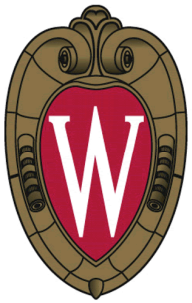

University of Wisconsin
SCHOOL OF MEDICINE
AND PUBLIC HEALTH

NeuroImage Analysis

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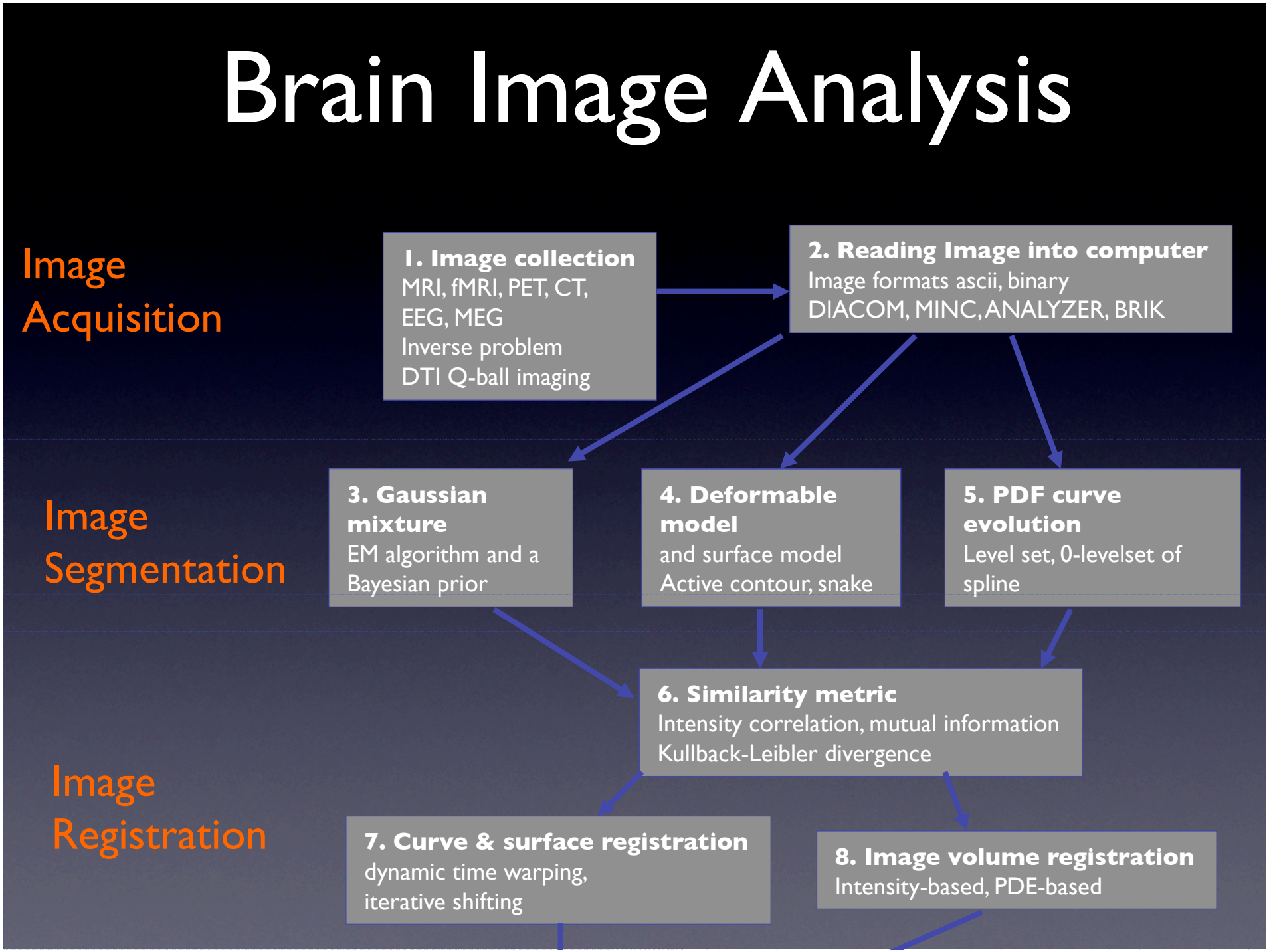
SNU PBCS lecture
October 4, 2011

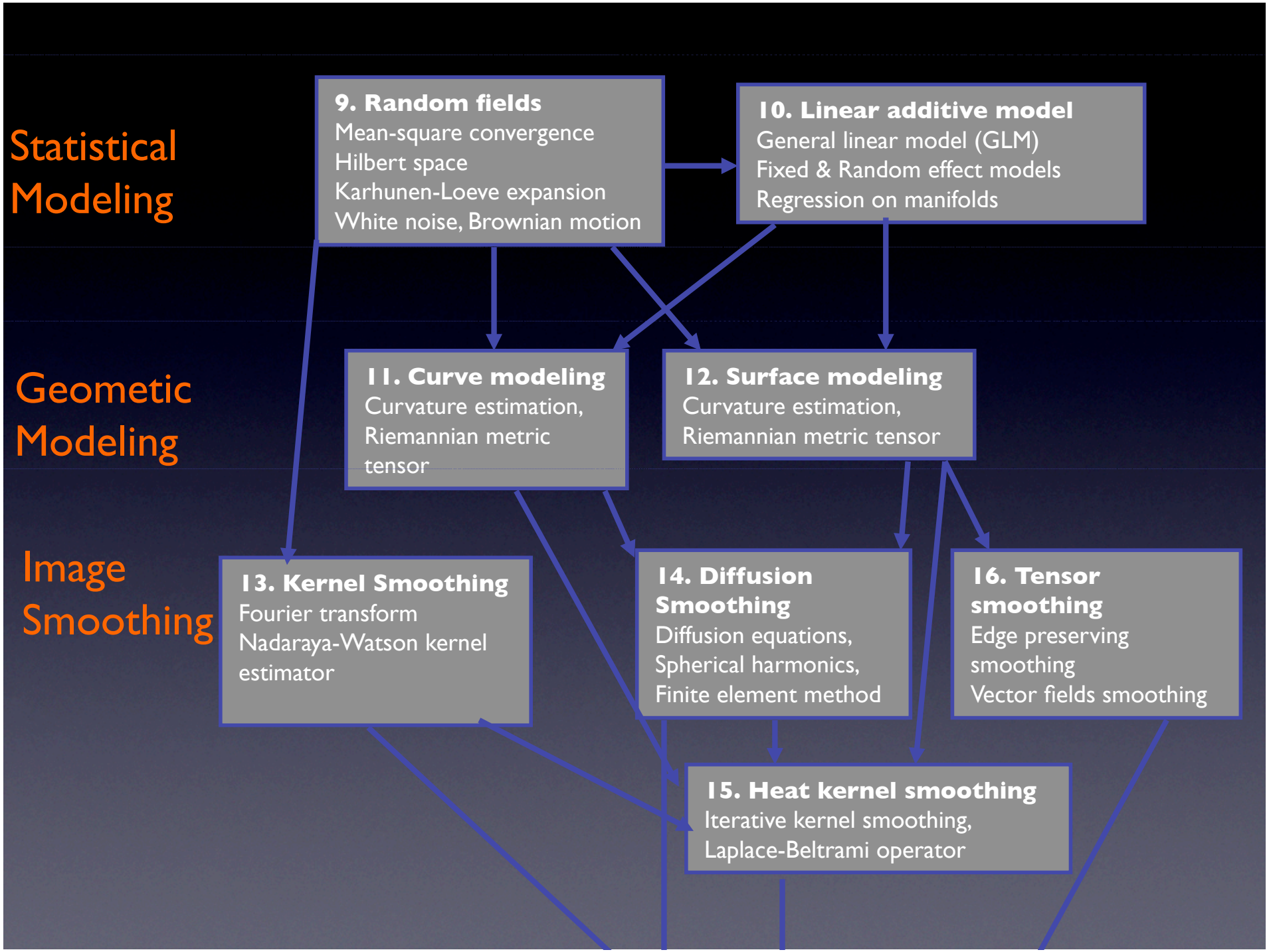
Where I work?

Waisman Laboratory for Brain Imaging and Behavior, Madison

http://brainimaging.waisman.wisc.edu

Brain Image Analysis




Statistical Modeling
Geometic Modeling
Image Smoothing
9. Random fields
Mean-square convergence
Hilbert space
Karhunen-Loeve expansion
White noise, Brownian motion
10. Linear additive model
General linear model (GLM)
Fixed & Random effect models
Regression on manifolds
11. Curve modeling
Curvature estimation,
Riemannian metric
tensor
12. Surface modeling
Curvature estimation,
Riemannian metric tensor
13. Kernel Smoothing
Fourier transform
Nadaraya-Watson kernel
estimator
14. Diffusion Smoothing
Diffusion equations,
Spherical harmonics,
Finite element method
16. Tensor smoothing
Edge preserving
smoothing
Vector fields smoothing
15. Heat kernel smoothing
Iterative kernel smoothing,
Laplace-Beltrami operator

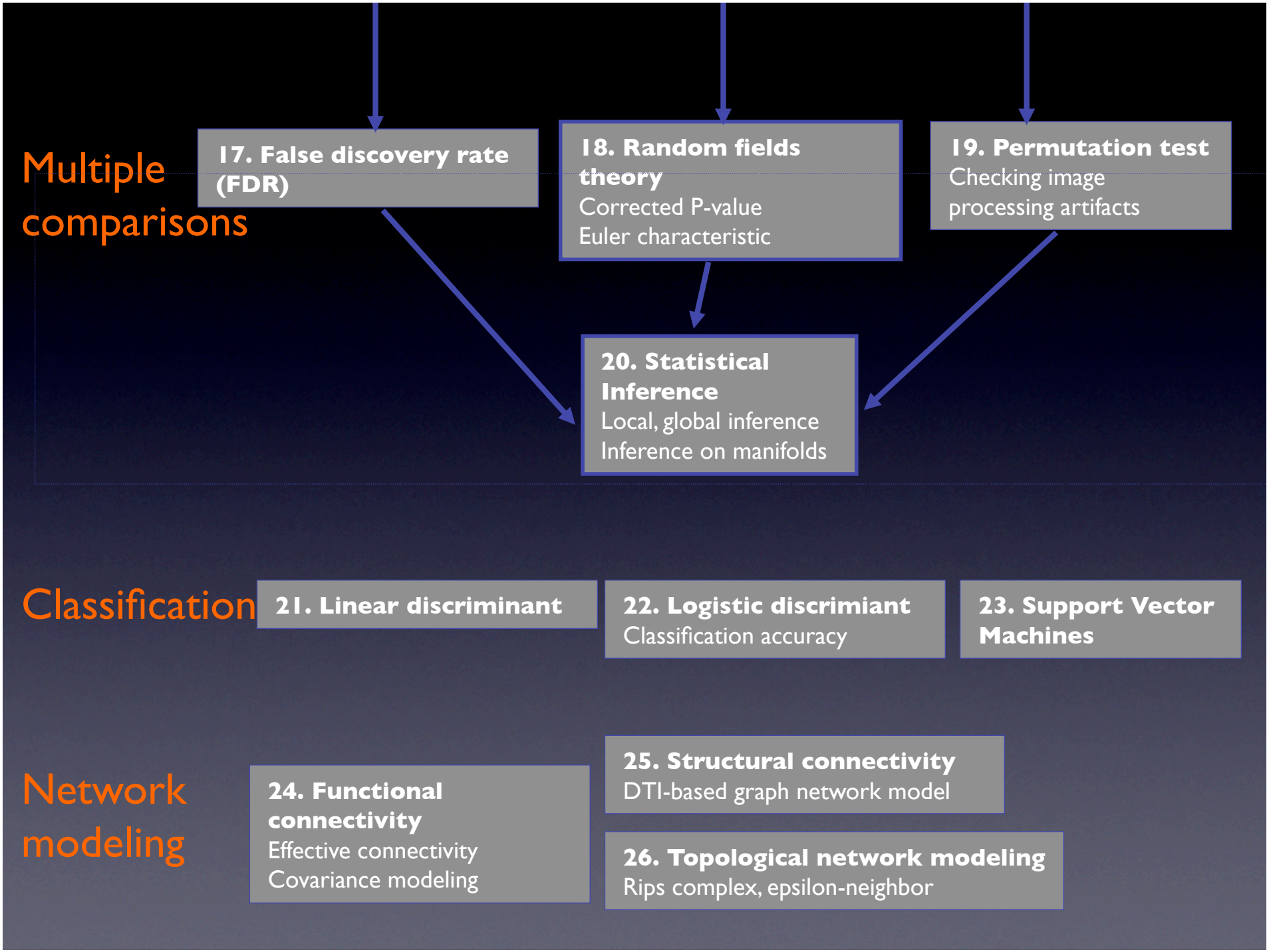
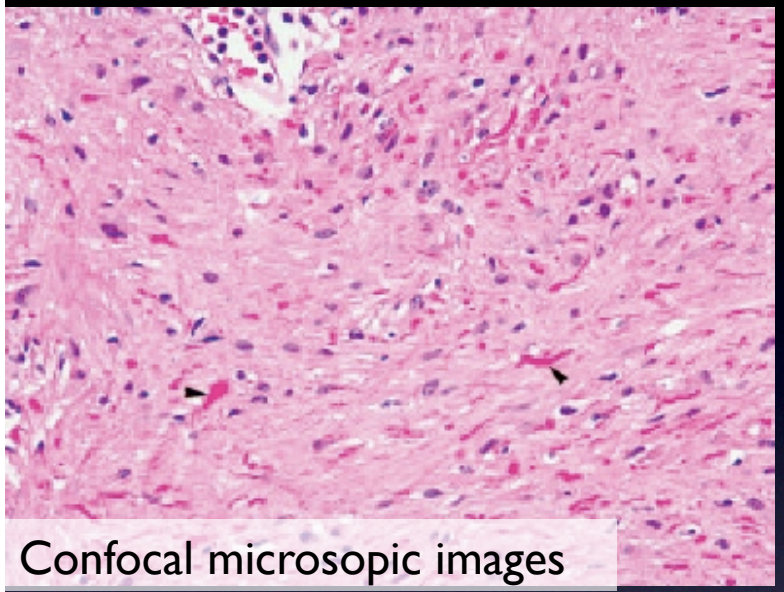

Multiple comparisons
17. False discovery rate (FDR)
18. Random fields theory
Corrected P-value
Euler characteristic
19. Permutation test
Checking image processing artifacts
20. Statistical Inference
Local, global inference
Inference on manifolds
Classification
21. Linear discriminant
22. Logistic discrimiant
Classification accuracy
23. Support Vector Machines
Network modeling
24. Functional connectivity
Effective connectivity
Covariance modeling
25. Structural connectivity
DTI-based graph network model
26. Topological network modeling
Rips complex, epsilon-neighbor

Image acquisition

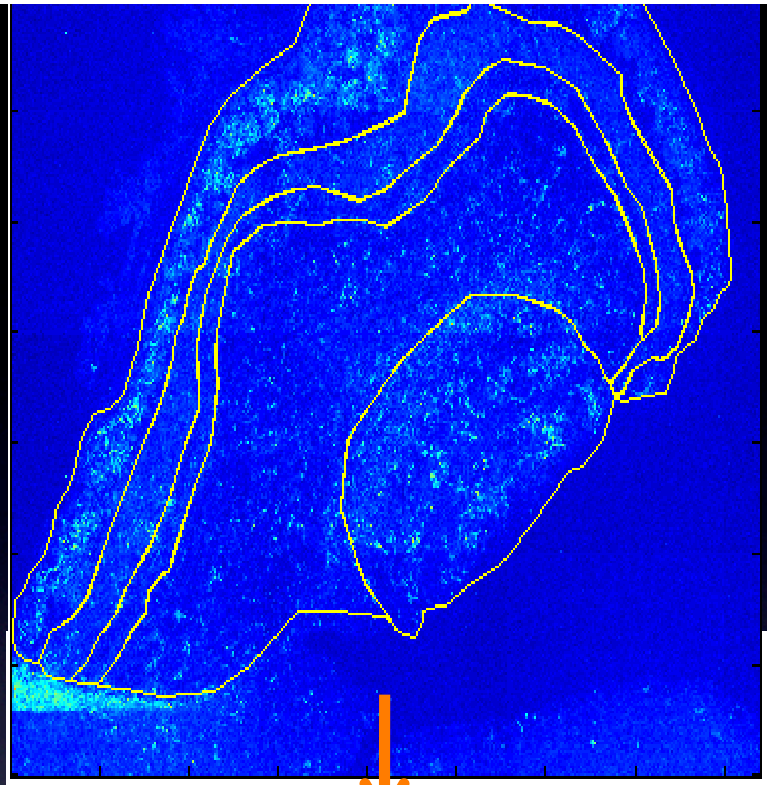
Microscope

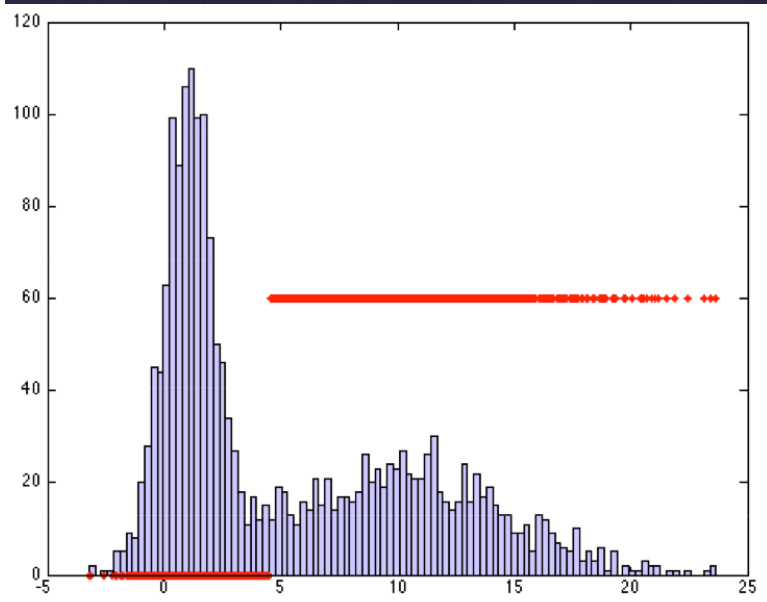
Rosenthal Fiber Segmentation
(mouse brain)



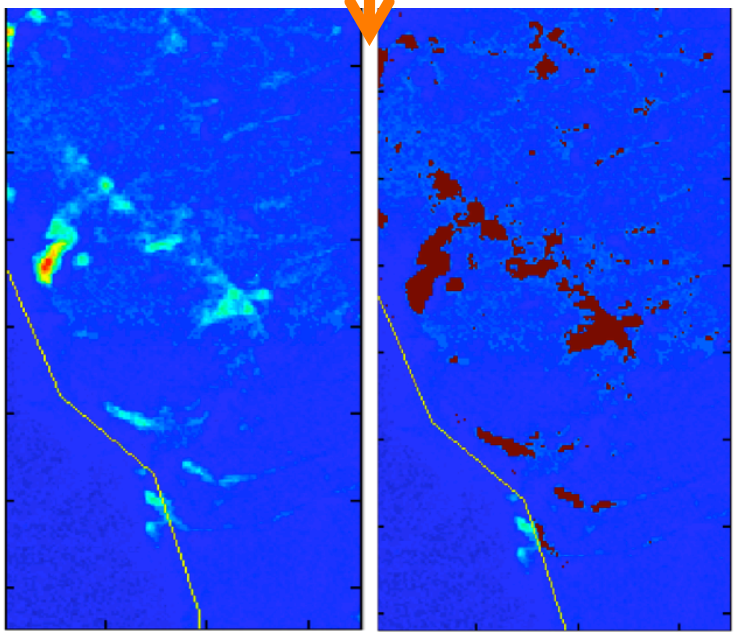
Confocal microsopic images

ROI-drawing



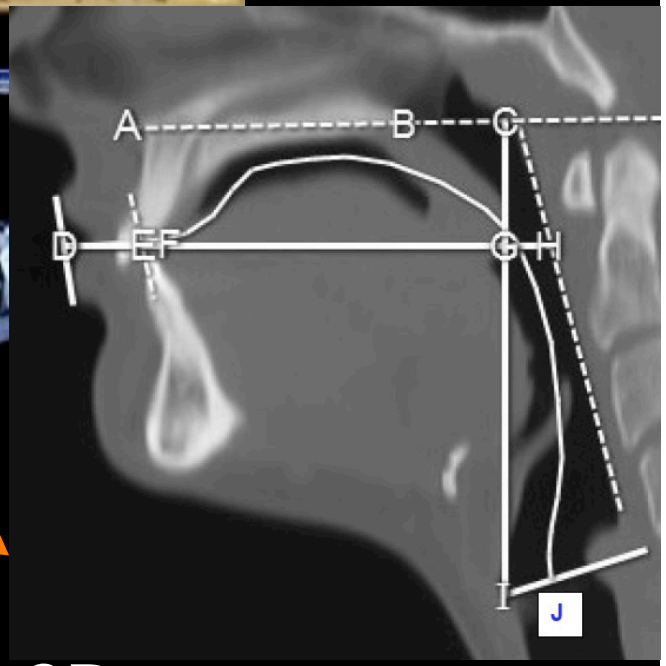


Gaussian
Mixture model

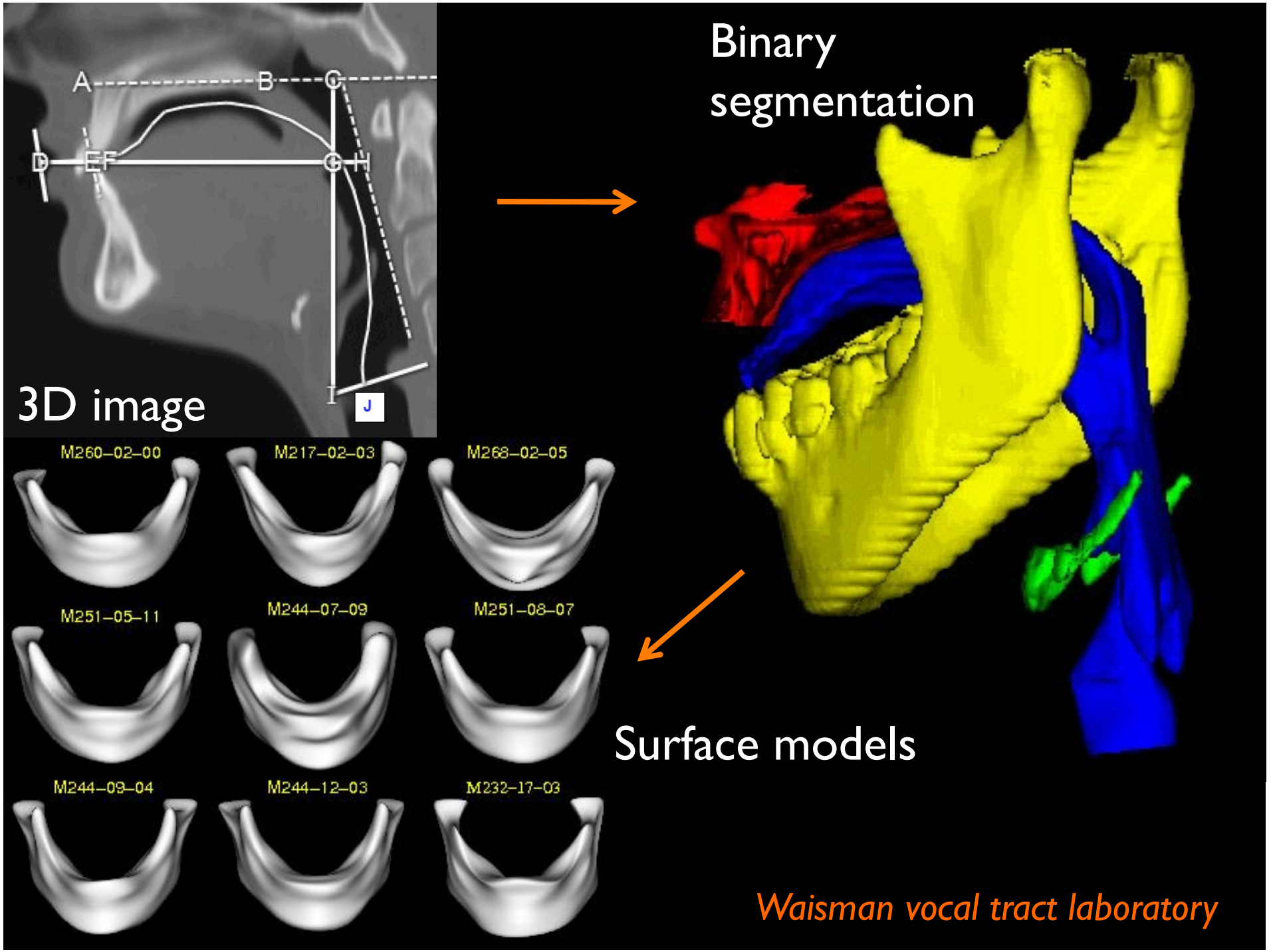


Computed Tomography (CT)

Hard tissues: bones, teeth

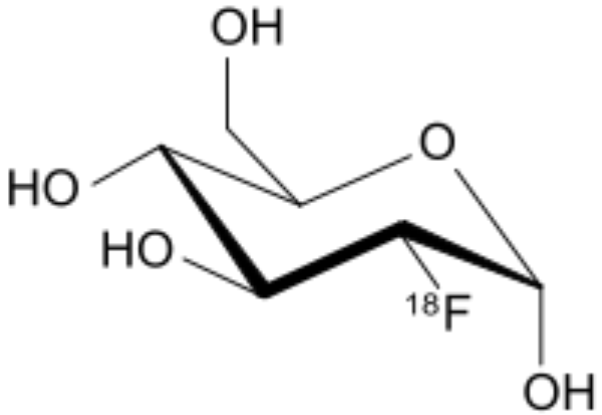


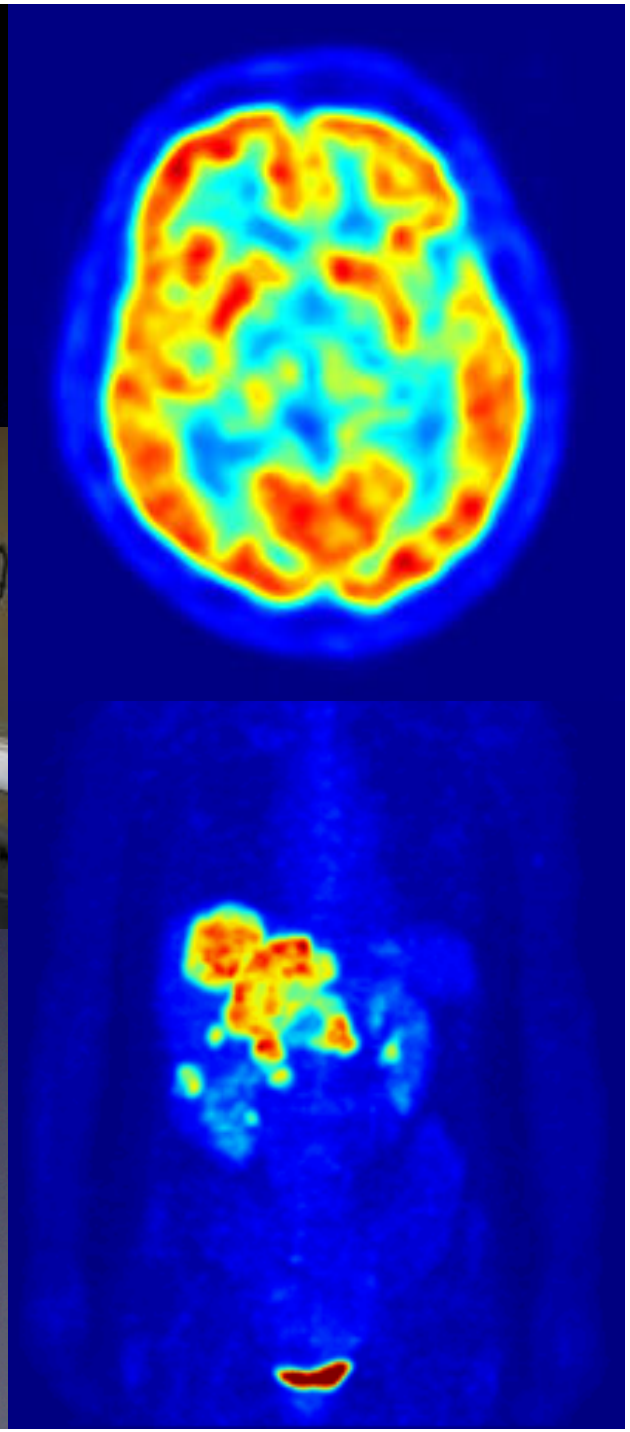
3D image


A
B
C
D
E
F
G
H
I
J
3D image
Binary segmentation
M260–02–00
M217–02–03
M268–02–05
M251–05–11
M244–07–09
M251–08–07
M244–09–04
M244–12–03
M232–17–03
Surface models
Waisman vocal tract laboratory

FDG-PET

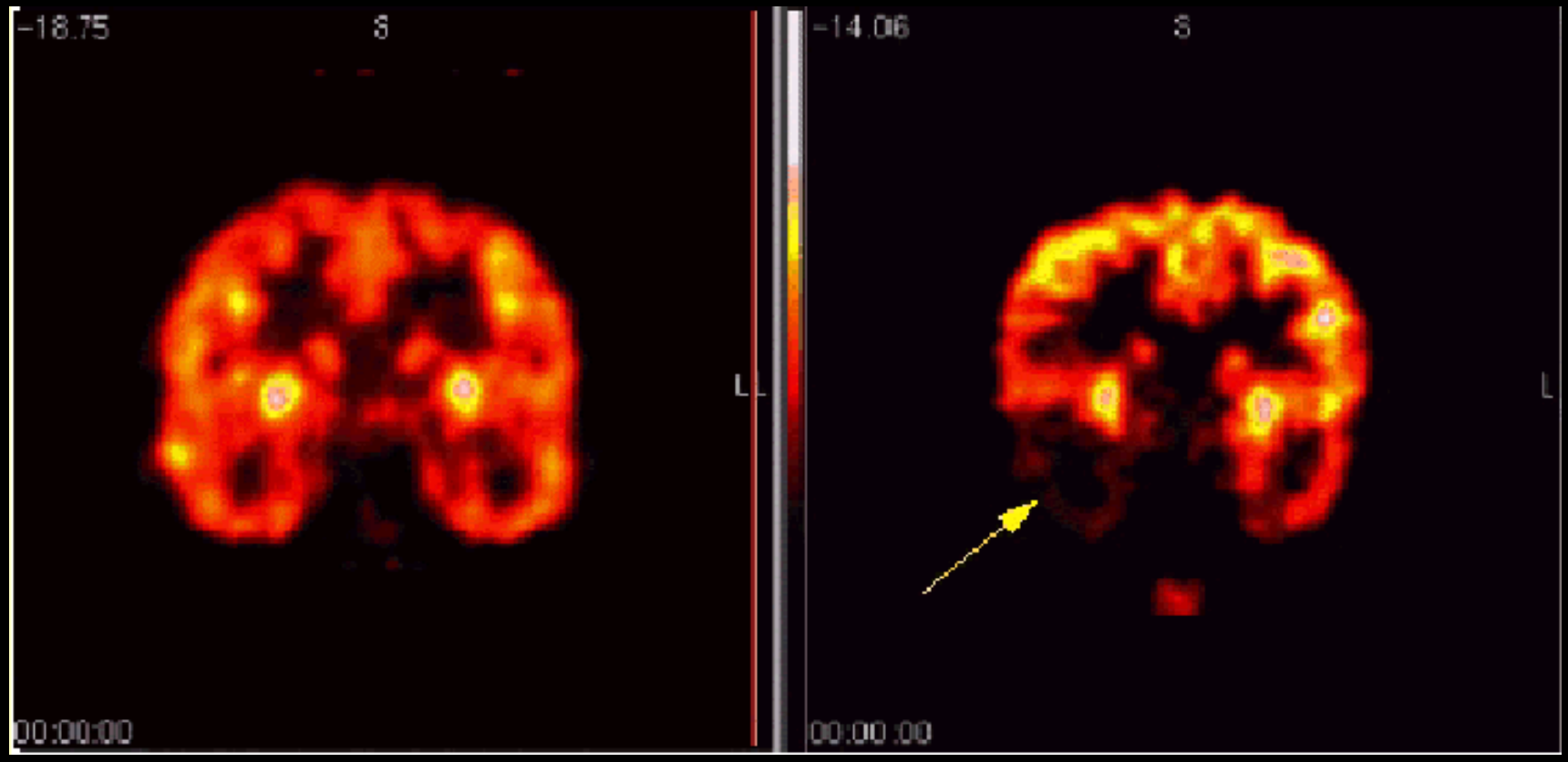
The PET scanner detects pairs of gamma rays emitted from a positron-emtting radioactive tracer.





