



Brain & Cognitive  
Sciences



University of Wisconsin  
**SCHOOL OF MEDICINE  
AND PUBLIC HEALTH**

# Computational Challenges in Brain Imaging

Moo K. Chung

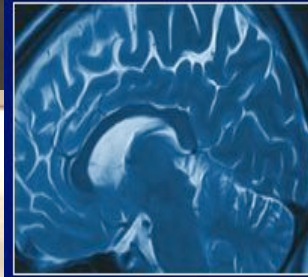
Department of Brain and Cognitive Sciences  
Seoul National University

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

[www.stat.wisc.edu/~mchung](http://www.stat.wisc.edu/~mchung)

SNU BCS DLS  
October 14, 2009

# University of Wisconsin, Madison



*The Waisman Laboratory  
for Brain Imaging and Behavior*



6 faculty members

MRI + PET + MicroPET + MEG+EEG + eye tracking device

5 staff members (2 computer support + 3 administrative/grant)

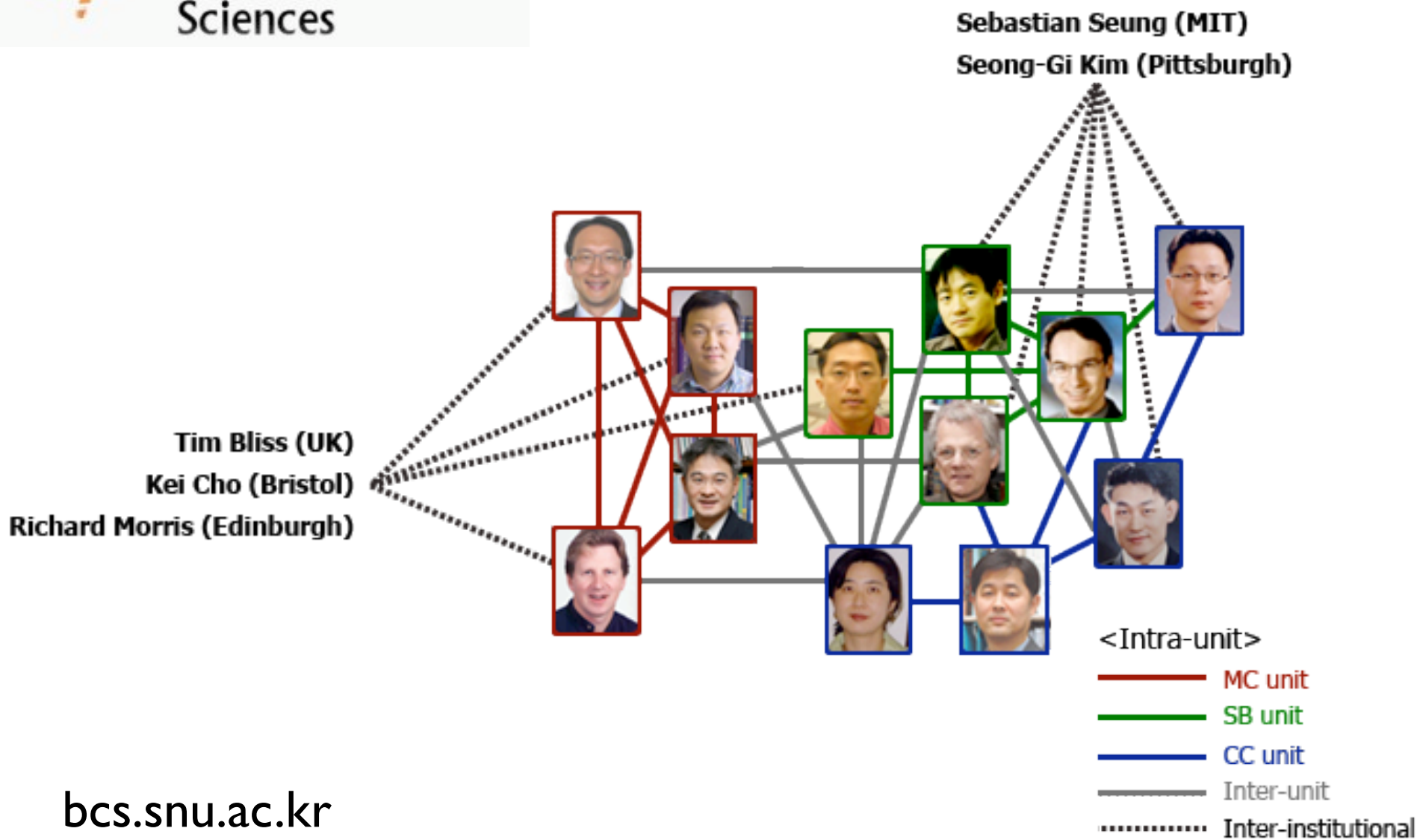
20 PhD level scientists + postdocs

100 graduate + undergraduate students

[brainimaging.waisman.wisc.edu](http://brainimaging.waisman.wisc.edu)



# Seoul National University



[bcs.snu.ac.kr](http://bcs.snu.ac.kr)

# Job Advertisement

We are looking for graduate students (masters, PhD) and postdoctoral students at **BCS** who will do brain research in general and computational aspect of brain imaging in particular.

Any student with math, stat, physics, CS and EE will find the field real easy.  
Send email to [mkchung@wisc.edu](mailto:mkchung@wisc.edu)

# Abstract

Computational neuroanatomy is an emerging field that utilizes various non-invasive brain imaging modalities such as magnetic resonance imaging (MRI) and diffusion tensor imaging (DTI) in quantifying the spatiotemporal dynamics of the human brain structures in both normal and clinical populations in macroscopic level. This discipline emerged about twenty years ago and has made substantial progress in the past decade. It usually deals with computational problems arising from the quantification of within- and between-subject variations associated with the structure and the function of the human brain. Major challenges in the field are caused by the massive amount of nonstandard high dimensional non-Euclidean imaging data that are difficult to analyze using traditional methods. This requires new computational solutions that incorporate geometric and topological nature of brain structures. Overview of various computational issues in neuroanatomy will be presented with example studies on autism.

# Outline

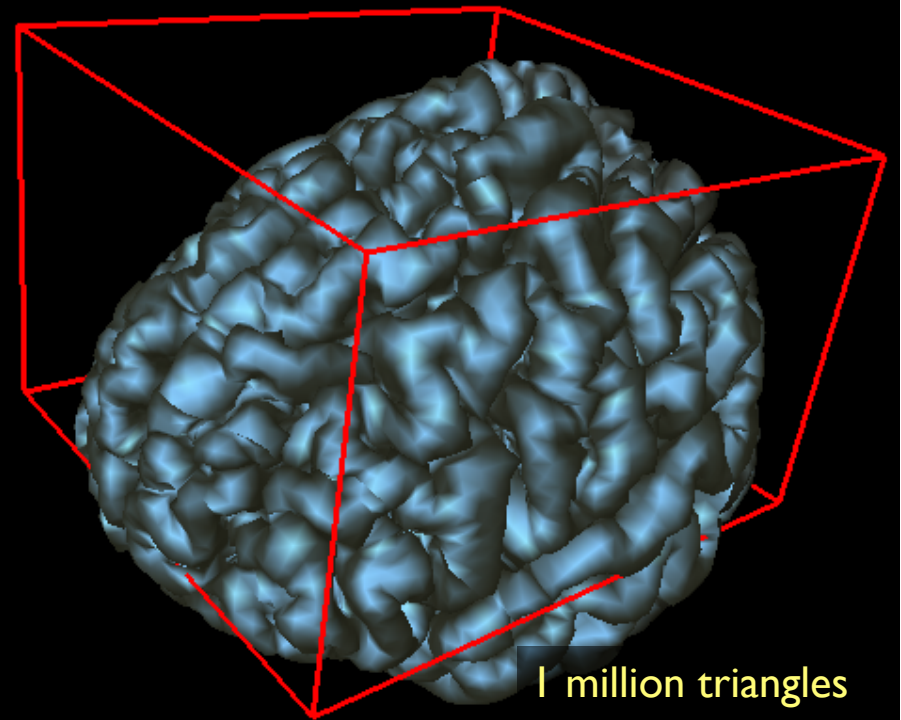
1. Brain images & problems
2. Intrinsic method
3. Extrinsic method
4. Computational Challenge I  
(extremely large least squares problem)
5. Computational Challenge II  
(extremely large 3D graph model)

Real brain

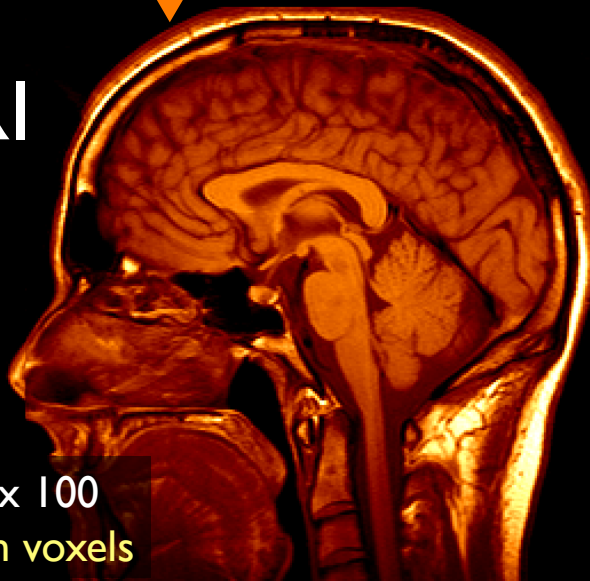


Magnetic Resonance Imaging

Cortical surface model



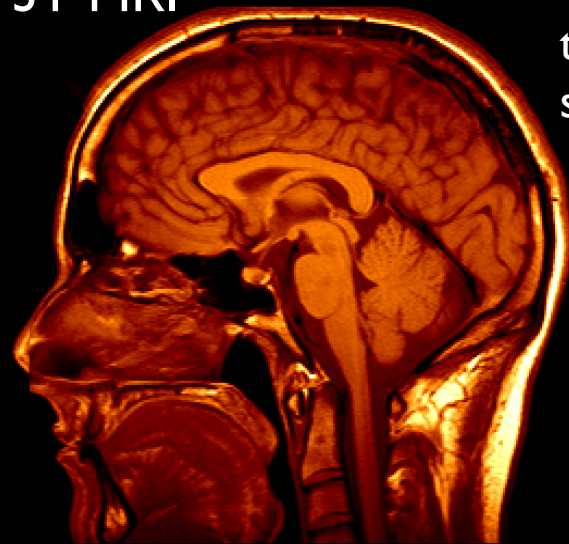
3T MRI



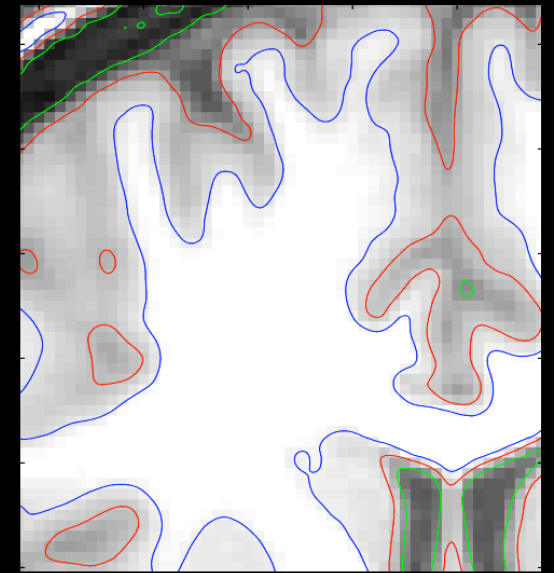
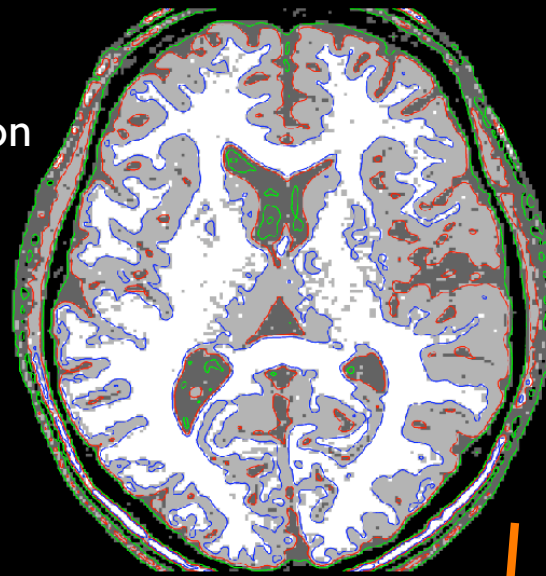
$200 \times 100 \times 100$   
= 2 million voxels

1 million triangles

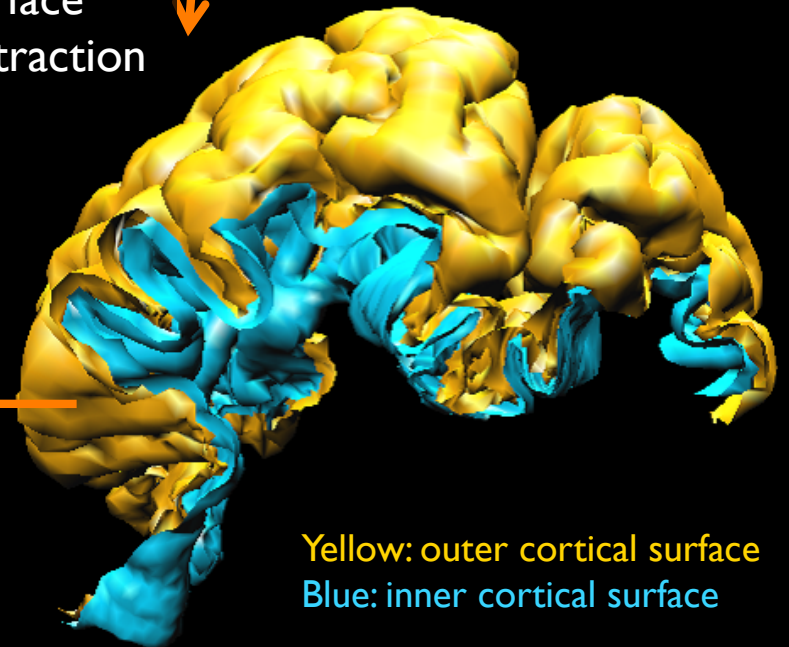
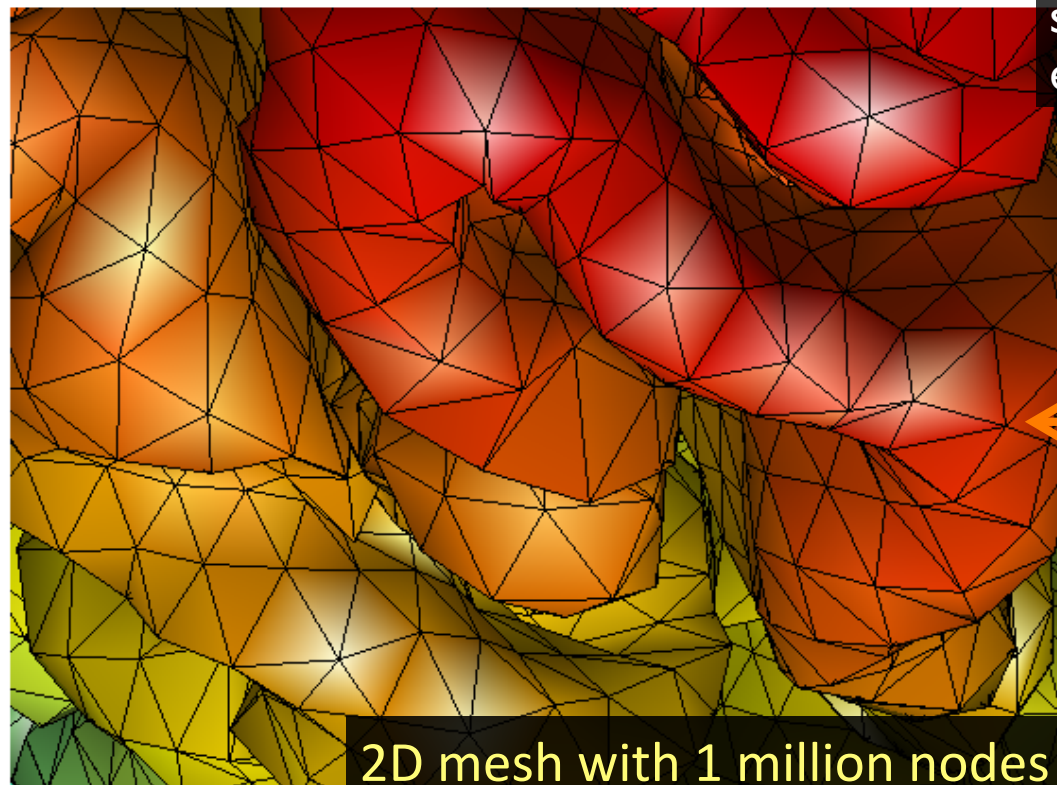
3T MRI



tissue  
segmentation



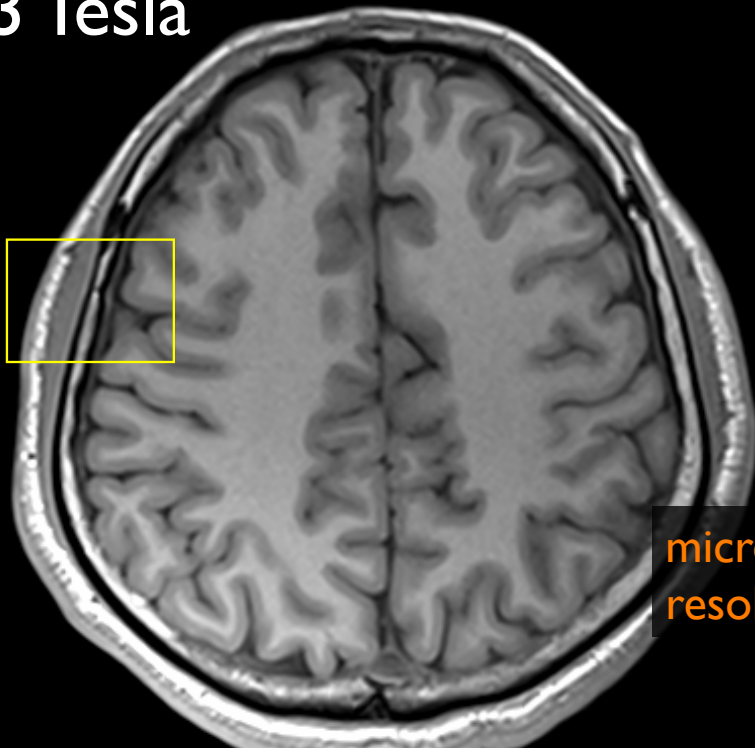
surface  
extraction



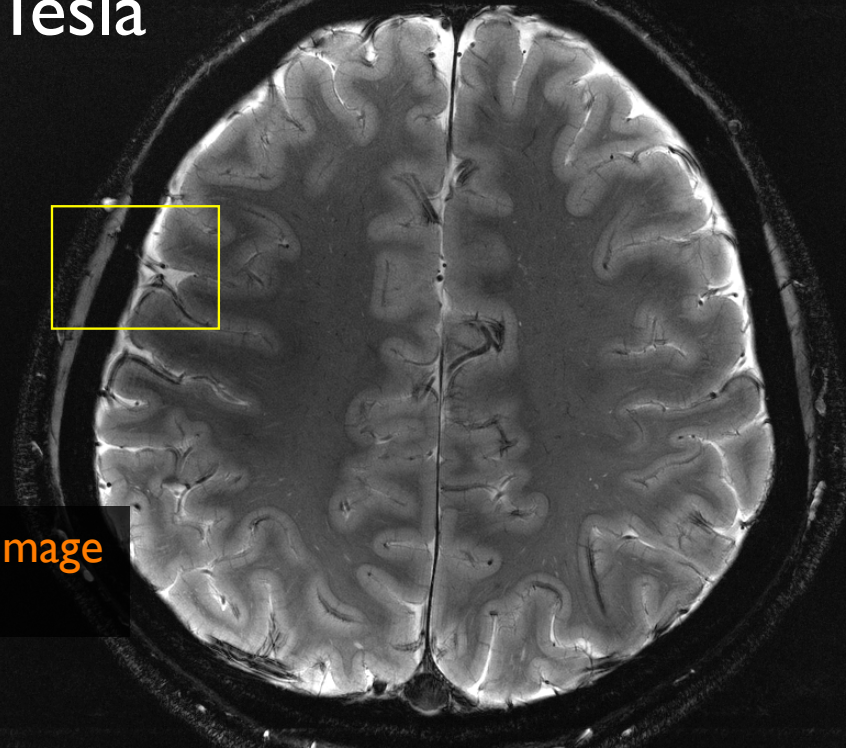
Yellow: outer cortical surface  
Blue: inner cortical surface



