Computational Methods in NeuroImage Analysis

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Lecture 9
Brain network modeling

November 5, 2010

KAIST/SNU Joint Workshop on Sparse Data Recovery and its Application to Medical Imaging

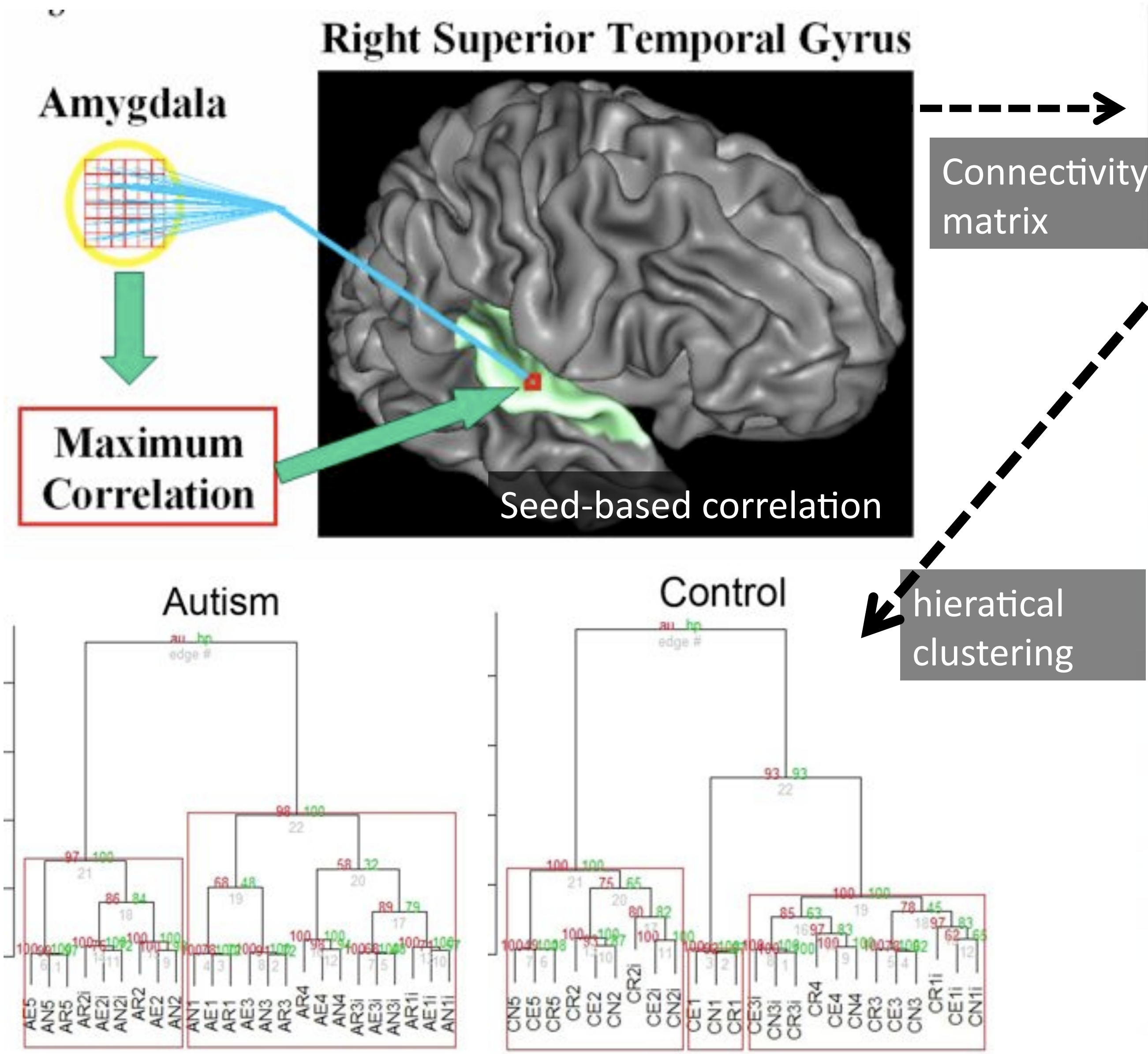
Sponsored by the Department of Brain and Cognitive Sciences (WCU), SNU

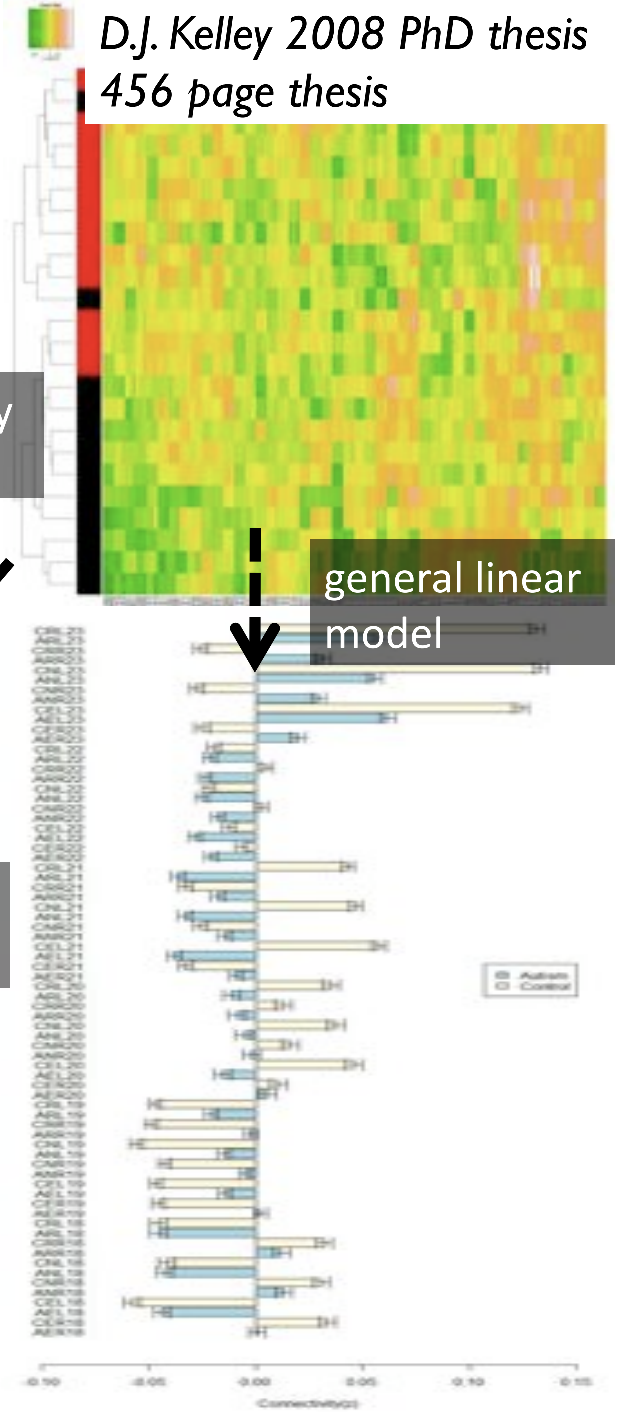
November 9, 2010. SNU Dental Hospital, Rm.807

9:30am-6:00pm

Sparse data recovery, compressed sensing, sparse regression, sparse-PCA, persistent homology, sparse network modeling, medical imaging applications.

functional (fMRI) connectivity study on face fixation





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

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.

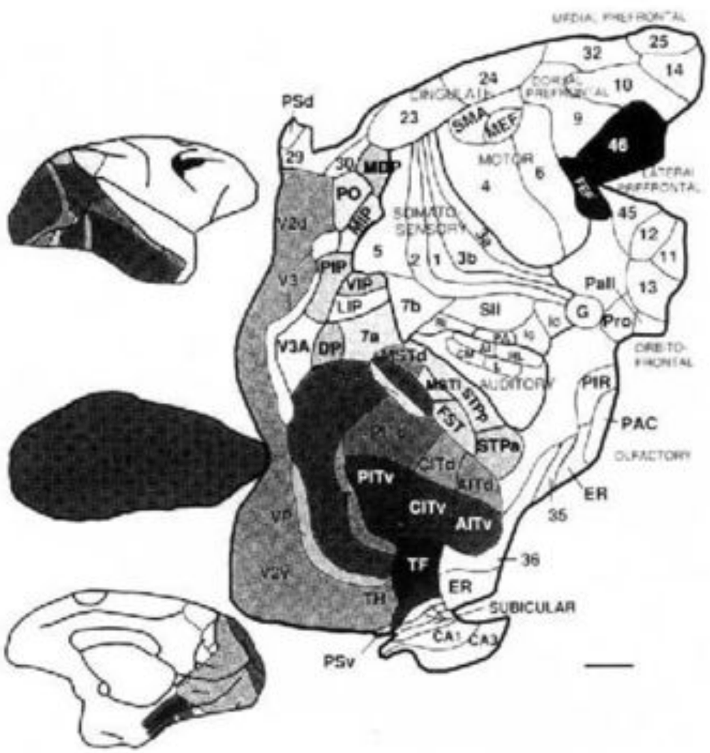
OVER the past 20 years there have been great advances in understanding the neuroanatomy of the macaque monkey, especially its cerebral cortex. We have learned much about the functional parcellation of the monkey's cortex from both anatomical and physiological studies. We know, for example, that rather

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

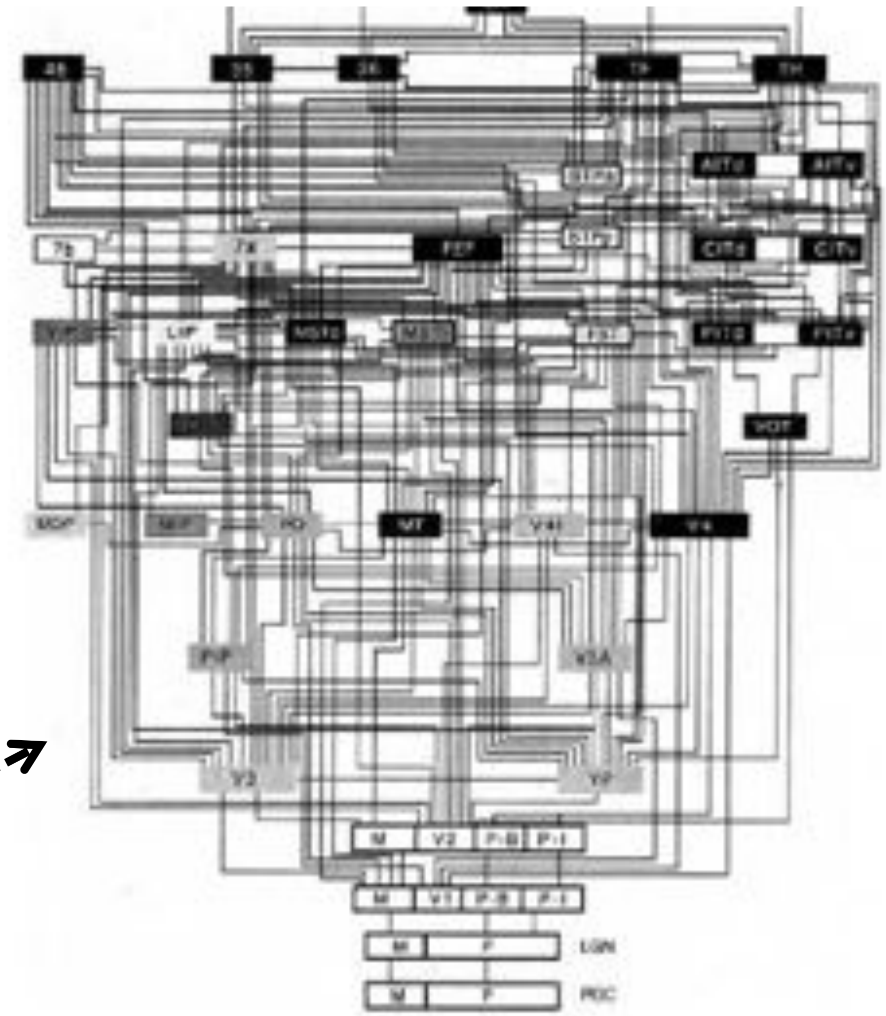
that for the macaque shown in Fig. 1? And what does the human equivalent of the connectional map of Fig. 2 look like? The shameful answer is that we do not have such detailed maps because, for obvious reasons, most of the experimental methods used on the macaque brain cannot be used on humans.

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

Macaque cortical map



Connectional map of visual area



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

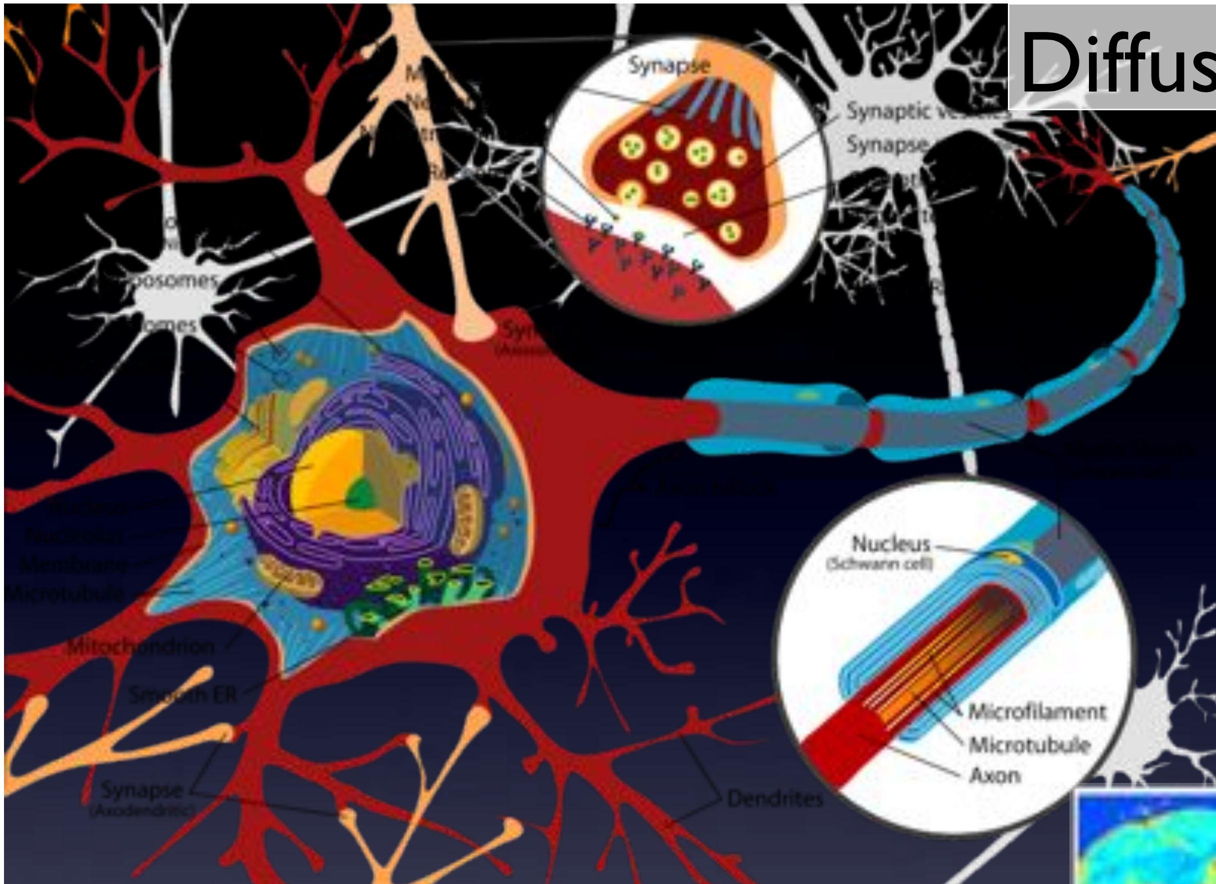
Outdated technique

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

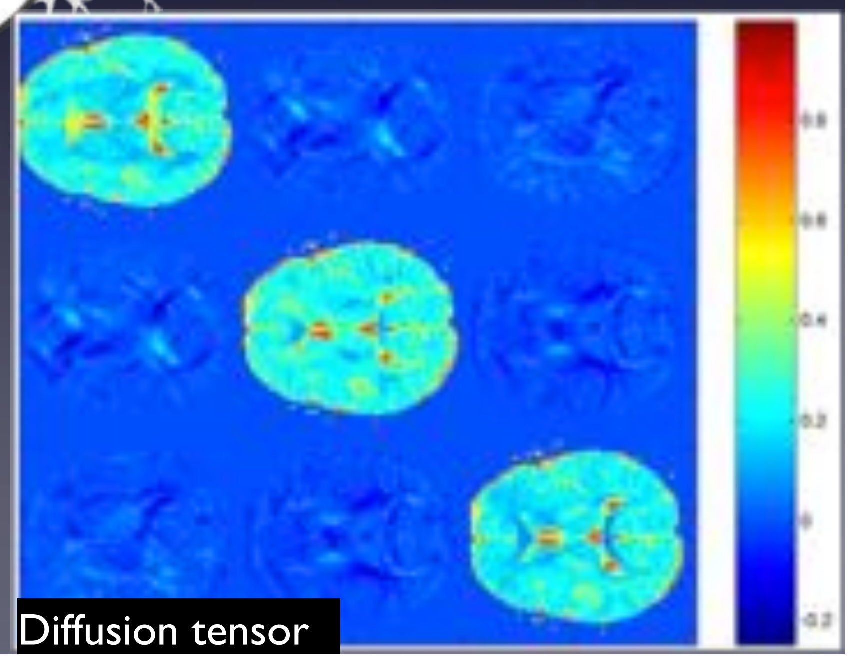
New technique

Diffusion Tensor Imaging (DTI)

Diffusion Tensor Imaging

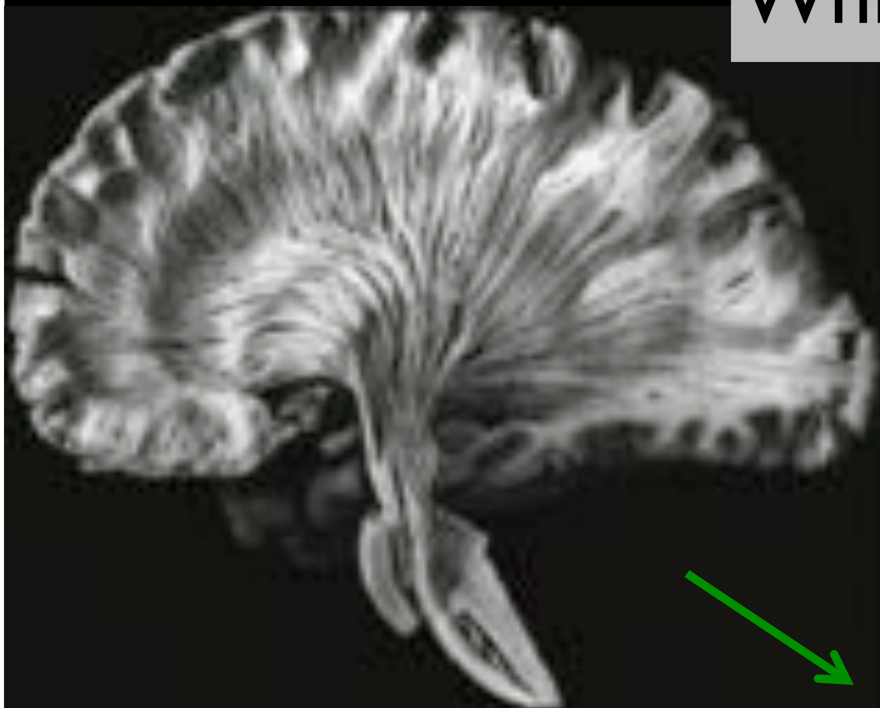


The movement of anisotropic water diffusion can be measured using DTI.

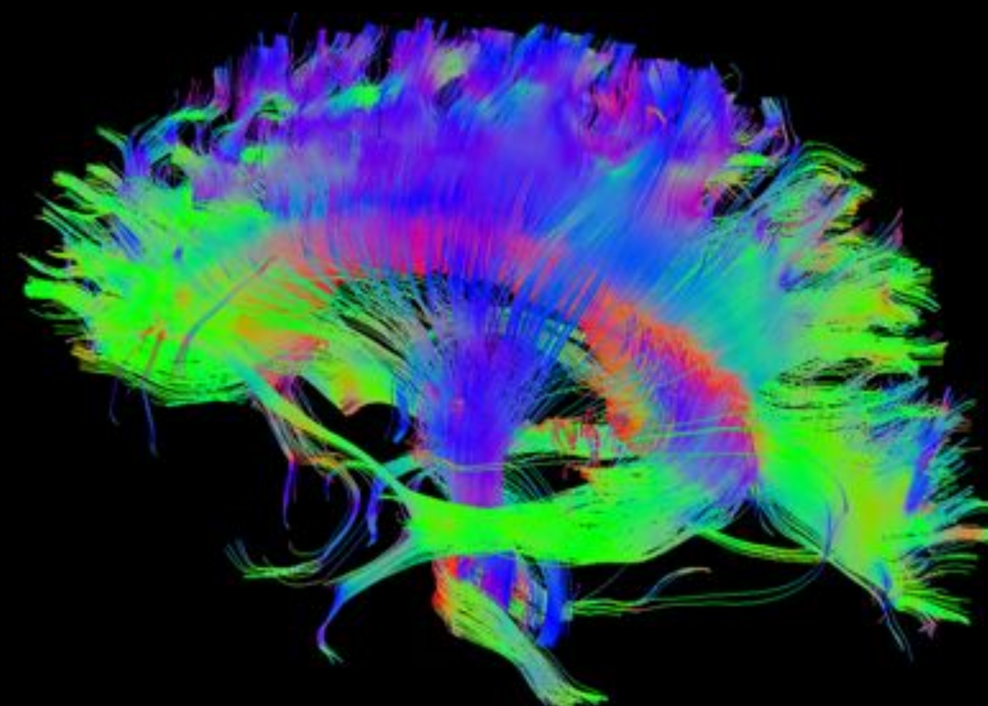


The direction of neuronal filaments in the axon dictates the movement of water diffusion.

