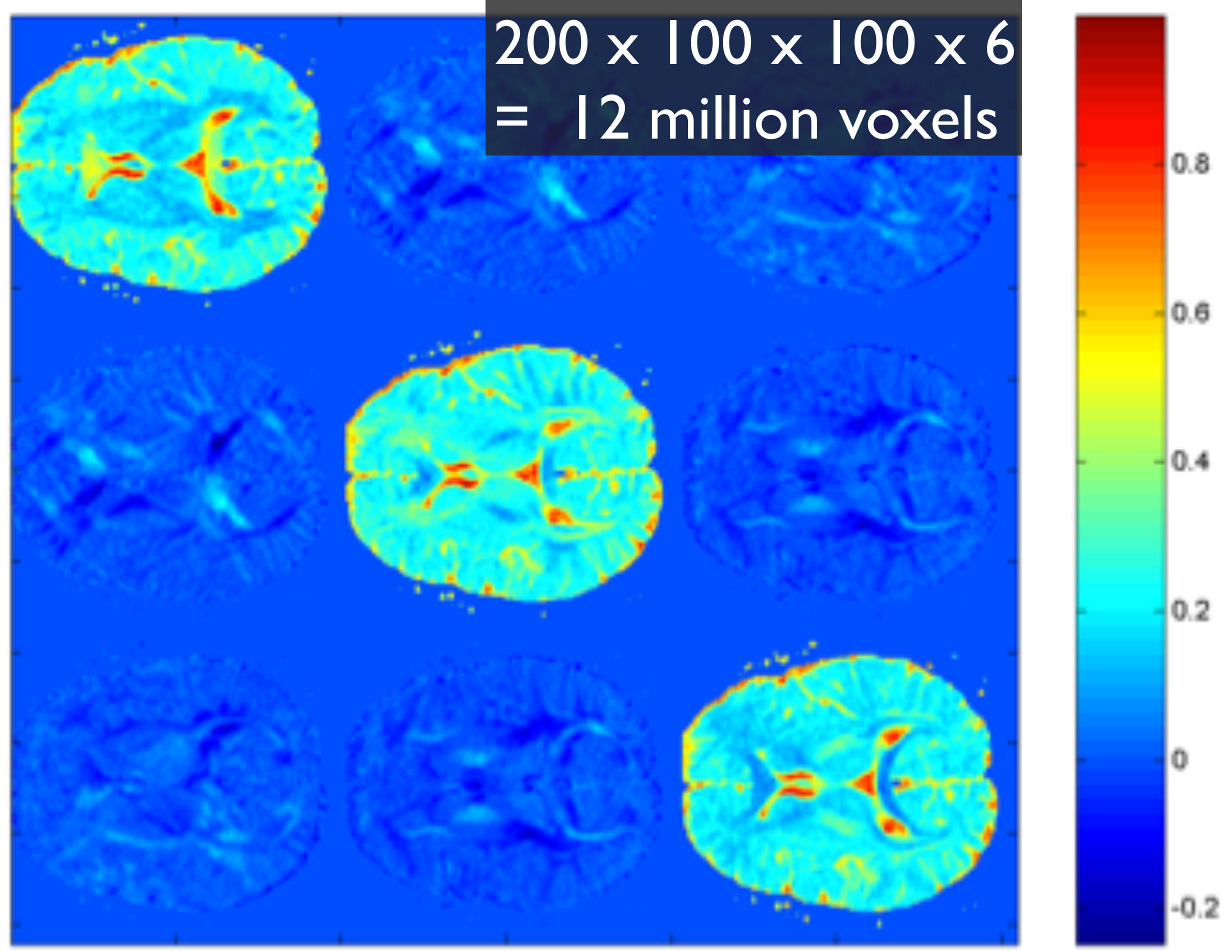


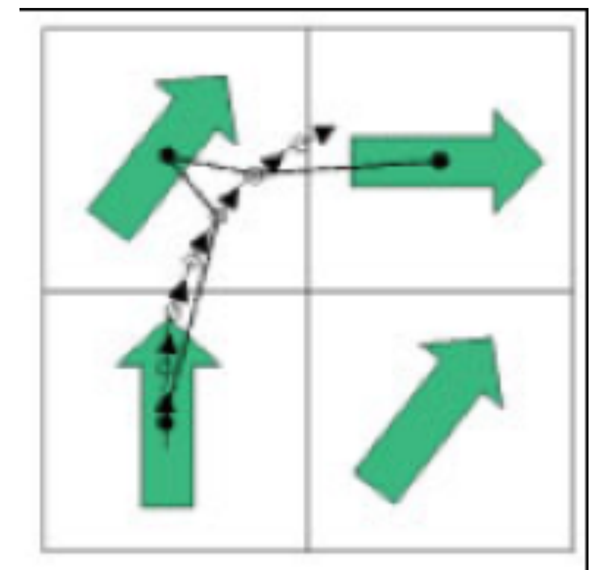
The movement of anisotropic water diffusion can be measured using DTI.

The direction of neuronal filaments in the axon dictates the movement of water diffusion.

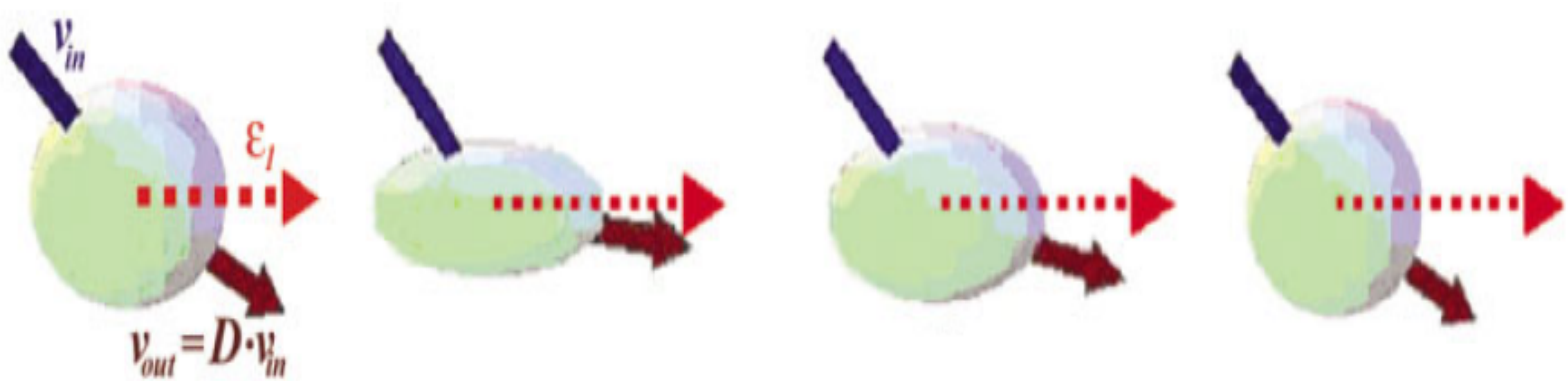


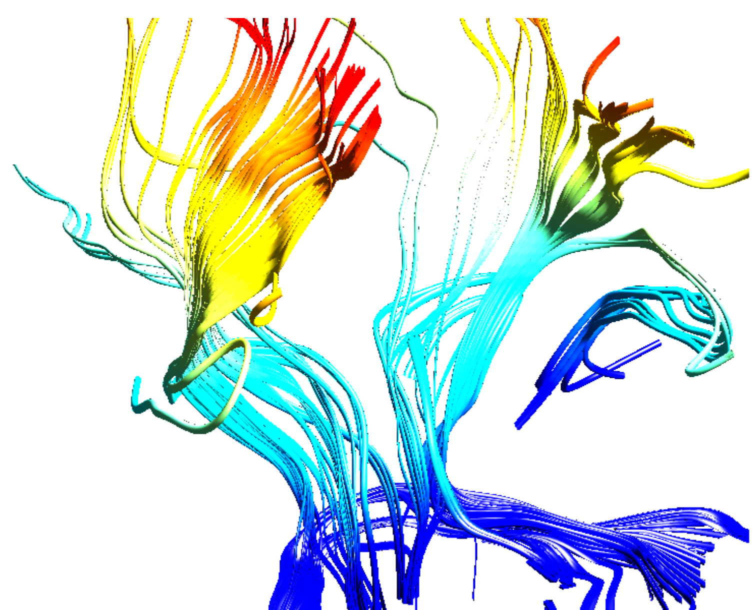
Fiber Tractography





TENsor Deflection (TEND) algorithm

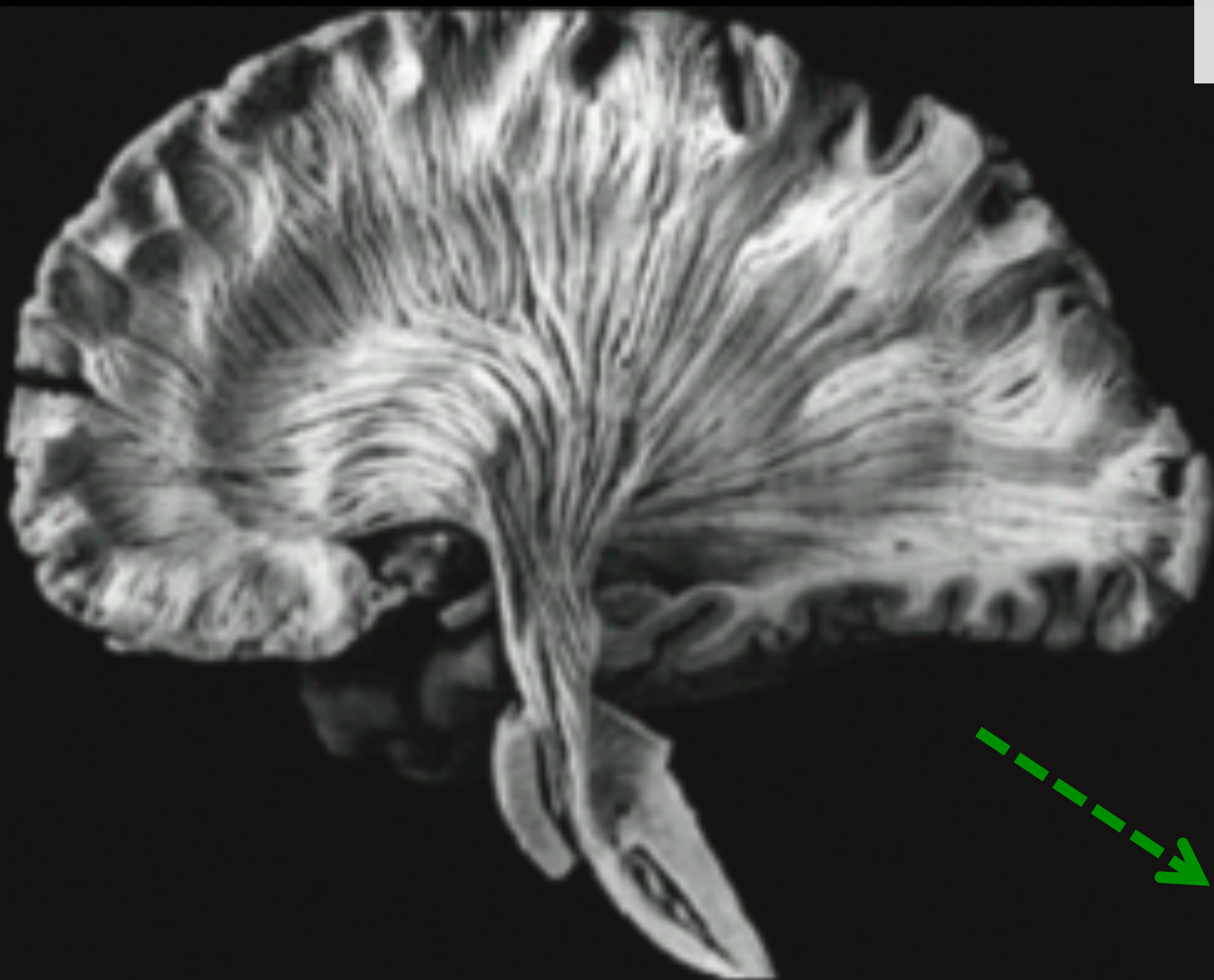




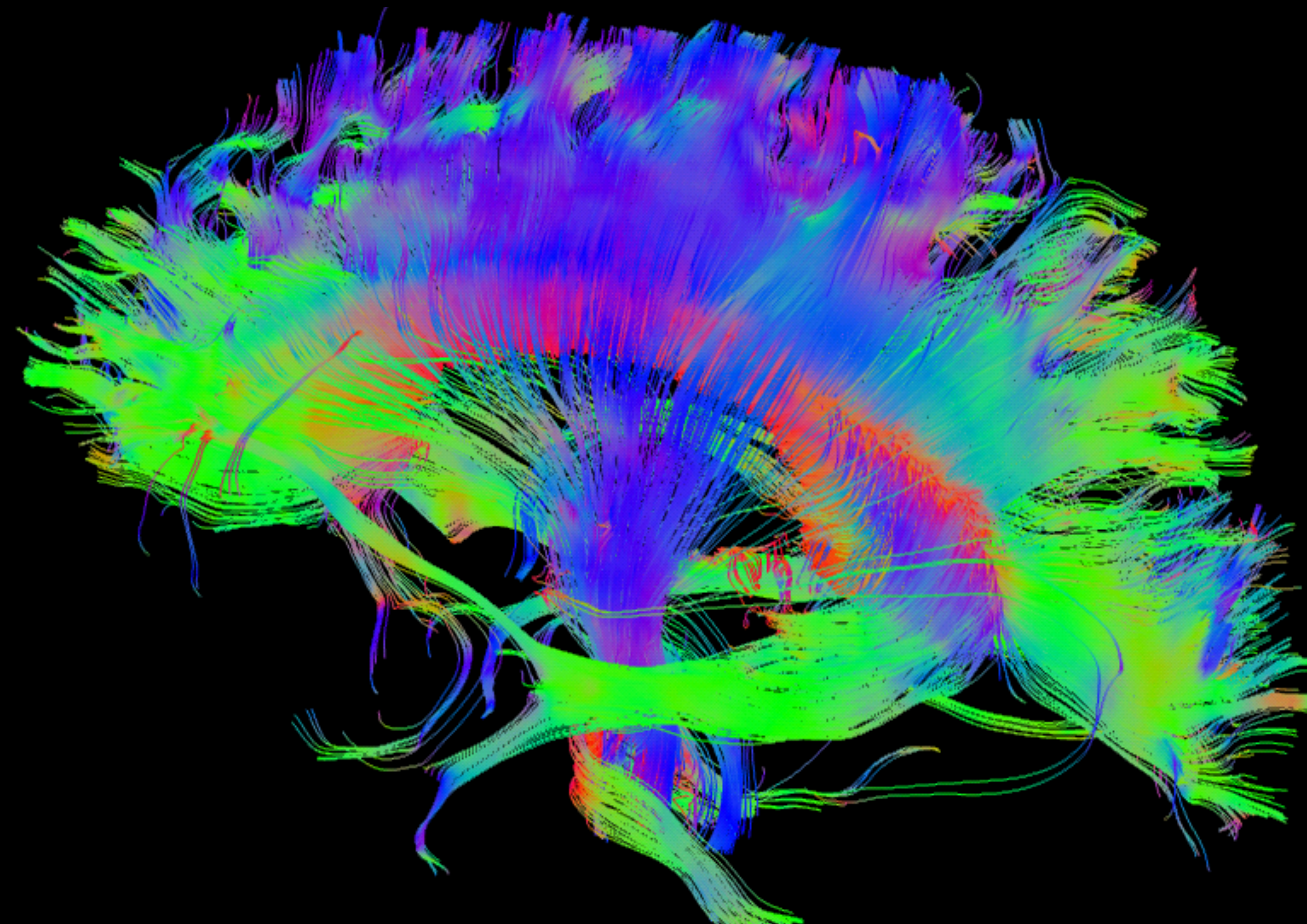
Second order Runge-Kutta algorithm with TEND

