The Waisman Laboratory for Brain Imaging and Behavior

University of Wisconsin SCHOOL OF MEDICINE AND PUBLIC HEALTH

White Mater Fiber Shape and Brain Network Analysis using Diffusion Tensor Imaging

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

Department of Brain and Cognitive Sciences
Seoul National University, Korea

www.stat.wisc.edu/~mchung

Montreal Workshop November XX, 2009

Abstract

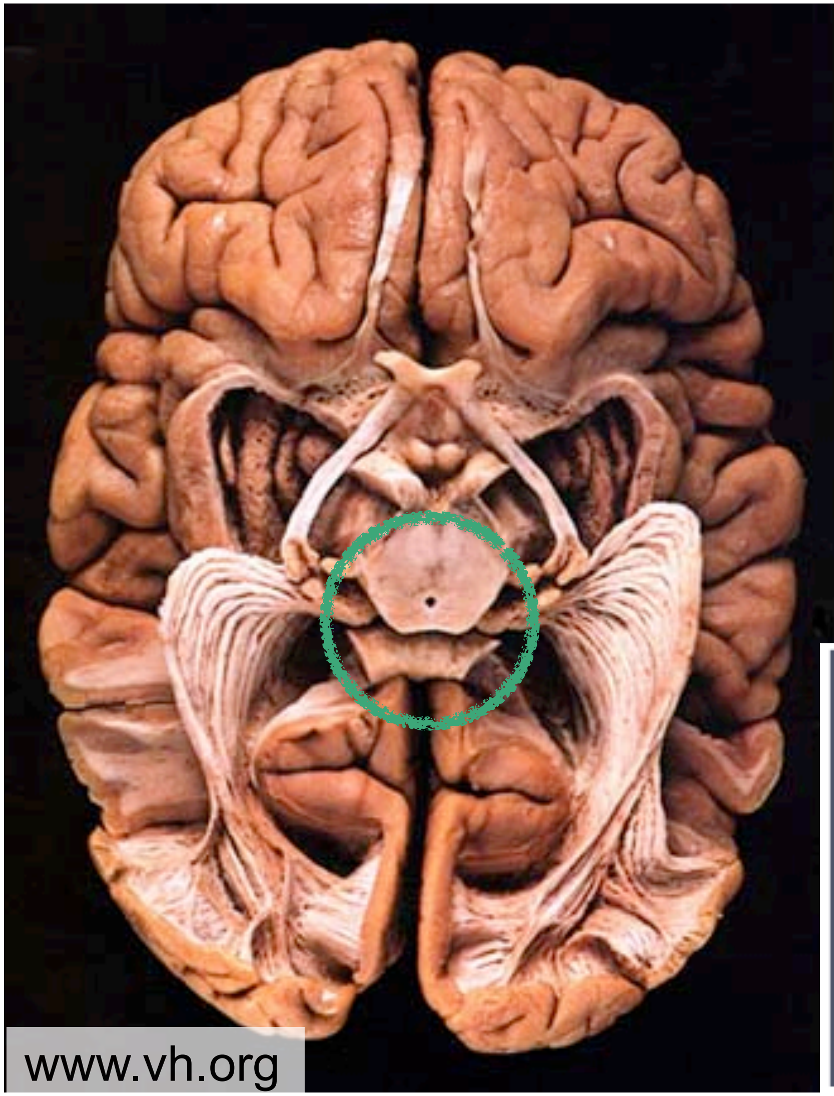
Diffusion tensor imaging offers a unique opportunity to characterize the trajectories of white matter fiber bundles non-invasively in the brain. Whole brain tractography studies routinely generate up to half million tracts per brain. The main computational challenge is to develop a unified and compact mathematical representation of large number of tracts. We have developed the cosine series representation (CSR) to parameterize, register and perform inference in a unified Hilbert space framework. CSR can be fairly useful in shape characterization of tracts but it cannot answer more complex hypothesis about brain connectivity. To address the brain connectivity problem, we built a scalable 3D graph network model and inference was performed in the ensemble of graphs for testing for over- and under-connectivity of the brain network. Computational issues and methods are illustrated with autism case studies.

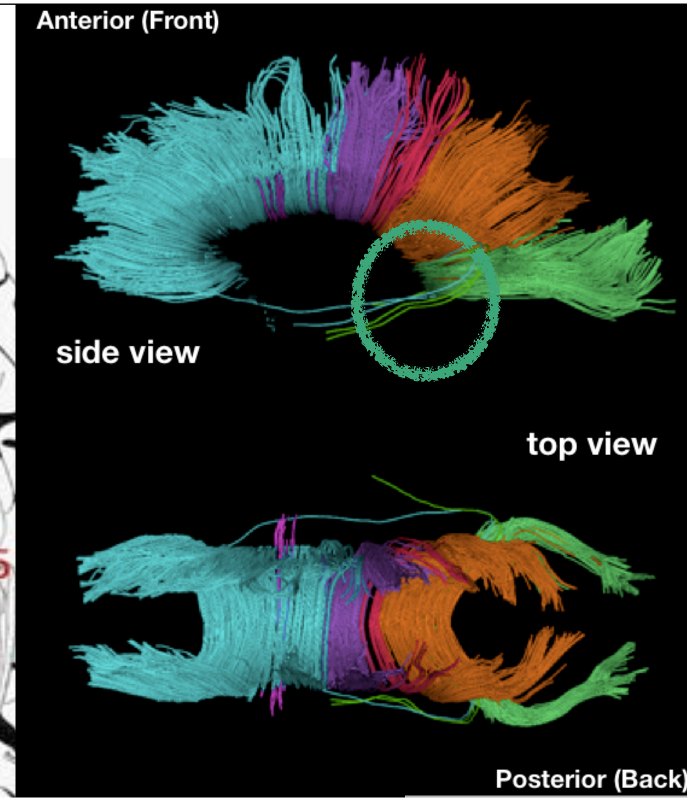
Acknowledgment

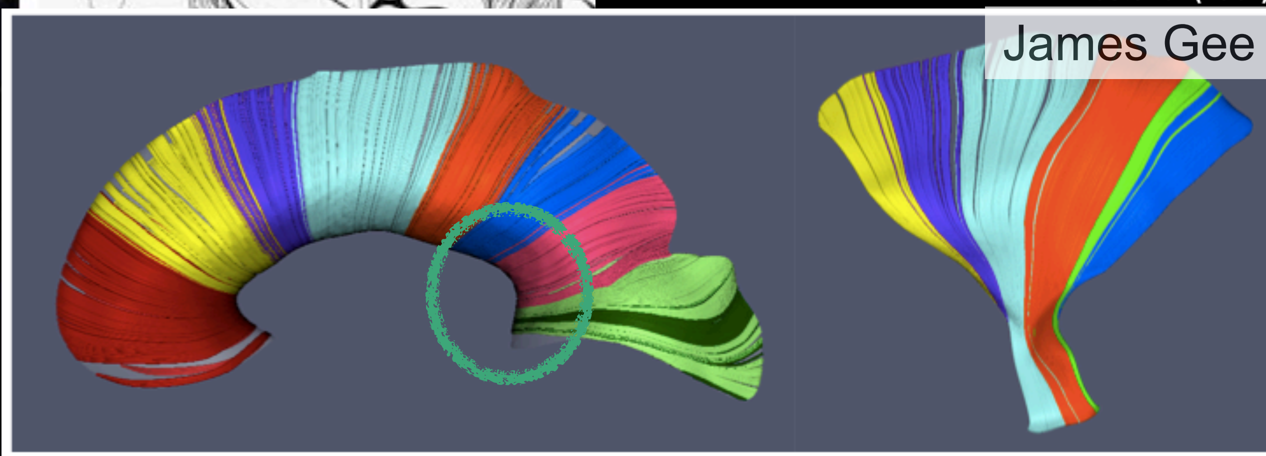
Nagesh Adluru, Jee Eun Lee, Mariana Lazar
Jane E. Lainhart, Andrew L. Alexander

University of Wisconsin-Madison

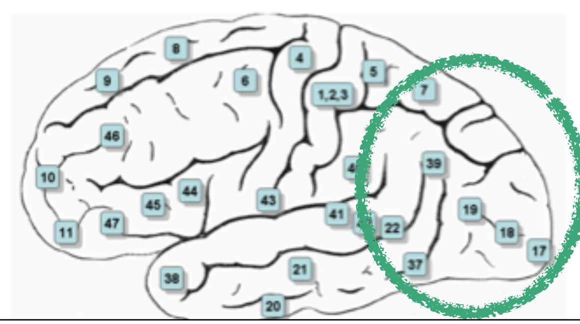
White matter fibers







Fibers passing through splenium of corpus callosum

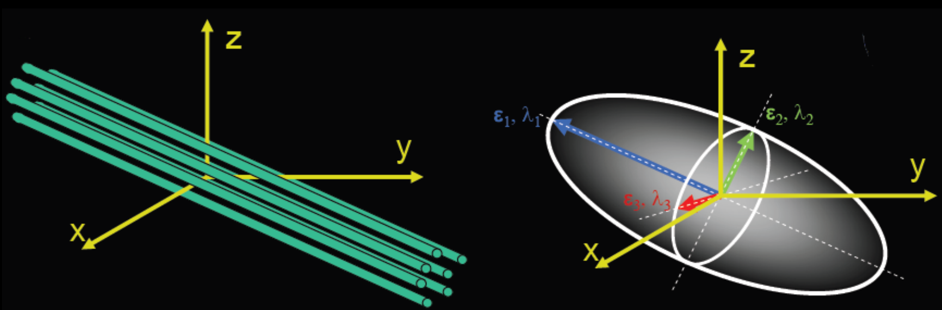


- Brodmann Area 2
- Brodmann Area 4
- Brodmann Area 5
- Brodmann Area 6
- Brodmann Area 7
- Brodmann Area 8
- Brodmann Area 9
- Brodmann Area 10
- Brodmann Area 18
- Brodmann Area 19

Tractography

isotropic diffusion

Mori and van Zijl NMR Biomed 2002

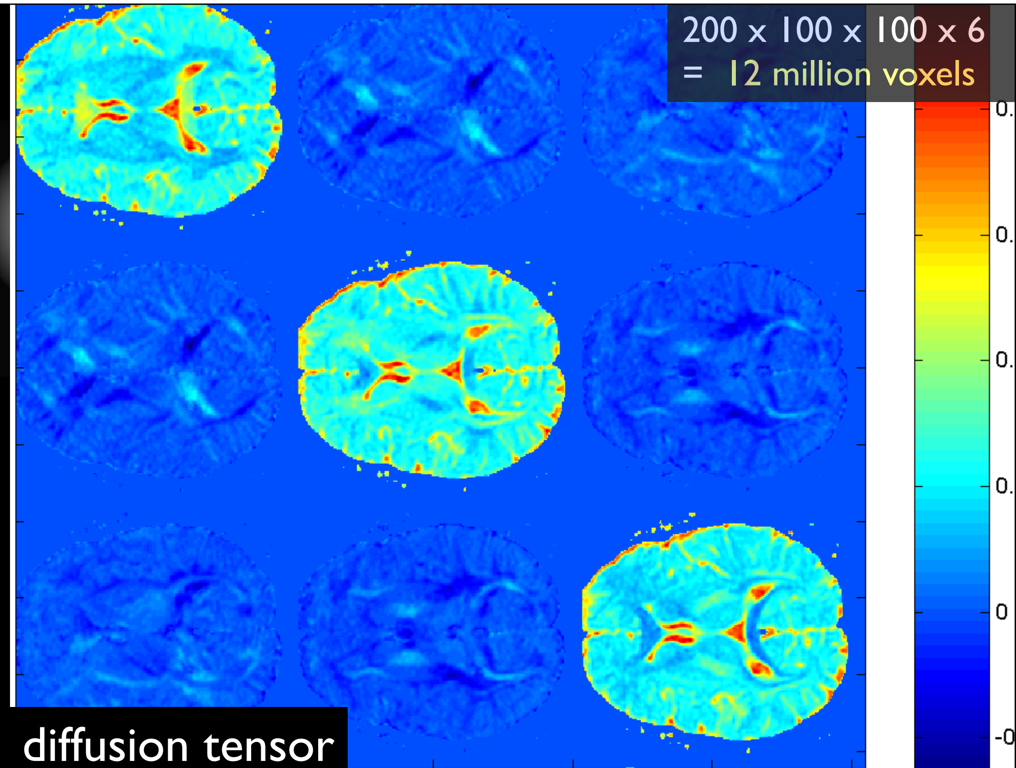


anisotropic diffusion

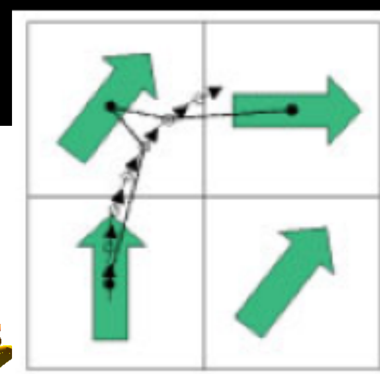
$$p(x \mid x_o, \tau) = \frac{1}{\sqrt{(4\pi\tau)^3 |\underline{D}|}} exp\left(\frac{-(x - x_0)^T \underline{D}^{-1} (x - x_0)}{4\tau} \right)$$

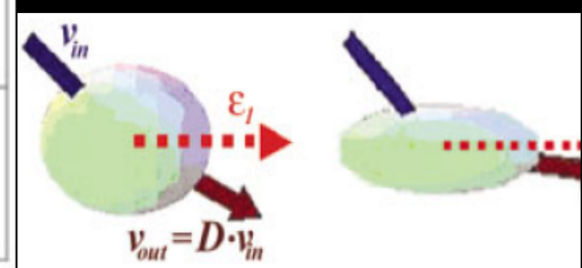
transition probability from x_0 to x

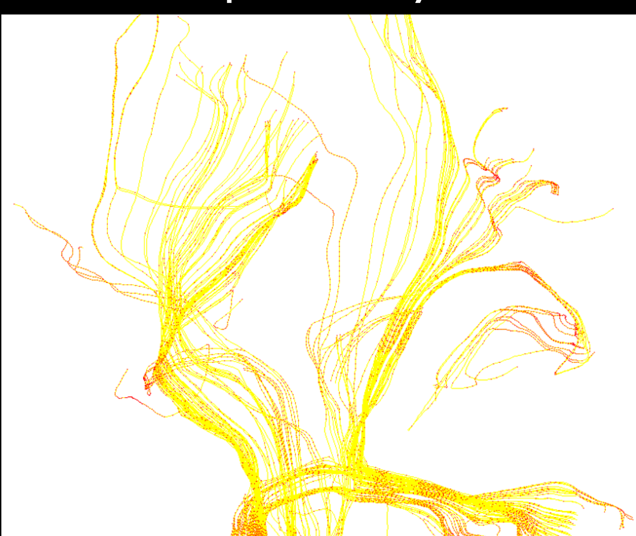
diffusion tensor

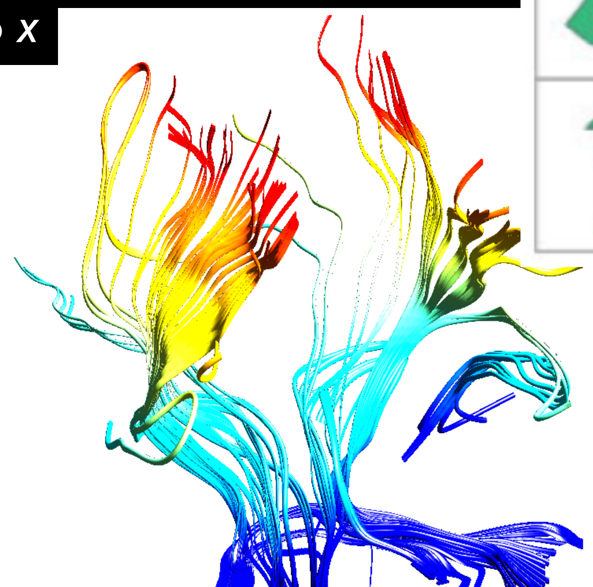


TENsor Deflection (TEND)



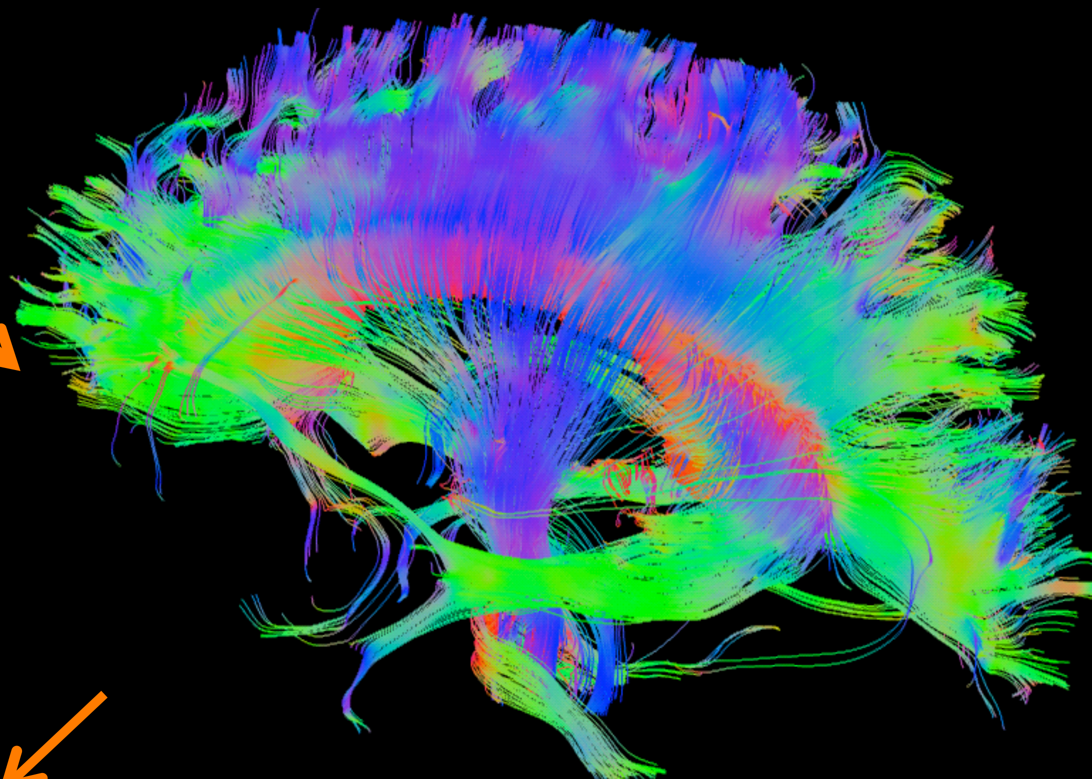






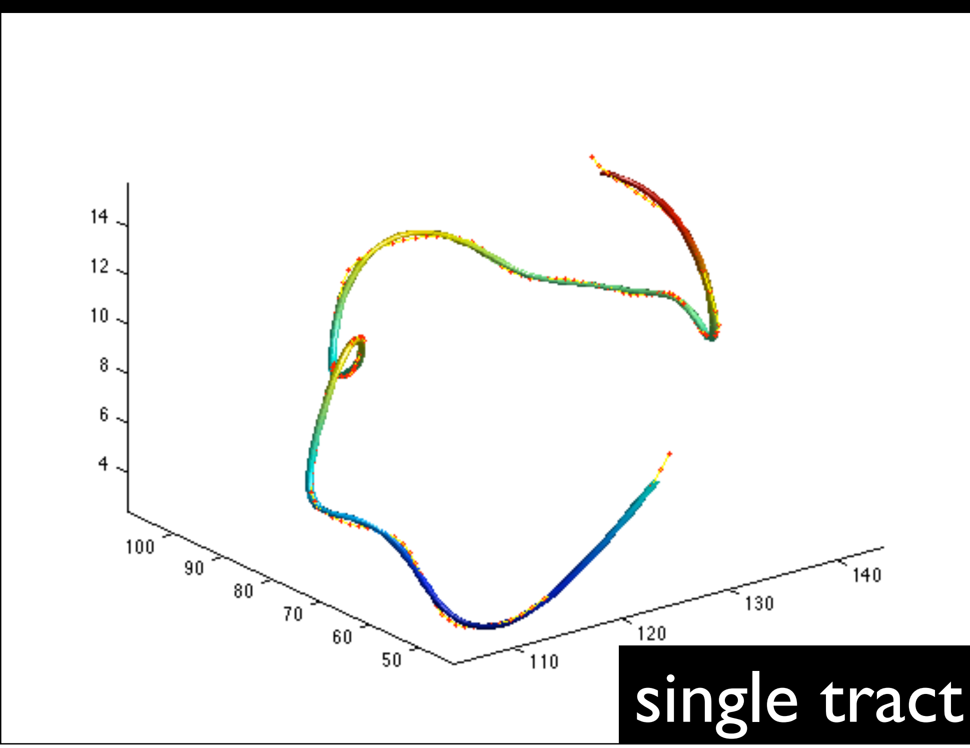
Second order Runge-Kutta algorithm with TEND (Lazar et al., HBM 2003)

White matter fiber tractography



Tractography result

0.5-1 million tracts



parameterization

Previous studies

Very limited research on parametric model of white fiber tracts

Clayden et al. IEEE TMI 2007

Cubic B-spline is used to model and match tracts.