White Matter Fiber Tractography



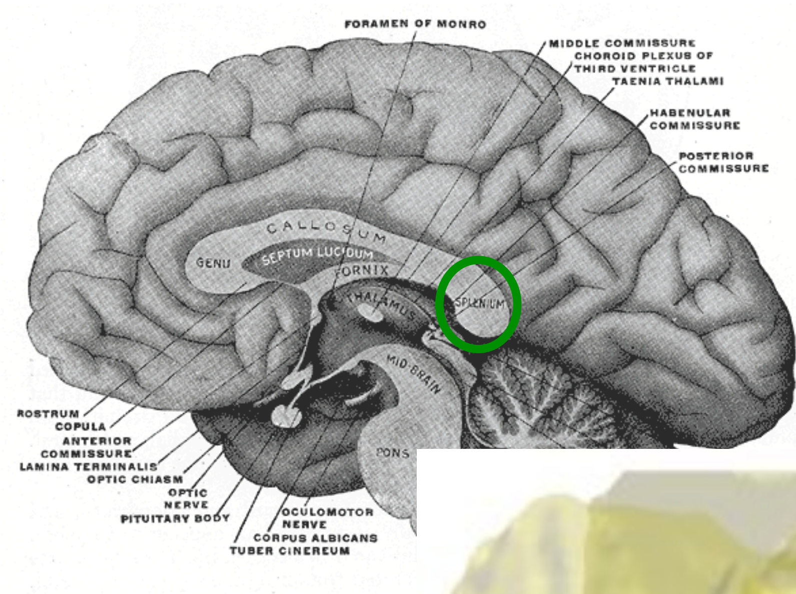
Postmortem



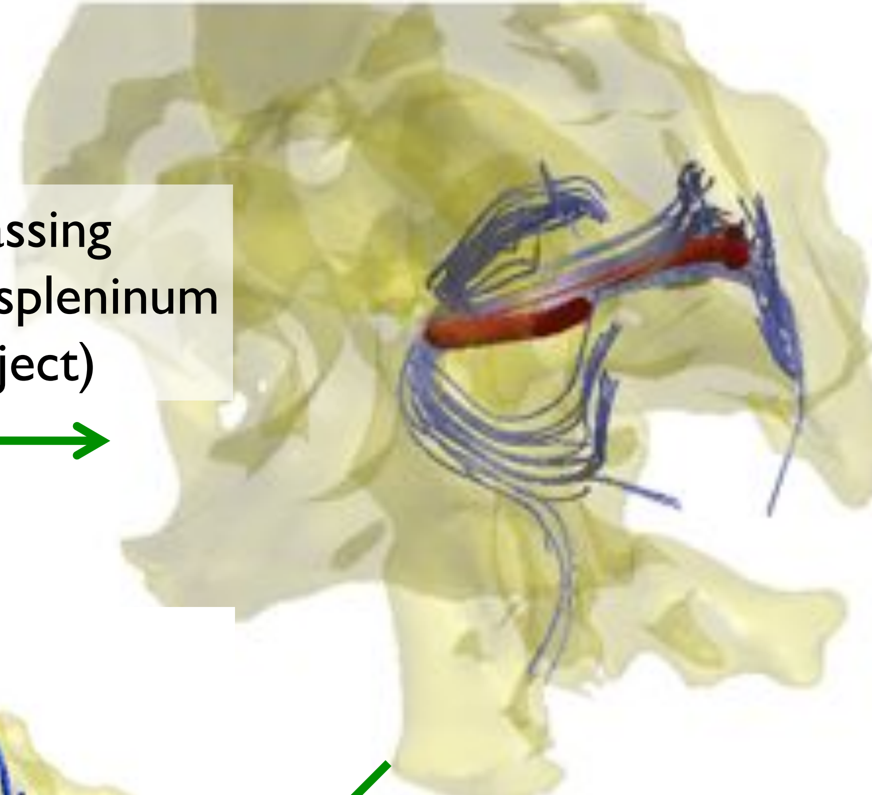
Reconstructed
0.5 million tracts

Tractography is done using the second order Runge-Kutta algorithm with TEND (Lazar et al., HBM 2003)

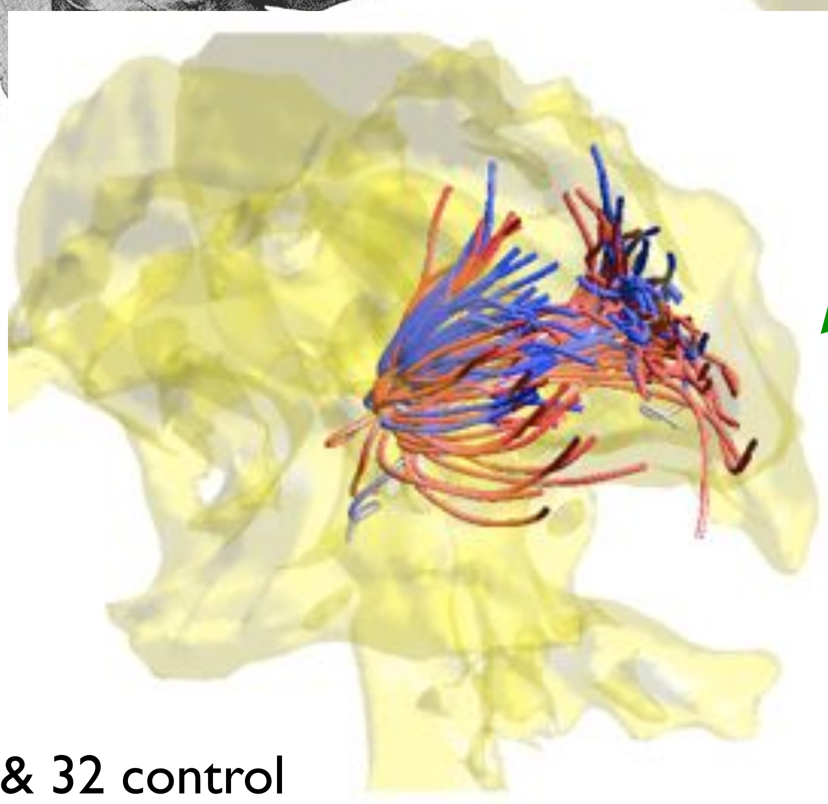
ROI based connectivity analysis



Tracts passing through spleninum (one subject)



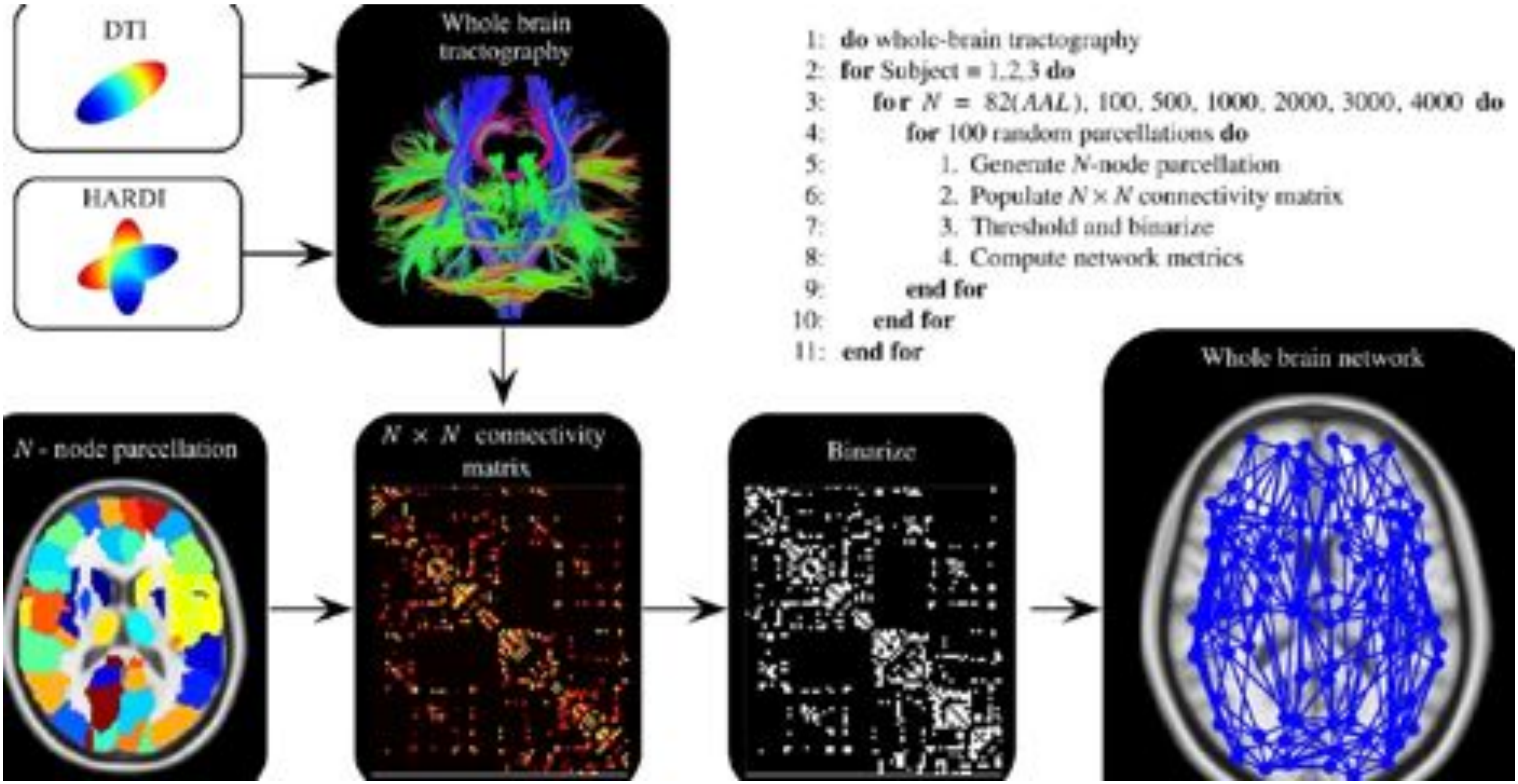
Average tracts



42 autistic & 32 control

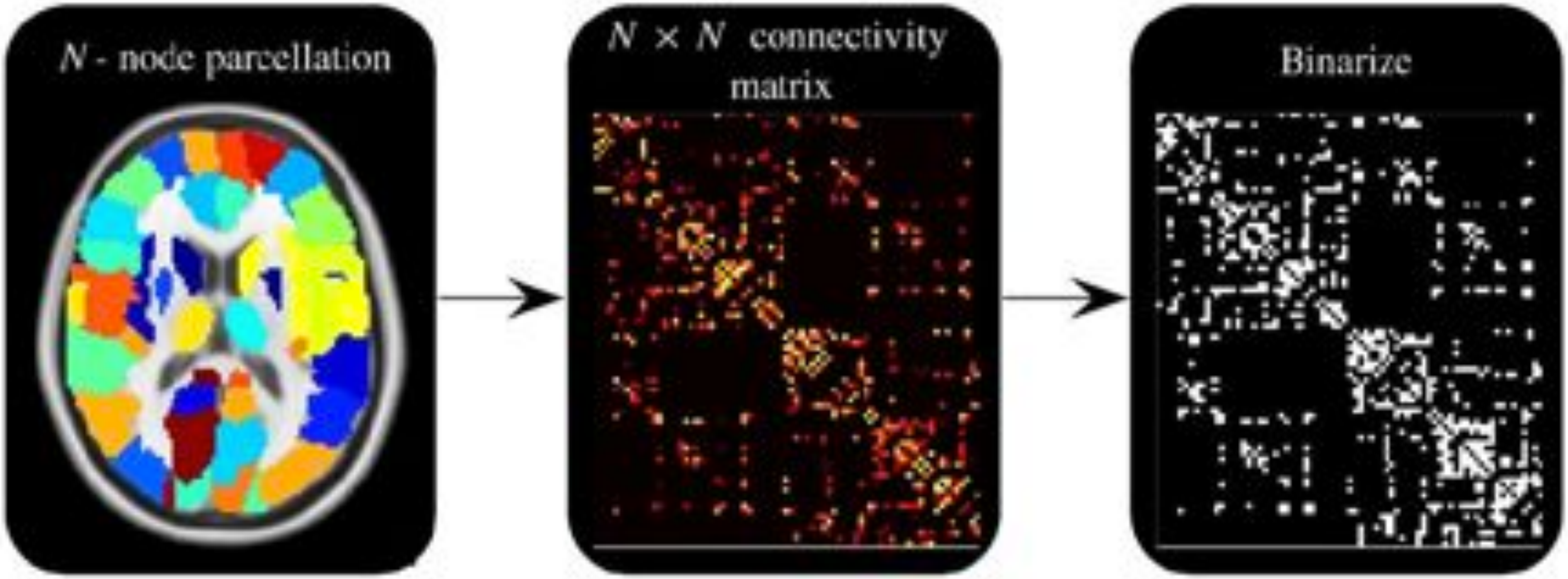
Chung et al. 2010

Multiple ROI-based connectivity analysis



Zalesky et al. 2010

What is wrong with traditional method?

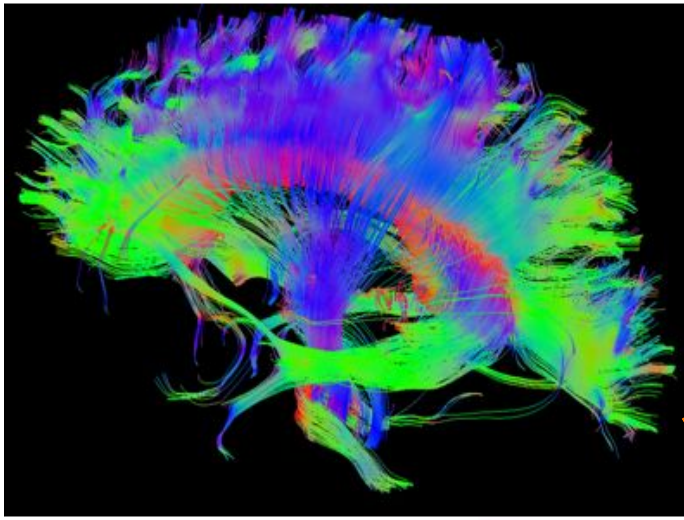


Need parcellation

Arbitrary thresholding

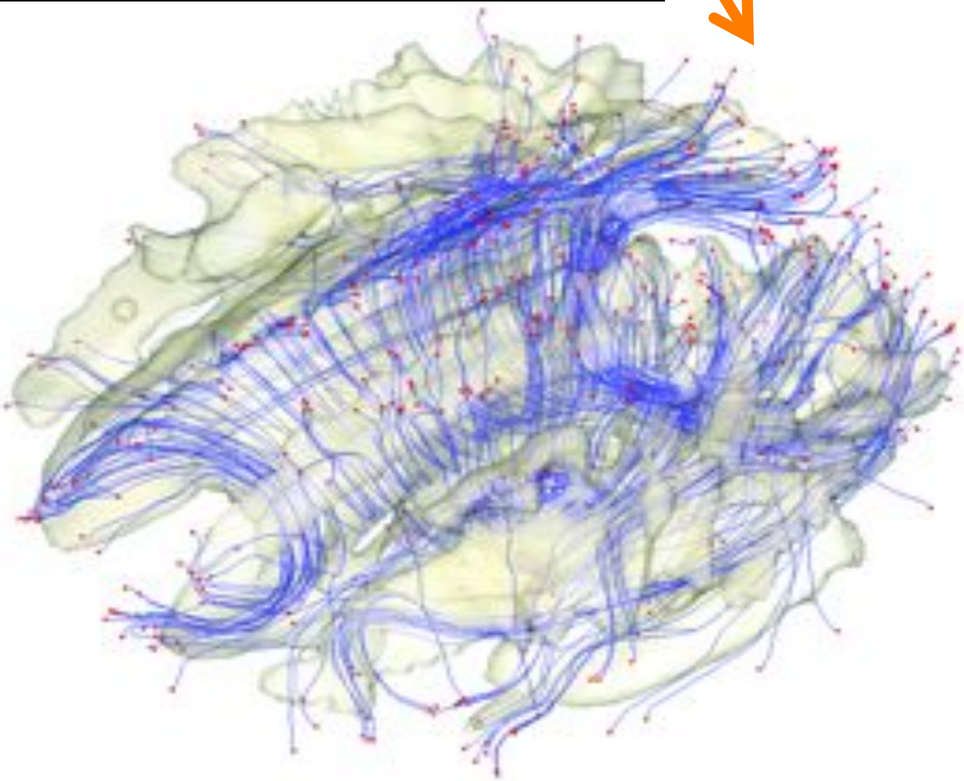
New method: epsilon-neighbor approach

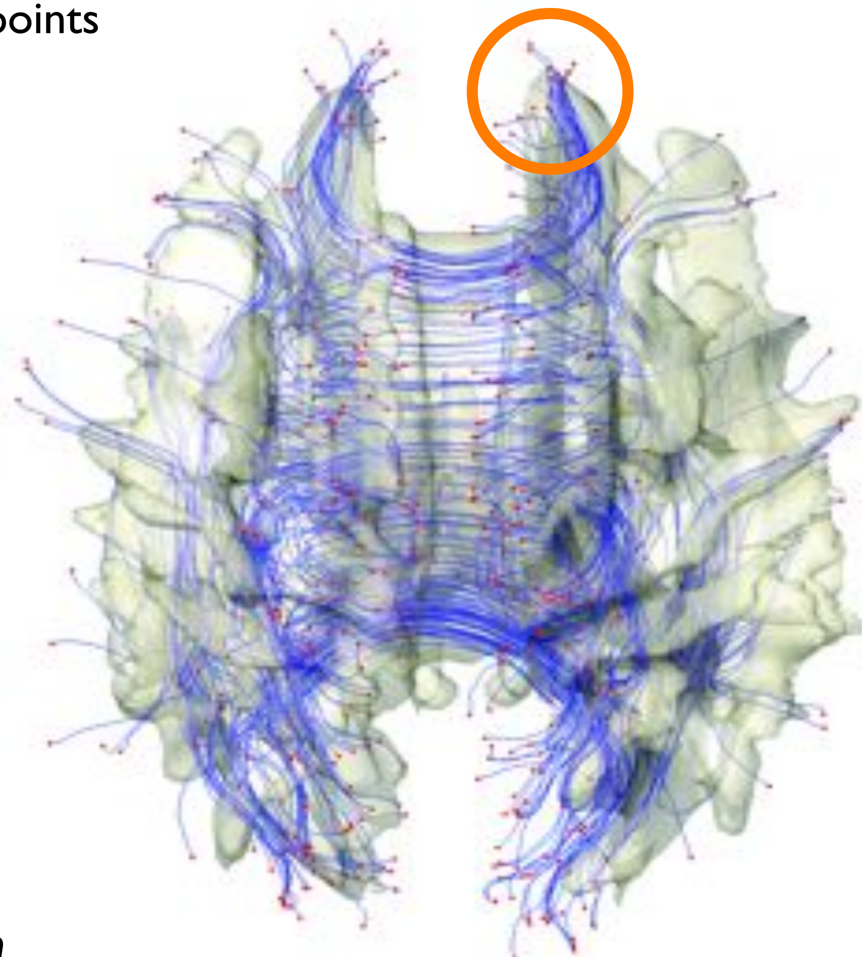
ε-neighbor graph



Identify end points

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

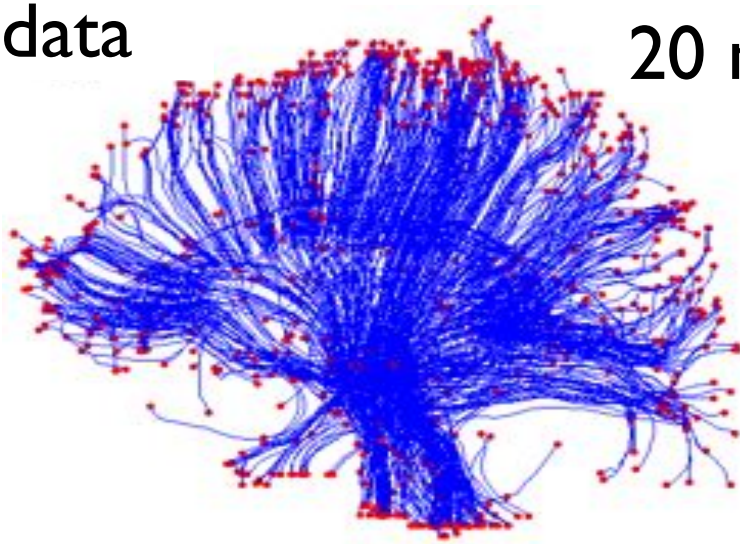




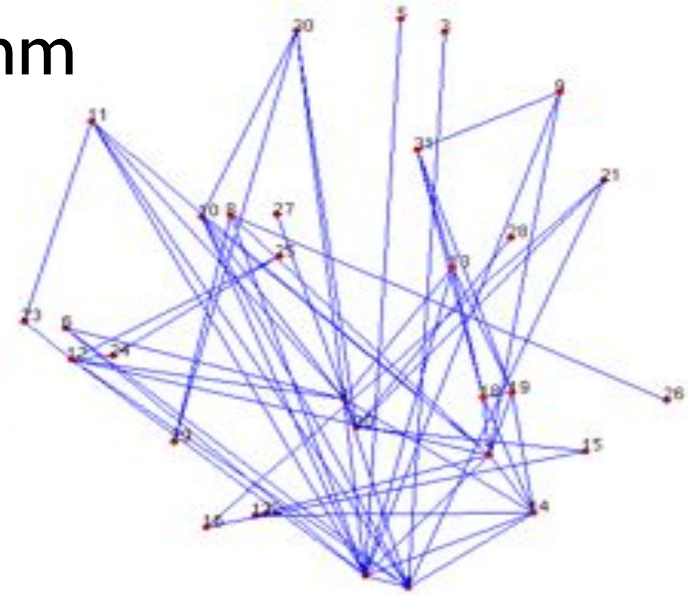
the first data-driven DTI structural network construction framework without any parcellation