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

Positron Emission Tomography (PET)



Normal Brain

Brain of 9 year old girl suffering from epilepsy

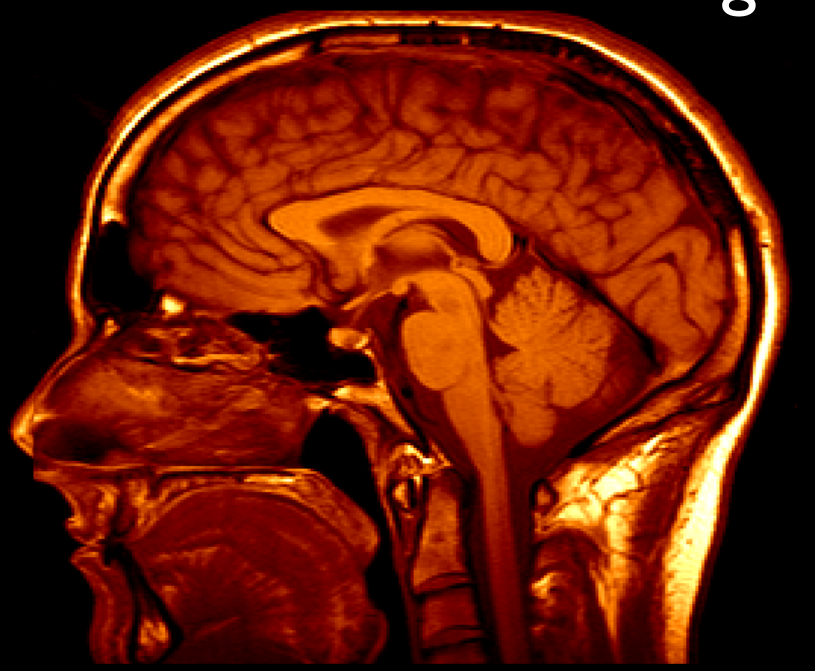
Montreal Neurological Institute

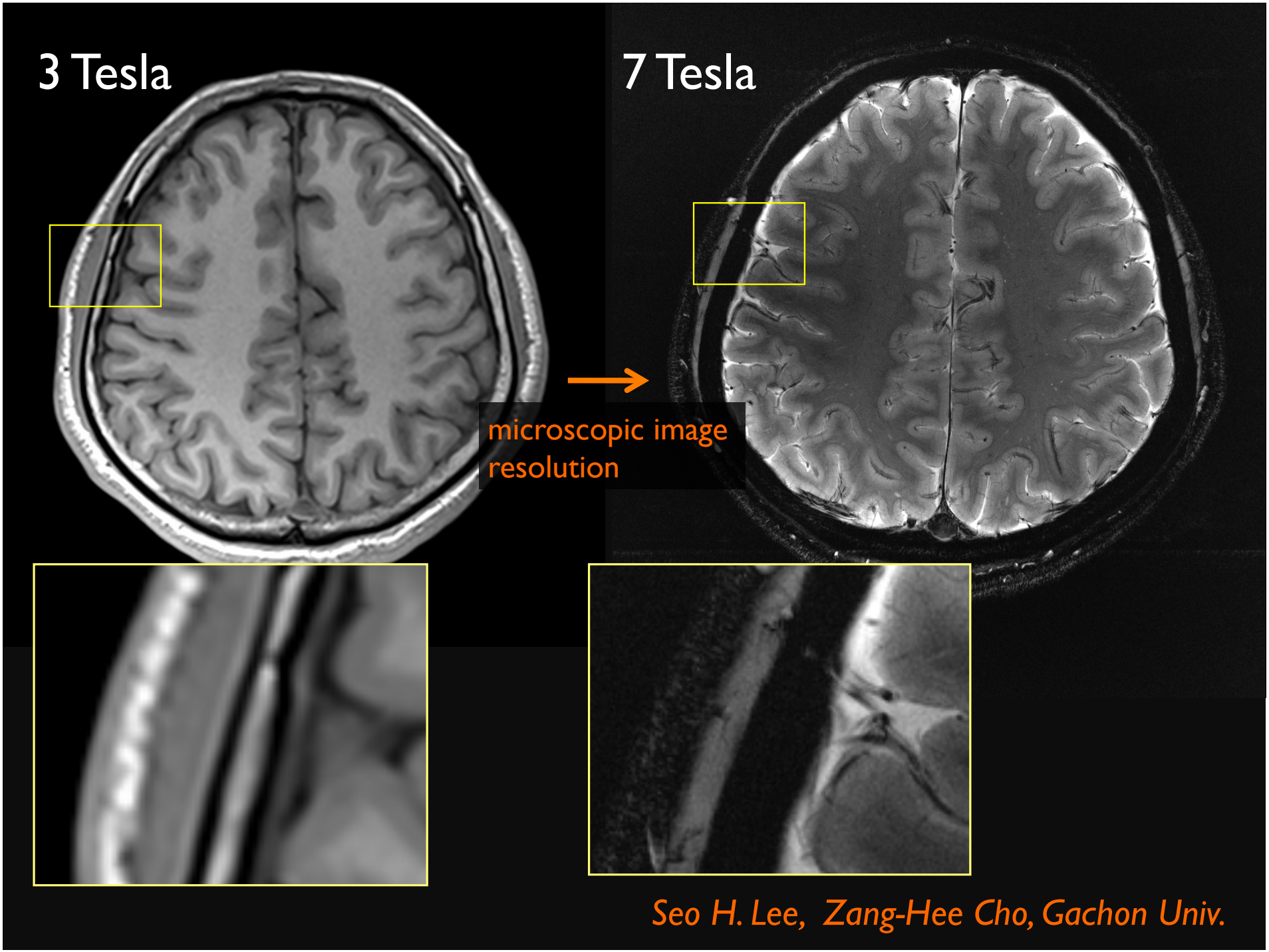
Magnetic Resonance Imaging (MRI)

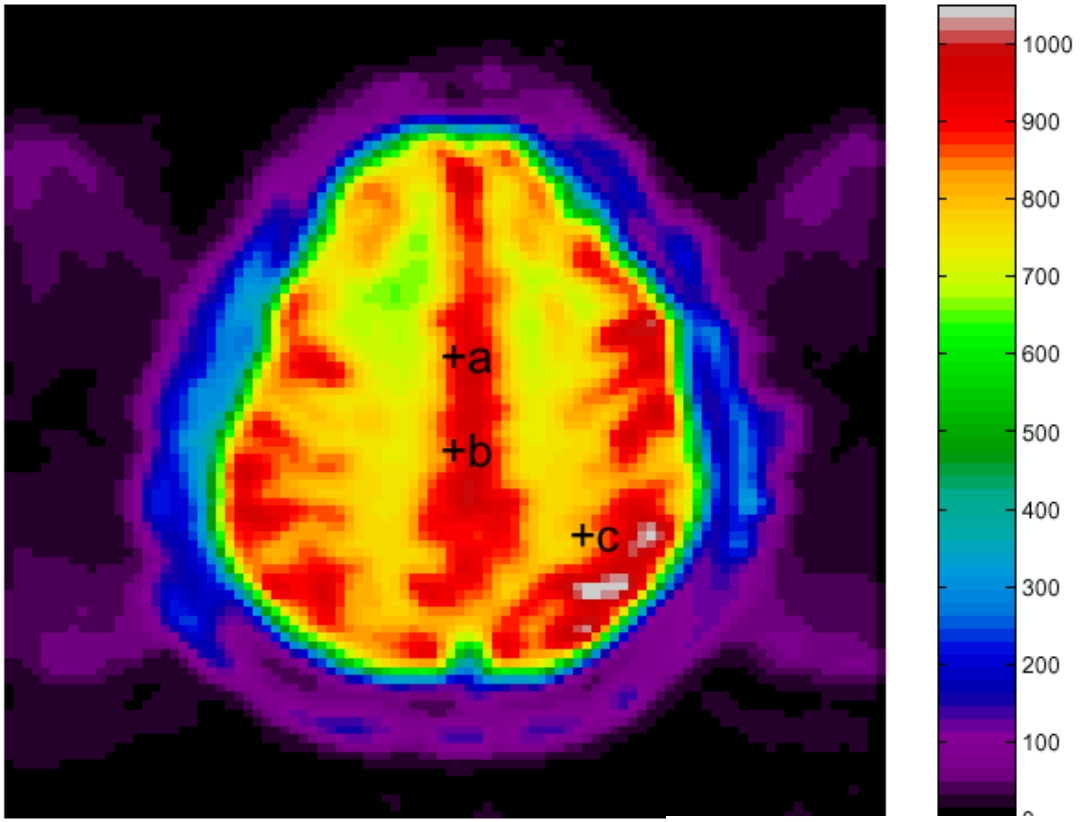
3.0 Tesla GE Scanner

Soft tissues

3D image

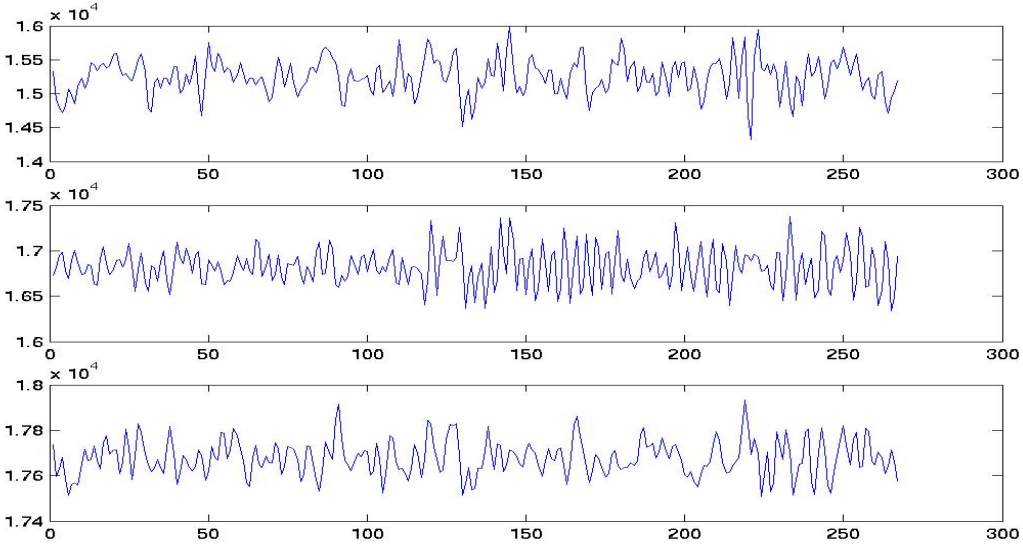



3 Tesla
7 Tesla
microscopic image
resolution
Seo H. Lee, Zang-Hee Cho, Gachon Univ.



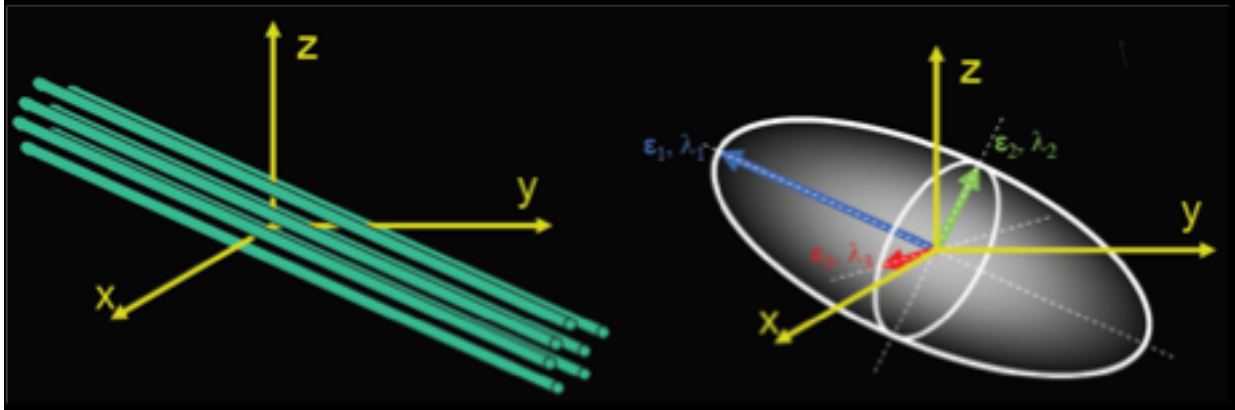
Functional MRI

Measures hemodynamic response (change in blood flow)

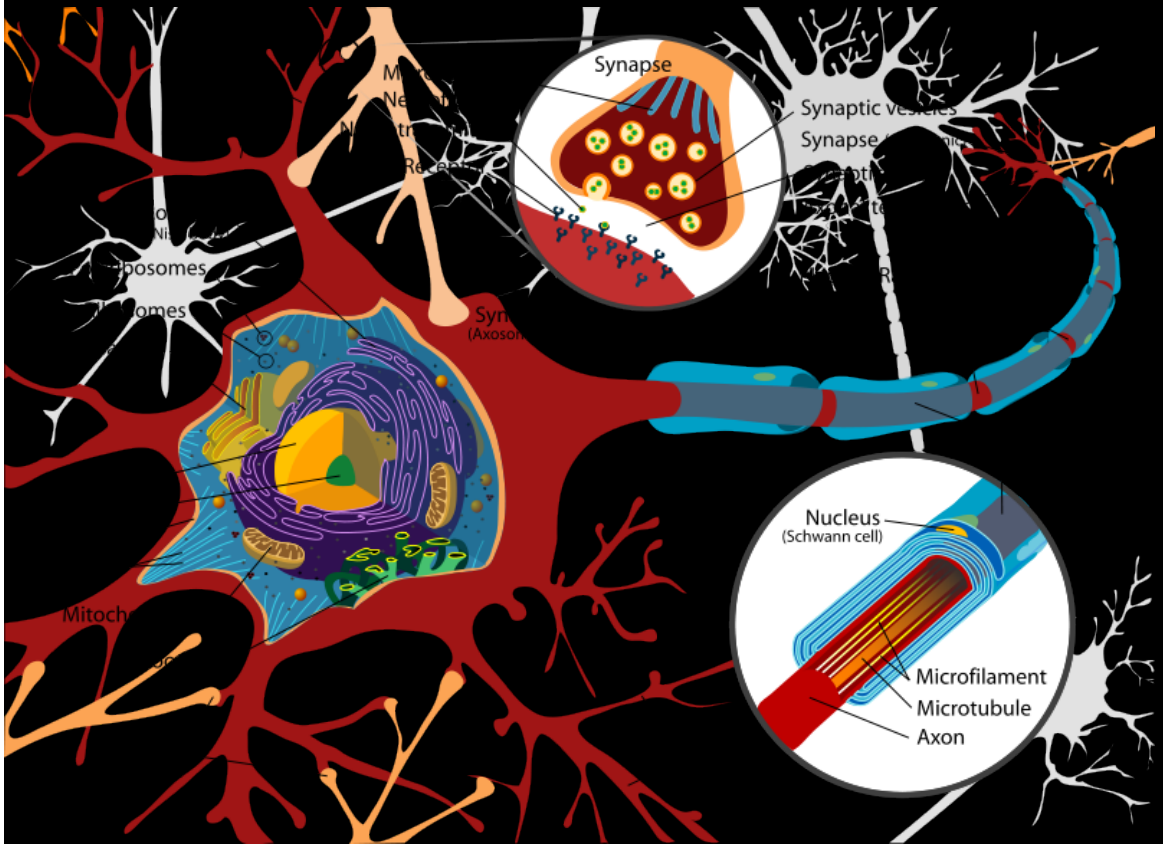


Diffusion Tensor Imaging

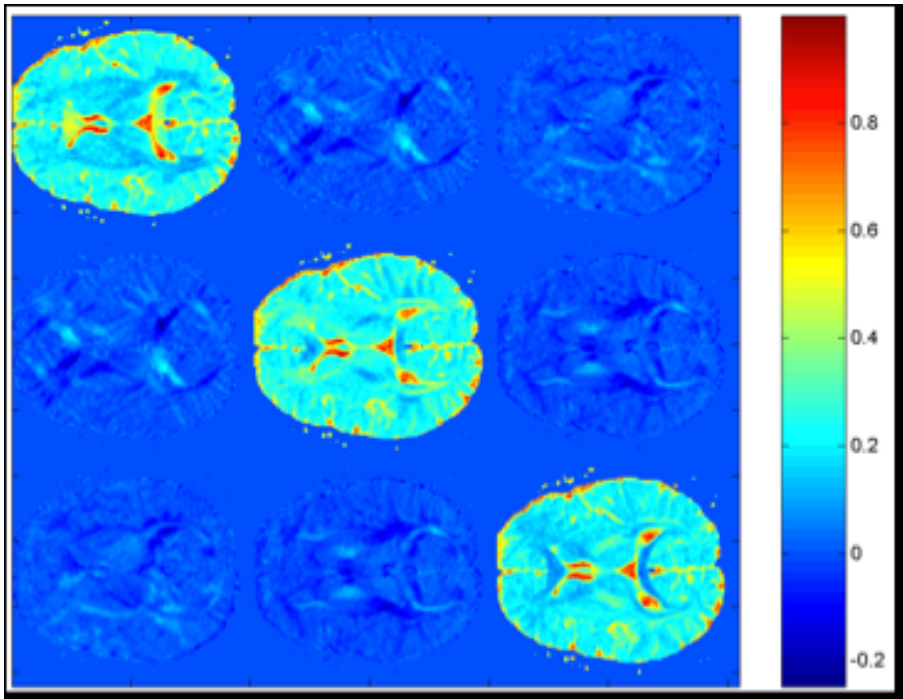
Mori and van Zijl NMR Biomed 2002



The movement of anisotropic water diffusion can be measured using DTI

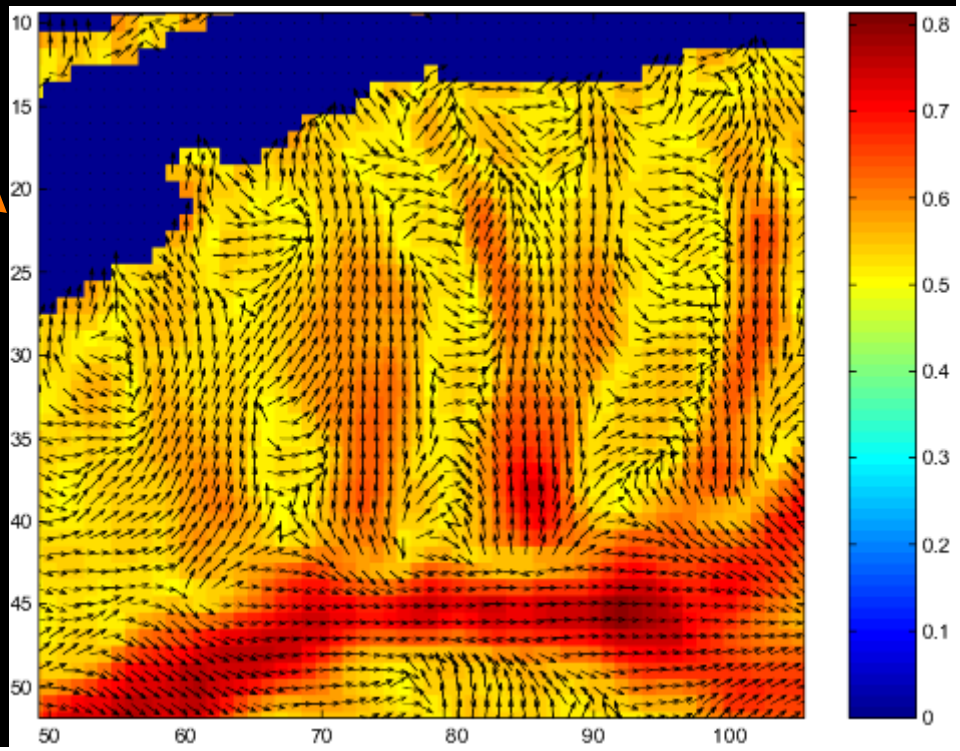


The direction of neuronal filaments in the axon dictates the movement of water diffusion.



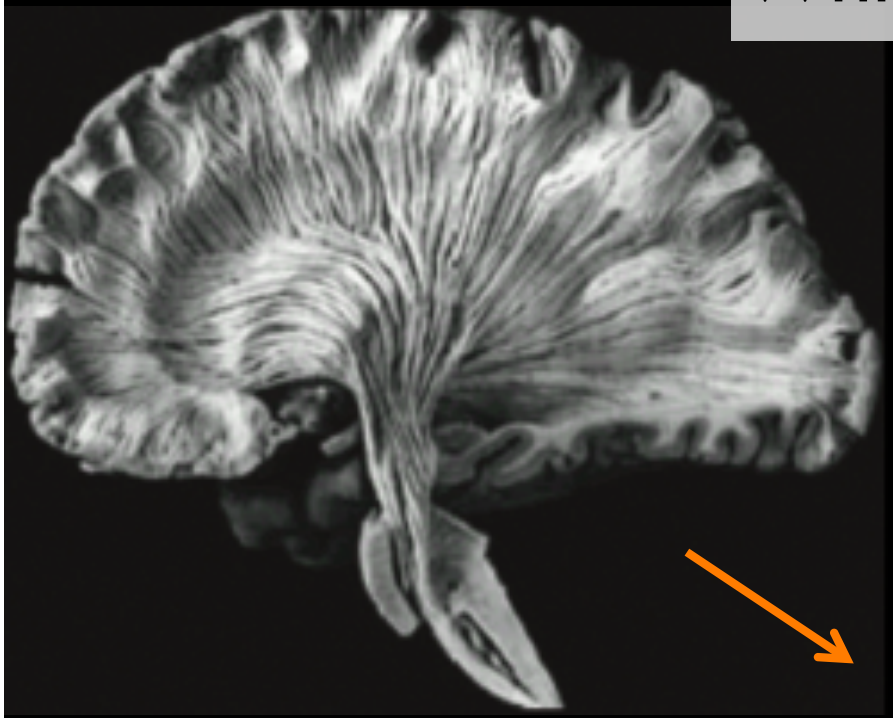
Direction of diffusion is encoded in 3x3 matrix *D* (diffusion tensor)

Principal eigenvectors of D

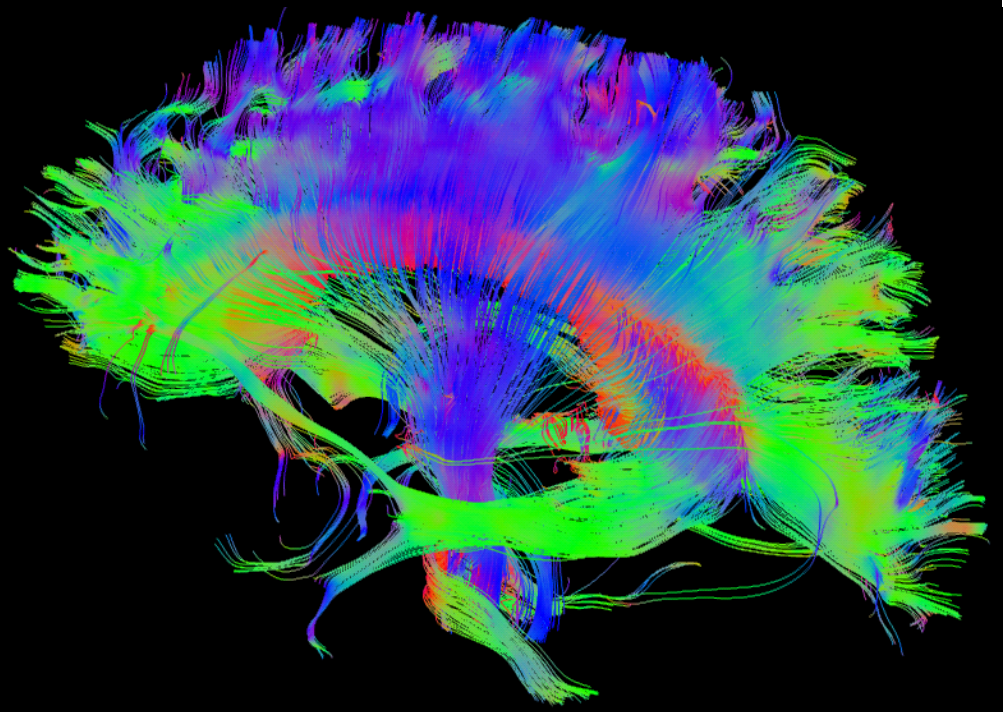


Tractography done using the second order Runge-Kutta algorithm with TEND (Lazar et al., HBM 2003)

White Matter Fiber Tractography



Postmortem

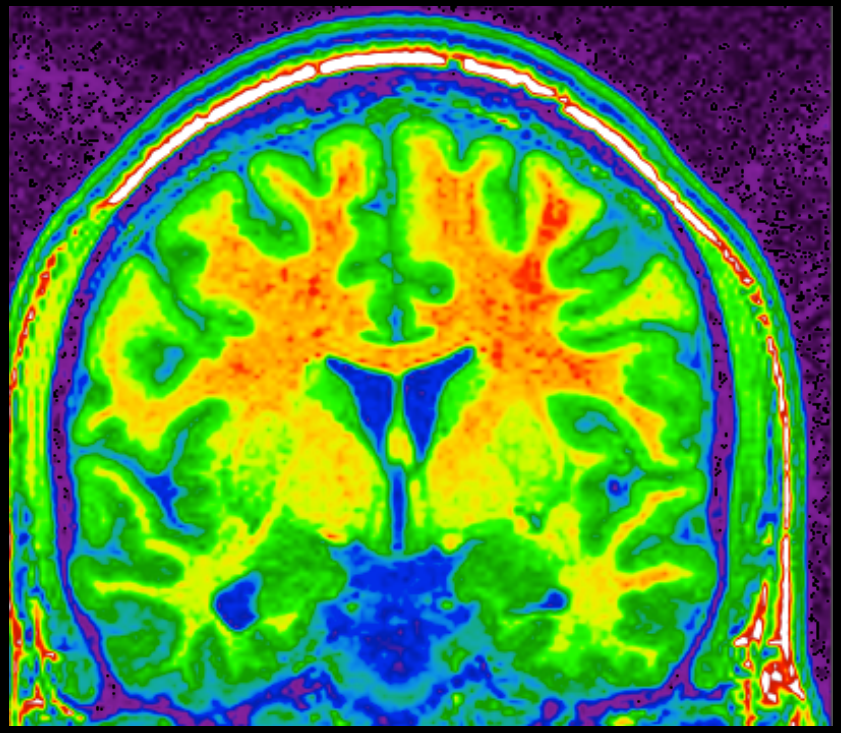


Reconstructed
0.5 million tracts

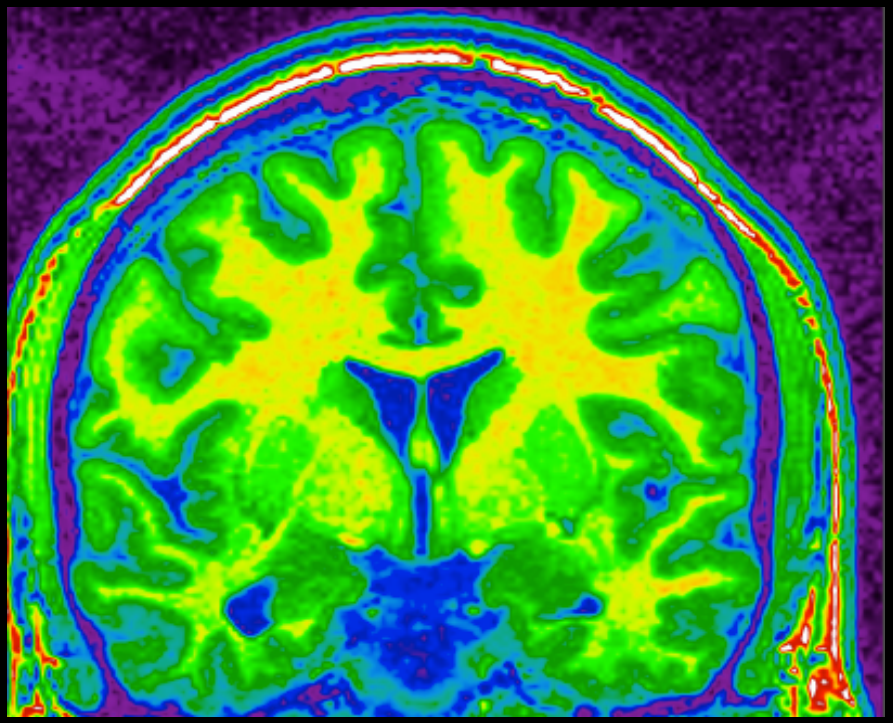
Image, tissue and structure segmentation