Lazar et al., HBM 2003

White Matter Fibers in Brain

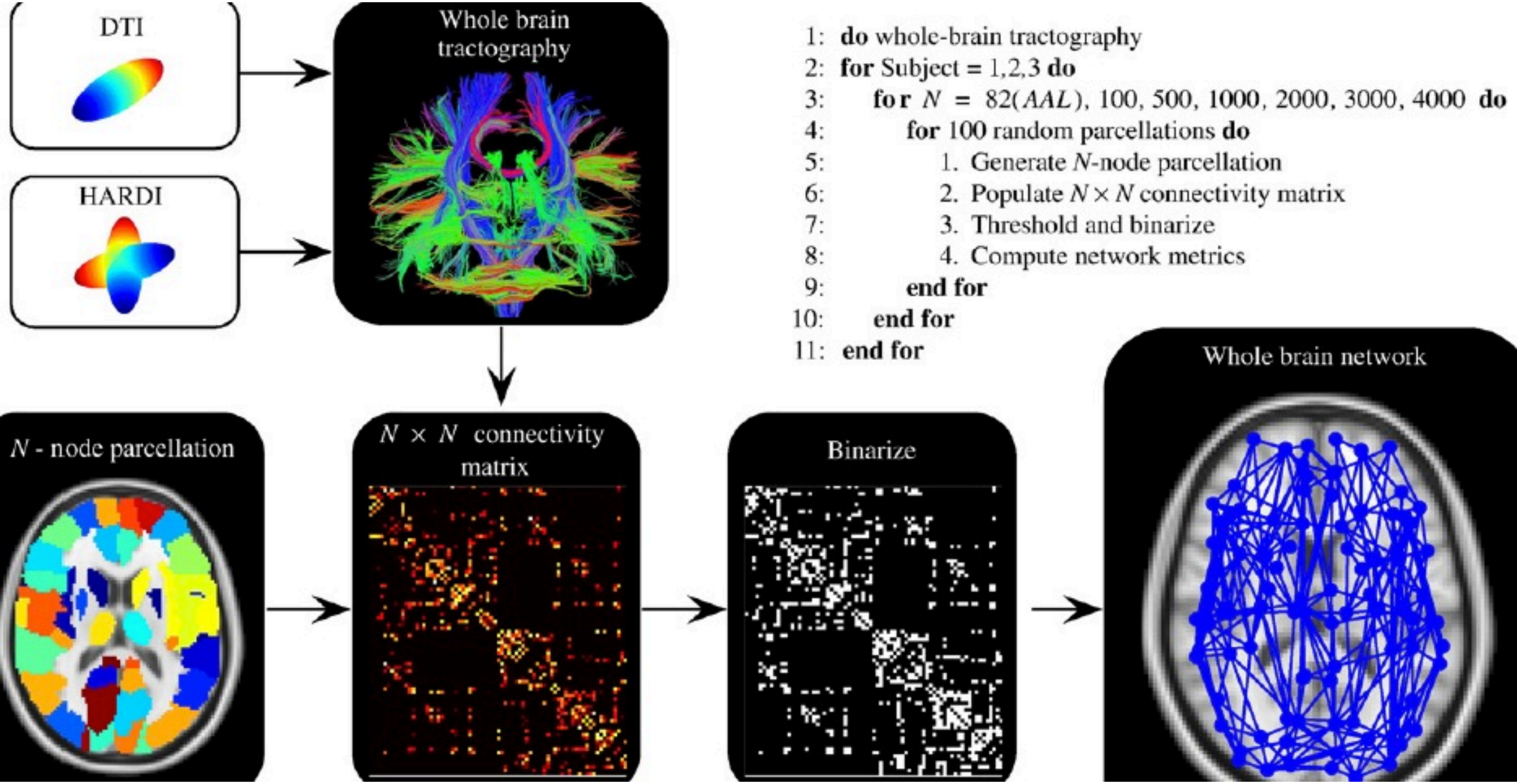


Postmortem



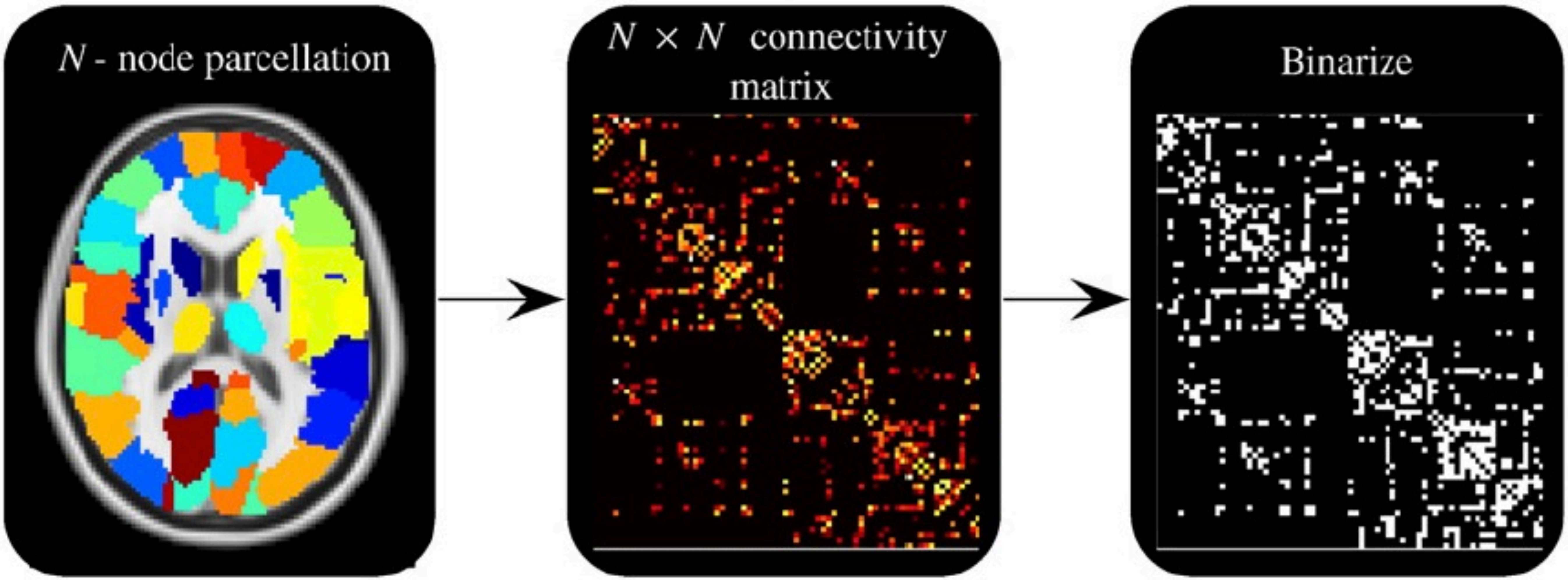
Half million tracts
600MB image per subject

Traditional brain network modeling flow



Zalesky et al. NeuroImage 2010

Two problems with the standard framework



Parcellation
70-100 regions

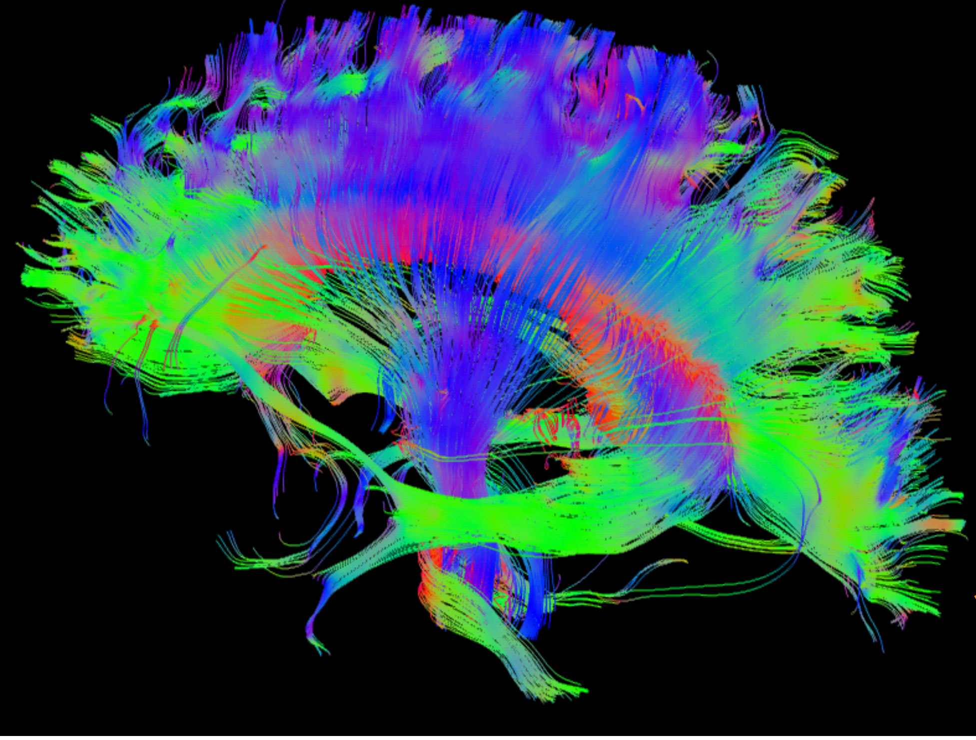
Arbitary thresholding

Brain Network Modeling without parcellation and thresholding

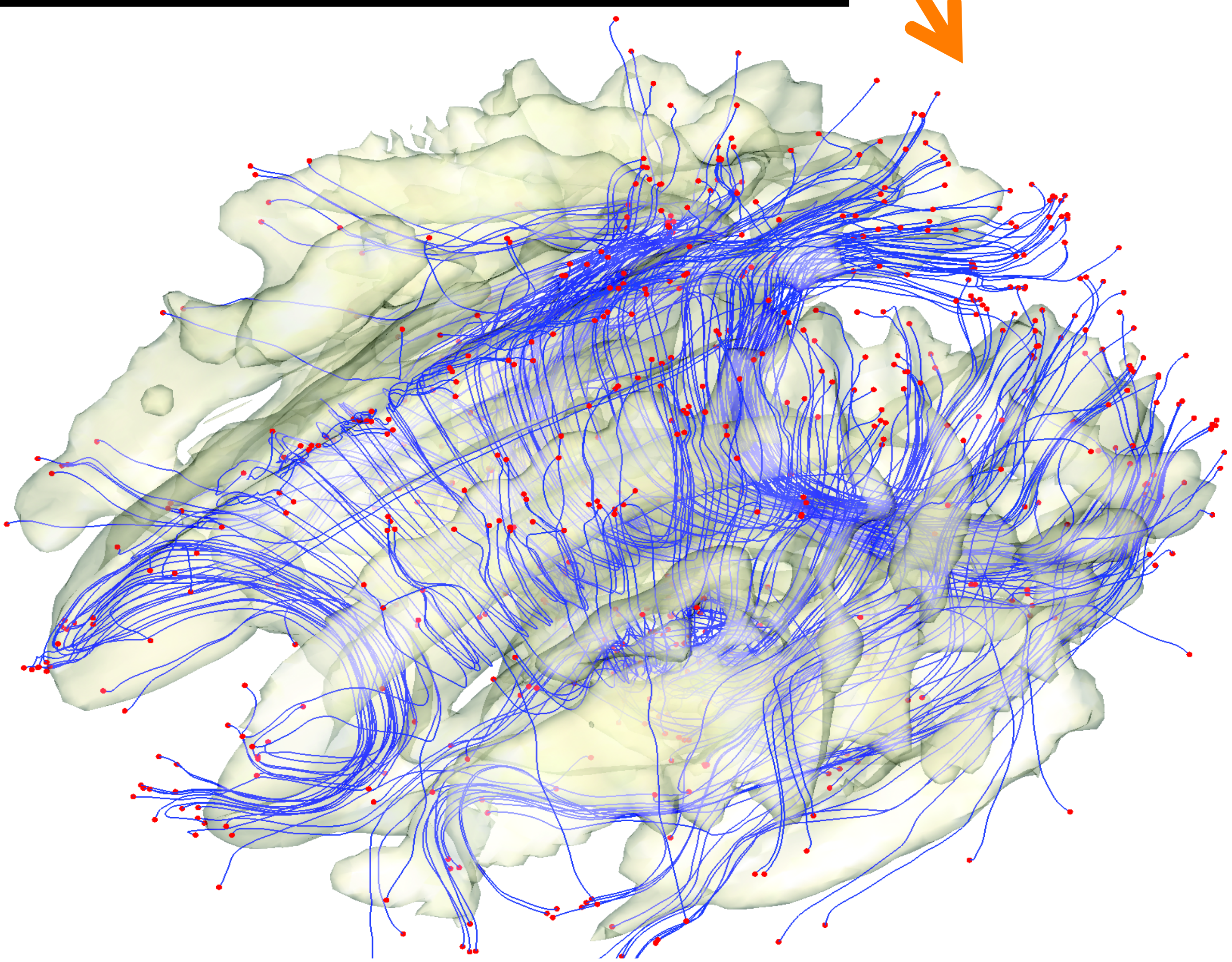
Epsilon-neighbor method

A different simplex construction technique

ε-neighbor graph simplication

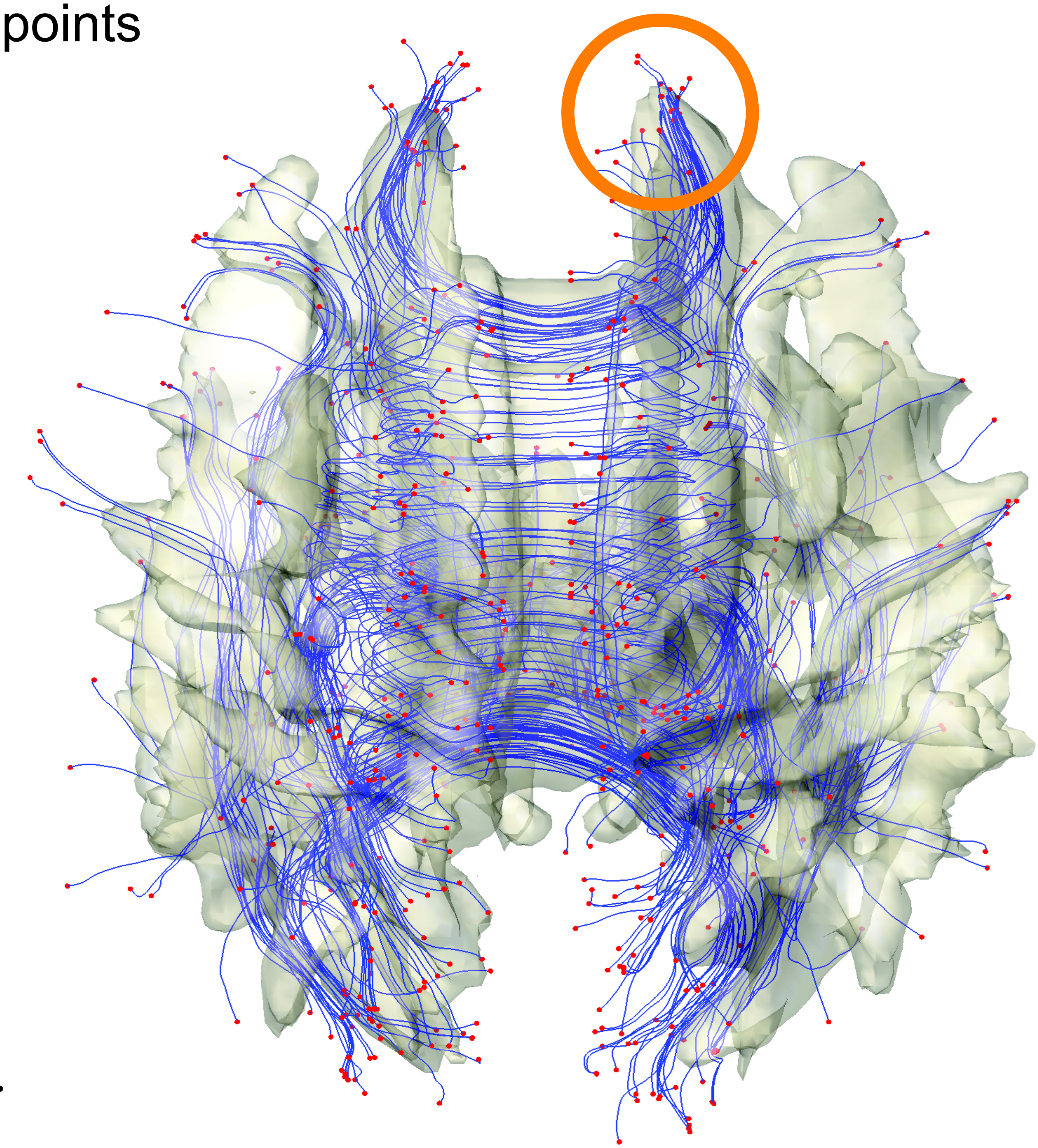


Identify end points

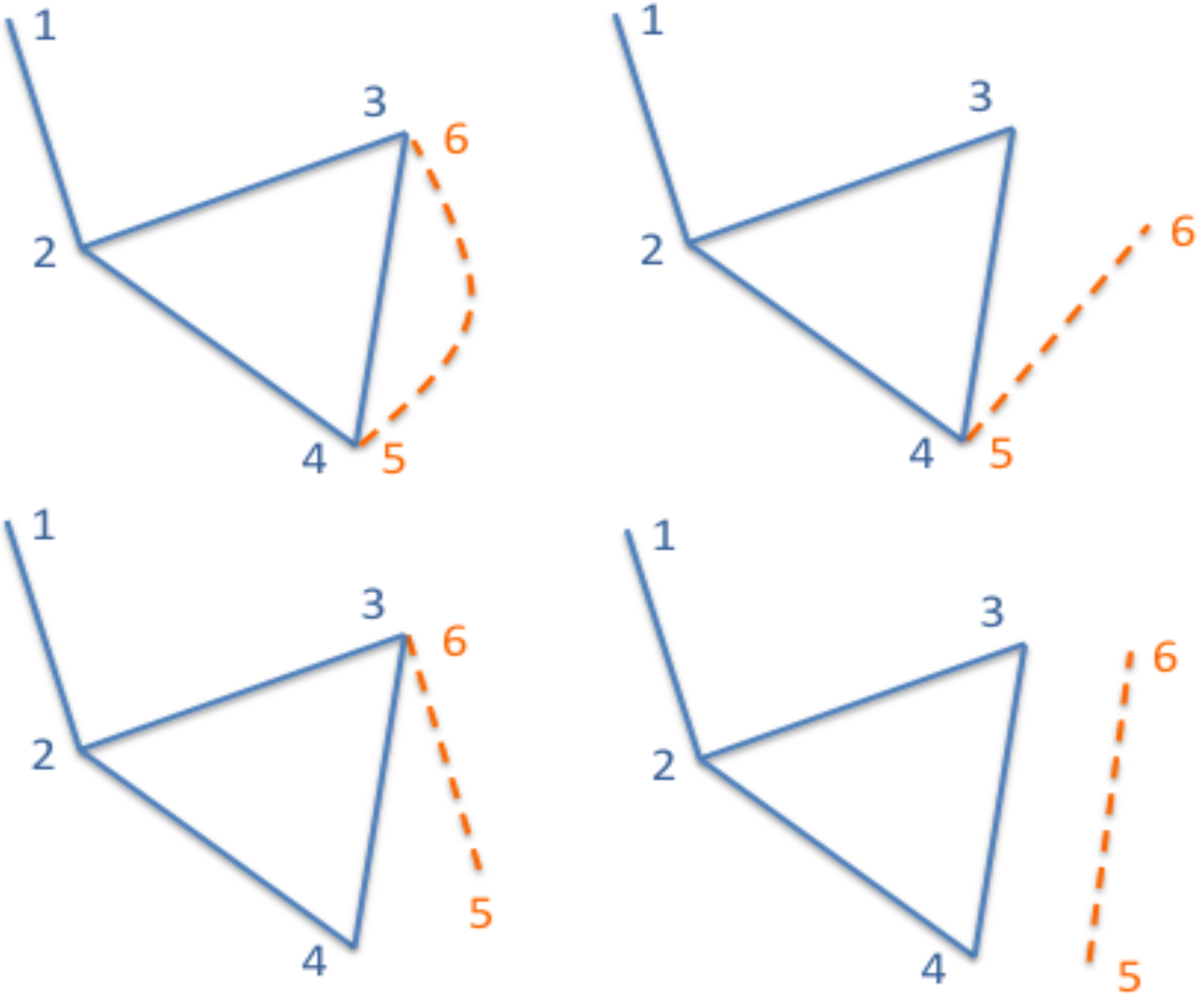


The first data-driven DTI structural network construction framework without any parcellation.