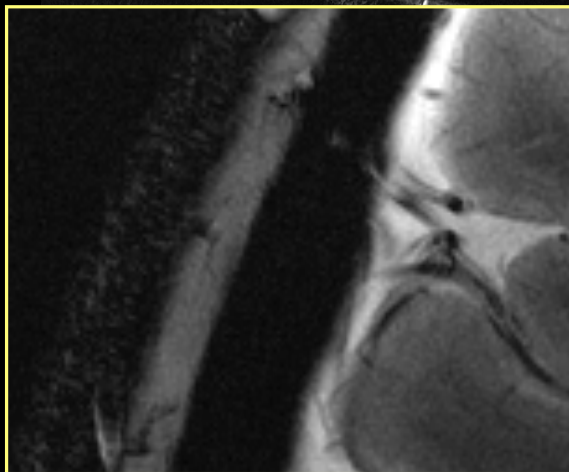
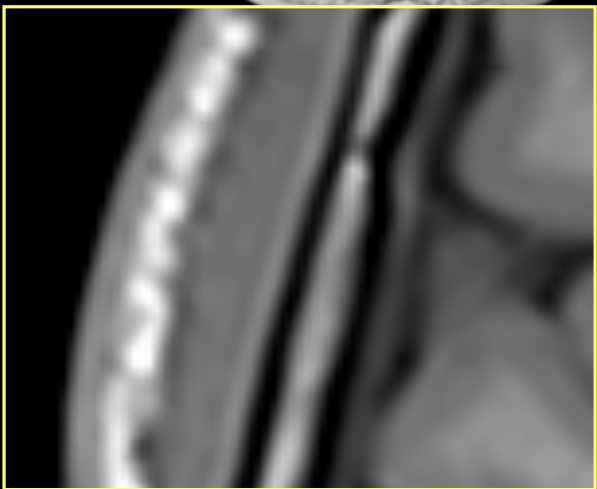
3 Tesla



7 Tesla



microscopic image resolution



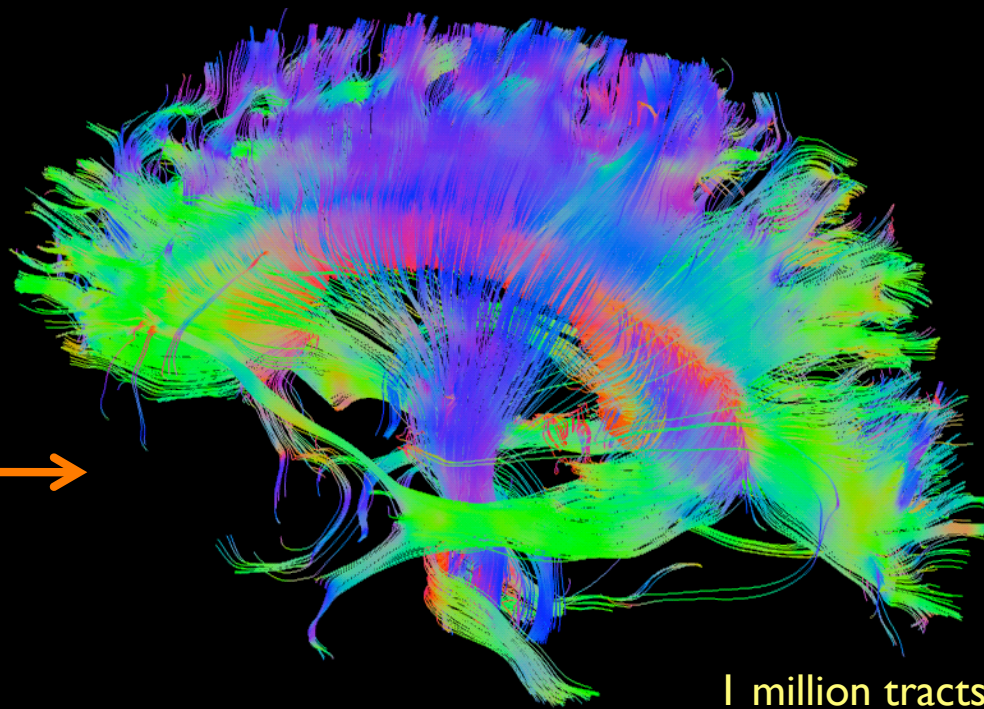
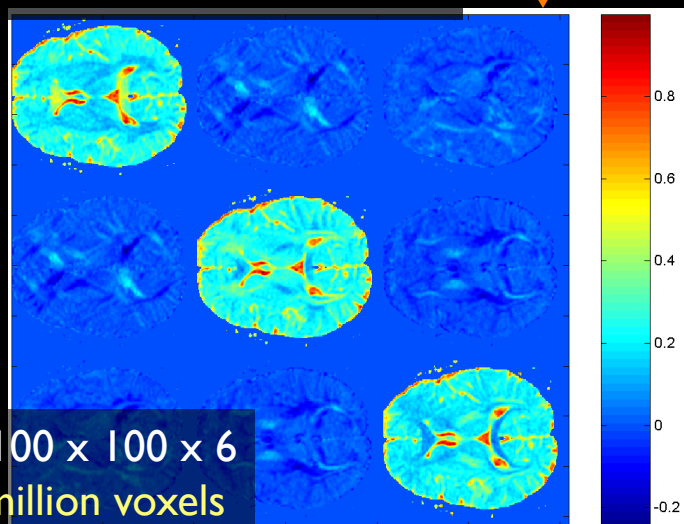
Real brain

Diffusion Tensor Imaging

White matter fiber tractography

Diffusion tensor

$200 \times 100 \times 100 \times 6$   
= 12 million voxels



1 million tracts



## Sample Computational Problems

Matrix inversion of size 1000000

Eigenvalue problem of size 1000000

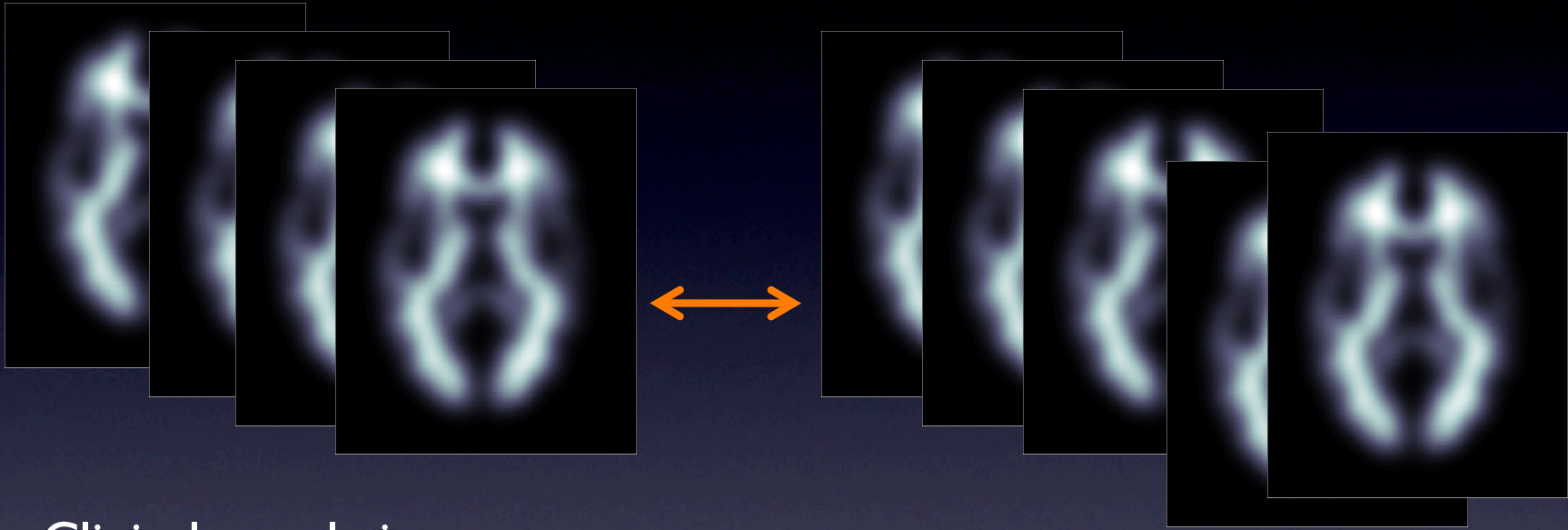
Computation on a mesh with 1000000 triangles

Computation on a collection of 1000000 fiber tracts

3D Graph with 1000000 nodes and 1000000 edges

# Typical question in computational neuroanatomy

Given a collection of images



Clinical population:  
autism, Parkinson's disease

Normal controls

1. Do brains differ in shape ?
2. How they differ?

# Intrinsic approach Spectral Geometry

# Intrinsic approach: spectral geometry

*Mark Kac, 1966.*

*Can one hear the shape of a drum?*

*American Mathematical Monthly*

If we know the shape of a drumhead, we know its frequency. Can we know the shape of the drumhead knowing its frequency?



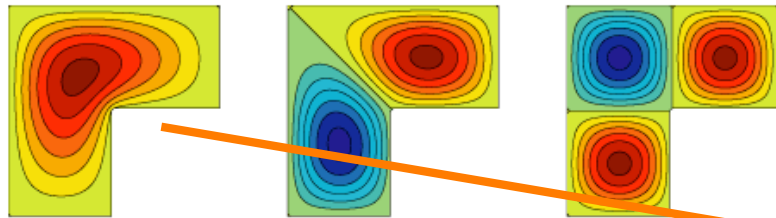
Shape characterization using spectrum

# Shape spectrum

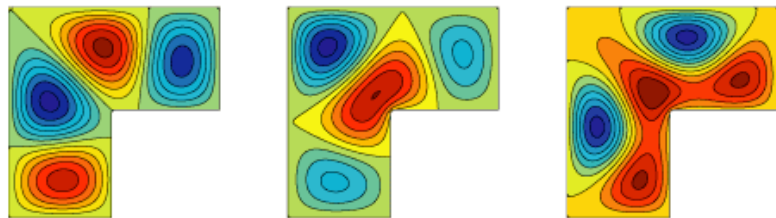
Steady-state oscillations in wave equation



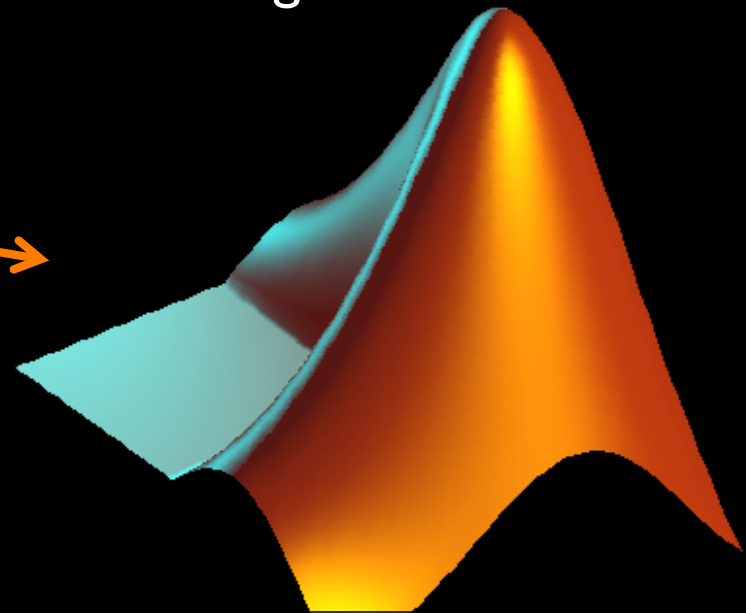
Helmholtz equation  $\Delta_X F = \lambda F$



L-shaped membrane

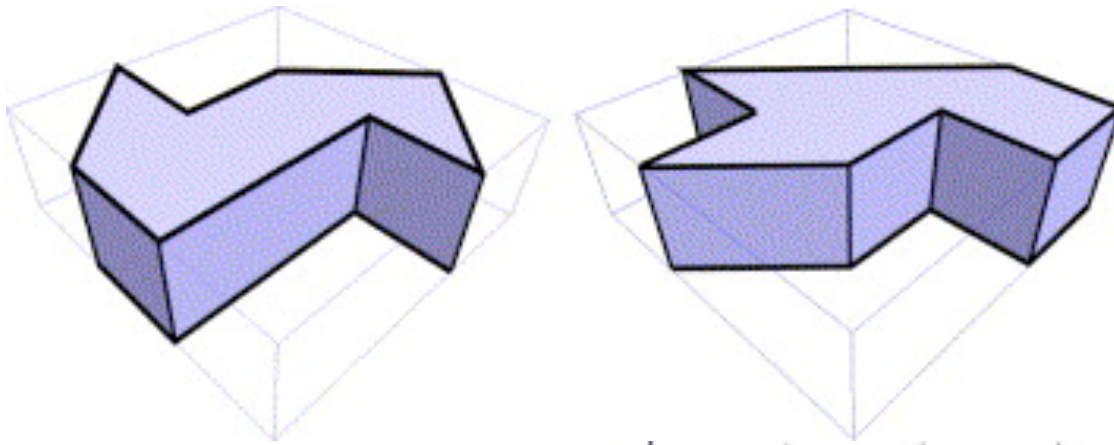


MATLAB logo

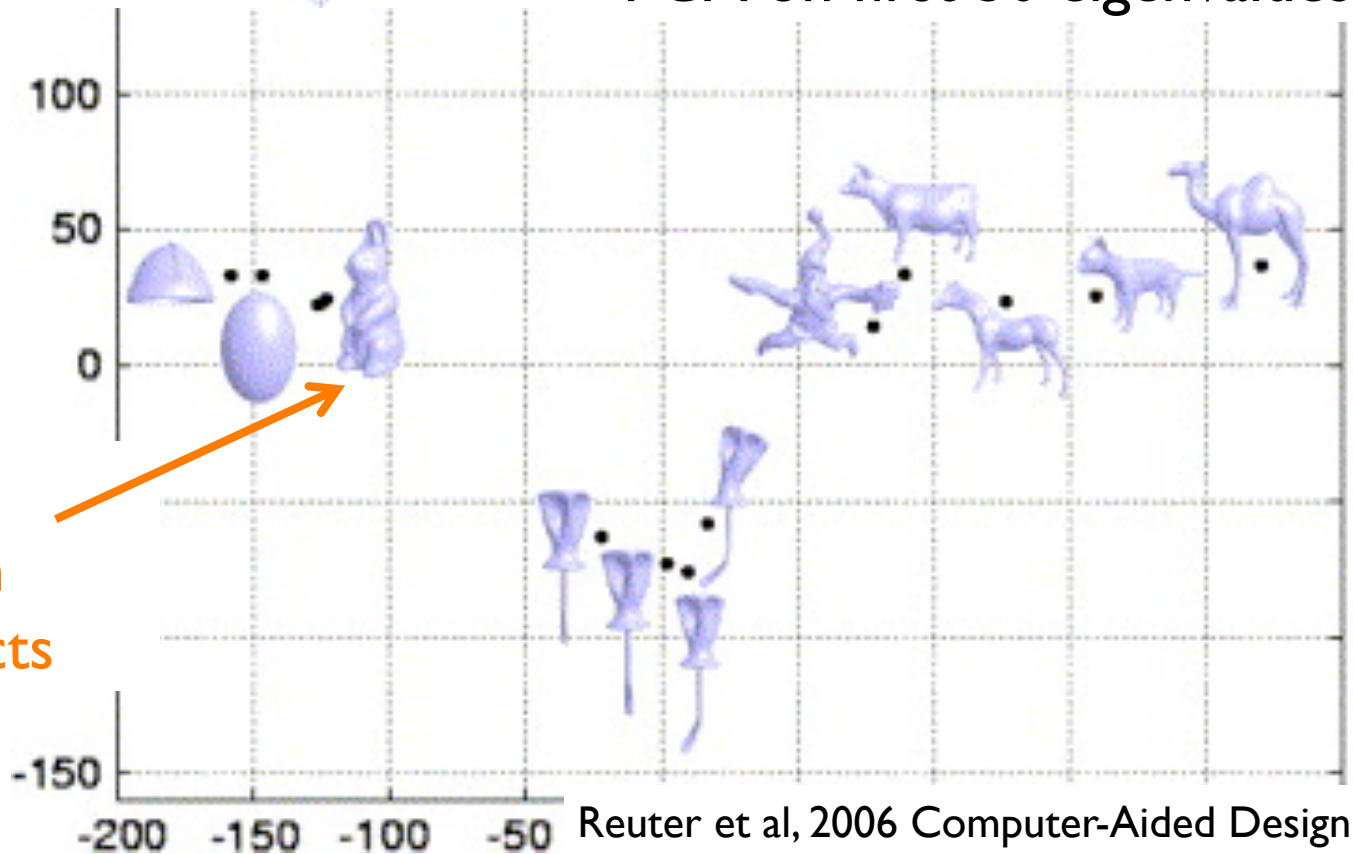


Isospectral shapes

# Shape spectrum



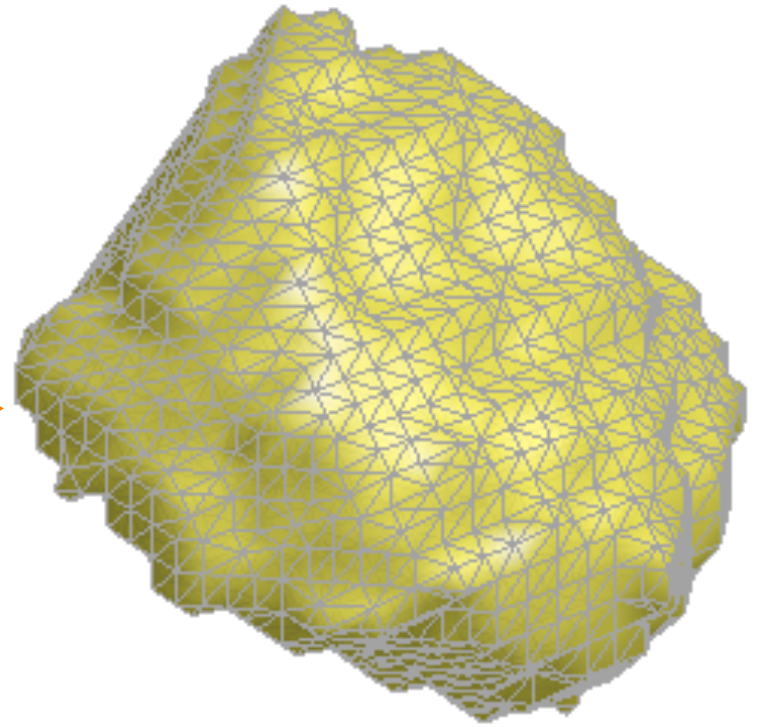
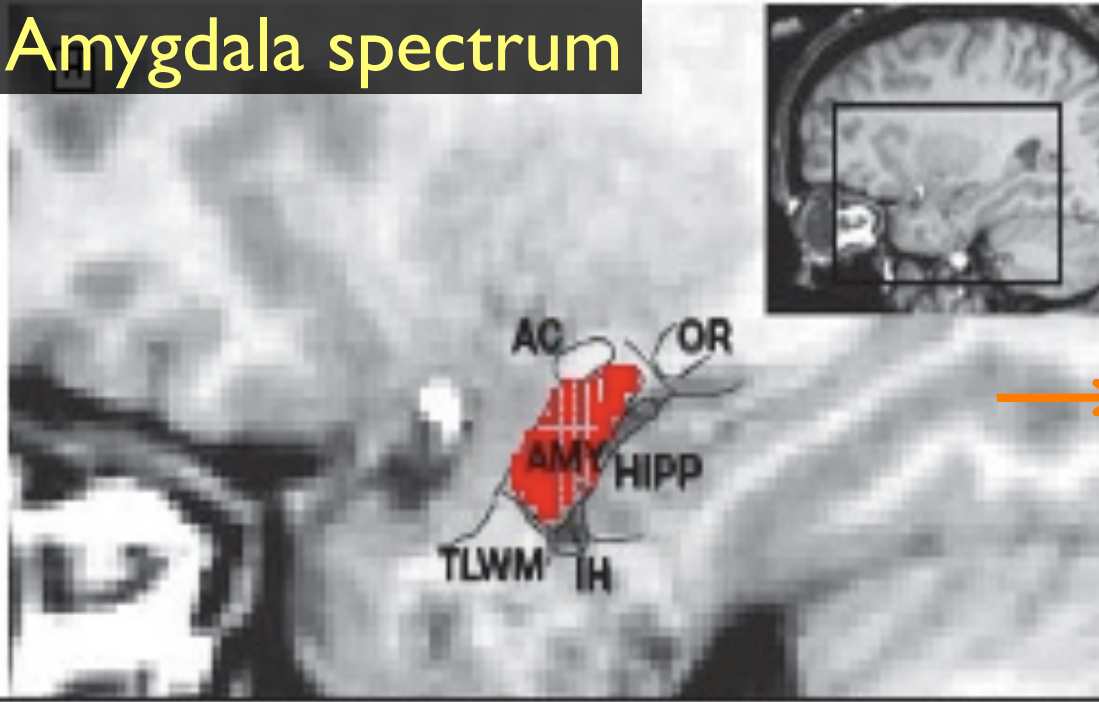
PCA on first 50 eigenvalues