ε-neighbor graphs with different ε

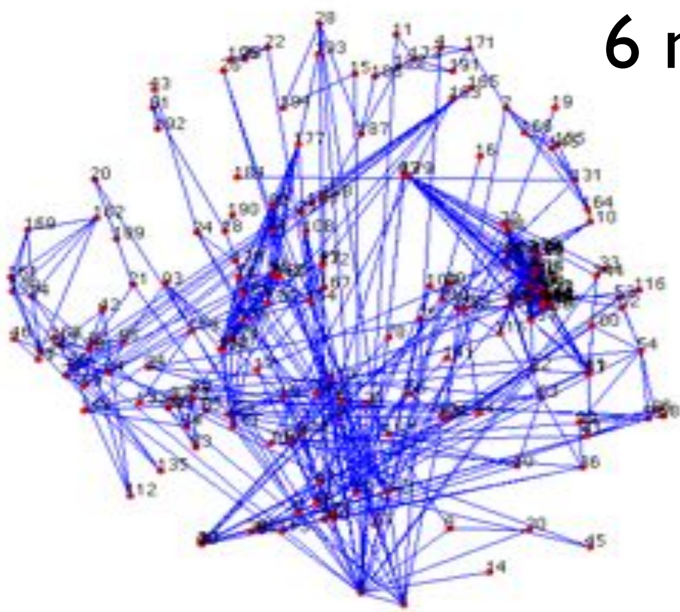
original data



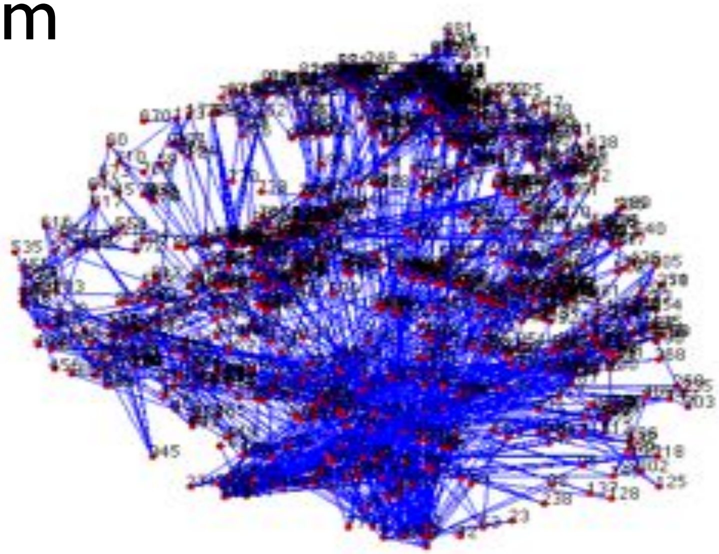
20 mm



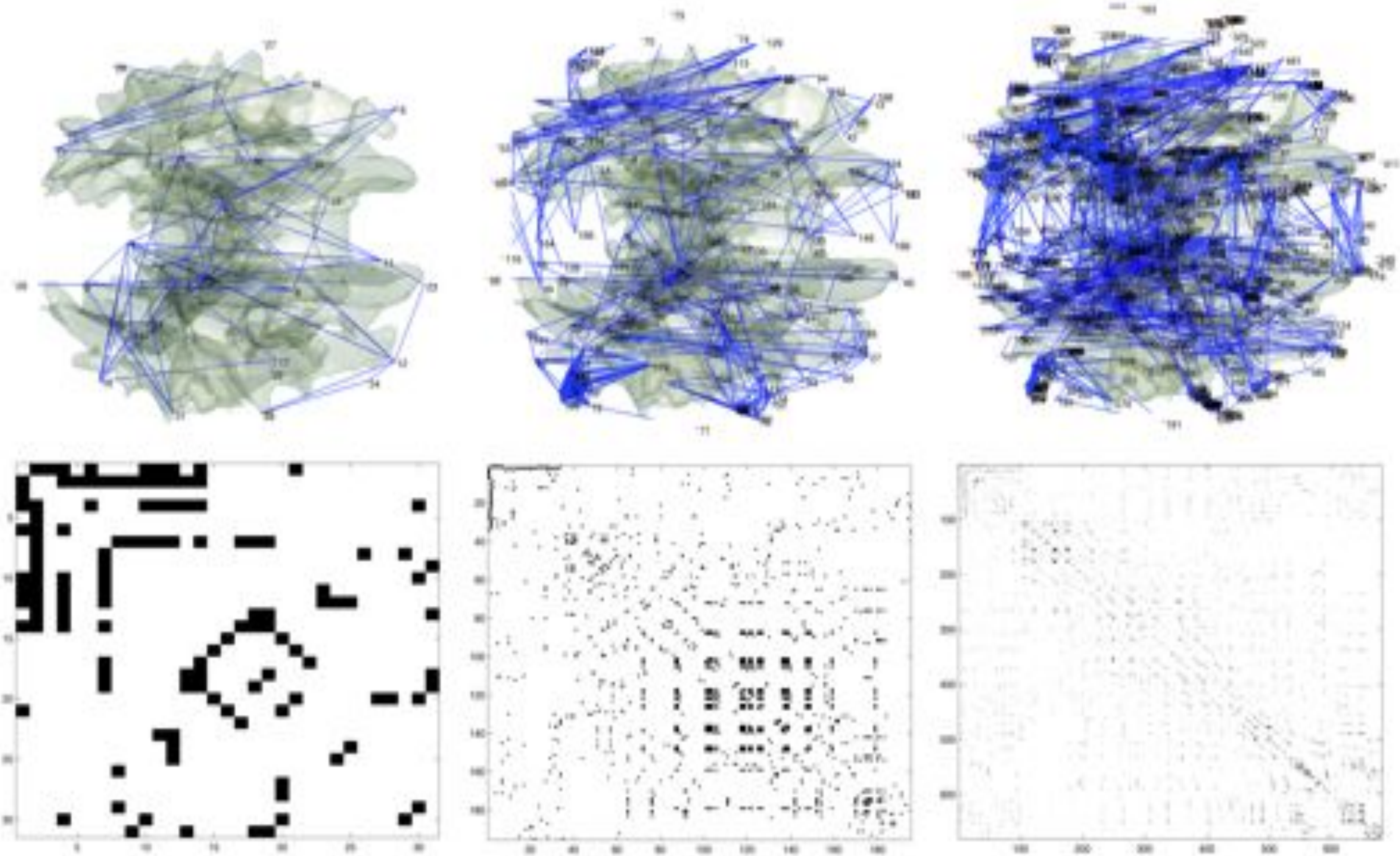
10 mm



6 mm



Adjacency matrix

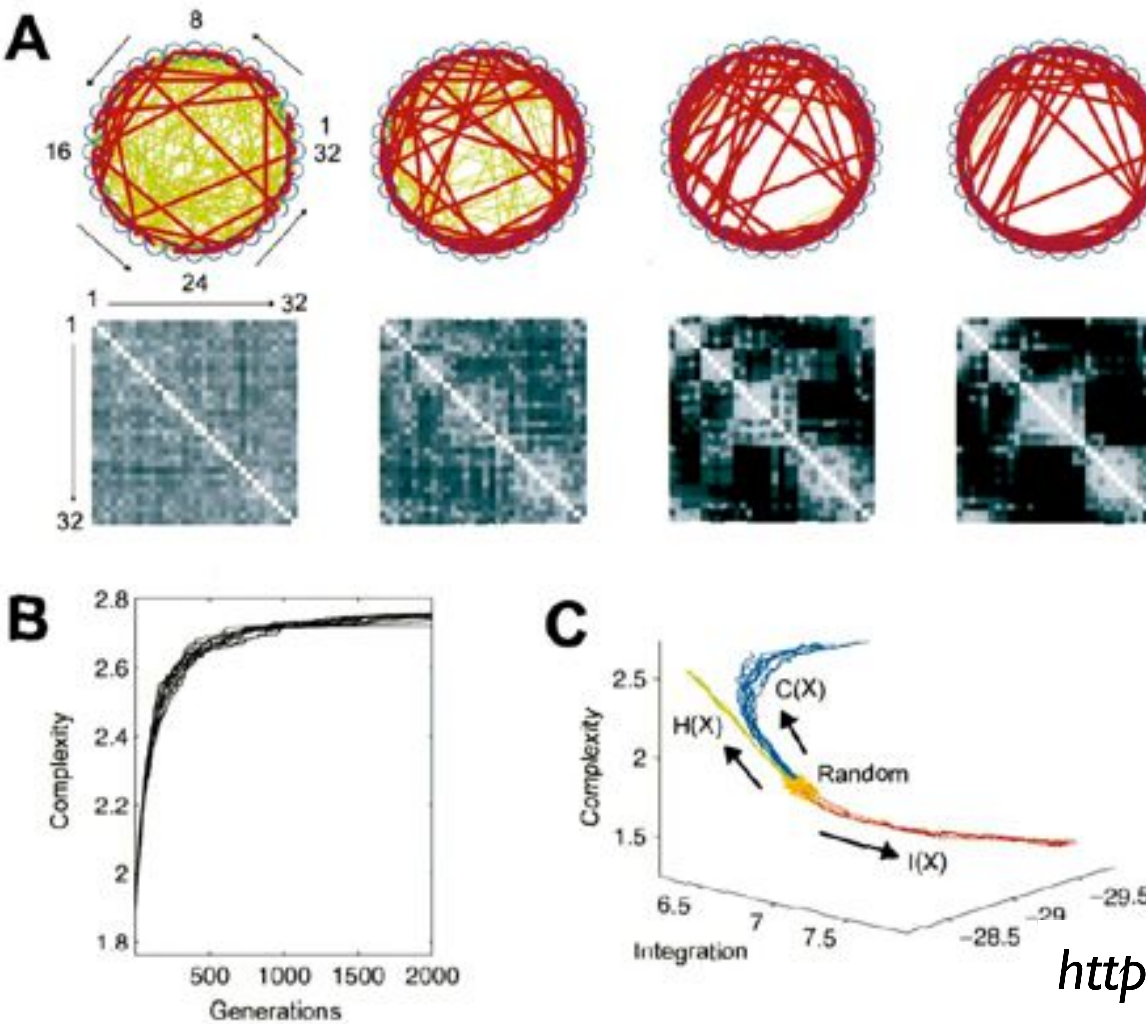


MATLAB demonstration

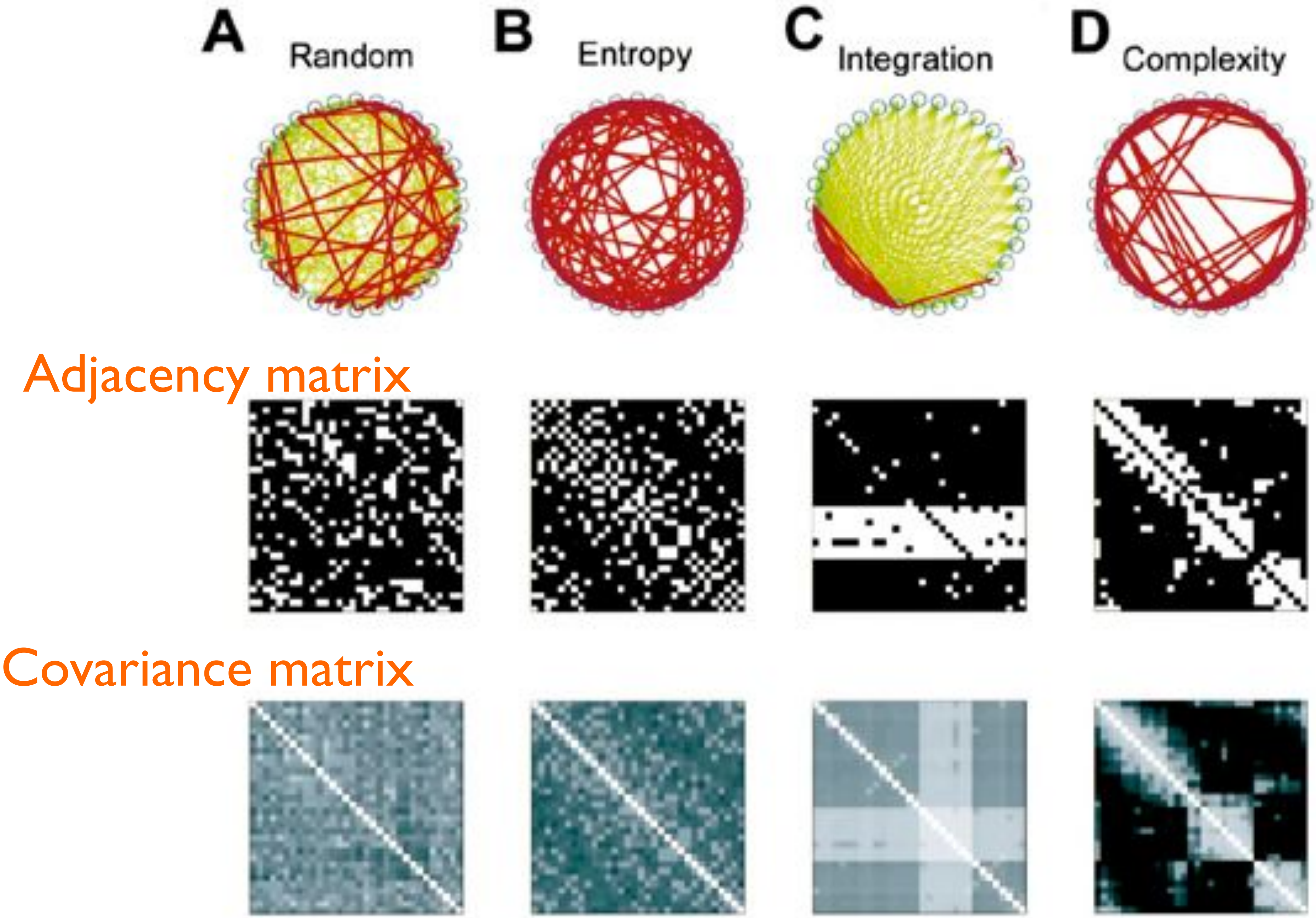
Theoretical Neuroanatomy: Relating Anatomical and Functional Connectivity in Graphs and Cortical Connection Matrices

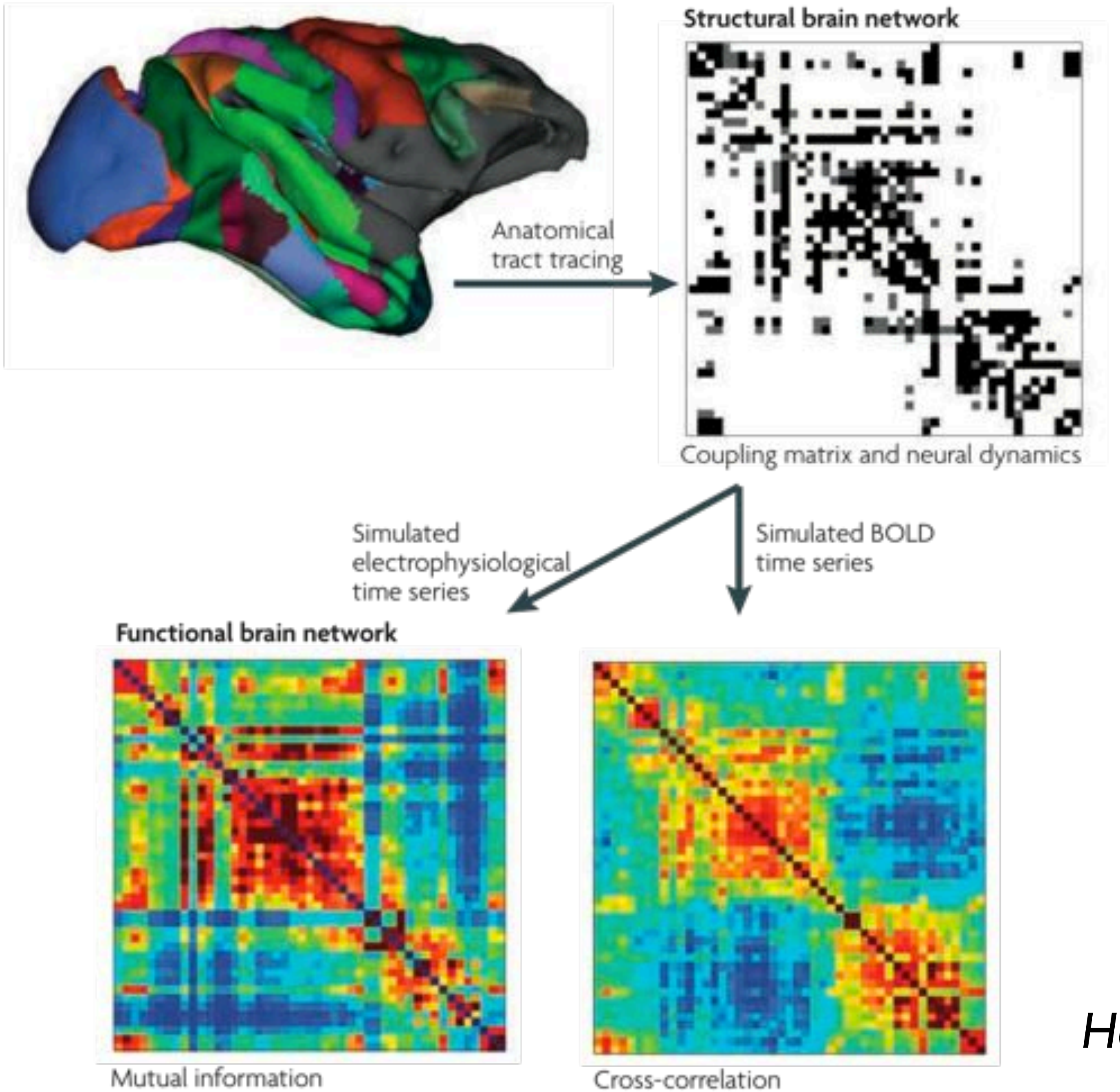
O. Sporns, G. Tononi and G.M. Edelman

The Neurosciences Institute, 10640 John Jay Hopkins Drive, San Diego, CA 92121, USA