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

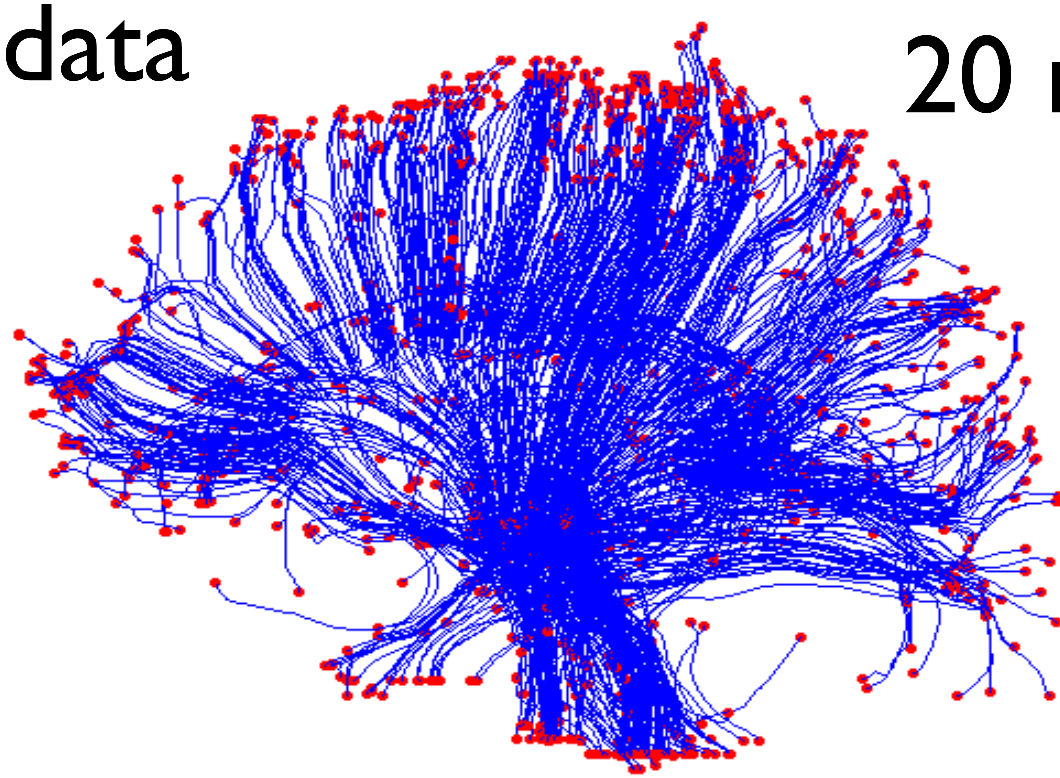


Iterative graph construction

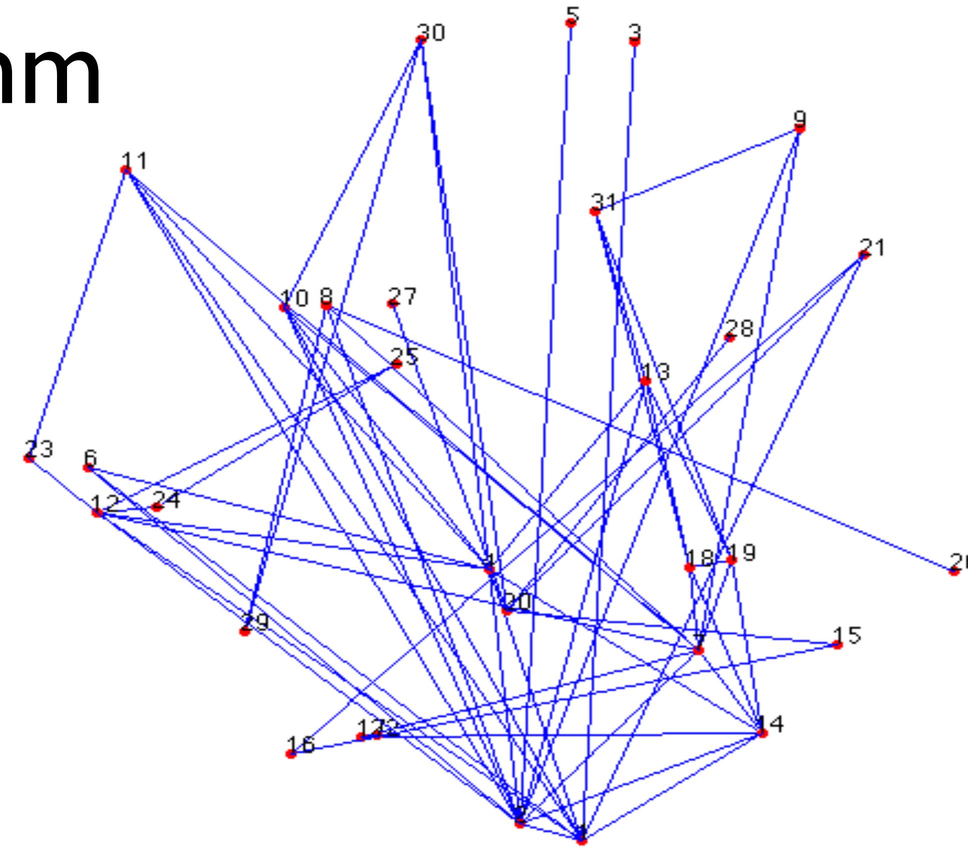


ε-neighbor graphs with different ε

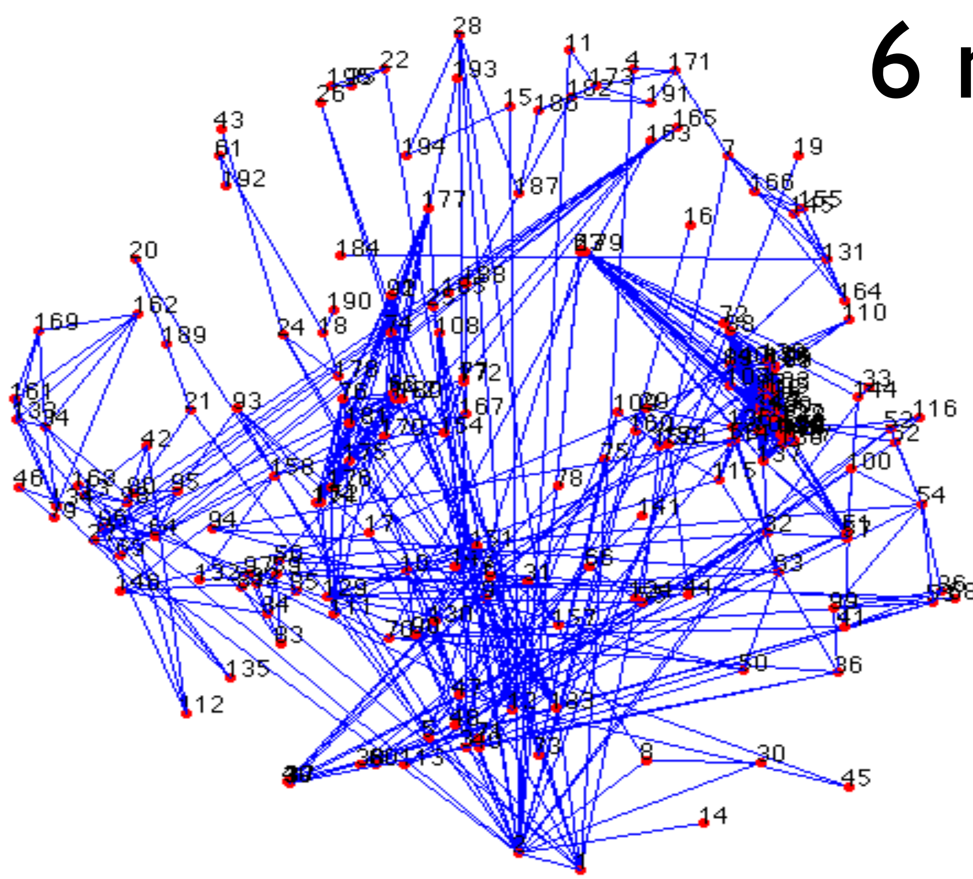
original data



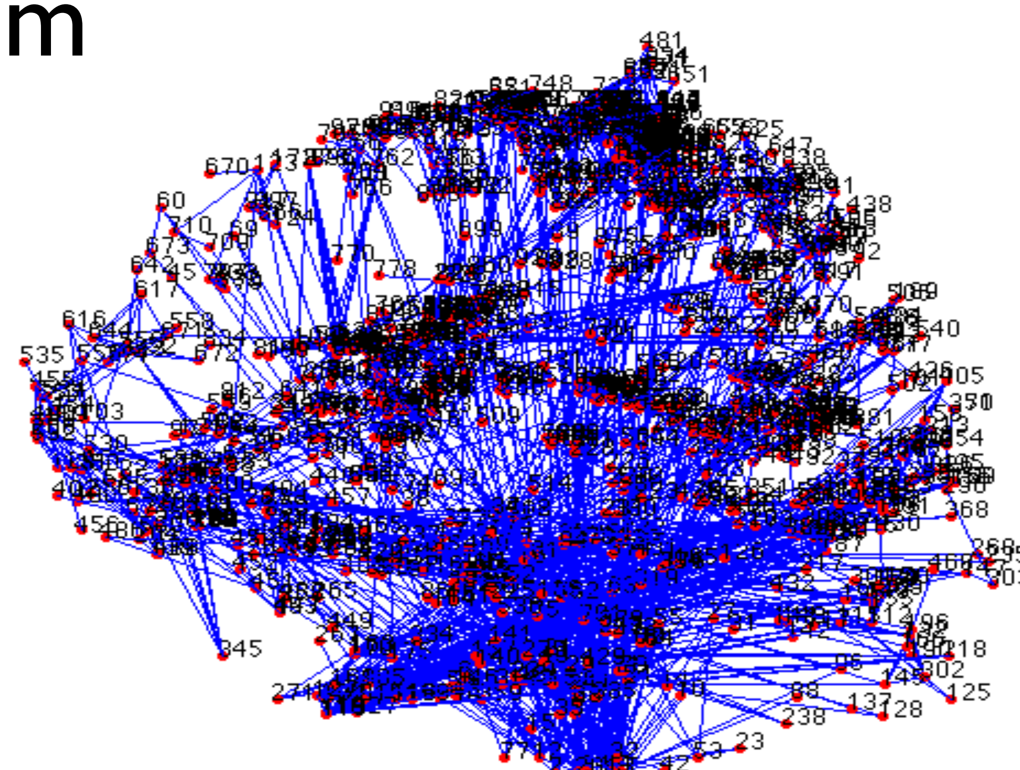
20 mm



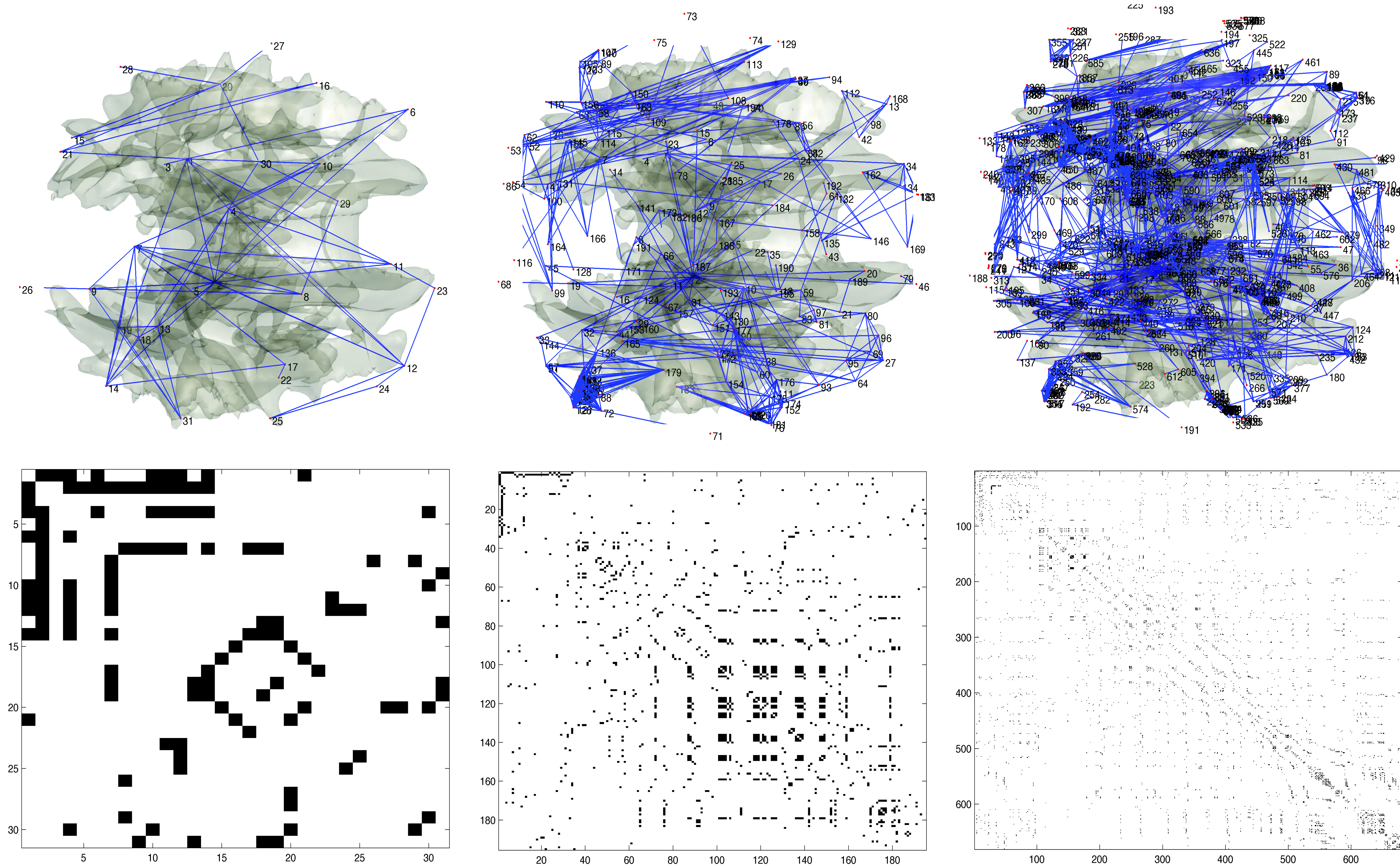
10 mm



6 mm



Adjacency matrix



MATLAB DEMO

Epsilon Neighbor method

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

Application to autism

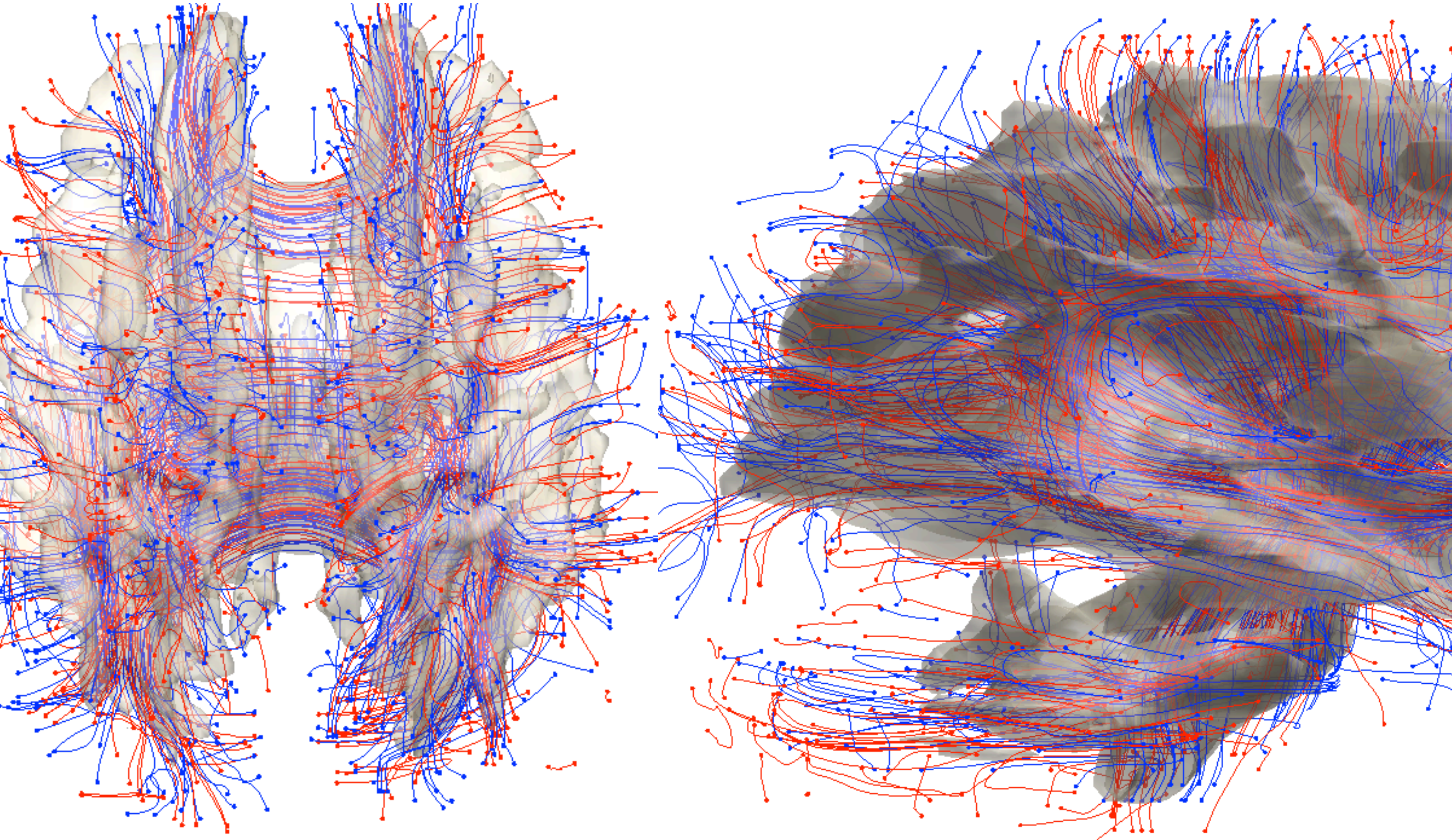
Autistic children (n=17)

Control subjects (n=14)