A bunny can't be distinguished from other stupid objects



# Amygdala spectrum



## Generalized eigenvalue problem

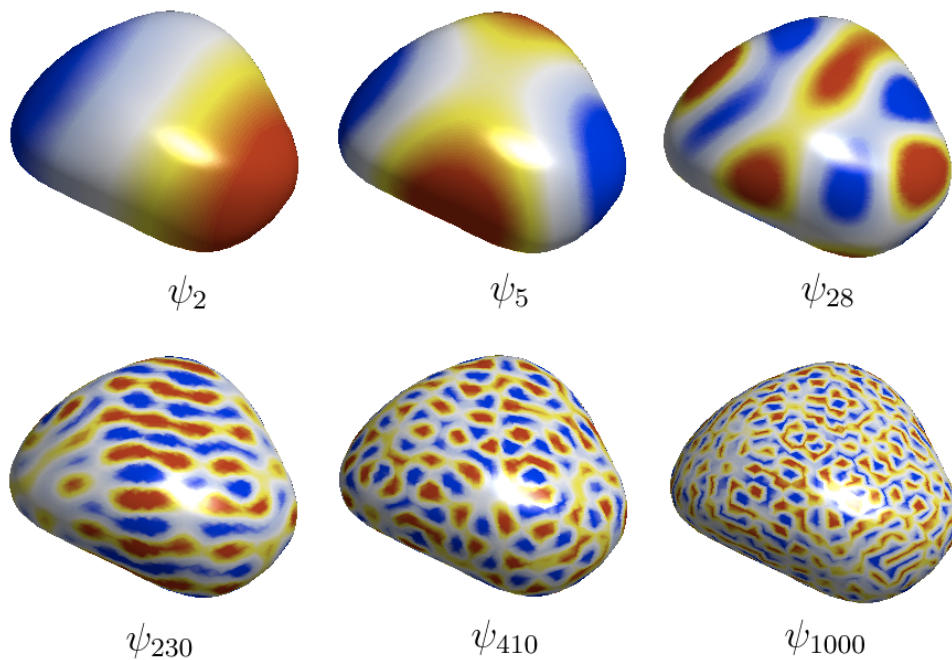
$$a_{ii} = \frac{1}{12} \sum_{p_j \in N(p_i)} T_{ij}^+ + T_{ij}^-$$

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

$$\Delta_X F = \lambda F$$

↓ discretization

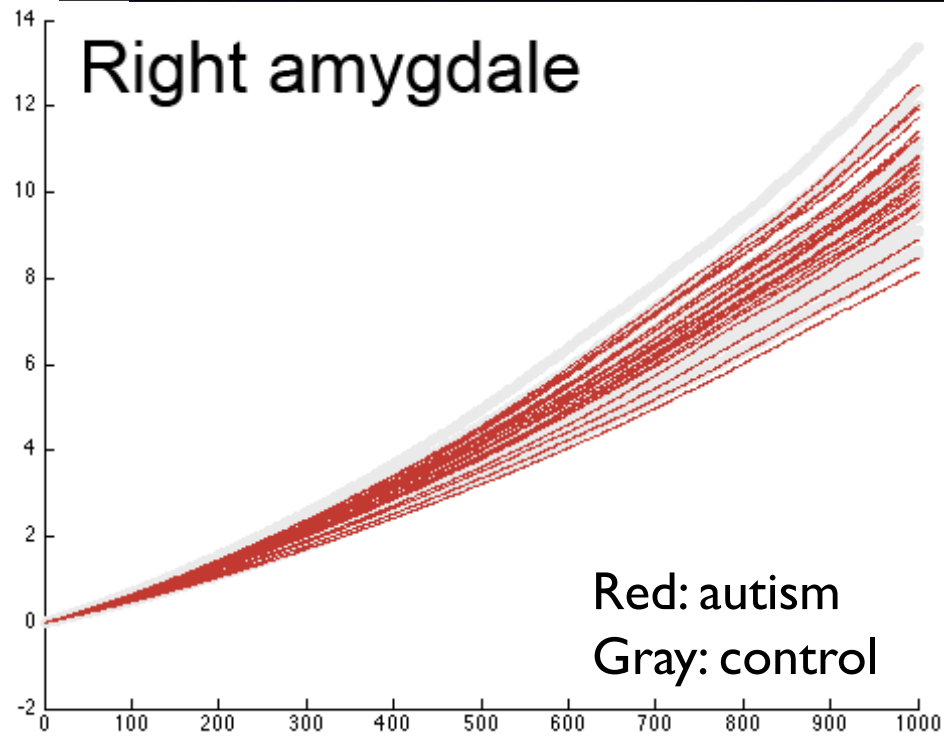
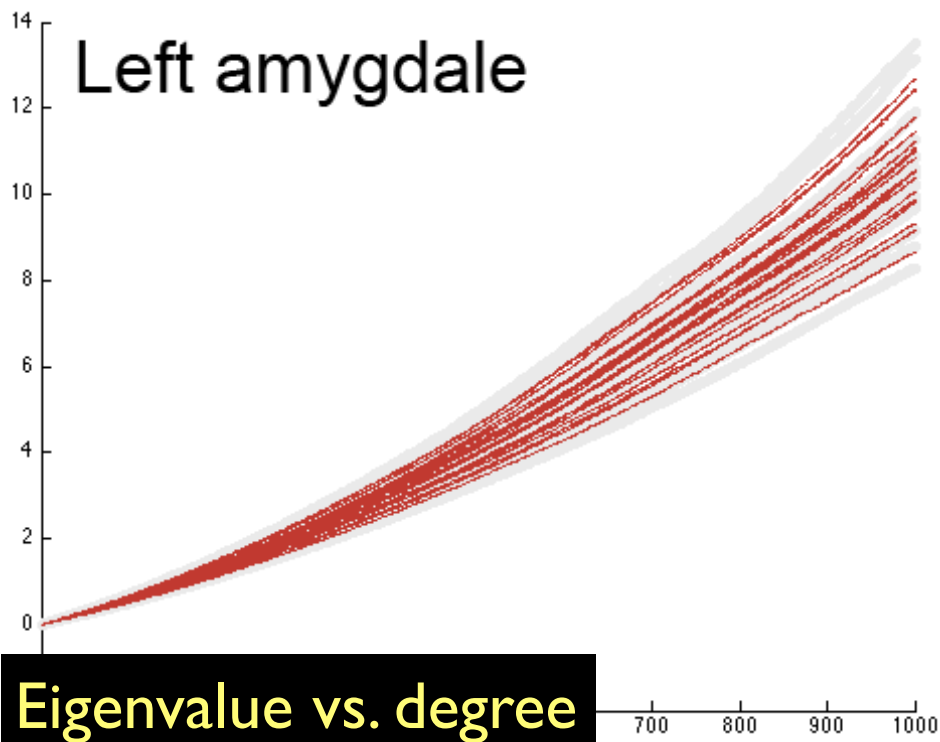
$$\lambda A \psi = C \psi$$



Weyl's formula

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

Eigenvalues can't discriminate similarly shaped objects.

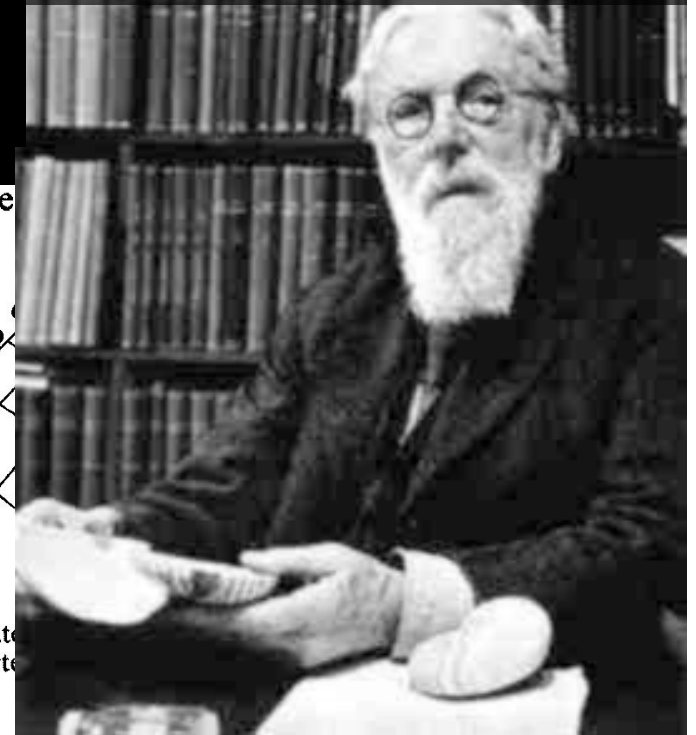


# Extrinsic approach

## Fourier Descriptors

# Extrinsic approach: Fourier Descriptors

D'Arcy Thompson 1860-1948



figuratively speaking, the

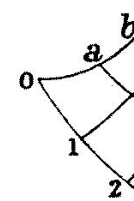


Fig. 178. Co-ordinates  
the Carte

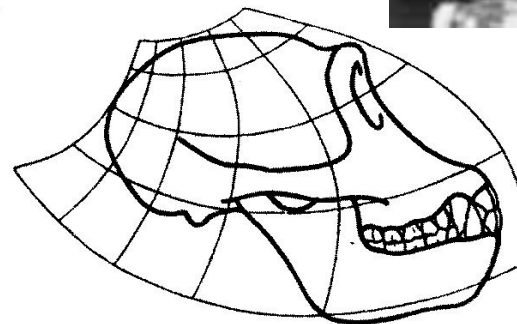


Fig. 179. Skull of chimpanzee.

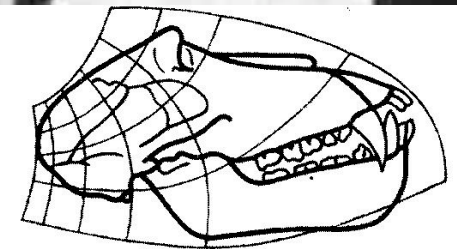


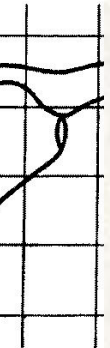
Fig. 180. Skull of baboon.

diagram  
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anthropo

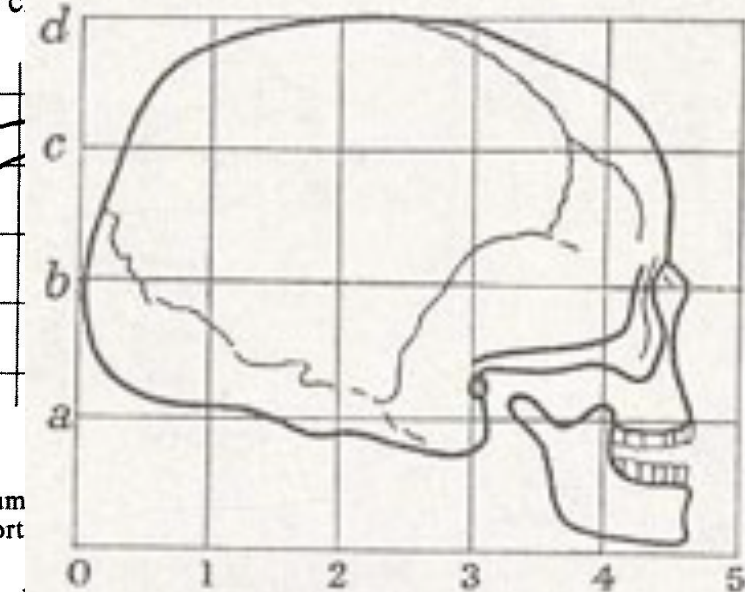
## On Growth and Form D'Arcy Thompson

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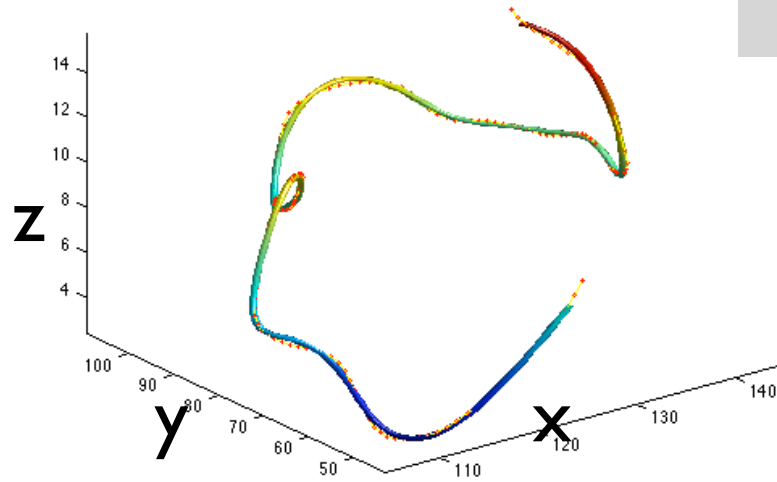


d  
c  
b  
a

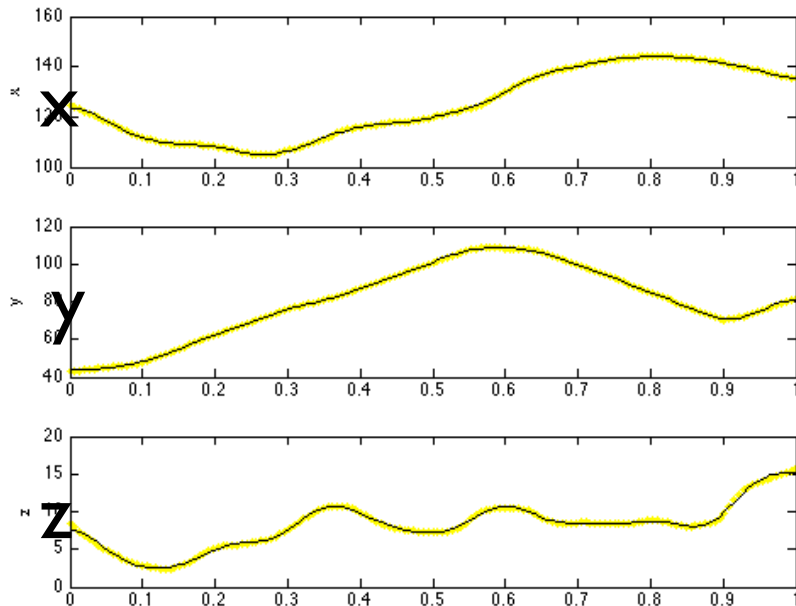


early a

# White matter fiber tract model



parameterization

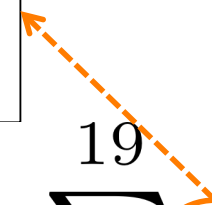


basis expansion

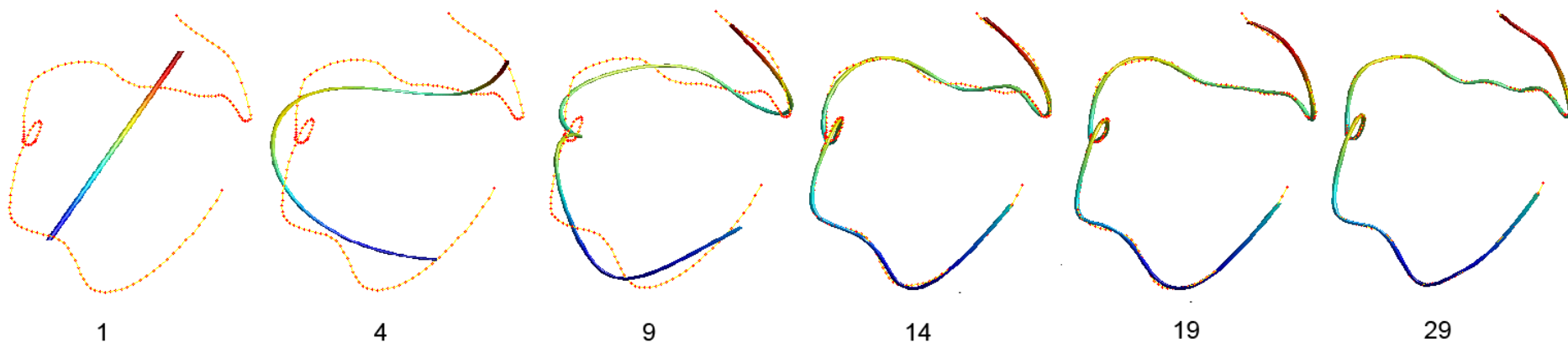
88.1799	56.6336	5.7367
-12.4775	-11.2552	-2.0791
2.4336	-15.4428	-0.4021
4.3956	2.2733	-0.9354
-0.0106	-0.0674	0.6999
2.1773	-2.4194	-0.1176
0.5808	0.8390	1.2942
0.0615	-0.1893	0.1188
-0.2629	0.7524	0.1089
0.7909	-0.7276	-0.1901
0.5458	0.6236	0.6939
0.4295	-0.4337	0.2185
0.2150	0.4157	0.0254
0.1584	-0.1973	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.