http://tononi.psychiatry.wisc.edu/research_overview.html

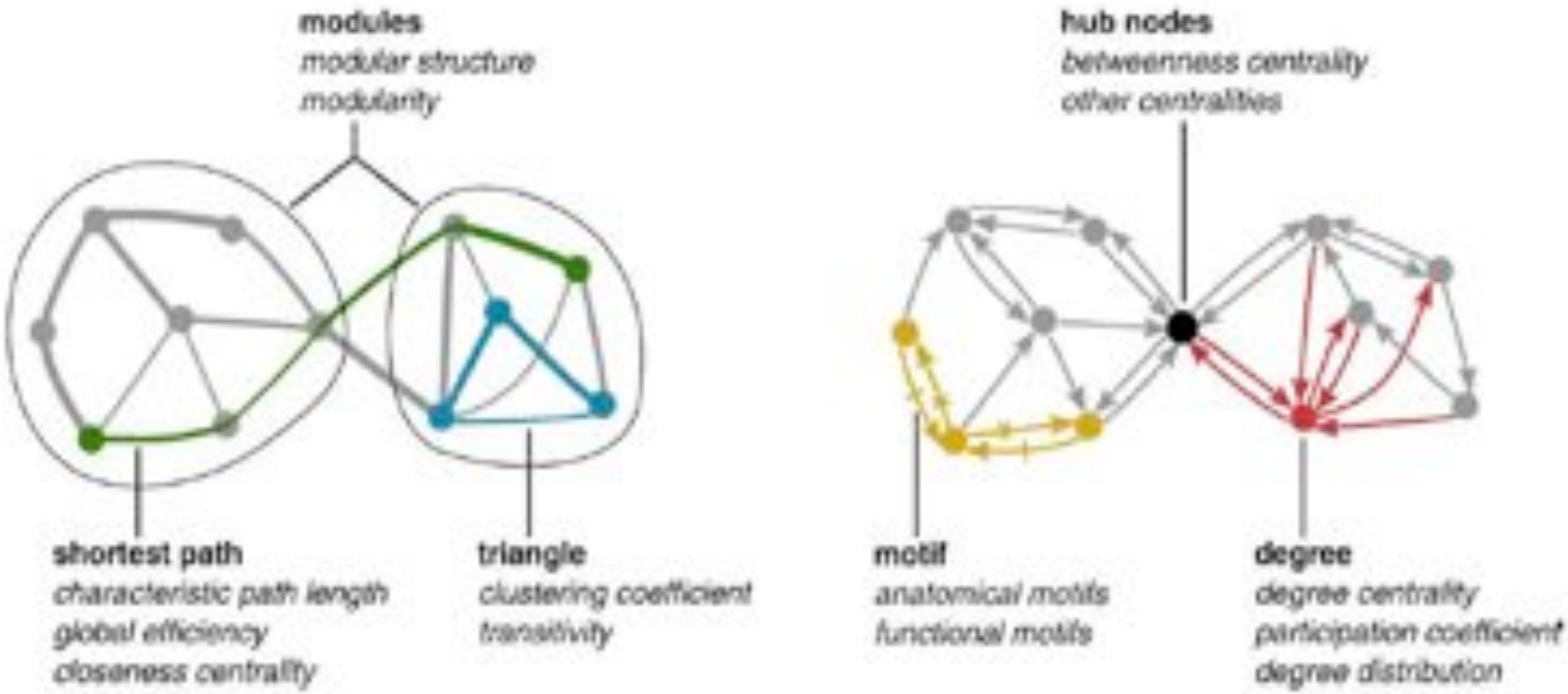

A
Random
B
Entropy
C
Integration
D
Complexity
Adjacency matrix
Covariance matrix



Honey, Kotter, 2007

Various network complexity measures

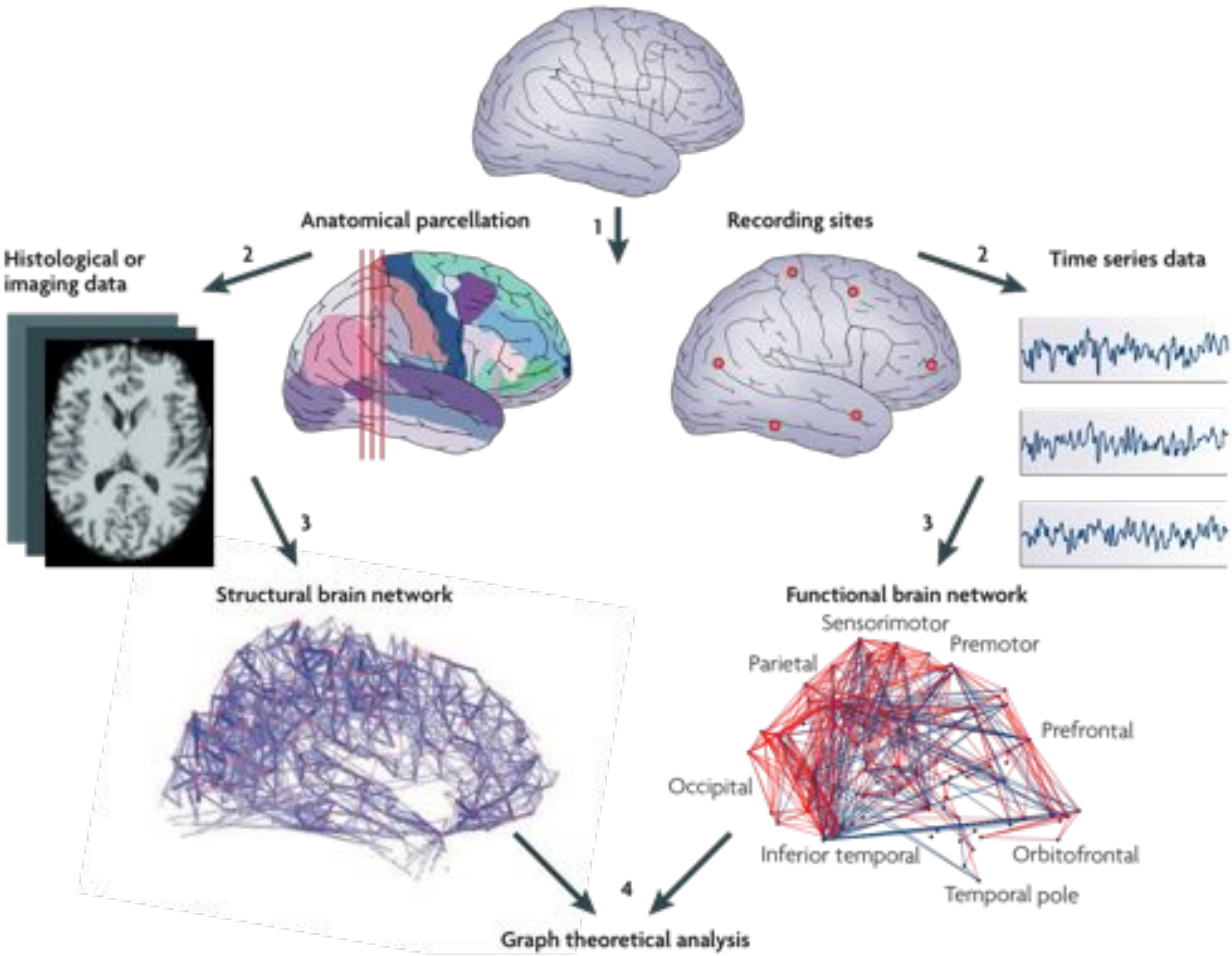
There are soooo many complexity measures….. ☹

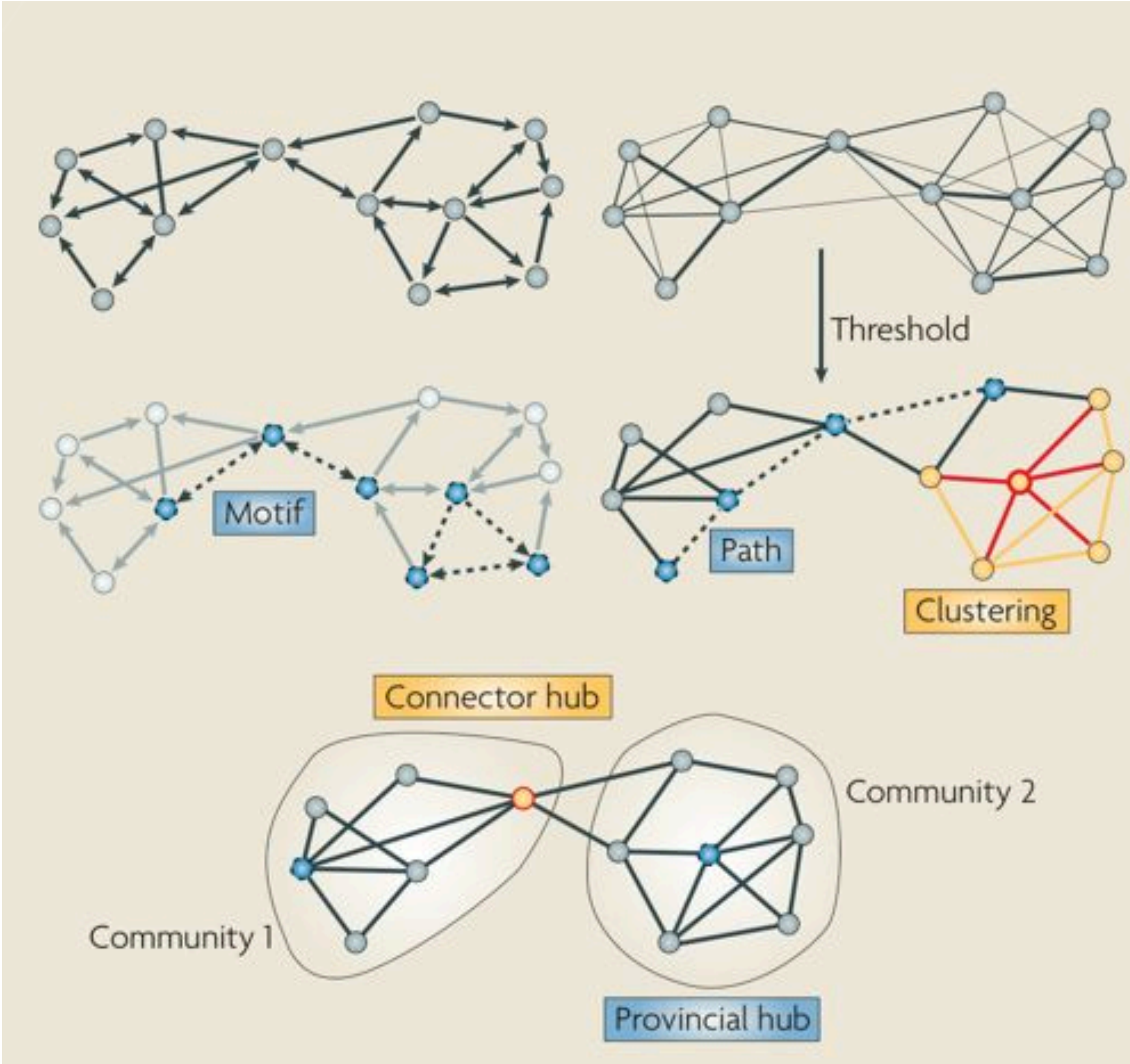


Rubinov and Sporns, Neuroimage, 2009

Complex brain networks: graph theoretical analysis of structural and functional systems

Ed Bullmore[*†] *and Olaf Sporns*[§]





Threshold
Motif
Path
Clustering
Connector hub
Community 2
Community 1
Provincial hub

Application to autism

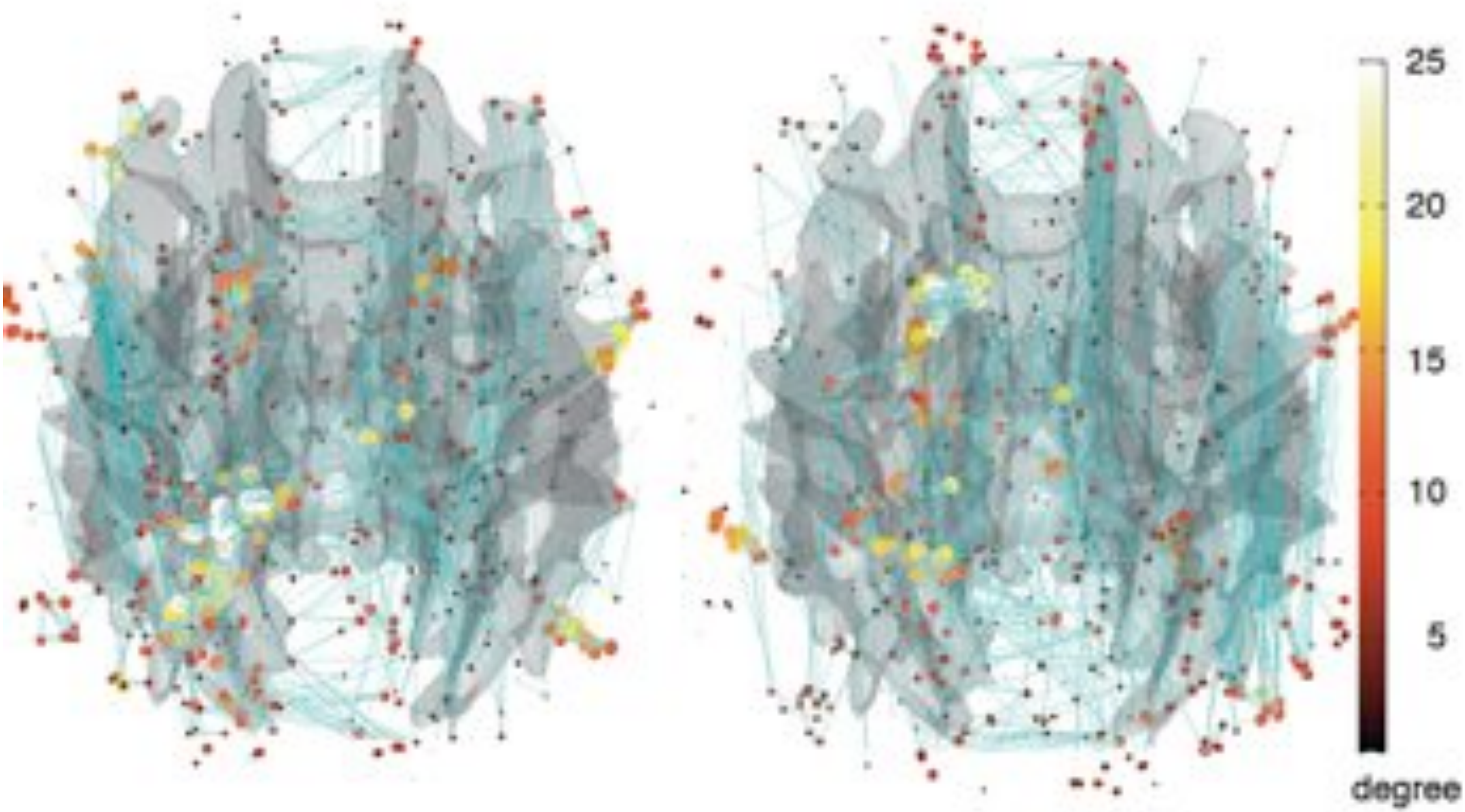
Autistic children (n=17)

Control subjects (n=14)

Matched for age, handedness, IQ and head size

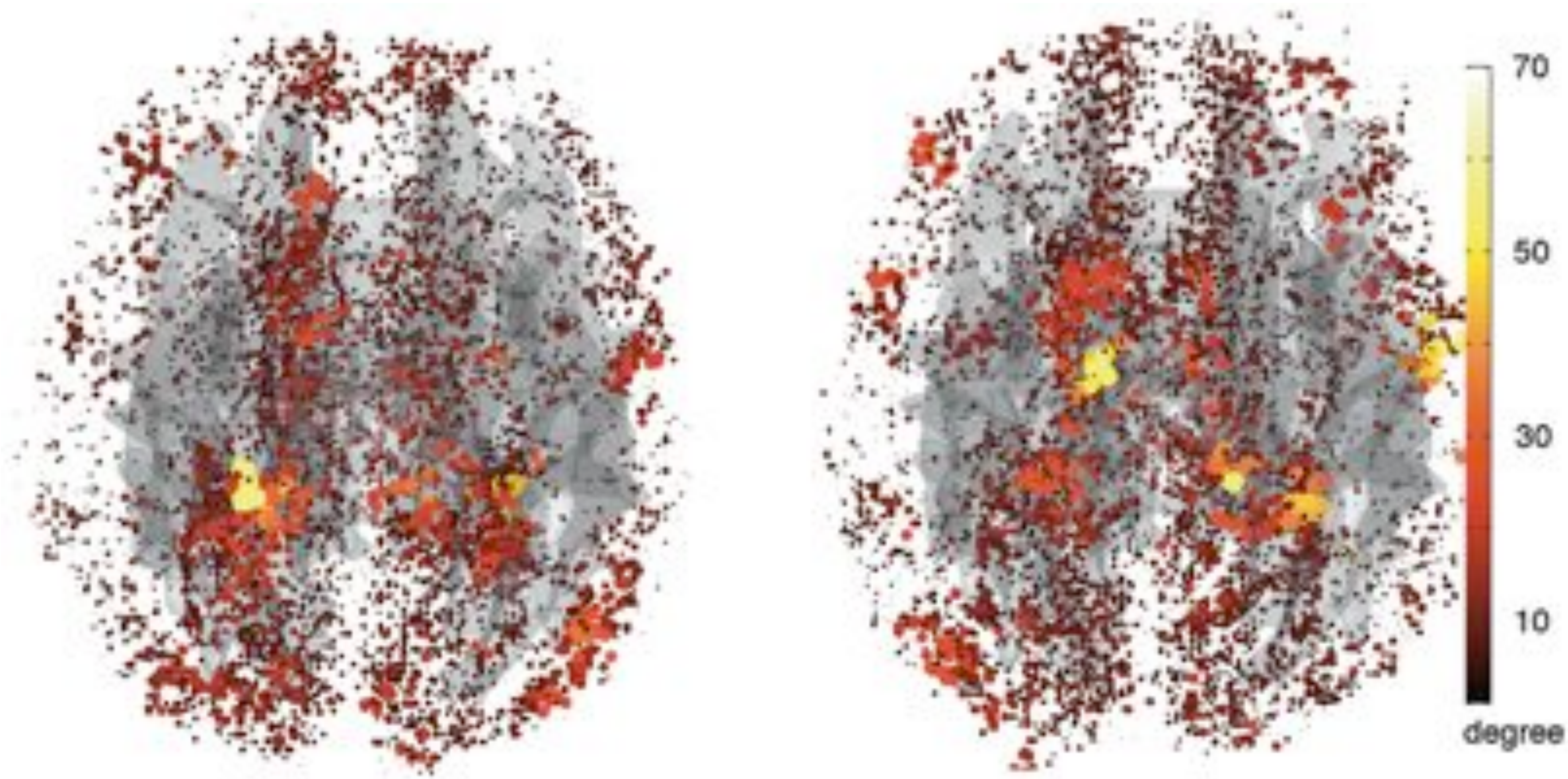
Abnormal connectivity hypothesis in autism:
local over-connectivity
long-range under-connectivity