:computational nightmare

Batchelor et al. MRM 2006

Sine and cosine Fourier descriptors are used to extract global shape features for classification

: inefficient representation

STATISTICS AND ITS INTERFACE Volume 0 (2010) 1–11

Cosine Series Representation of 3D Curves and Its Application to White Matter Fiber Bundles in Diffusion Tensor Imaging

MOO K. CHUNG, NAGESH ADLURU, JEE EUN LEE, MARIANA LAZAR, JANET E. LAINHART AND ANDREW L. ALEXANDER

accepted

Our contribution

1. More efficient Fourier descriptor (uses less number of basis than before).

2. Developed registration and averaging framework for 3D curves without numerically demanding optimization routines as in splines.

Orthonormal basis in [0,1]

$$\Delta f + \lambda f = 0$$

Eigenfunctions form orthonormal basis

Solve it with periodic constraint

$$f(t+2) = f(t)$$

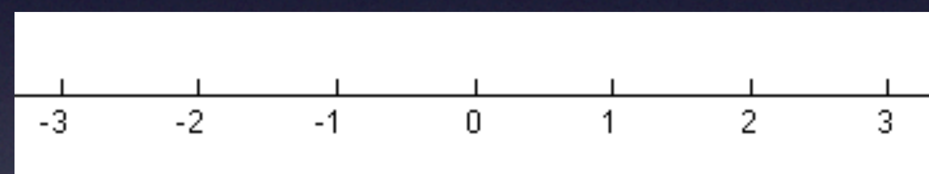
$$\sin(l\pi t), \cos(l\pi t)$$

Additional symmetric constraint

$$f(t) = f(-t)$$

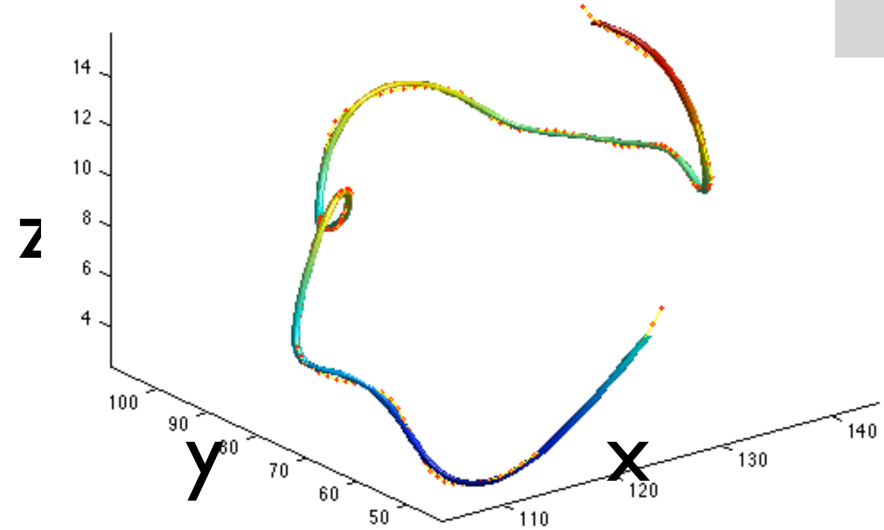
$$\lambda_l = -l^2\pi^2$$

$$\psi_0 = 1, \psi_l = \sqrt{2}\cos(l\pi t)$$

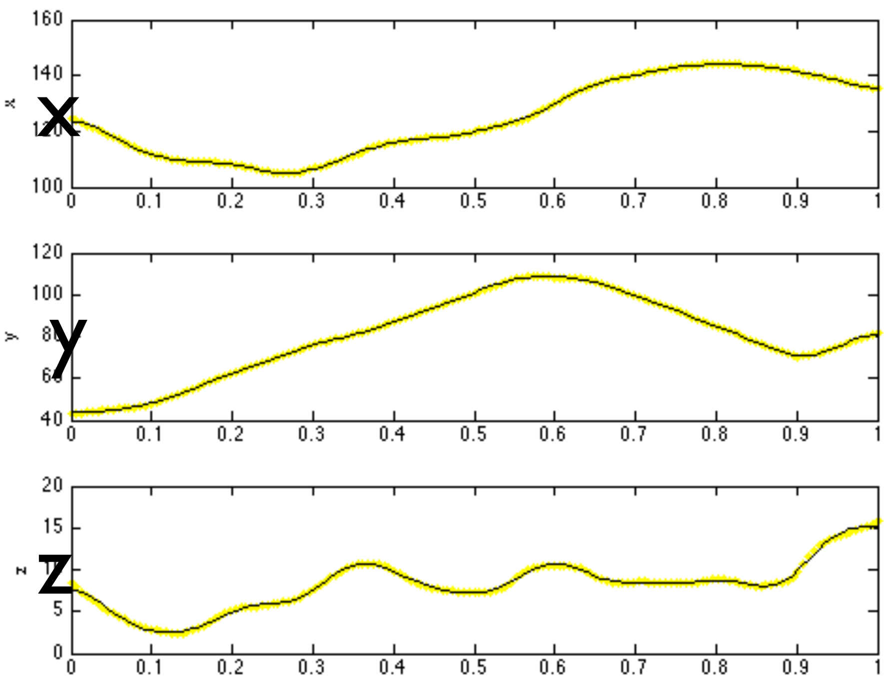


Make it only valid in [0,1]

White matter fiber tract model



parameterization



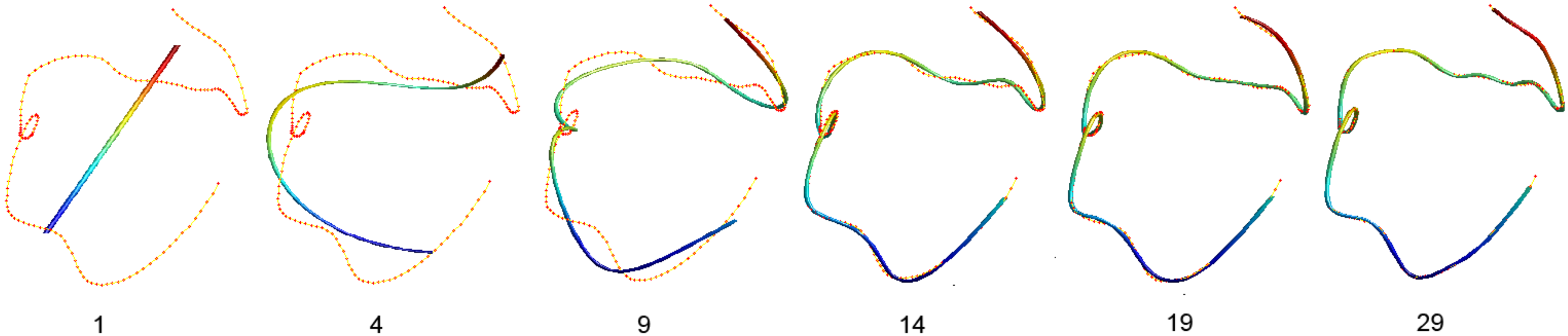
basis expansion

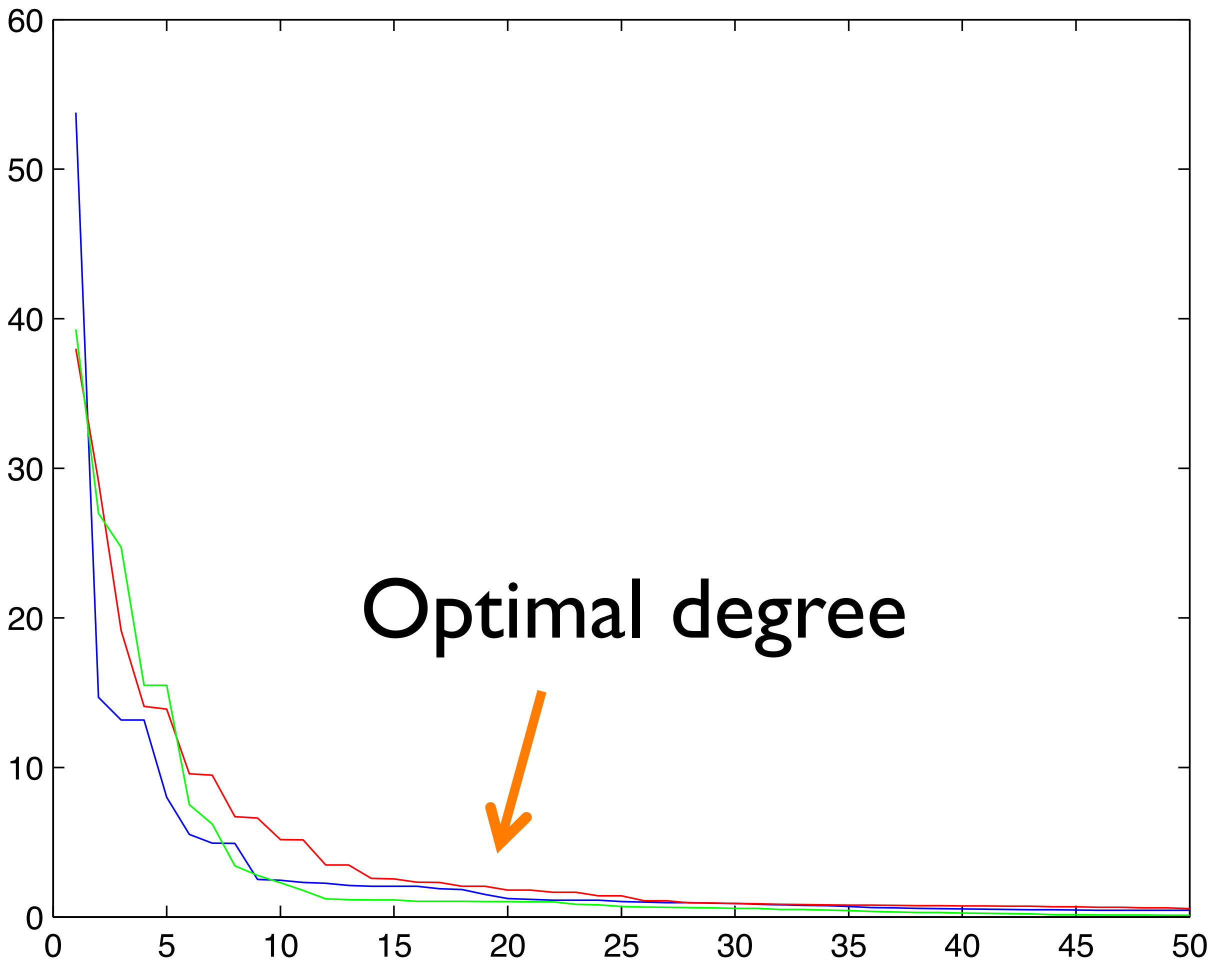
88.1799	56.6336	5.7367
-12.4775	-11.2552	-2.0791
2.4336	-15.4428	-0.4021
4.3956	2.2733	-0.9354
-0.0106	-0.0674	0.6999
2.1773	-2.4194	-0.1176
0.5808	0.8390	1.2942
0.0615	-0.1893	0.1188
-0.2629	0.7524	0.1089
0.7909	-0.7276	-0.1901
0.5458	0.6236	0.6939
0.4295	-0.4337	0.2185
0.2150	0.4157	0.0254
0.1584	-0.1973	0.0762
-0.1557	0.2466	-0.1086
0.0632	-0.0978	-0.0208
0.0389	-0.0143	-0.0284
-0.0014	-0.1193	0.1970
0.0004	0.0129	-0.0198
0.1342	0.0002	0.0260

Any tract can be compactly parameterized with only 60 coefficients.

$$(x, y, z)' = \sum_{l=0}^{19} \beta_l \cos(l\pi t)$$

Cosine series representation





Optimal degree chosen using the forward model selection method.

Least squares estimation

x, y, z coordinate at p_i $\longrightarrow$ $$f(p_i) = \sum_{j=0}^{k} \beta_j \psi_j(p_i)$$

$$\mathbf{f} = (f(p_1), \cdots, f(p_n))' \quad \beta = (\beta_0, \cdots, \beta_k)'$$

$$\mathbf{Y} = \begin{bmatrix} \psi_0(p_1) & \cdots & \psi_k(p_1) \\ \vdots & \ddots & \vdots \\ \psi_0(p_n) & \cdots & \psi_k(p_n) \end{bmatrix}$$

$$\mathbf{f} = \mathbf{Y}\beta \longrightarrow \beta = (\mathbf{Y}'\mathbf{Y})^{-1}\mathbf{Y}'\mathbf{f}$$

Discrepancy measure between two tracts

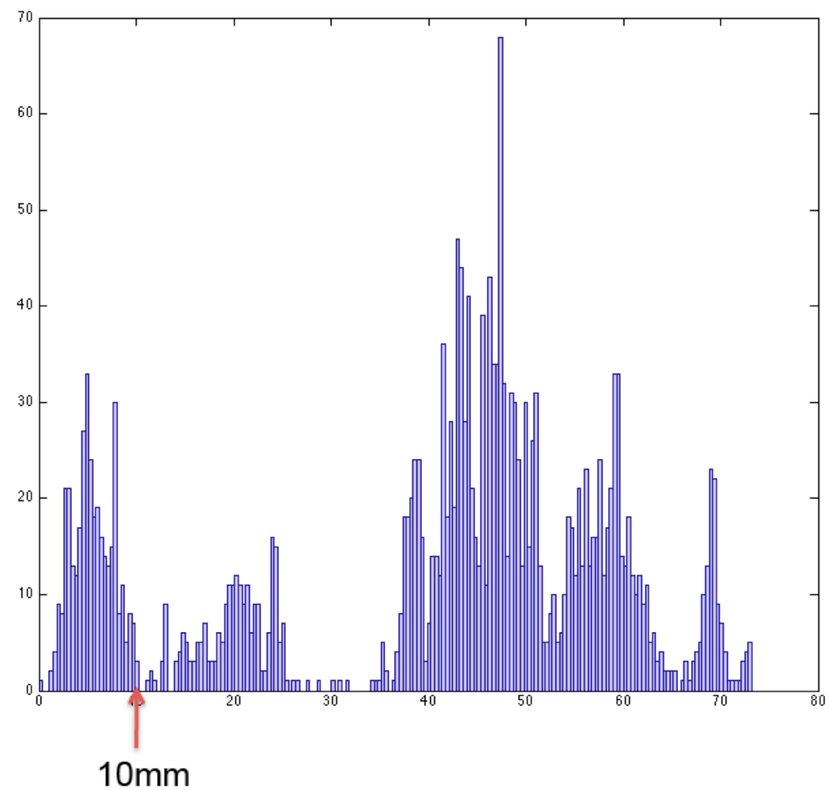
$$\boldsymbol{\zeta}(t) = \sum_{l=0}^{k} \boldsymbol{\zeta}_l \psi_l(t) \qquad \boldsymbol{\eta}(t) = \sum_{l=0}^{k} \boldsymbol{\eta}_l \psi_l(t)$$

$$\rho(\boldsymbol{\zeta}, \boldsymbol{\eta}) = \int_0^1 \|\boldsymbol{\zeta}(t) - \boldsymbol{\eta}(t)\|^2 \, dt$$

$$= \int_0^1 \sum_{j=1}^{3} \left[\sum_{l=0}^{k} (\zeta_{lj} - \eta_{lj}) \psi_l(t) \right]^2 dt$$

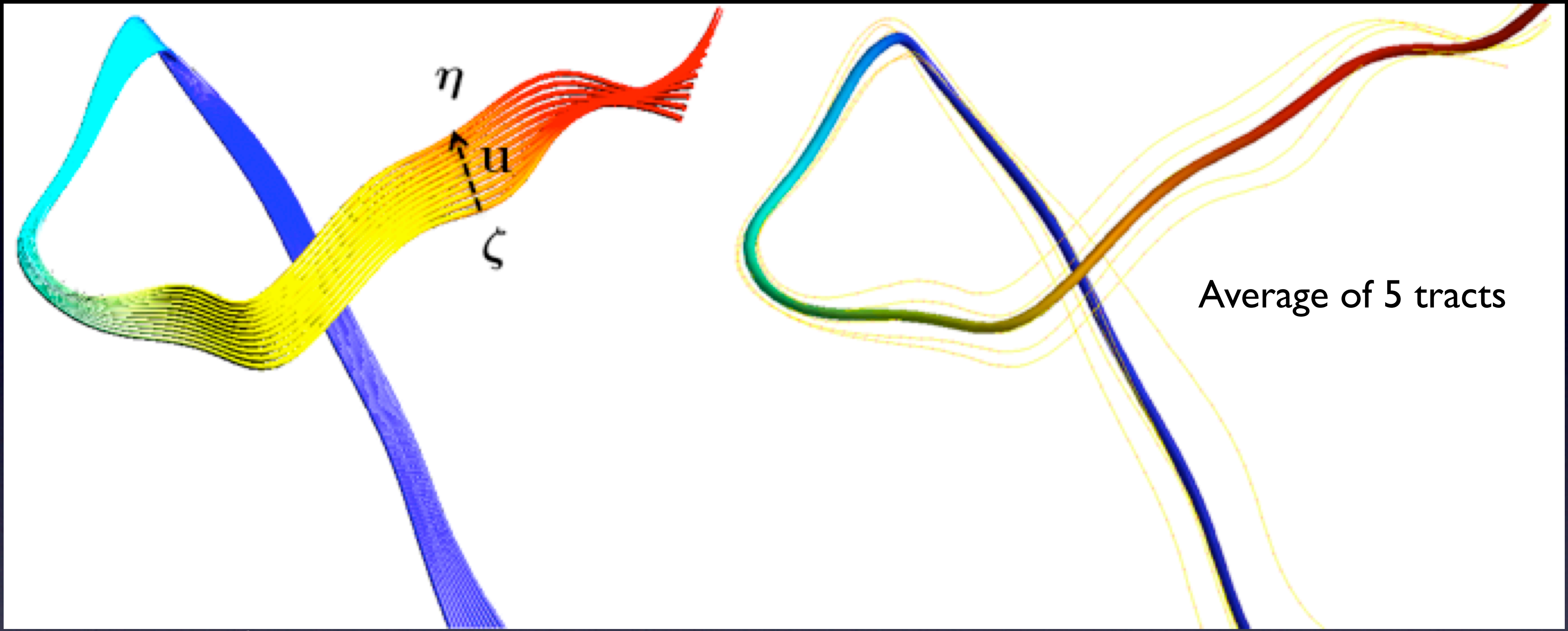
$$= \sum_{j=1}^{3} \sum_{l=0}^{k} (\zeta_{lj} - \eta_{lj})^2$$

The discrepancy measure can quantify the closeness of tract shapes



Histogram of discrepancy measure

Registering tracts



$$\zeta(t) = \sum_{l=0}^{k} \zeta_l \psi_l(t)$$

$$\eta(t) = \sum_{l=0}^{k} \eta_l \psi_l(t)$$

$\longrightarrow$

optimal displacement

$$\mathbf{u}^*(t) = \arg \min_{u_1, u_2, u_3} \rho(\boldsymbol{\zeta} + \mathbf{u}, \boldsymbol{\eta})$$

Minimum is taken over the subspace spanned by the basis functions.

optimal displacement based on our discrepancy measure

$$\mathbf{u}^*(t) = \arg \min_{u_1, u_2, u_3} \rho(\boldsymbol{\zeta} + \mathbf{u}, \boldsymbol{\eta})$$

$$= \sum_{l=0}^{k} (\boldsymbol{\eta}_l - \boldsymbol{\zeta}_l) \psi_l(t)$$

In a Hilbert space, Fourier series achieve optimality with respect to L2 norm.