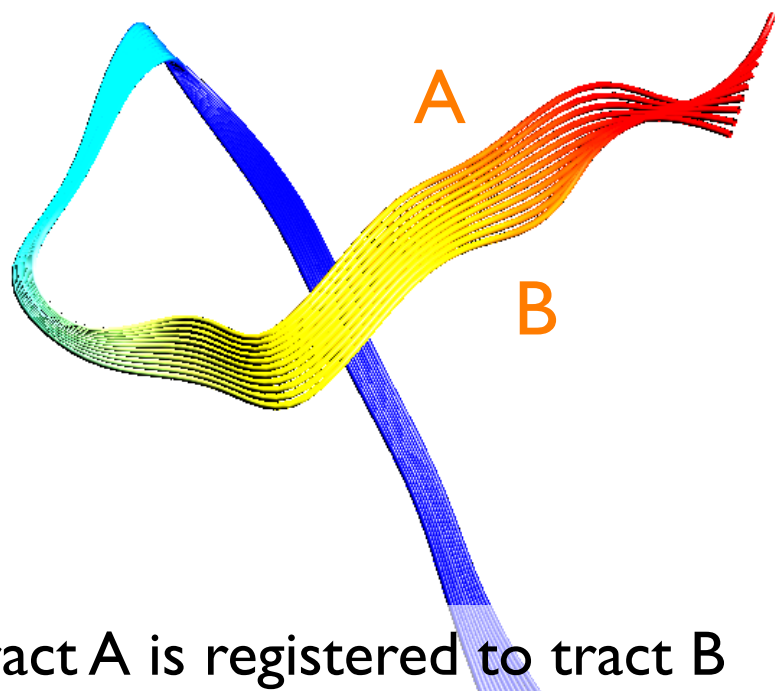
$$(x, y, z)' = \sum_{l=0}^{19} \beta_l \cos(l\pi t)$$



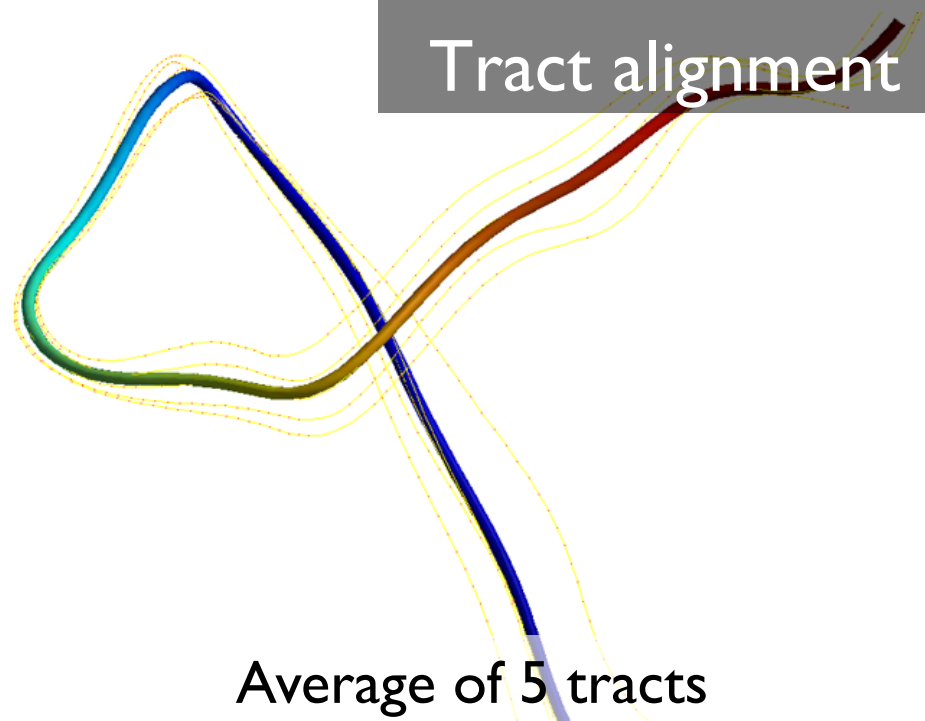
# Cosine series representation



# Tract alignment

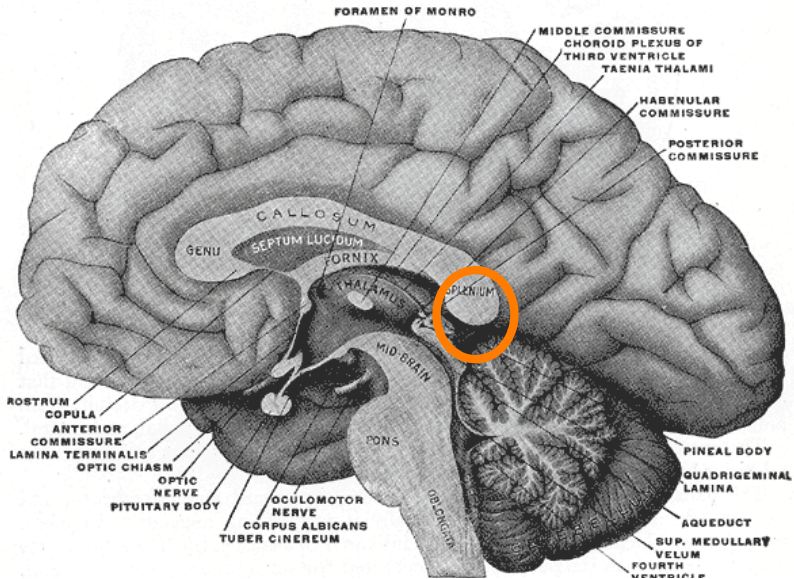


Tract A is registered to tract B

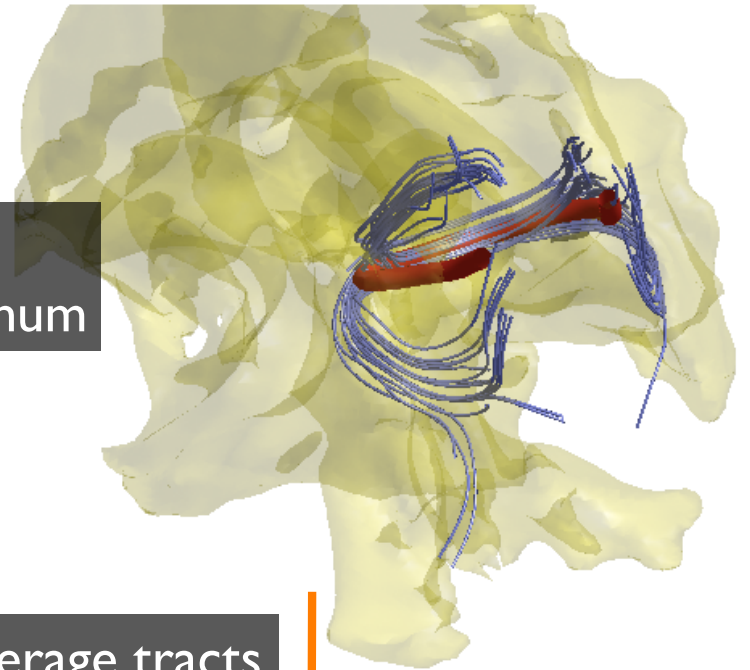


Average of 5 tracts

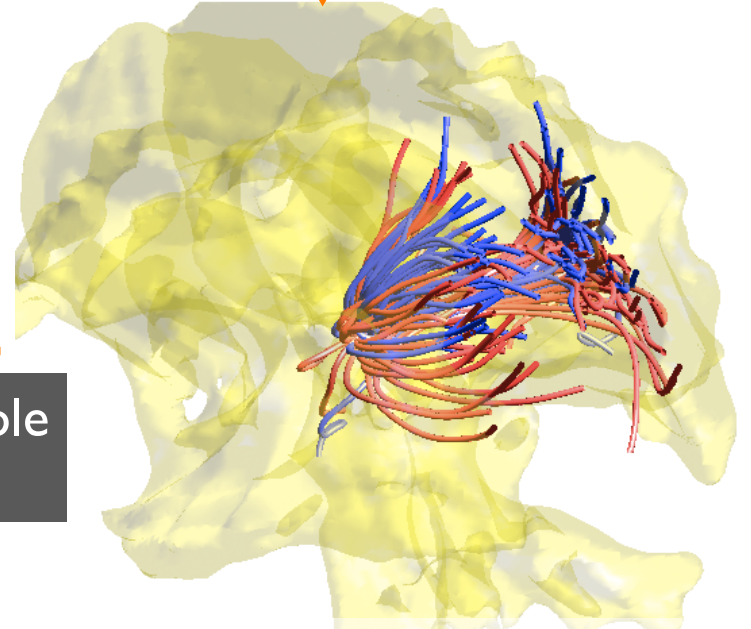
# Fiber concentration analysis



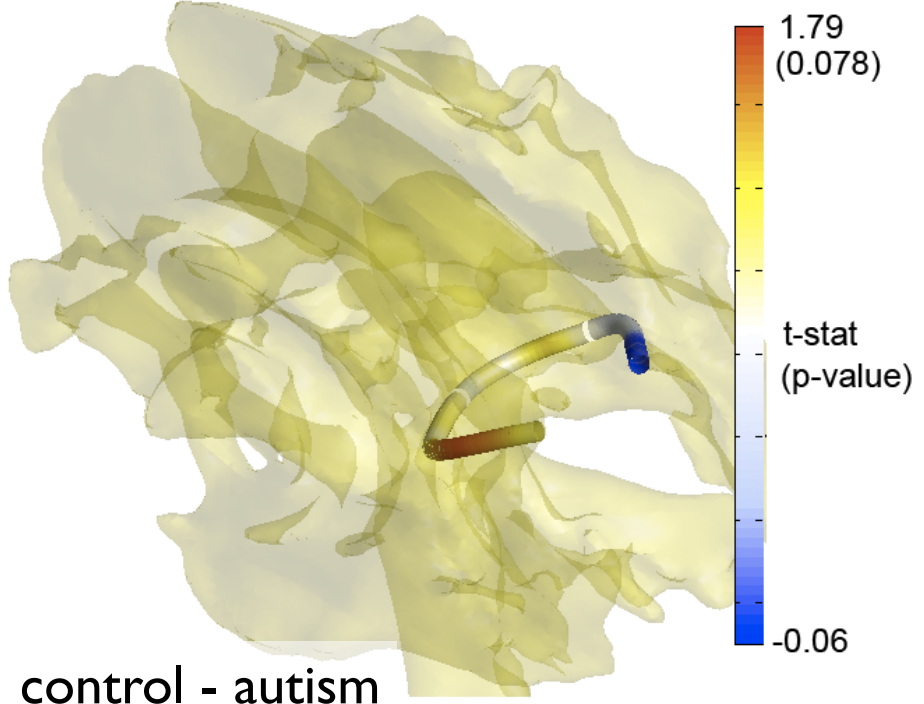
tracts passing through splenium



Average tracts

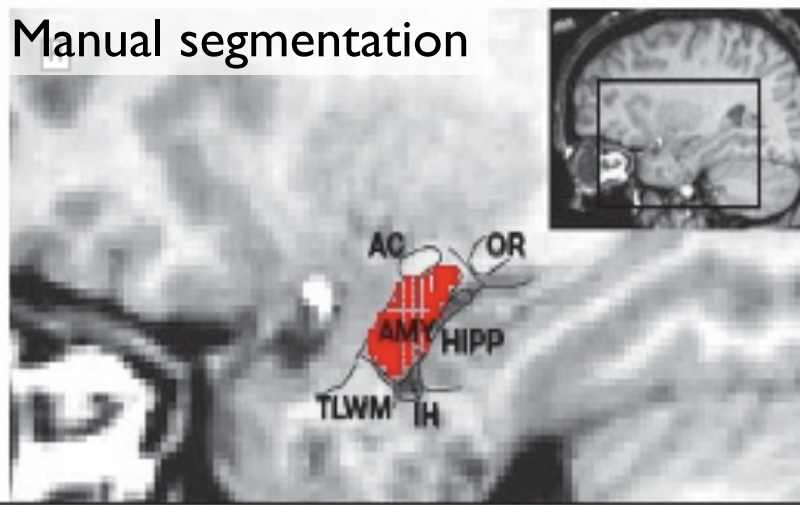


two sample t-test

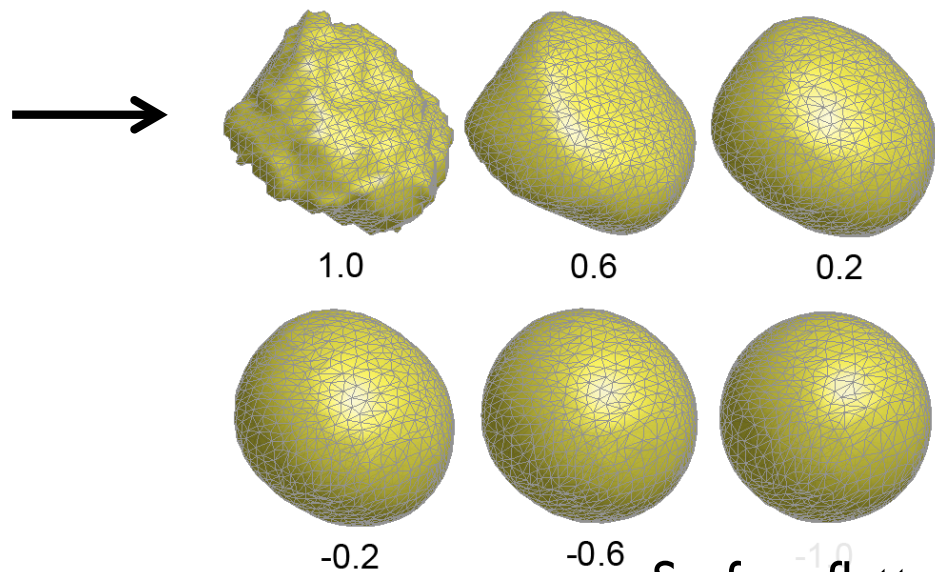


42 autistic & 32 control

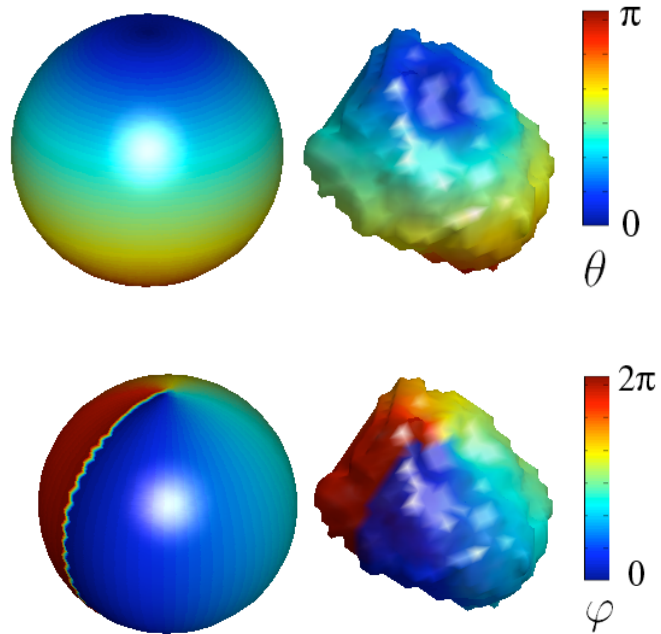
## Manual segmentation



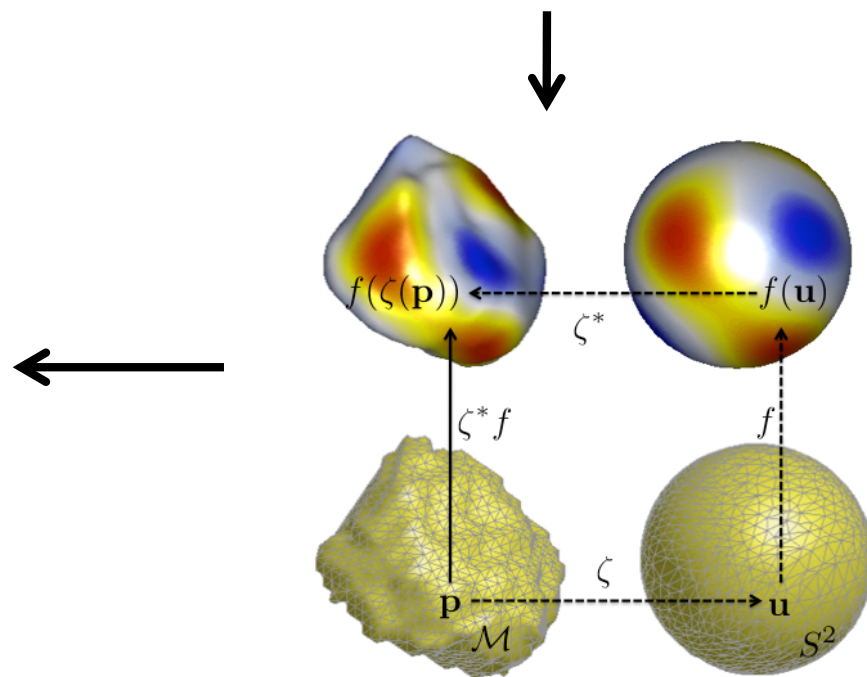
## Spherical coordinates on amygdala



## spherical angles



## Surface flattening





# Fourier Descriptors

## Real hard example

566

IEEE TRANSACTIONS ON MEDICAL IMAGING, VOL. 26, NO. 4, APRIL 2007

### Weighted Fourier Series Representation and Its Application to Quantifying the Amount of Gray Matter

Moo K. Chung\*, Kim M. Dalton, Li Shen, Alan C. Evans, and Richard J. Davidson

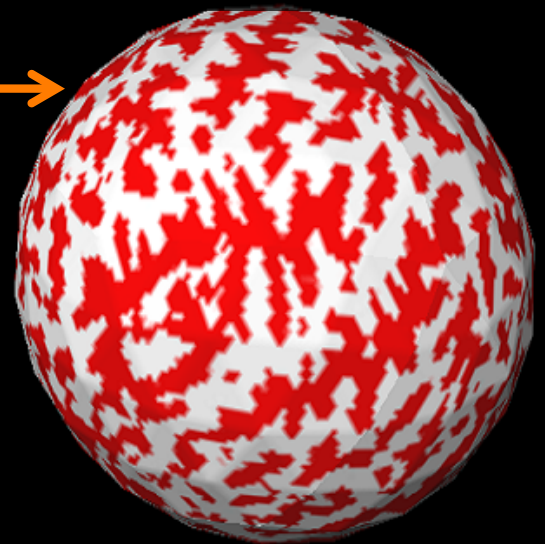
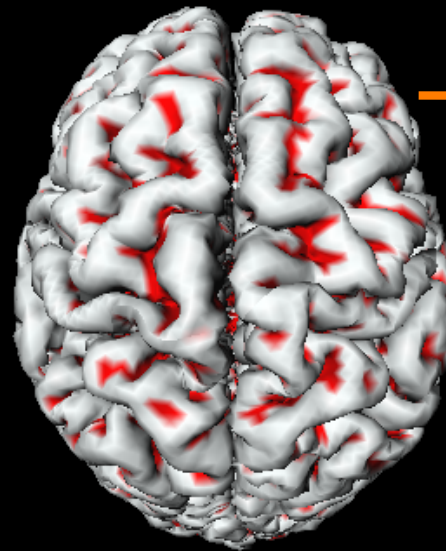
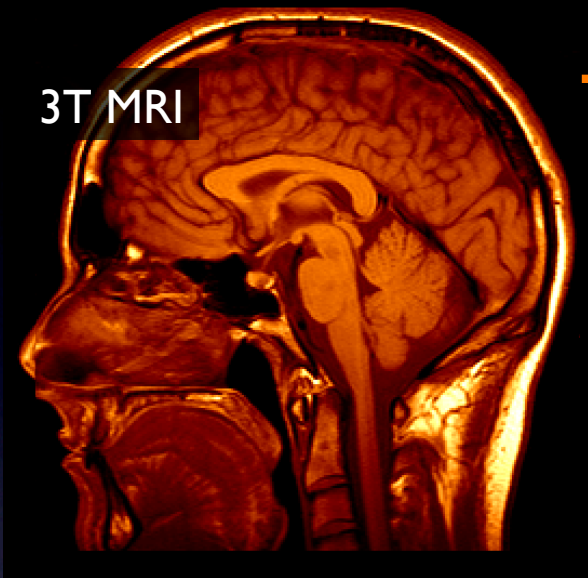
This problem was beyond the capability of average PC (Pentium-3 with 1GB memory) in 2005.