Degree of nodes for a single subject



control #001 autism #120

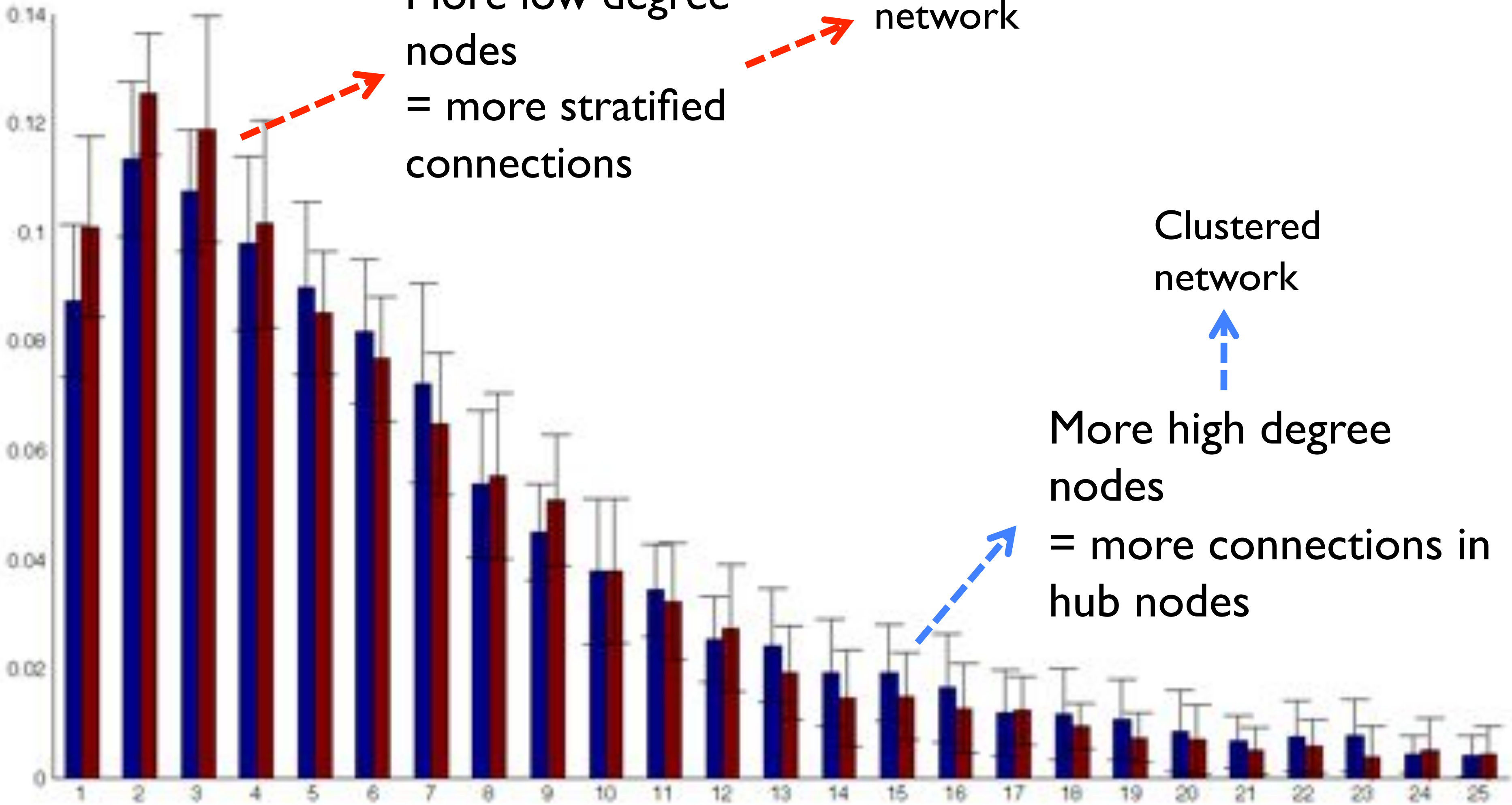
Degree of nodes for all subjects



Control   Autism

Degree distribution

red: autism
blue: control



More low degree nodes
= more stratified connections

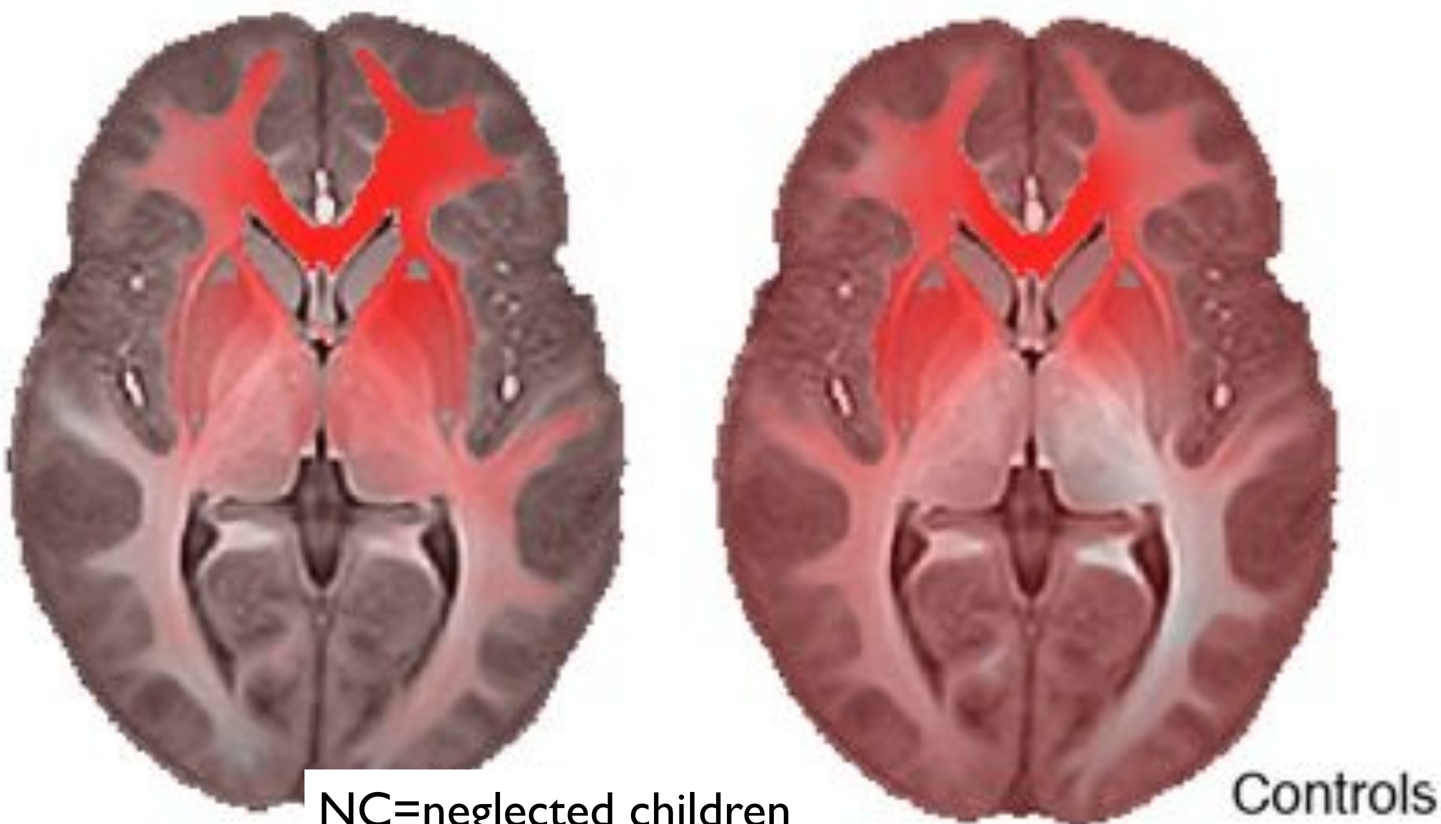
Stratified network

More high degree nodes
= more connections in hub nodes

Clustered network

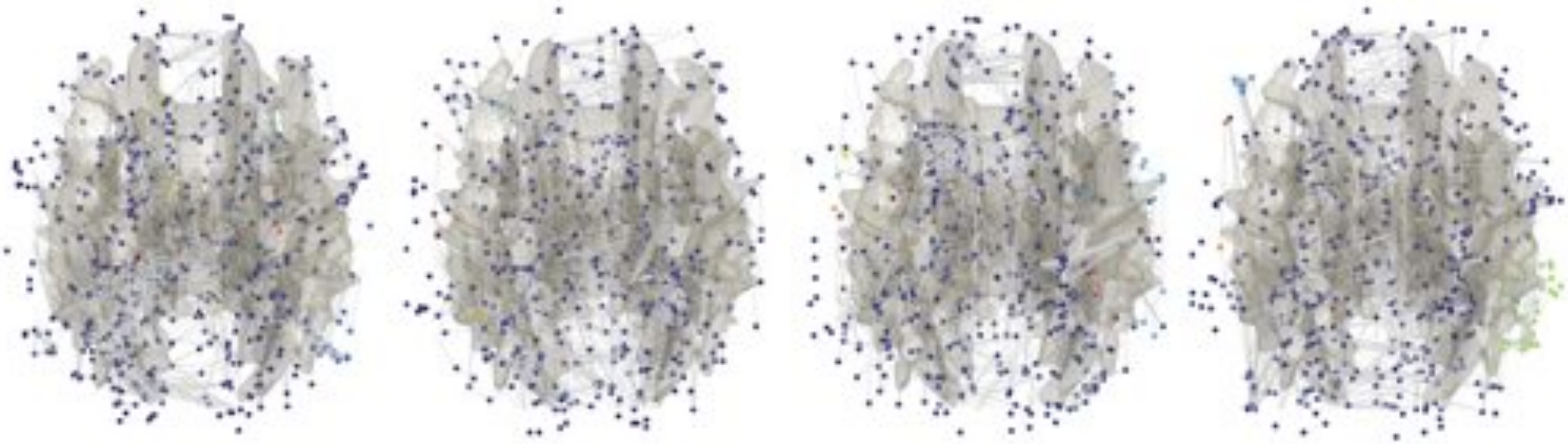
pvalues = 0.024, 0.015 and 0.080 for degrees 1, 2 and 3.

White matter connectivity based on correlating Jacobian determinant



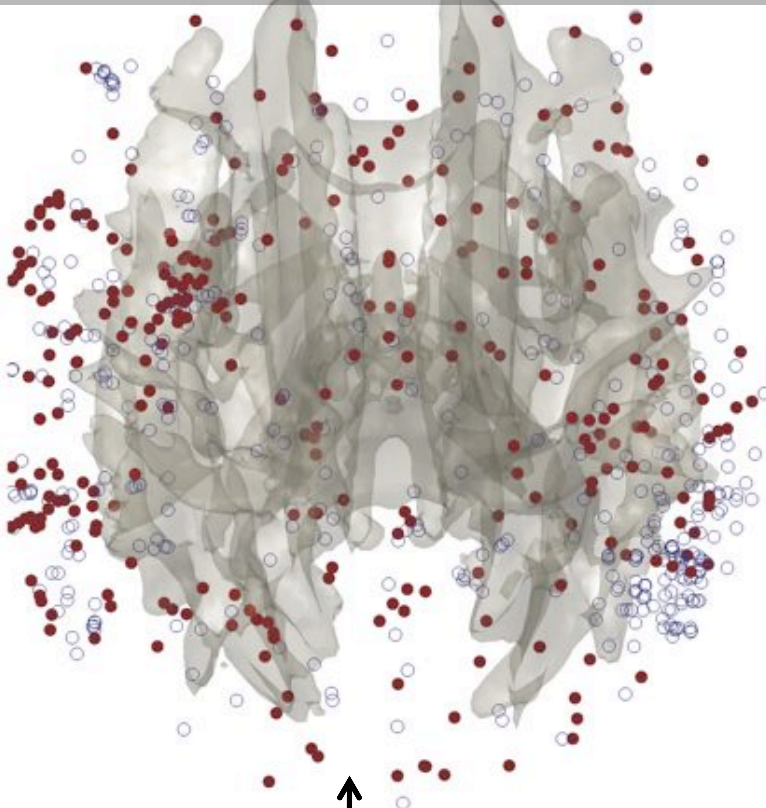
NC=neglected children

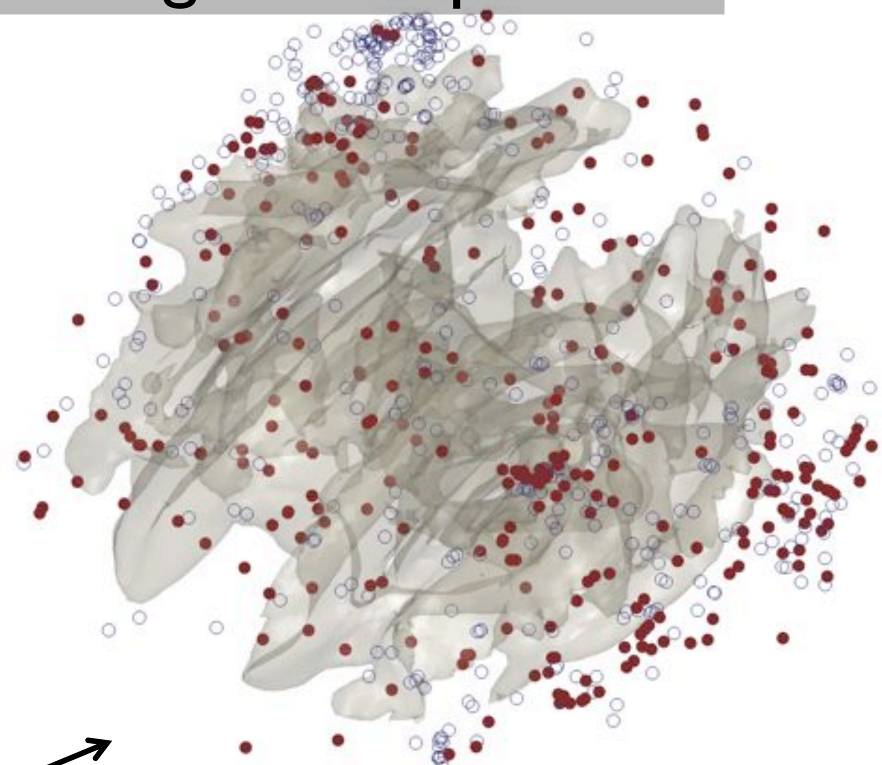
Largest connected component for 4 subjects



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 largest component





Disconnected components

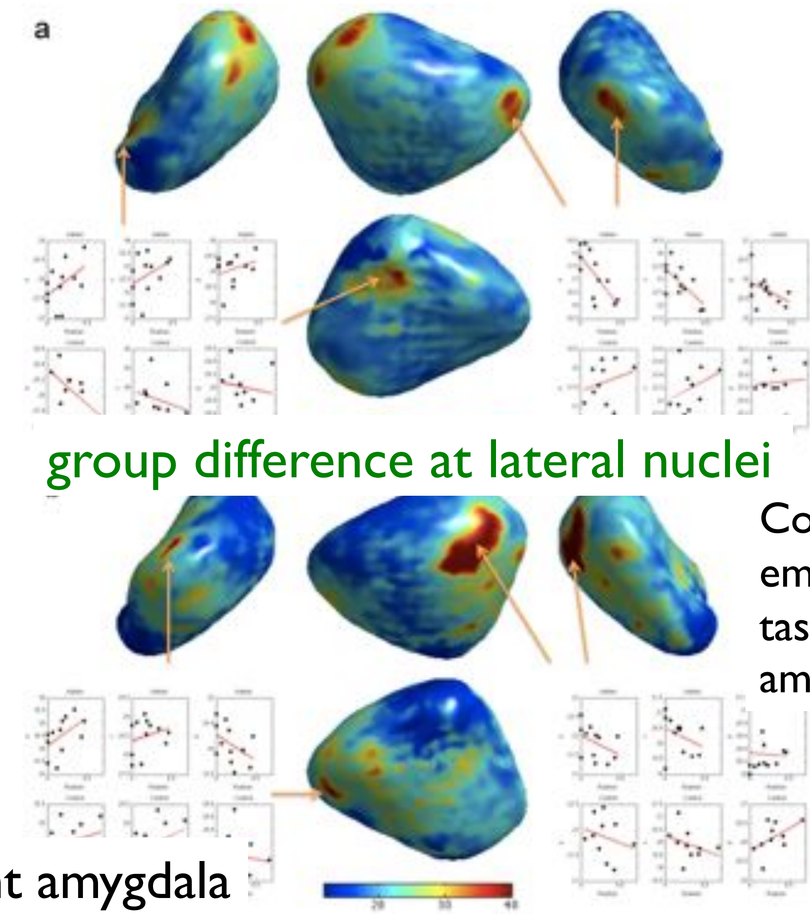
Control=blue
Autism=red

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

Chung, Worsley et al., Neuroimage 2010

Discussion

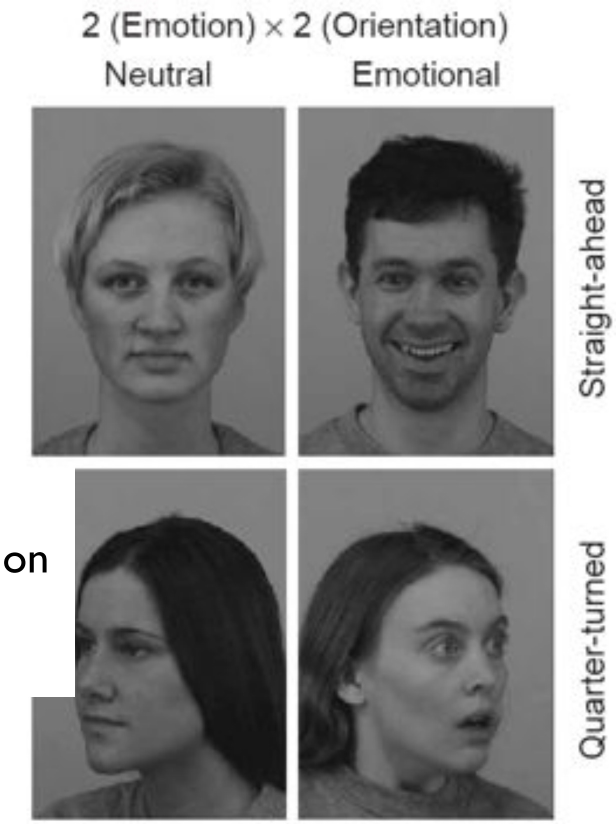
Left amygdala



group difference at lateral nuclei

Right amygdala

Correlating facial emotion discrimination task response and amygdala shape



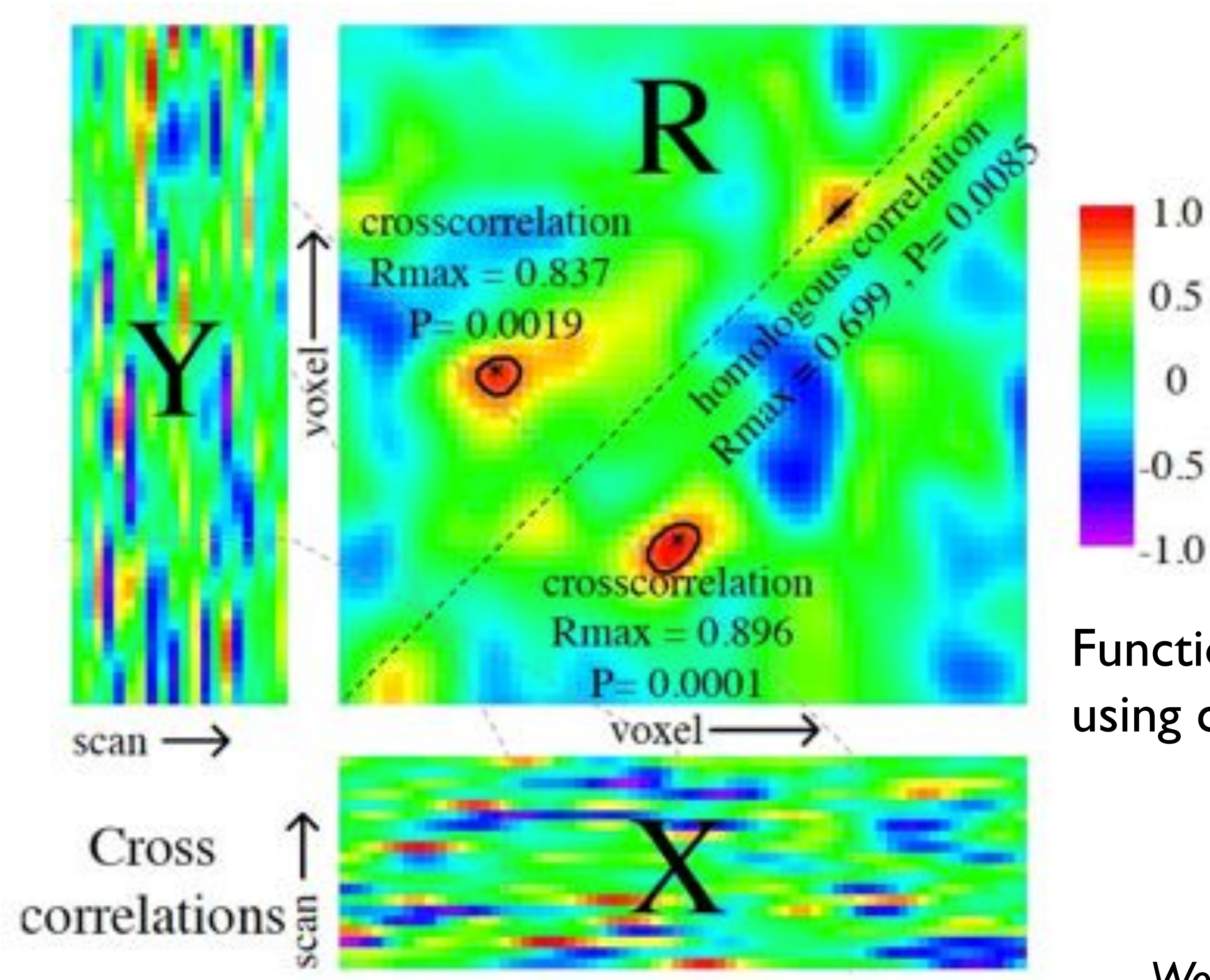
Amygdala network correlated with behavioral measures

Having said that we need DTI
for structural connectivity analysis…

This is not entirely true. We don’t really need DTI to do structural connectivity.

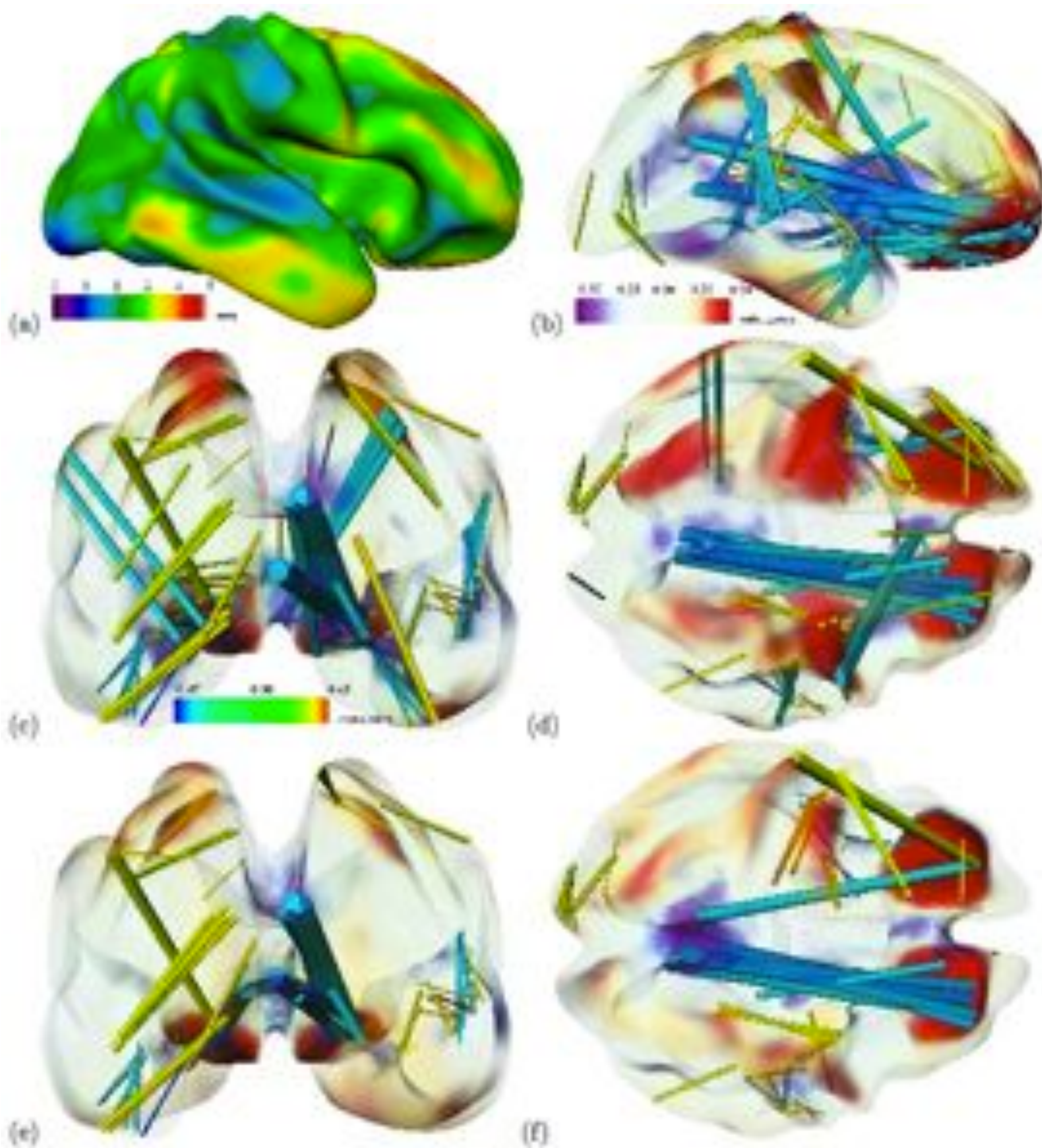
How?

Keith J. Worsley's evolving idea of anatomical connectivity. Let's see how he did it.