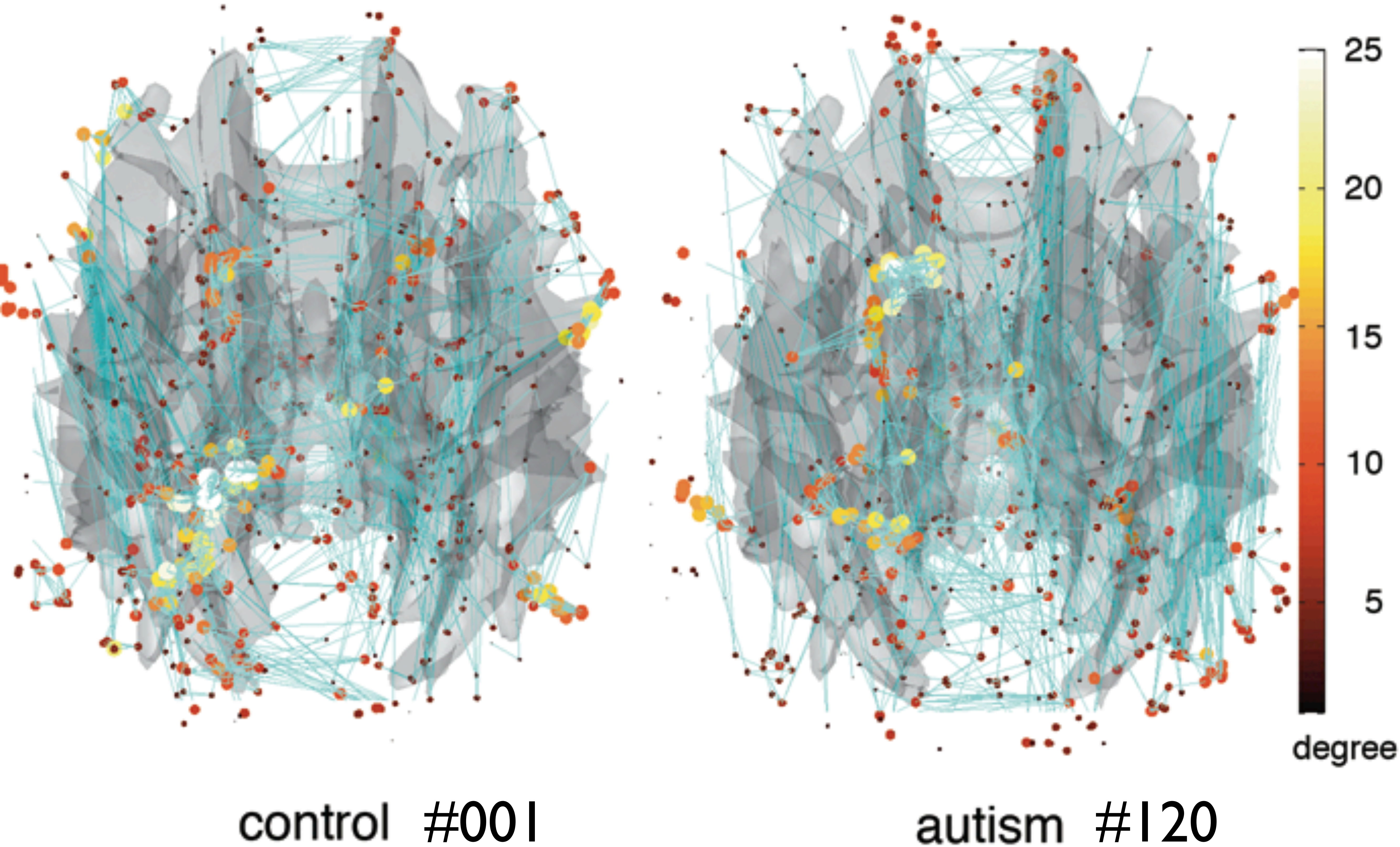
Matched for age, handedness, IQ and head size

Abnormal connectivity in autism ?

DTI registration

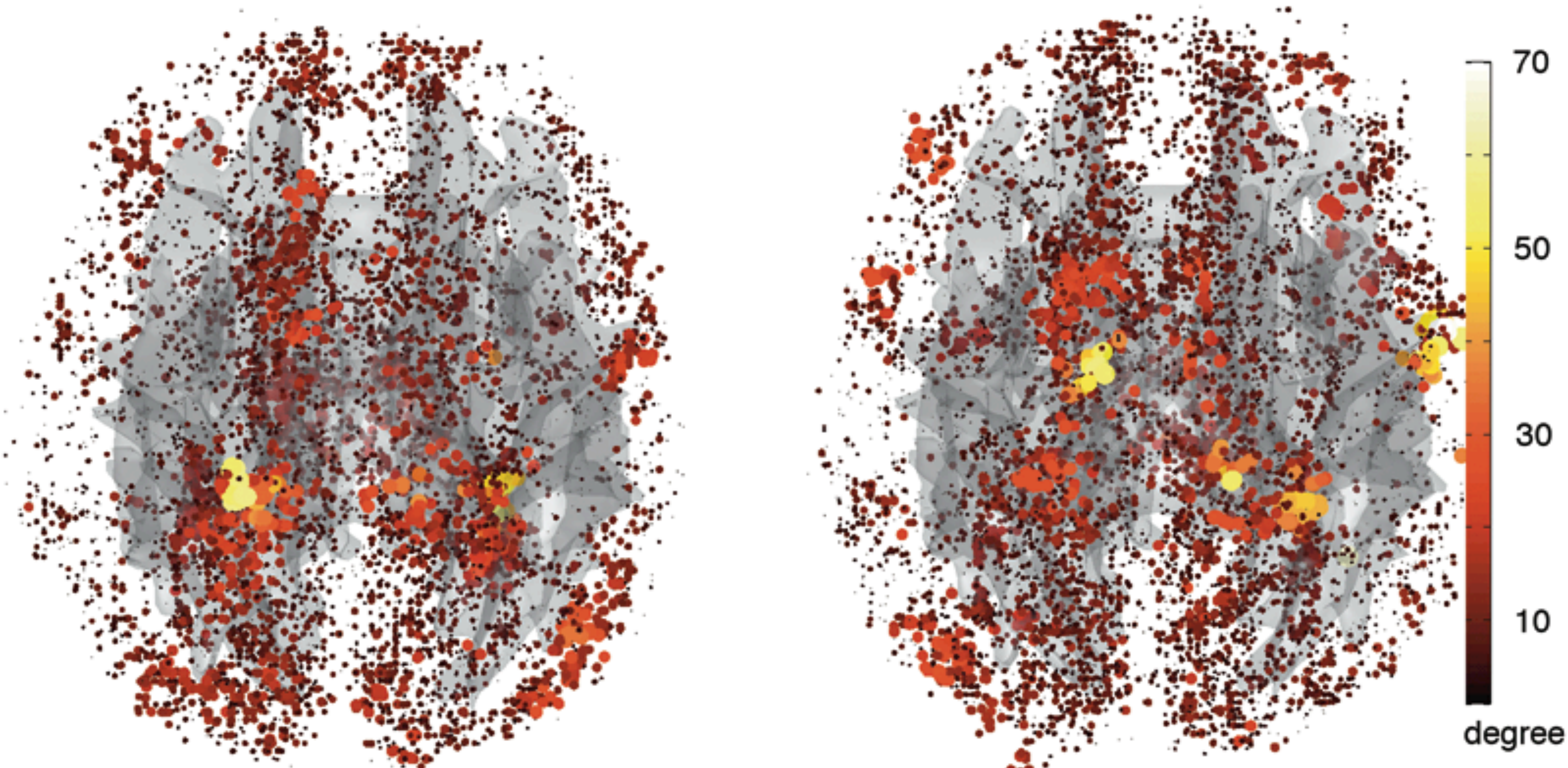


Degree of nodes for a single subject



Local inference on degree

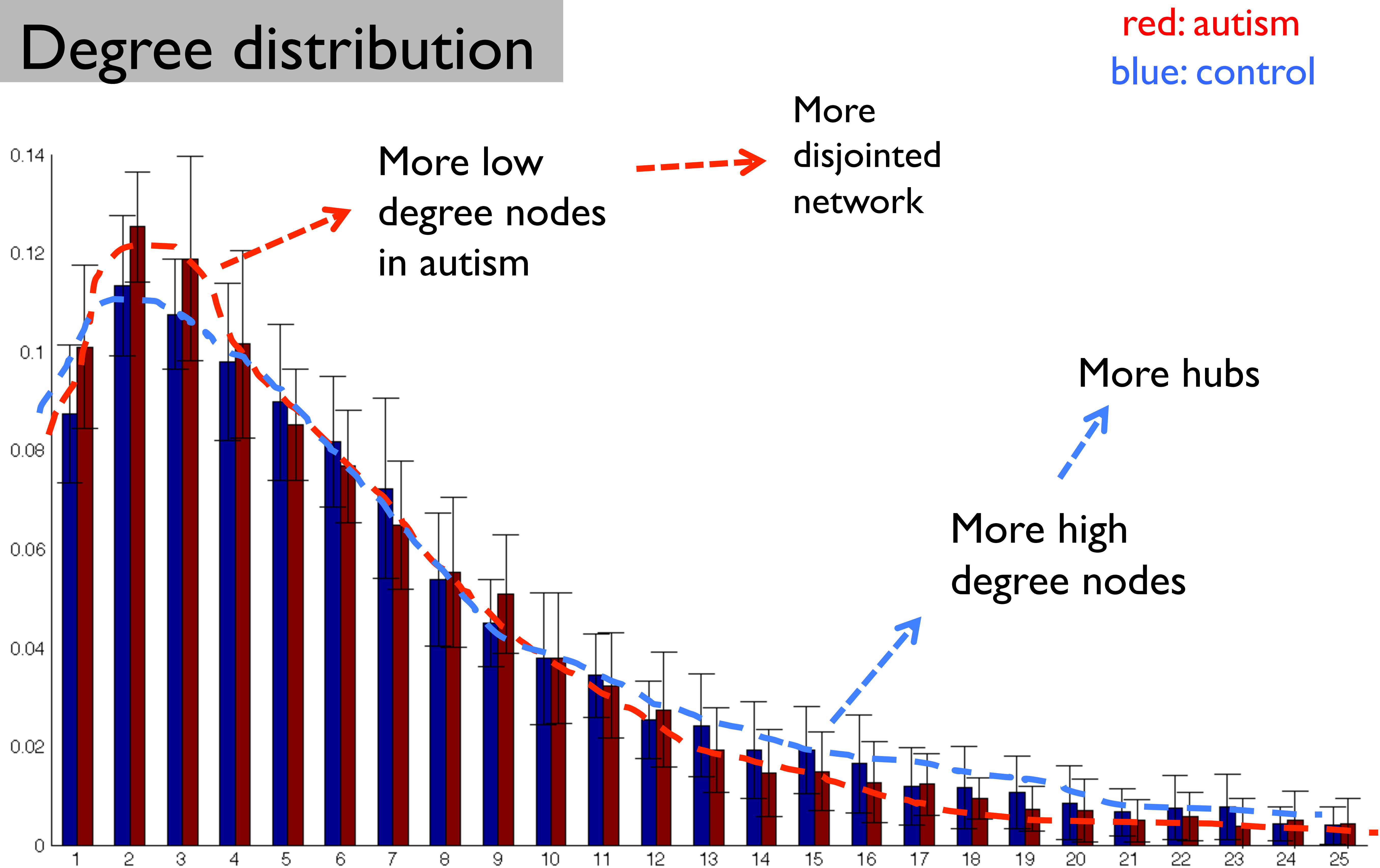
Superimposition of every subjects



Control

Autism

Degree distribution

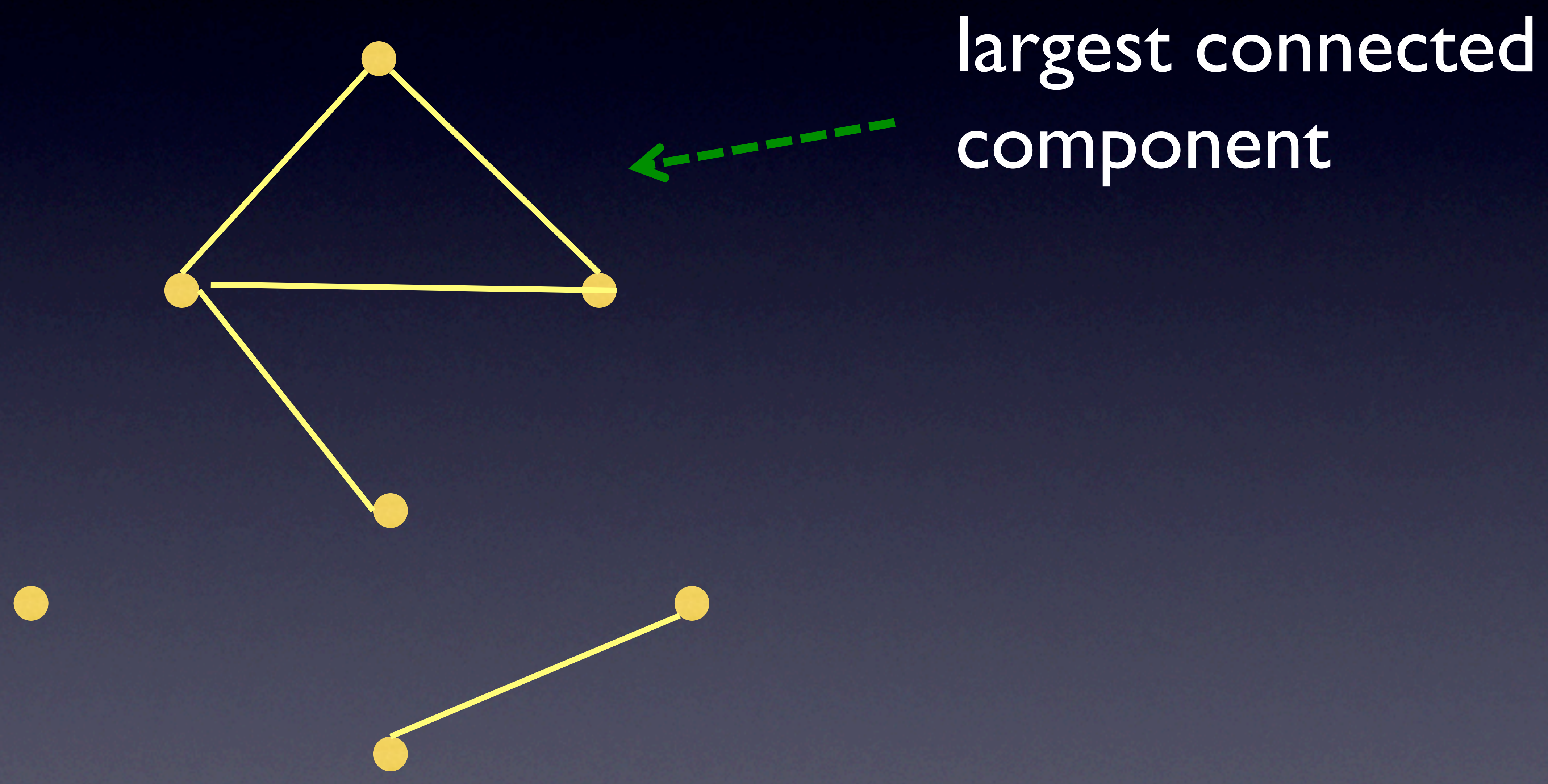


pvalues = 0.024, 0.015 and 0.080 for degrees 1, 2 and 3.

Persistent homological approach

Graph Filtration

Connected component



Filtration on ε-neighbor graphs

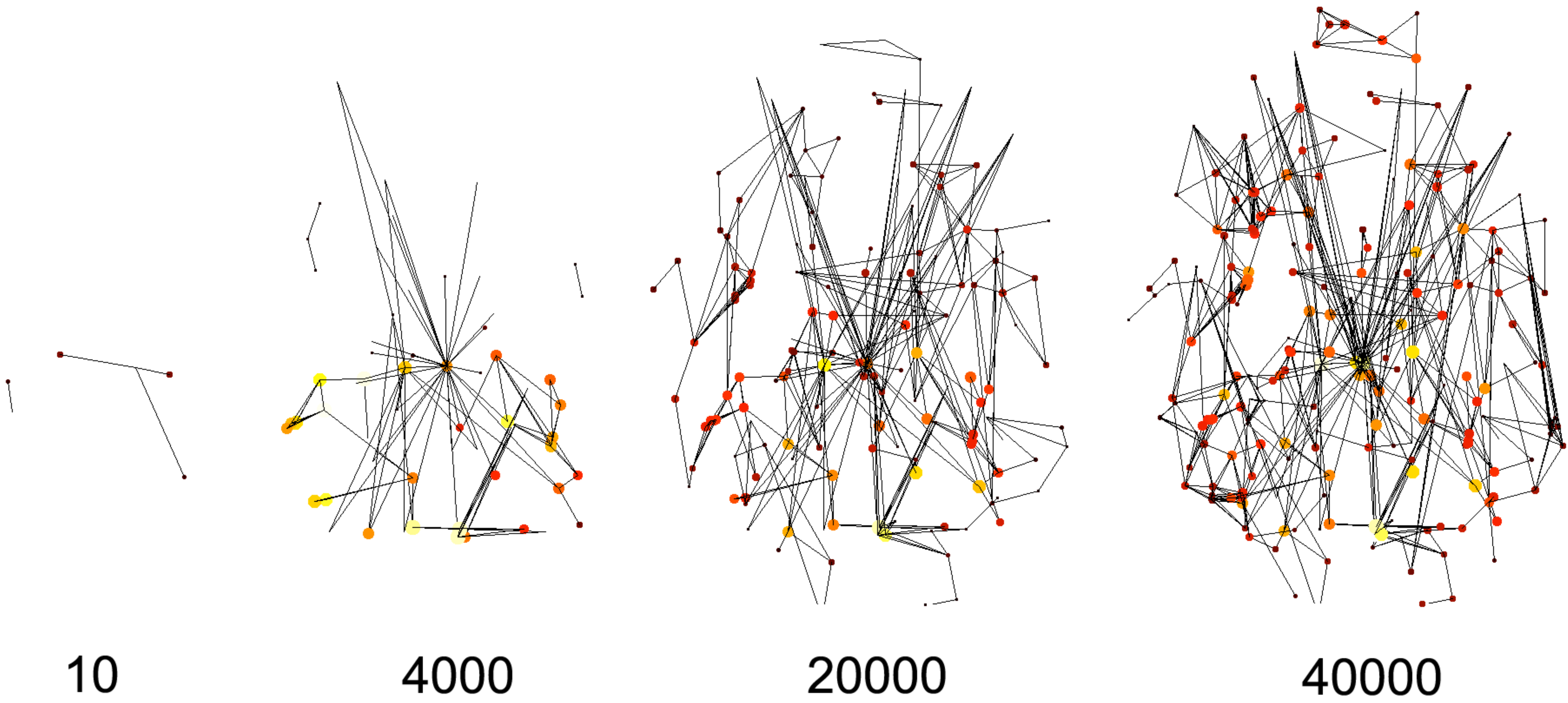
ε-neighbor graph at the *i*-th iteration $\mathcal{G}_i$