But can be solved with 9 year old laptop with 500MB memory.

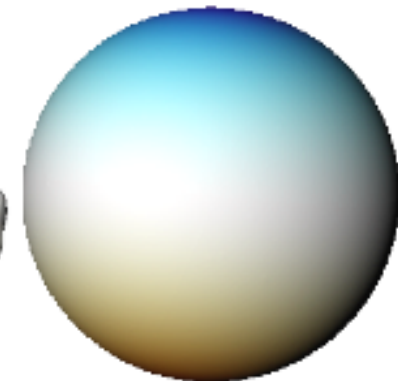
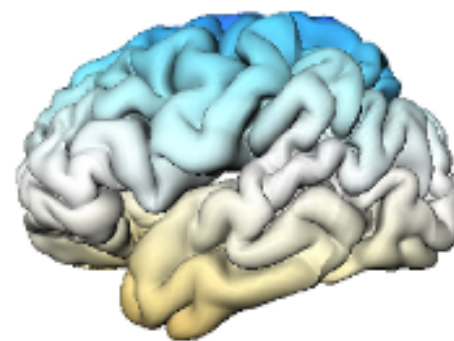
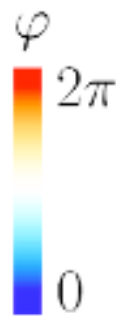
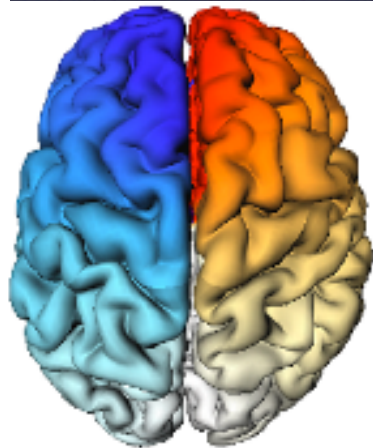
# Spherical Coordinates on Cortex

Deformable surface algorithm

3T MRI

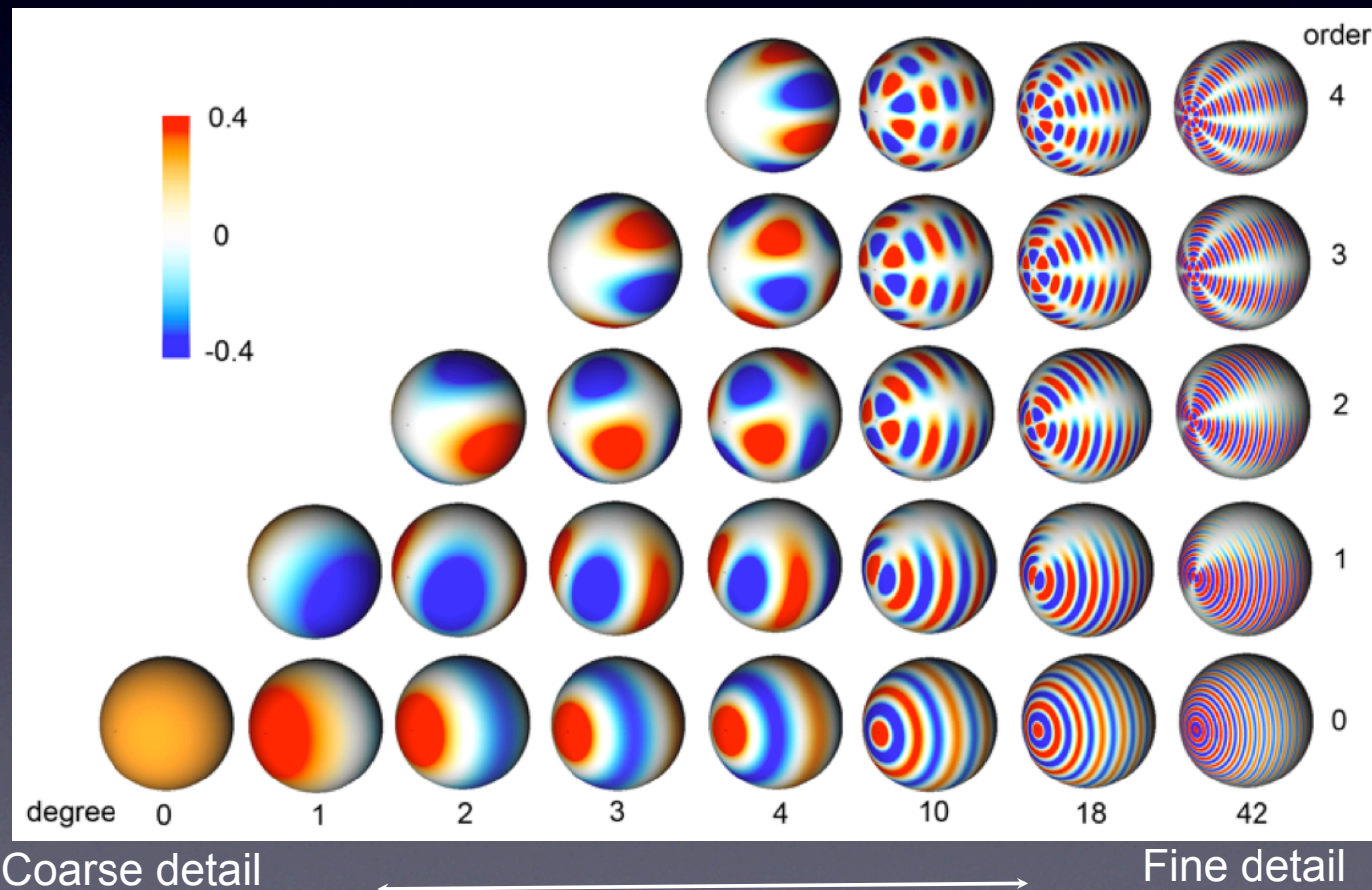


Parameterization



# Spherical harmonic of degree $l$ and order $m$

$$Y_{lm} = \begin{cases} c_{lm} P_l^{|m|}(\cos \theta) \sin(|m|\varphi), & -l \leq m \leq -1, \\ \frac{c_{lm}}{\sqrt{2}} P_l^0(\cos \theta), & m = 0, \\ c_{lm} P_l^{|m|}(\cos \theta) \cos(|m|\varphi), & 1 \leq m \leq l, \end{cases}$$



## Spherical harmonic expansion of cortical thickness

$$\sum_{l=0}^k \sum_{m=-l}^l f_{lm} Y_{lm}(\theta, \varphi) \rightarrow f$$

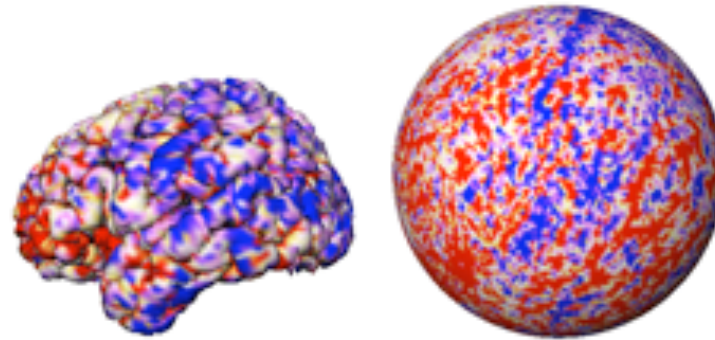
$$f_{lm} = \int_{S^2} f(\theta, \varphi) Y_{lm}(\theta, \varphi) d\theta d\varphi$$

Decomposition of signal on unit sphere

# Spherical harmonic expansion of cortical thickness

white matter

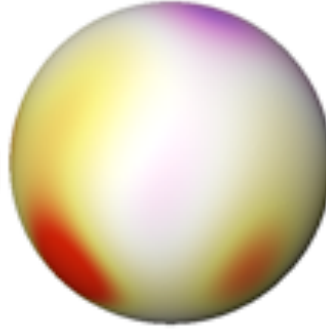
gray matter



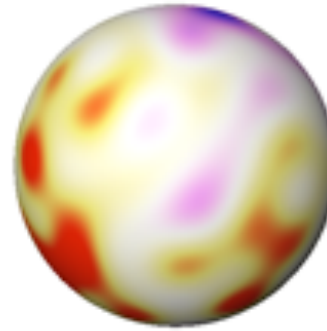
$\sum_{i=1}^k$  k-th degree Expansion



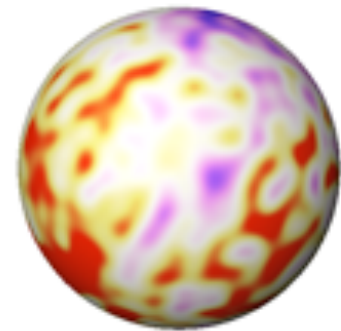
k=1



7



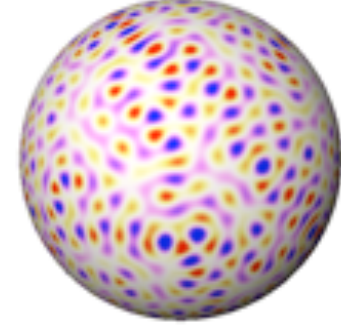
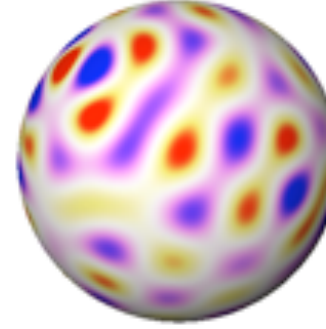
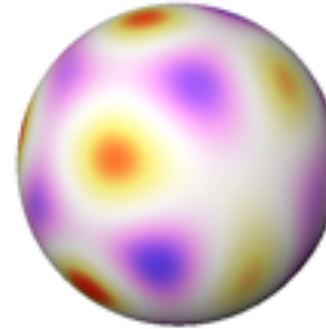
14



42

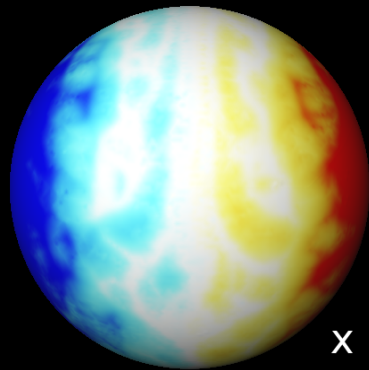


spherical harmonic basis

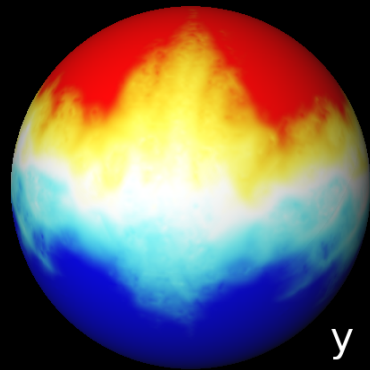


# Fourier expansion of cortex

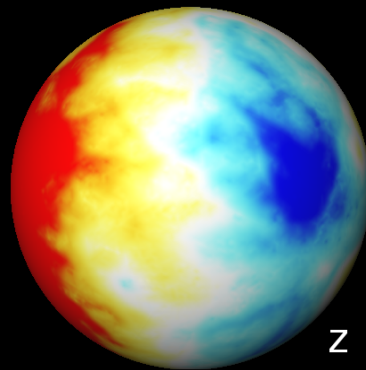
Coordinate functions



x



y

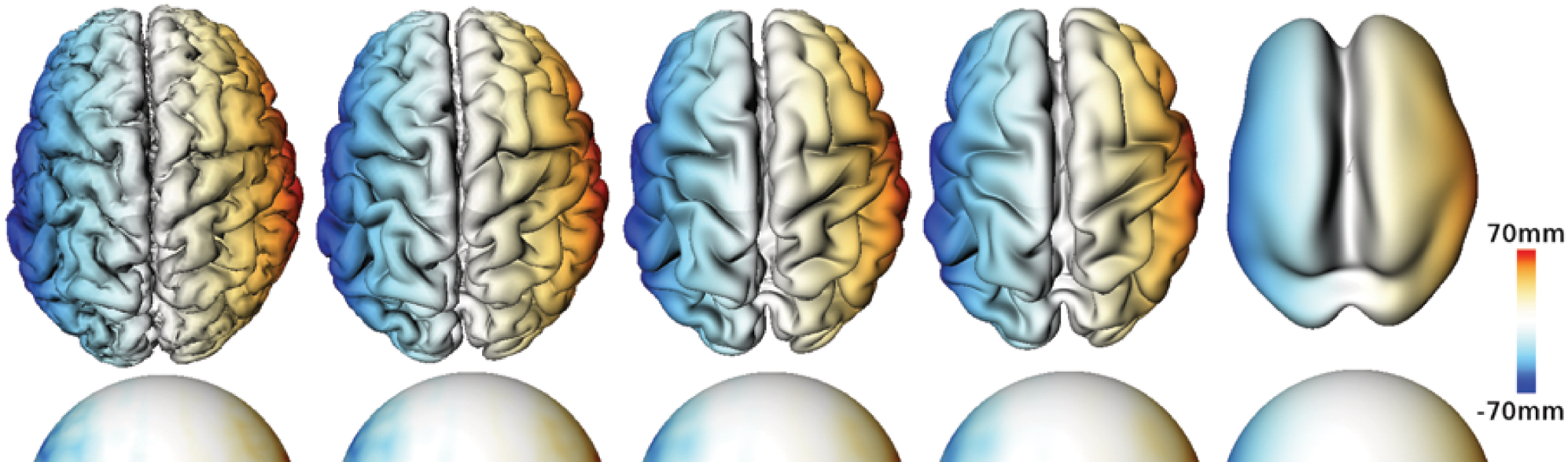


z

cortical  
flattening



Fourier expansion  
of coordinate functions



# Computing Fourier coefficients

$$f_{lm} = \int_{S^2} f(\theta, \varphi) Y_{lm}(\theta, \varphi) d\theta d\varphi$$

Compute for all  $l$  and  $m$  and three coordinates  
= 20000 coefficients. MATLAB (LAPACK) breaks down after order 80. No imaging papers beyond order 40.

*dd*

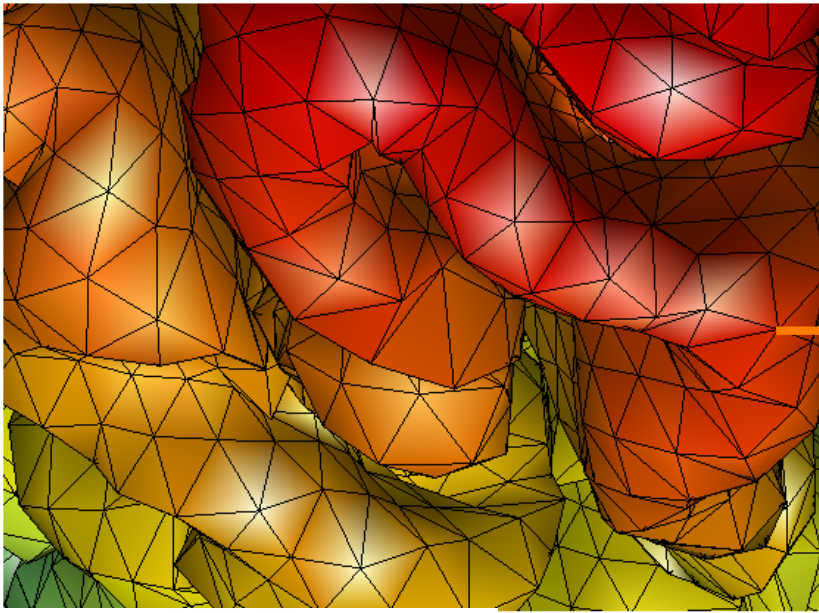
## Available techniques:

Direct numerical & Monte-Carlo integration

Fast spherical harmonic transform

Least squares

# Least squares estimation



at the  $i$ -th vertex  $p_i$

$$f(p_i) = \sum_{l=0}^k \sum_{m=-l}^l \beta_{lm} Y_{lm}(p_i)$$

$$\mathbf{f} = \mathbf{Y} \boldsymbol{\beta}$$

Matrix inversion  
up to size 1 million!

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



After two months of  
stupid struggle,  
I was like this in 2006



# Iterative residual fitting (IRF) algorithm

Step 1. measurements  $f(p_1), \dots, f(p_n)$

Step 2. Set initial degree=0  $k = 0$

Step 3. Solve  $f(p_i) = \sum_{m=-k}^k \beta_{km} Y_{km}(p_i)$  Project data into a finite subspace

Step 3.5.  $f \leftarrow f - \hat{f}$  Once low frequency parts are estimated, we throw them away

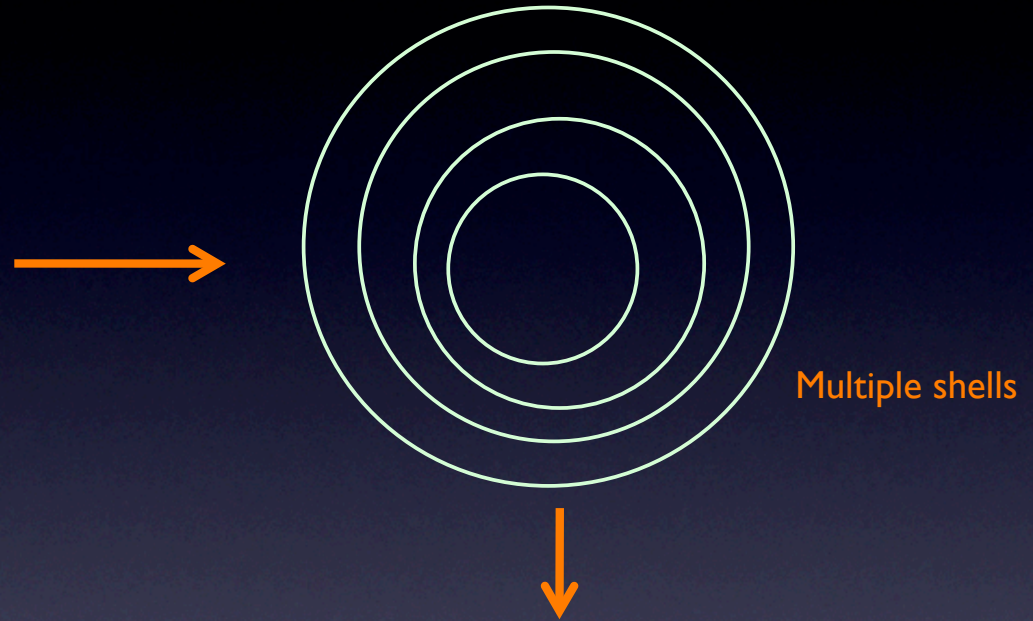
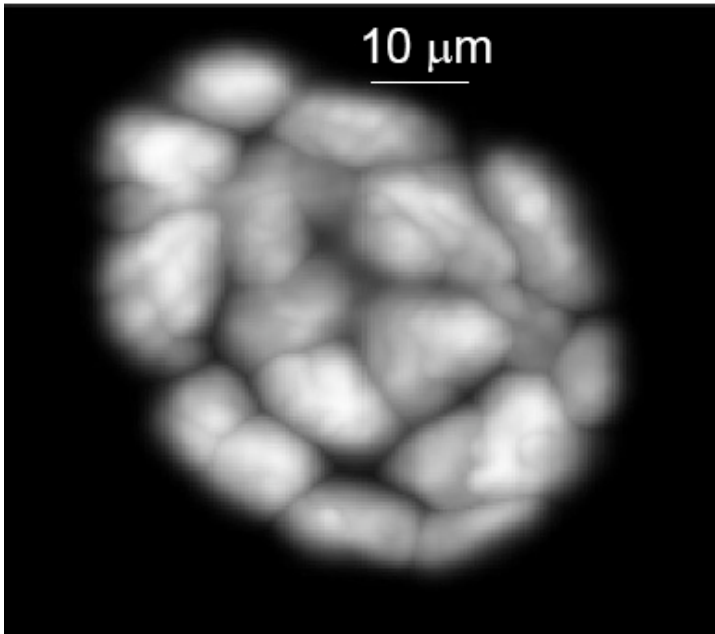
Step 4. Set degree  $k \leftarrow k + 1$