Functional connectivity using cross-correlation

Worsley et al. 1998. HBM



Anatomical connectivity in cortical thickness

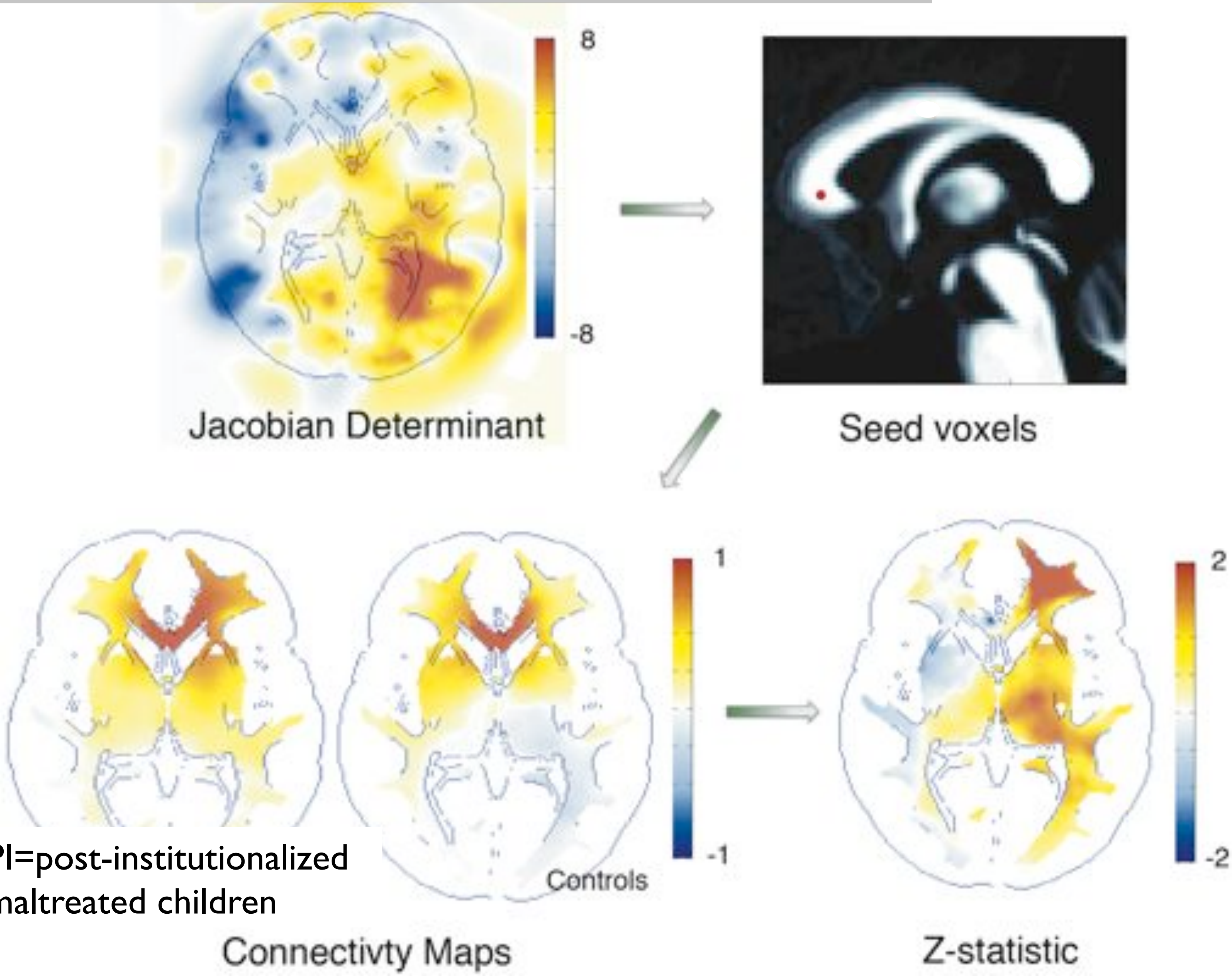
Took 6 years to get from functional to anatomical connectivity.

Worsely et al. 2004 NeuroImage

After Worsely et al. (2004) there has been a flood of studies on anatomical connectivity using cross-correlation. ,

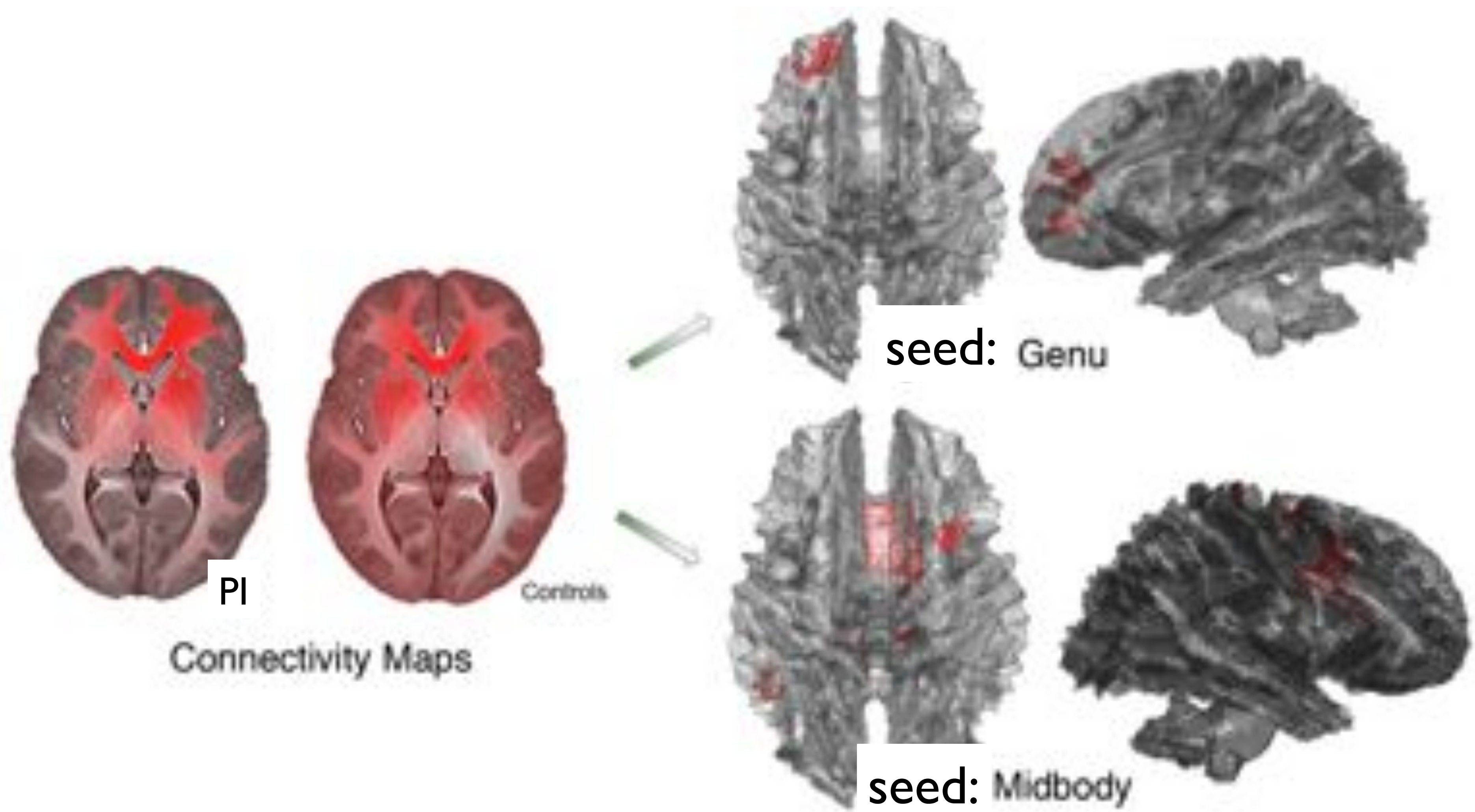
Lerch et al. 2006. NeuroImage
He et al. 2007. Cerebral cortex
Chen et al. 2008. Cerebral cortex
Gong et al., 2009. Cerebral cortex
….

Connectivity in tensor-based morphometry

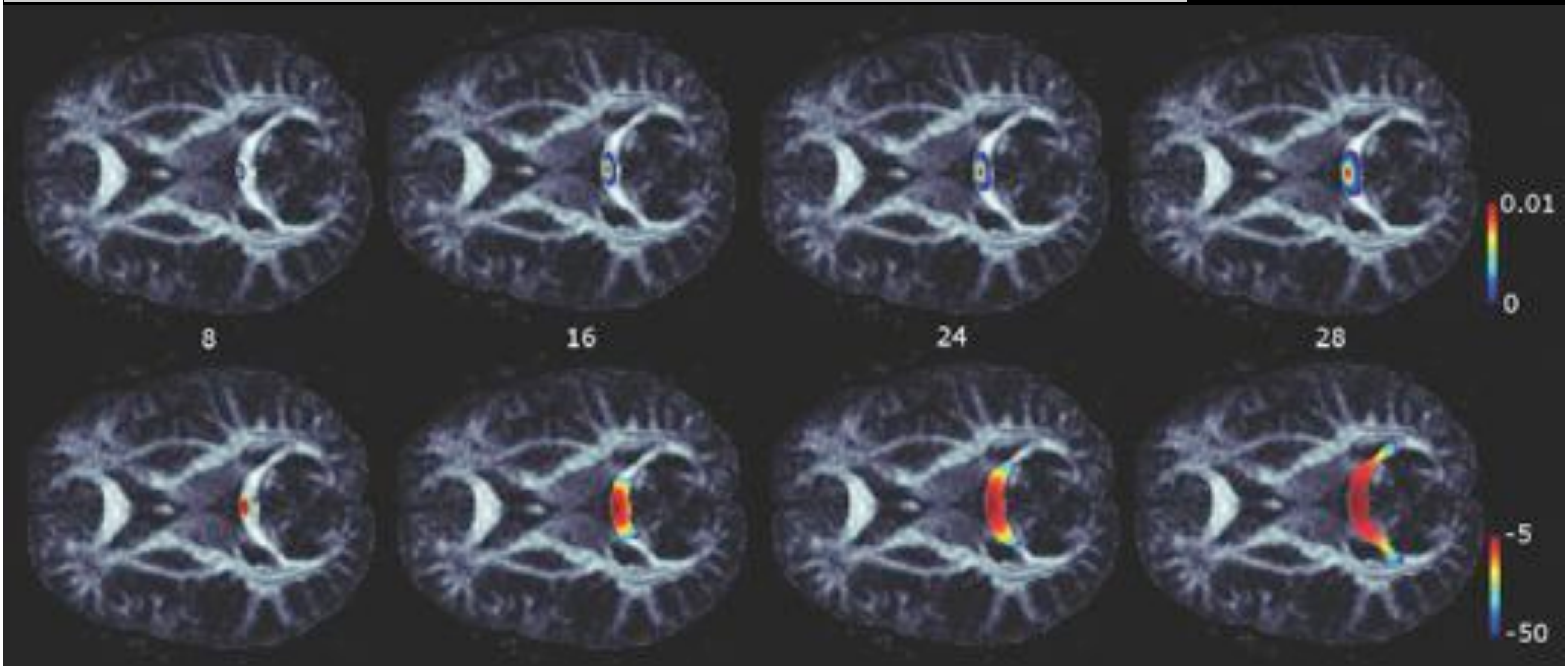


PI=post-institutionalized
maltreated children

No need for DTI doing structural connectivity analysis



Compare our maps to probabilistic connectivity maps in DTI



Transition probability of random walk is iteratively computed from the seed voxel (spleninum).

NeuroImage

www.elsevier.com/locate/ynimg
NeuroImage 31 (2006) 993 – 1003

Mapping anatomical correlations across cerebral cortex (MACACC) using cortical thickness from MRI

Jason P. Lerch,[a] Keith Worsley,[a] W. Philip Shaw,[b] Deanna K. Greenstein,[b] Rhoshel K. Lenroot,[b] Jay Giedd,[b] and Alan C. Evans[a,*]

Correlation on residual

$$thick_i = c1 + c2*age_i + e_i$$

Correlation

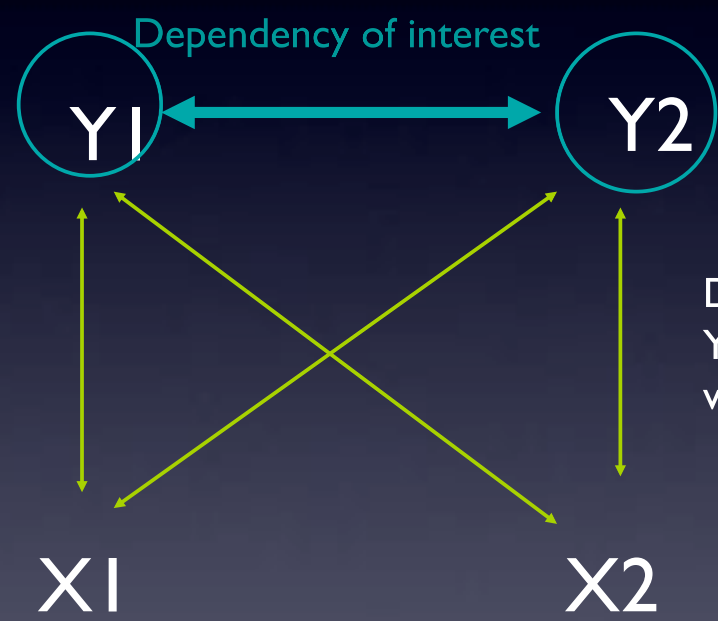
Partial Correlation

$$thick_j = c1 + c2*age_j + e_j$$

Are they same or different?

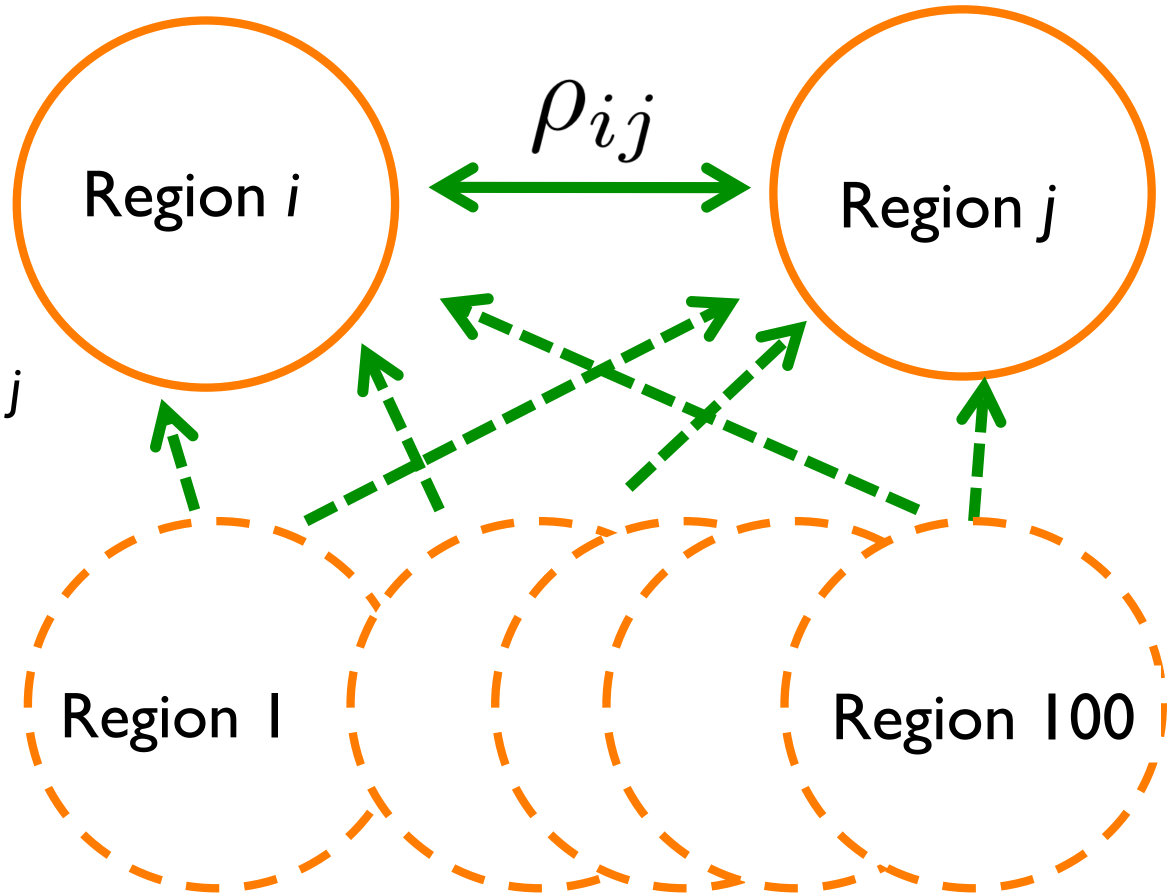
Partial correlation

Measure of dependency while removing the effect of other variables.



Dependency between Y1 and Y2 is influenced by other variables X1 and X2

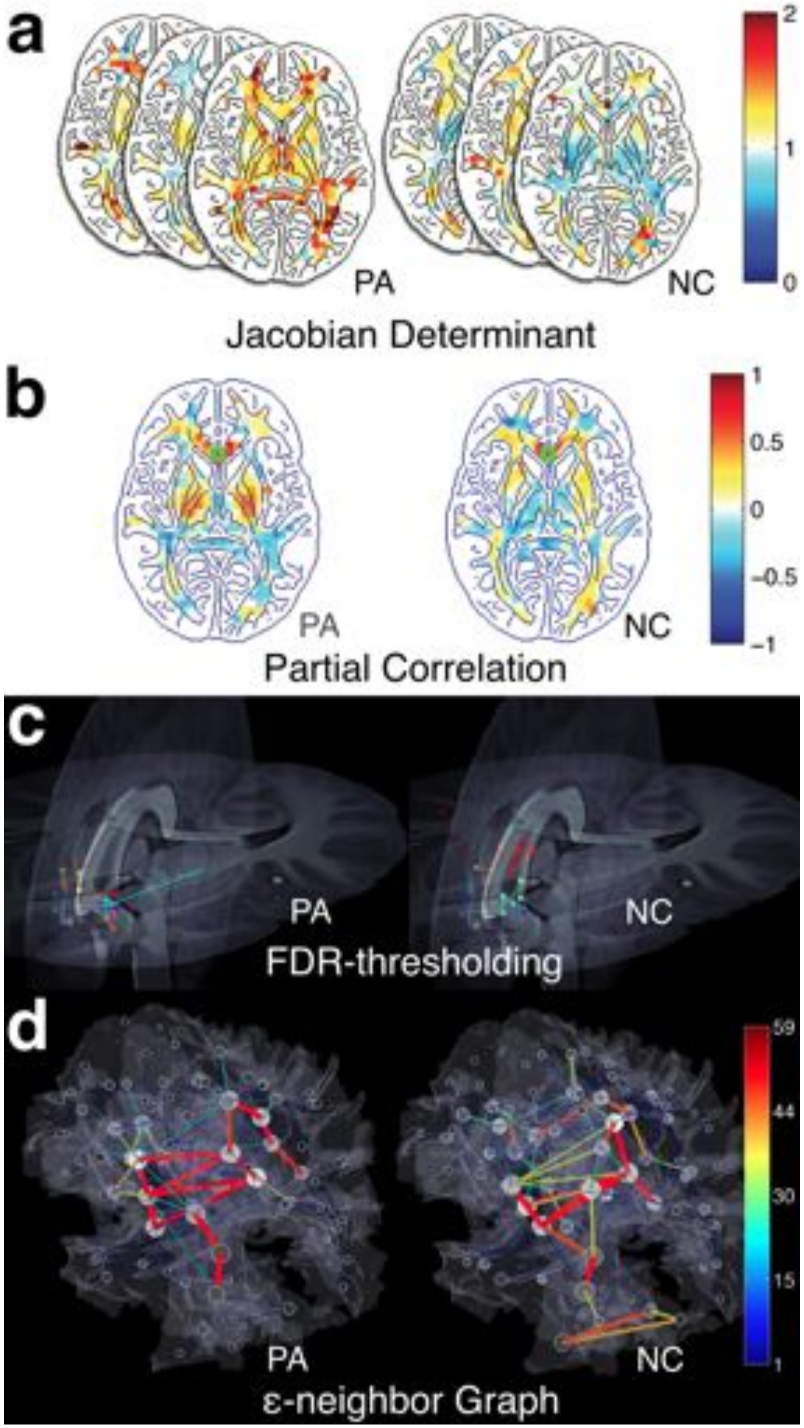
Connectivity analysis for multiple regions



Correlation of regions *i* and *j* while accounting for the effect of other regions

Inverse covariance matrix: $\Sigma^{-1} = (\sigma^{ij})$

Partial correlations: $\rho_{ij} = -\dfrac{\sigma^{ij}}{\sqrt{\sigma^{ii}\sigma^{jj}}}$