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

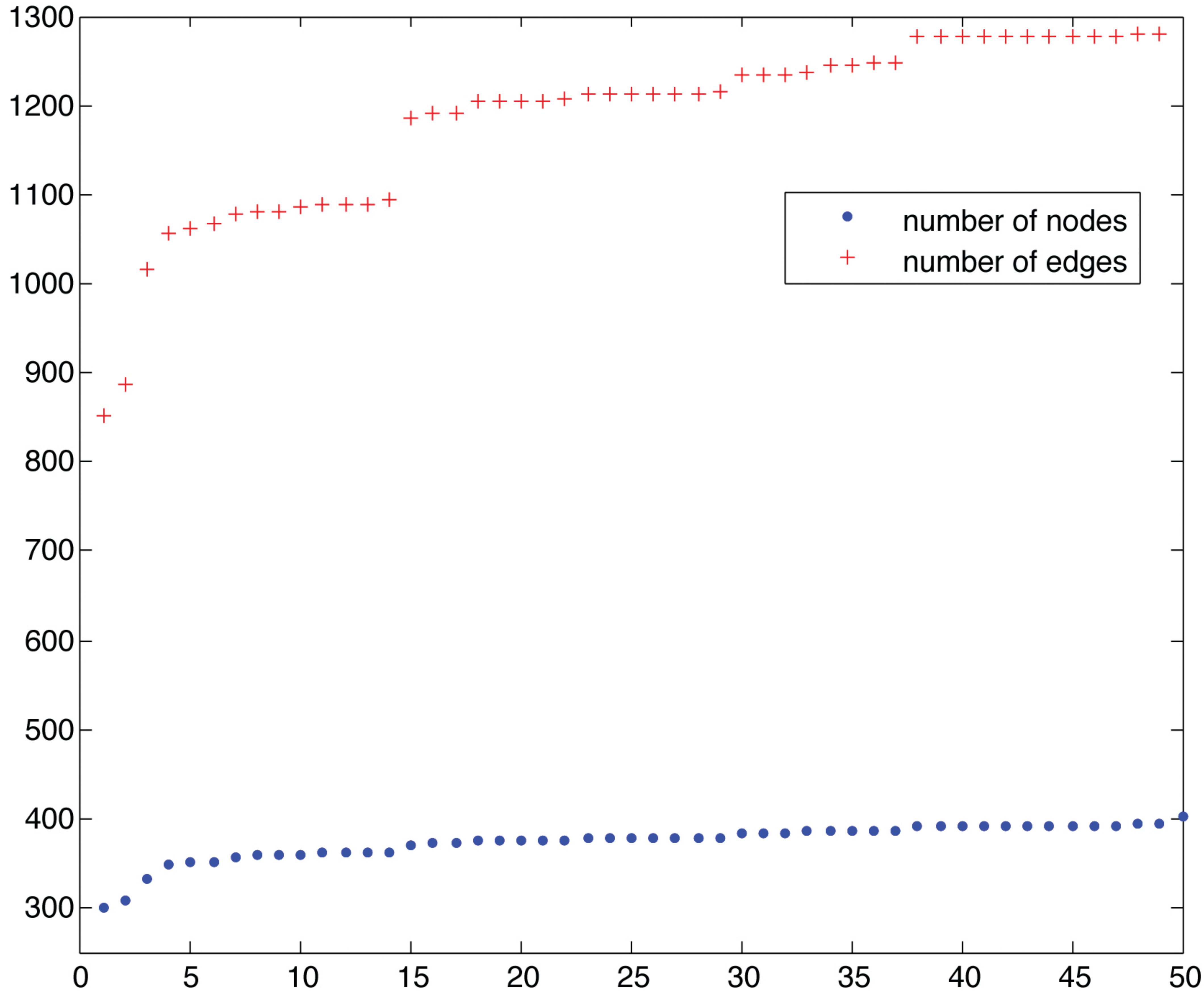
The size of the *i*-th graph is an increasing function:

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

Filtration on ε-neighbor graphs

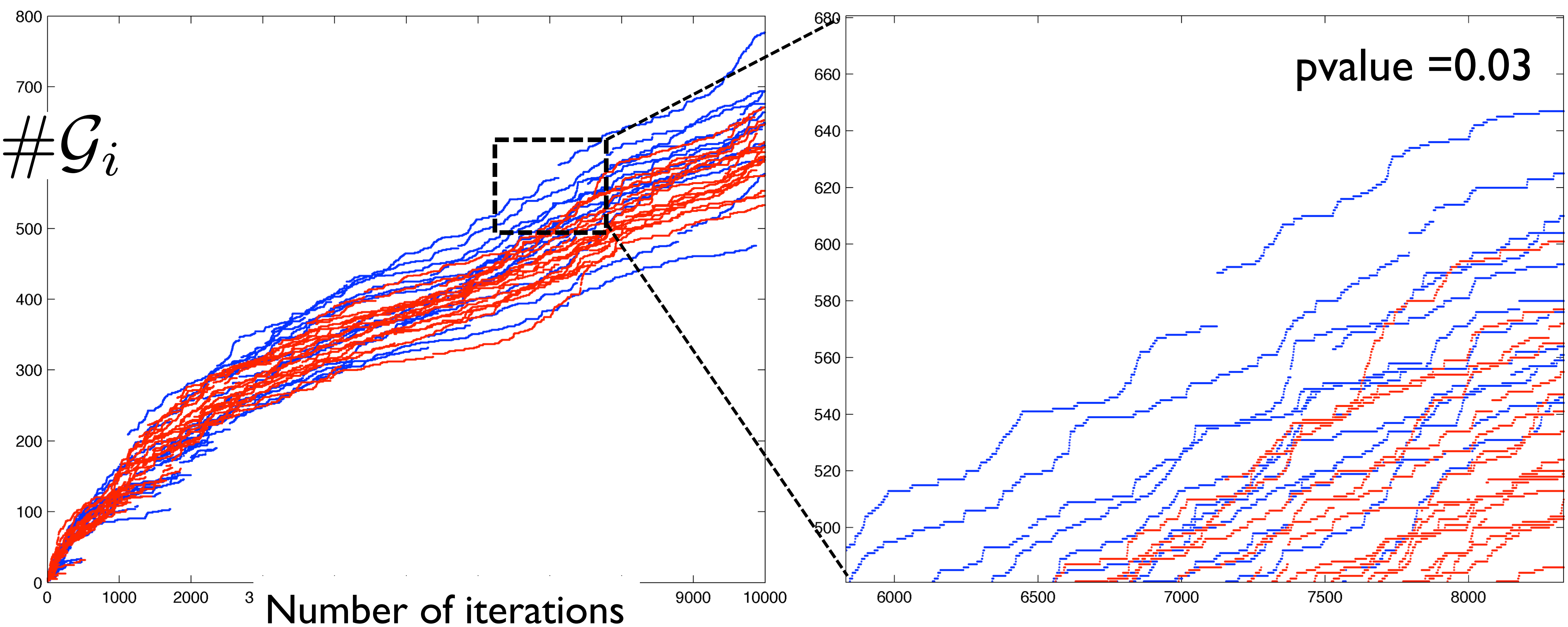


Number of edges and nodes in filtration



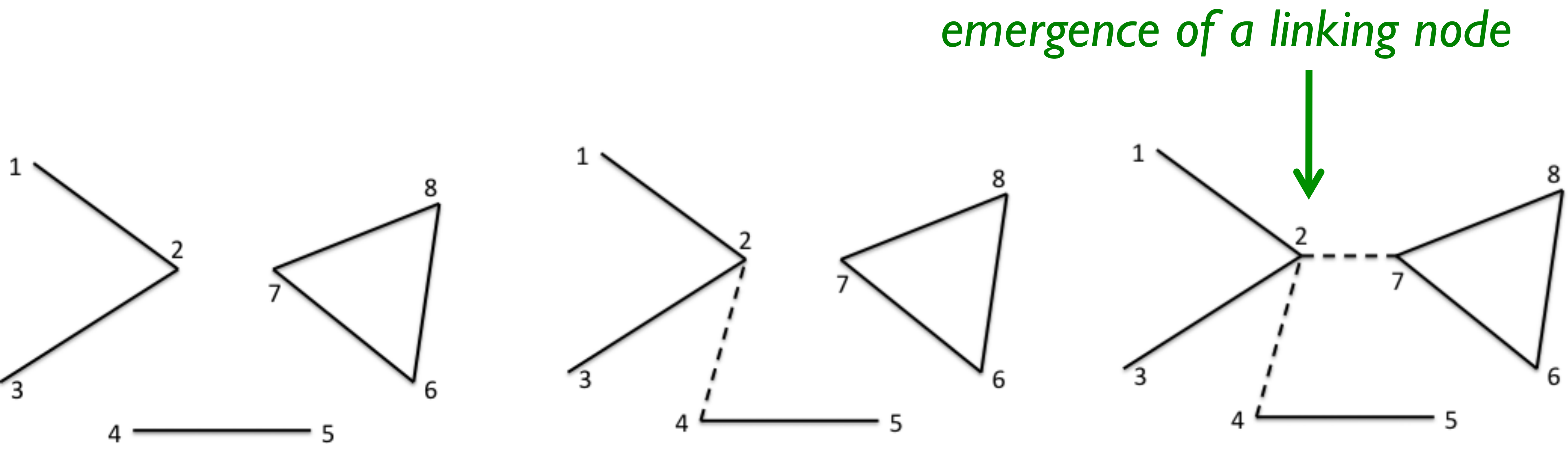
Network integration difference

Control=blue
Autism=red



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

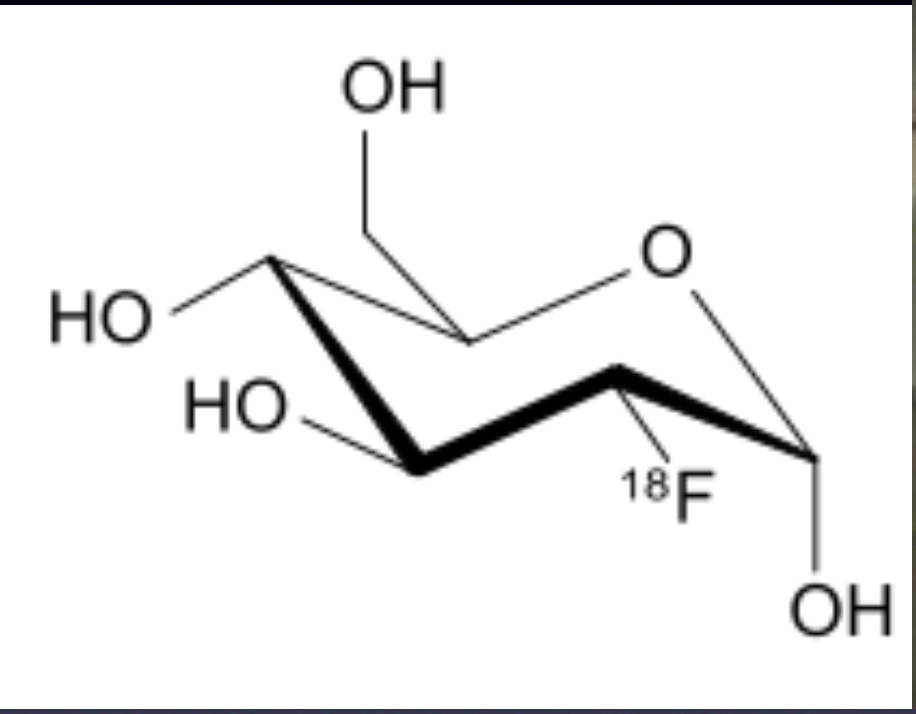
The size of the largest connected component

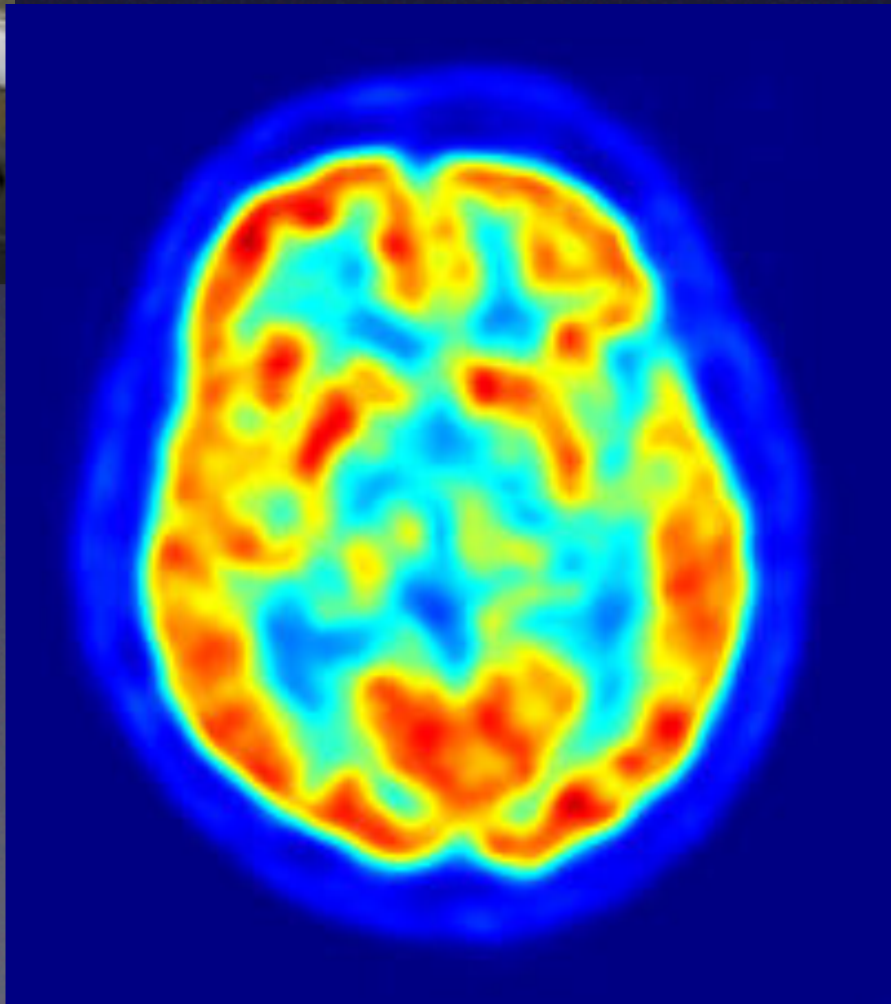


Size: 3 5 8

FDG-PET imaging

The PET scanner detects pairs of gamma rays emitted from a positron-emtting radioactive tracer.

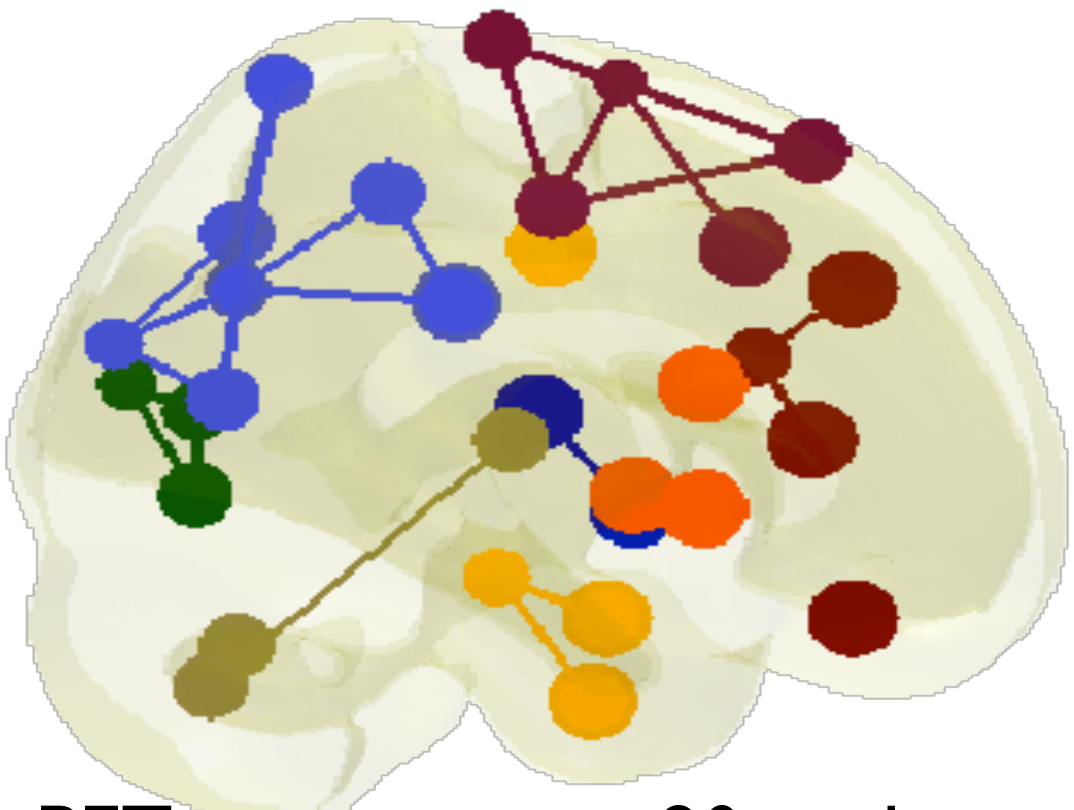




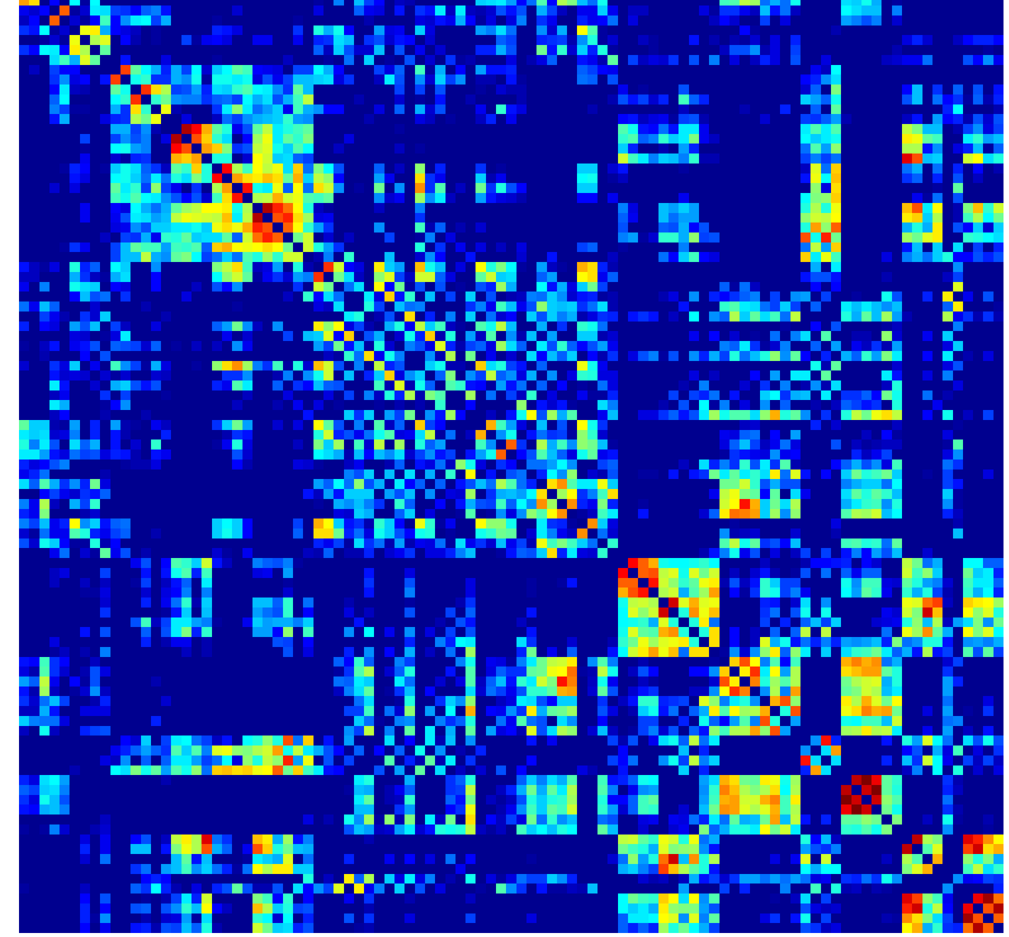
^{18}F-FDG is the most widely used tracer used for measuring tissue metabolic activity, in terms of regional glucose uptake in the brain.