Image intensity non-uniformity correction

Original MRI

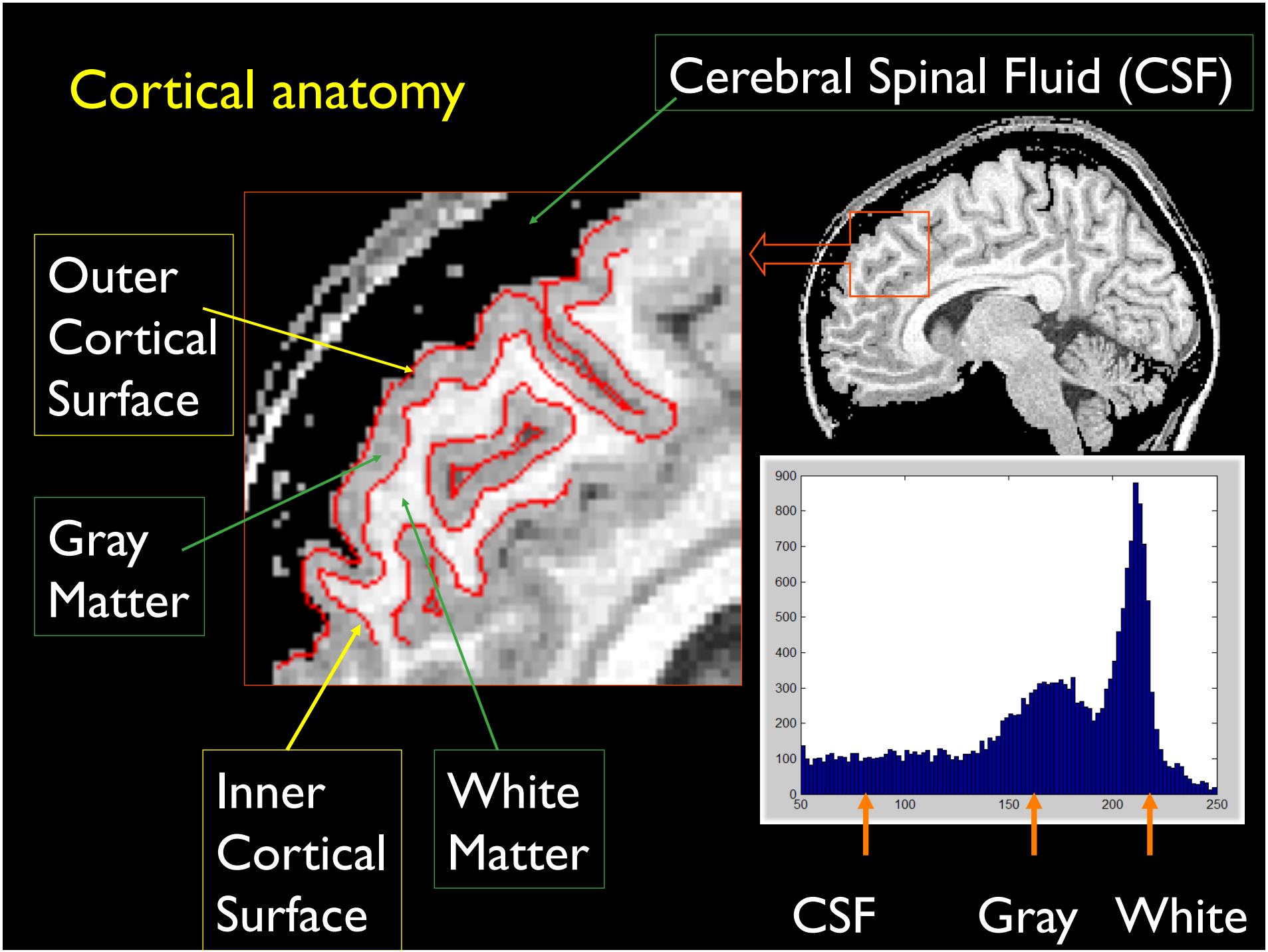


Corrected



McConnell Brain Imaging Center, MNI

Cortical anatomy

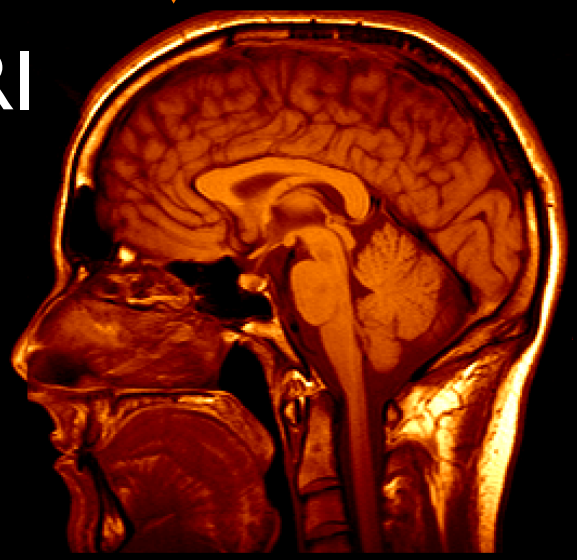


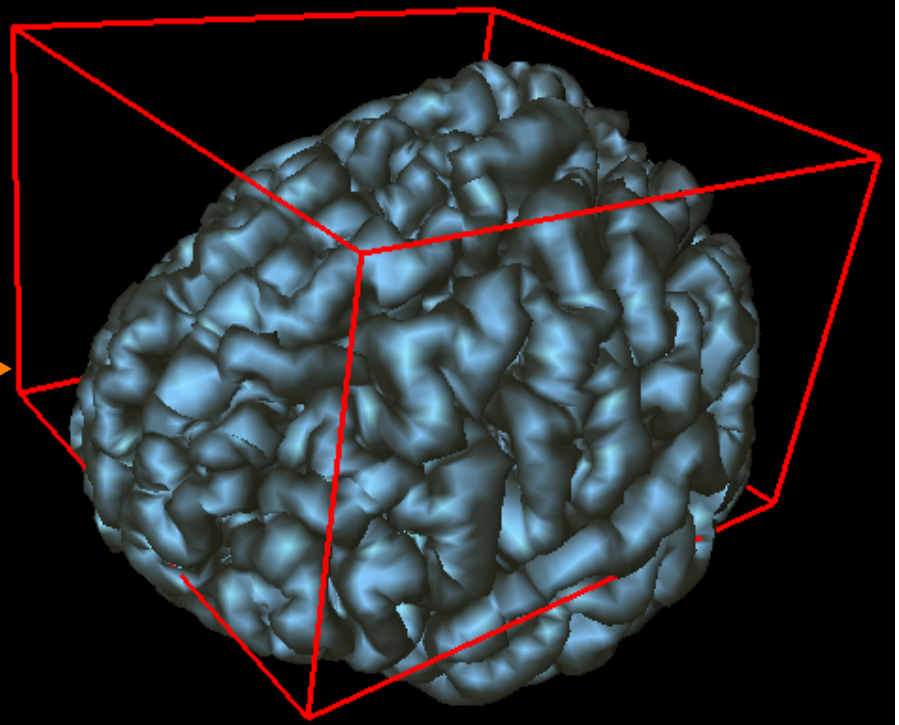
Real brain

Image & structure segmentation

Cortical surface model

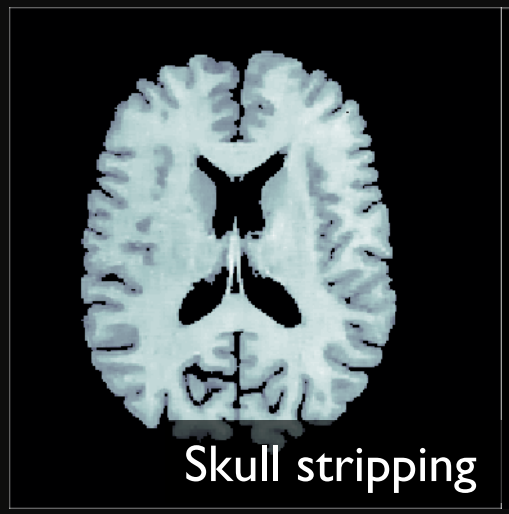
3T MRI

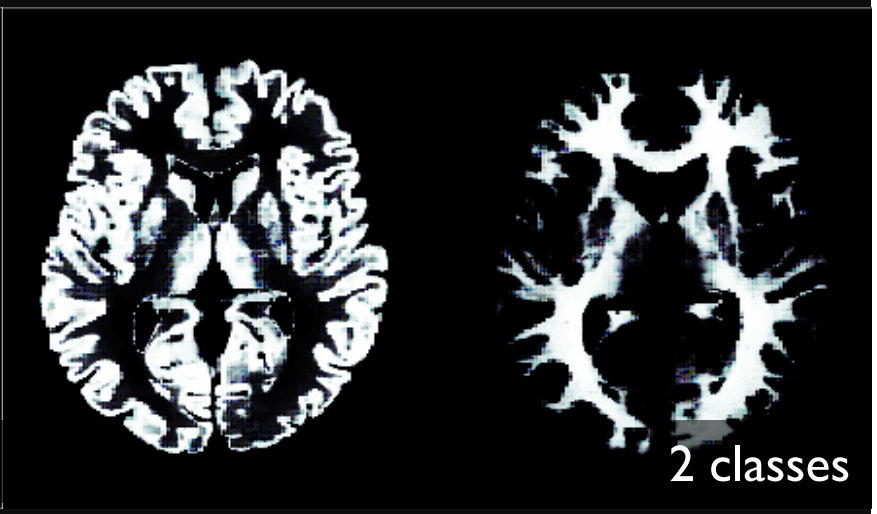




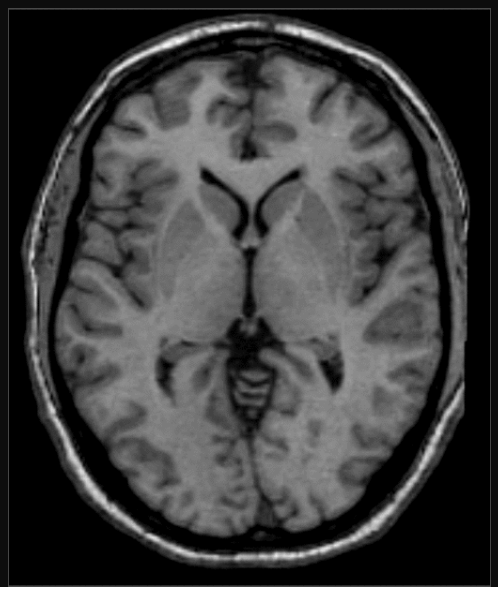
Gaussian mixture modeling


SPM approach

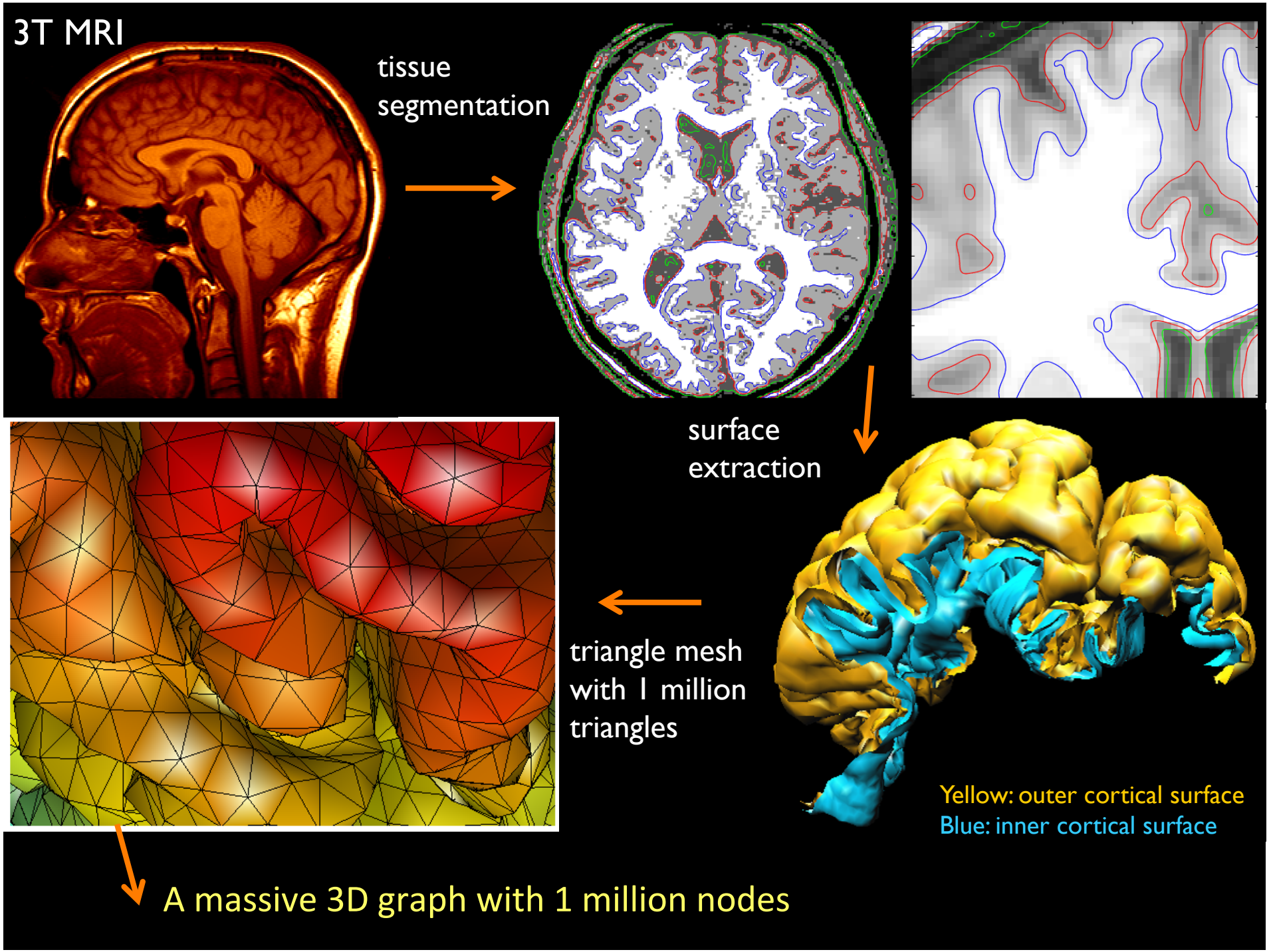

Skull stripping


2 classes

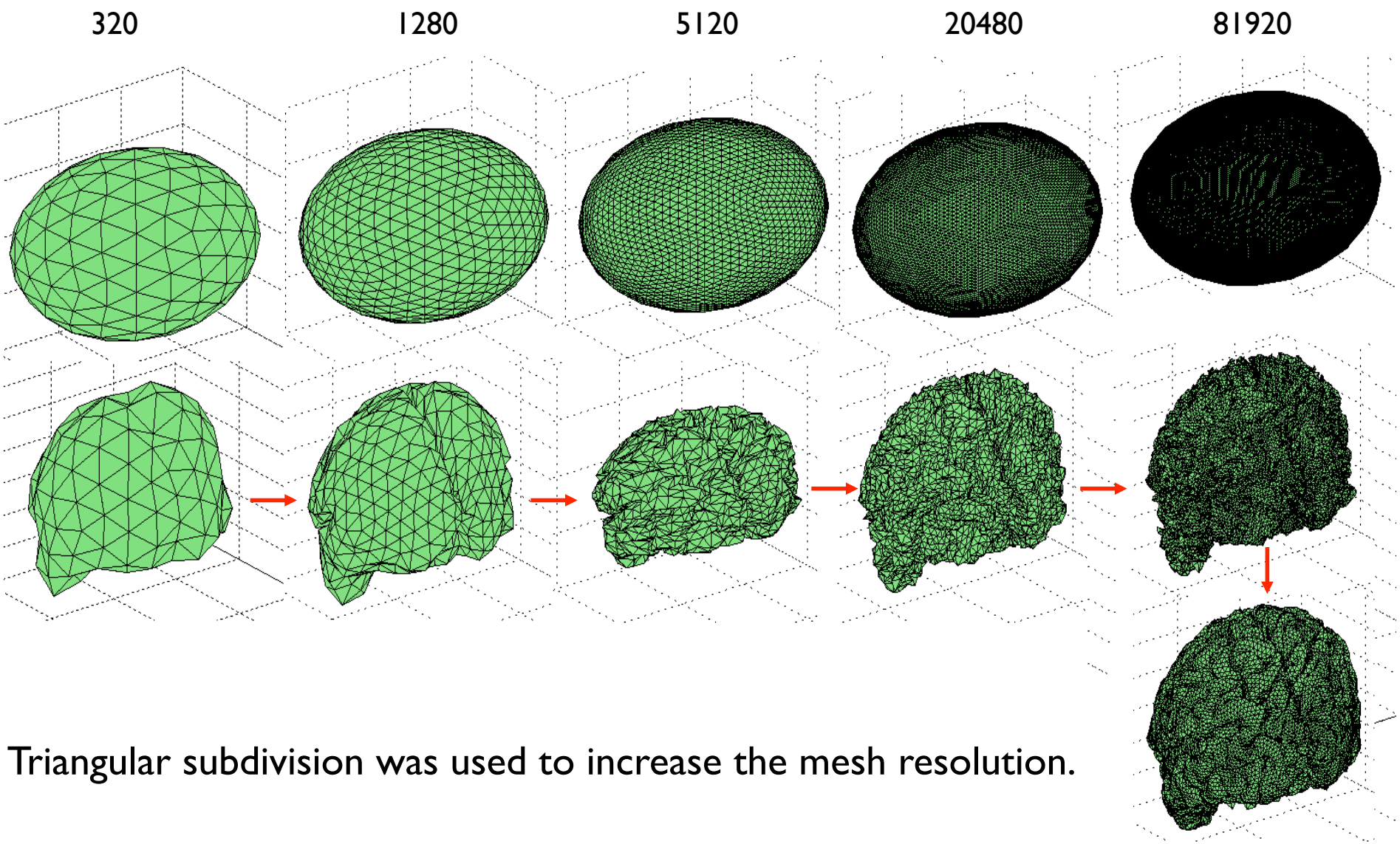
MNI Neural network classifier



3 classes

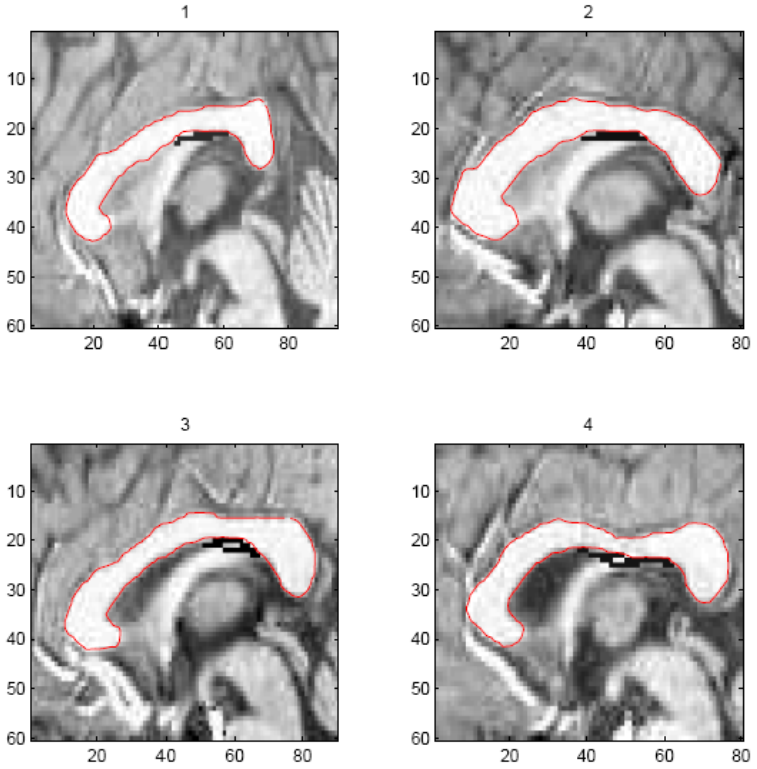

3T MRI
tissue segmentation
surface extraction
triangle mesh with 1 million triangles
Yellow: outer cortical surface
Blue: inner cortical surface
A massive 3D graph with 1 million nodes

Deformable surface algorithm for cortical surfaces

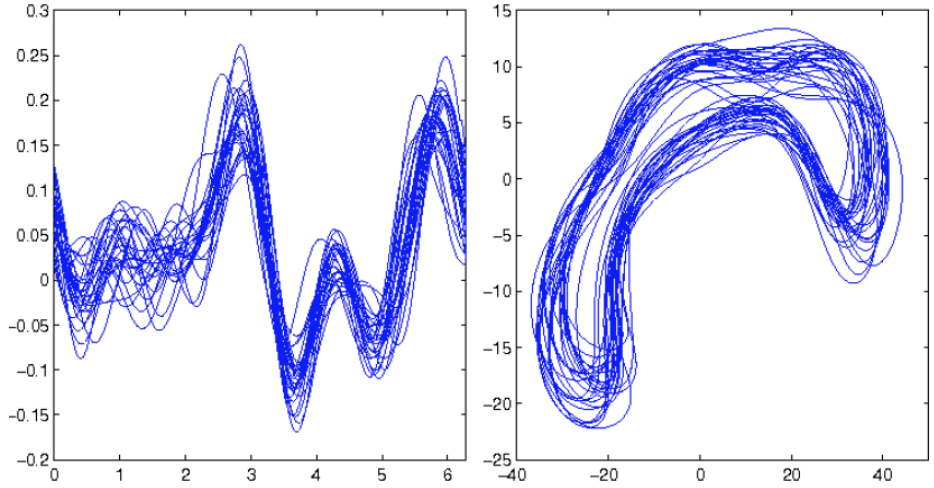


Triangular subdivision was used to increase the mesh resolution.

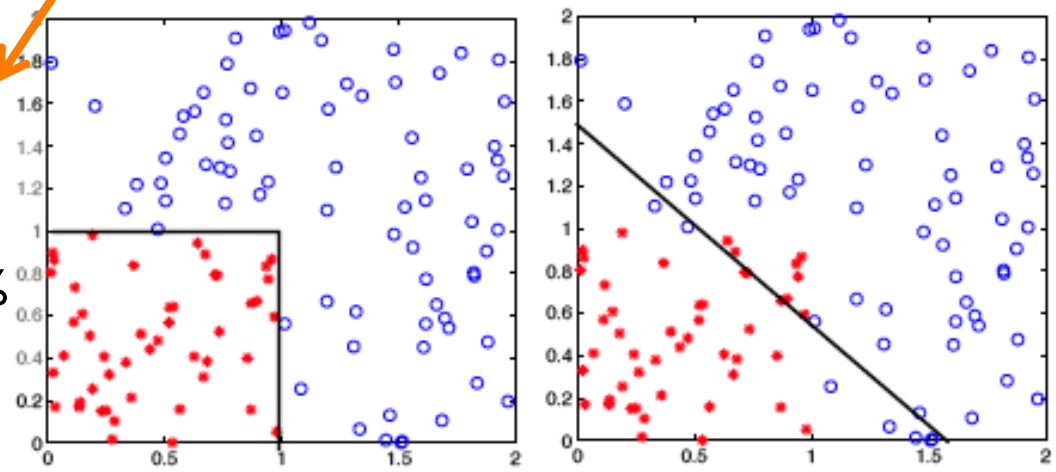
Active contour (snake) segmentation



Corpus callosum segmentation and modeling



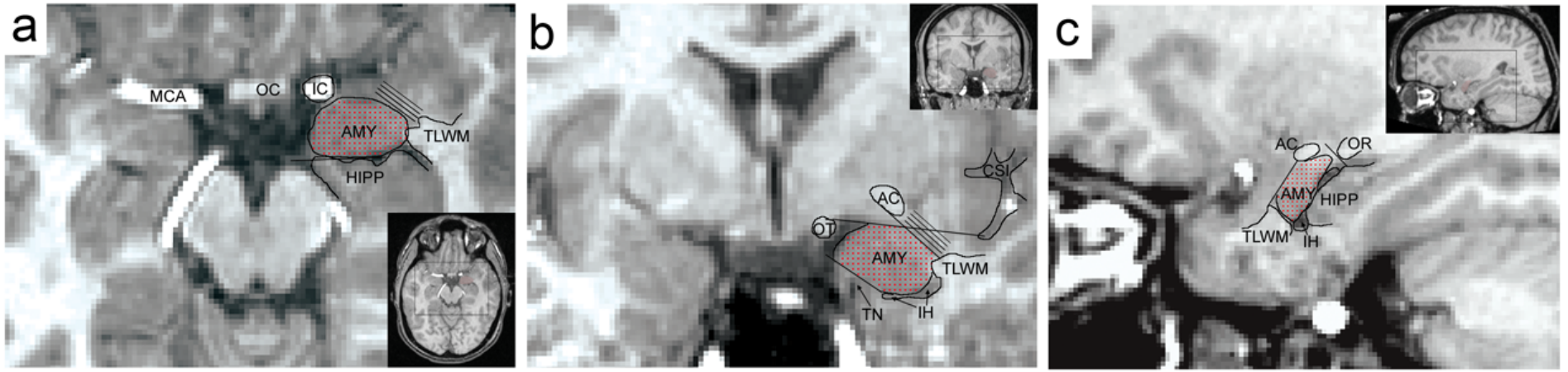
Active contour (snake) segmentation



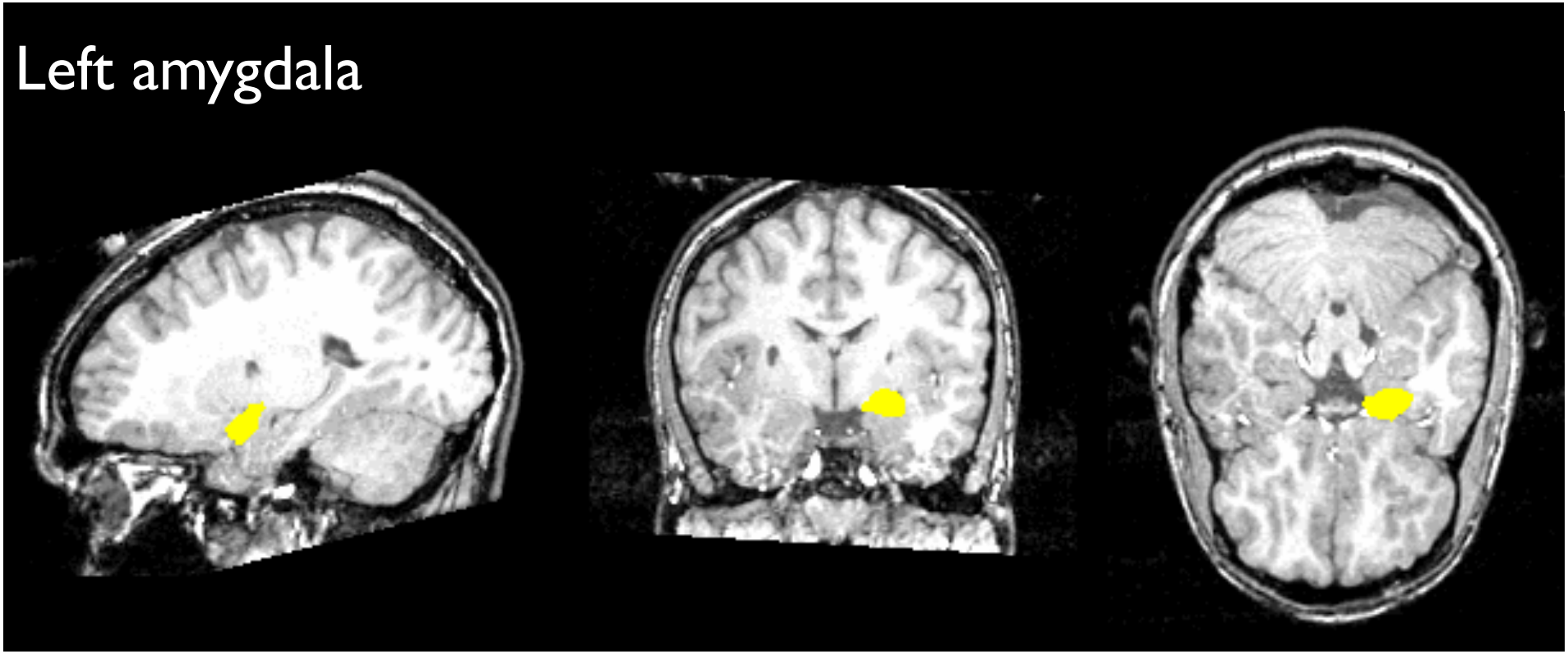
Classification result

Linear discriminant analysis (LDA) 75%
Regression tree 85%

Manual segmentation

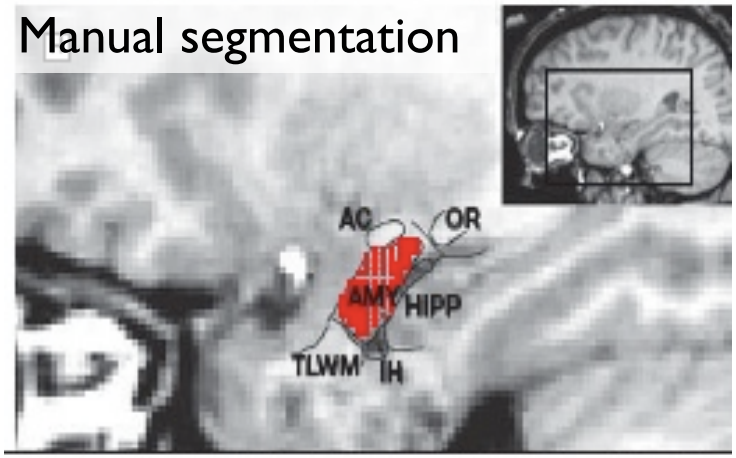


Left amygdala

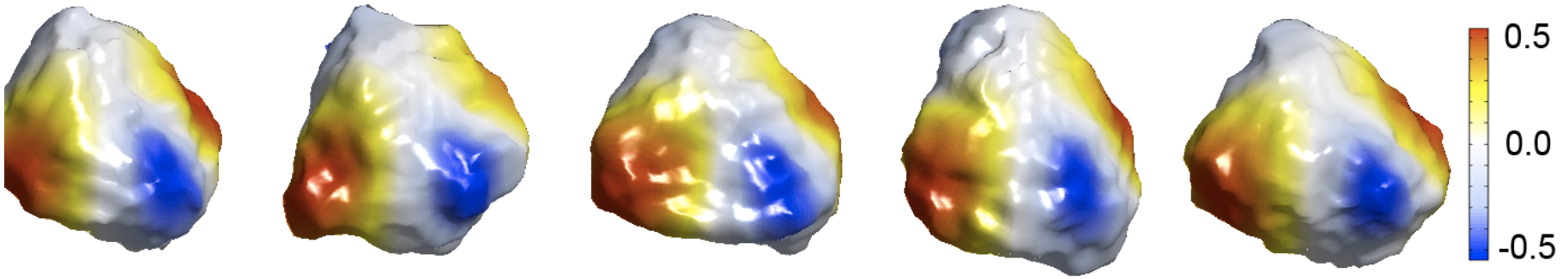


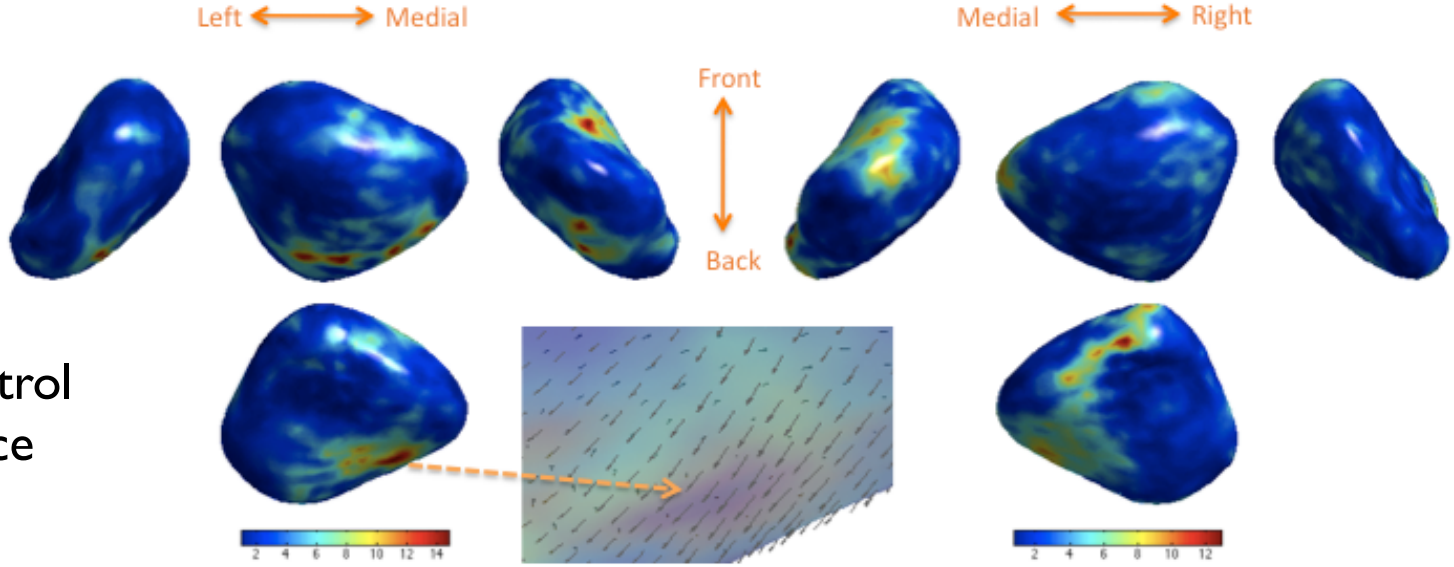
Amygdala shape modeling

Chung et al. 2010, NeuroImage



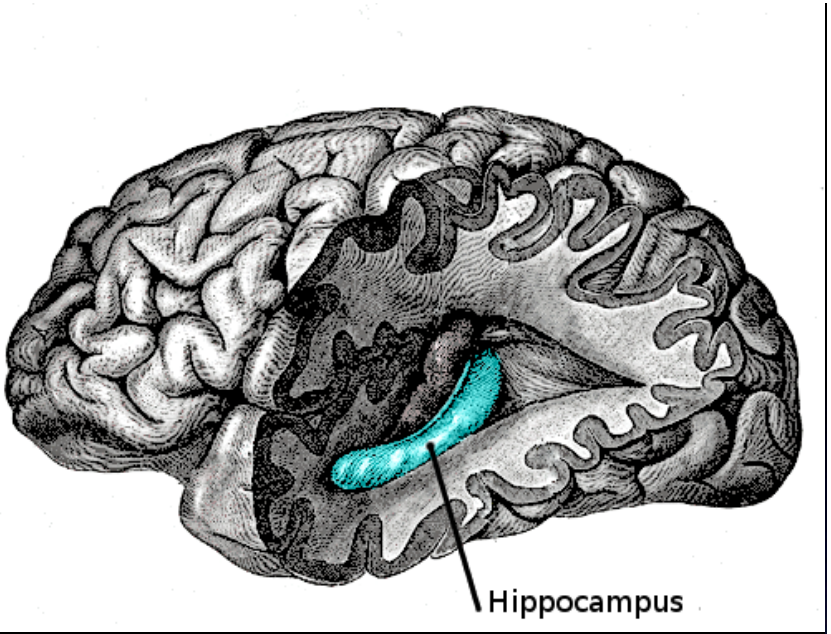
Amygdala registration via spherical harmonic representation