Voxel-wise measure

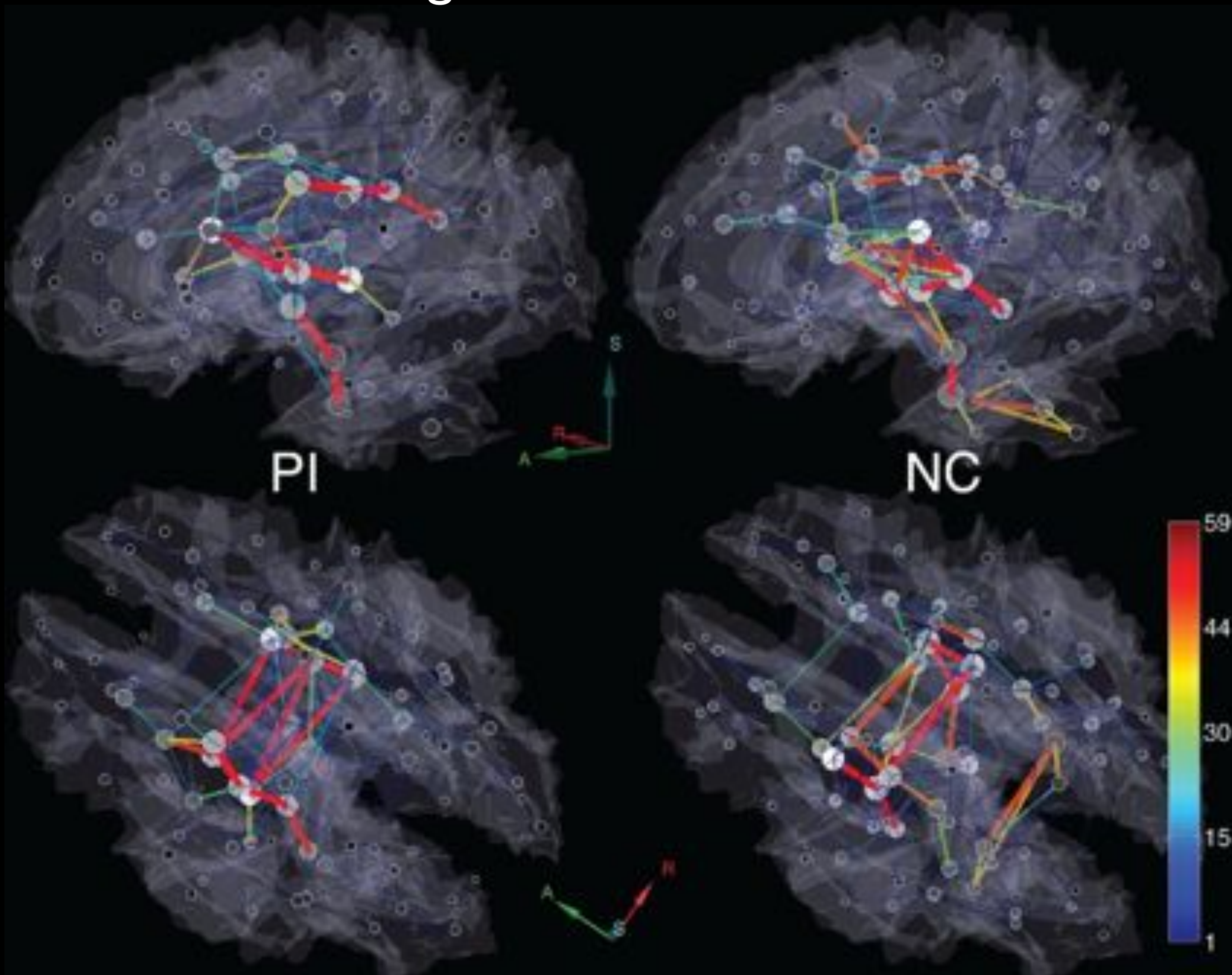
Connectivity maps with million nodes

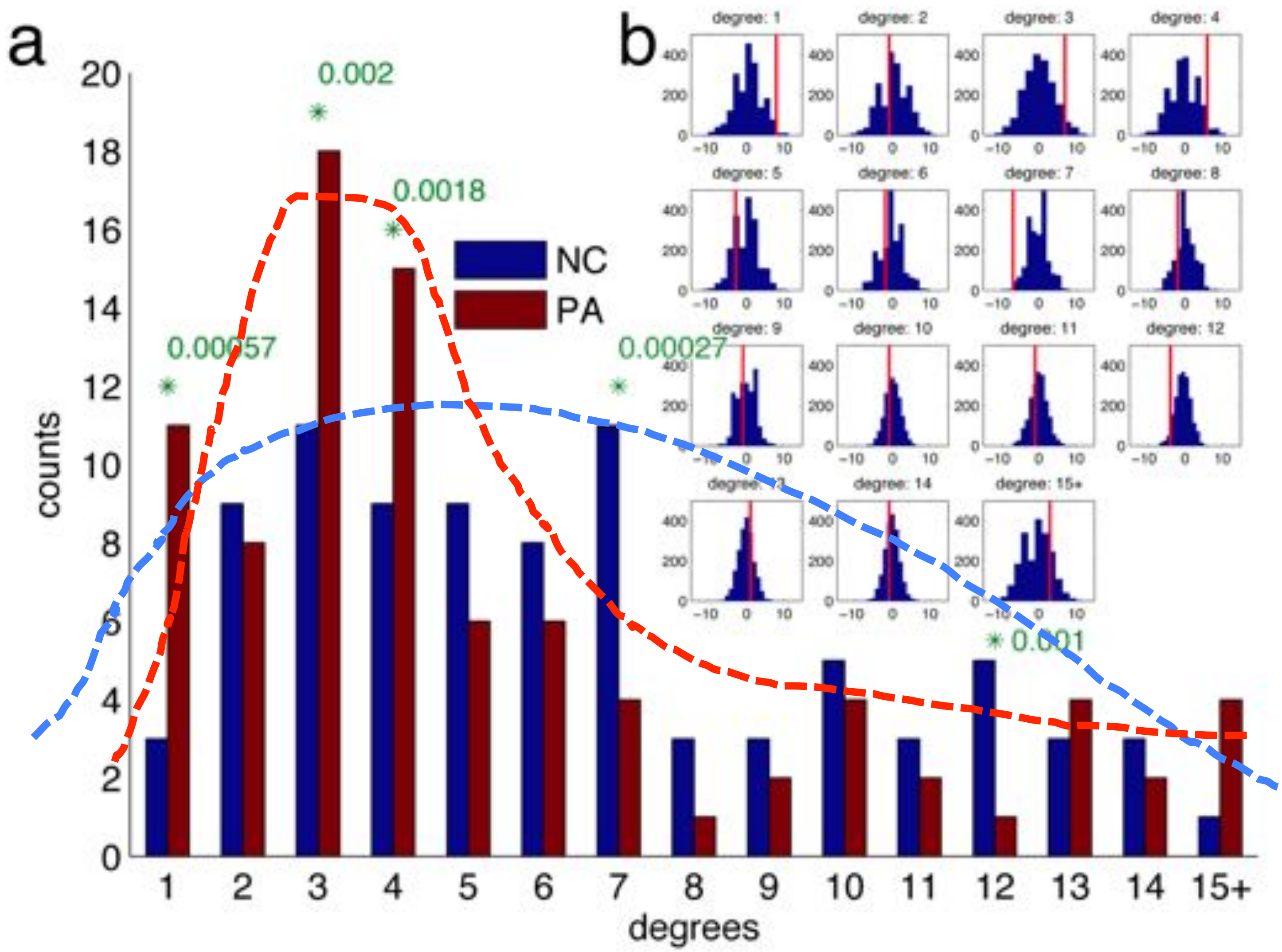
FDR-thresholding

Epsilon-neighbor graph construction

Kim et al. ISBI, 2009 submitted

Strength of connections



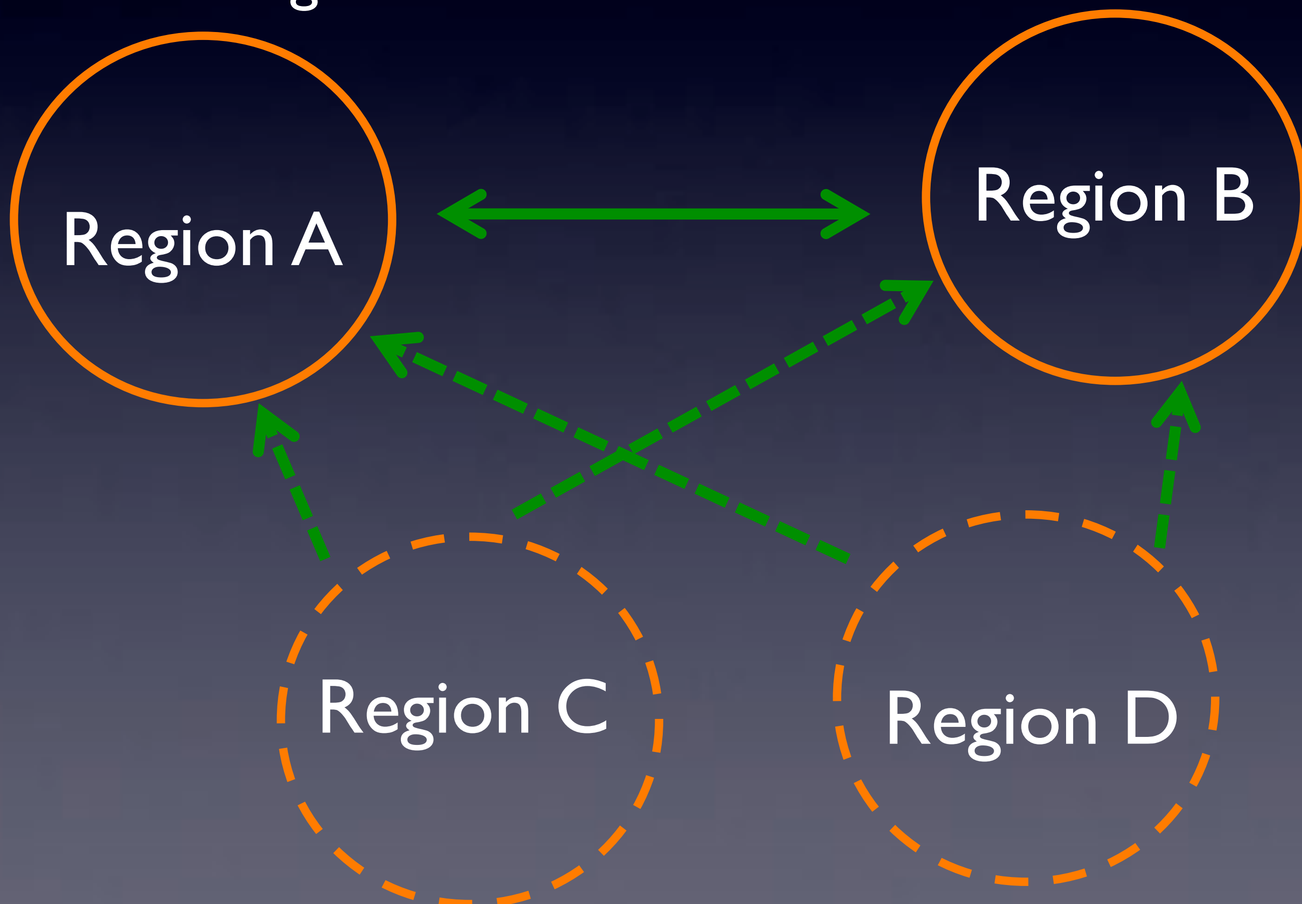


Degree distribution difference

Brain network modeling under compressed sensing

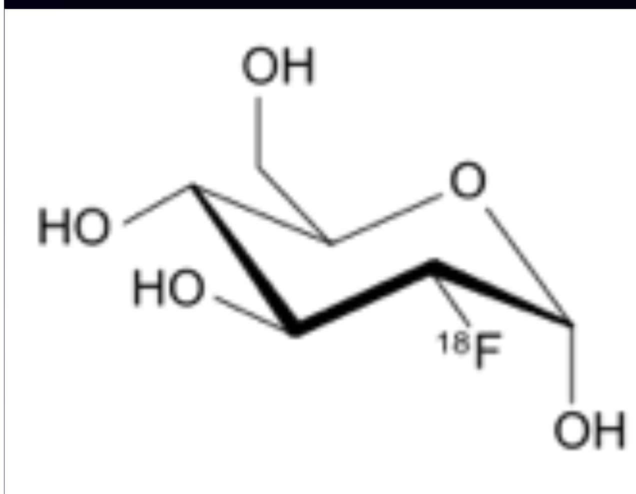
Lee et al. 2011. IEEE Transactions on Medical Imaging. submitted
Lee et al. 2011. SPIE Medical Imaging.

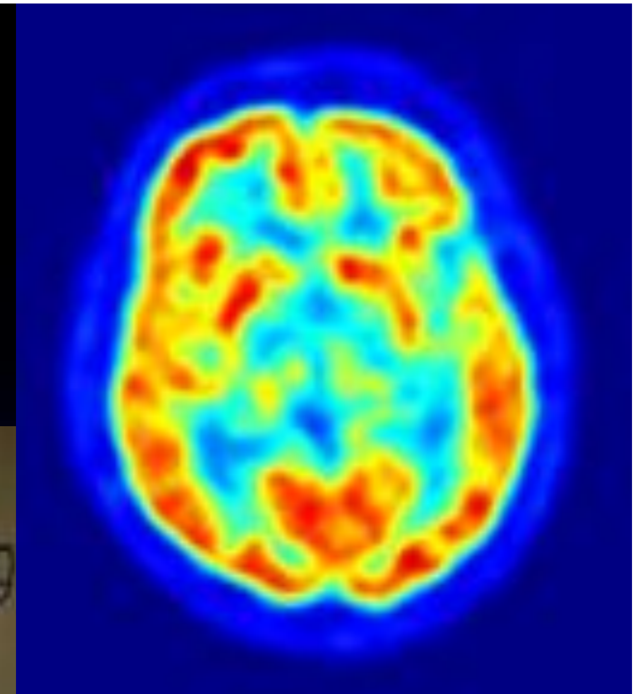
How change in A is related to change in B while accounting for the effect of other regions.

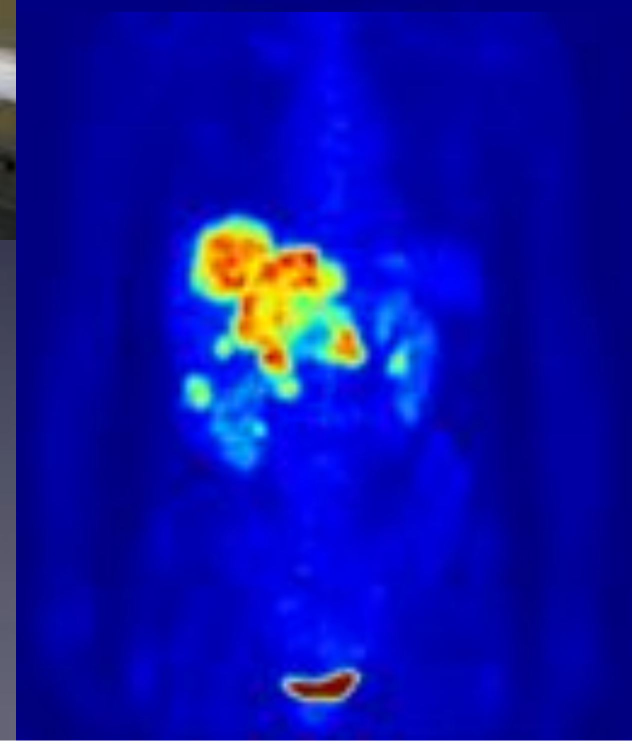


FDG-PET

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.

Large-p small-n problem

p (100-1000) regions >> n (20-50) subjects

97 regions 37 subjects (26 autistic, 11 control)

i-th subject: $\mathbf{x}_i = (x_{i1}, \cdots, x_{ip})'$

assumption:

$$\mathbb{E}\mathbf{x}_i = 0, \cdots \mathbb{E}(\mathbf{x}_i \mathbf{x}_i') = \Sigma$$

The dependency among p-regions is characterized by the covariance matrix.

Inverse covariance matrix: $\Sigma^{-1} = (\sigma^{ij})$

Partial correlations as sparse regression

Sparse linear regression:

$$\mathbf{x}_i = \sum_{j \neq i} \beta_{ij} \mathbf{x}_j + \epsilon_i$$

Residual:

$$r_i = \mathbf{x}_i - \sum_{j \neq i} \widehat{\beta}_{ij} \mathbf{x}_j$$

Partial correlation:

$$\rho_{ij} = \mathrm{corr}\ (r_i, r_j)$$

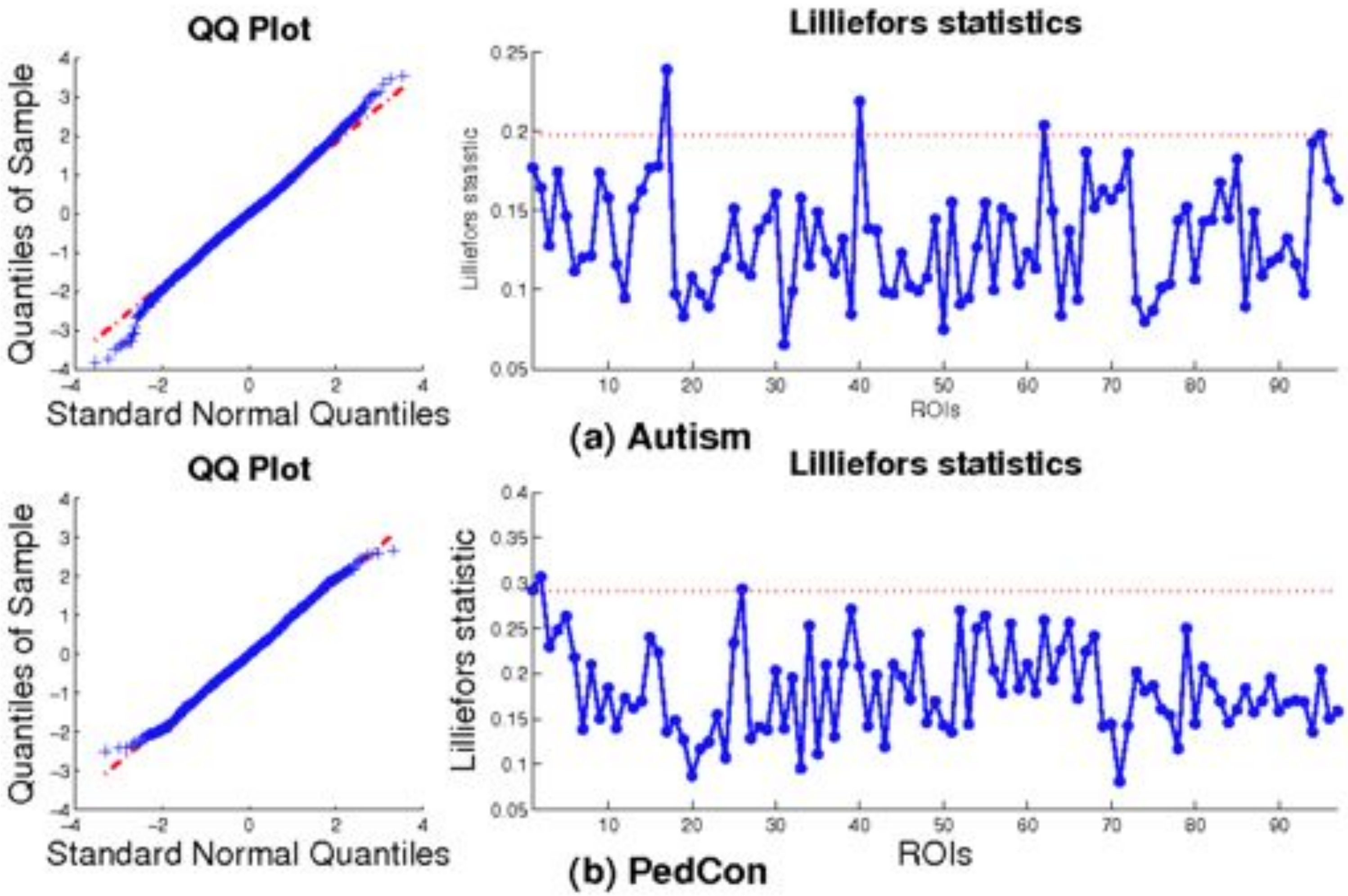
LASSO(least absolute shrinkage and selection operator)

Goodness-of-fit: $$L = \sum_{i=1}^{p} \|\mathbf{x}_i - \sum_{j \neq i} \beta_{ij} \mathbf{x}_j\|^2$$