Pet metabolic connectivity

Lee et al., 2011 MICCAI



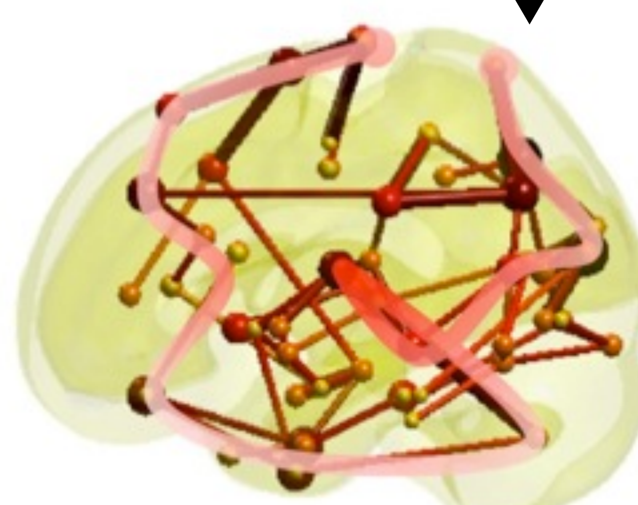
PET measures on 90 nodes



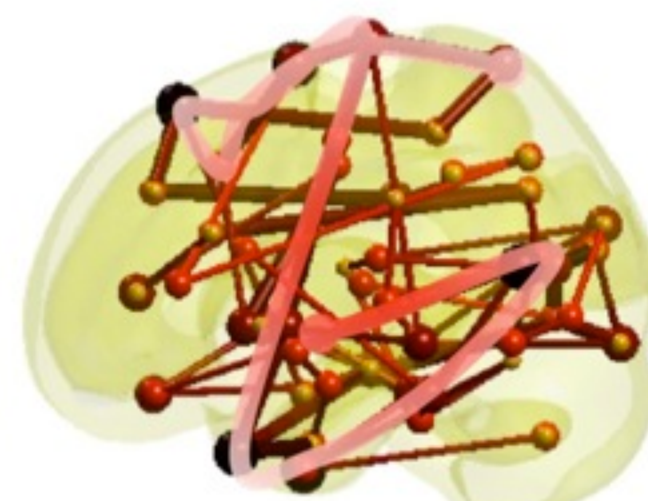
90 x 90 correlation map

Graph filtration

Attention deficit



Autism



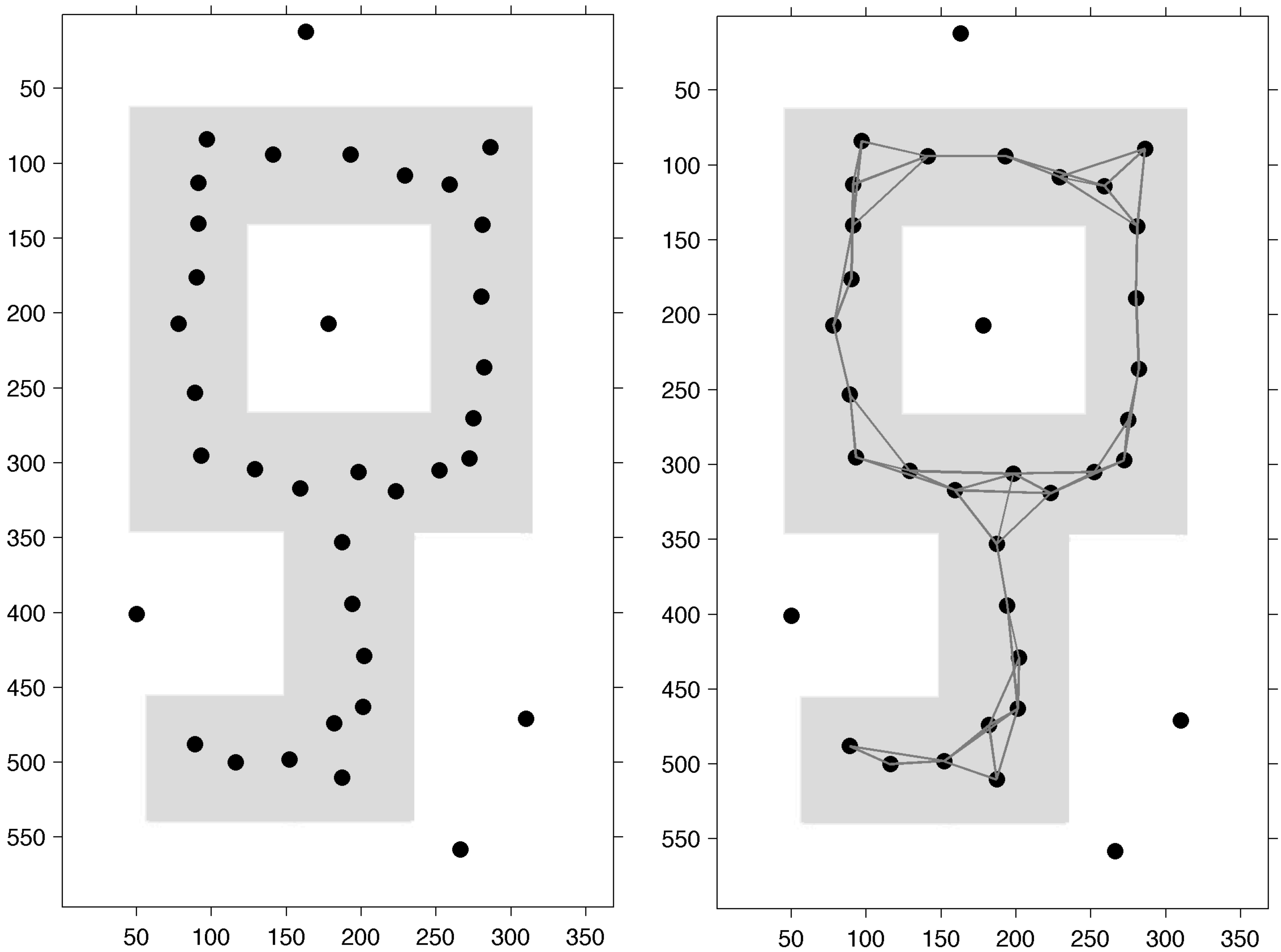
Control

Rips complex of point cloud data

Rips complex approximates the topology of the point cloud data by connecting two point cloud data, x_i and x_j, if $d(x_i, x_j) < \varepsilon$

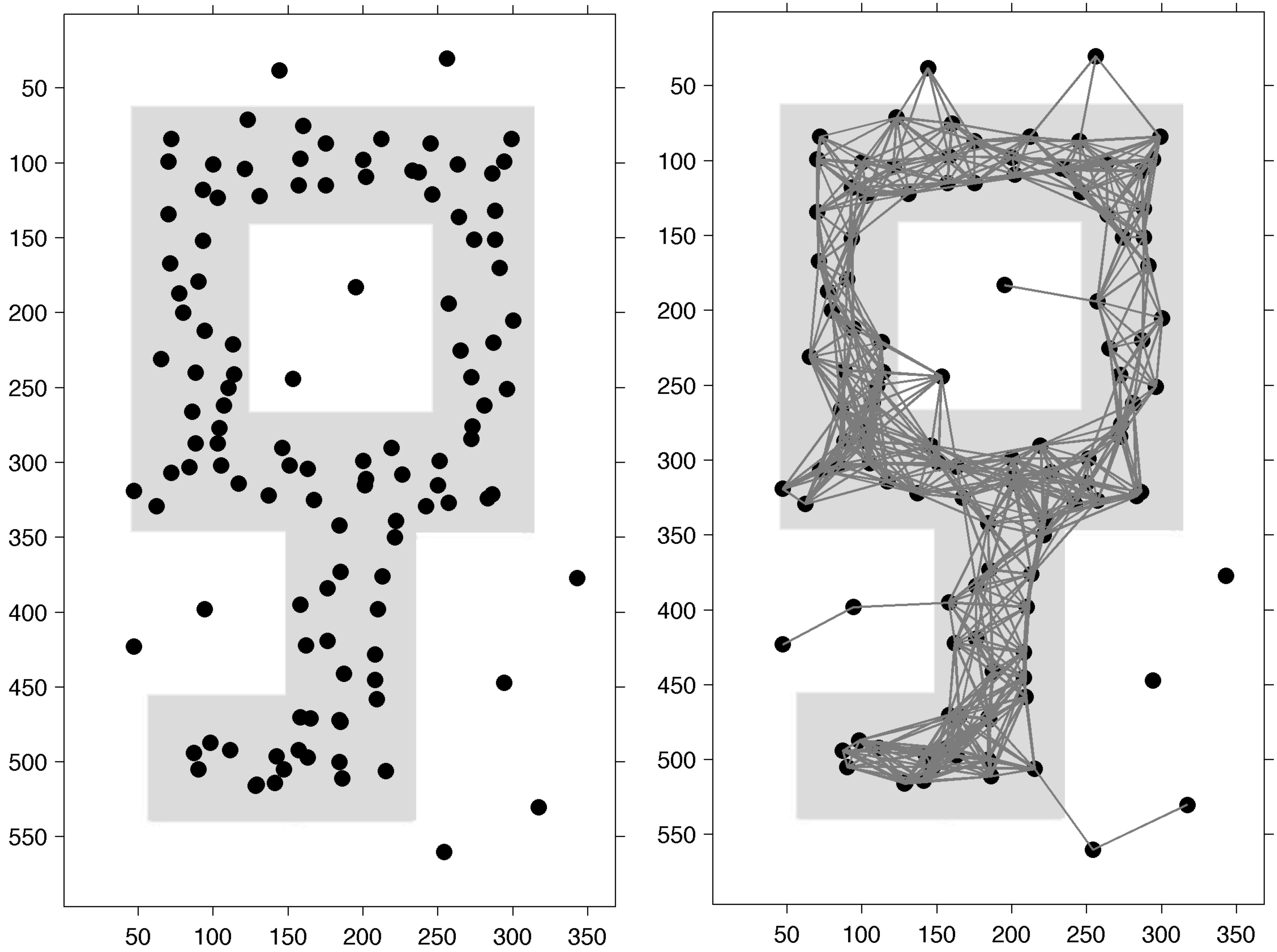
Rips complex of point cloud data

ε = 70mm



What's wrong with Rips complex

ε = 70mm



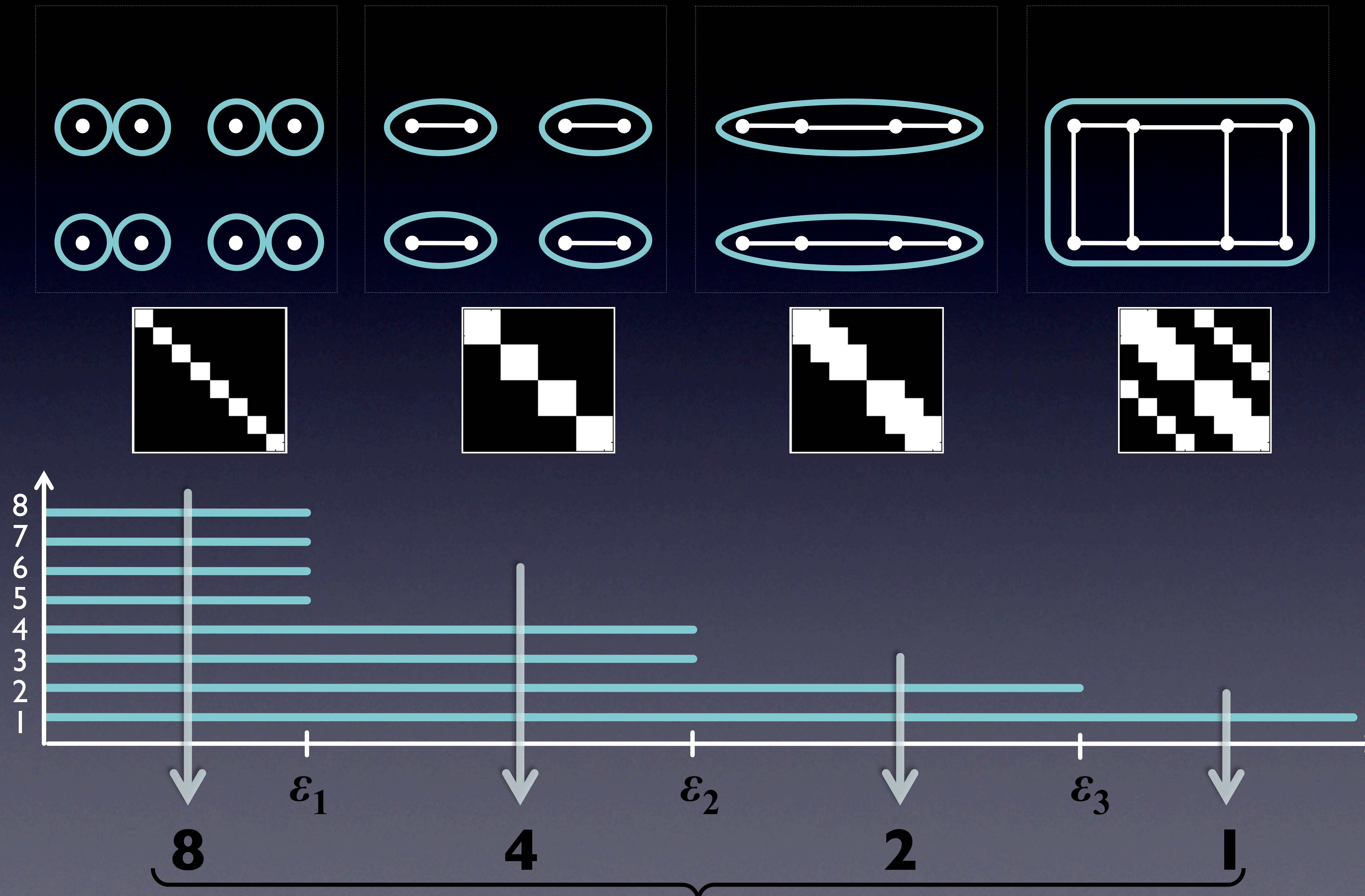
MATLAB DEMO

Epsilon Neighbor method

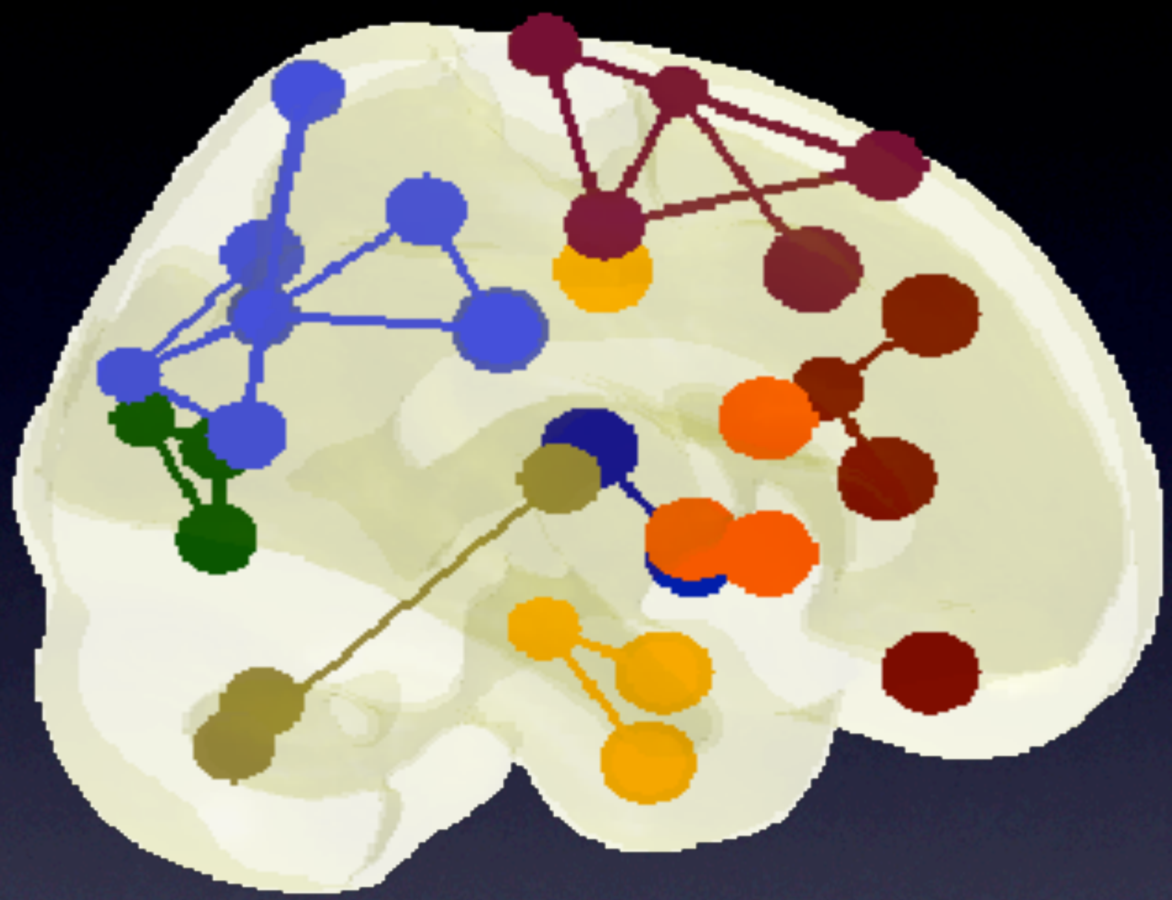
/adjacency.matrix/matlab/DEMO.2011.07.09.IMSchina.m