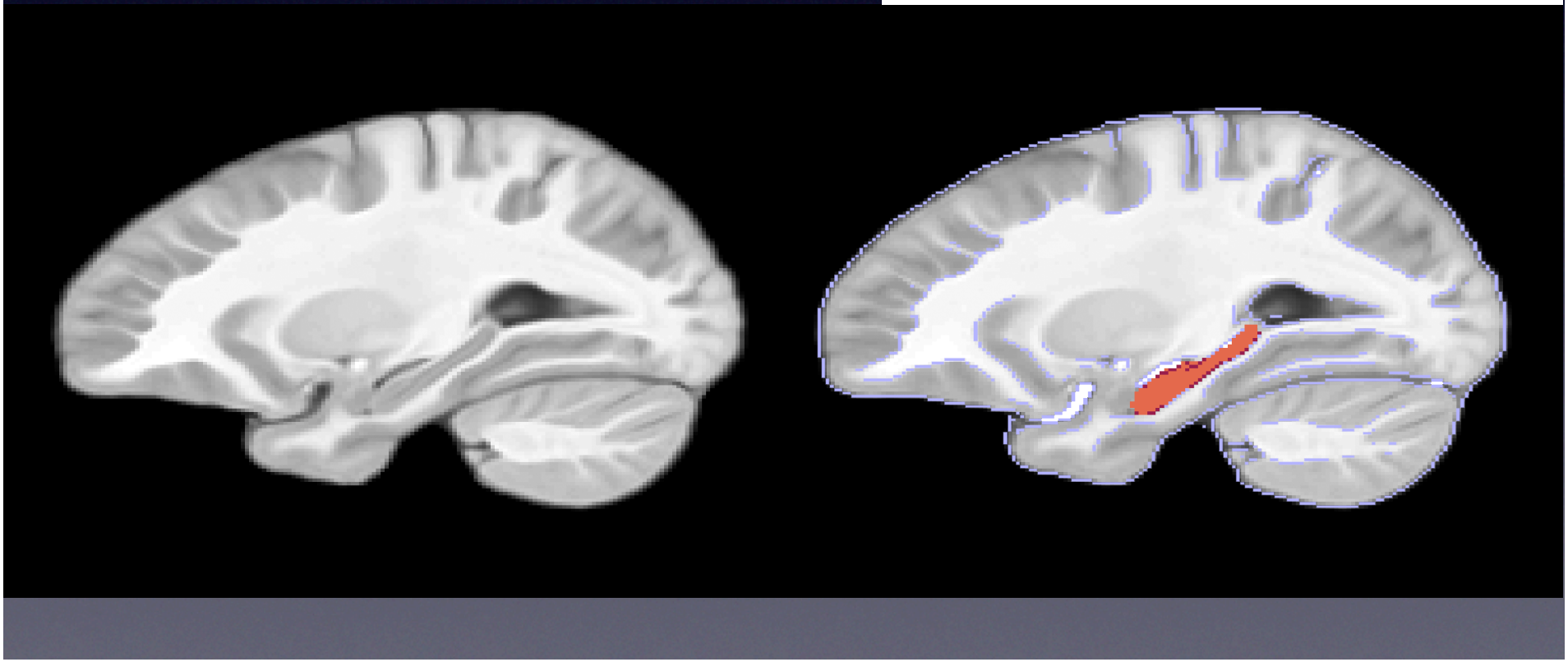




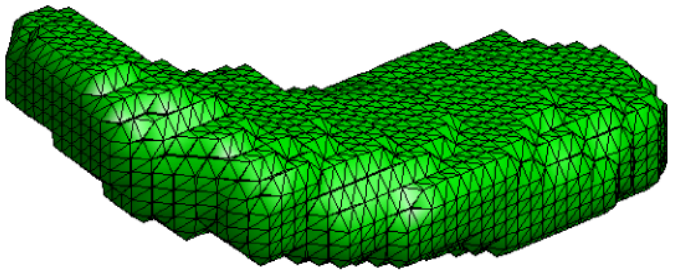
Autism vs. control group difference

Manual hippocampus segmentation on MRI template



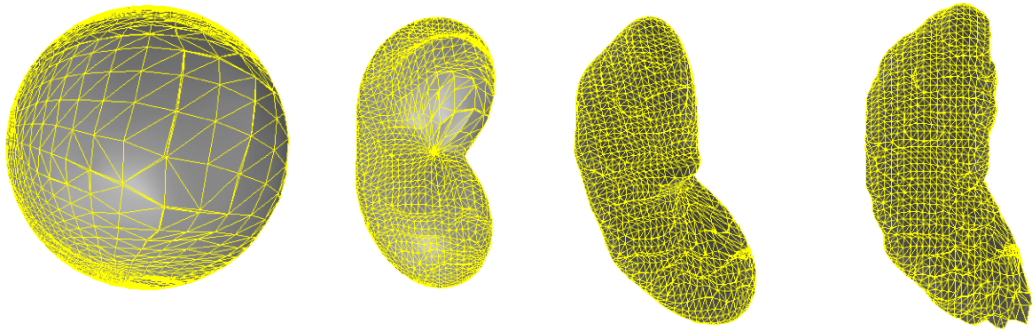


Hippocampus segmentation and modeling

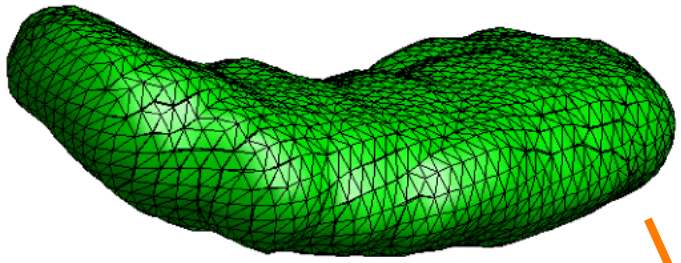


Manual segmentation

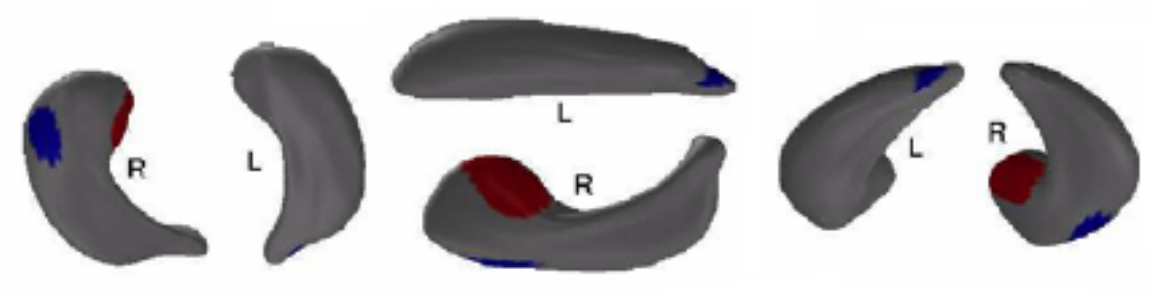
Spherical harmonic parameterization



degree 1 degree 5 degree 10 degree 50



Parametric model

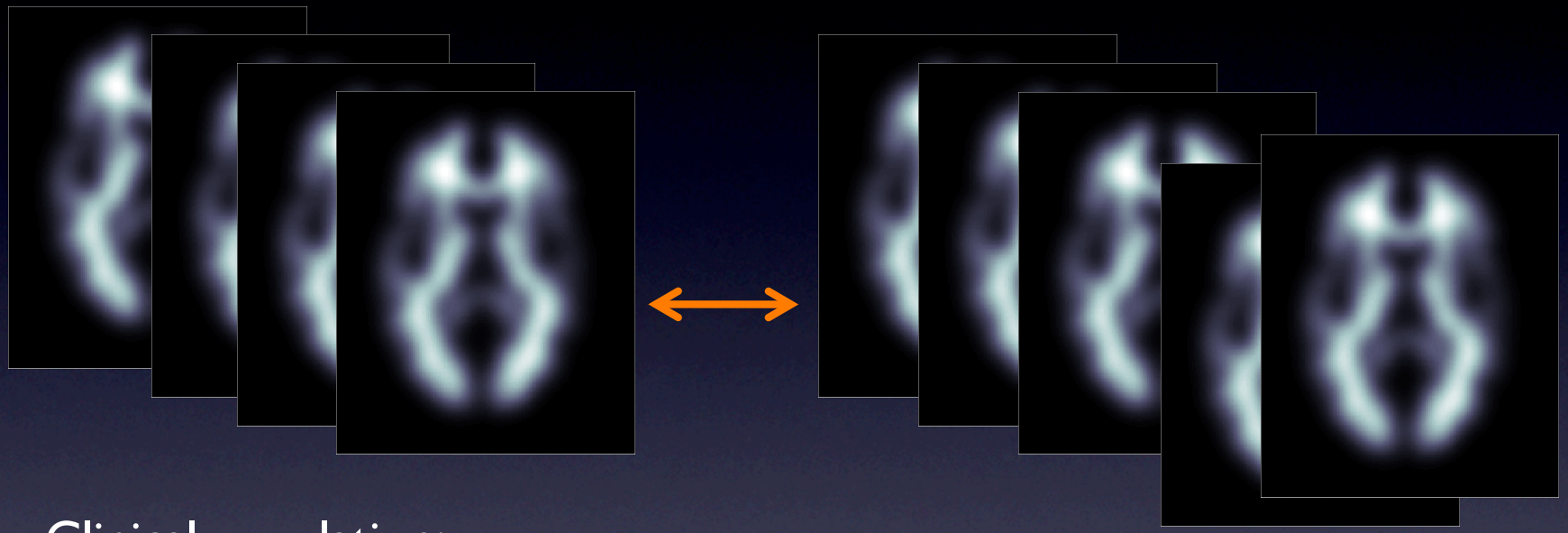


Mild cognition impairment (MCI) - control at p=0.05

Image registration

Typical question in computational neuroanatomy

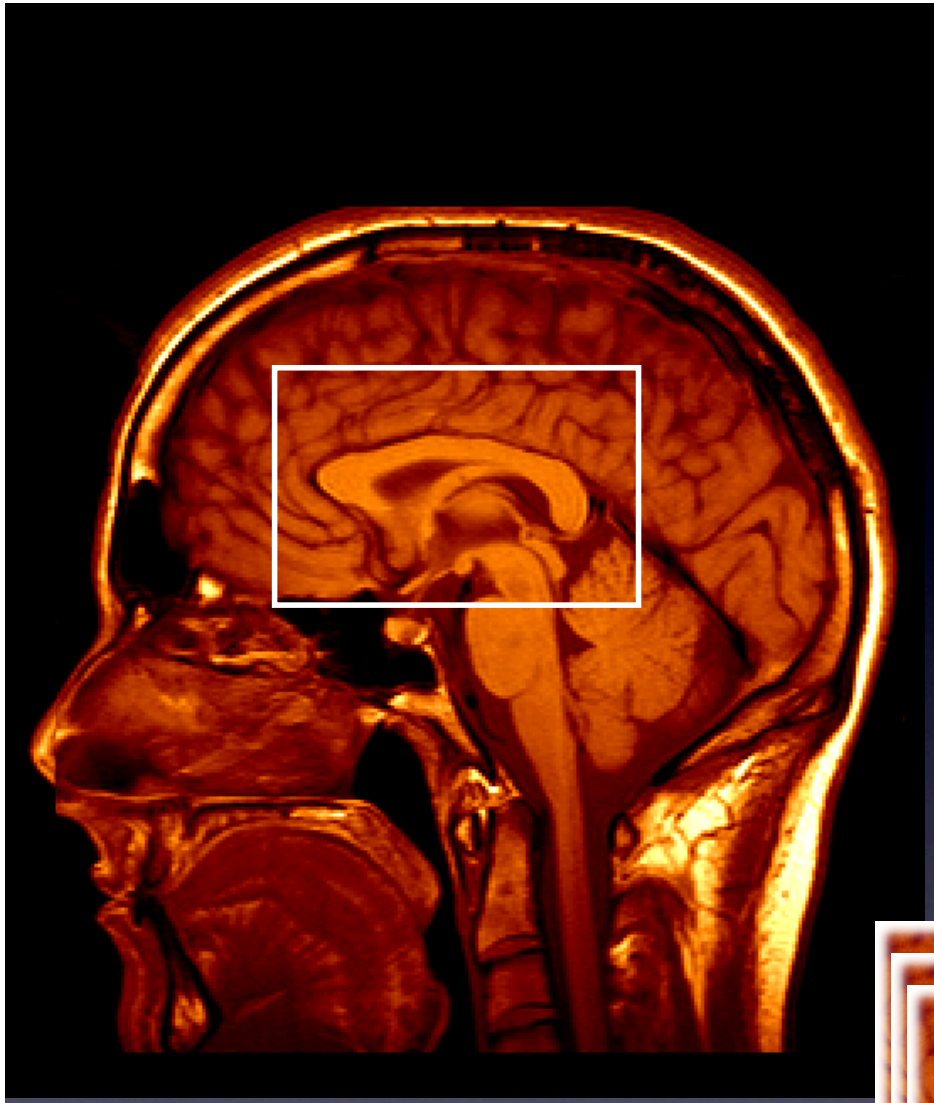
Given a collection of images



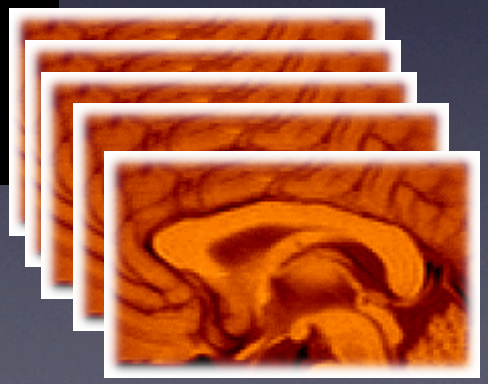
Clinical population:
autism, Parkinson's decease

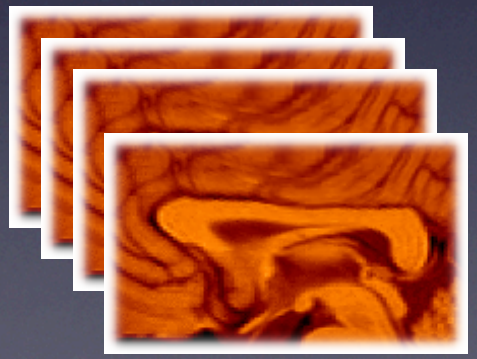
Normal controls

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



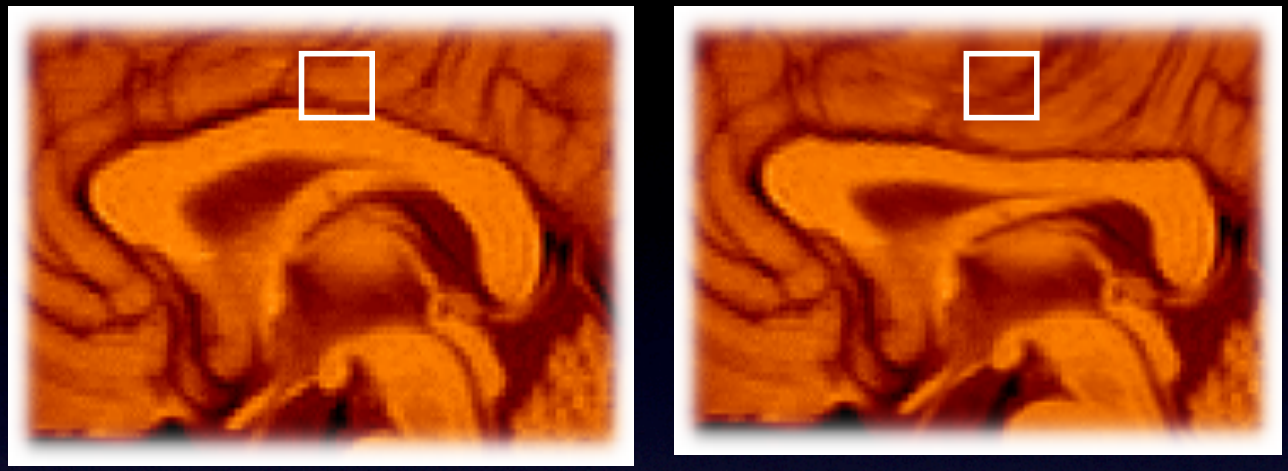
Each subject has different brain shape. So how do we compare shape difference across subjects?





Group 1

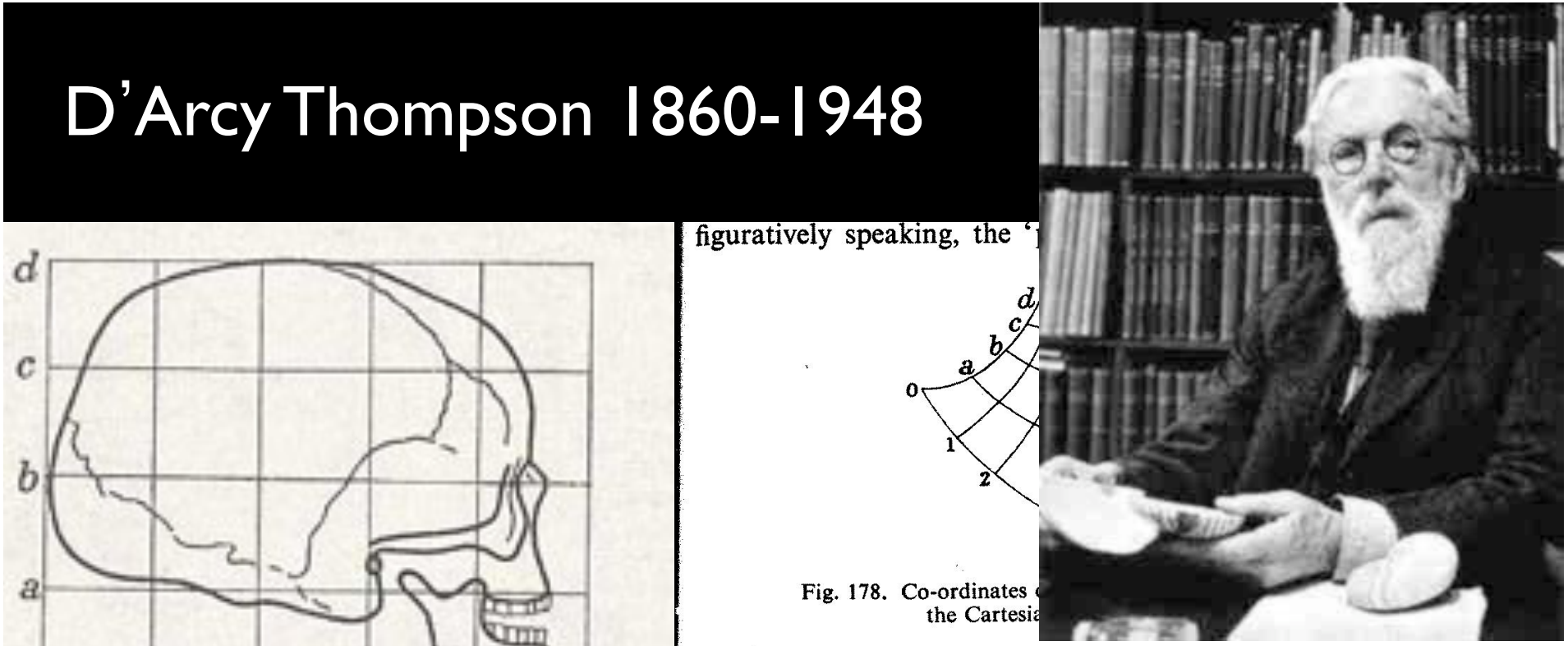
Group 2



Direct voxel-to-voxel comparison causes anatomical mismatching.

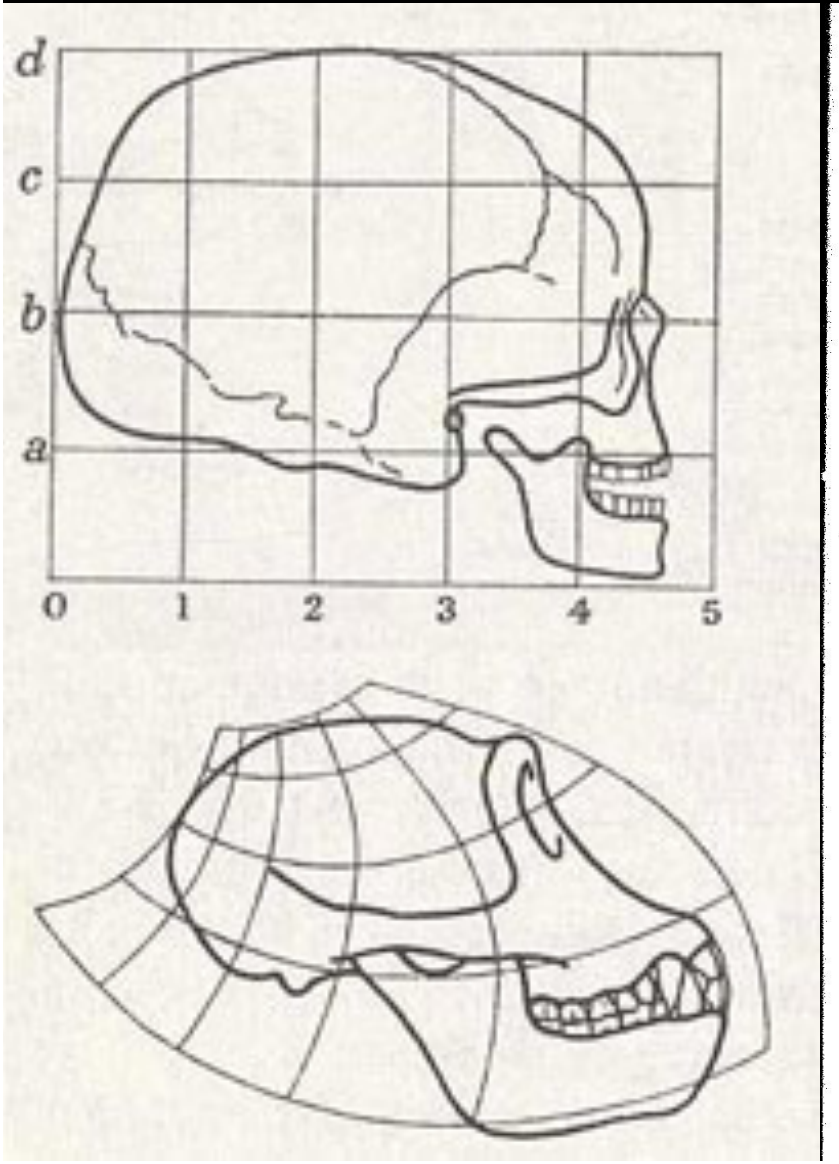
Image registration: The aim of image registration is to find a smooth one-to-one mapping that matches homologous anatomies together.

D'Arcy Thompson 1860-1948



figuratively speaking, the '

Fig. 178. Co-ordinates
the Cartesia



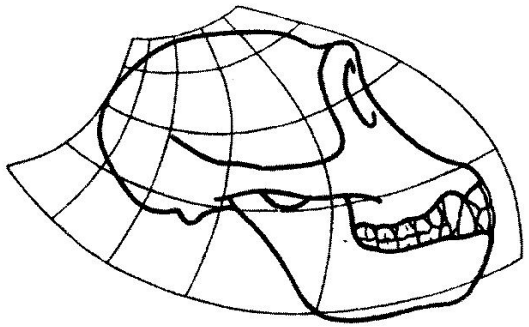


Fig. 179. Skull of chimpanzee.

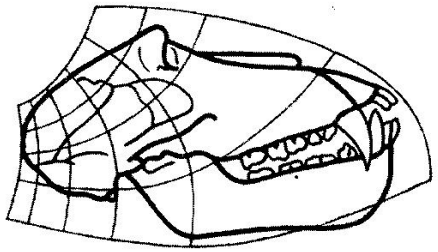


Fig. 180. Skull of baboon.

diagram
I have sh
is obviou
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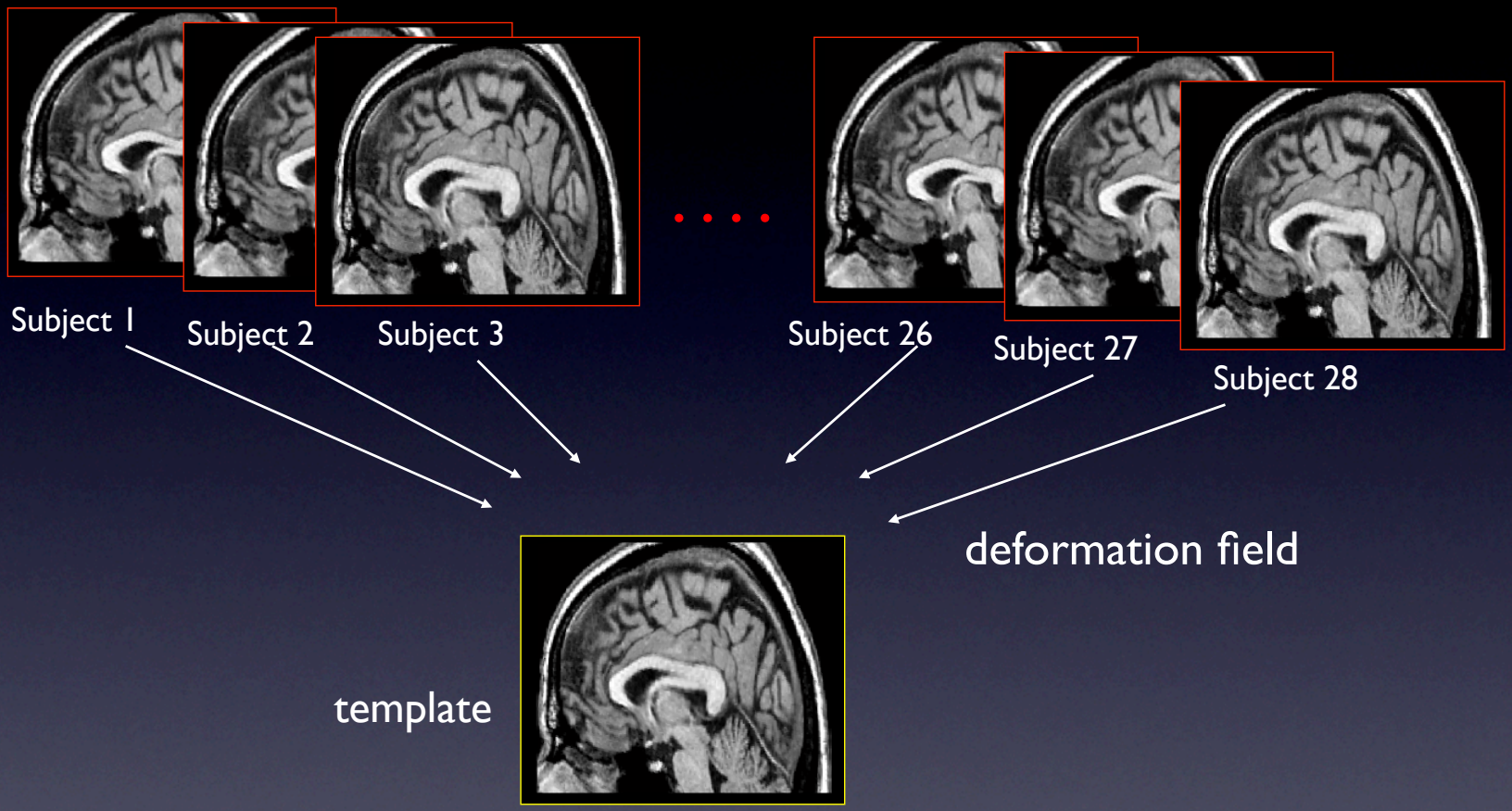
anthropo

n Fig. 180
oon, and it
order, and
ion.[1] These
another by

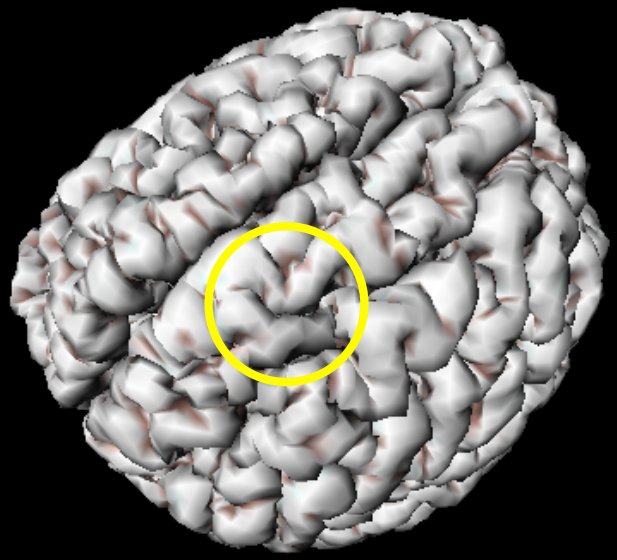
On Growth and Form
D'Arcy Thompson

Deformable template framework

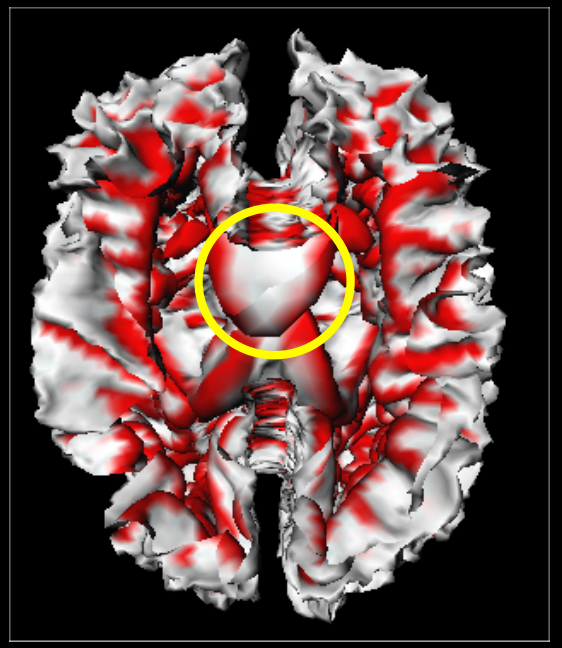


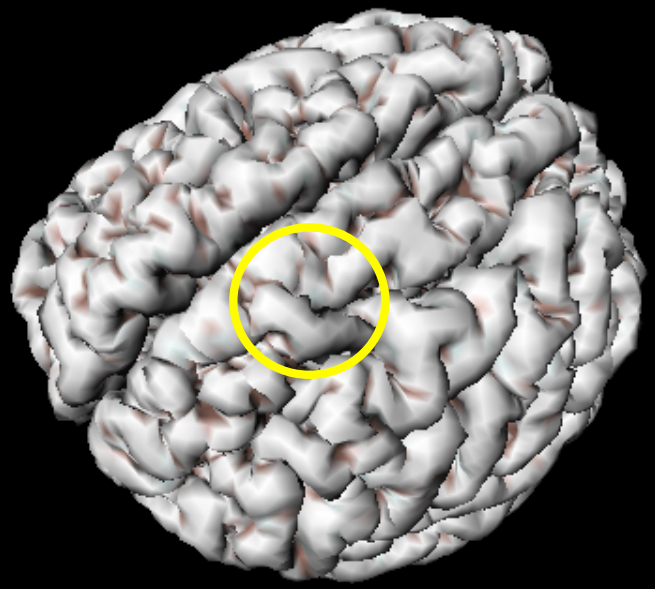
MRIs will be warped into a template and anatomical differences can be compared at a common reference frame.