Defining average tract

Given m representations $\zeta^1, \ldots, \zeta^m$

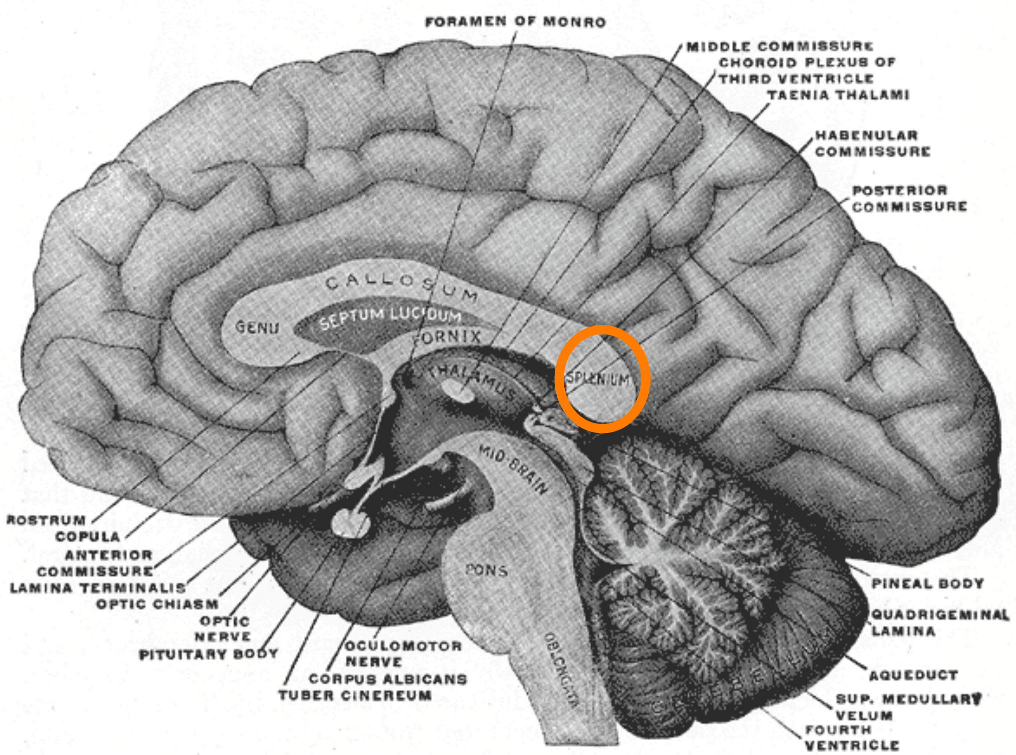
we define the average tract as

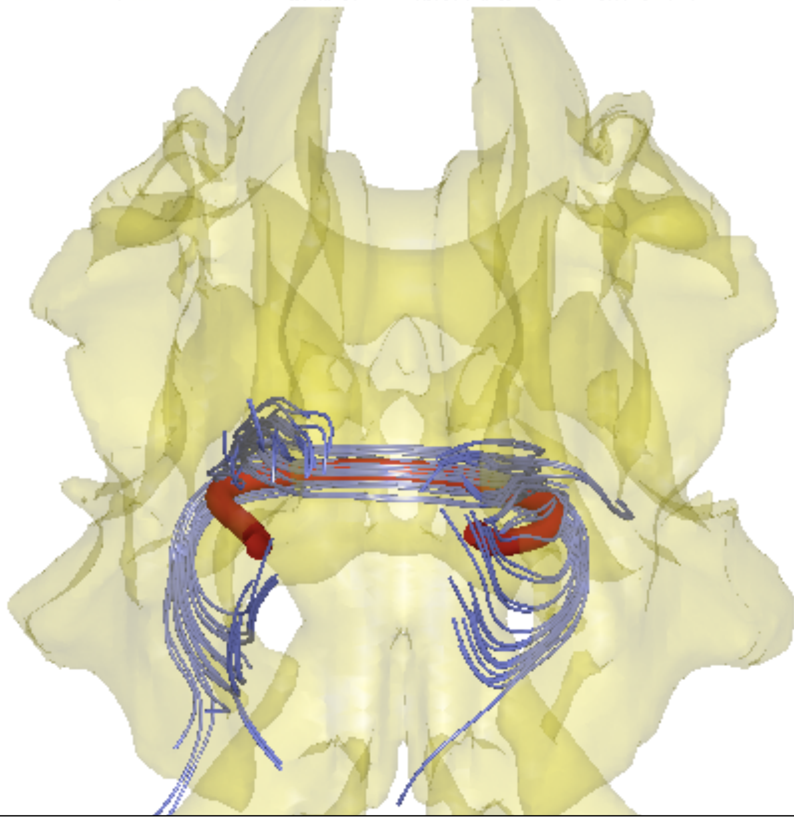
$$\overline{\zeta}(t) = \arg\min_{\zeta} \sum_{j=1}^{m} \rho(\zeta^j, \zeta)$$

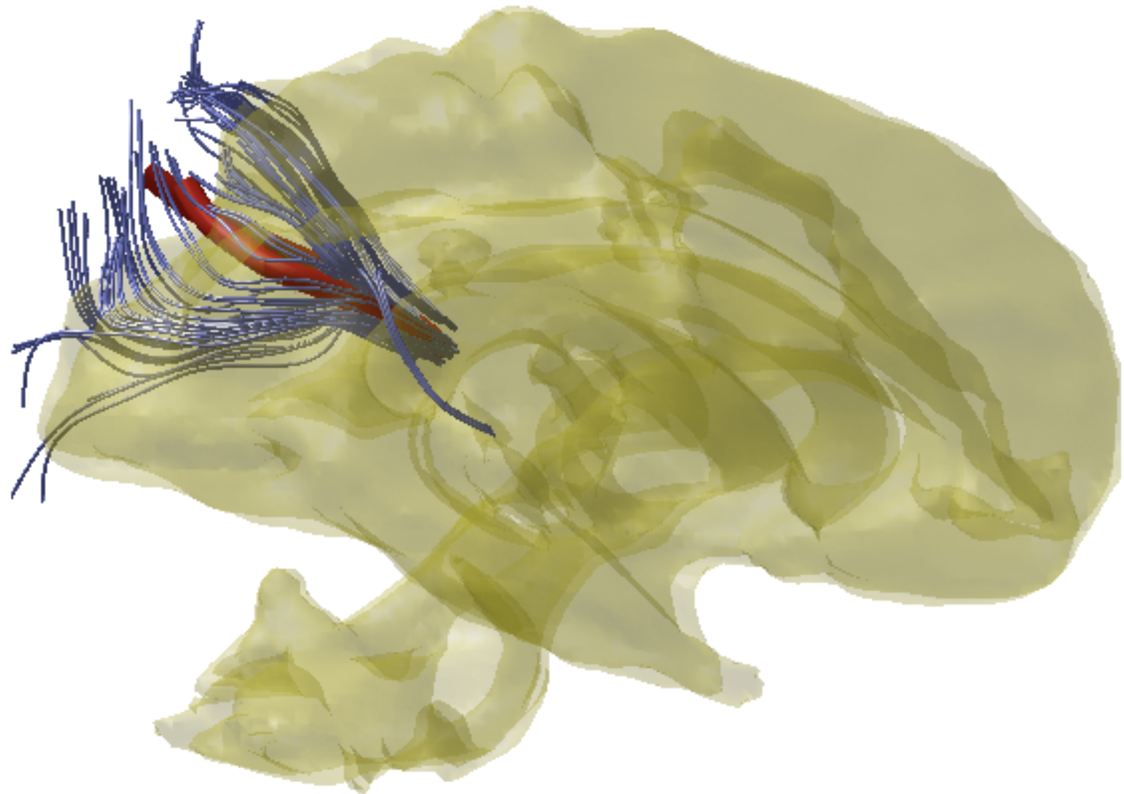
$$= \sum_{l=0}^{k} \overline{\zeta}_l \psi_l(t)$$

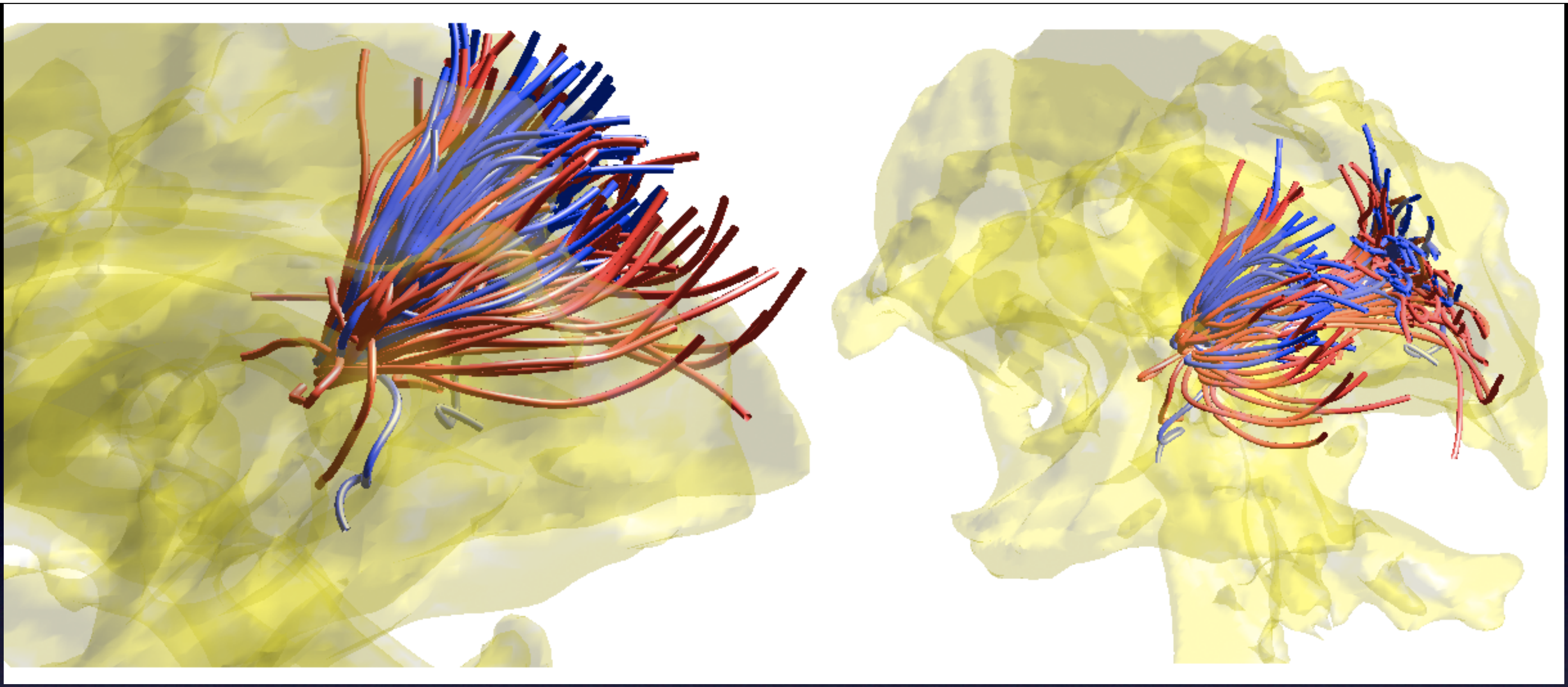
The average tract is simply given by averaging coefficients.

Tracts passing through the splenium of the corpus callosum



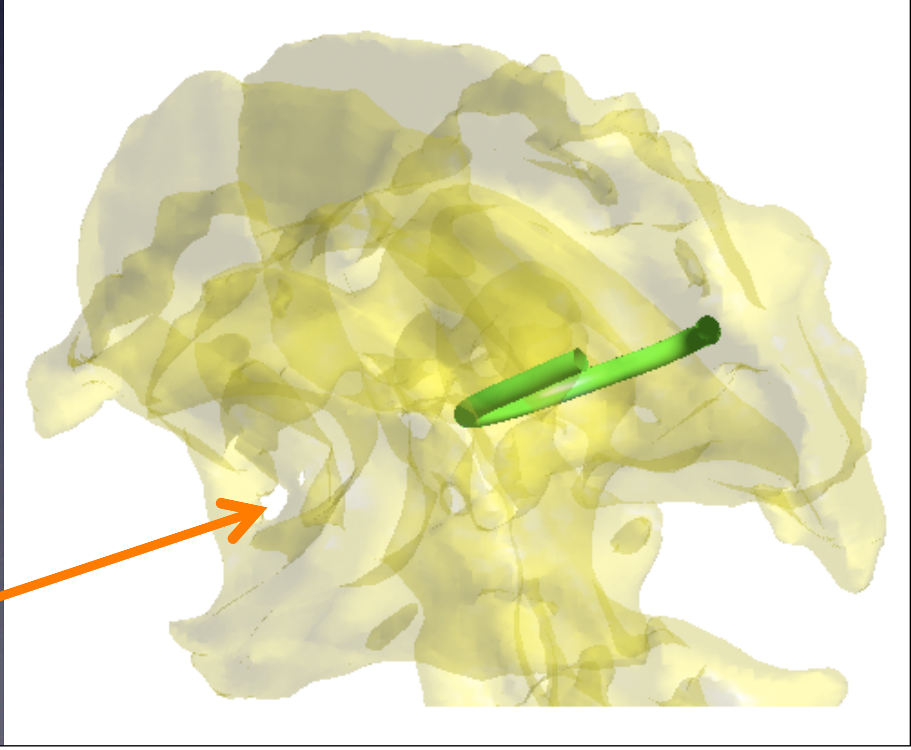




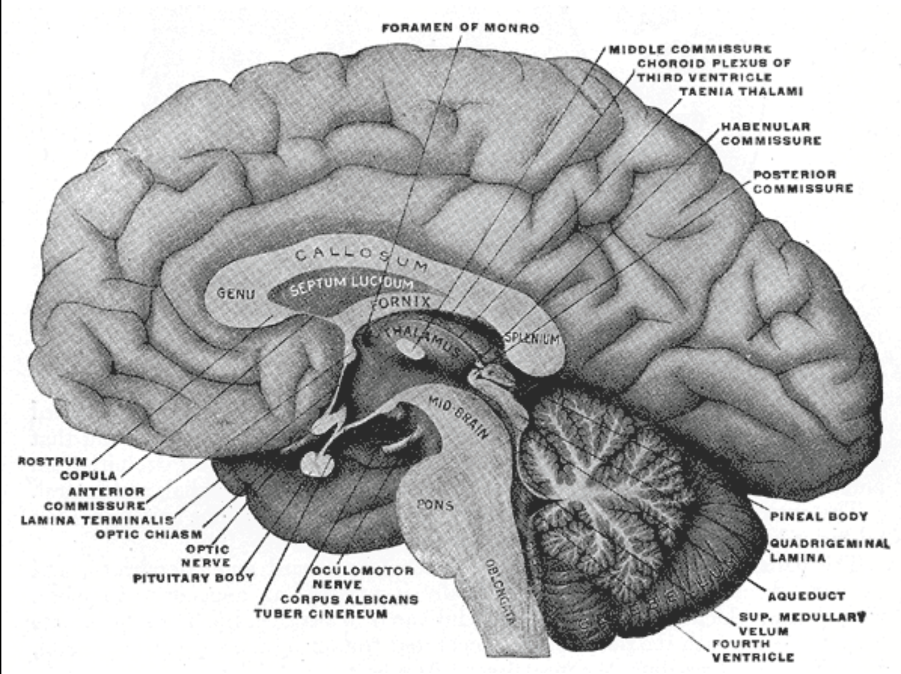


Average tracts across 74 subjects
(42 autistic 32 control)

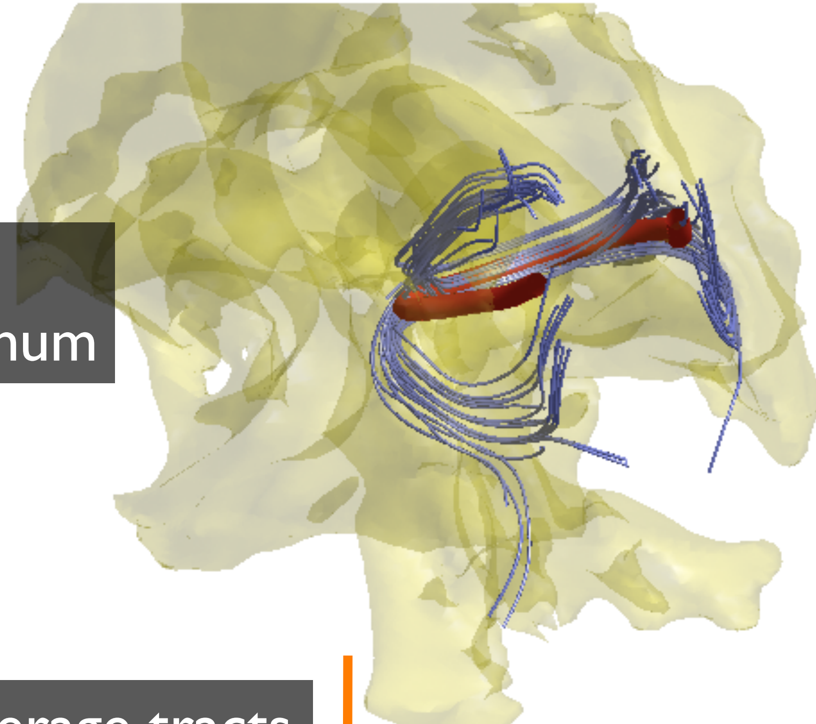
Average of average



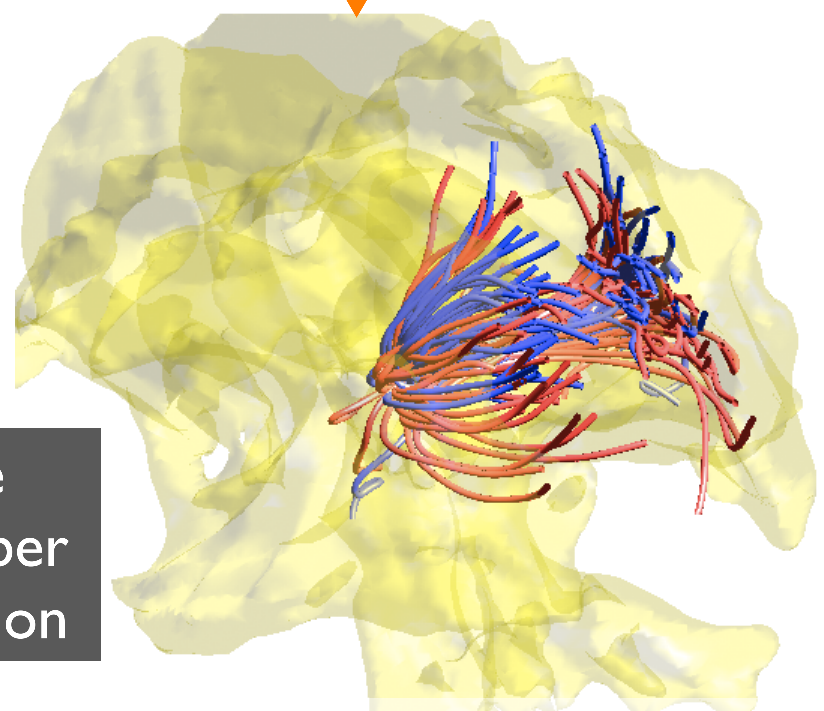
Fiber concentration analysis



tracts passing through spleninum

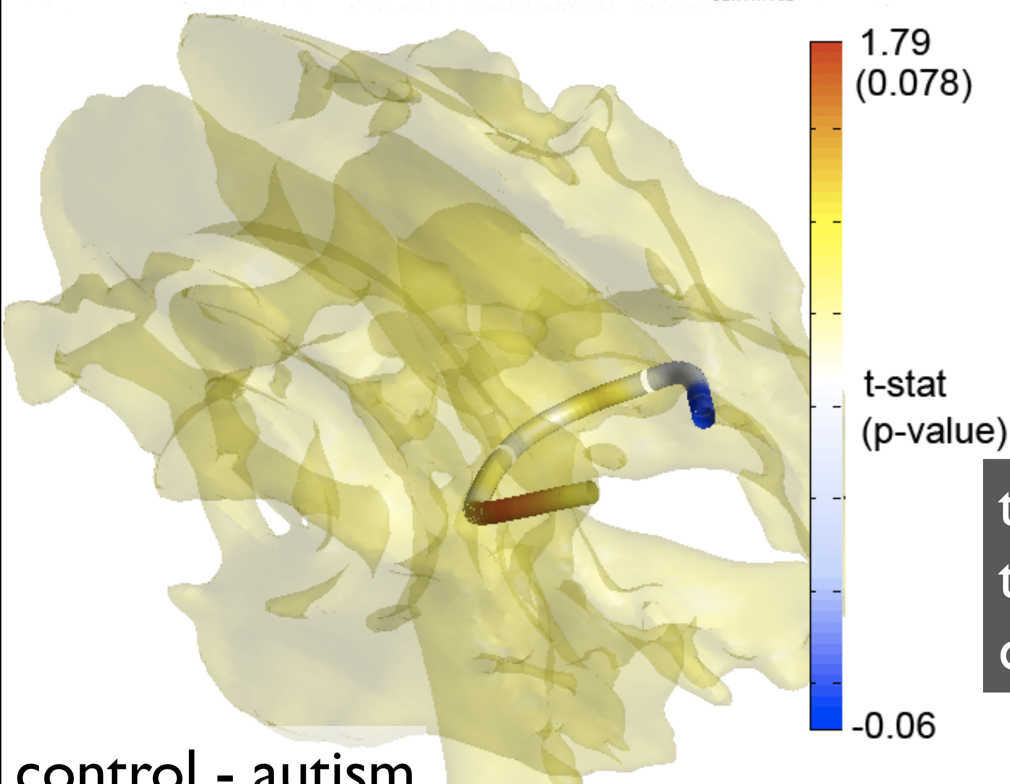


Average tracts



42 autistic & 32 control

two sample t-test on fiber concentration



control - autism

Inference on representation

Compare tract shapes between the groups

$$\boldsymbol{\zeta}^1, \cdots, \boldsymbol{\zeta}^m \longleftrightarrow \boldsymbol{\eta}^1, \cdots, \boldsymbol{\eta}^n$$