MATLAB code available at <http://www.stat.wisc.edu/~mchung/>

# Direct application of IRF

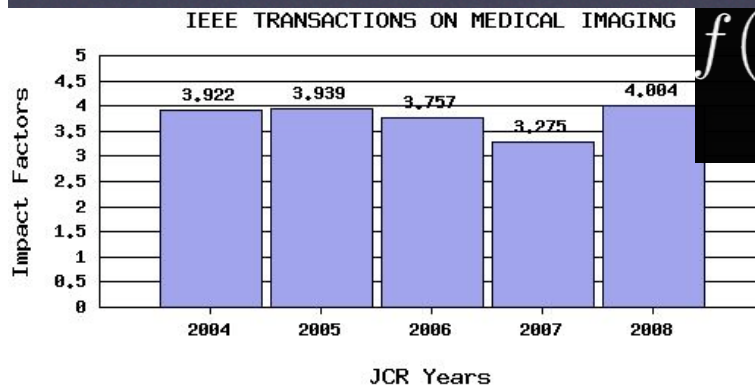
Reconstruction of 3D microscopic image data using spherical harmonics



TMI 2007: 9 references

TMI 2008: 11 references

Humongous linear system involving spherical harmonics



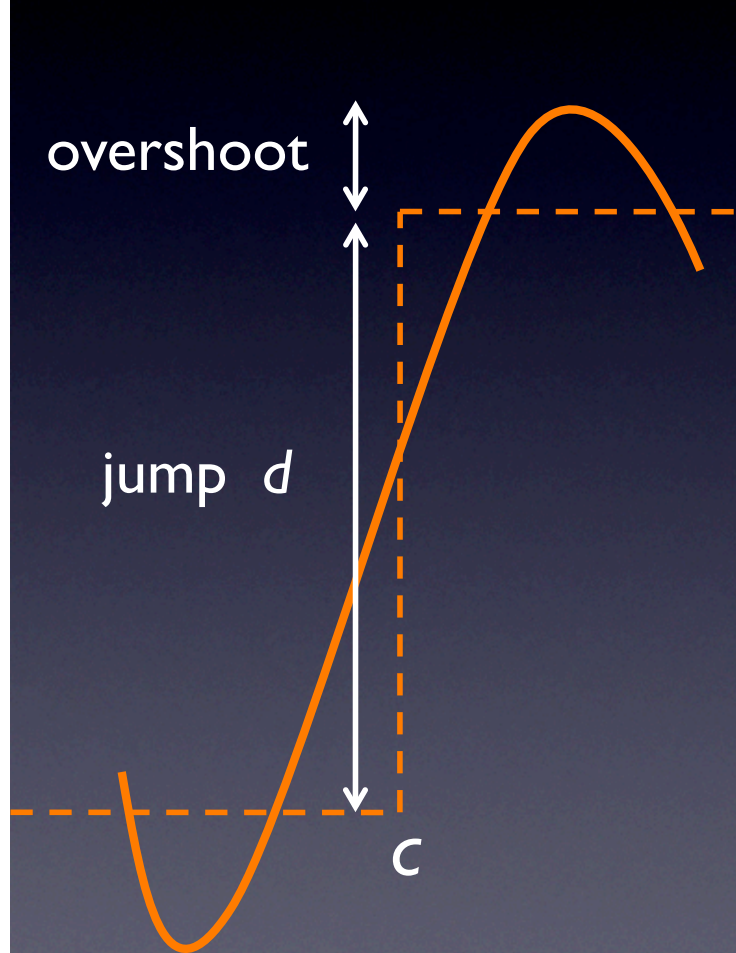
$$f(\theta, \varphi, r) = \sum_i \sum_j \sum_k \beta_{ijk} Y_{ijk}(\theta, \varphi, r)$$

Khairy et al., 2008 MICCAI

Fourier approach is not perfect

**Gibbs phenomenon**

Spherical harmonic expansion is only good for smooth & continuous signal

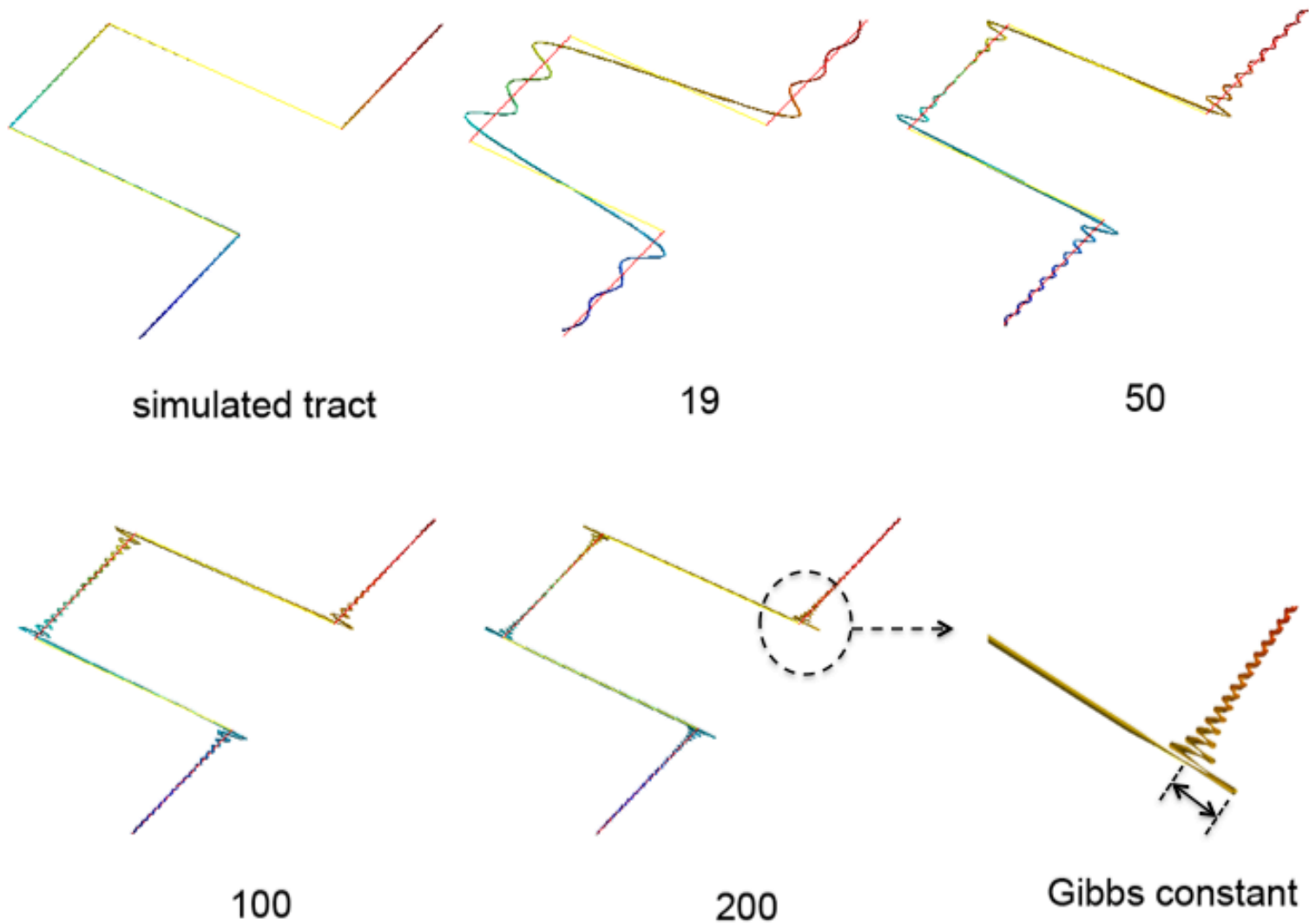


## Gibbs Phenomenon

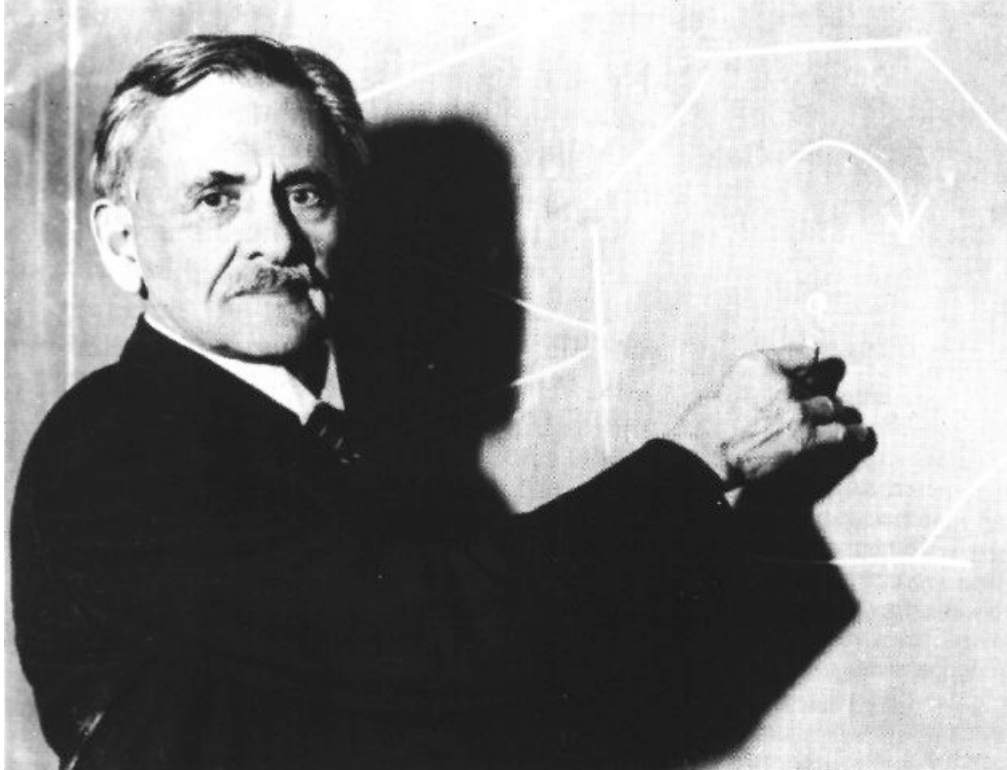
Mathematician Henry Willbraham published a paper on Gibbs phenomenon in 1848 but did not attract any attention.

# Gibbs phenomenon on a simulated white matter tract

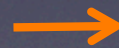
## Overshooting at jump discontinuity



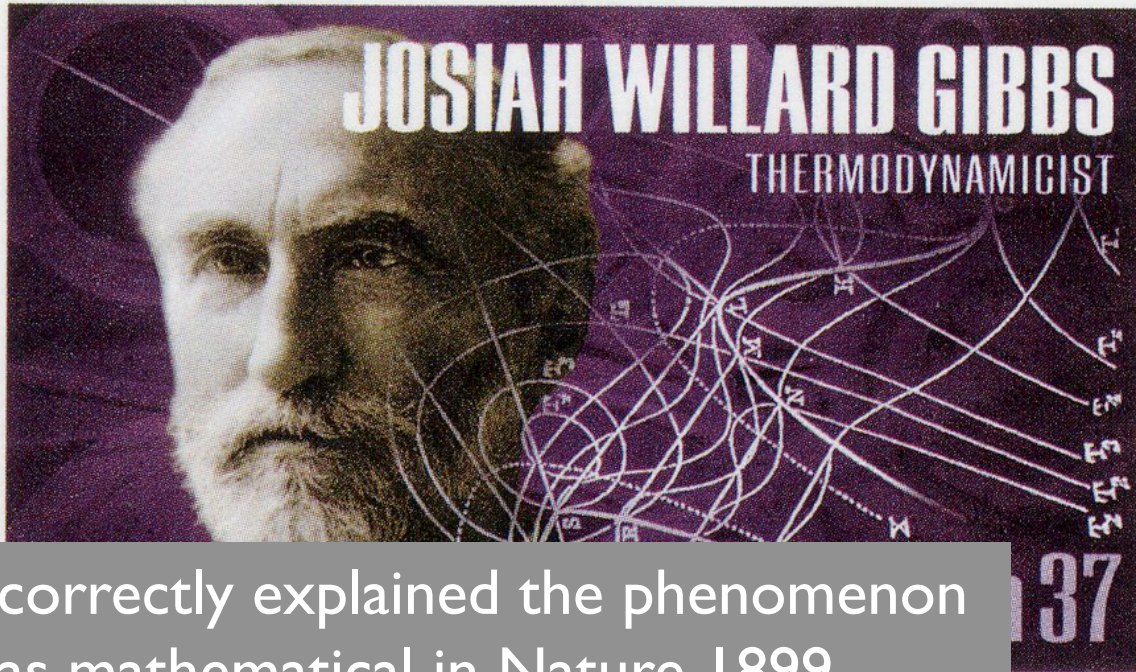
# Albert Abraham Michelson



The Michelson-Stratton harmonic analyzer, one of the first mechanical analogue computers, recorded data from spectroscopic experiments.



Observed the phenomenon but assumed it to be mechanical error

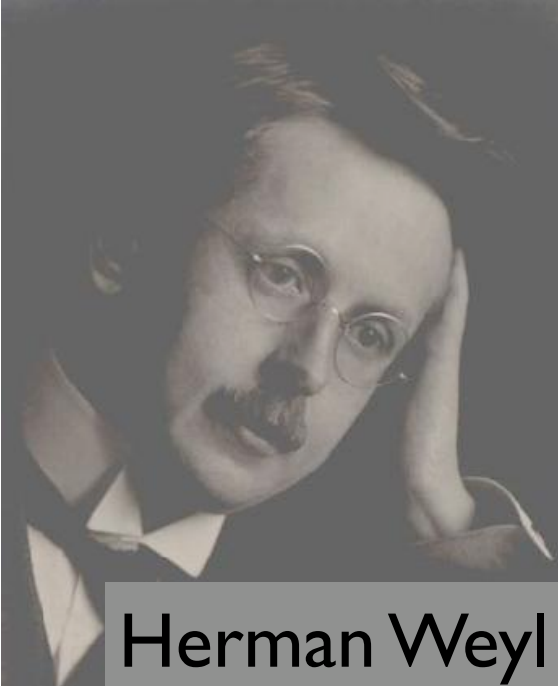


correctly explained the phenomenon as mathematical in Nature 1899.

Maxime Bocher



Gave detailed mathematical analysis and named it Gibbs phenomenon in 1906.

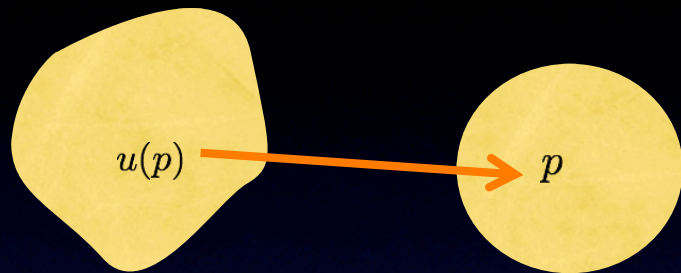


Herman Weyl

Investigated the Gibbs phenomenon associated with spherical harmonics in 1968.

# How do we reduce the Gibbs phenomenon?

## Weighted Fourier Analysis



manifold  $\mathcal{M}$

parameter space  $\mathcal{N}$

tracts, amygdala,  
hippocampus,  
cortical surface

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

Input signal

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

Weighted Fourier series

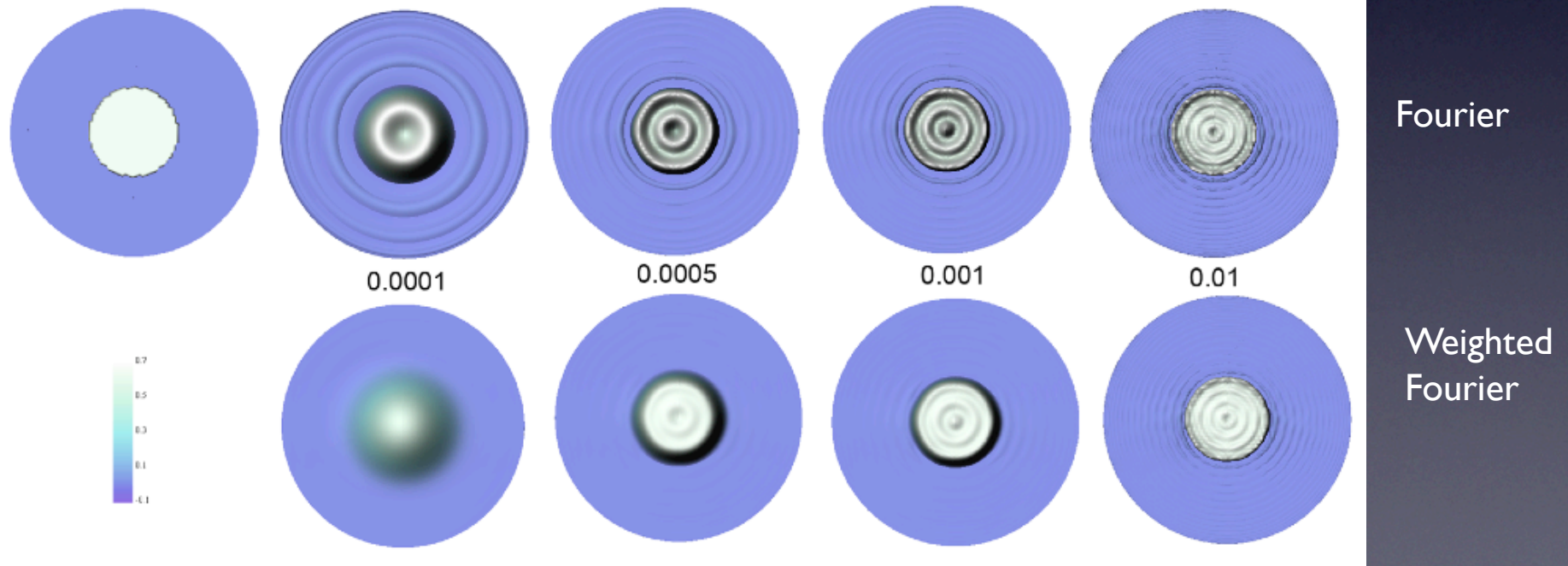
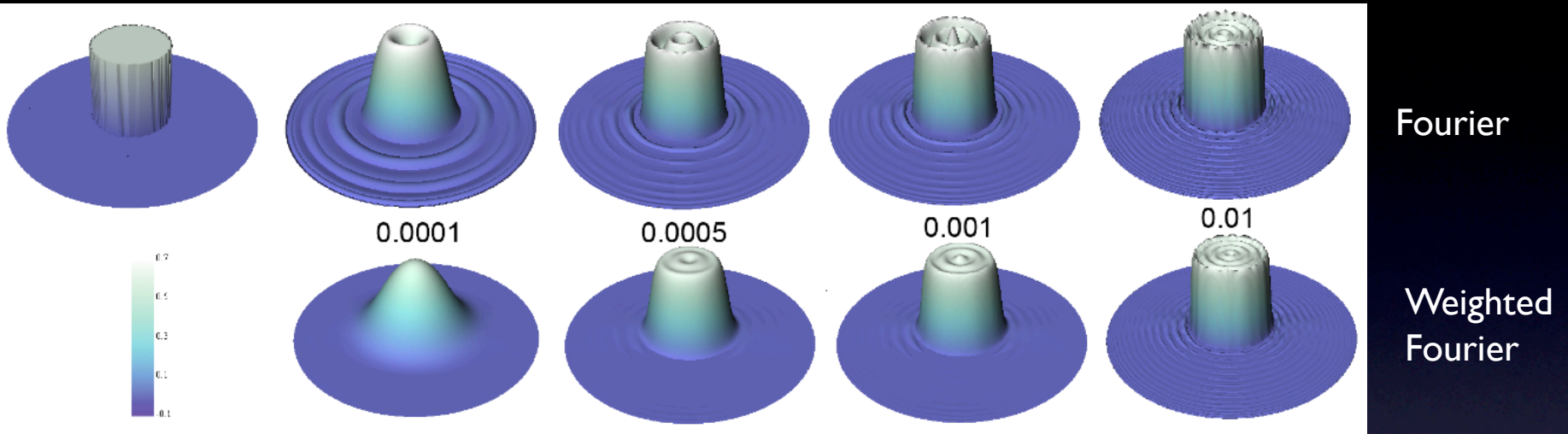
$$g(p, t) = \sum_{j=0}^{\infty} e^{-\lambda_j t} \langle f, \psi_j \rangle \psi_j(p)$$