Motivation for 2D cortical surface matching

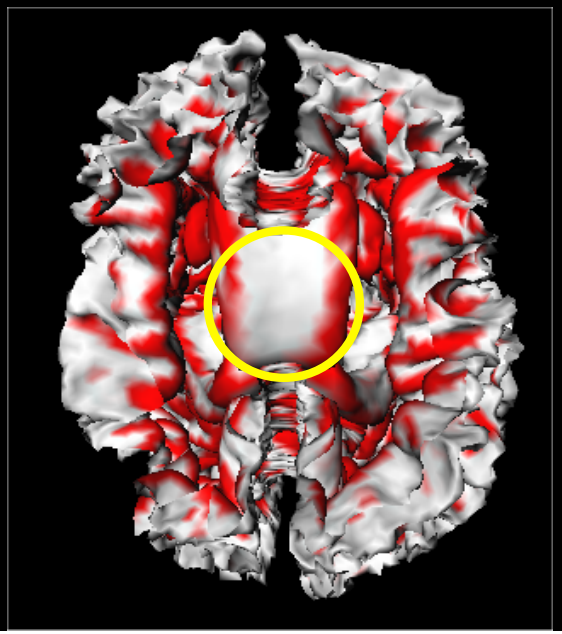


14 year old

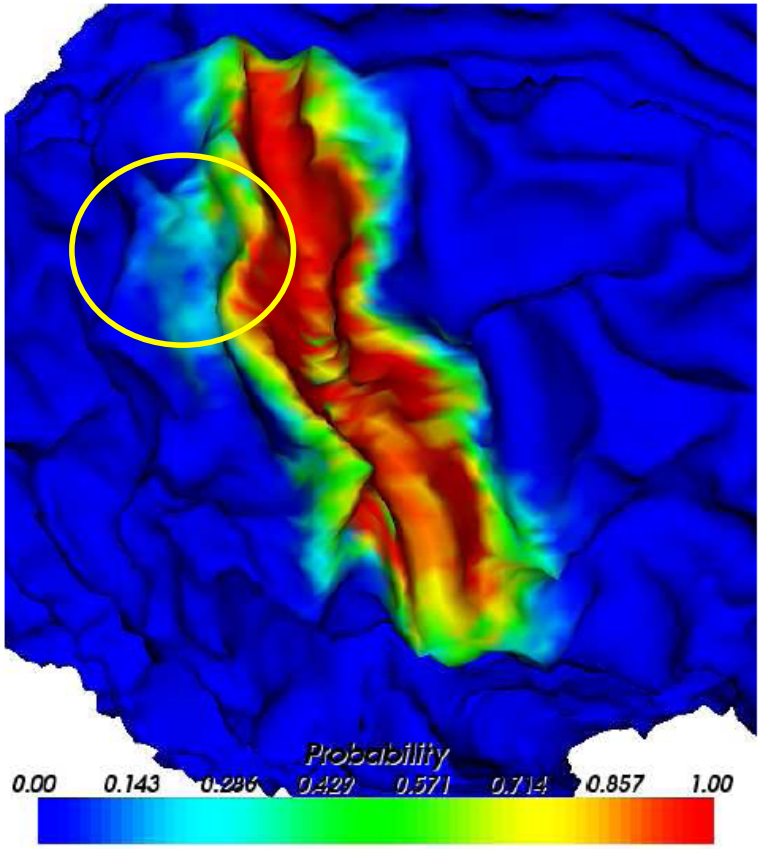


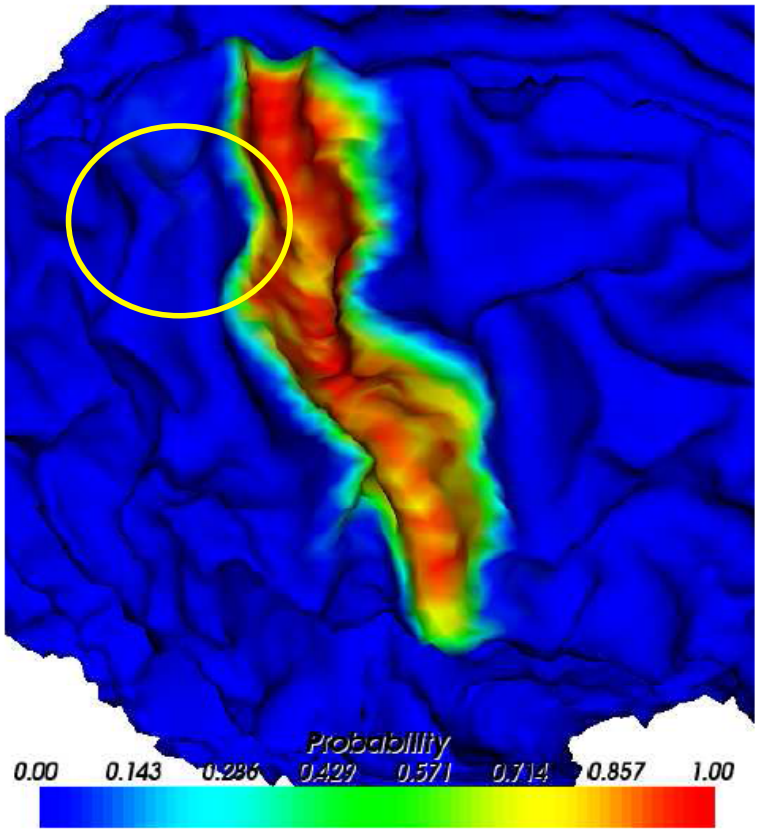


19 year old



Probability of matching in right central sulcus





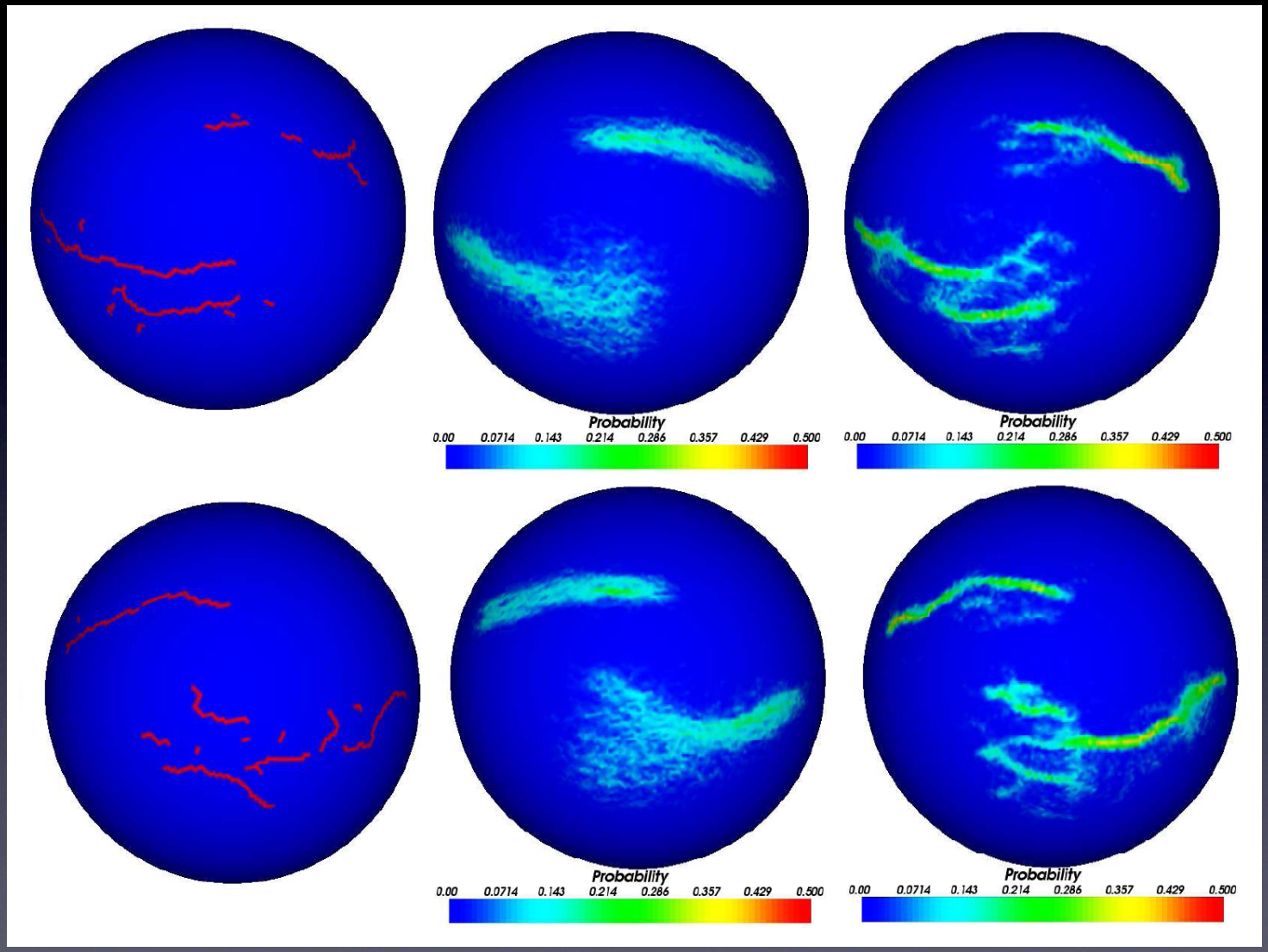
3D volume registration

2D surface registration

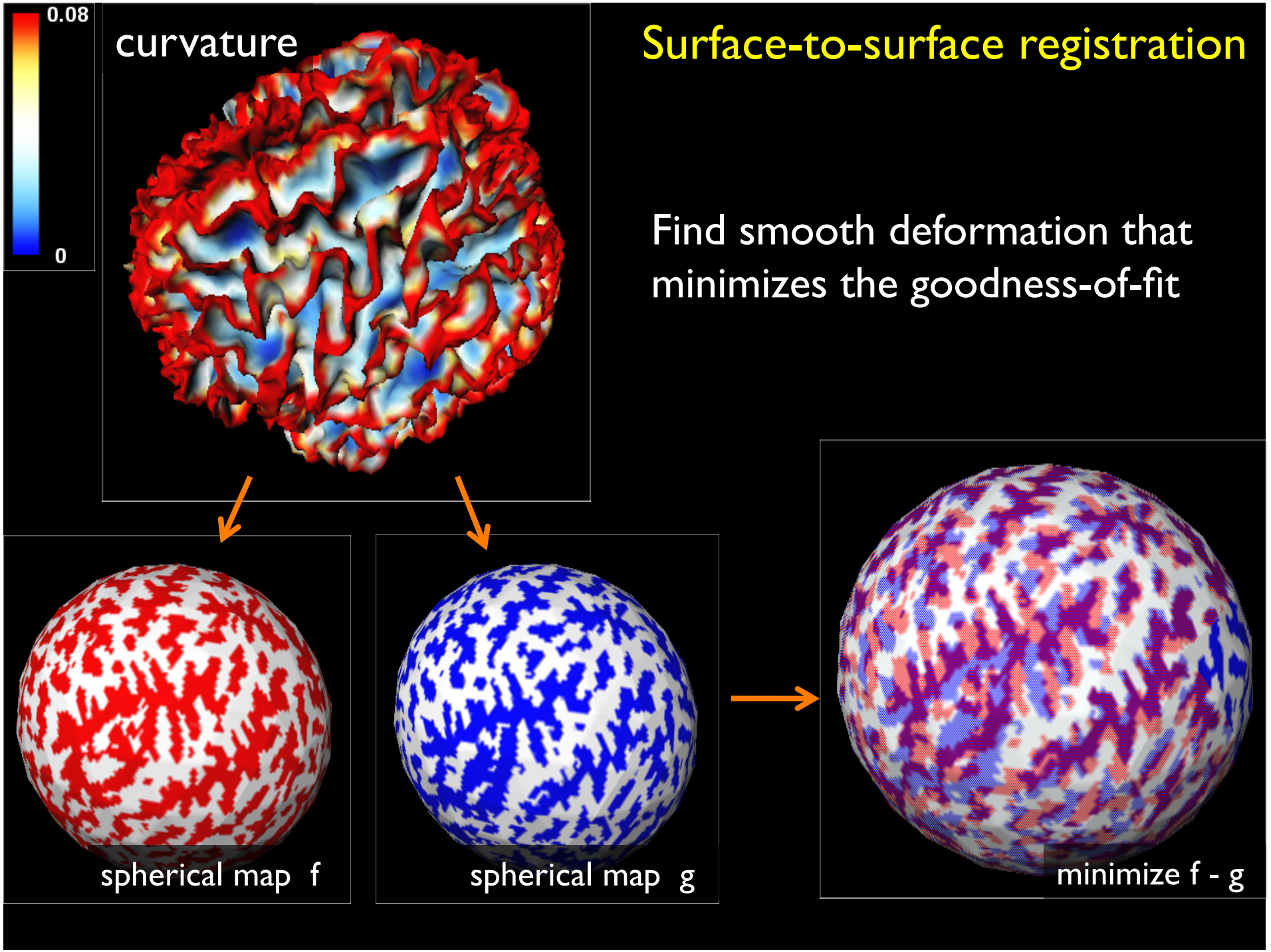
Chung et al., 2005 NeuroImage

Validation of surface registration (149 subjects)

Central & temporal sulci



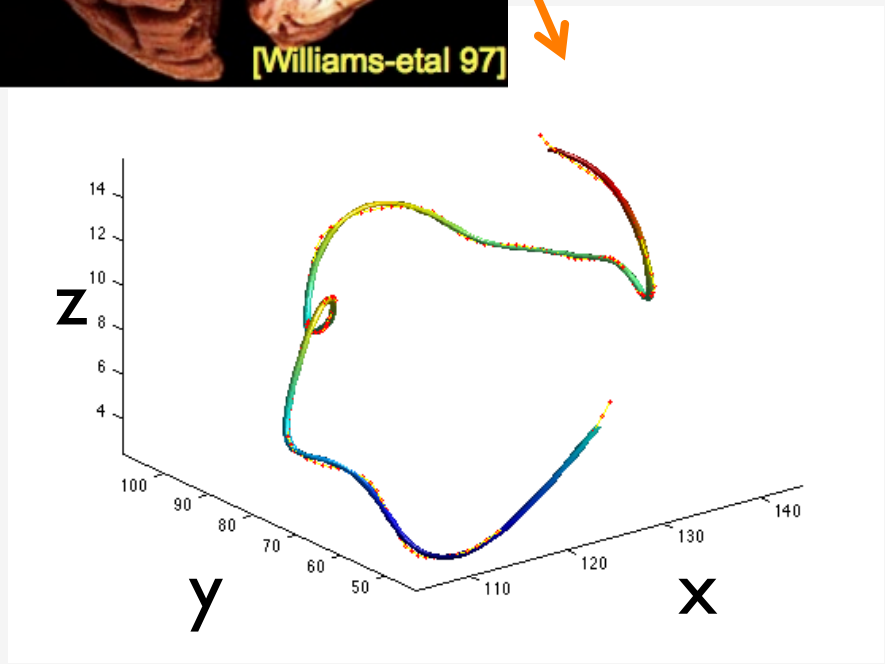
NeuroImage (2005)

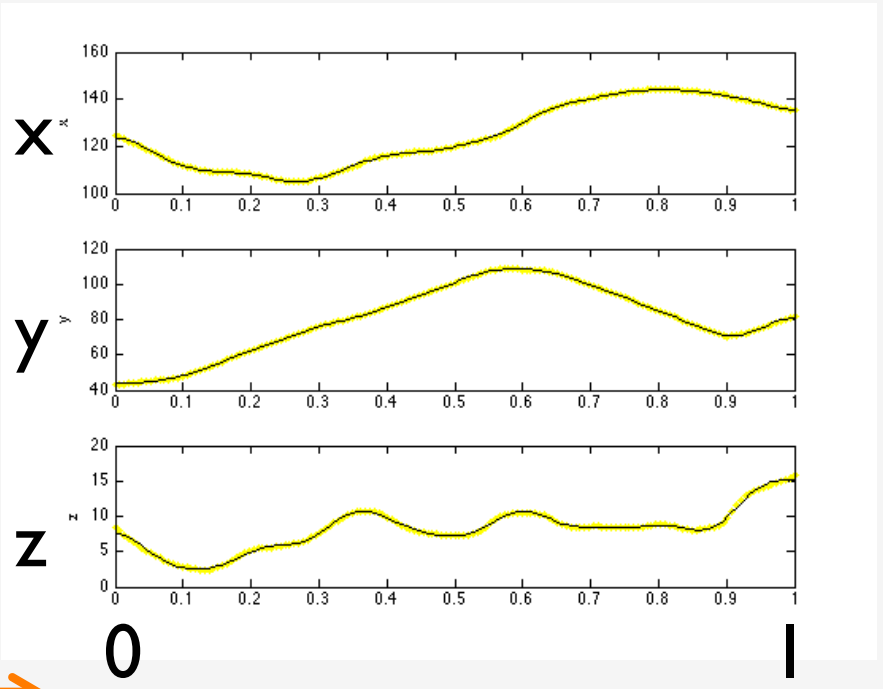

0.08
0
curvature
Surface-to-surface registration
Find smooth deformation that
minimizes the goodness-of-fit
spherical map f
spherical map g
minimize f - g

Shape representation and modeling

DTI white matter fiber tracts

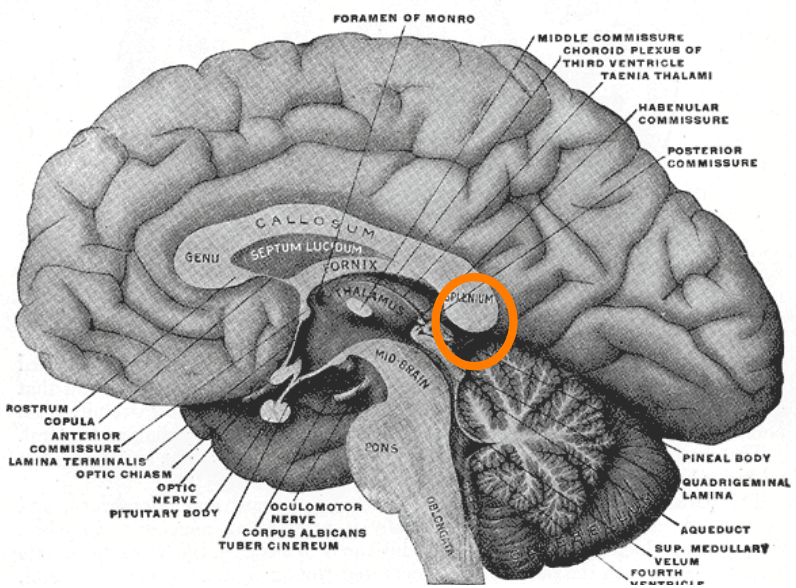
Image acquisition
& processing



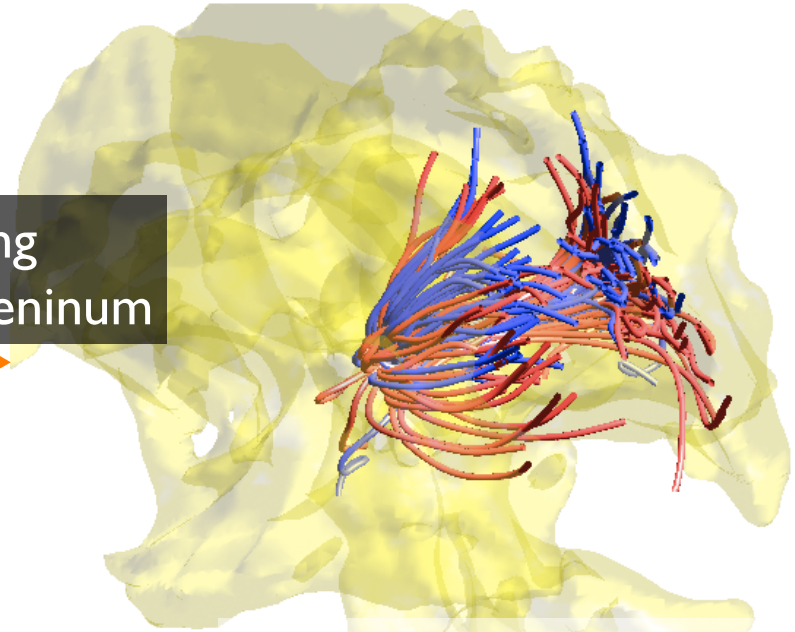


parameterization

Fiber concentration analysis in splenium

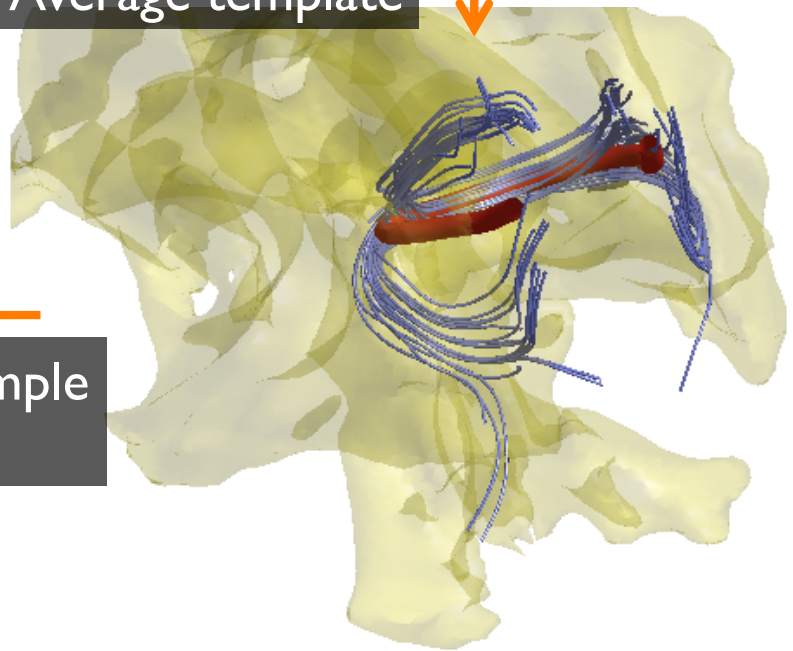


tracts passing through spleninum

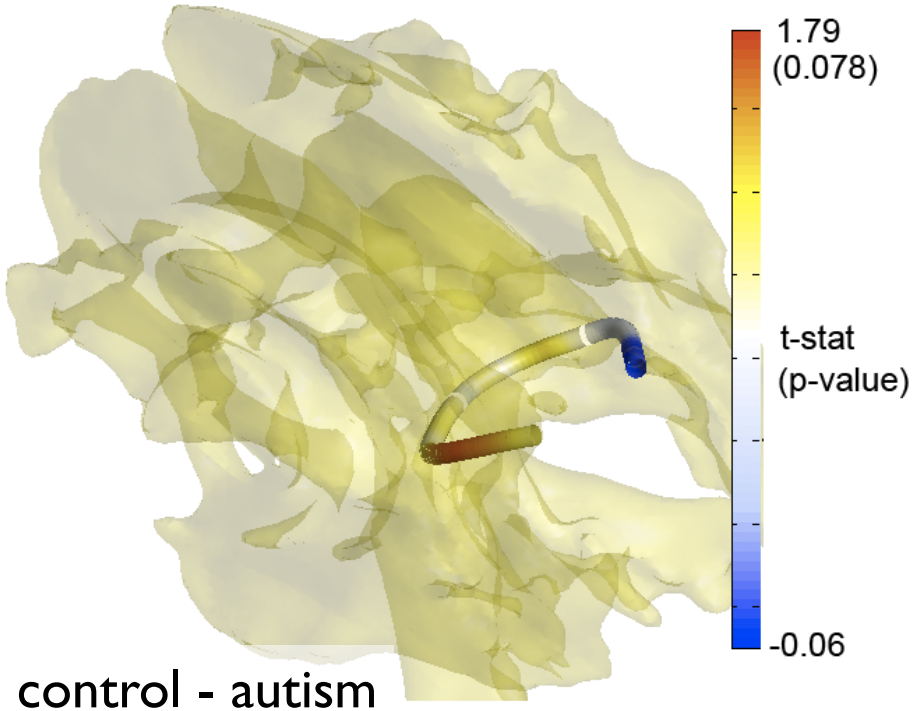


42 autistic & 32 control

Average template

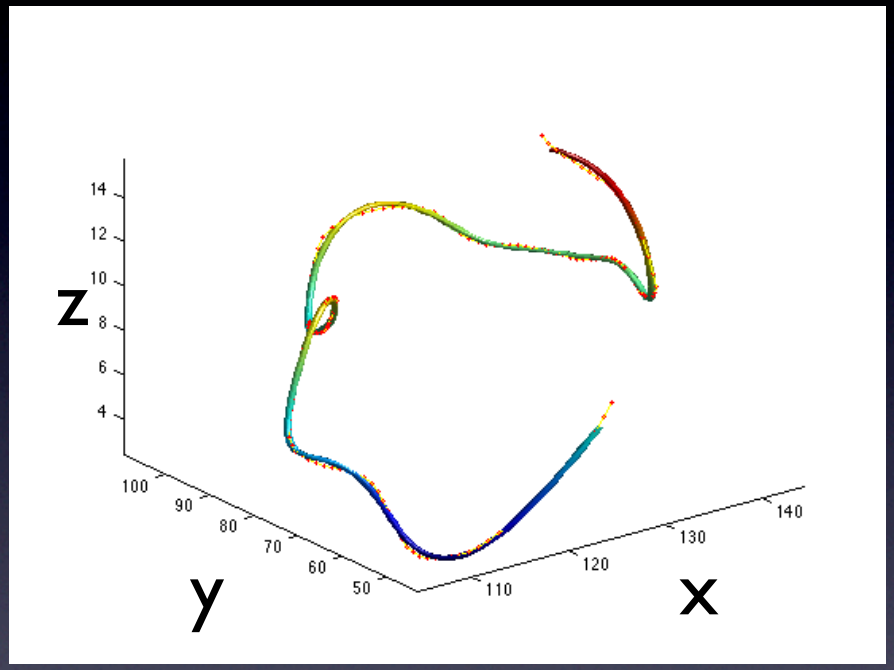


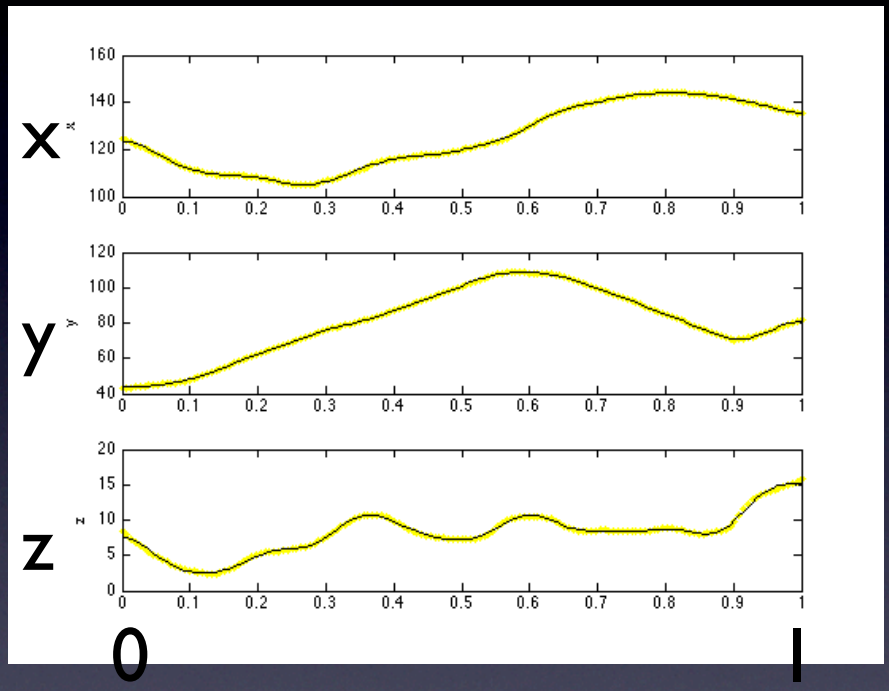
two sample t-test



control - autism

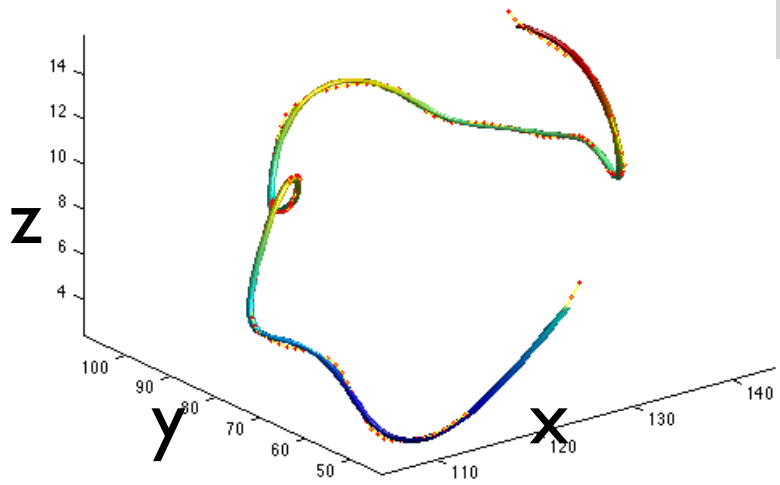
DTI Tract parameterization



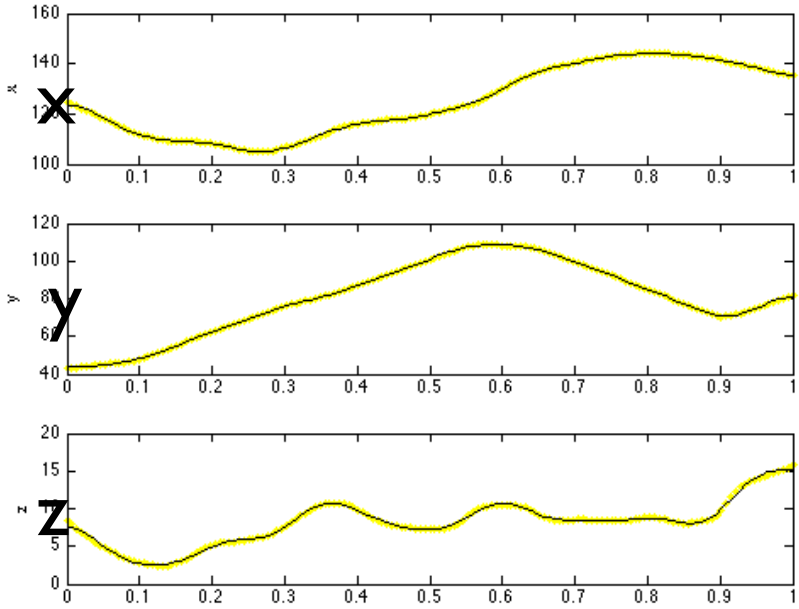


x, y, z coordinate functions are mapped onto a unit interval

Cosine series representation



parameterization



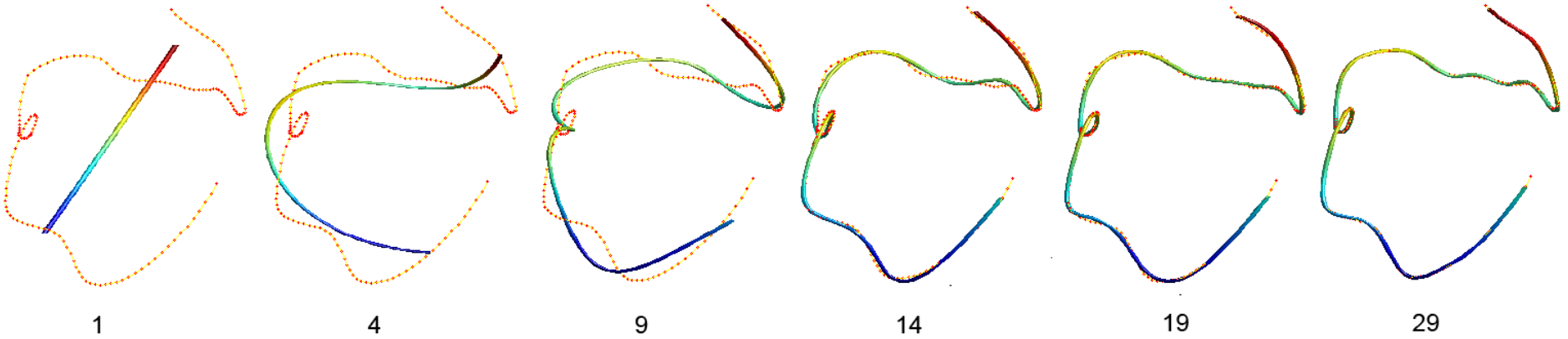
basis expansion

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

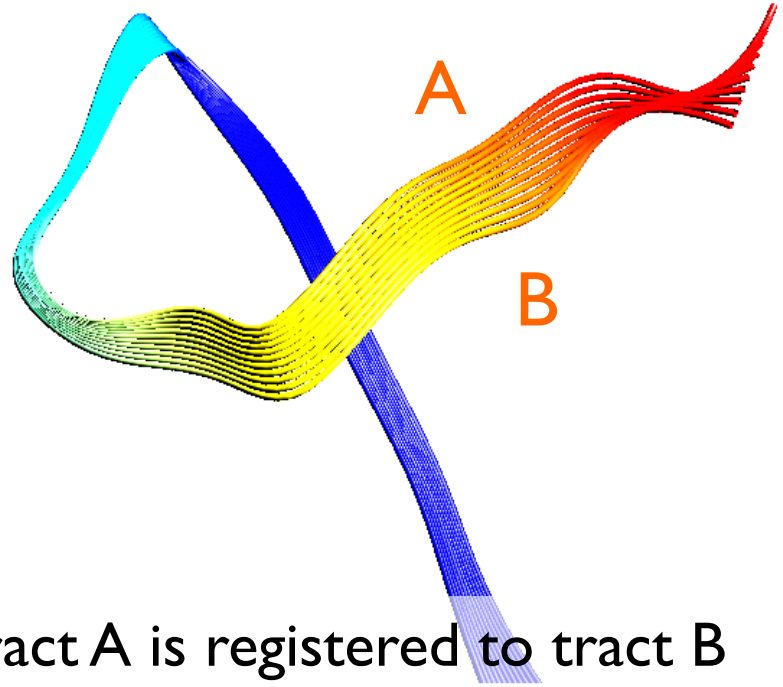
Any tract can be compactly parameterized with only 60 coefficients.