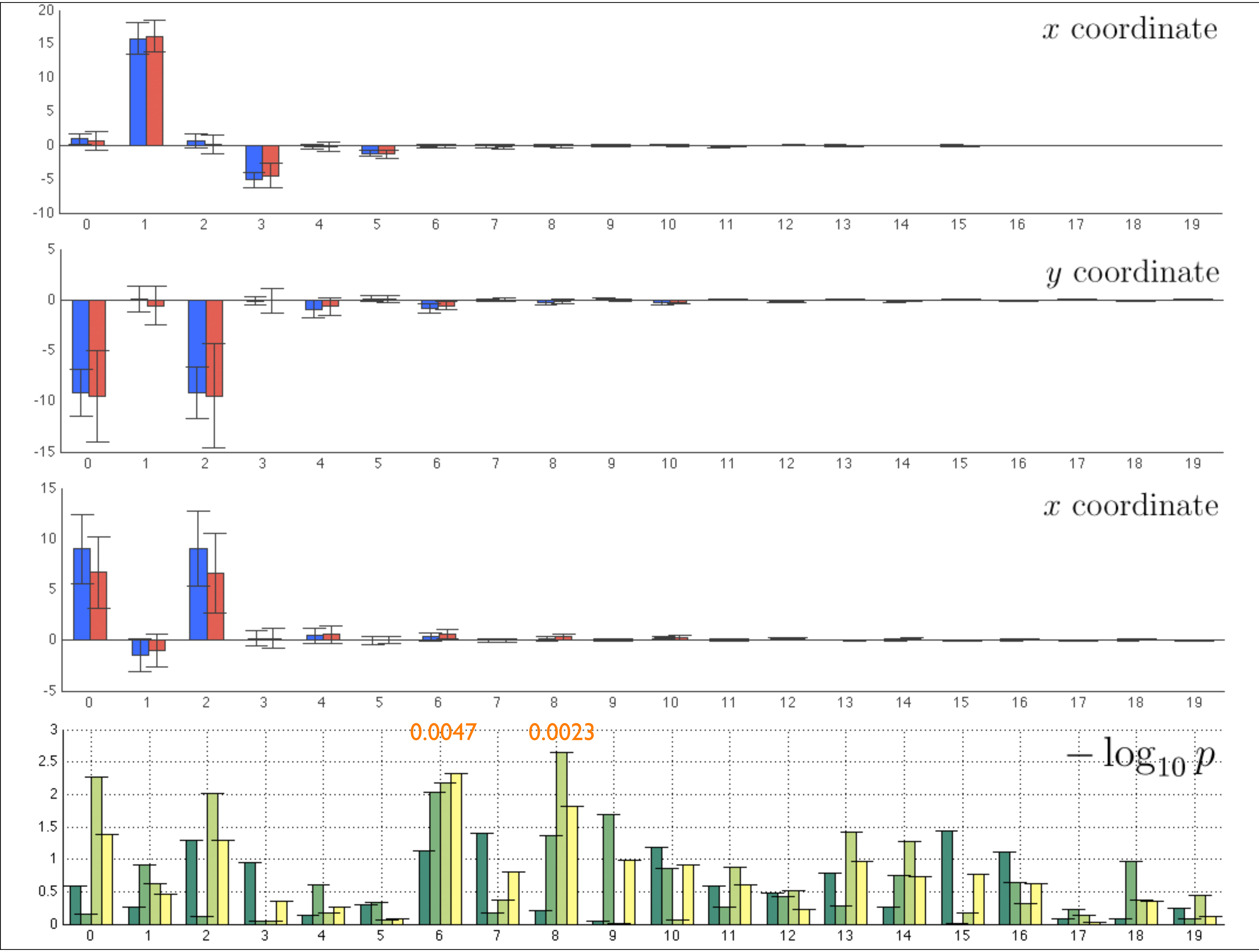
This is done by testing the equality of mean tracts between the groups

$$H_0 : \overline{\boldsymbol{\zeta}} = \overline{\boldsymbol{\eta}}$$

Equivalent hypothesis

$$H_0' : \overline{\boldsymbol{\zeta}}_1 = \overline{\boldsymbol{\eta}}_1, \cdots, \overline{\boldsymbol{\zeta}}_k = \overline{\boldsymbol{\eta}}_k$$

Two cosine representations are equivalent if and only if the coefficients match



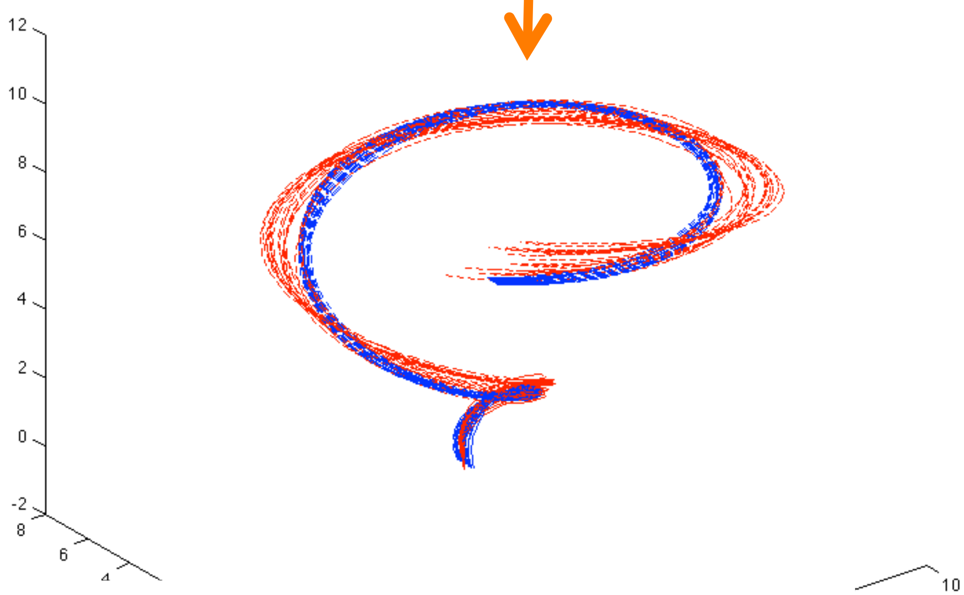
x coordinate
y coordinate
x coordinate
$-\log_{10} p$
0.0047
0.0023

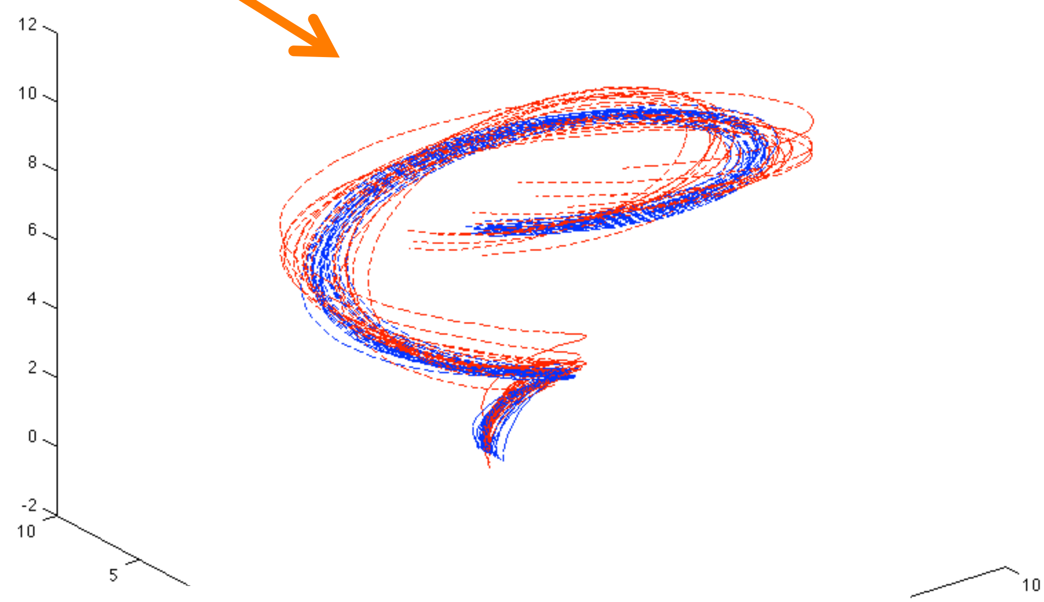
Validation via Random curve simulation

Basic model

$$(x, y, z) = (s \sin s, s \cos s, s), \;\; s \in [0, 10]$$

Add noise to the basic model

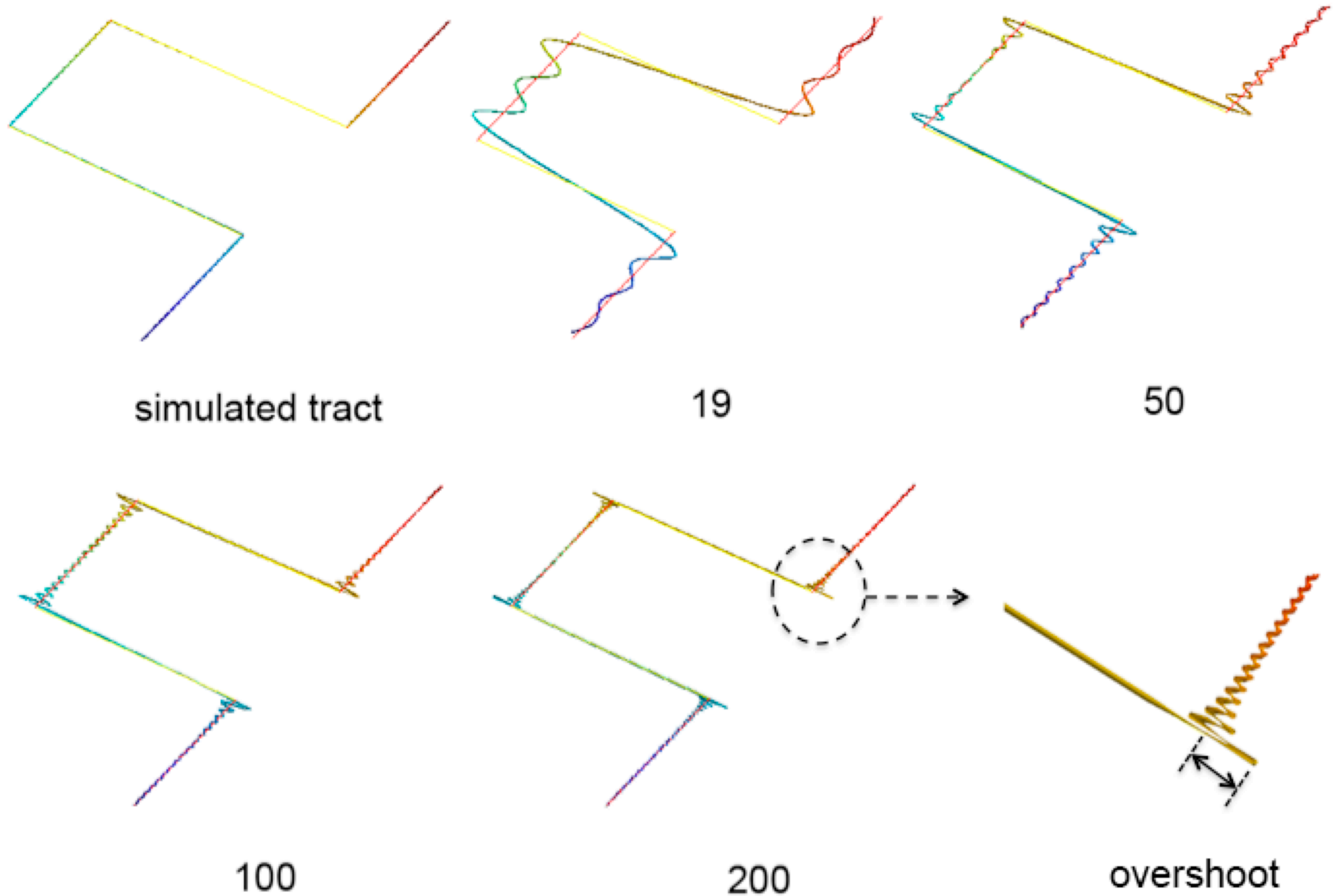




Bonferroni corrected pvalue 0.00005

Bonferroni corrected pvalue 0.294

Discussion: Gibbs phenomenon



Diffusion smoothing

The Canadian Journal of Statistics
Vol. 28, No. 2, 2000, Pages 225–240
La revue canadienne de statistique

Differential equation models for statistical functions[1]

James O. RAMSAY

Wealth concentration in Montreal area

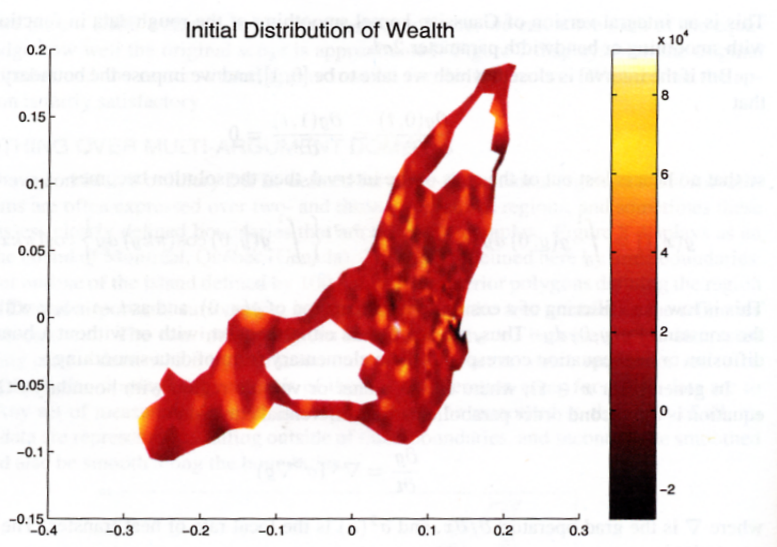


FIGURE 10: The distribution of wealth on the Island of Montréal. This defines the initial state $g(x, 0)$ of the system described by partial differential equation (15) and boundary condition (16).

Solve diffusion equation →

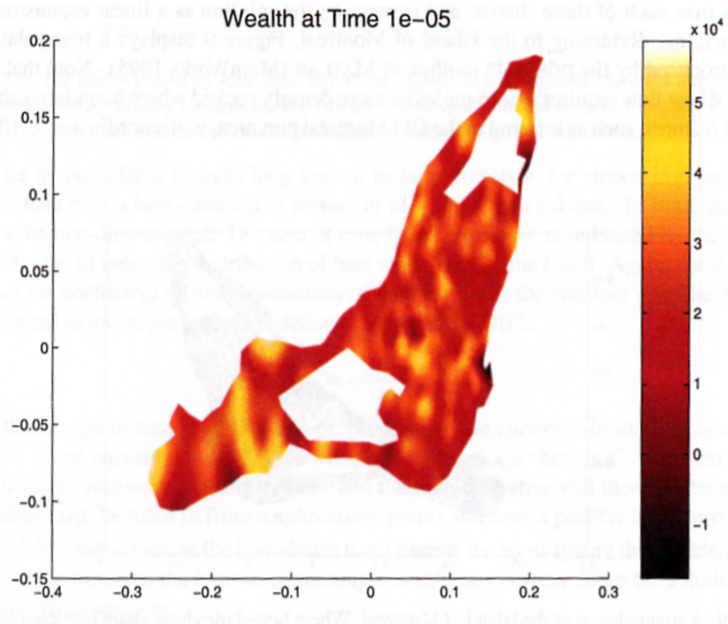


FIGURE 11: The distribution of wealth at time 0.00001.

How to fix Gibbs phenomenon in Fourier expansion?

Weighted Fourier Analysis, Weighted Spherical harmonic representation: Chung et al., IEEE Trans. Medical Imaging. 2007, 2008
23 citations so far

Exponentially weight the cosine series representation and make the representation converges faster

$$\zeta(t) = \sum_{l=0}^{k} \zeta_l \psi_l(t)$$

add expontional weight

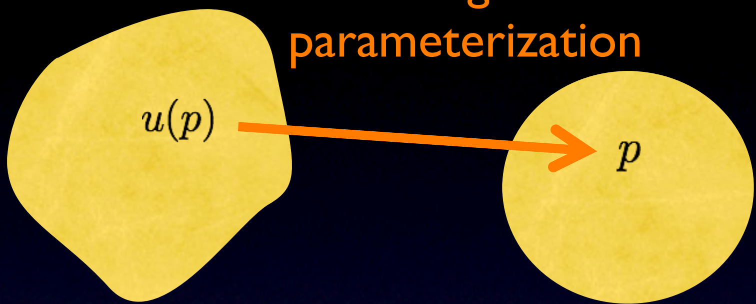
diffusion:

$$e^{-\lambda_l \sigma}$$

$$\frac{\partial}{\partial \sigma} g = \Delta g, \; g(t, \sigma = 0) = \zeta(t)$$

Weighted Fourier Analysis

Flattening parameterization



manifold $\mathcal{M}$ parameter space $\mathcal{N}$

tracts, amygdala, hippocampus, cortical surface

Self-adjoint operator:

$$\langle \mathcal{L}g_1, g_2 \rangle = \langle g_1, \mathcal{L}g_2 \rangle$$

$$\mathcal{L}\psi_j = \lambda_j \psi_j$$

Input signal

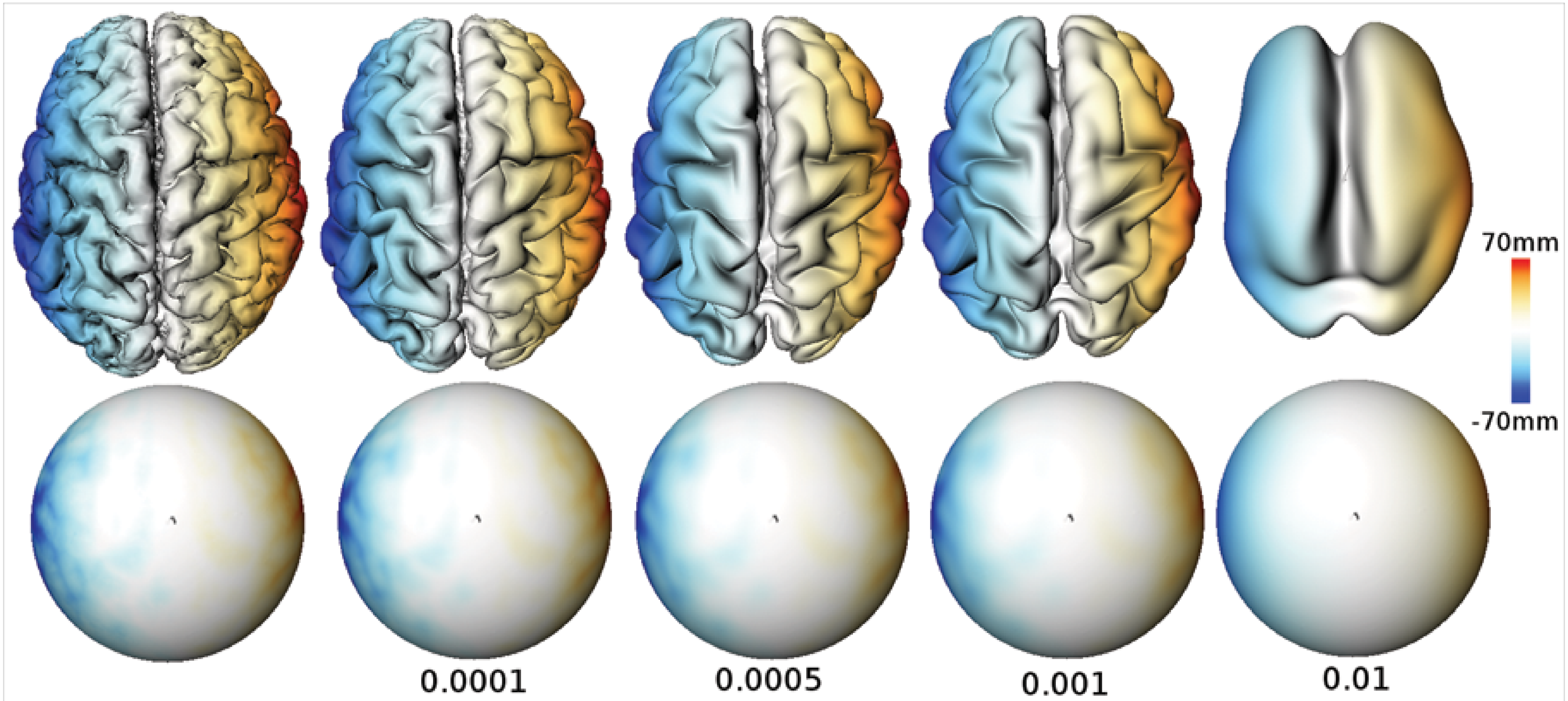
PDE: $\partial_t g + \mathcal{L}g = 0, g(p, t = 0) = f(p)$