Kernel smoothing

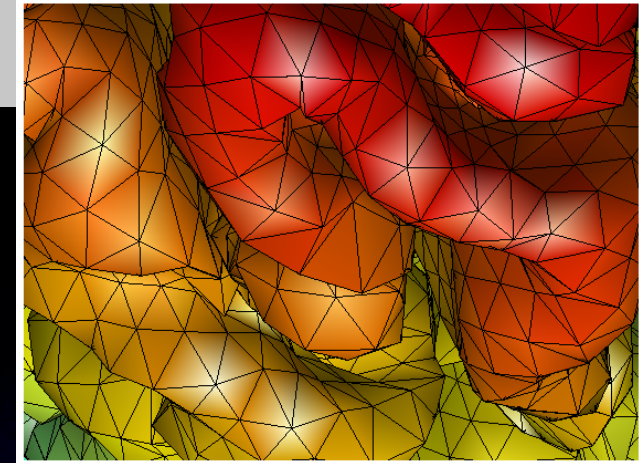
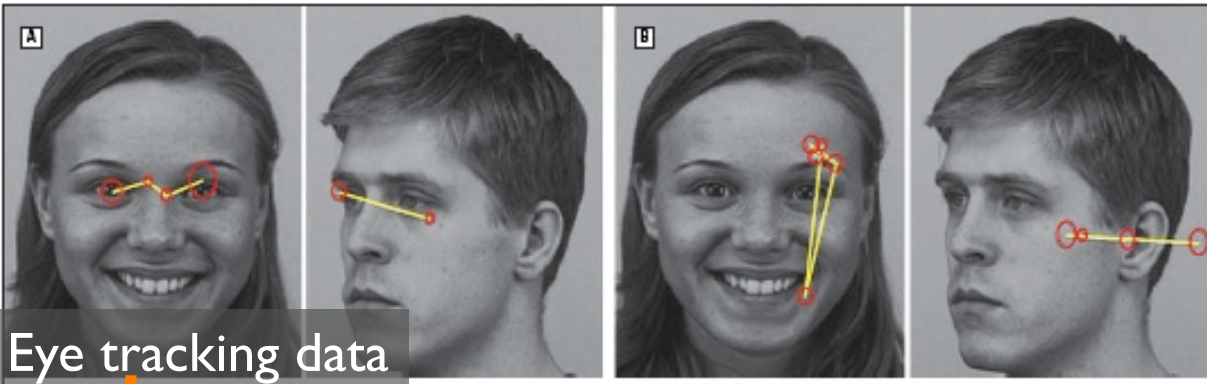
$$= \int_{\mathcal{N}} K_t(p, q) f(q) d\mu(q)$$



# Gibbs phenomenon on hat shaped surface

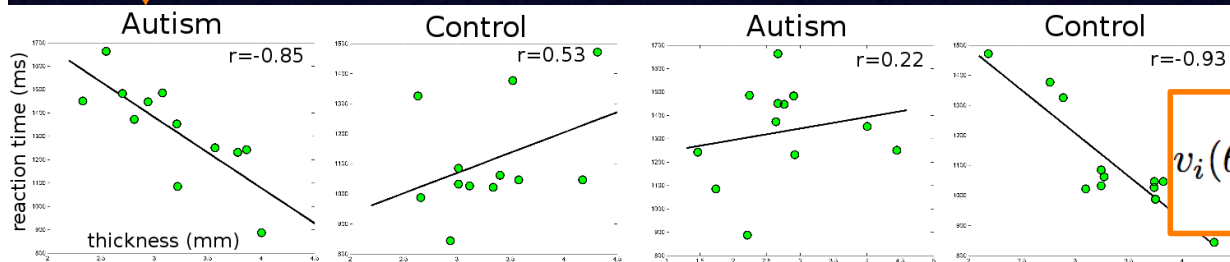


# Brain & behavior correlation

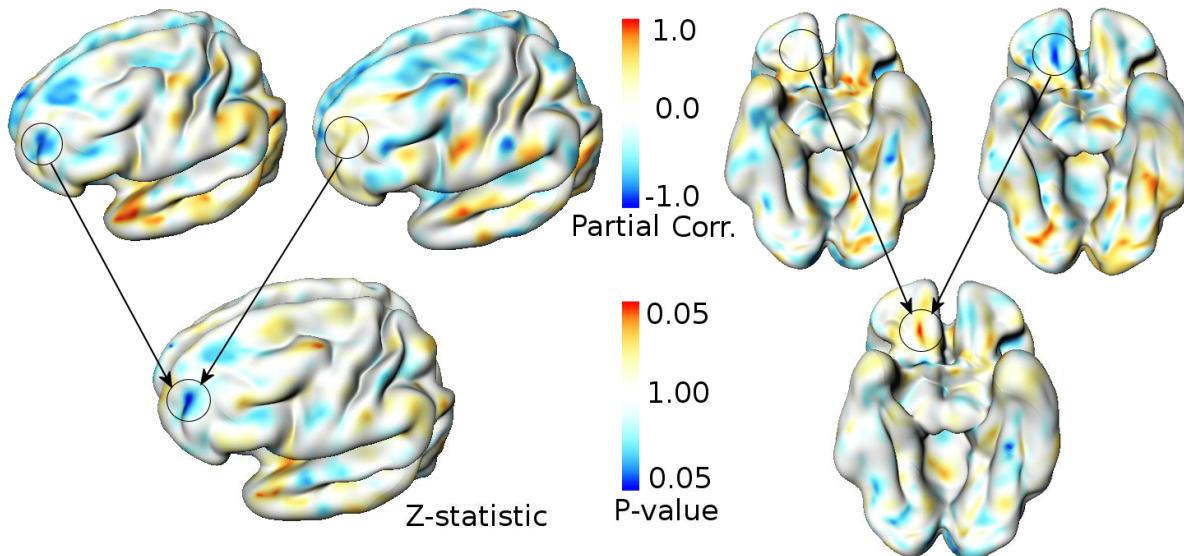


Partial correlation of thickness & gaze duration

Weighted Fourier representation



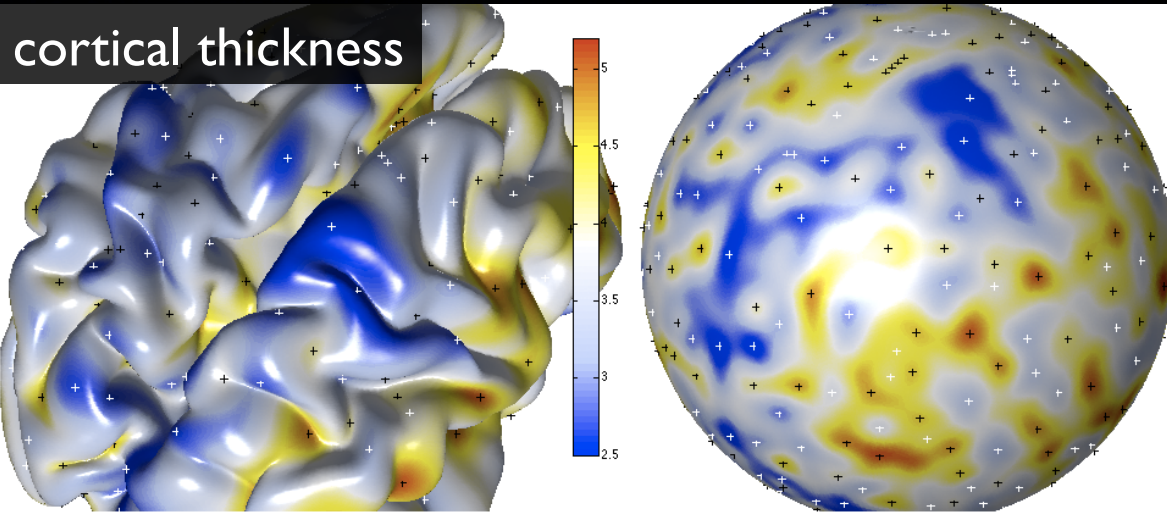
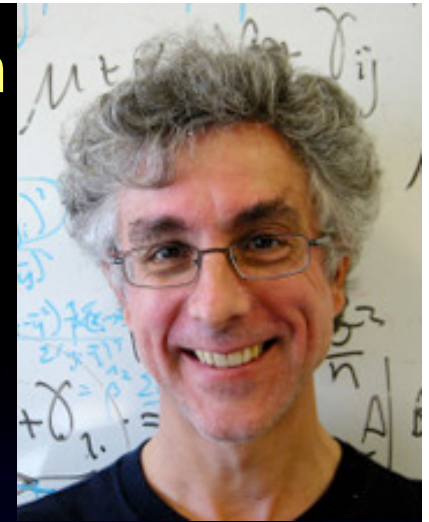
$$v_i(\theta, \varphi) = \sum_{l=0}^k \sum_{m=-l}^l e^{-l(l+1)\sigma} f_{lm}^i Y_{lm}(\theta, \varphi)$$



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
.....		

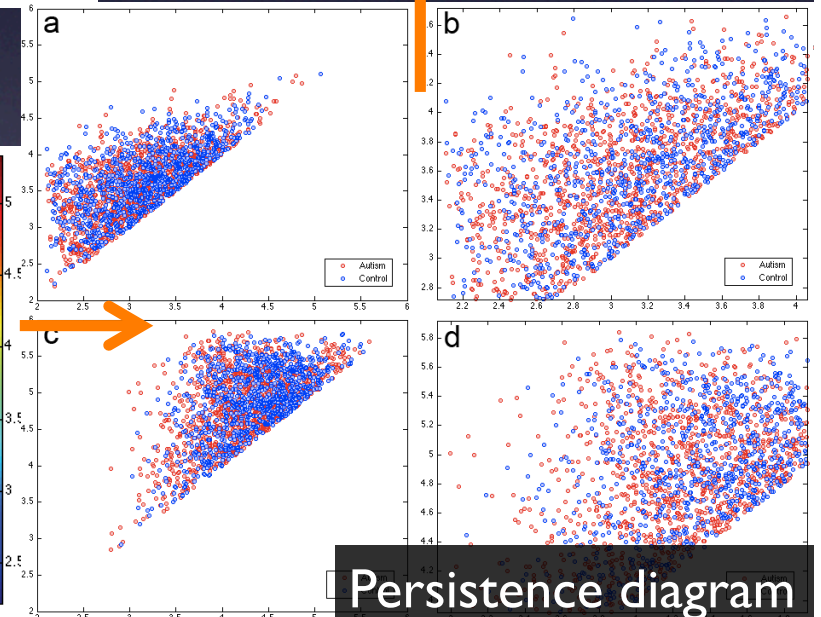
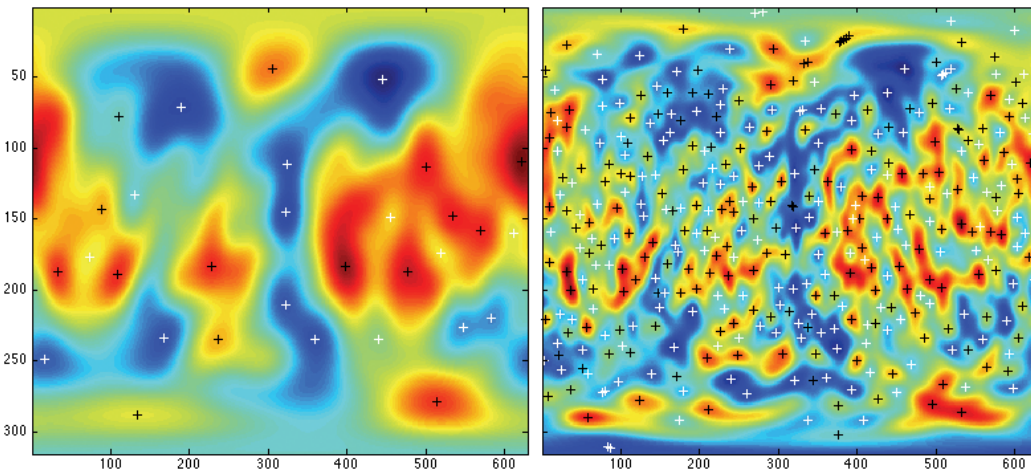
# Persistence homology based signal detection

*Euler characteristic, Betti numbers, Morse functions, Worsley's random field theory.*



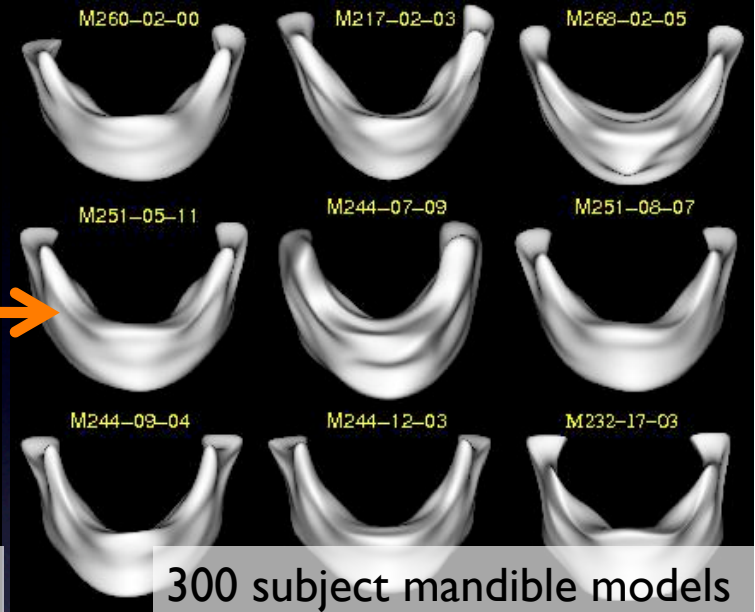
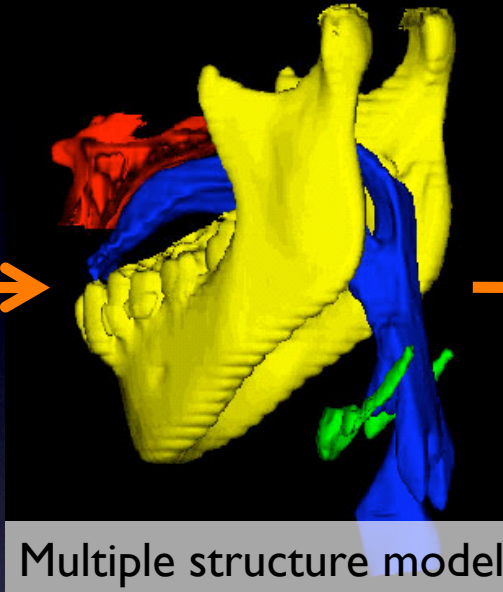
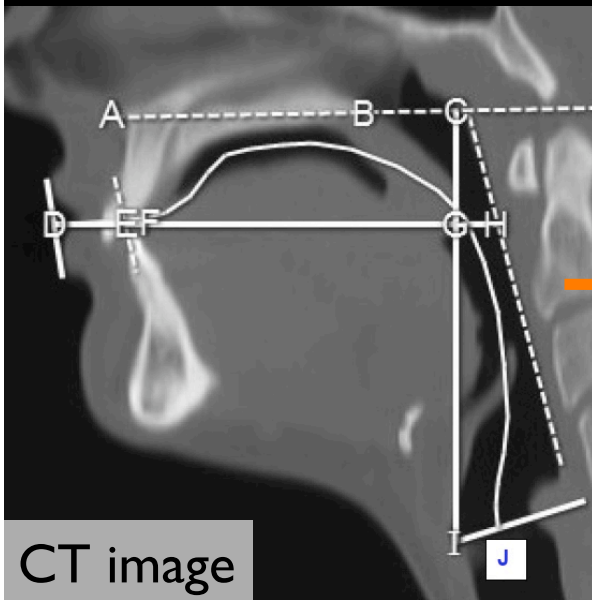
Topological classification 96%  
Previous method 90%

cortical flattening



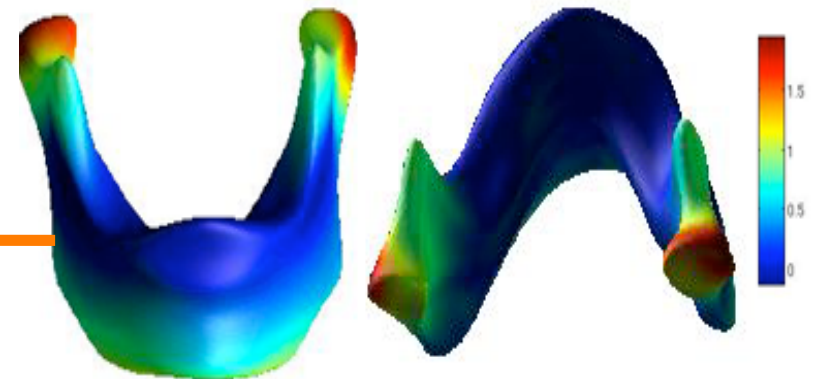
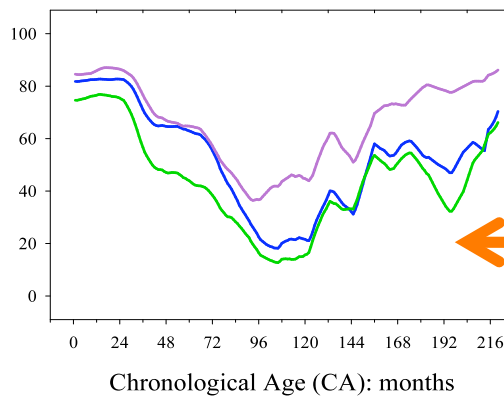
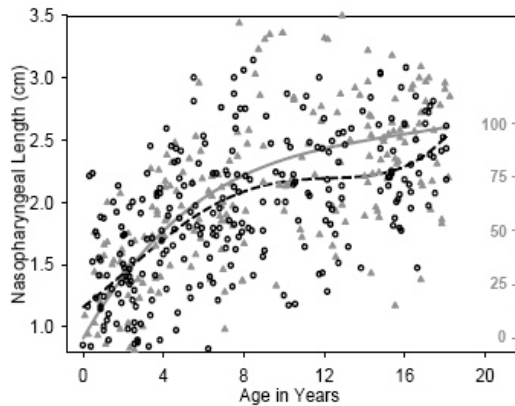
Persistence diagram

# Longitudinal growth modeling on mandible CT images



Longitudinal modeling

Growth rate modeling  
with weighted Fourier



# WCU-Project till the end of 2011

with Drs. Dong Soo Lee and Jae-Sung Lee (SNU), and  
Drs. Andrew Alexander and Richard Davidson (Madison)  
plus many *hardworking postdocs* in both places

## Brain connectivity analysis

### Wiring brain

↓ teaching

Neuroimage processing (2009 fall)

Computational Methods in neuroImage Analysis (2010 fall)