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

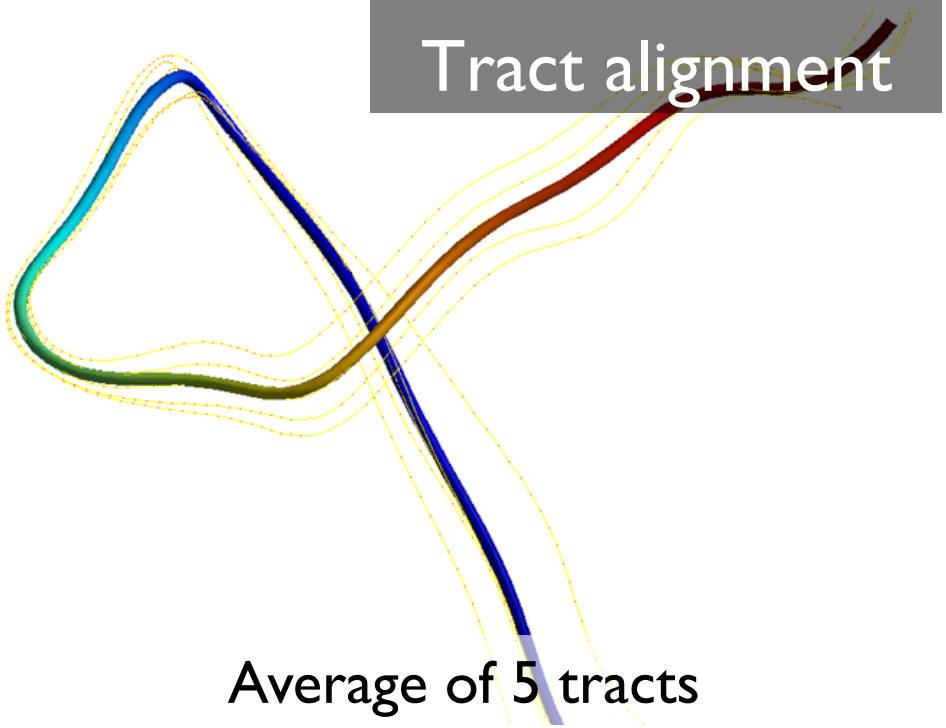
Cosine representation



Tract alignment

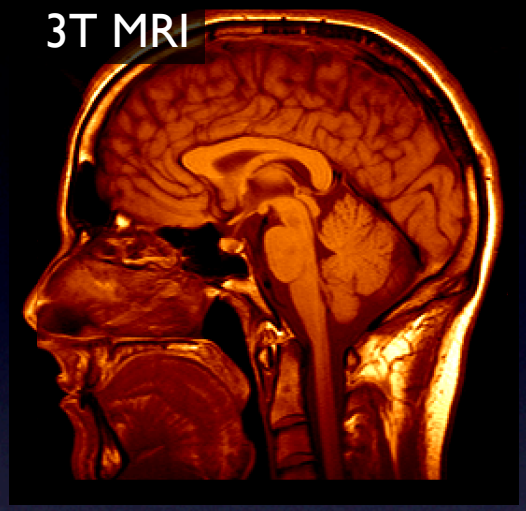


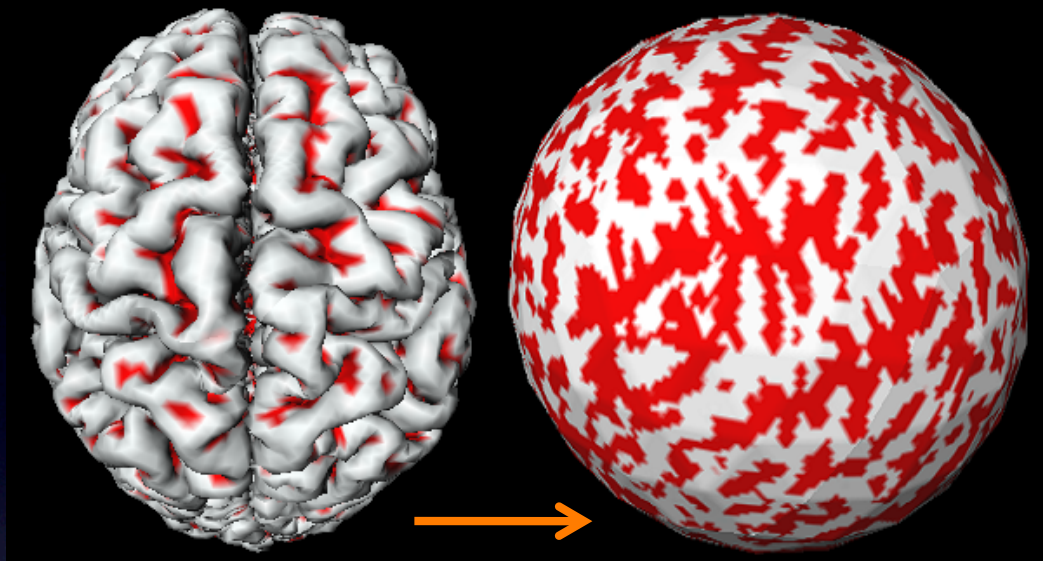
Tract A is registered to tract B



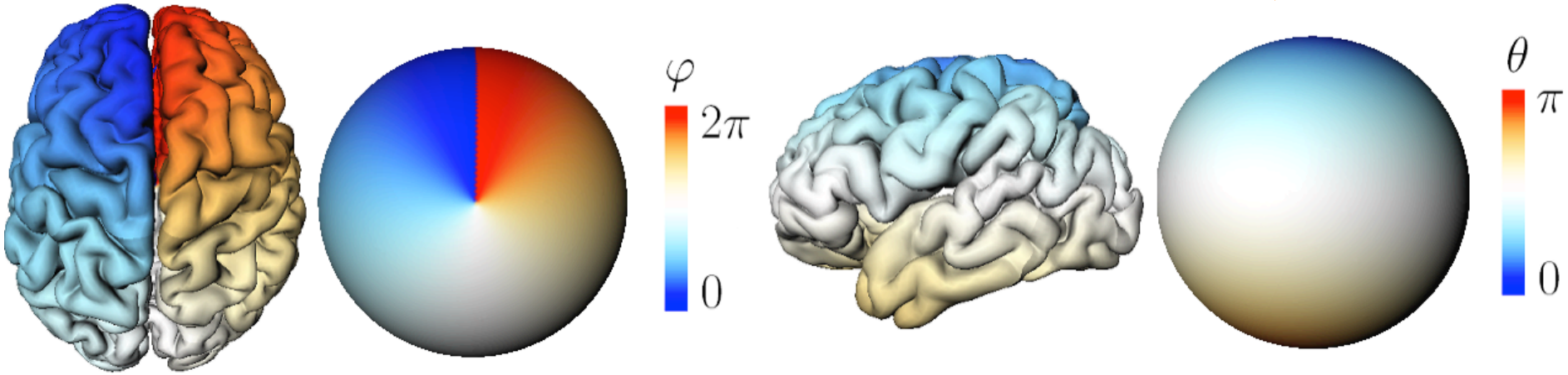
Average of 5 tracts

Cortical Surface Modeling





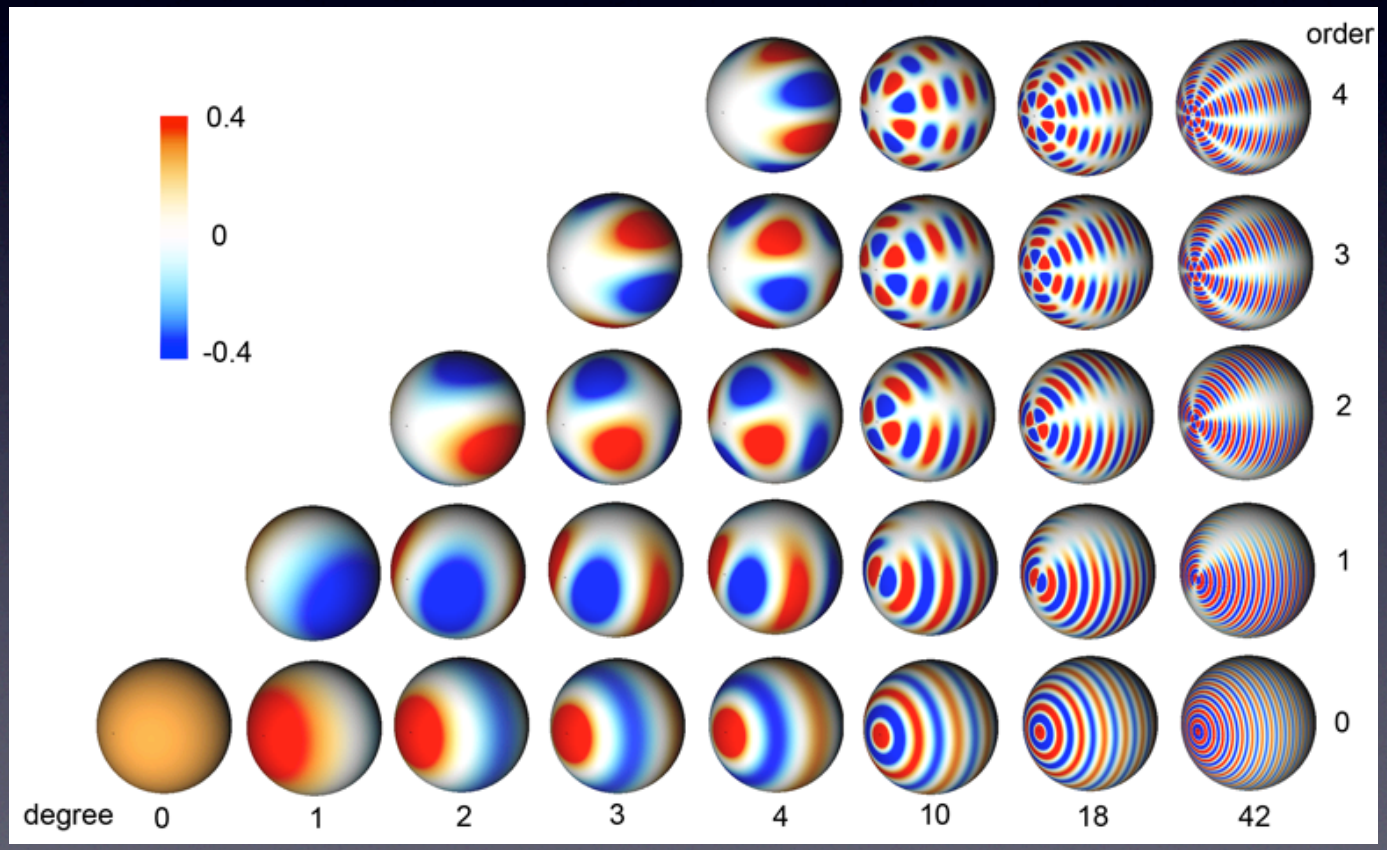
Deformable surface algorithm



Spherical angle based coordinate system

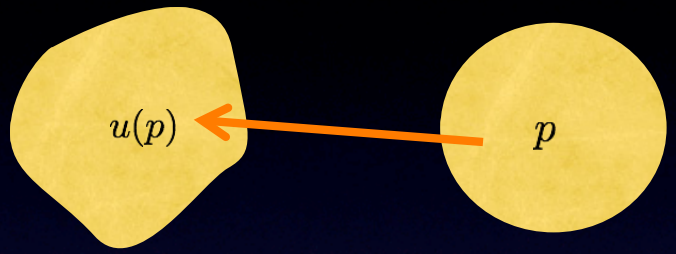
Spherical harmonic of degree *l* and order *m*

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



Coarse detail ⟷ Fine detail

Cortical manifold and function defined on the manifold



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

Anatomical manifold $\mathcal{M} \in \mathbb{R}^d$

tracts, amygdala, hippocampus, cortical surface

Flattening/ parameterization

Parameter space $\mathcal{N} \in \mathbb{R}^m$

Hilbert space $L^2(\mathcal{N})$ with inner product

$$\langle g_1, g_2 \rangle = \int_{\mathcal{N}} g_1(p) g_2(p) \mu(p)$$

Self-adjoint operator $\mathcal{L}$

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

Basis function

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

Weighted Fourier Analysis

t = scale, bandwidth, diffusion time

Input signal

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

Analytic solution

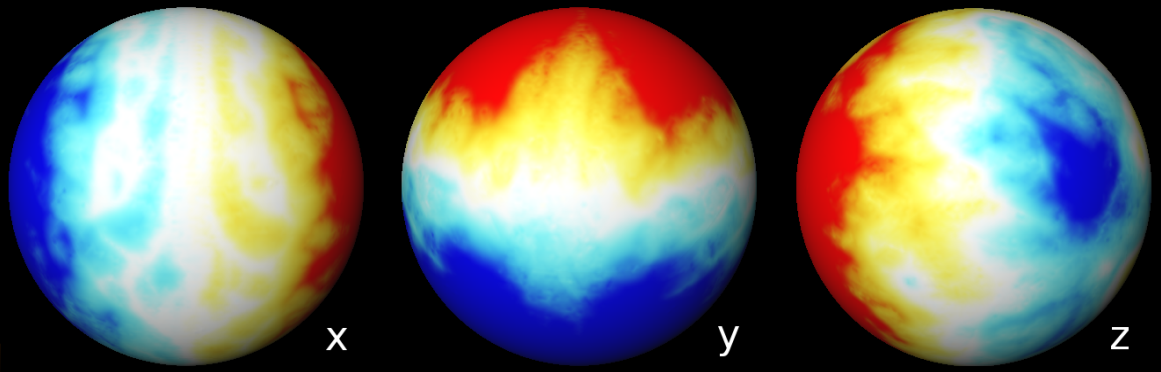
Weighted Fourier series $g(p,t) = \sum_{j=0}^{\infty} e^{-\lambda_j t} \langle f, \psi_j \rangle \psi_j(p)$

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

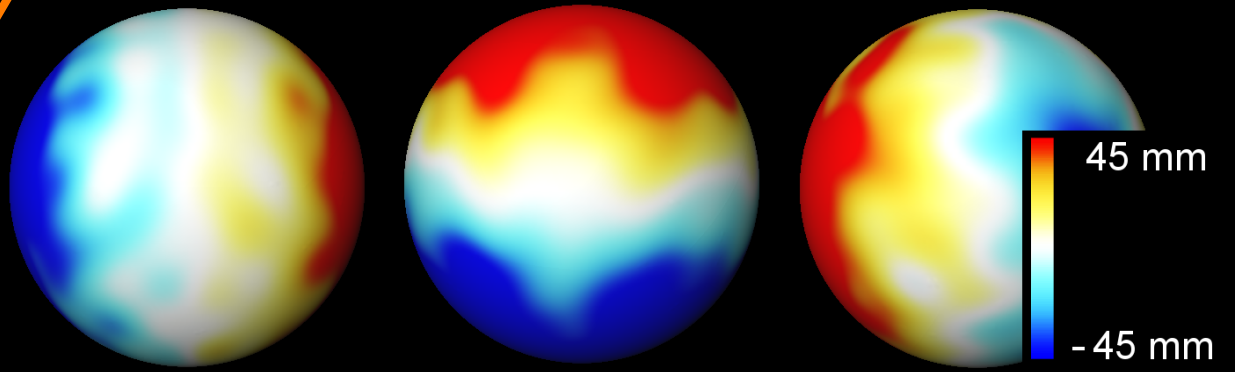
Spherical harmonic representation

Surface flattening

Coordinate functions



Weighted-SPHARM

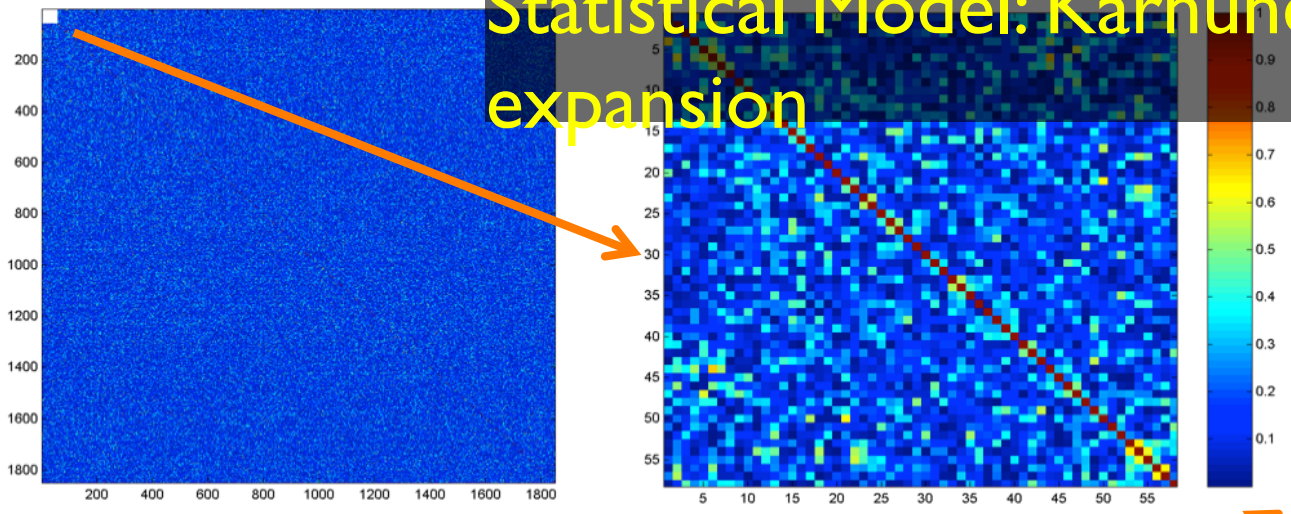


Coordinates are represented in a functional form:

$$\sum_{l=0}^{k} \sum_{m=-l}^{l} e^{-l(l+1)t} \langle f, Y_{lm} \rangle Y_{lm}(\theta, \varphi)$$

Let's take 15min break!

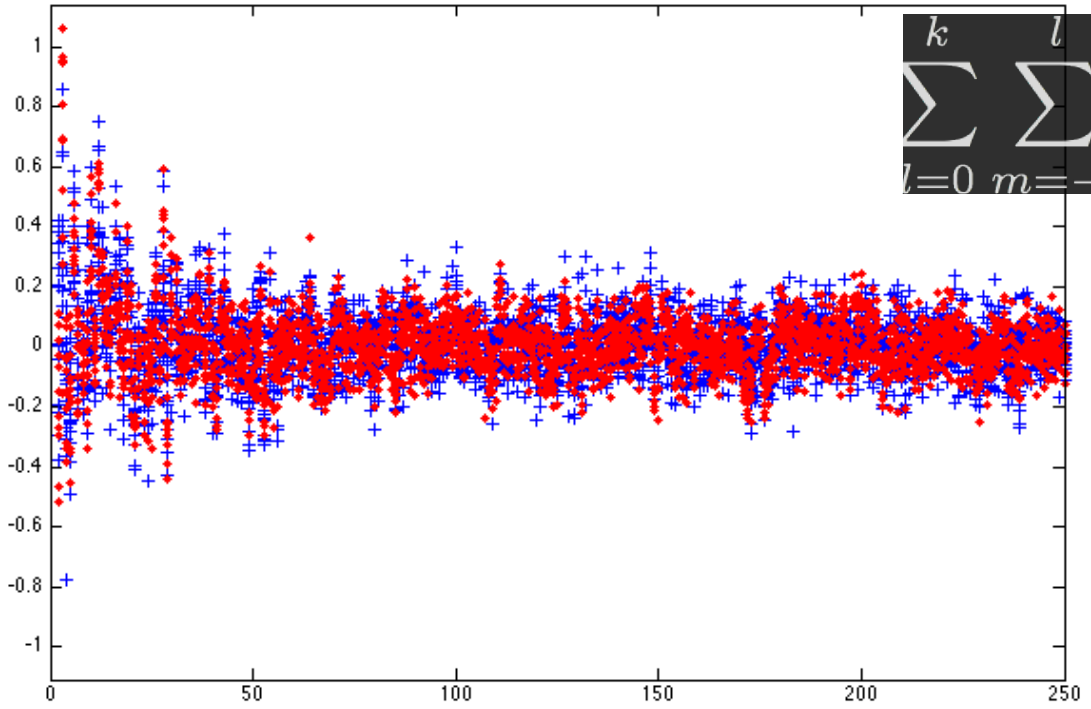
Statistical Model: Karhunen-Loeve expansion



Cross correlations

uncorrelated normal

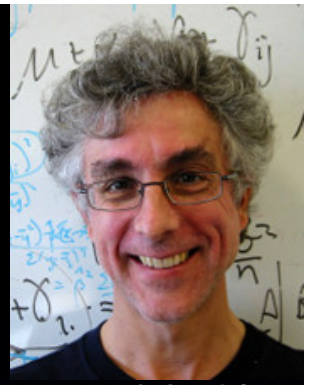
$$\sum_{l=0}^{k} \sum_{m=-l}^{l} e^{-l(l+1)t} \langle f, Y_{lm} \rangle Y_{lm}(\theta, \varphi)$$



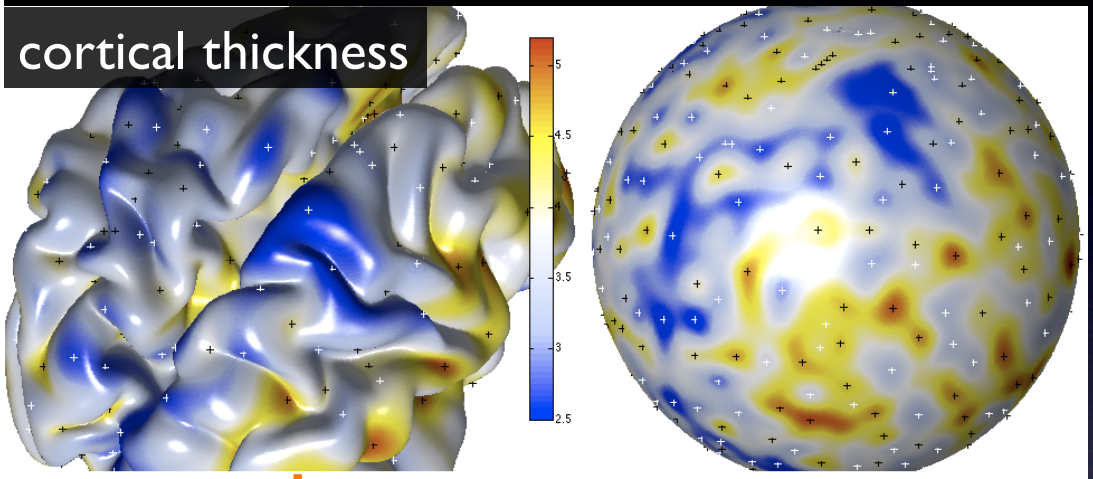
Classification ?

Persistent homology based signal detection (IPMI, 2009)

concept coming from algebraic topology, related to Euler characteristic, Betti numbers, Morse functions, Worsley's random field theory.



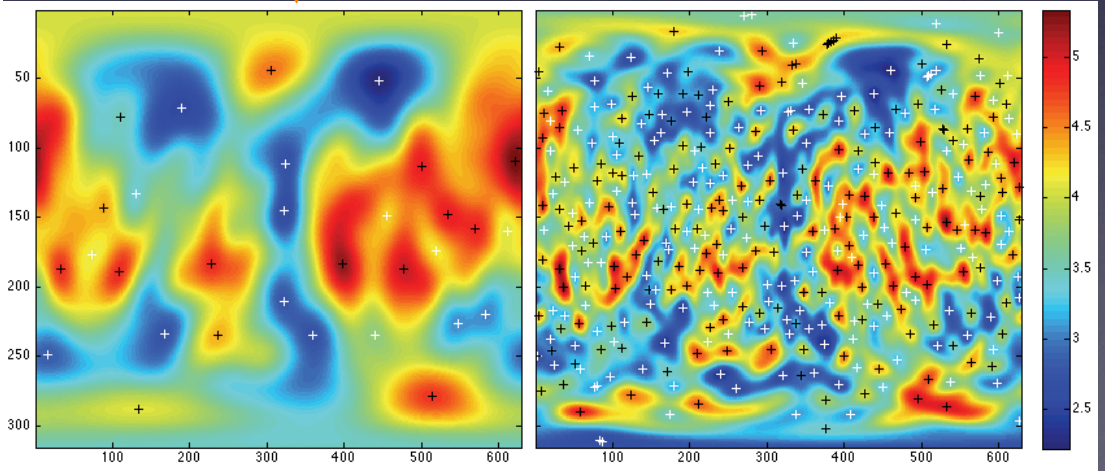
cortical thickness

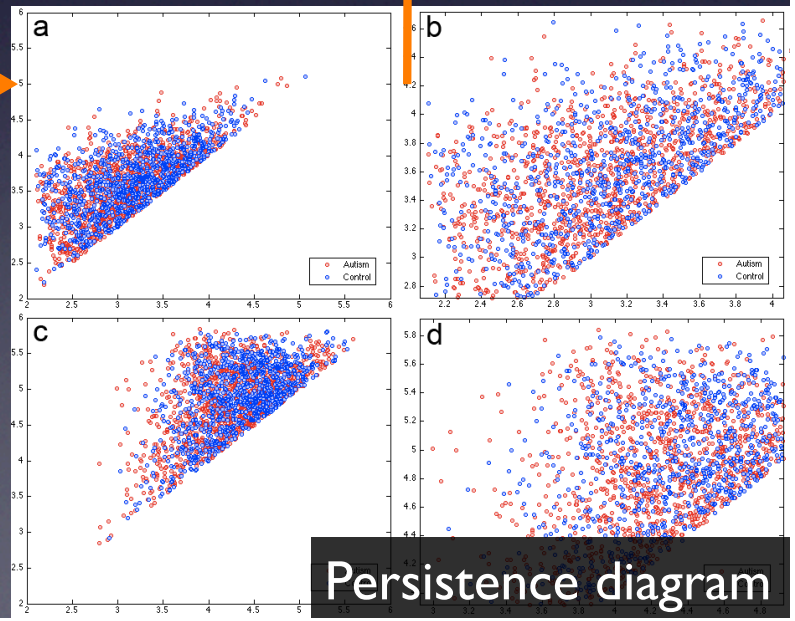


Classification accuracy of 96% using a simple support vector machine

Best available thickness analysis technique with Ada-boost 90%

cortical flattening



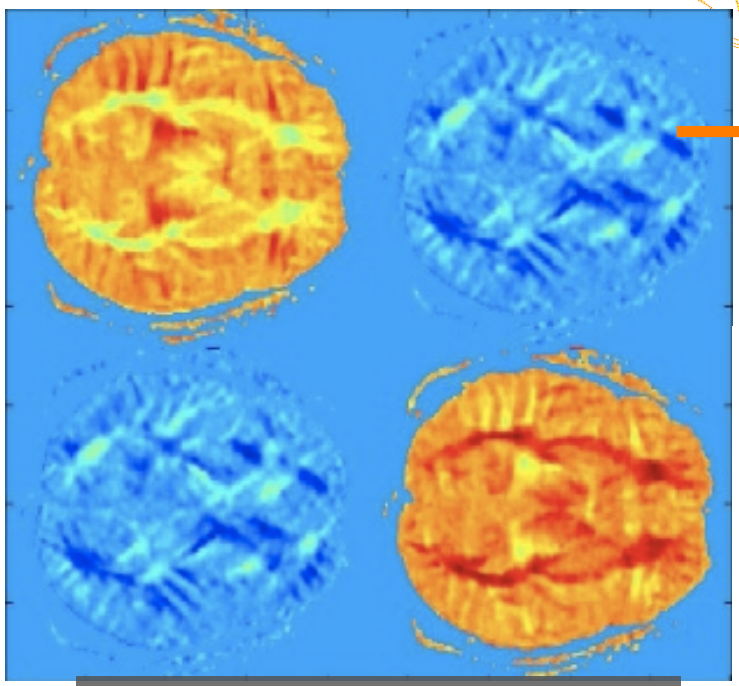


Persistence diagram

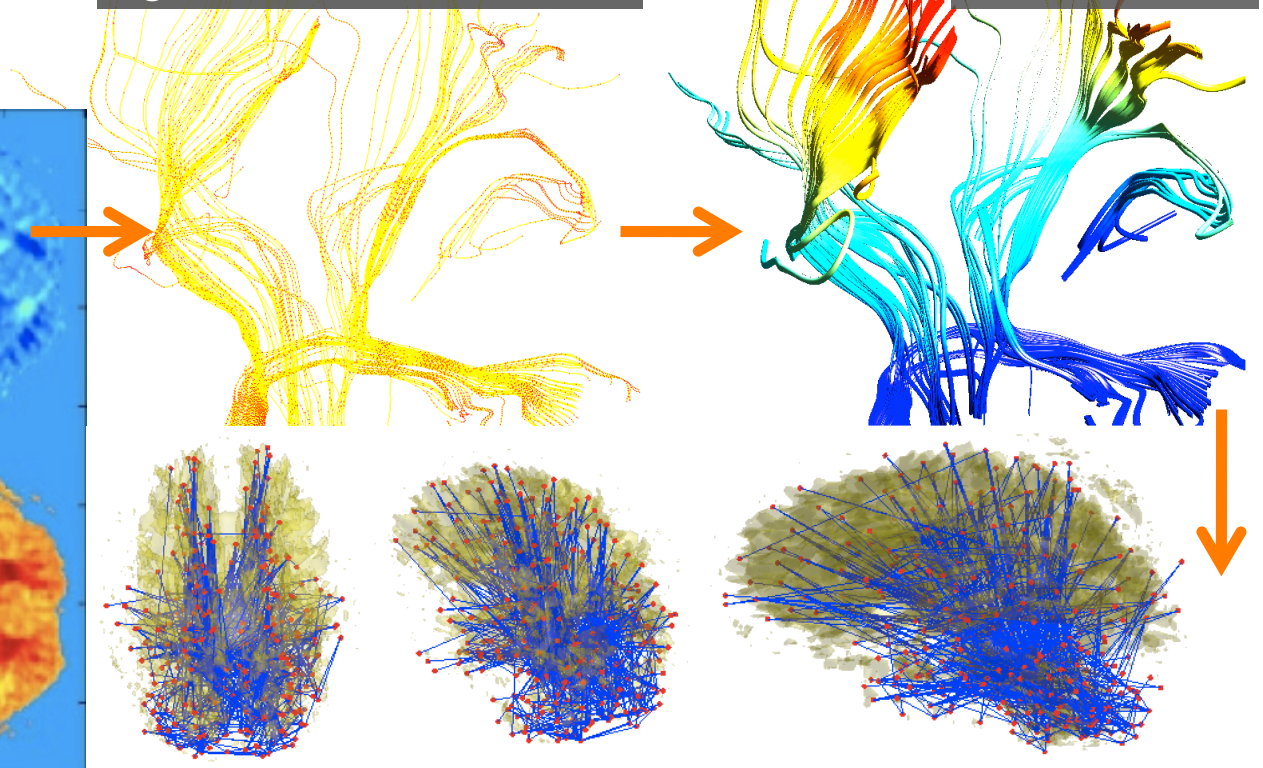
DTI connectivity model

Second order Runge-Kutta streamline algorithm

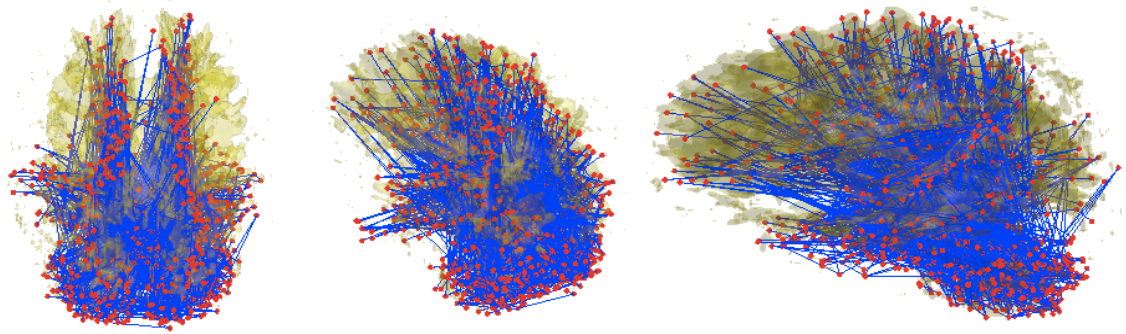
Cosine series representation



Diffusion tensor imaging (DTI)