Weighted Fourier series: $$g(p,t) = \sum_{j=0}^{\infty} e^{-\lambda_j t} \langle f, \psi_j \rangle \psi_j(p)$$

Kernel smoothing: $$= \int_{\mathcal{N}} K_t(p,q) f(q) \, d\mu(q)$$

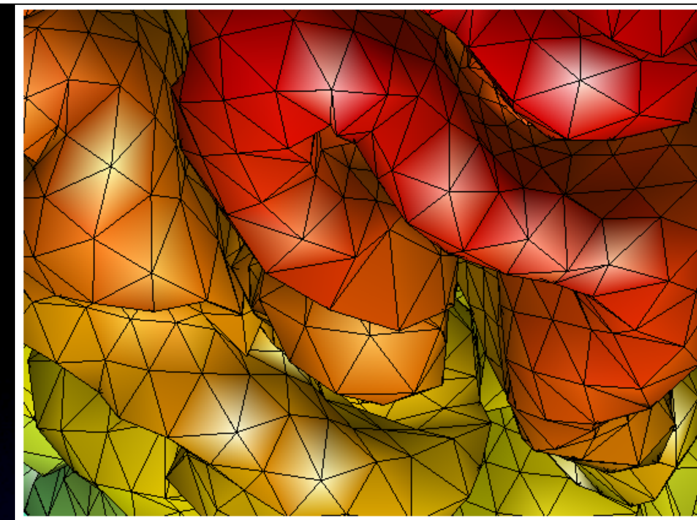
WFS representation for cortical shape

Color scale: X-coordinate value



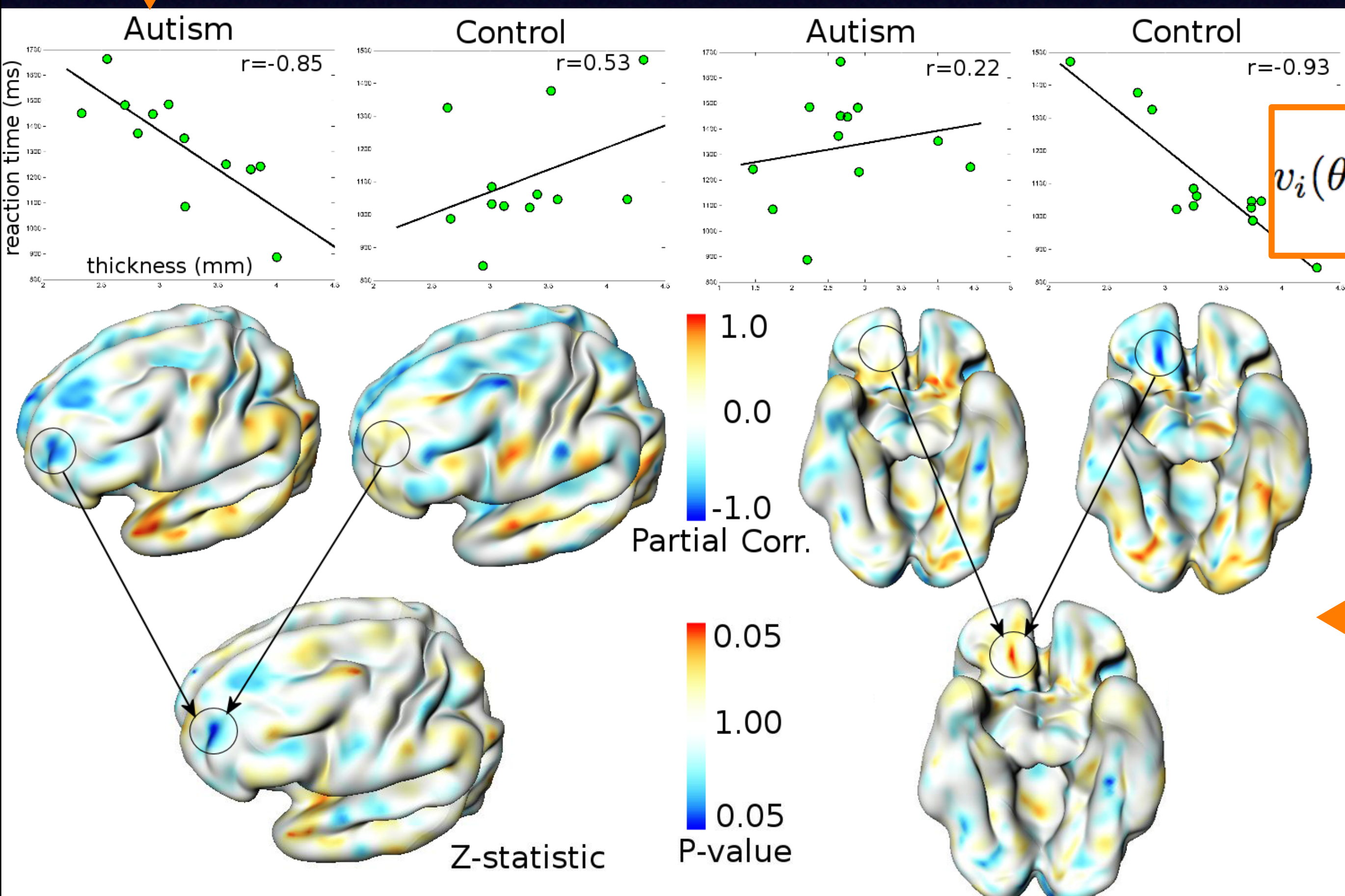
bandwidth

Brain & behavior correlation



Partial correlation of thickness & gaze duration

Weighted Fourier representation



$$v_i(\theta,\varphi) = \sum_{l=0}^{k} \sum_{m=-l}^{l} e^{-l(l+1)\sigma} f_{lm}^{i} Y_{lm}(\theta,\varphi)$$

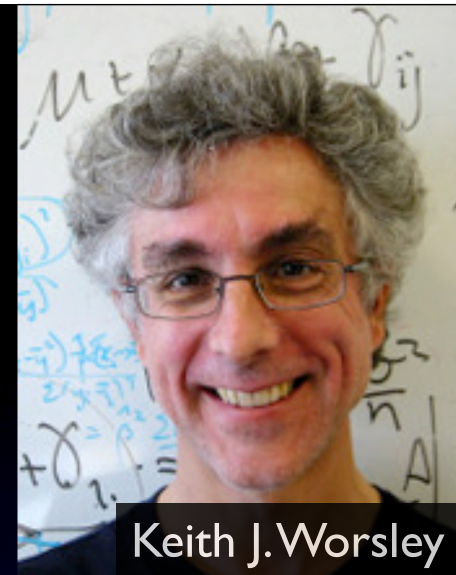
88.1799	56.6336	5.7367
-12.4775	-11.2552	-2.0791
2.4336	-15.4428	-0.4021
4.3956	2.2733	-0.9354
-0.0106	-0.0674	0.6999
2.1773	-2.4194	-0.1176
0.5808	0.8390	1.2942
0.0615	-0.1893	0.1188
-0.2629	0.7524	0.1089
0.7909	-0.7276	-0.1901
0.5458	0.6236	0.6939

....

Persistence homology based image analysis

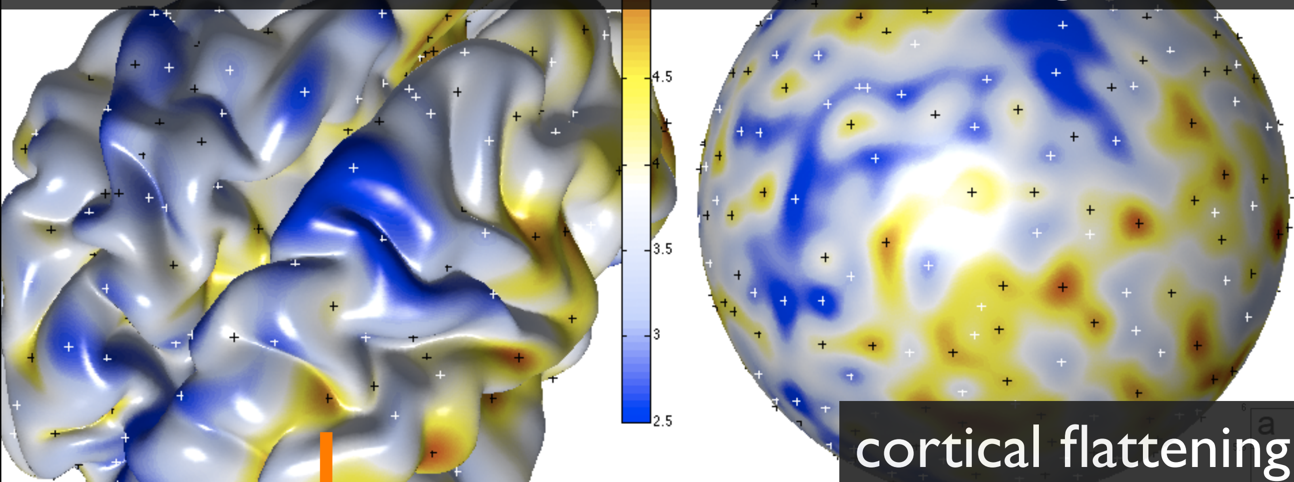
joint work with Peter Kim: IPMI 2009, MICCAI 2009

related to Euler characteristic, Betti numbers,
Morse functions, Worsley's random field theory

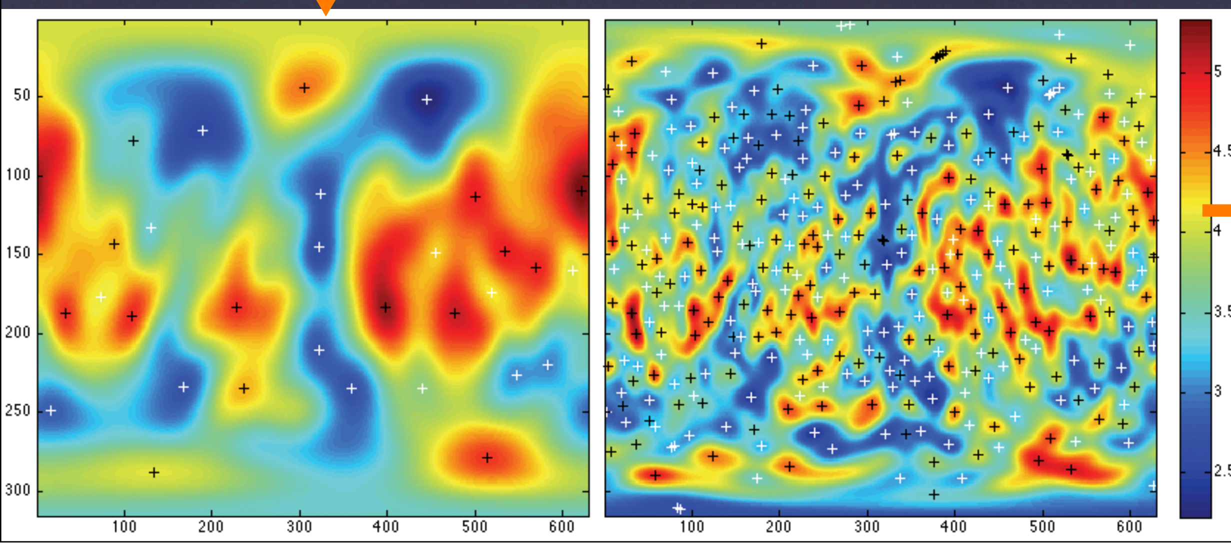


Keith J. Worsley

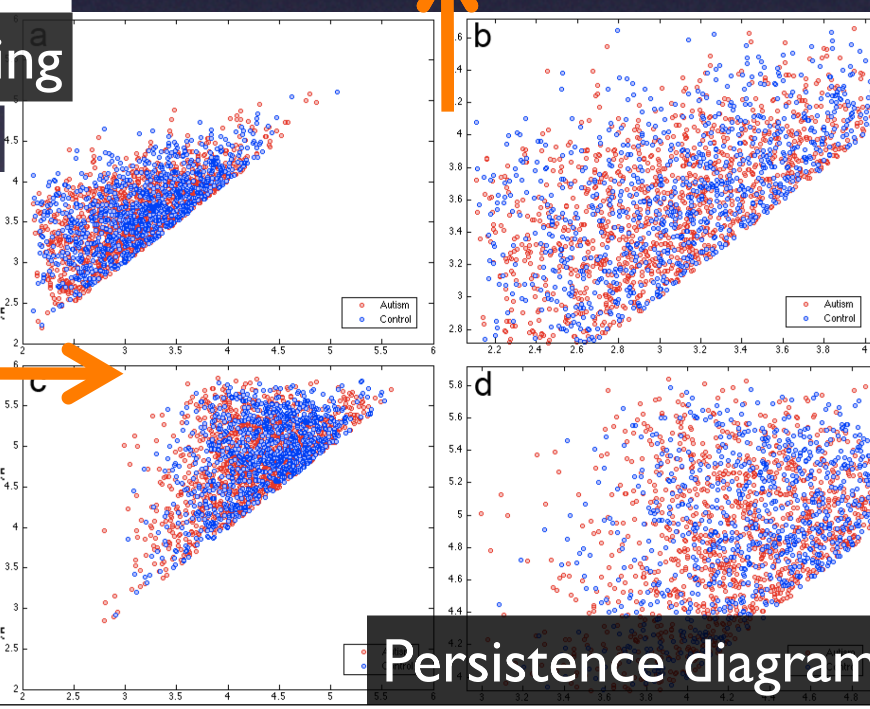
cortical thickness smoothed with the weighted Fourier method



cortical flattening

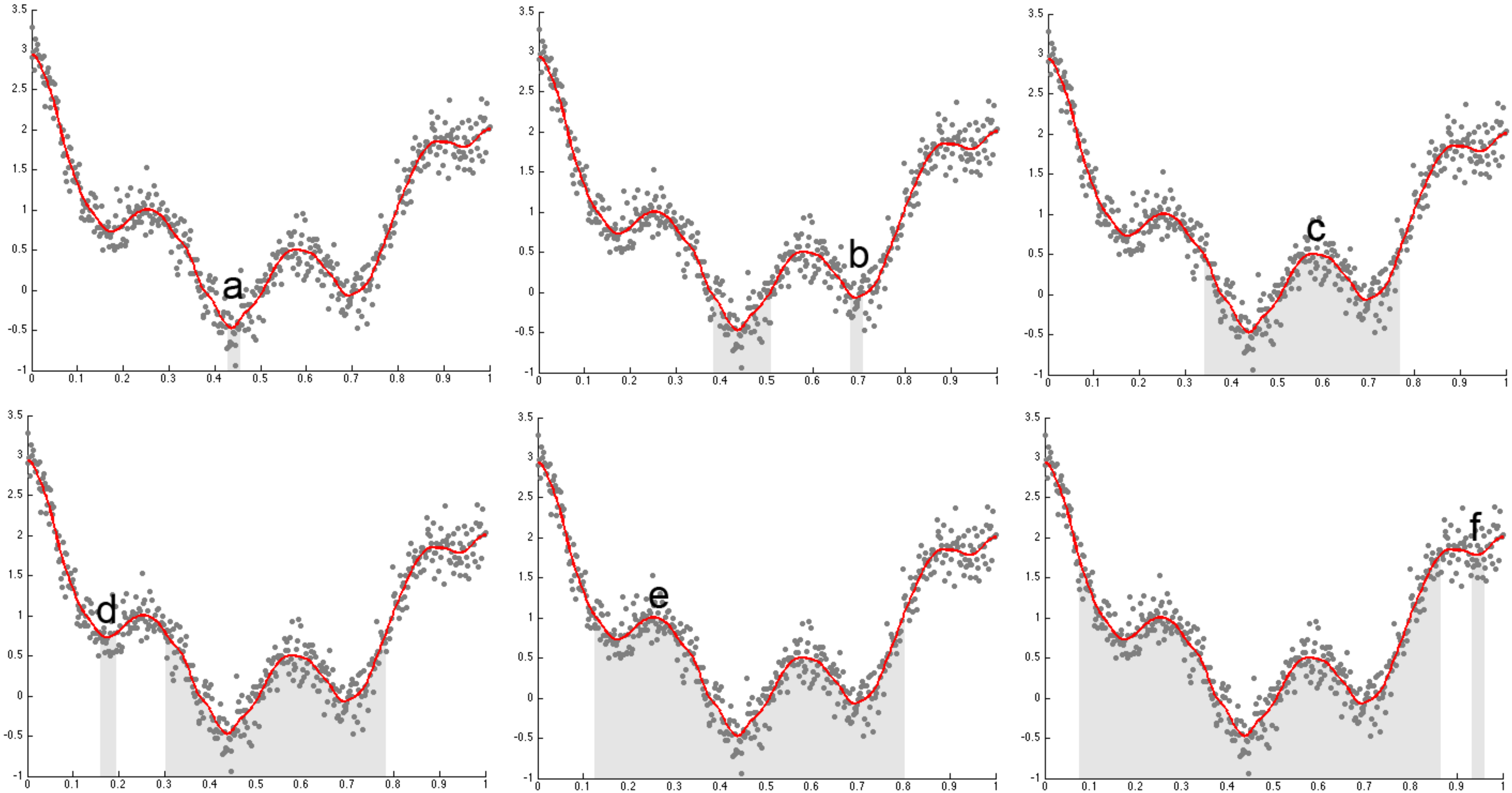


Topological classification 96%
Previous method 90%



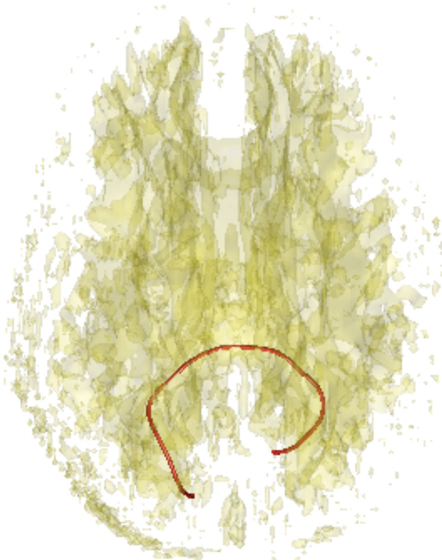
Persistence diagram

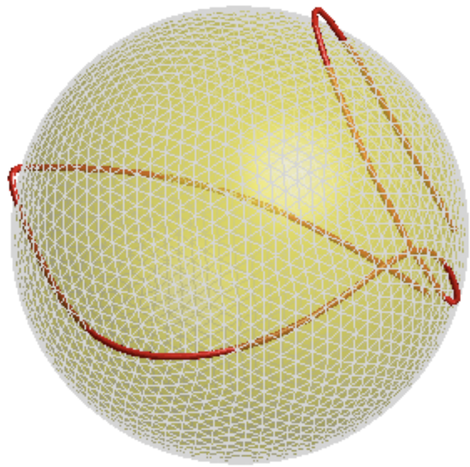
Persistence on weighted Fourier represent of 1D signal



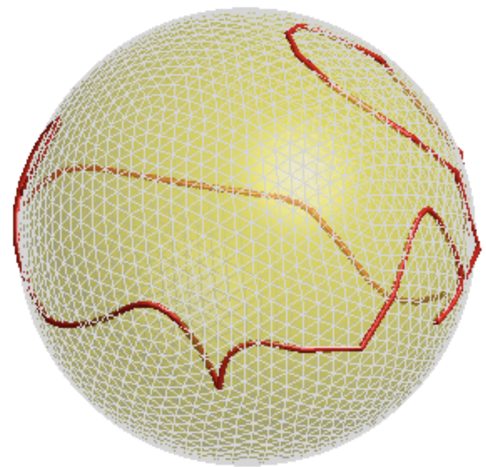
IPMI 2009

Discussion: spherical embedding of cosine series representation

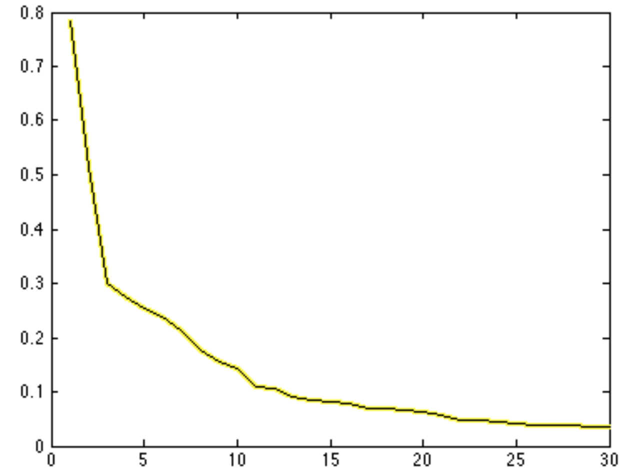




10



30



average reconstruction error

How to make cosine series representation invariant under translation, rotation and scaling?

$$P : v_i \rightarrow w_i = \frac{v_i}{\|v_i\|}$$

spherical projection

$$\zeta_o(t_j) = \sum_{l=0}^{k} c_{lo}\psi_l(t_j)$$

cosine series representation

I just can't transform this into standard quadratic optimization problem!