Statistical methods in neuroimage analysis (2011 fall)

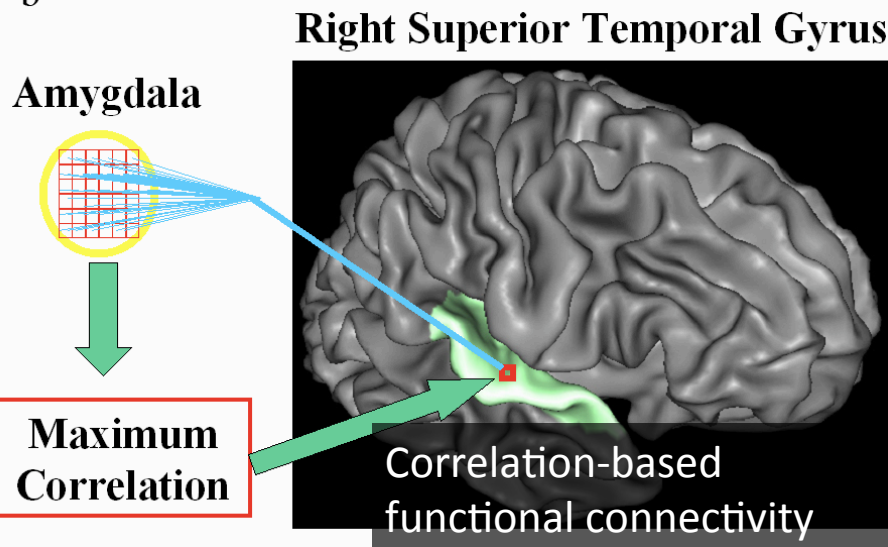
↓ book publication

Computational Neuroanatomy (2011)

Statistical and Computational Methods in Brain Image Analysis (2012)

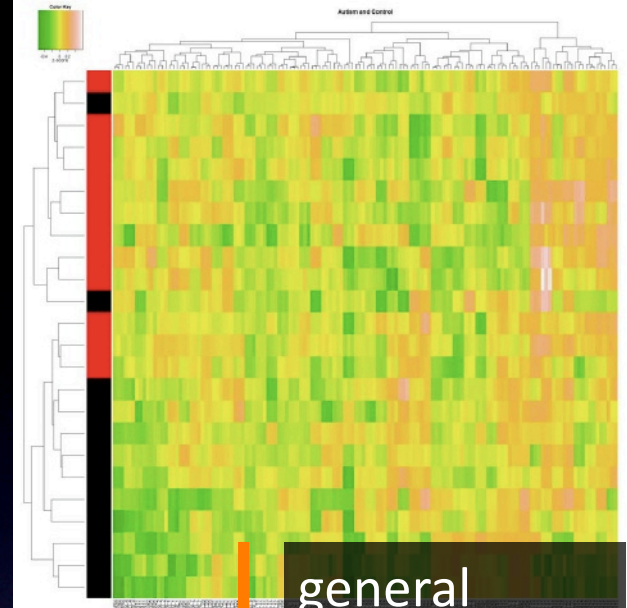
# functional (fMRI) connectivity: effective style

Daniel J. Kelley PhD thesis

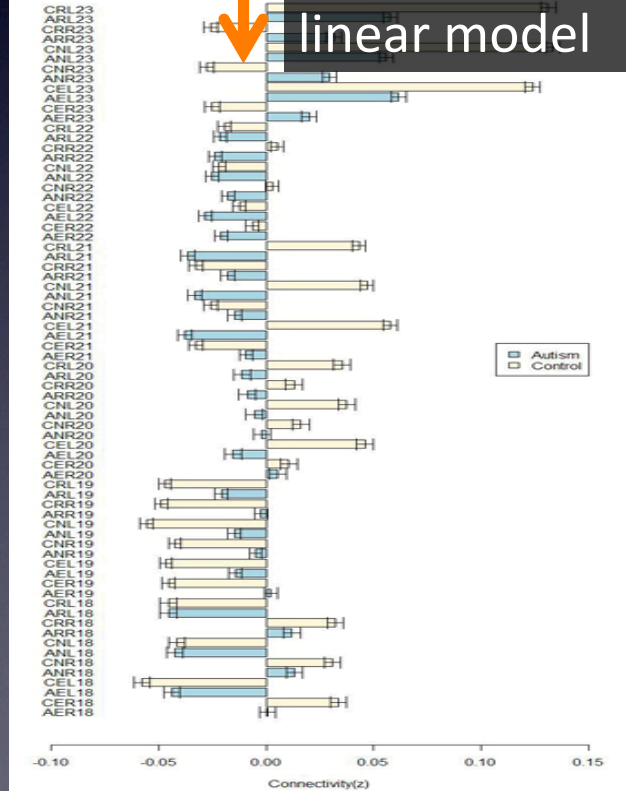


distance on correlation

hieratical clustering

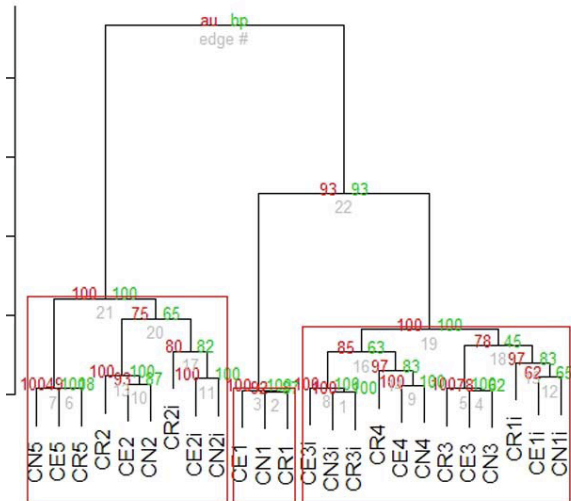
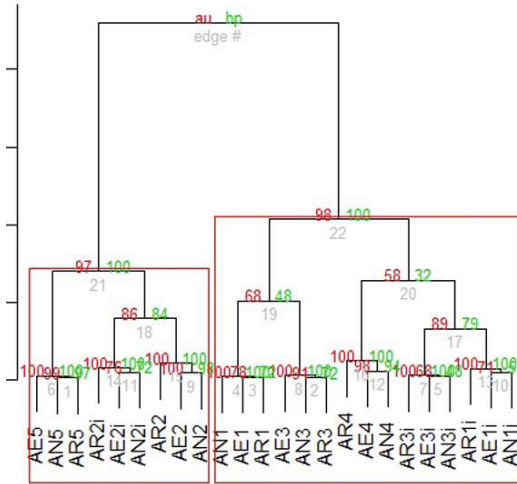


general linear model

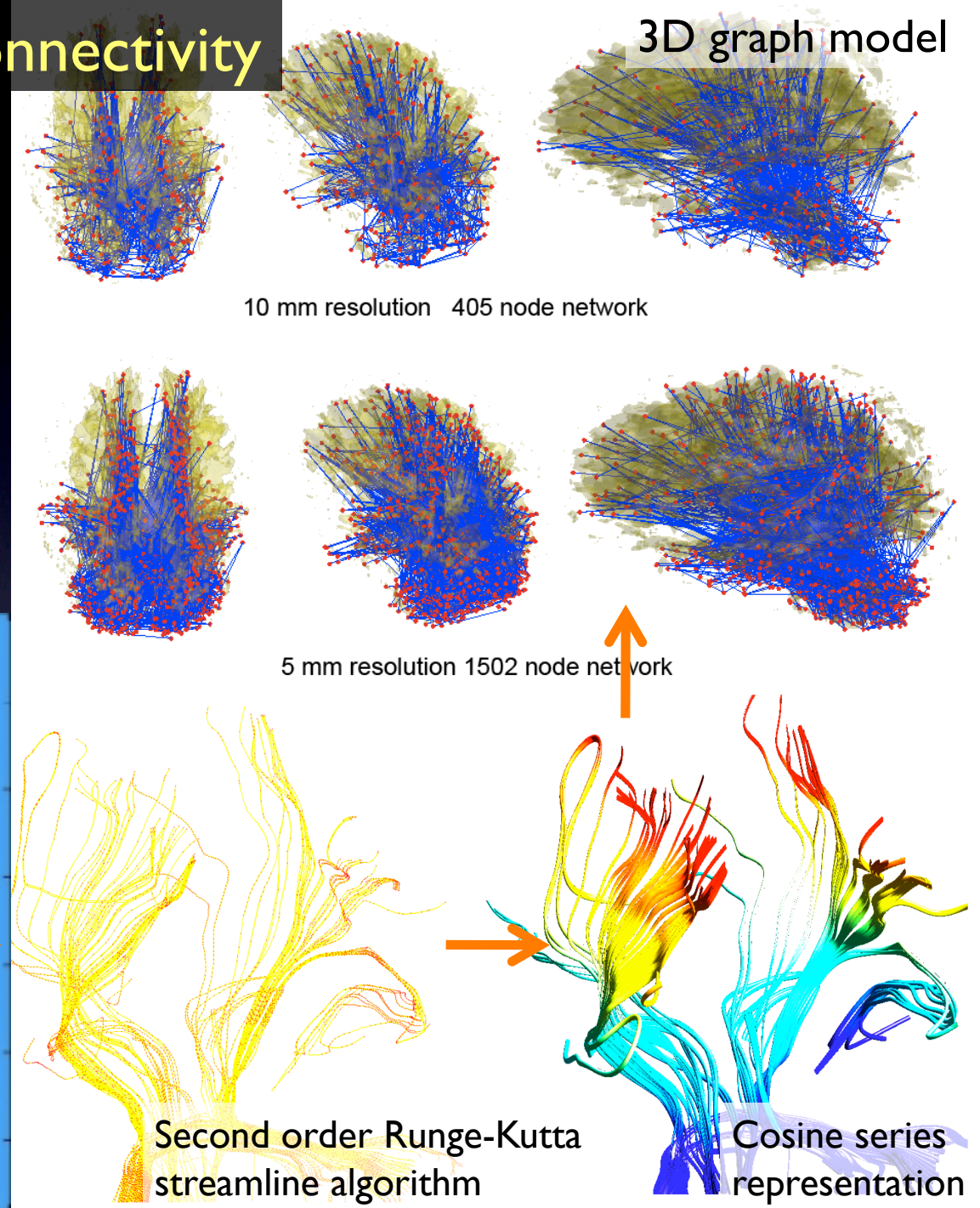
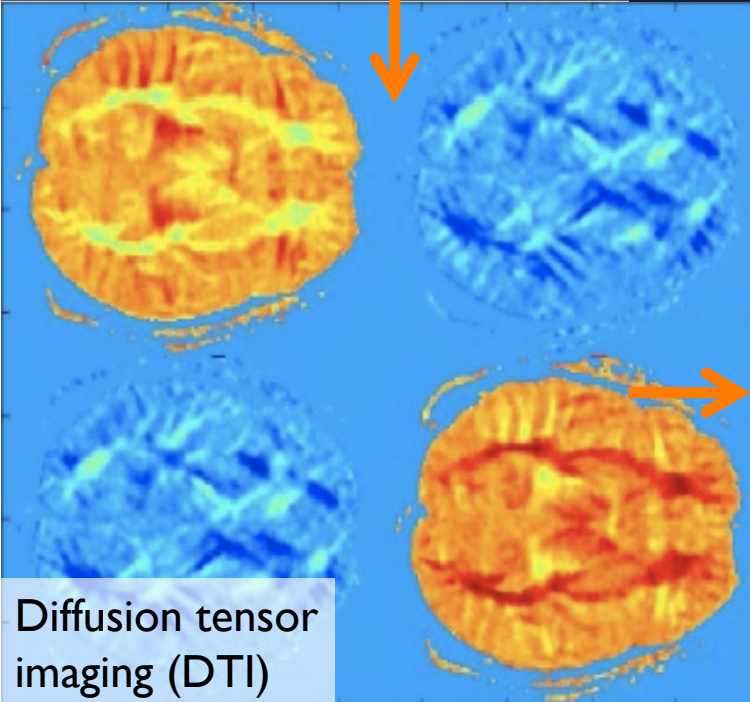


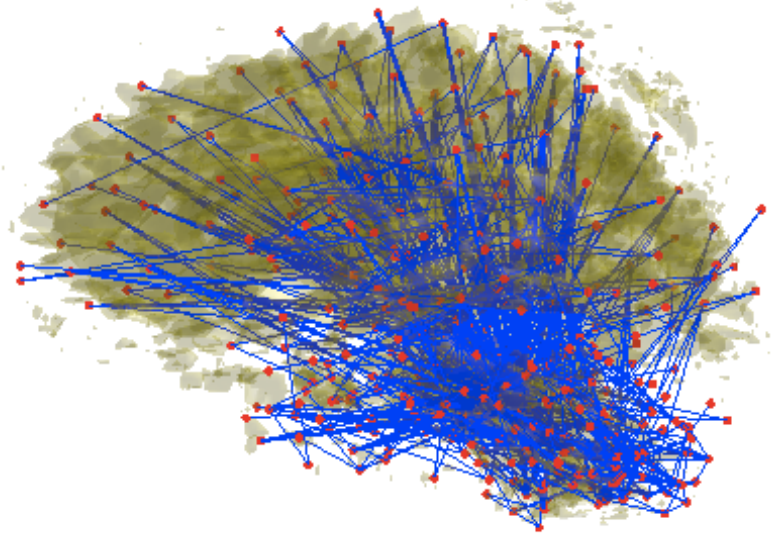
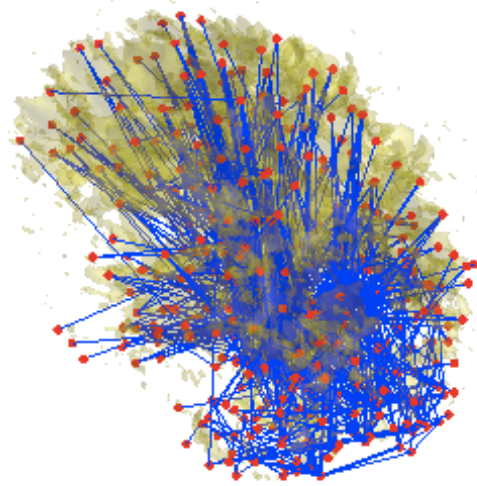
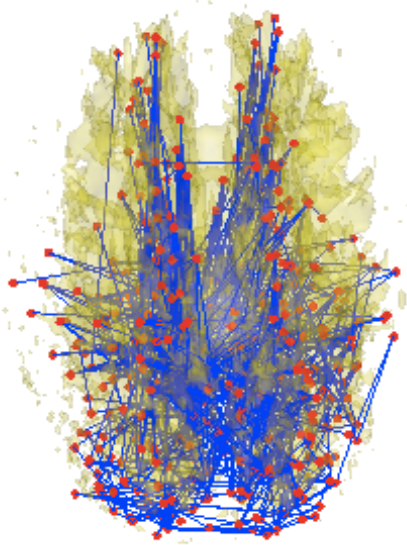
Autism

Control

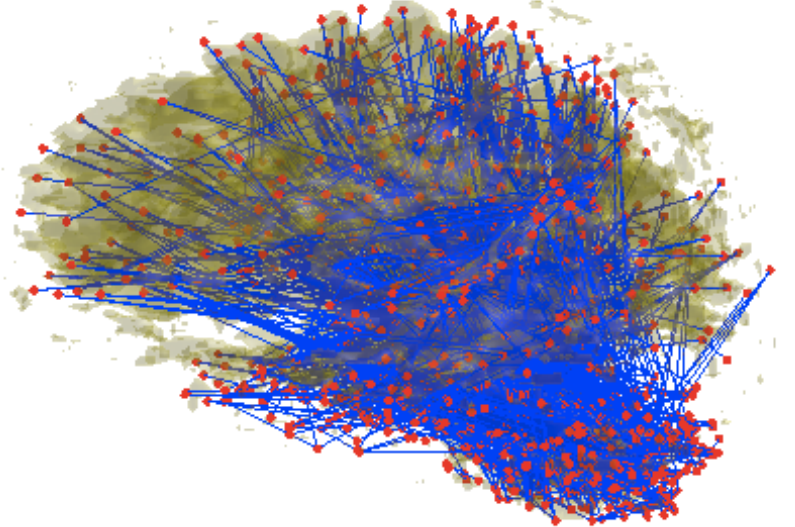
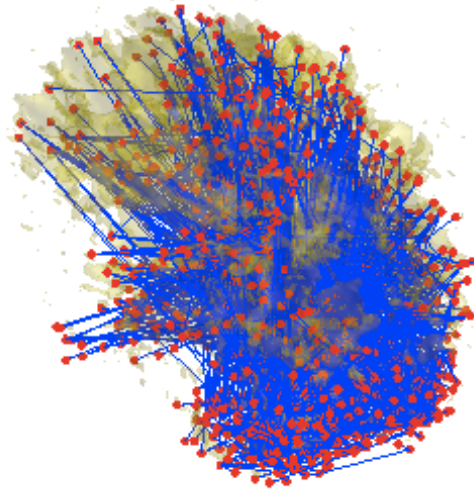
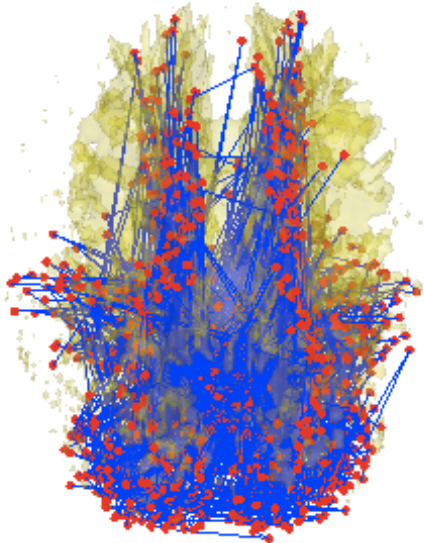


# White Matter Fiber Connectivity



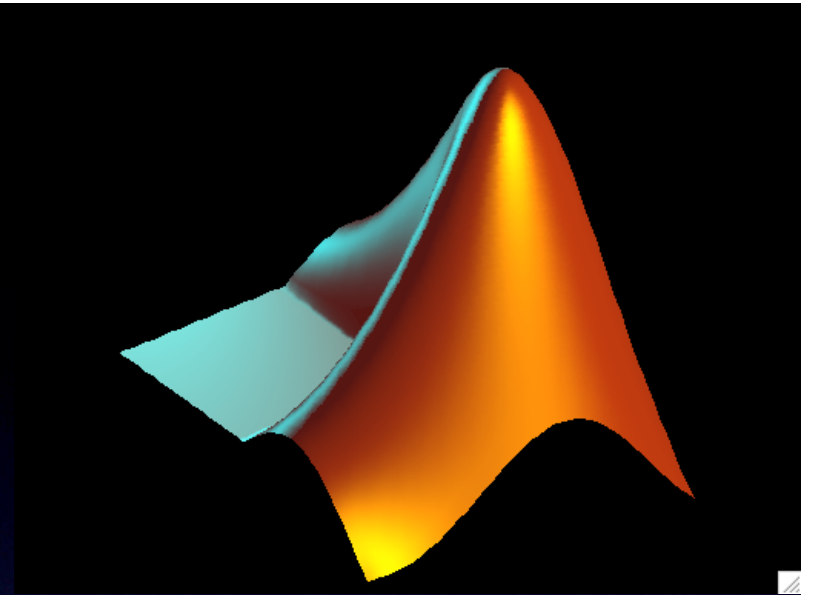


10 mm resolution 405 node network



5 mm resolution 1502 node network





# MATLAB

## demonstration

# Acknowledgement

Andrew Alexander, Jee Eun Lee,  
Richard Davidson, Kim Dalton,  
Nagesh Aldur, Houri Voperian,  
Daniel Kelley, Brendon Nacewicz

University of Wisconsin-Madison



Thank you.  
send email for whatever questions,  
collaboration request to  
[mkchung@wisc.edu](mailto:mkchung@wisc.edu)