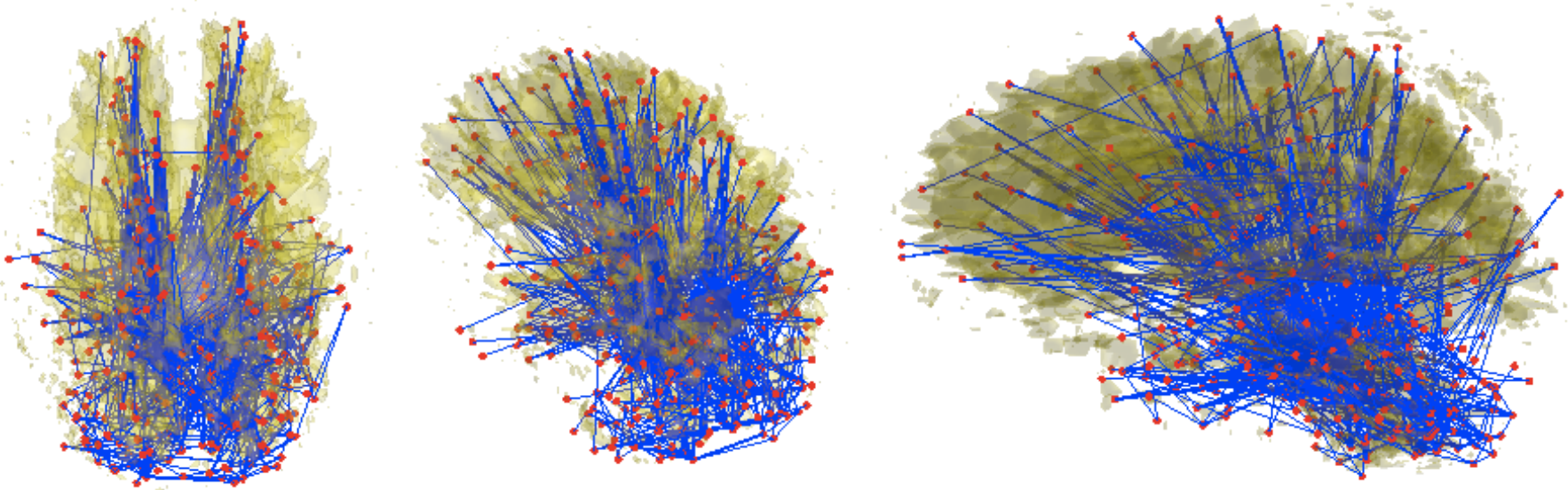


10 mm resolution 405 node network

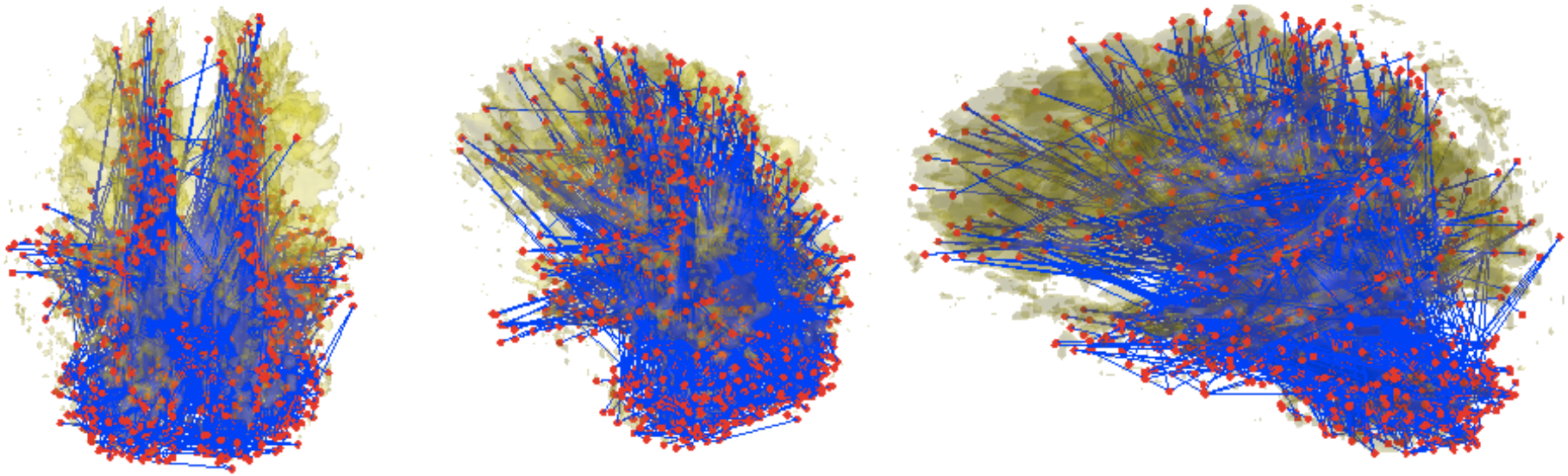


5 mm resolution 1502 node network

Multiscale 3D graph



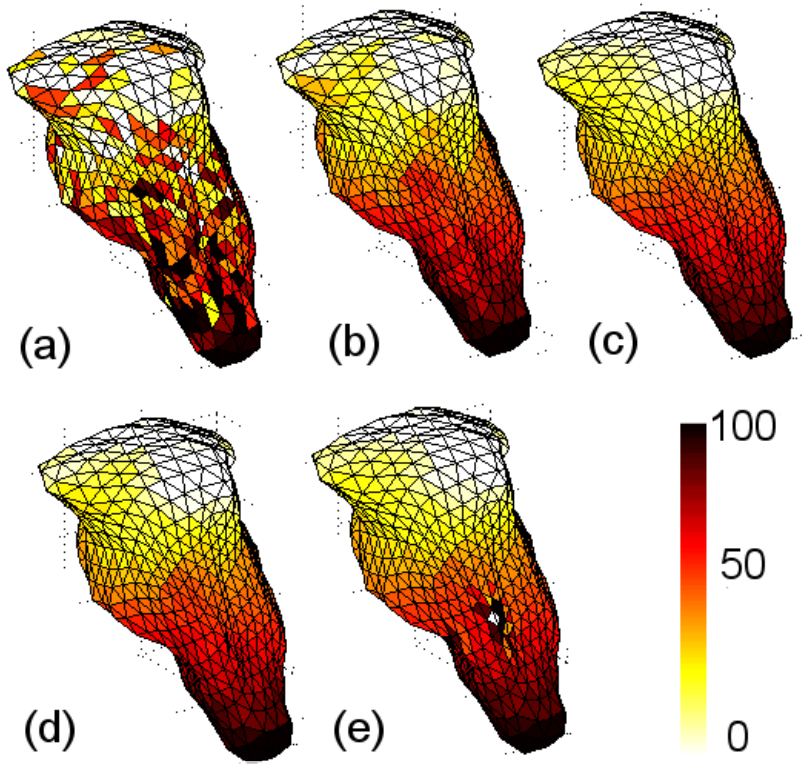
10 mm resolution 405 node network



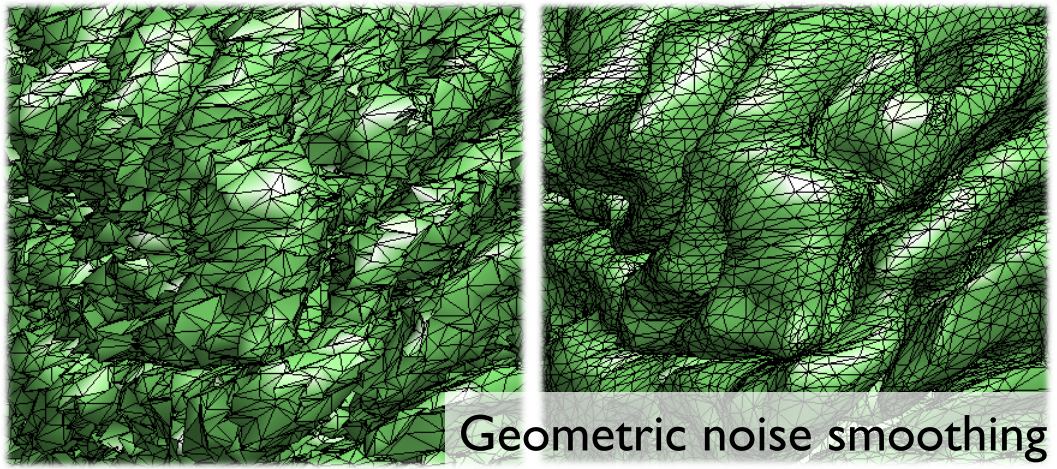
5 mm resolution 1502 node network

Image smoothing

Smoothing on anatomical boundary



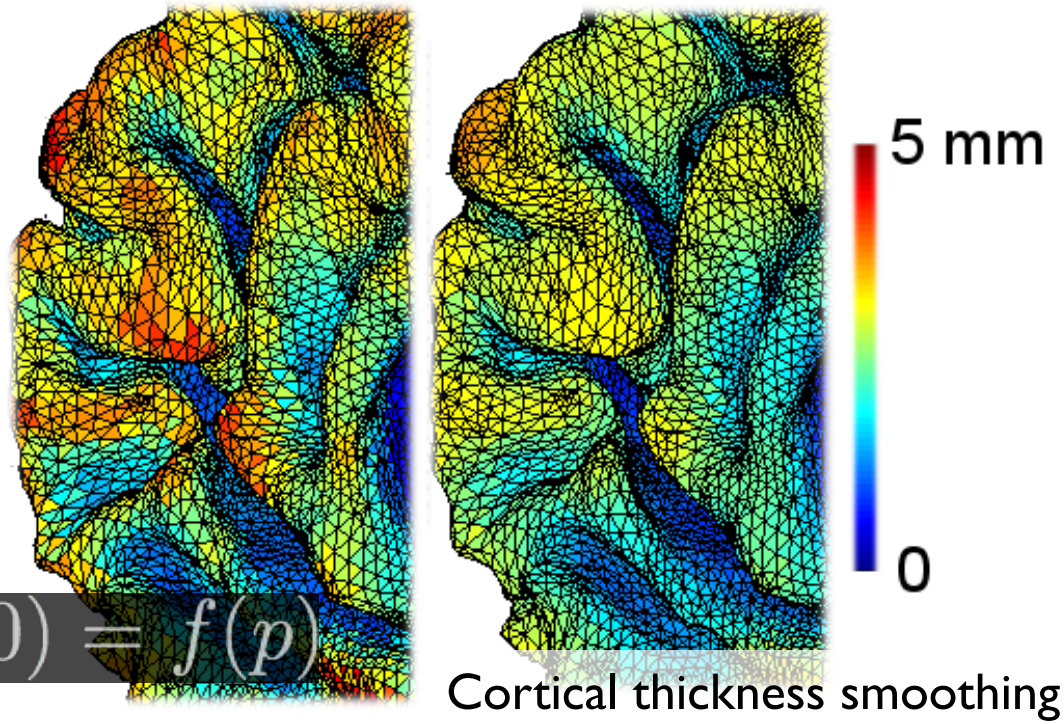
Diffusion smoothing on brain stem



Geometric noise smoothing

Diffusion equation

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



Cortical thickness smoothing

3D Gaussian kernel smoothing will blur measurements between A and B in different hemisphere

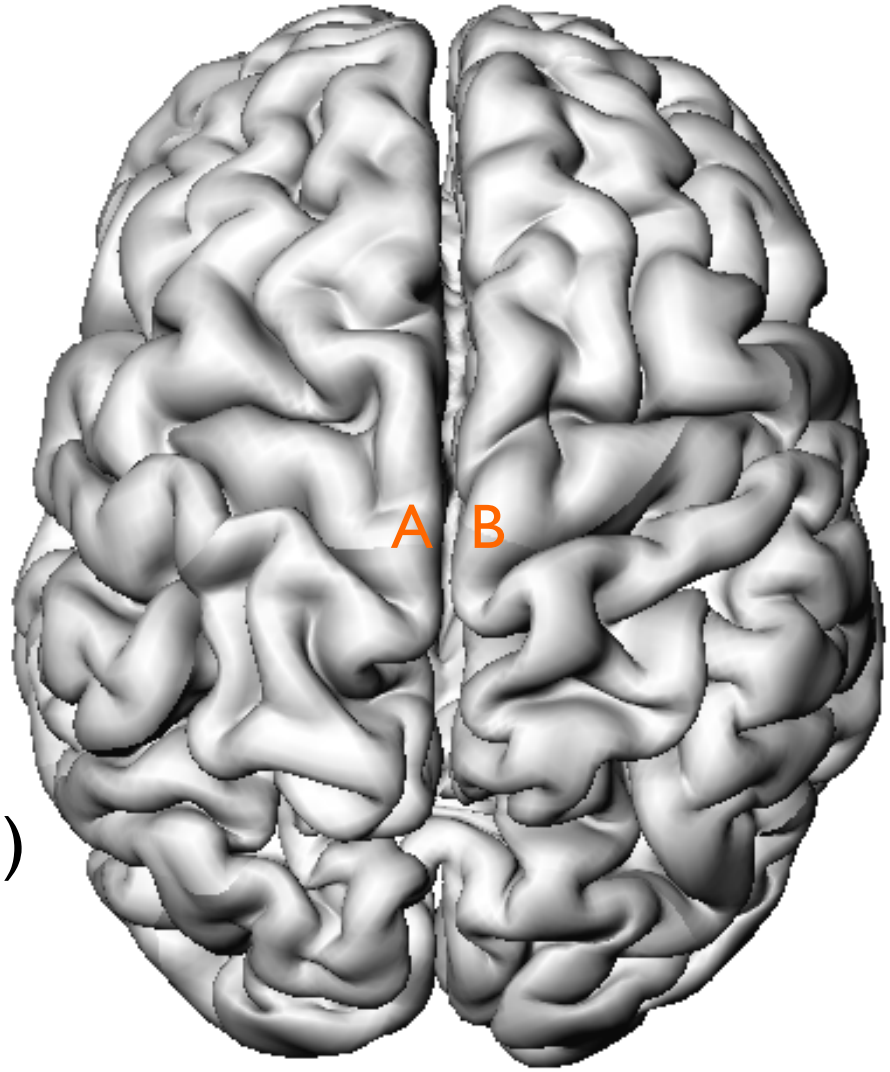
↓

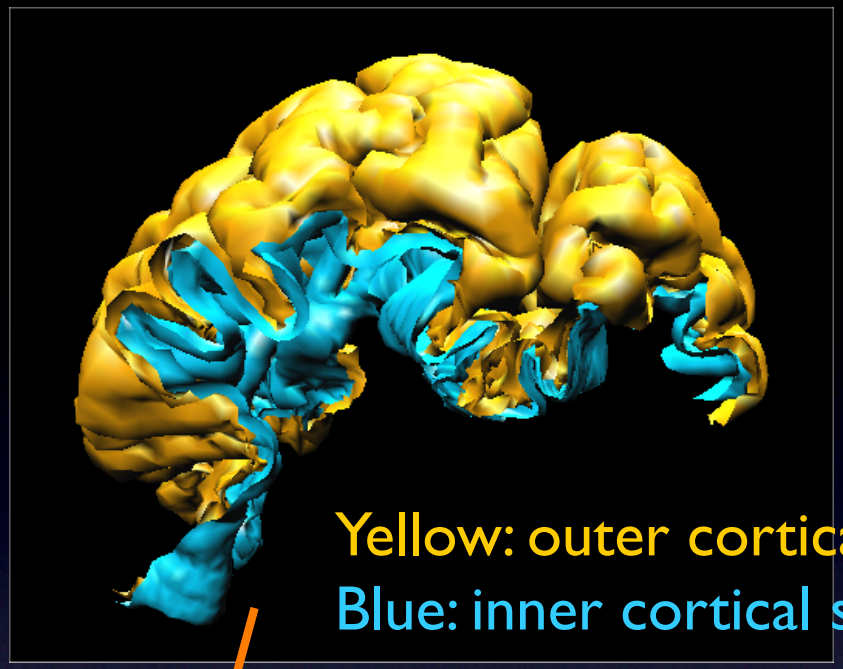
Need to smooth along the surface

↓

Diffusion smoothing (2001, 2003)
Heat kernel smoothing (2005)

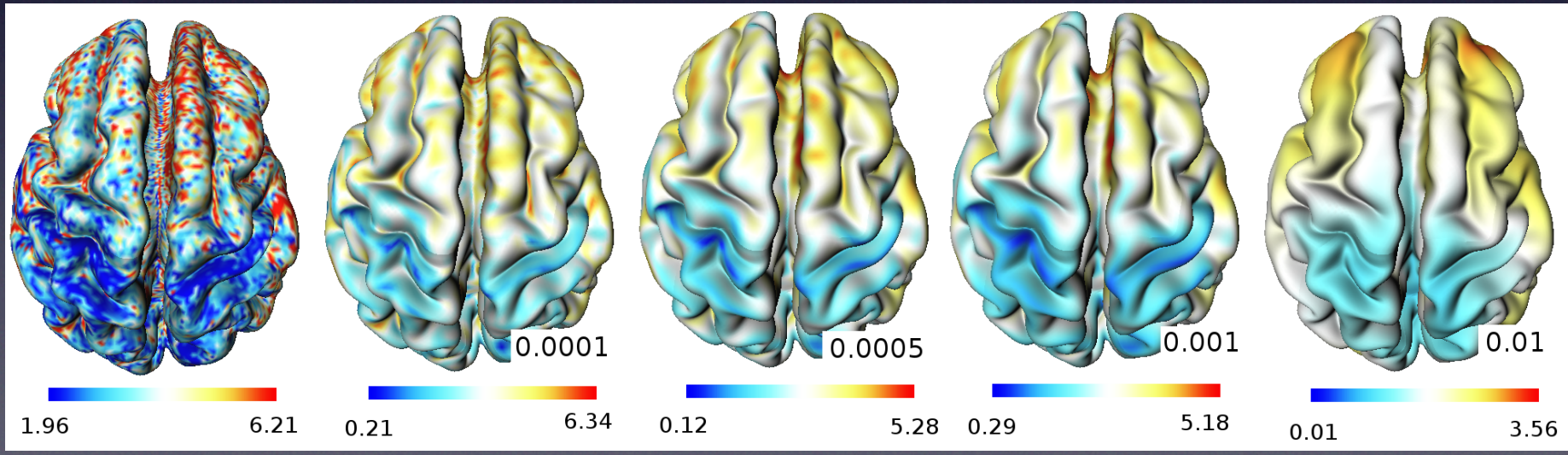
Most widely used cortical smoothing techniques



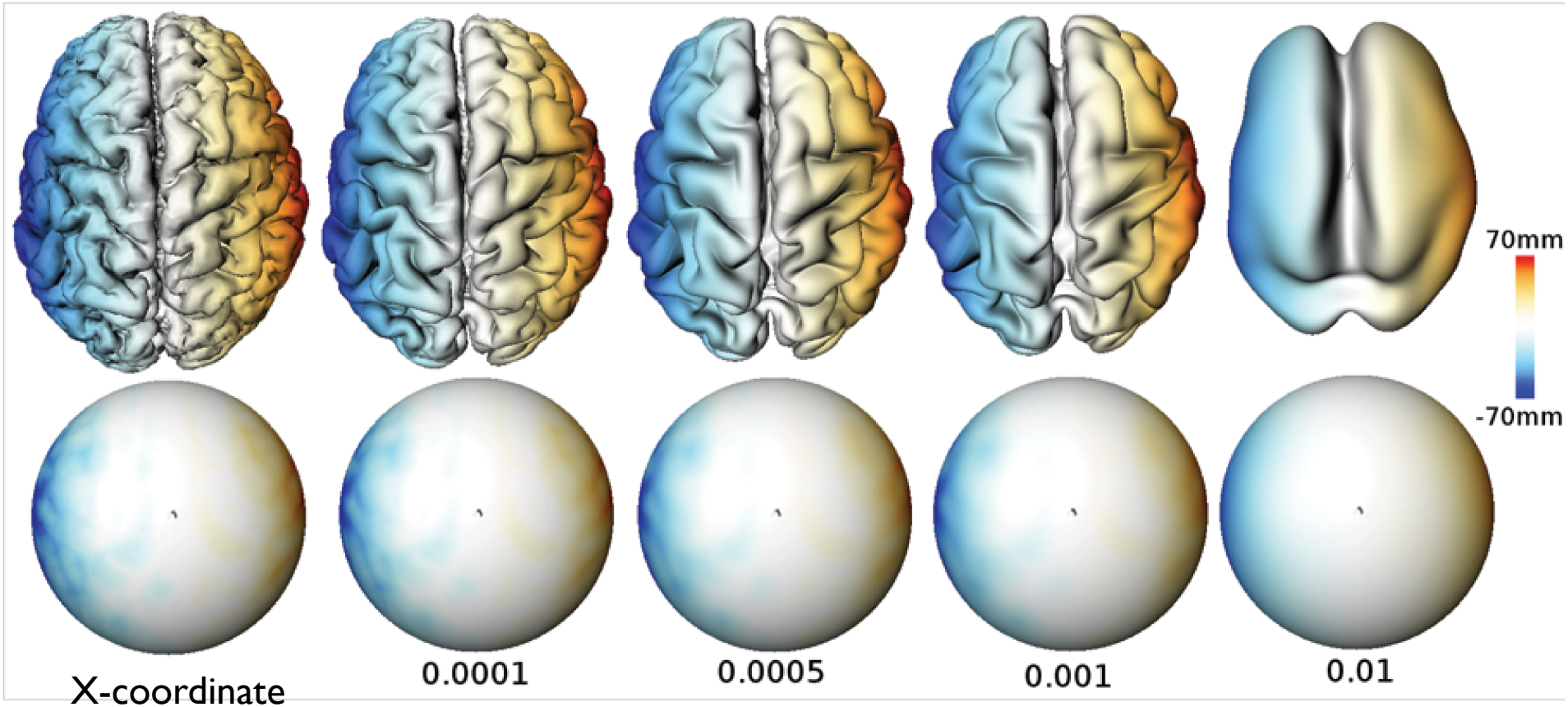


Yellow: outer cortical surface
Blue: inner cortical surface

Weighted Fourier representation of cortical thickness



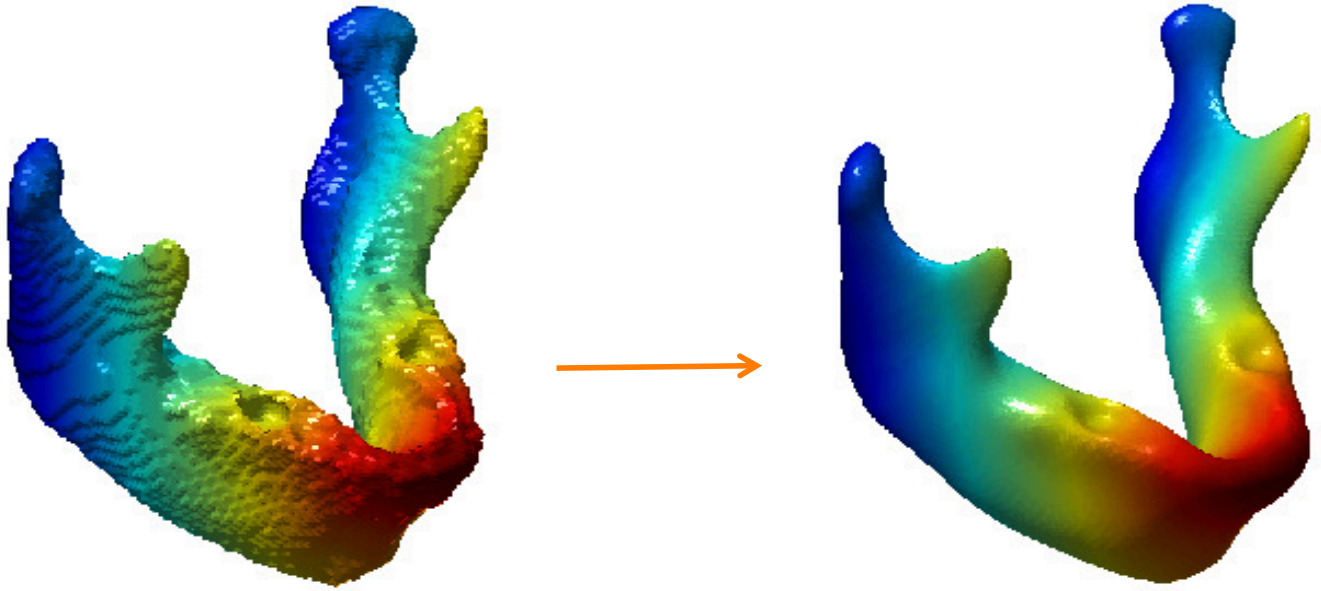
Multiscale representation of anatomy via weighted-SPHARM



Heat kernel smoothing on surface

Heat kernel: $$K_t(p,q) = \sum_{i=0}^{\infty} e^{-\lambda_i t} \psi_i(p) \psi_i(q)$$

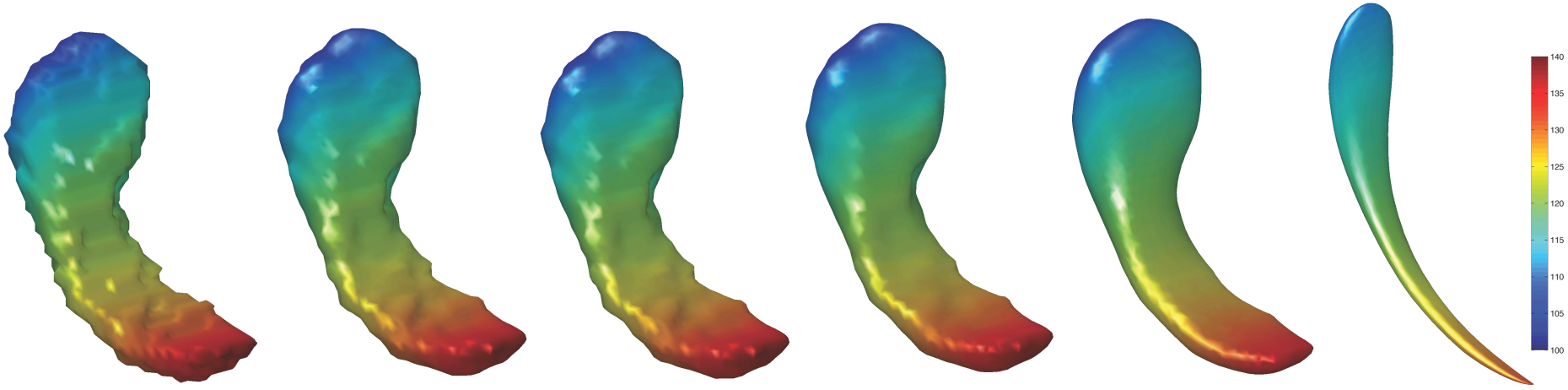
$$K_t * f = \int_{\mathcal{M}} K_t(p,q) f(q)\, dq$$



X-coordinate on mandible surface

smoothed with bandwidth 10 and 1269 eigenfunctions

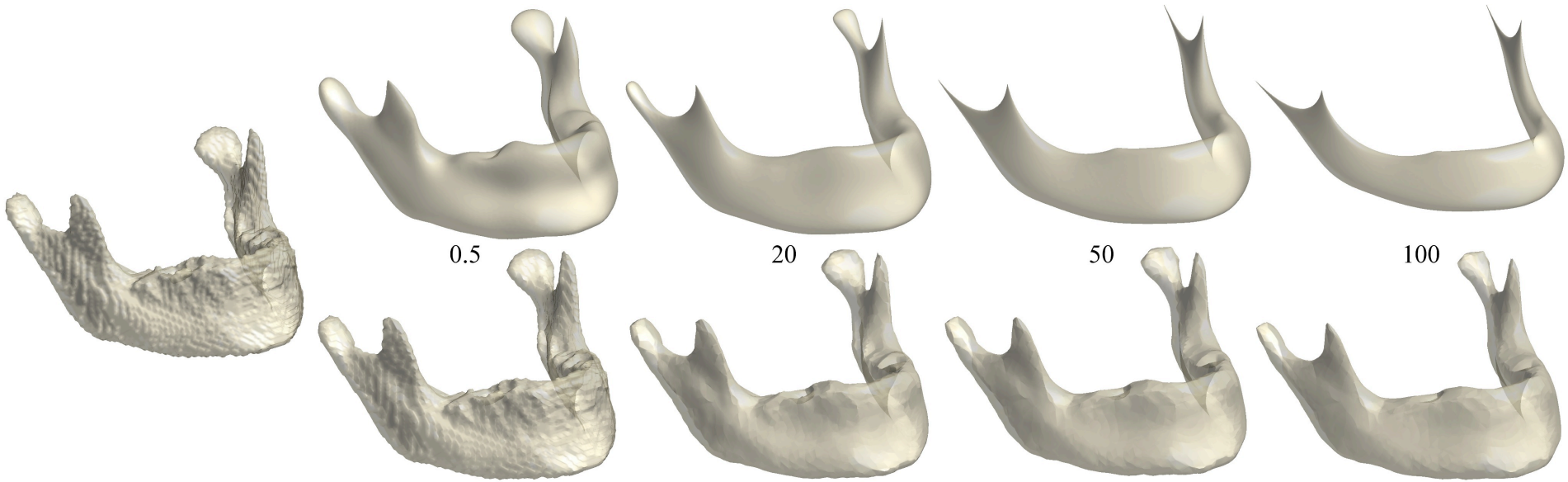
Heat kernel smoothing of hippocampus



Original 0.01 0.1 1 10 100

Heat kernel smoothing on mandible shape

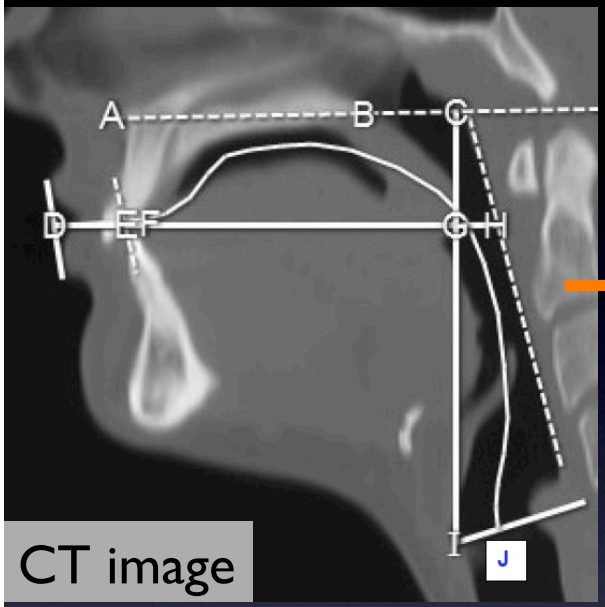
Heat kernel smoothing (Seo et al., 2010 MICCAI)



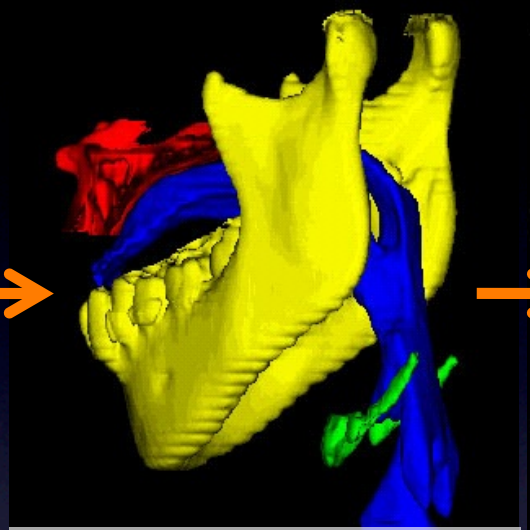
Iternated kernel smoothing (Chung et al., 2005 NeuroImage)

Statistical models

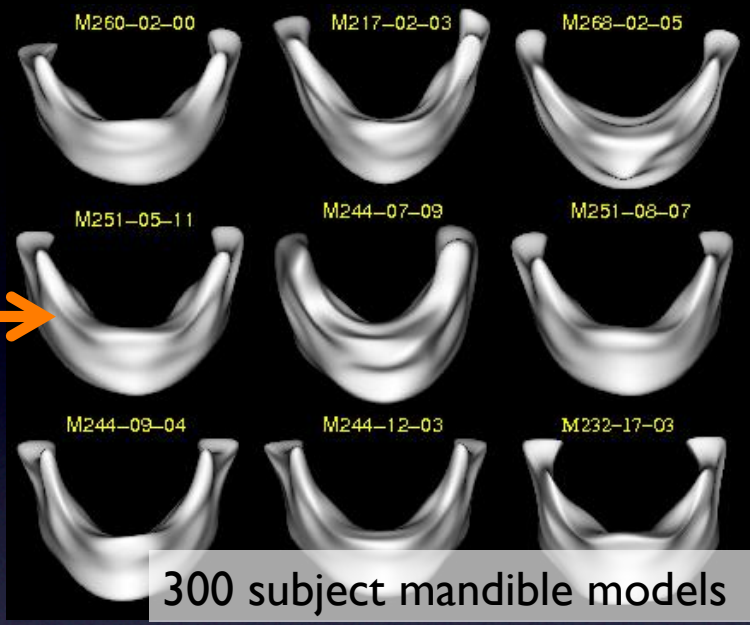
Longitudinal growth modeling on mandible CT images



CT image



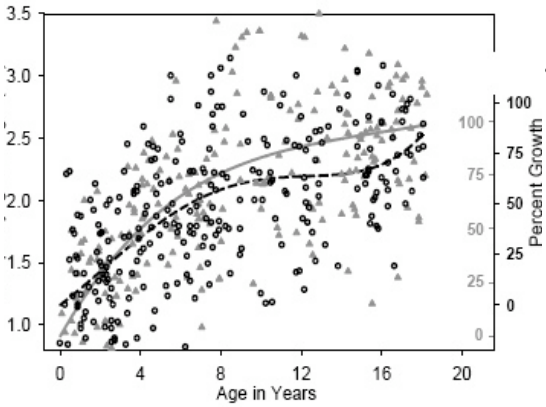
Multiple structure model

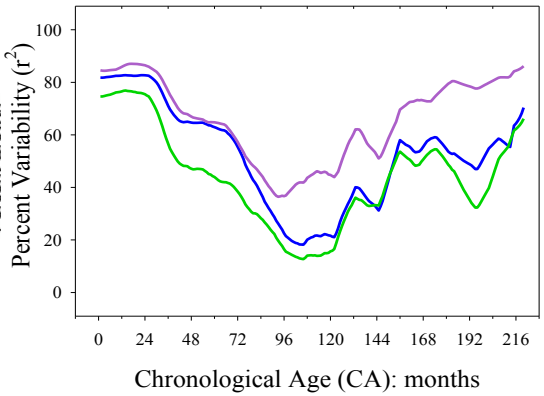


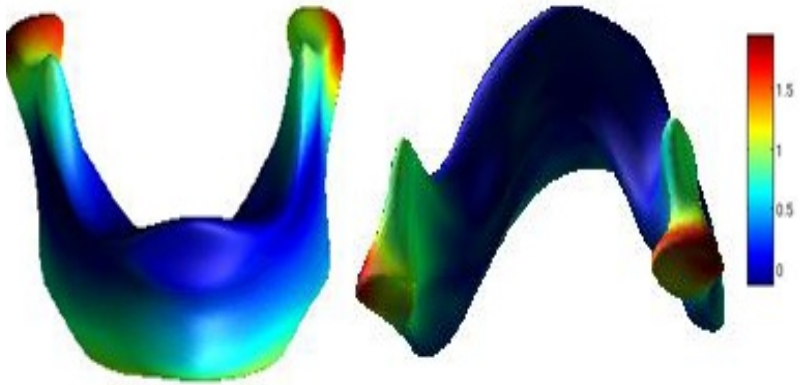
300 subject mandible models

Longitudinal modeling

Growth rate analysis

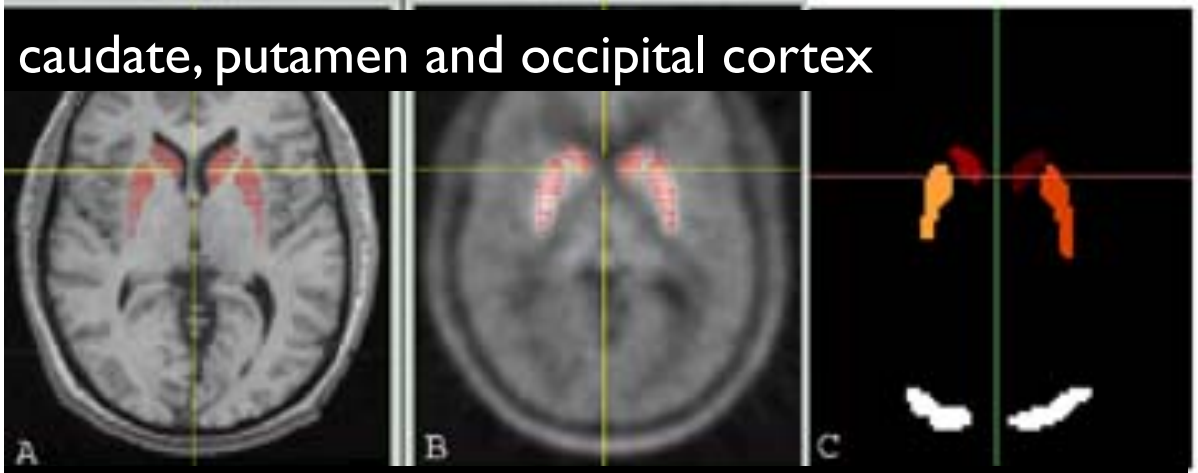


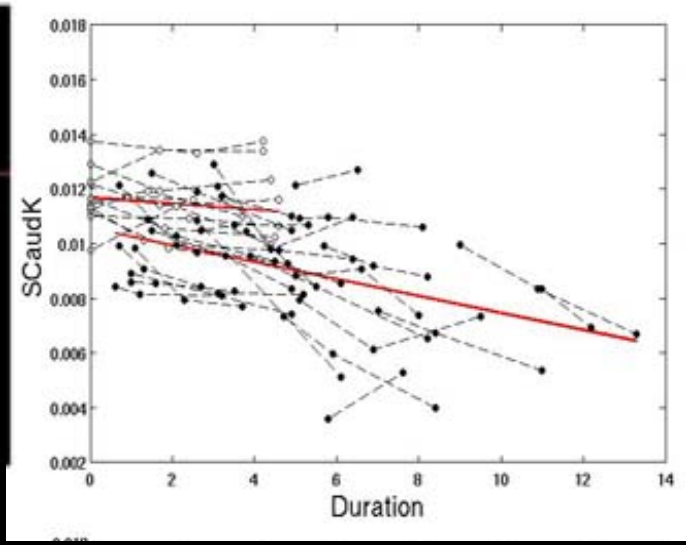




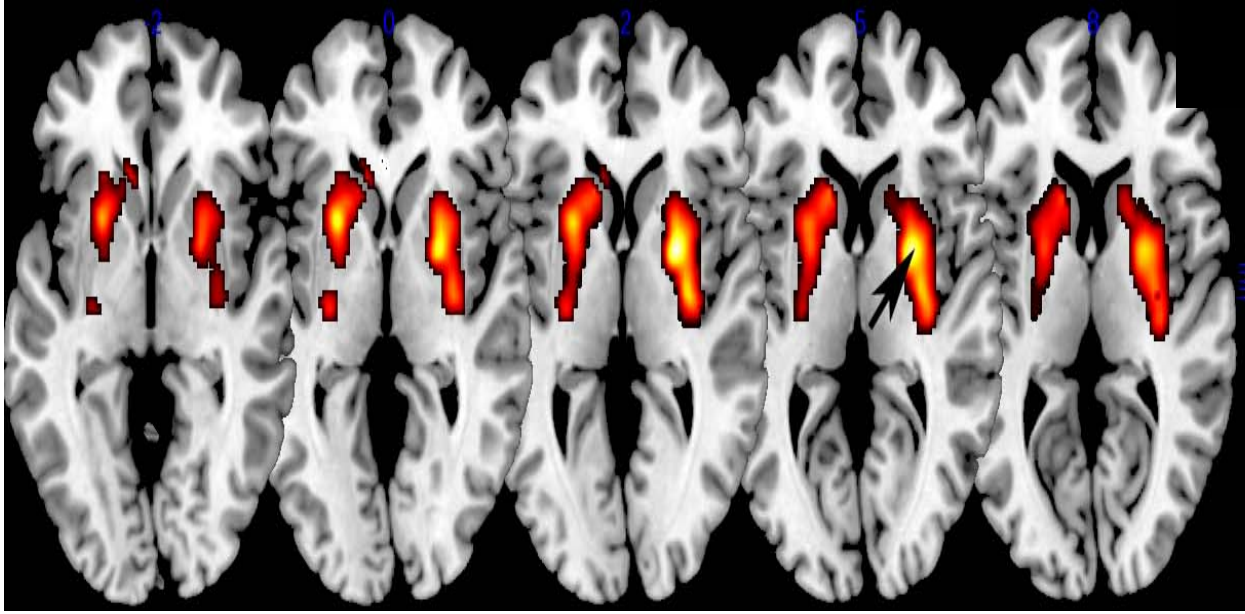
A longitudinal study of regional differences in the rate of striatal FDOPA uptake decline in Parkinson disease (PD)