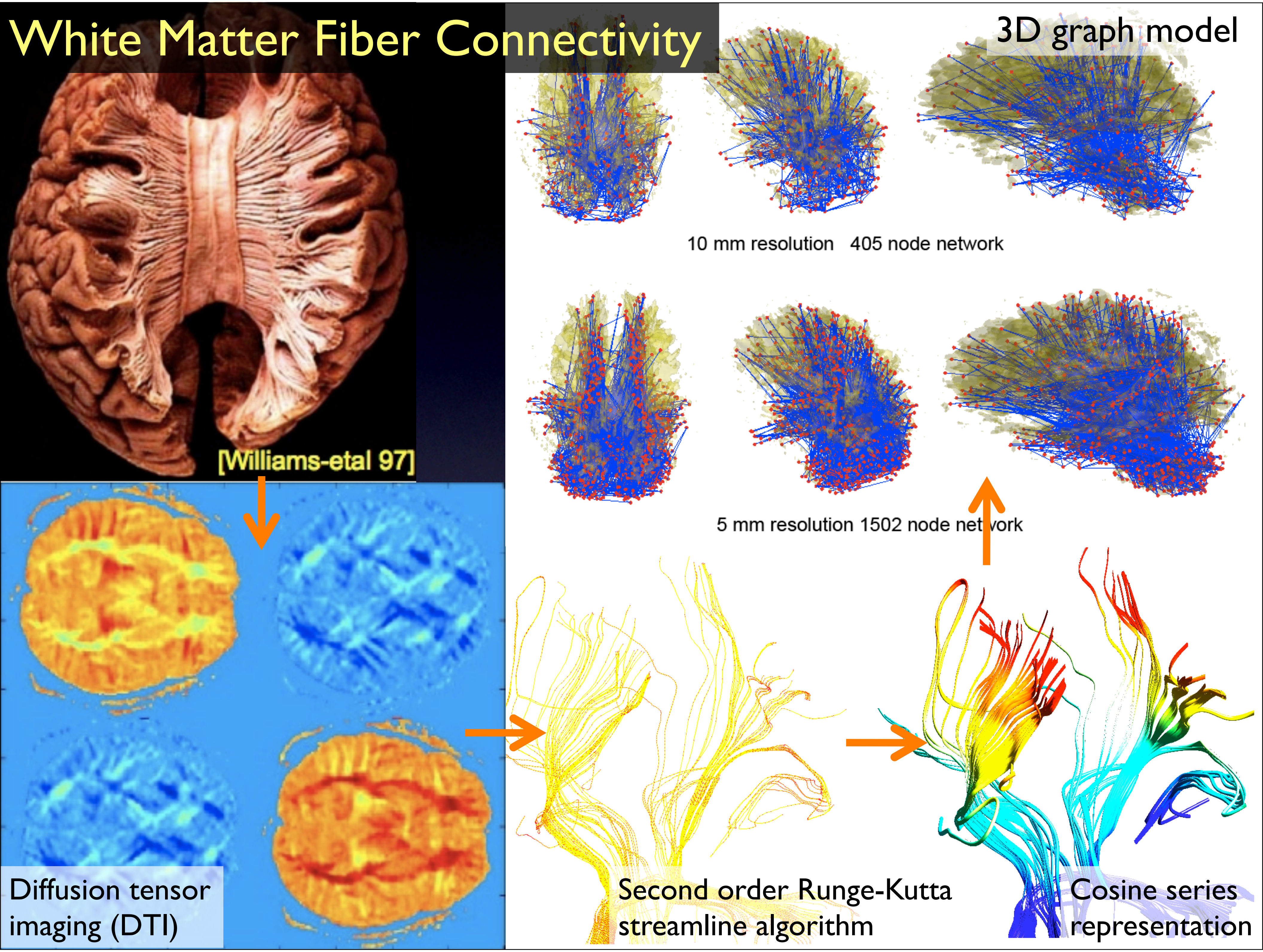
$$\sum_{o=1}^{3}\left[\sum_{l=0}^{k} c_{lo}\psi_l(t_j)\right]^2 = 1$$

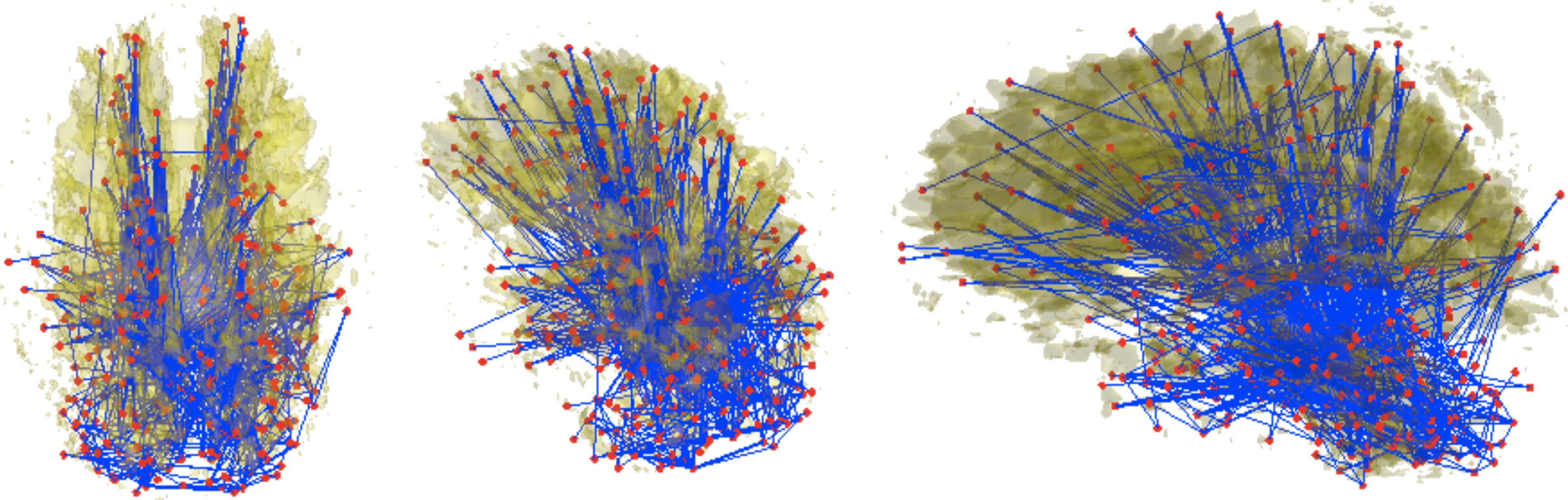
quadratic constraint

Limitation of tract shape analysis

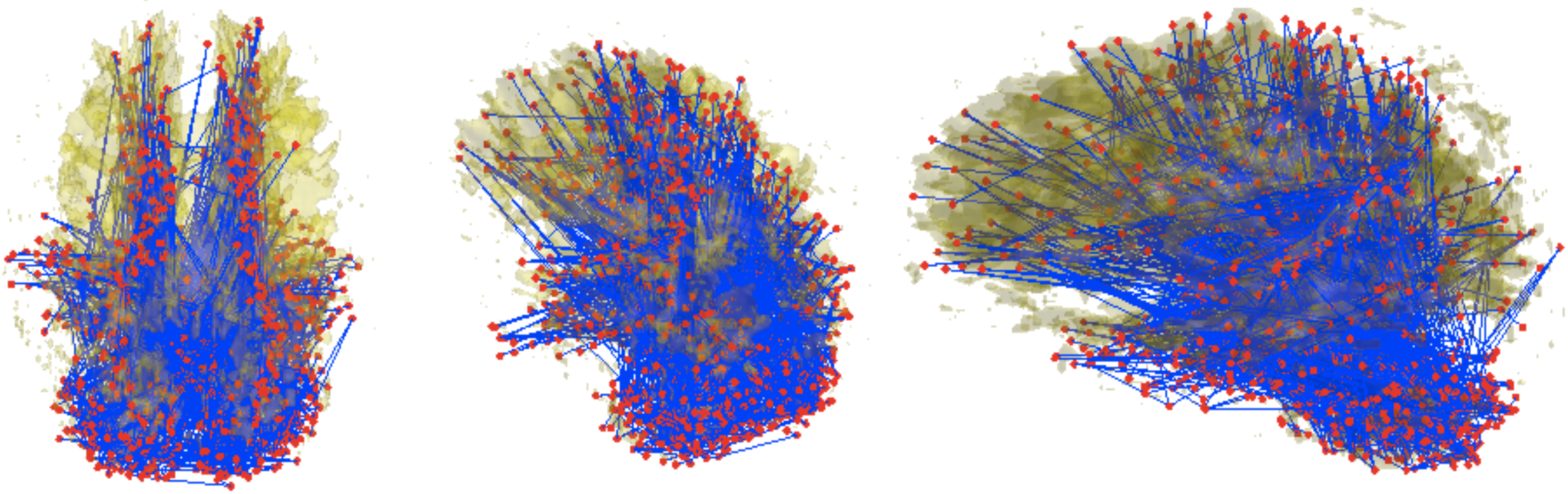
Difficult to do shape-to-shape correlation analysis

Can’t do brain connectivity analysis


White Matter Fiber Connectivity
3D graph model
10 mm resolution 405 node network
5 mm resolution 1502 node network
[Williams-etal 97]
Diffusion tensor imaging (DTI)
Second order Runge-Kutta streamline algorithm
Cosine series representation



10 mm resolution 405 node network

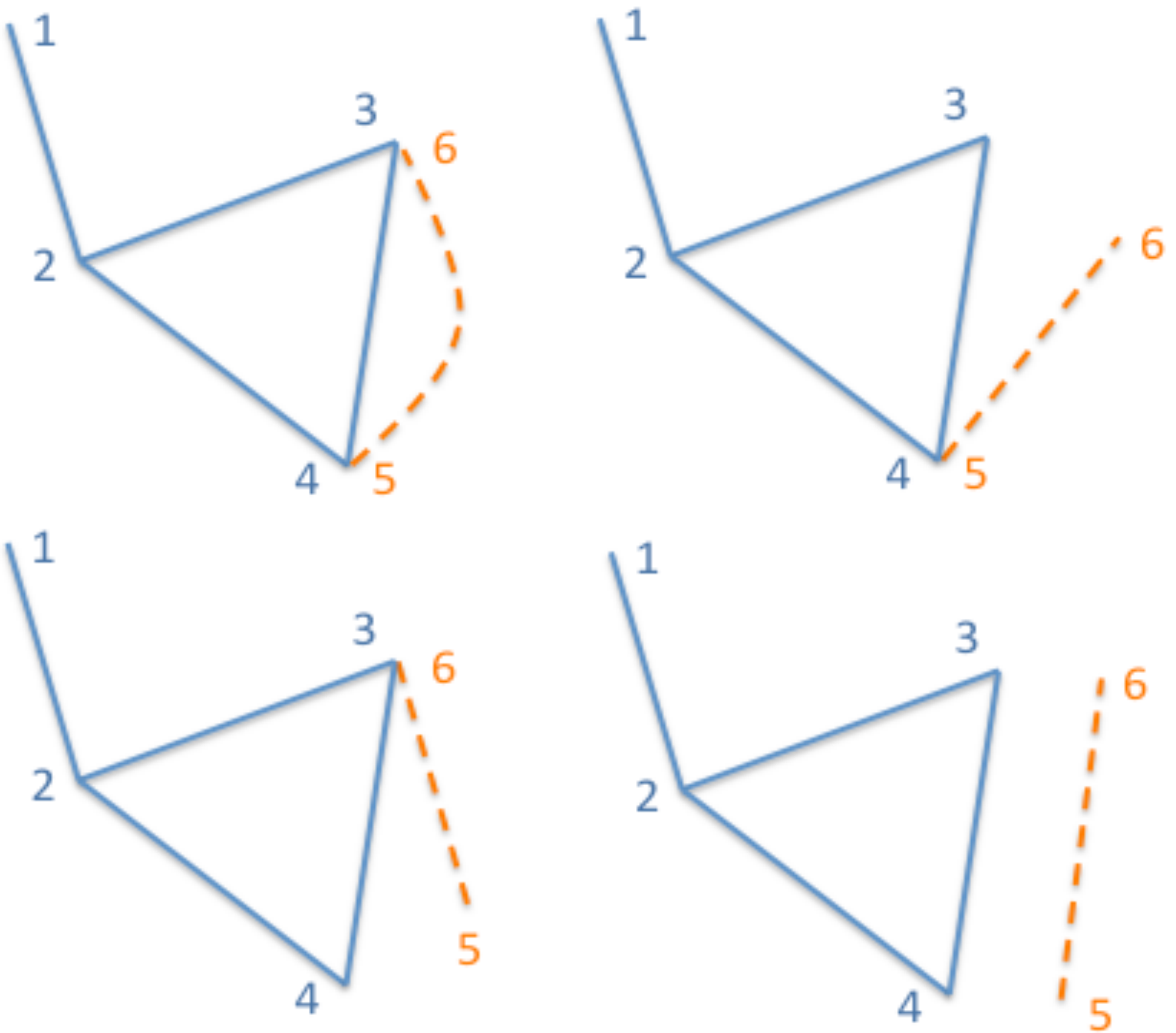


5 mm resolution 1502 node network

How did I generate the 3D network graphs ?