Rips Complex

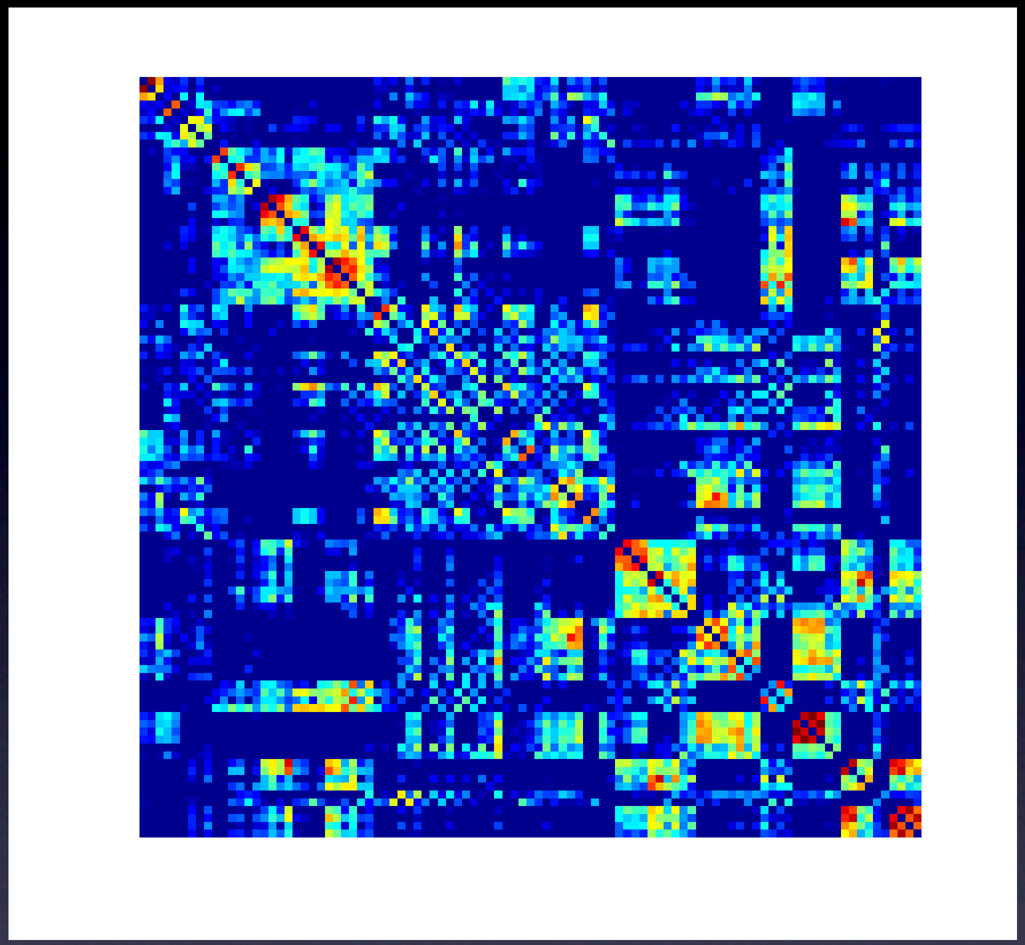
0-th Betti number over epsilon



Bar codes for brain network



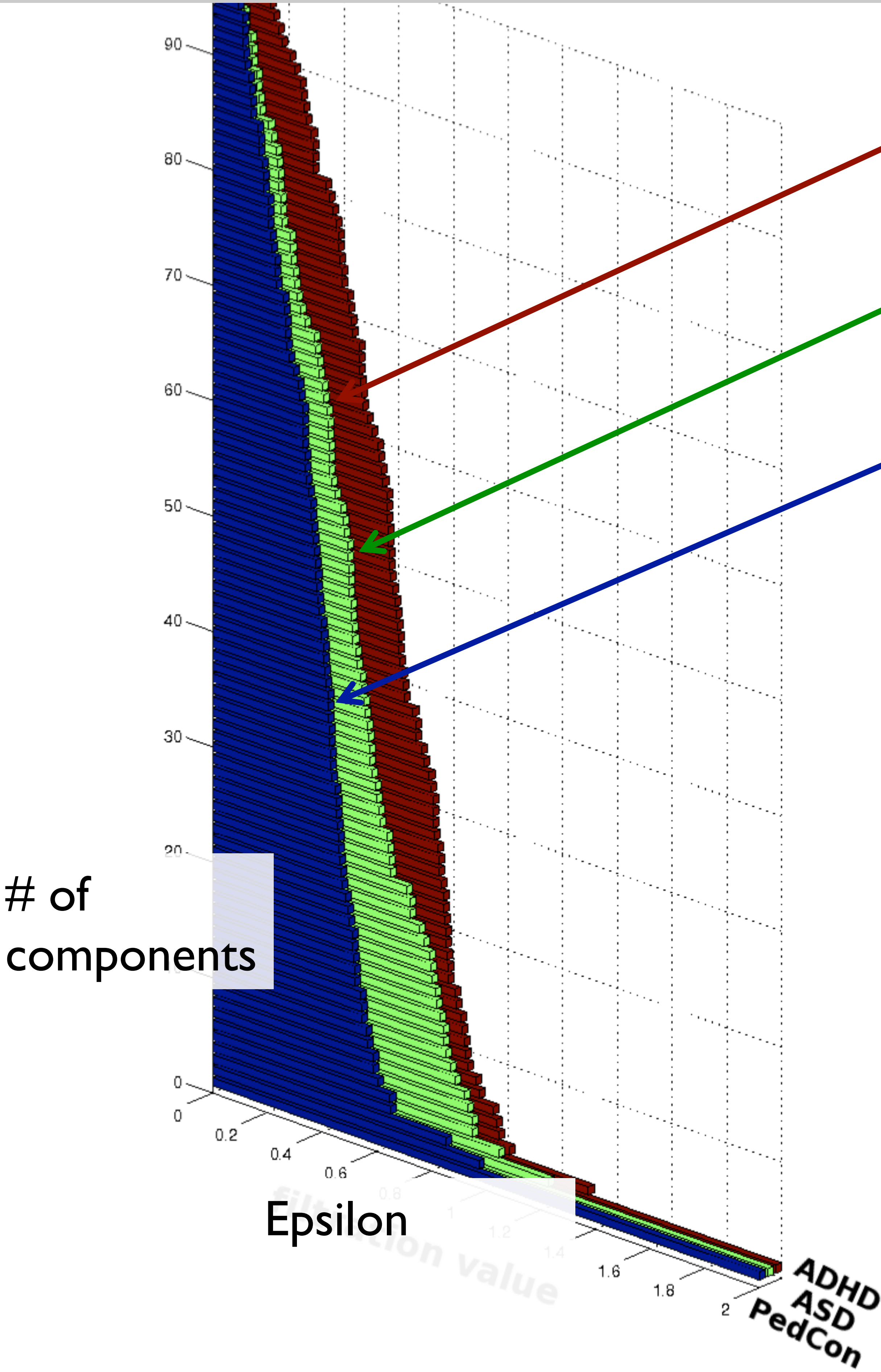
PET measures on nodes



Correlation

Distance = 1- correlation

Bar code on graph filtration



24 attention deficit hyperactivity disorder (ADHD) children

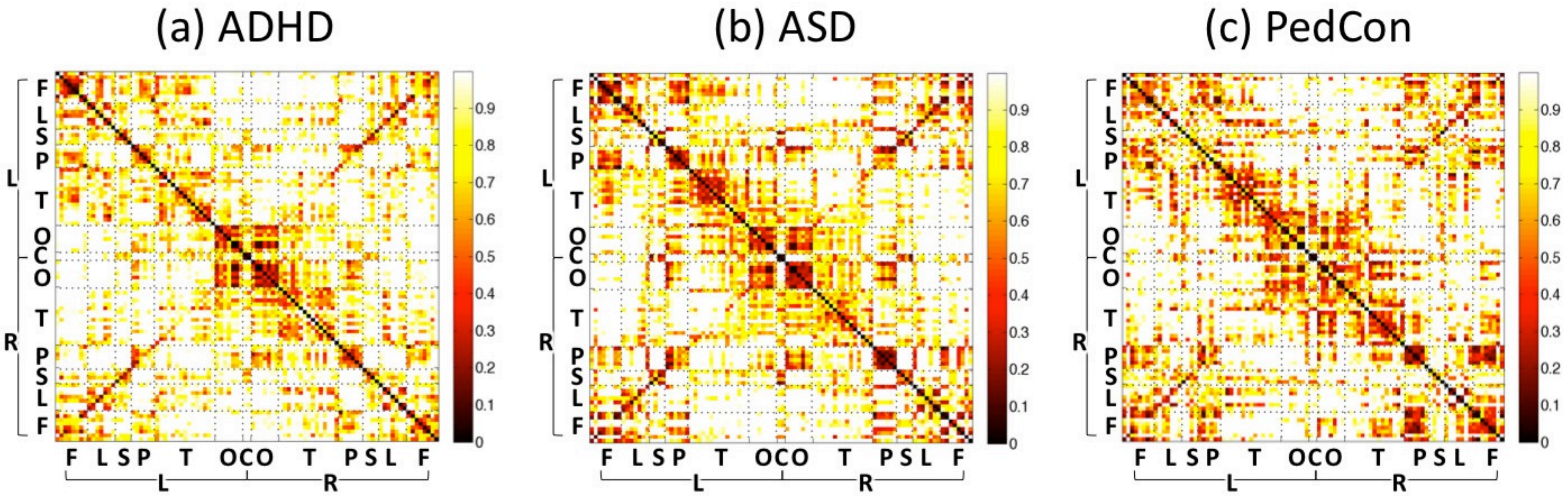
26 autism spectrum disorder (ASD) children

11 pediatric control subjects

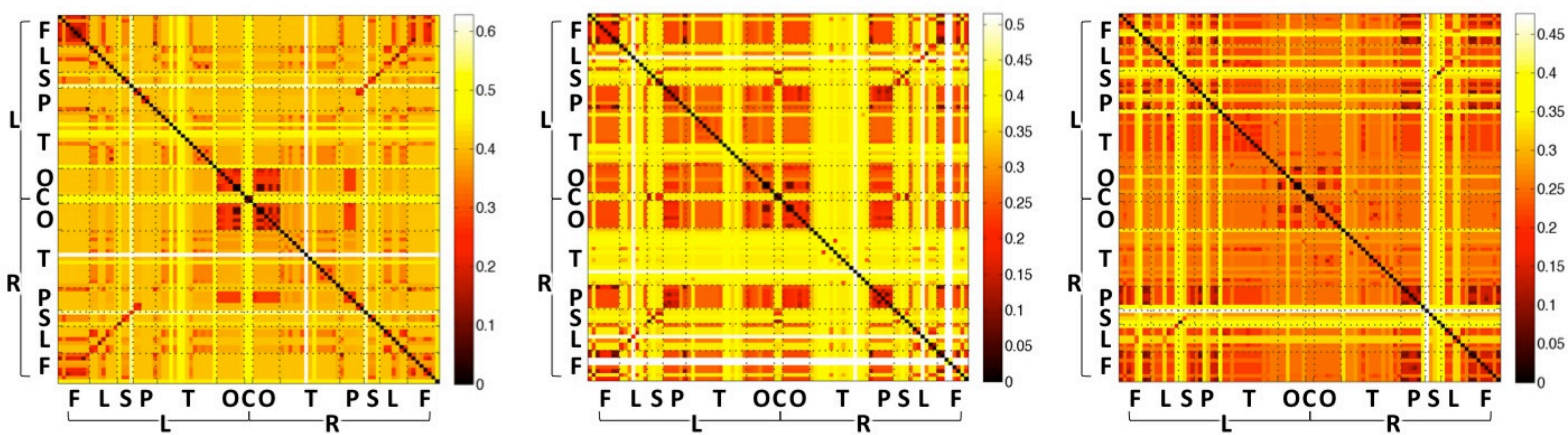
The brain network in control subjects merges to a single component faster than other populations!

Lee et al., 2011. ISBI

Connectivity matrix of brain network



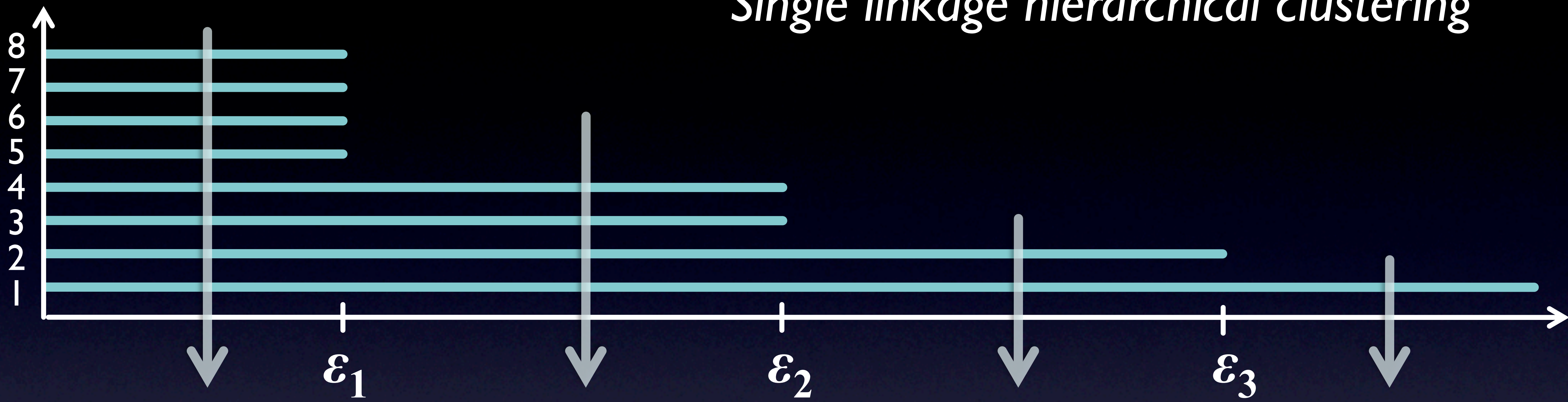
(d) Pairwise Distance Matrix = 1 - correlation