LASSO penalty: $$J = \sum_{i<j} |\beta_{ij}|$$

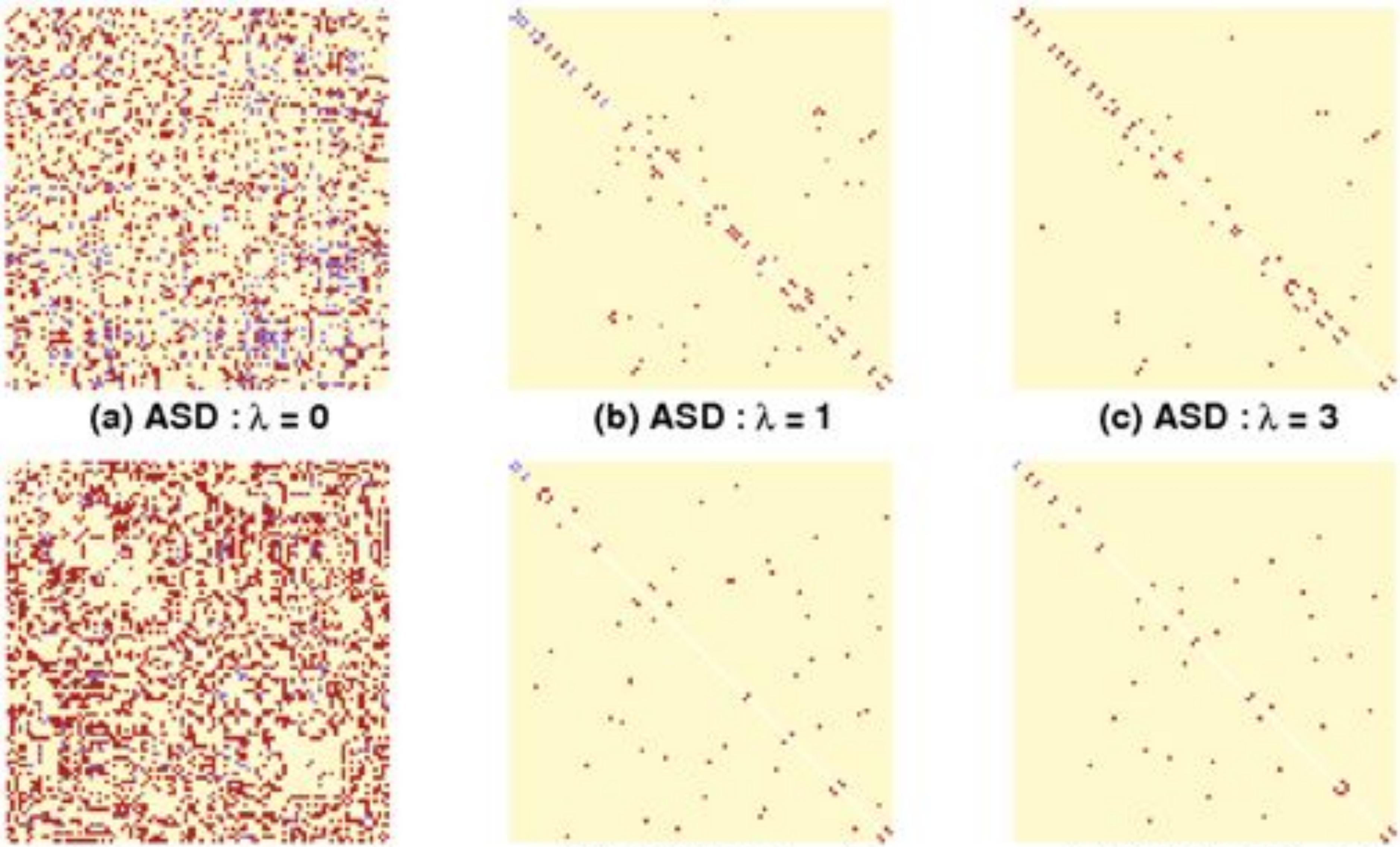
Minimize $$L + \lambda J$$

Gaussian model assumption



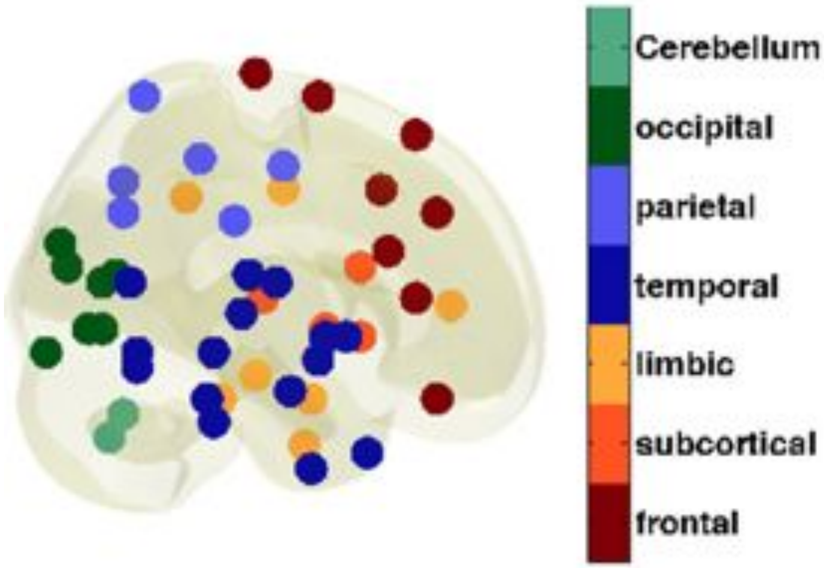
The sparse recovery of parameters can be done with overwhelmingly large probability under Gaussian assumption and $n \geq c \log p$ (Candes & Tao, 2006).

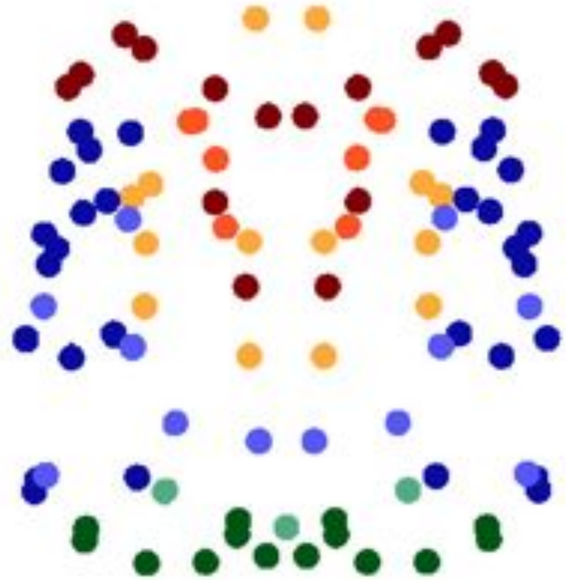
Sparsity vs. tuning parameter



(a) ASD : λ = 0 (b) ASD : λ = 1 (c) ASD : λ = 3

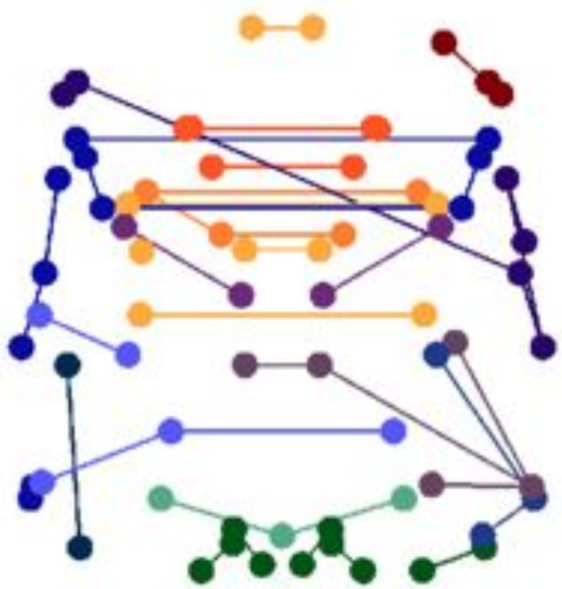
(d) PedCon : λ = 0 (e) PedCon : λ = 1 (f) PedCon : λ = 3



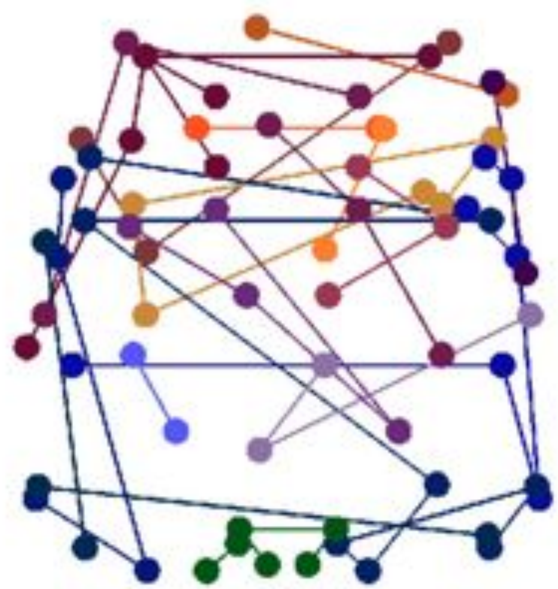


(a) ROIs in 3-dimensional space

(b) 2-dimensional embedding of ROIs

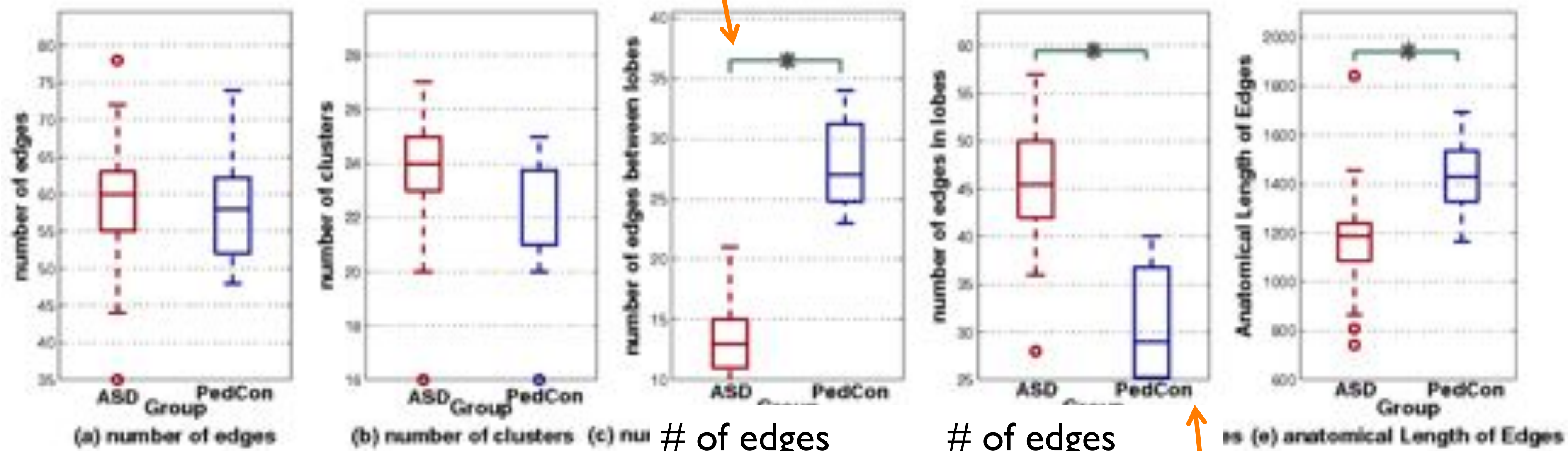


(c) ASD



(d) PedCon

Global (long range) under-connectivity



# of edges
between lobes

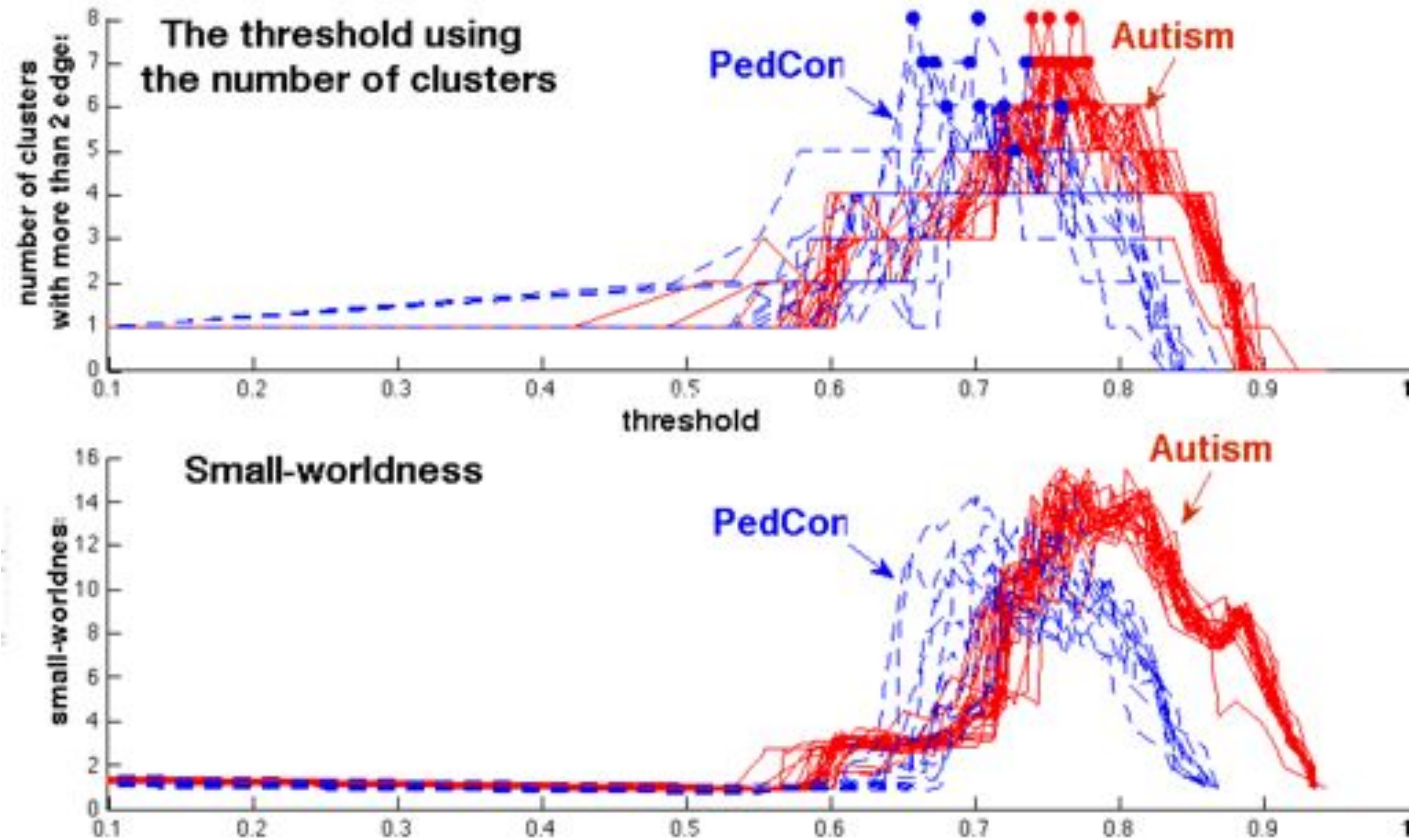
# of edges
within a lobe

Local over-connectivity

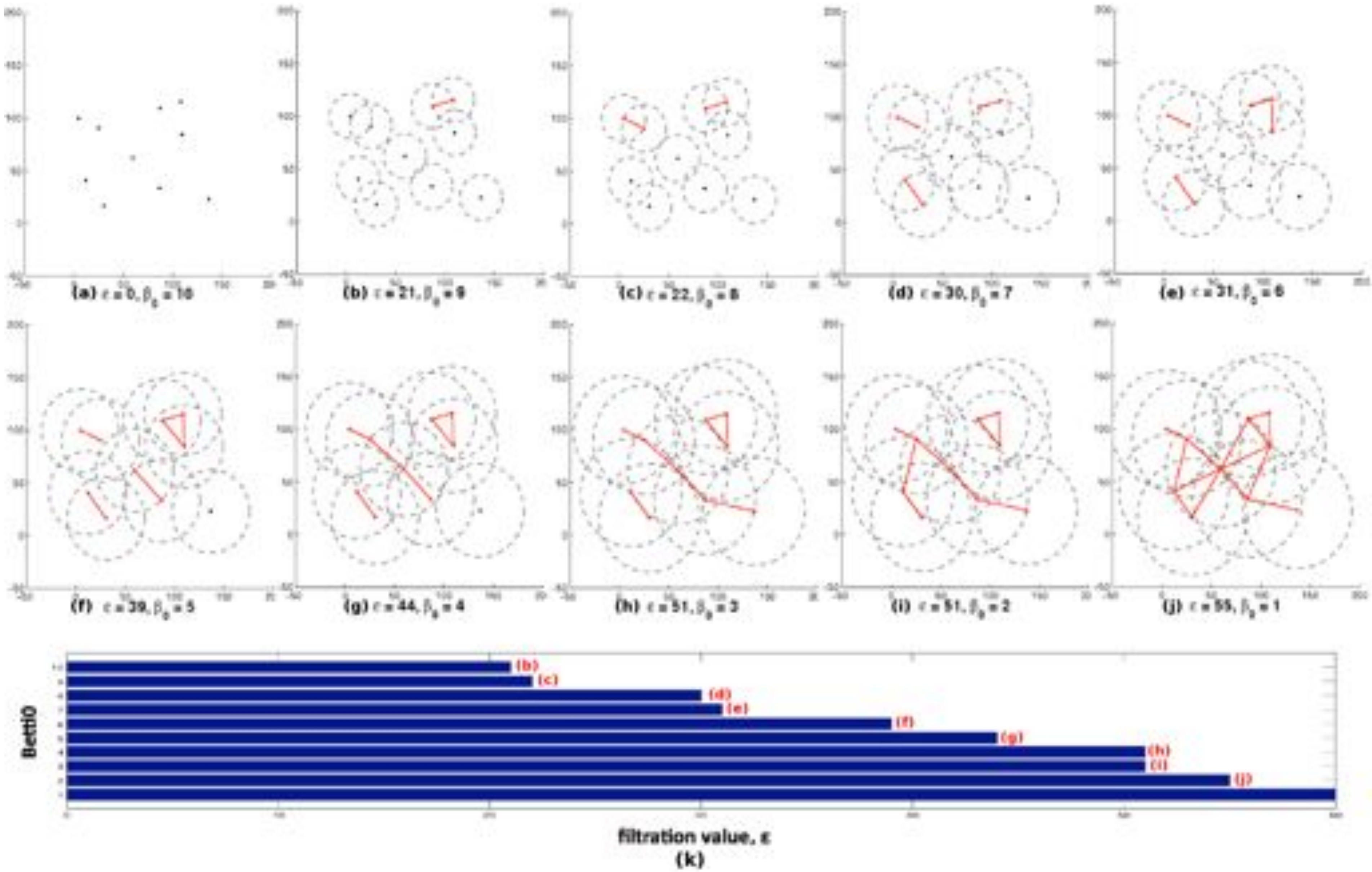
This is for functional network. What about structural network?

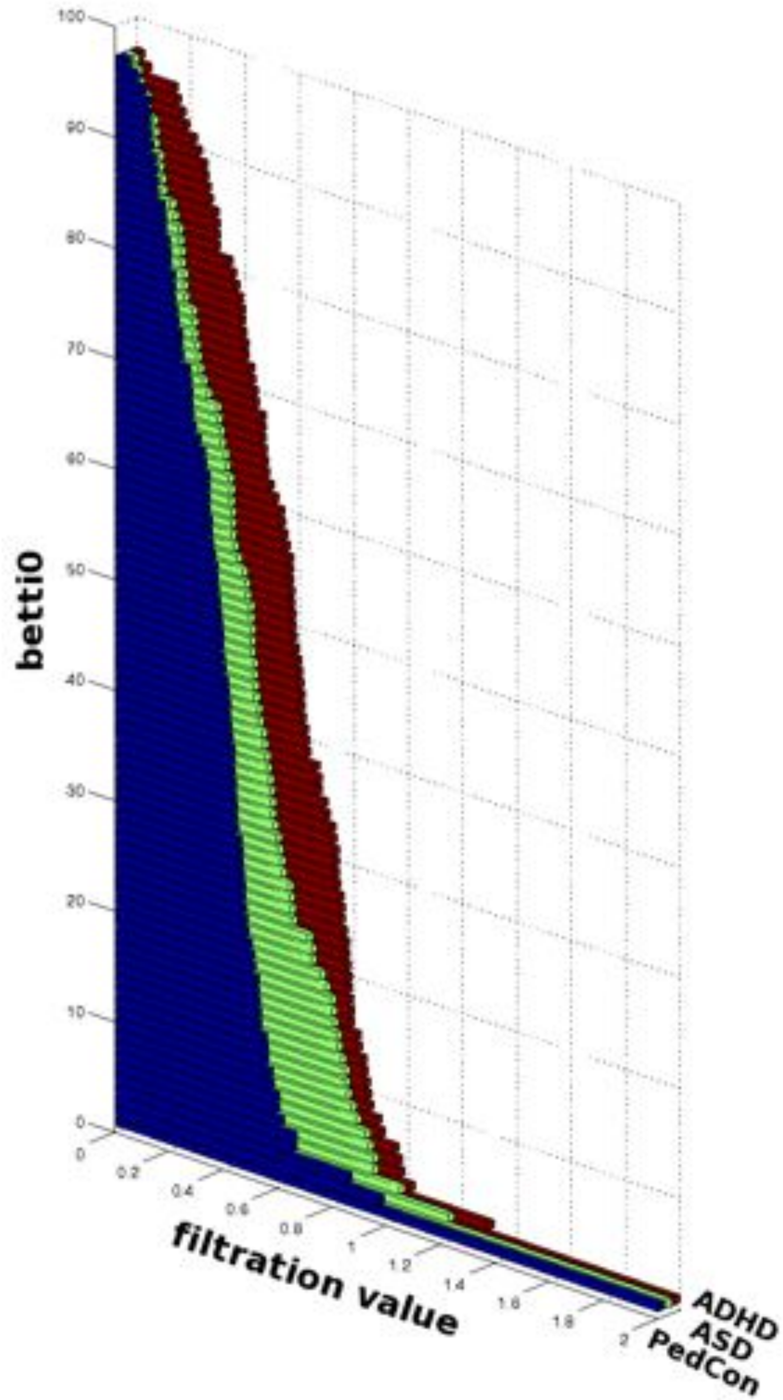
Discussion

Why do we have to pick one particular threshold?



Rips filtration and barcode





24 attention deficit hyperactivity disorder (ADHD) children
26 autism spectrum disorder (ASD) children
11 pediatric control subjects

Rate of decline difference:
Brain network in control subjects merges to a single component faster than other populations!

What about all other Betti numbers?

Lecture 10 topics

Asymmetry analysis
Logistic regression
Logistic discriminant analysis

Read chung.2008.mmbia.pdf
chung.2008.sinica.pdf