Building DTI-based brain network graph

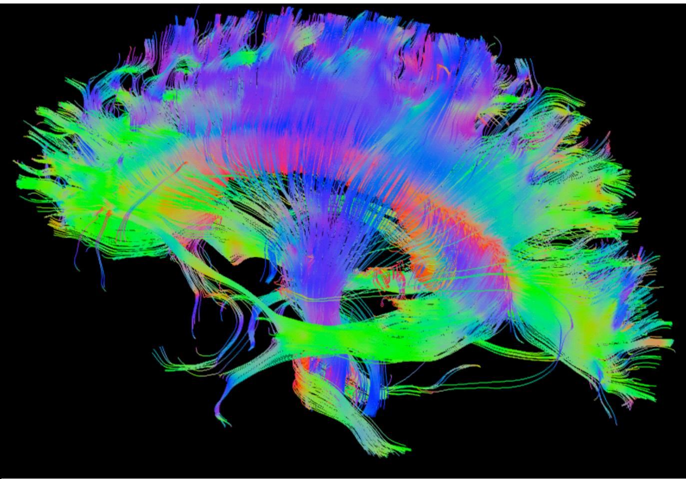
iteratively add one tract at a time



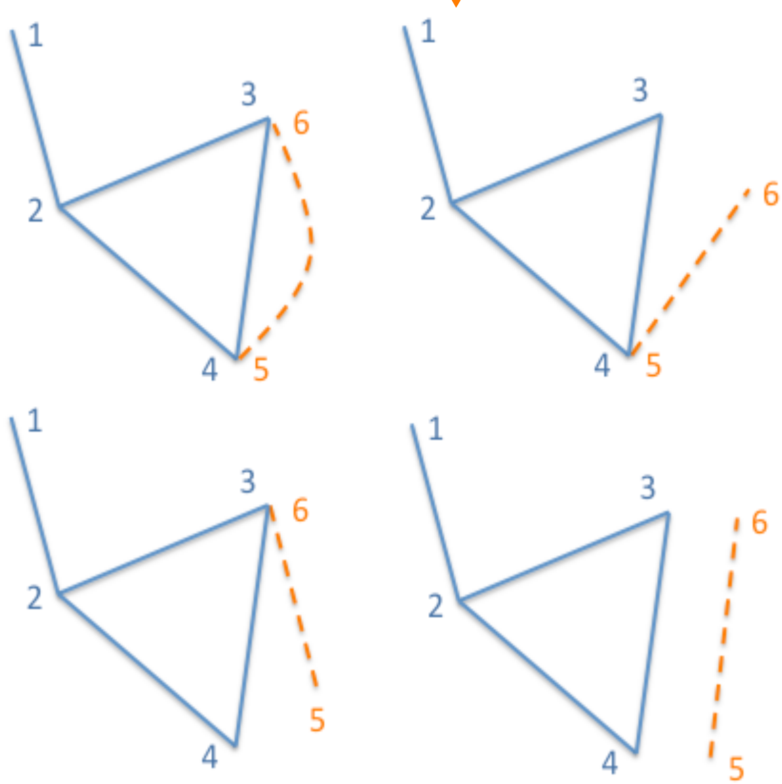
Blue: graph consisting of 4 tracts

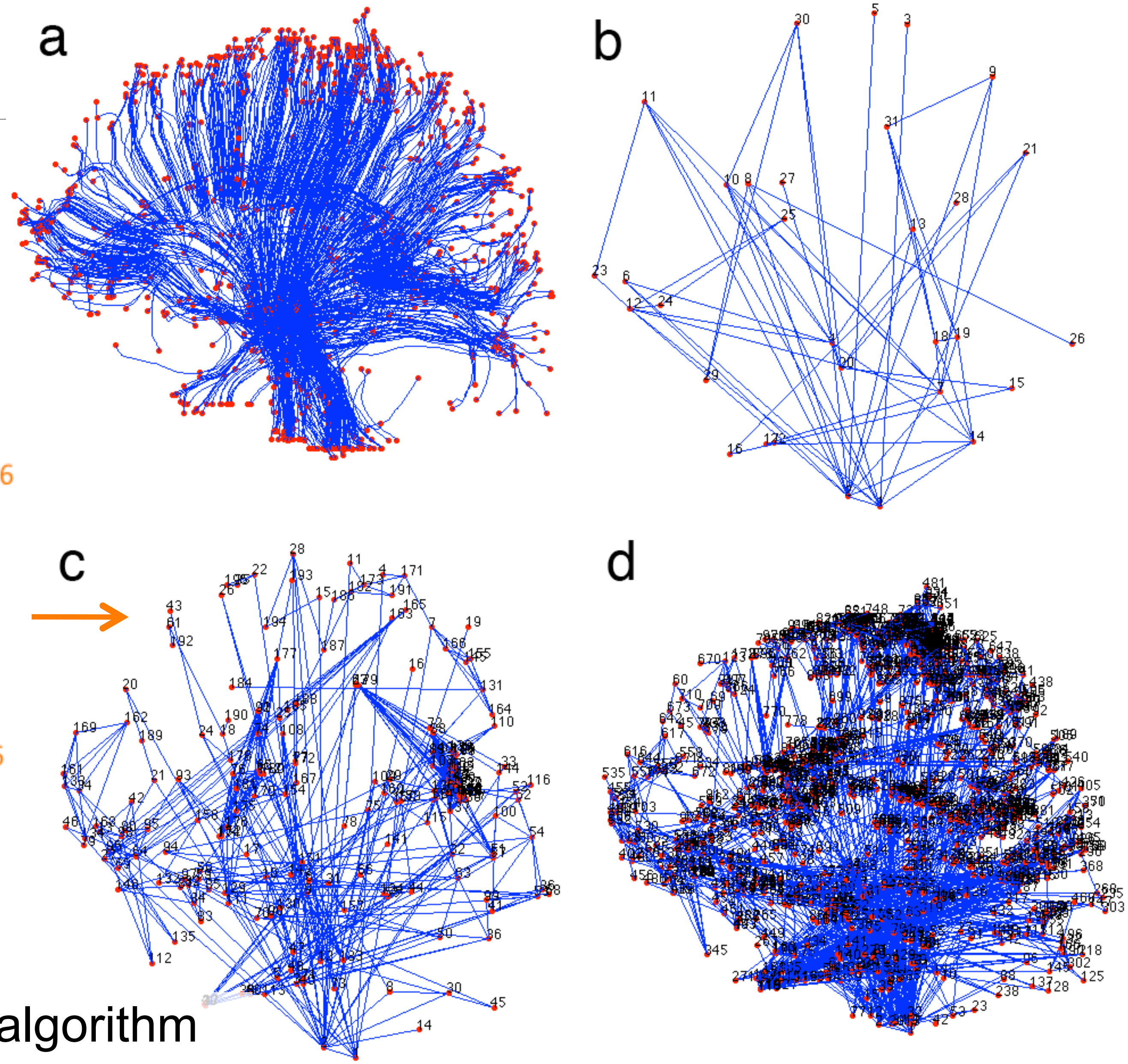
Orange: additional tract to be added

Iterative DTI network graph



Whole brain white matter fiber tractogpray

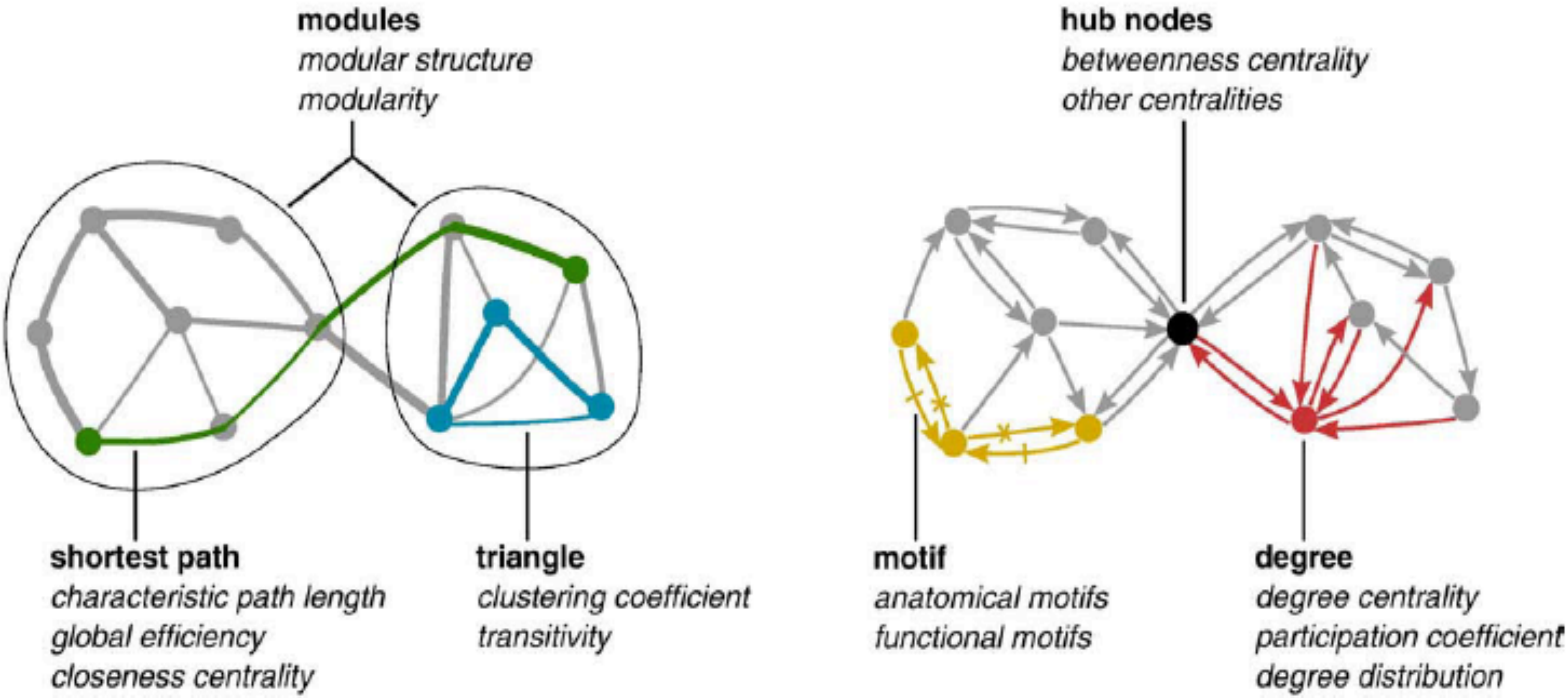




Iterative graph construction algorithm

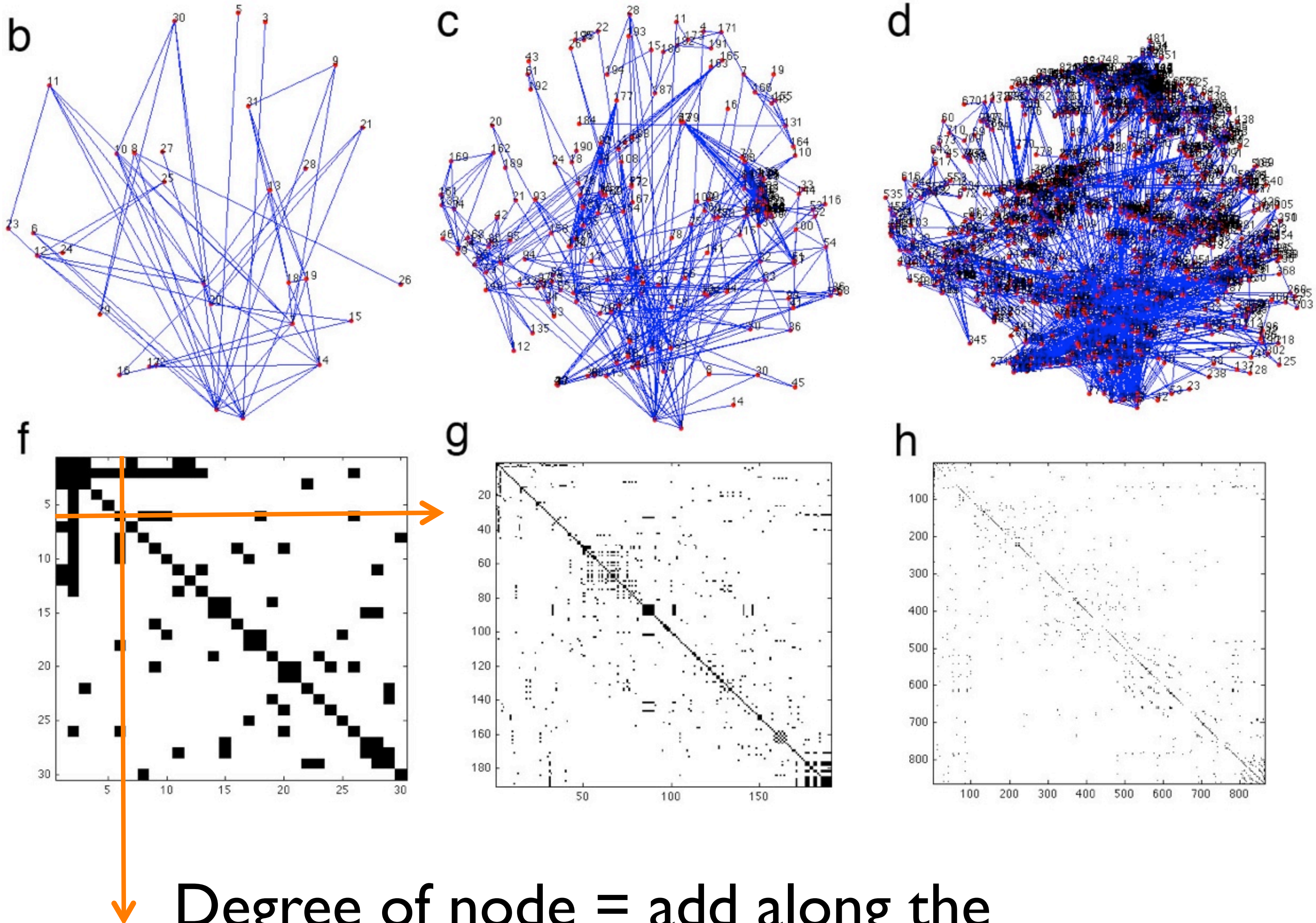
MATLAB demonstration

Various network complexity measures



Rubinov and Sporns, Neuroimage, 2009

Adjacency matrix

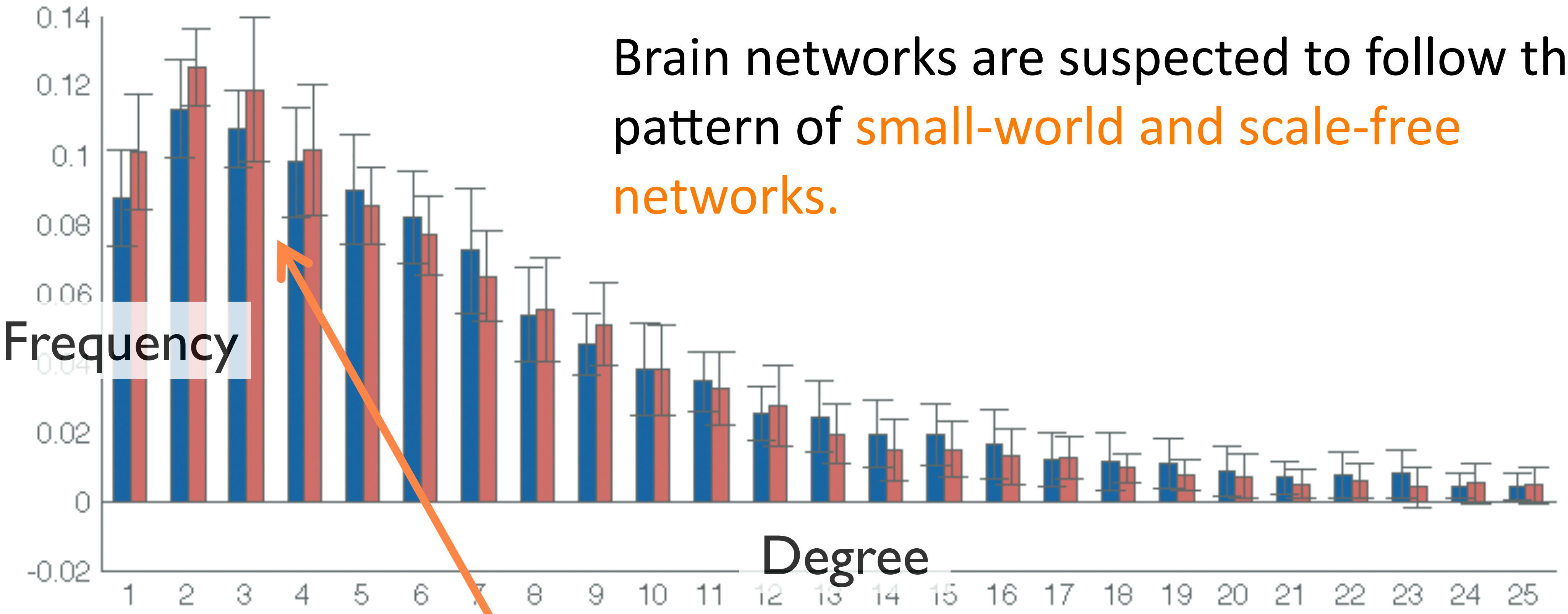


Degree of node = add along the vertical or horizontal direction

Degree distribution

Brain network is known to have higher clustering coefficient, shorter path length and power law form of $P(k) \sim k^{-x^{\wedge}3}$

Brain networks are suspected to follow the pattern of small-world and scale-free networks.



Blue: control

Red: autism

Higher frequency in lower degree = Over-connectivity in sparsely connected brain region

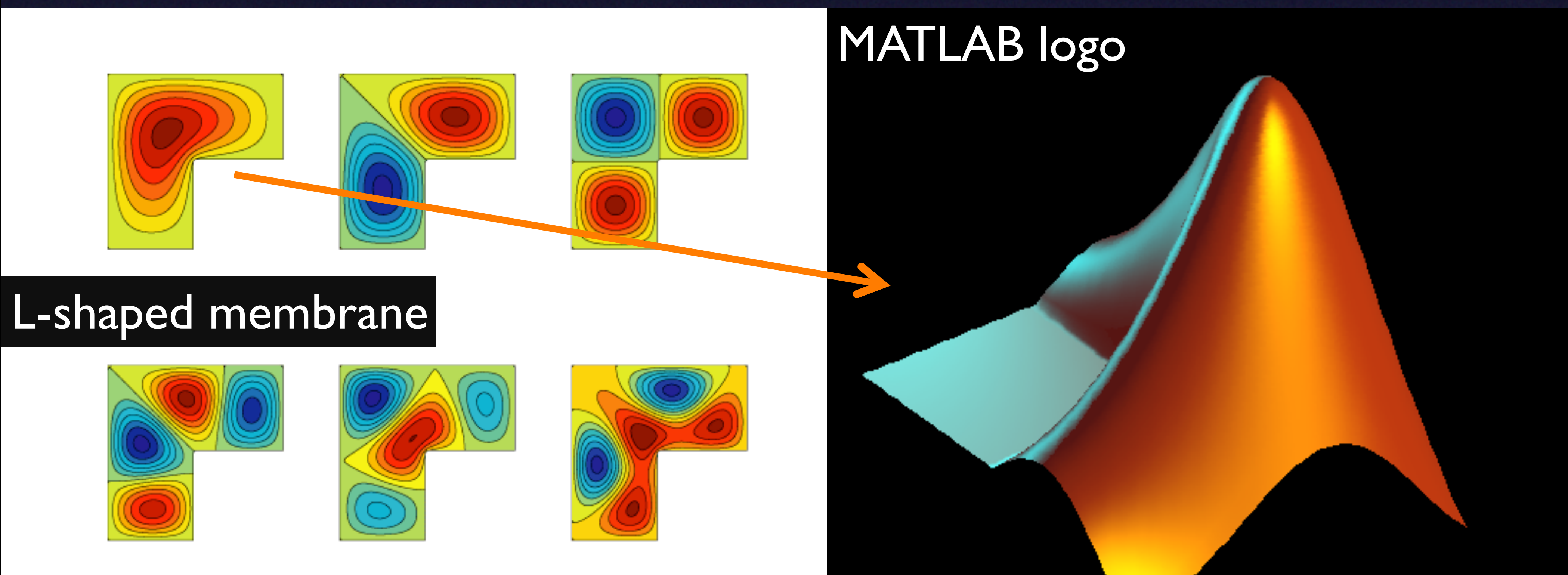
Intrinsic approach: spectral geometry

Steady-state oscillations in wave equation

↓

Helmholtz equation $$\Delta_X F = \lambda F$$

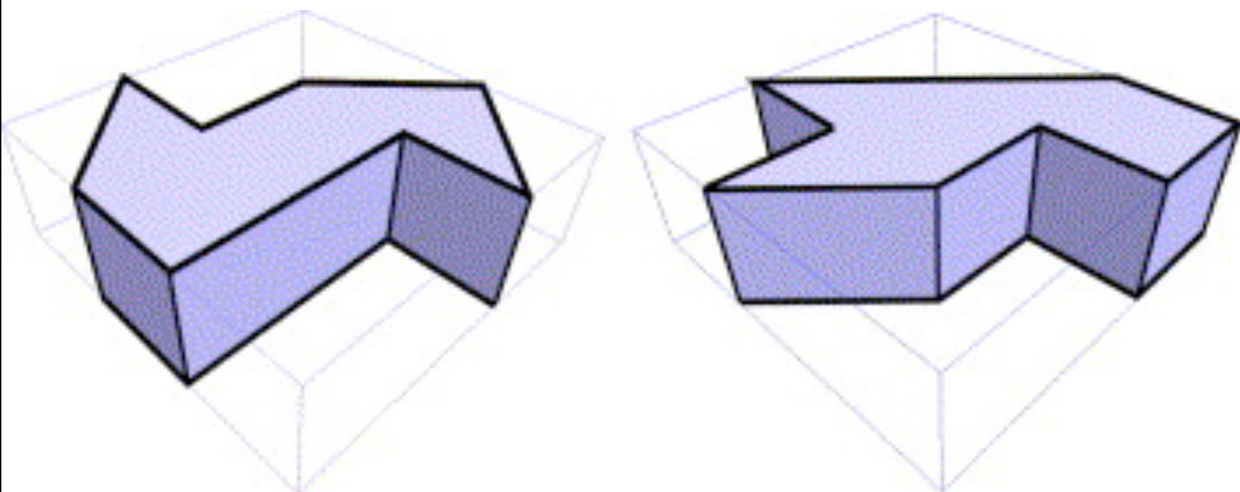
↓



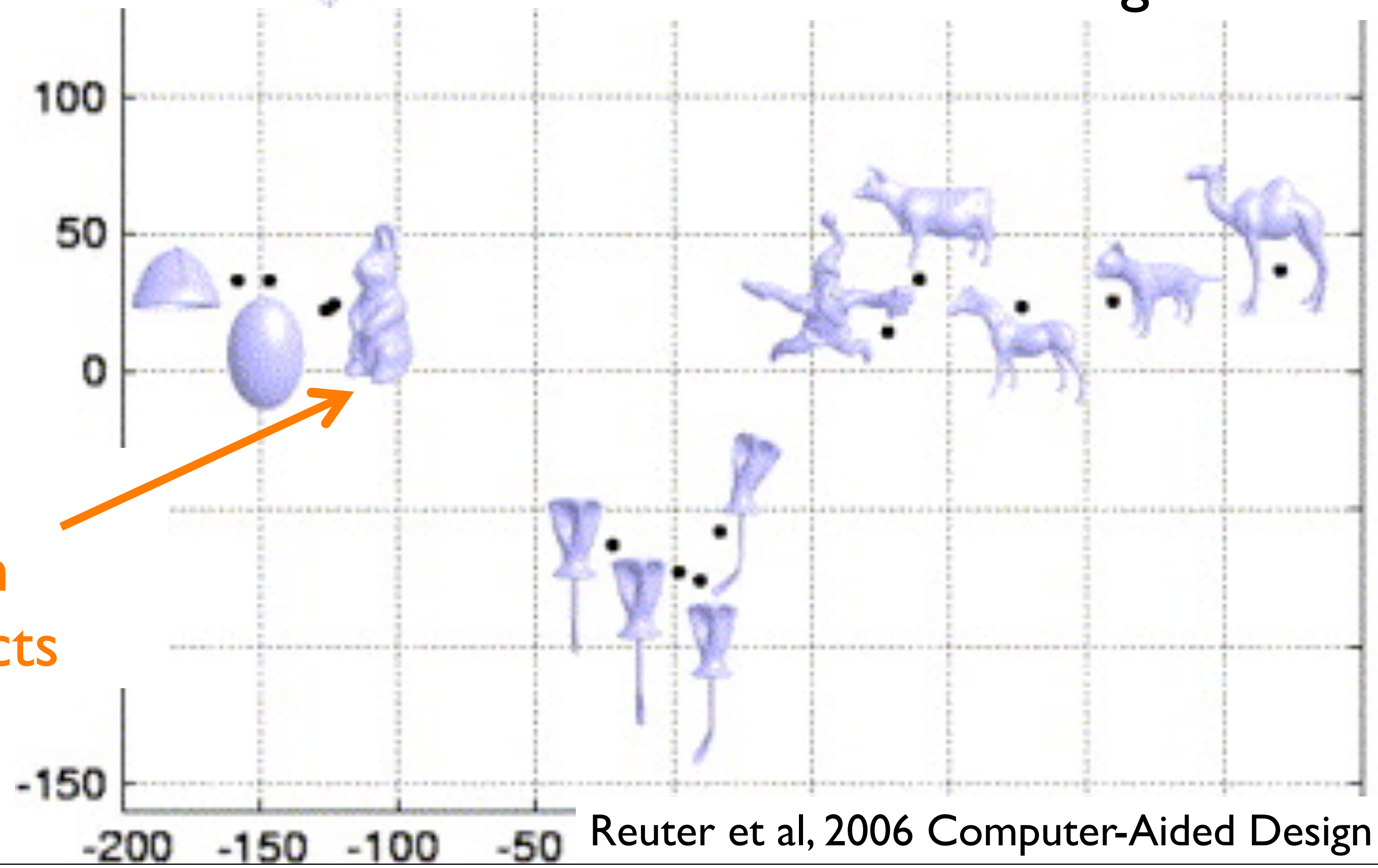
http://www.mathworks.com/company/newsletters/news_notes/clevescorner/win03_cleve.html