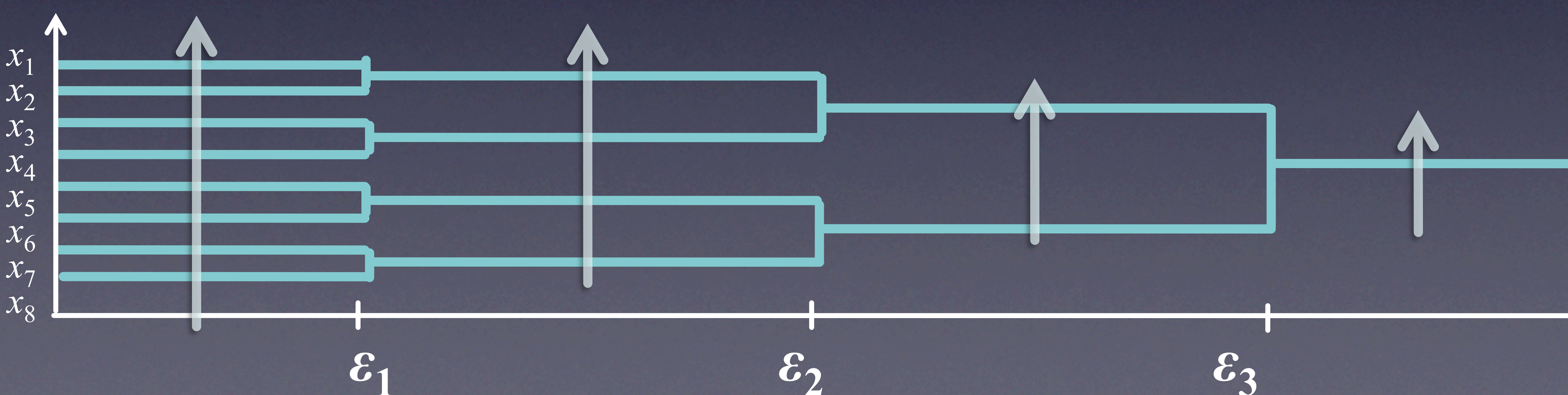
(e) Single Linkage Connectivity matrix

Permuted bar code = Dendrogram

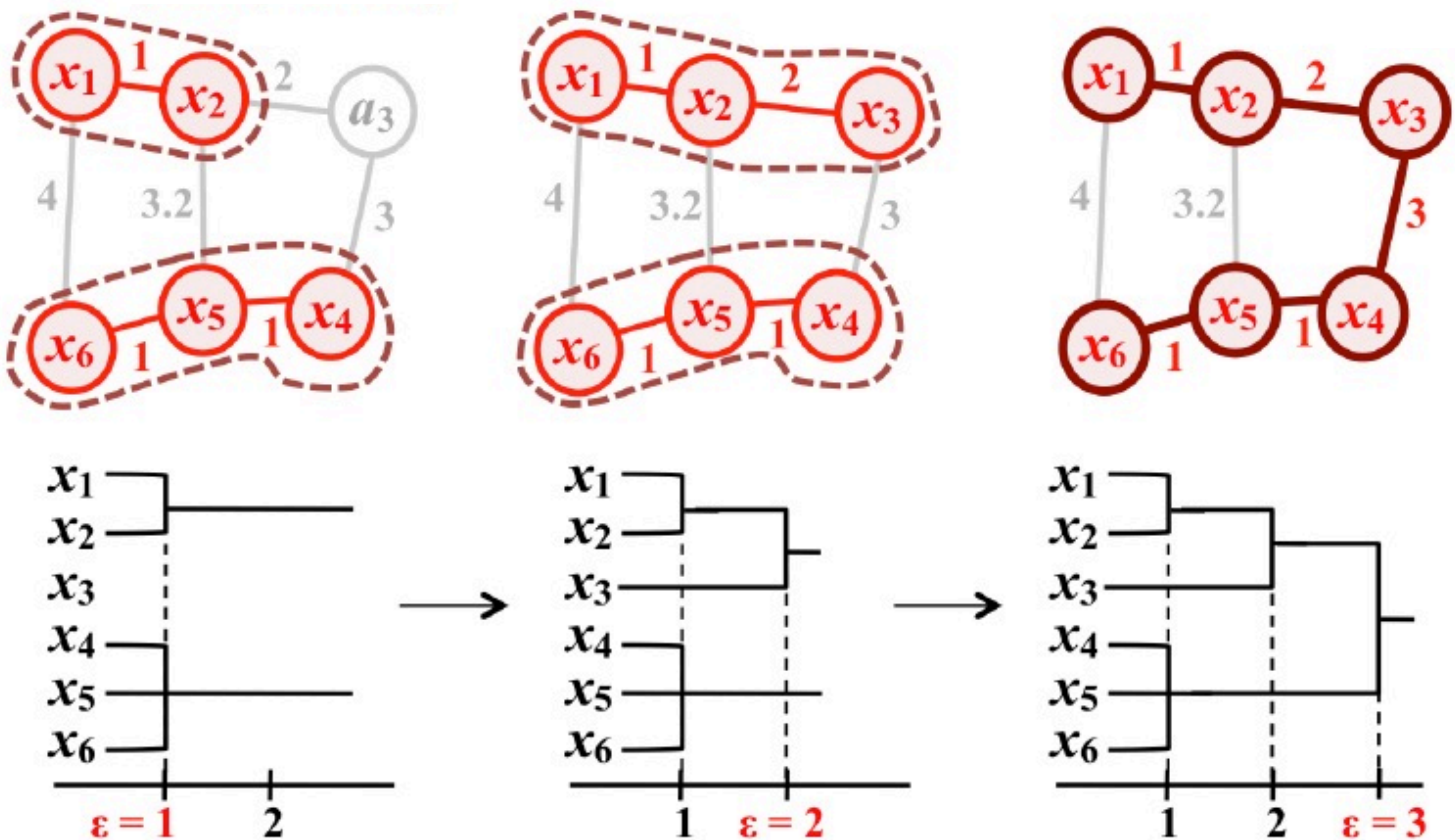
Single linkage hierarchical clustering



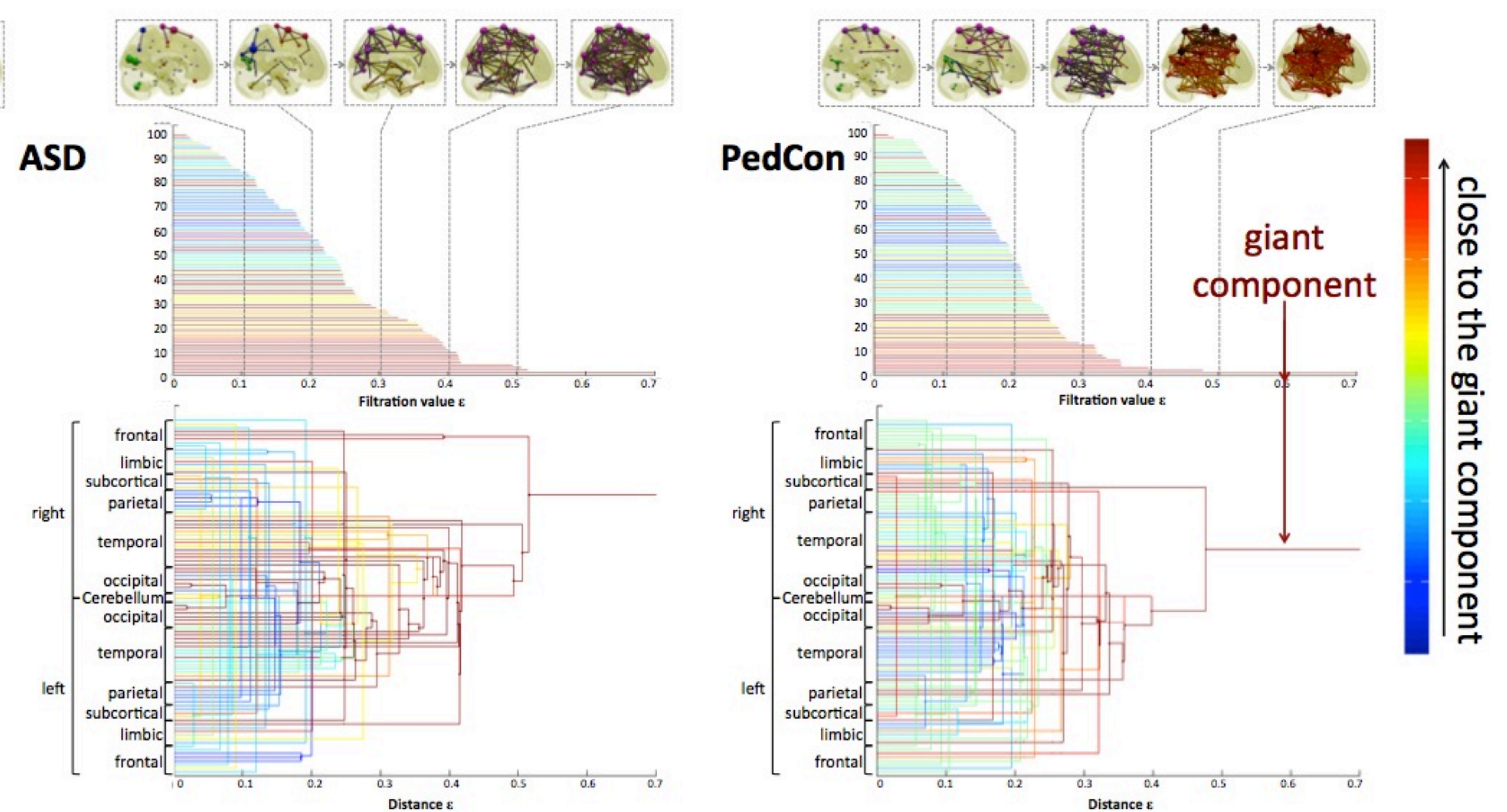
Rearrange the barcode according to the node index



Network filtration = dendrogram construction



Brain network as dendrogram



The network difference can be measured in terms of the dendrogram shape difference.

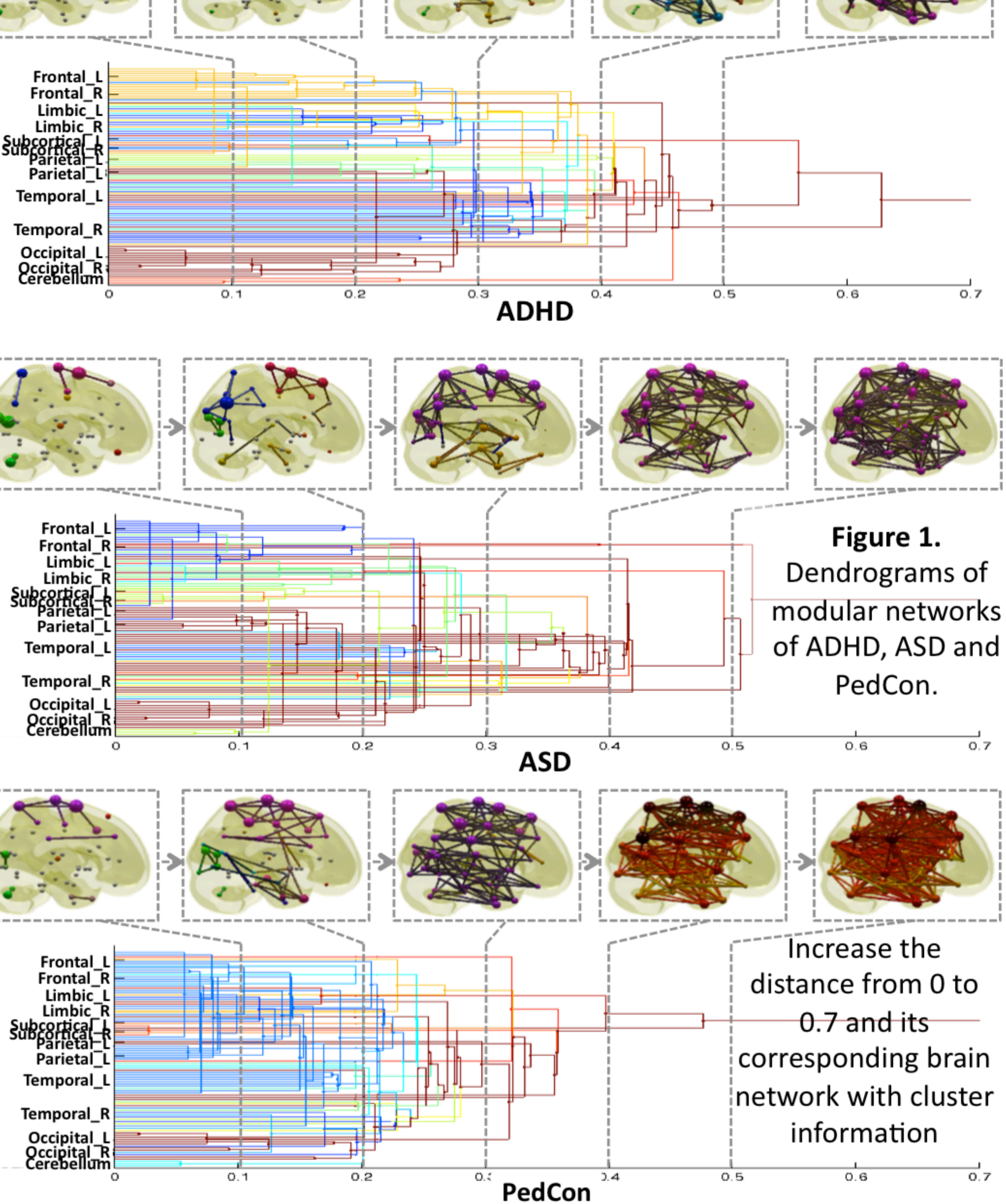
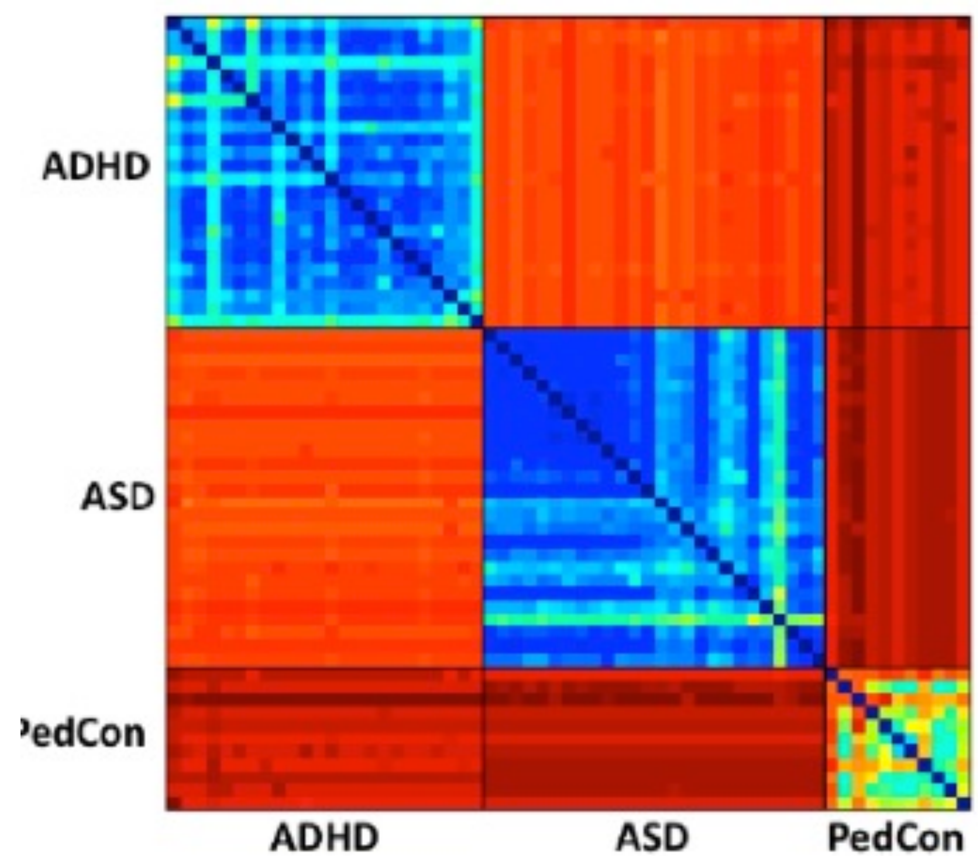
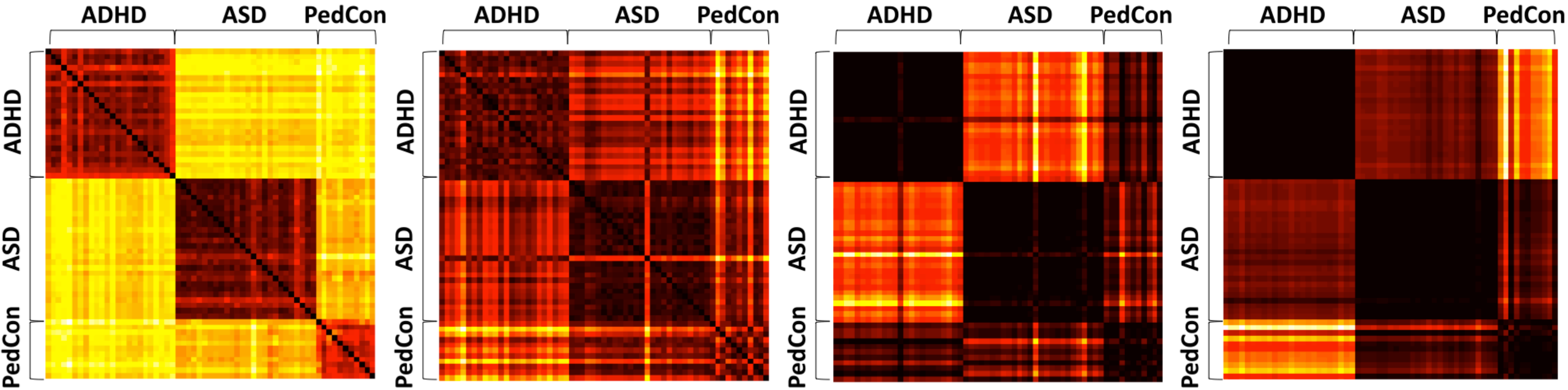


Figure 1. Dendrograms of modular networks of ADHD, ASD and PedCon.



Gromov-Hausdorff distance

Discrimination Accuracy

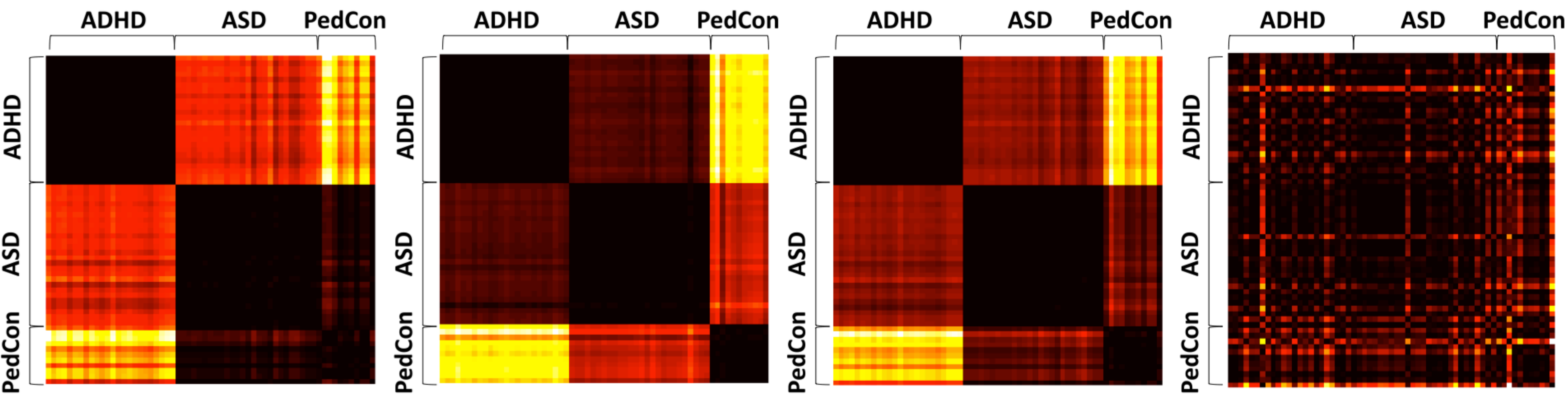


(a) GH distance
cluster_acc = 100 %
|w-b| = 0.4904

(b) Bottleneck distance
cluster_acc = 52.46 %
|w-b| = 0.1879

(c) Assortativity
cluster_acc = 77.05 %
|w-b| = 0.2982

(d) Betweenness Centrality
cluster_acc = 83.61 %
|w-b| = 0.2321



(e) Clustering Coefficient
cluster_acc = 85.25 %
|w-b| = 0.3382

(f) Characteristic Path Length
cluster_acc = 100 %
|w-b| = 0.3015

(g) Small-worldness
cluster_acc = 100 %
|w-b| = 0.2867

(h) Modularity
cluster_acc = 45.90 %
|w-b| = 0.0274

Thank you

Papers and MATLAB codes can be downloaded from www.stat.wisc.edu/~mchung