Shape spectrum

Isospectral shapes



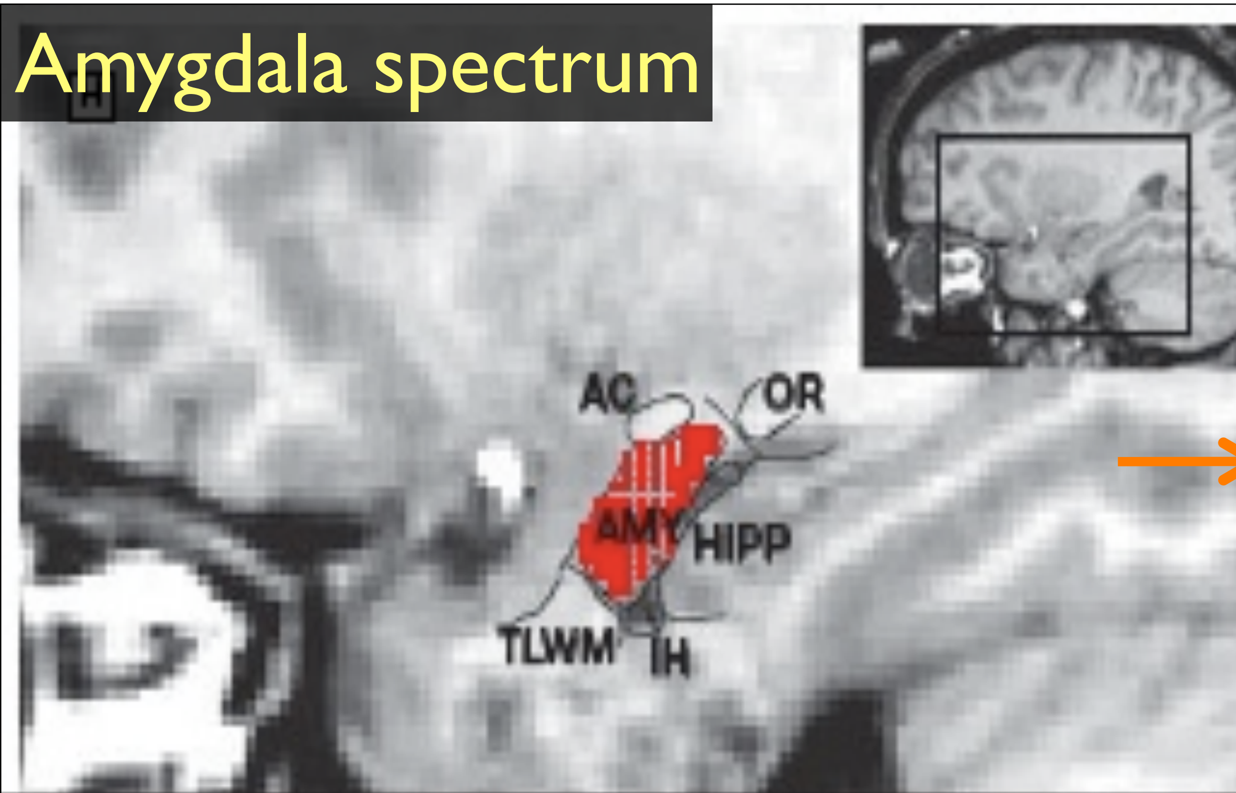
PCA on first 50 eigenvalues

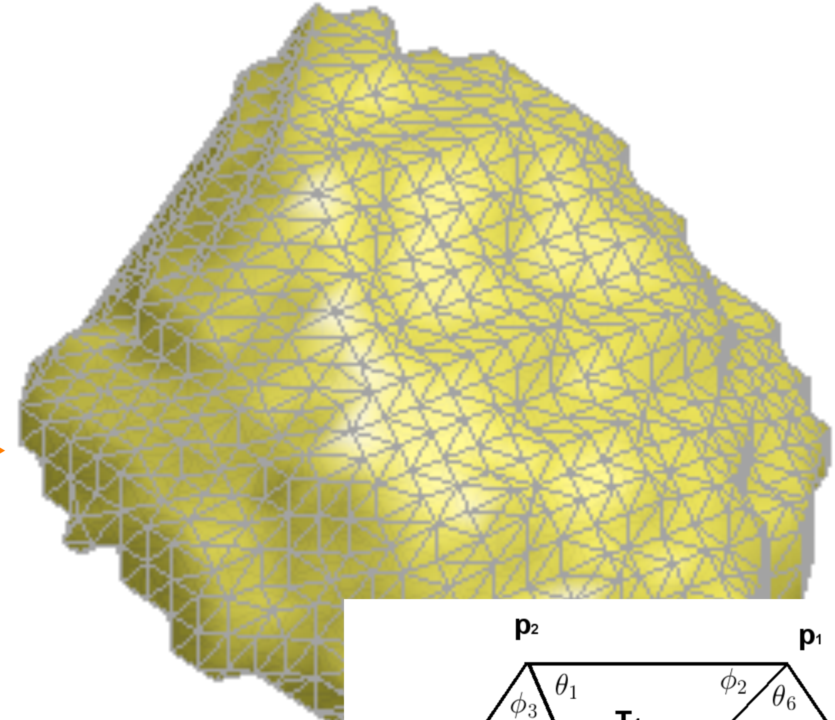


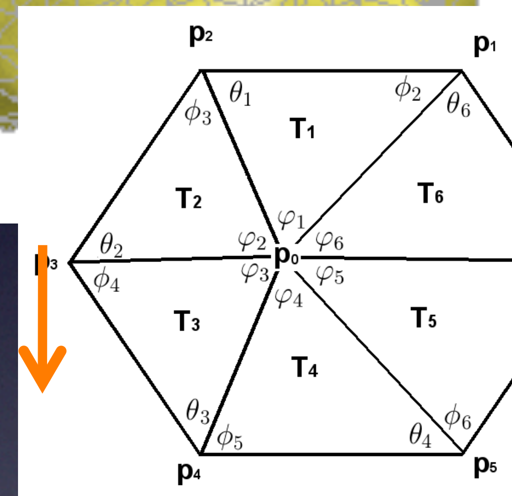
A bunny can't be distinguished from other stupid objects

Reuter et al, 2006 Computer-Aided Design

Amygdala spectrum







Generalized eigenvalue problem

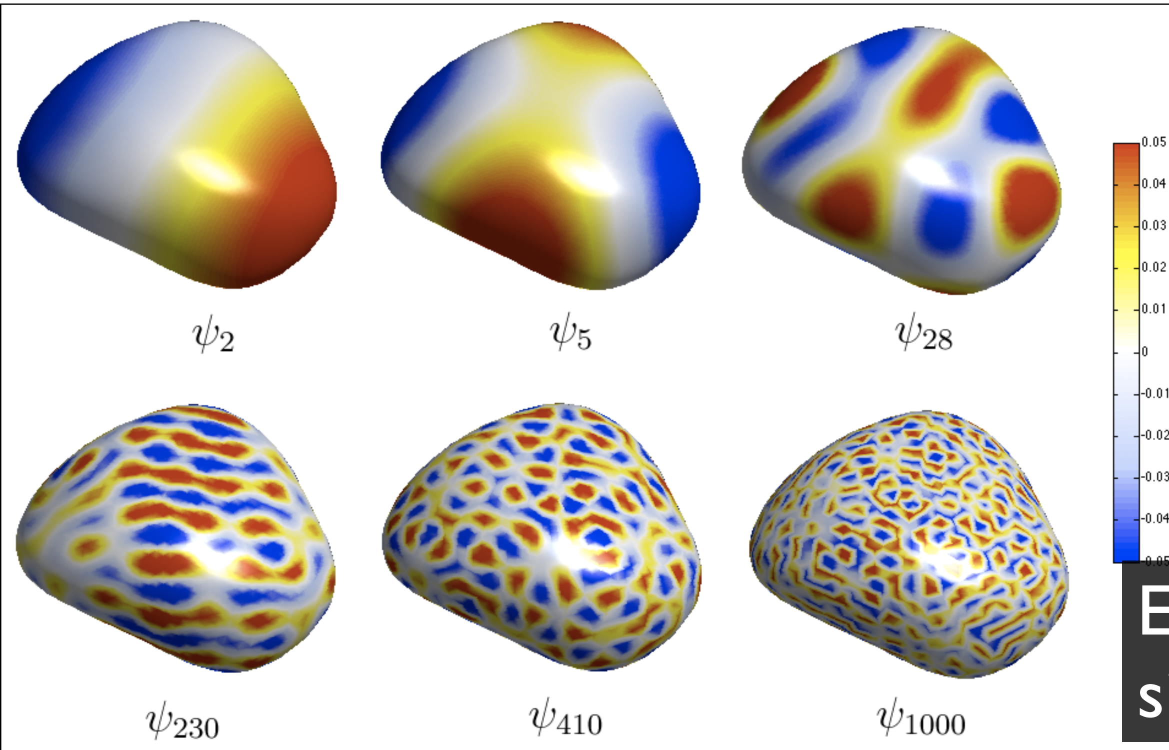
$$a_{ii} = \frac{1}{12} \sum_{p_j \in N(p_i)} T^{+}_{ij} + T^{-}_{ij}$$

$$c_{ii} = \frac{1}{2} \sum_{p_j \in N(p_i)} (\cot\theta_{ij} + \cot\phi_{ij})$$

$$\Delta_X F = \lambda F$$

discretization

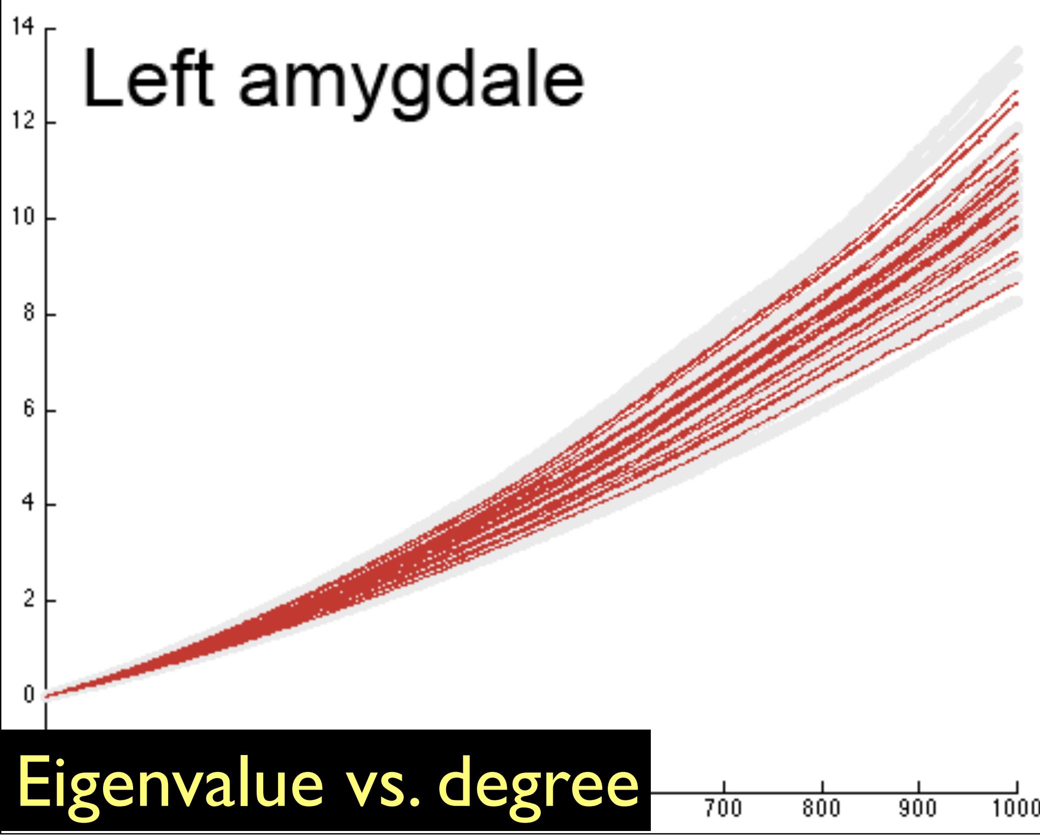
$$\lambda A\psi = C\psi$$

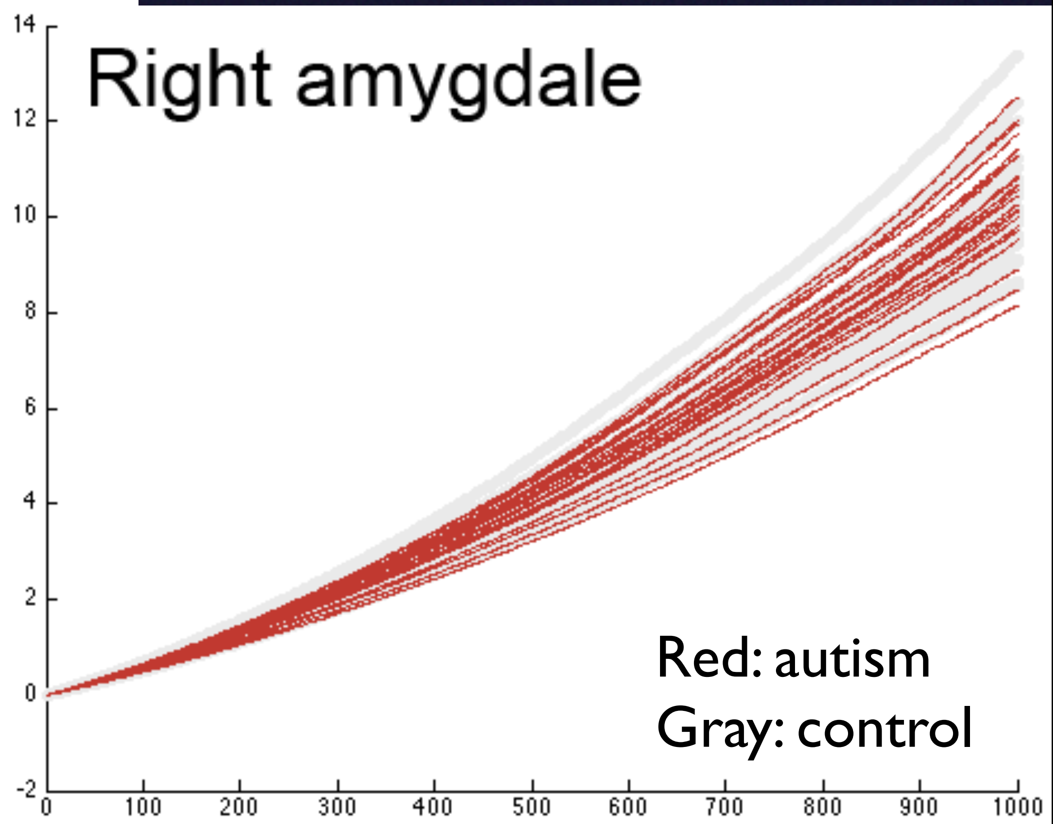


Weyl's formula

$$\lambda_k \to \frac{4\pi k}{\mu(\mathcal{M})}$$

Eigenvalues can't discriminate similarly shaped objects.





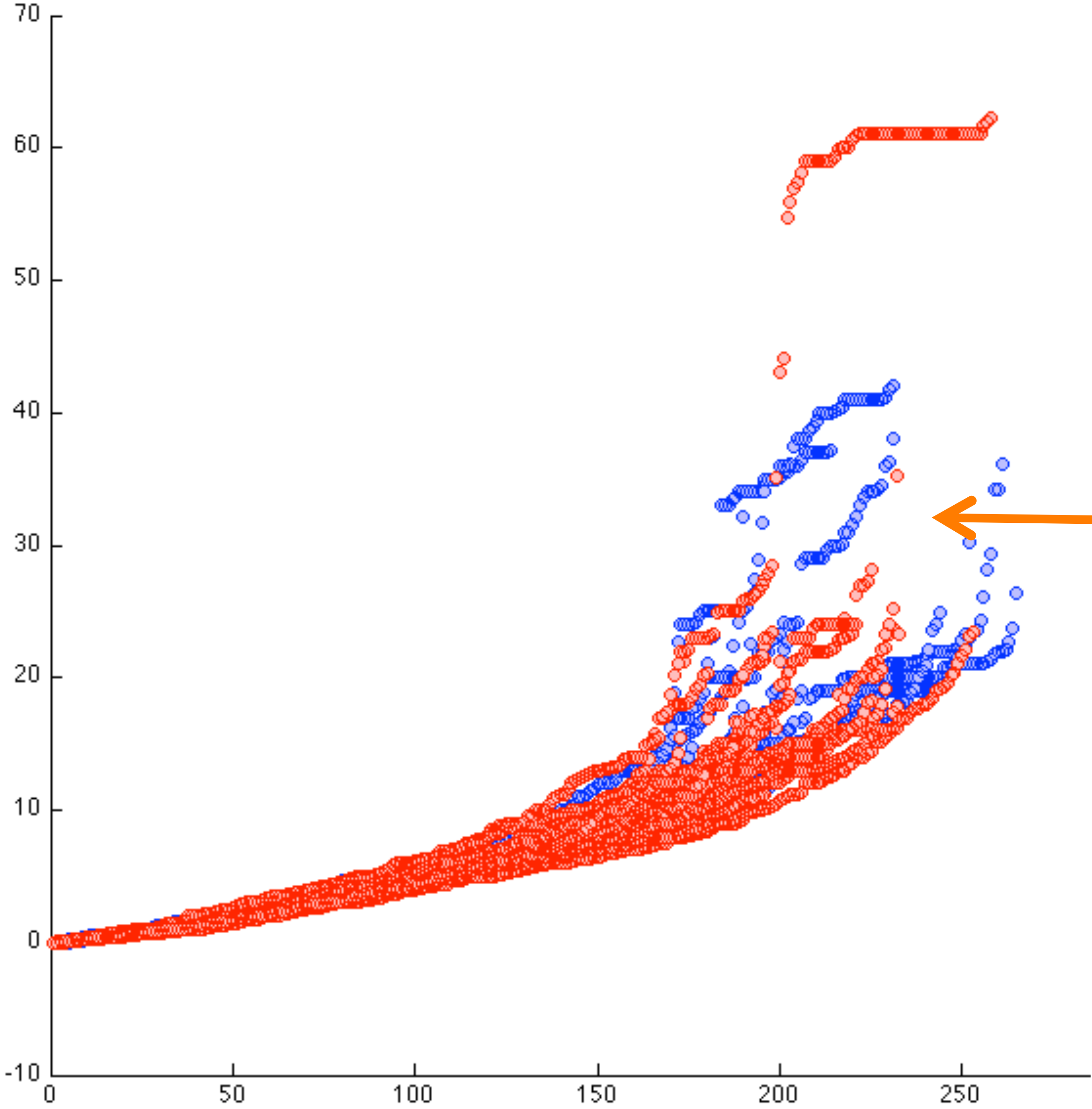
Eigenvalue vs. degree

Red: autism
Gray: control

Spectrum of adjacency matrix

Blue: control

Red: autism

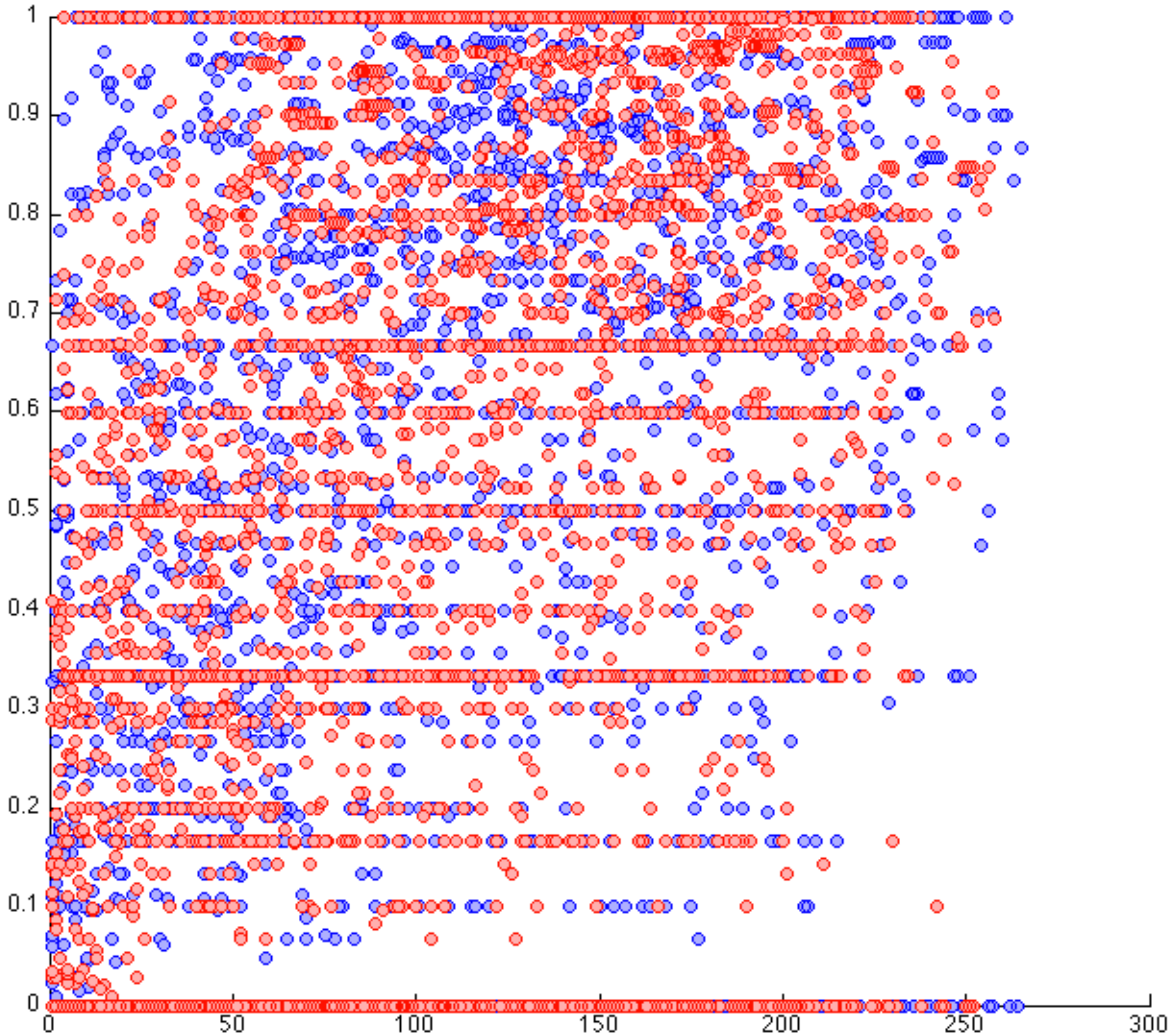


At higher frequency, we see group difference

Discretized version of Laplace-Beltrami operator was used

Clustering coefficients

Watts et al. Science 1998, Milo et al Science 2002



Space of adjacency matrices

Graph isomorphism problem

Given adjacency matrices of same size A_1 and A_2,

$$A_2 = P A_1 P'$$ ← permutation matrix

↓

Space of random permutation matrices

↓

Now we can construct statistics on graphs and do power computation