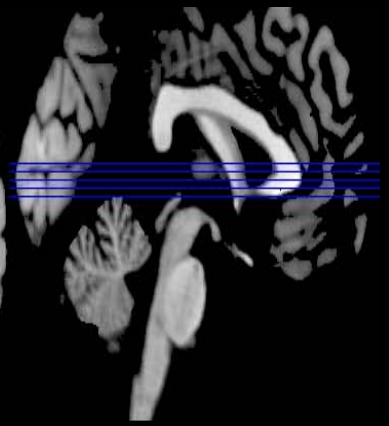
caudate, putamen and occipital cortex





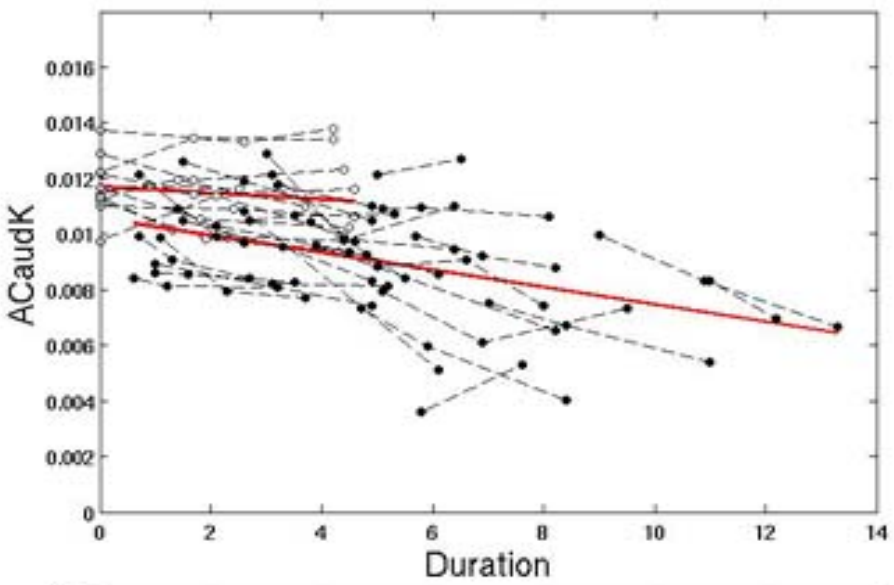
spaghetti plot
Mixed effect model

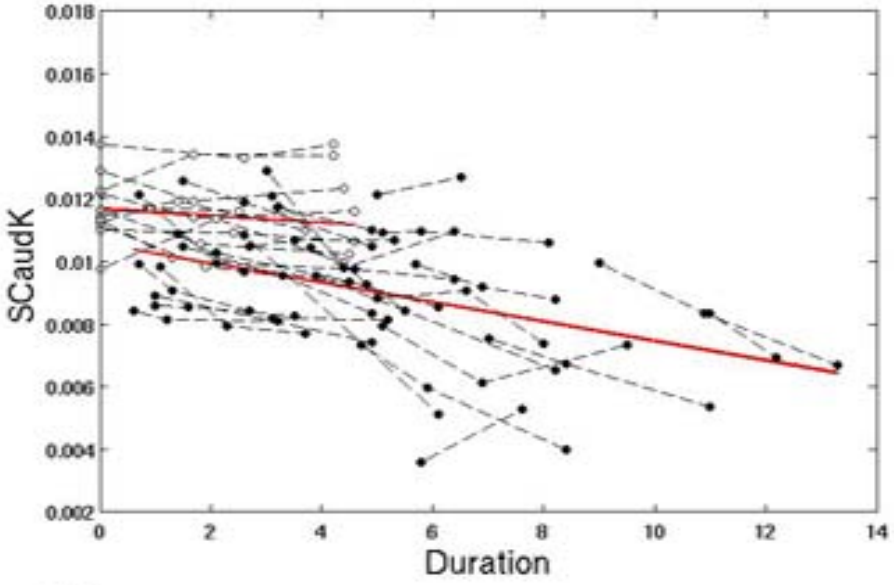


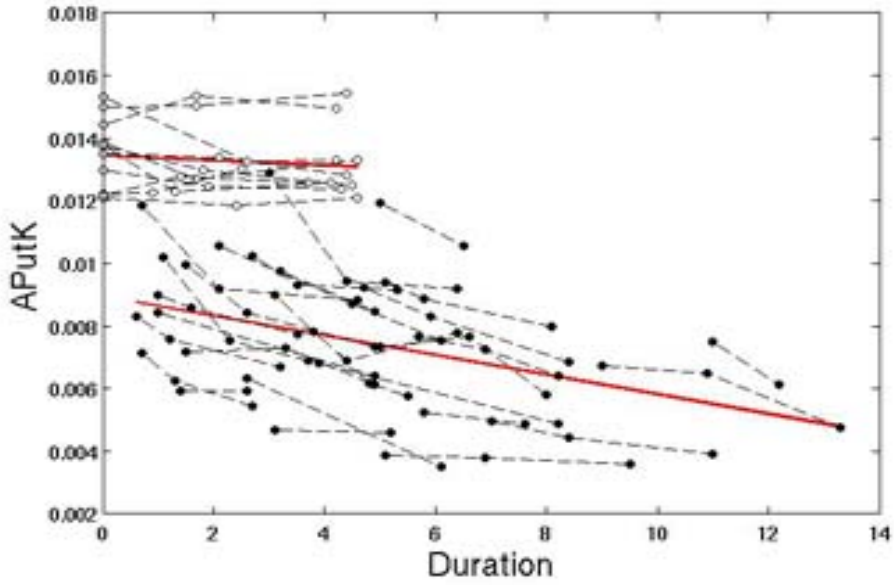


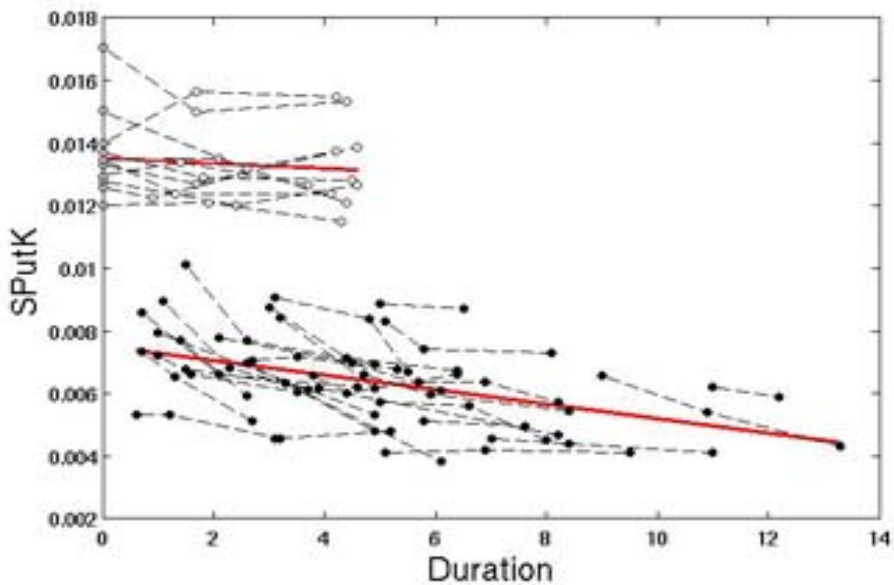
PD vs. control

Asymtomatic putamen, symptomatic caudate uptake





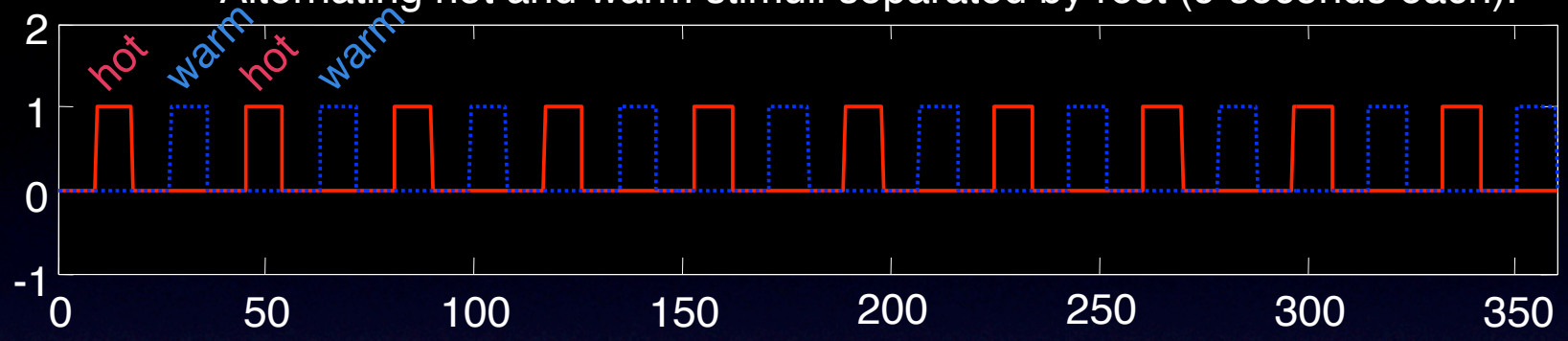




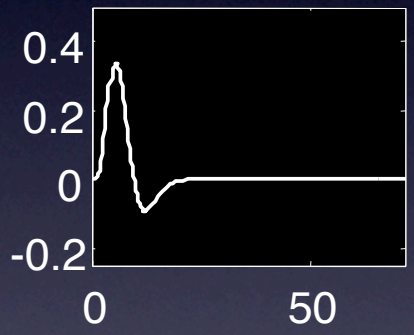
Pain perception fMRI study

Keith Worsley

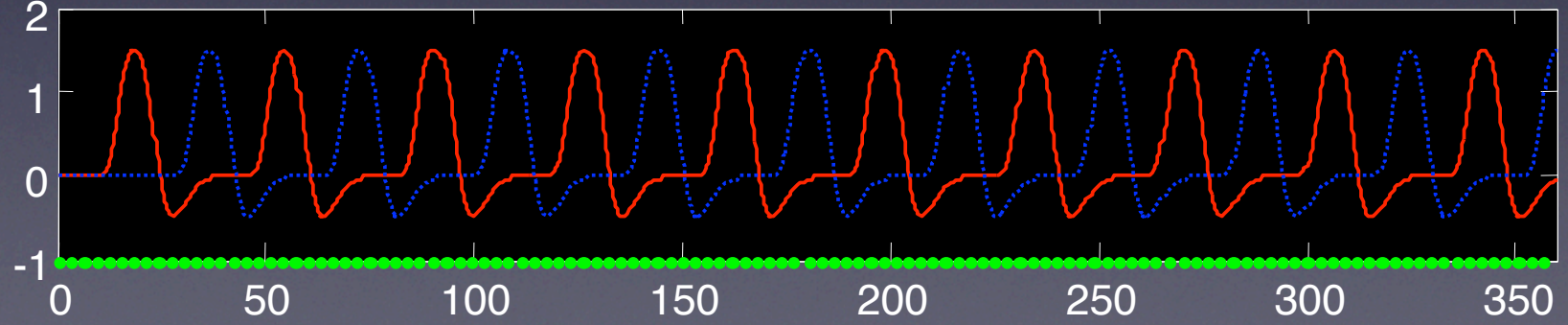
Alternating hot and warm stimuli separated by rest (9 seconds each).



Hemodynamic response function: difference of two gamma densities



Responses = stimuli * HRF, sampled every 3 seconds



Time, seconds

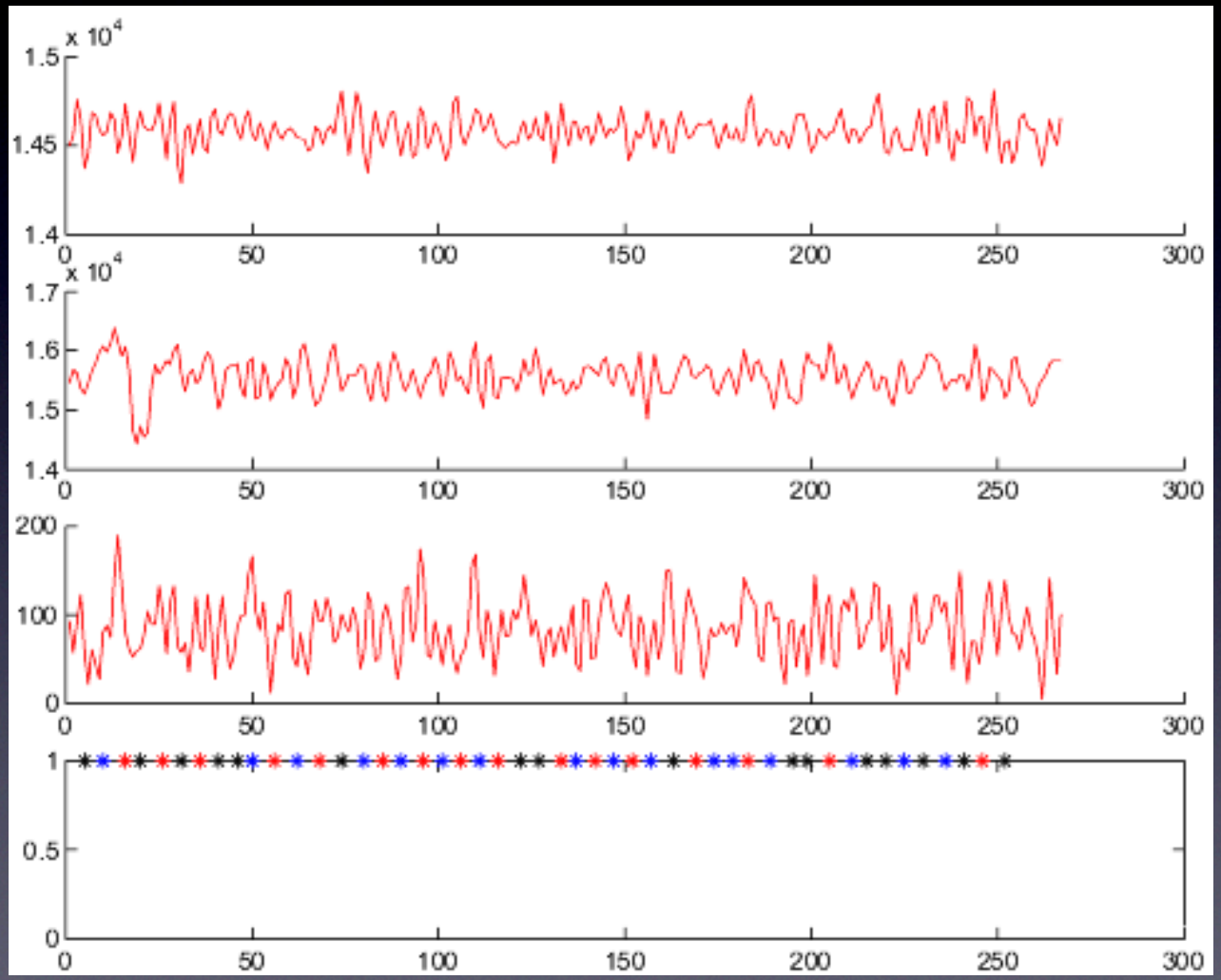
Event-related fMRI design of fear response in amygdala

Right Amygdala

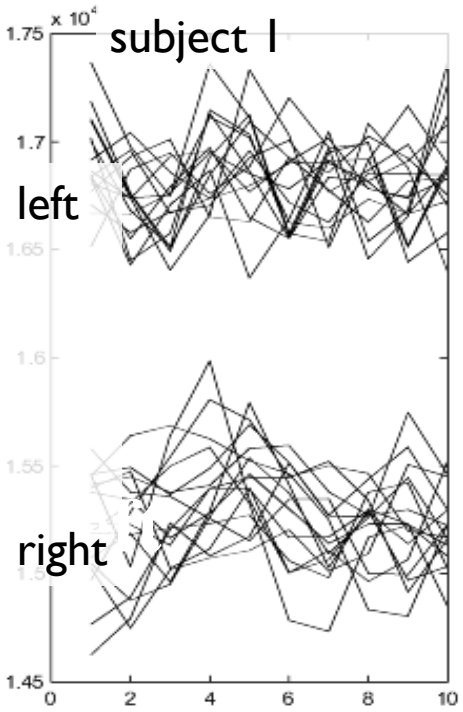
Left Amygdala

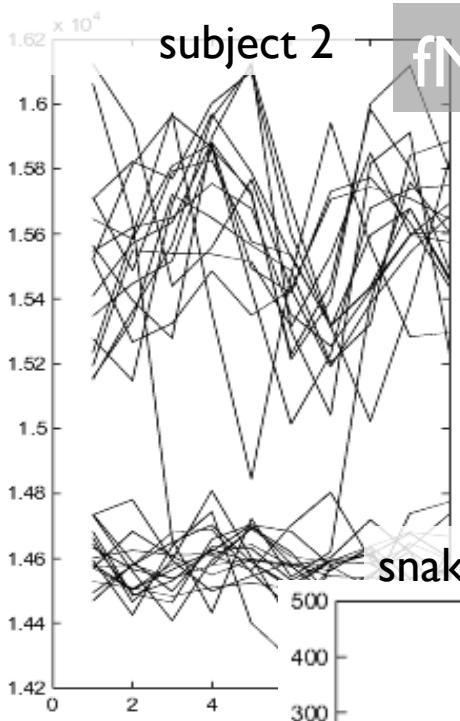
Background Noise

Stimuli



fMRI fear response in amygdala





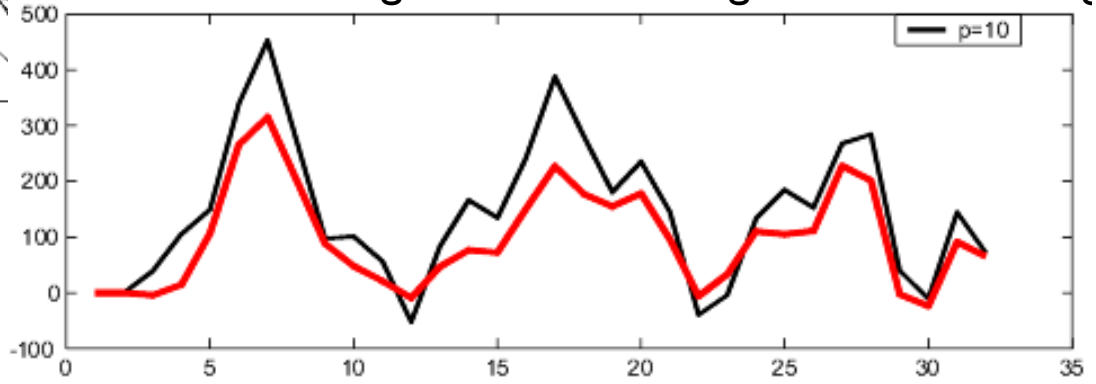
Hemodynamic response modeling

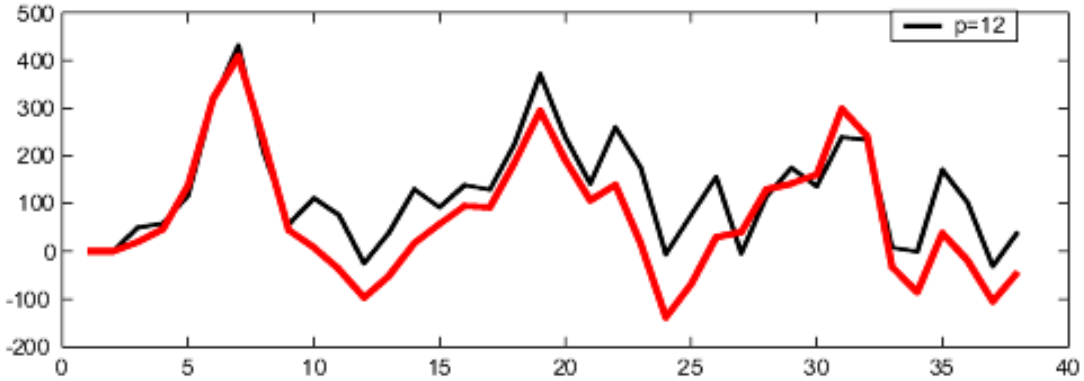
$$y(t) = \int_0^t H(t-s) f(s) ds + e(t)$$

Weighted least squares

Least squares

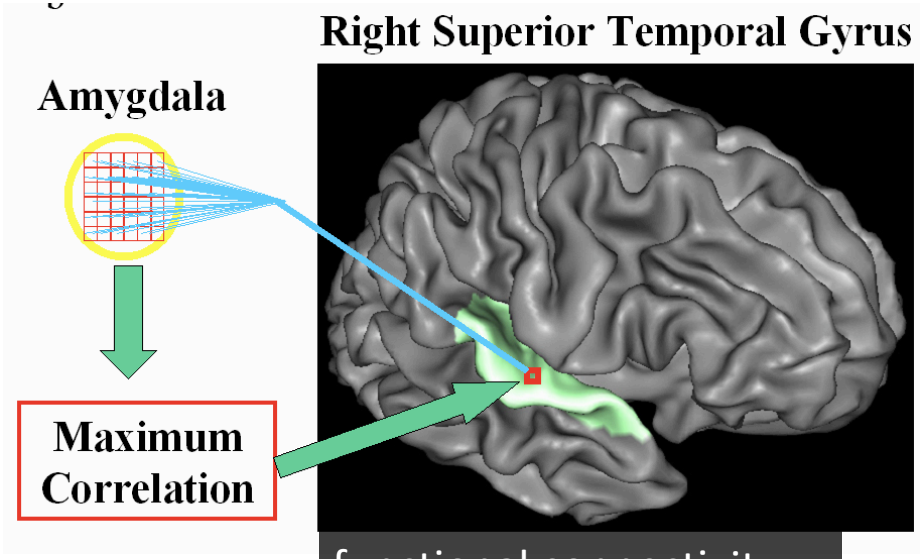
snake attacking snake crawling fish swimming





Effective fMRI connectivity

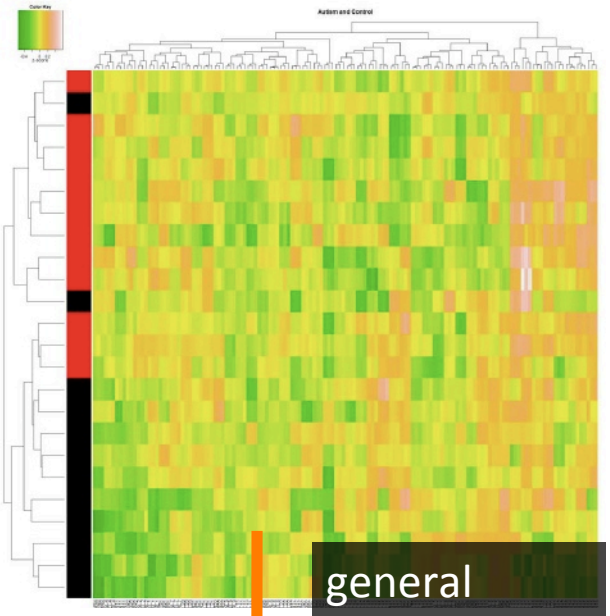
D. J. Kelley



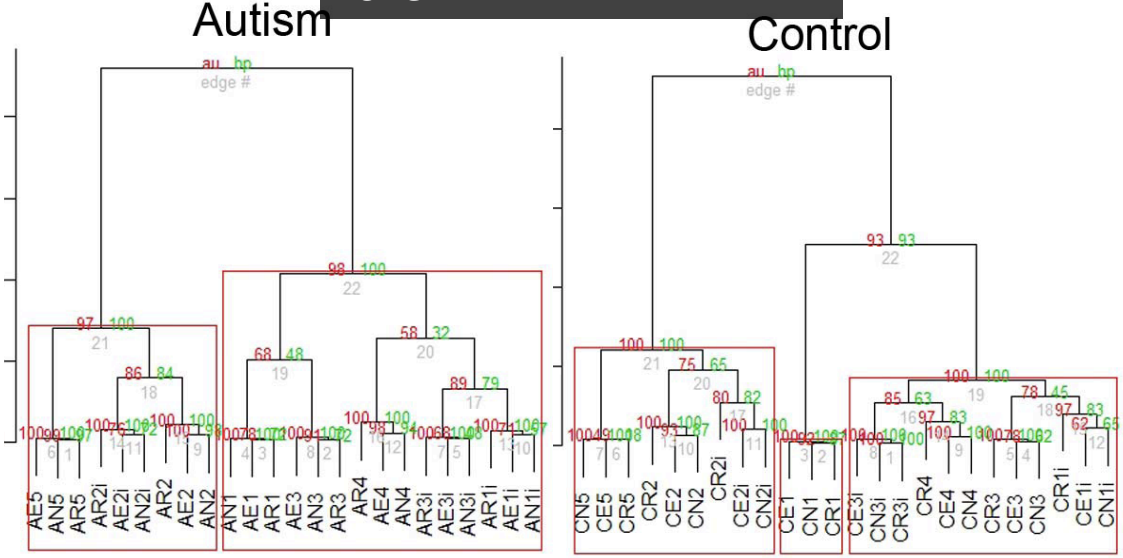
functional connectivity from amygdala seed voxel

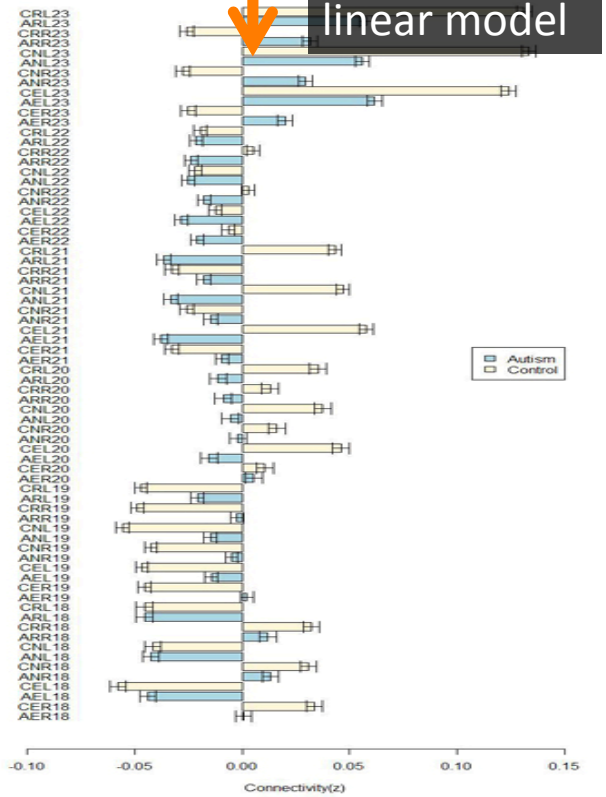
distance on correlation

hieratical clustering



general linear model

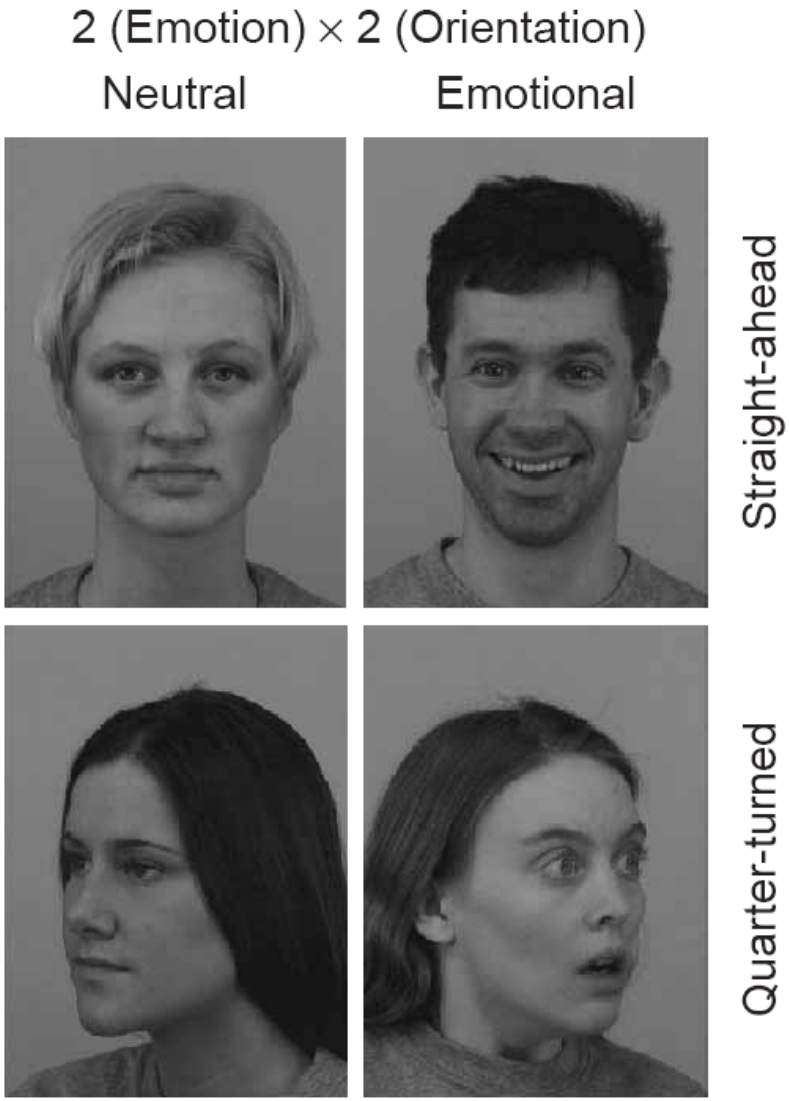




Inside fMRI scanner

Input:
24 emotional faces
16 neutral faces

Output:
Response time

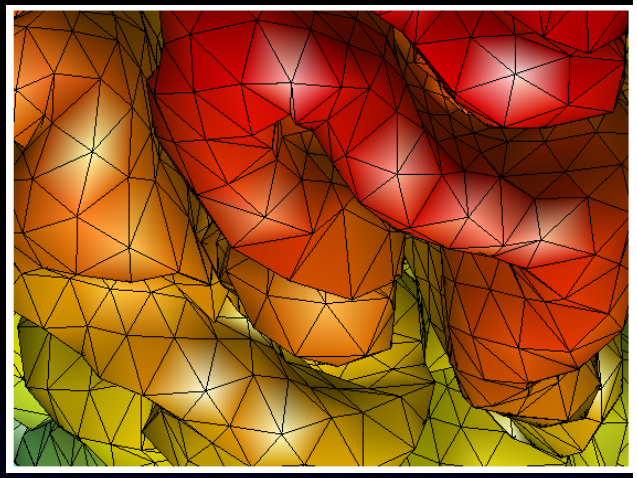


nature neuroscience

Gaze fixation and the neural circuitry of face processing in autism

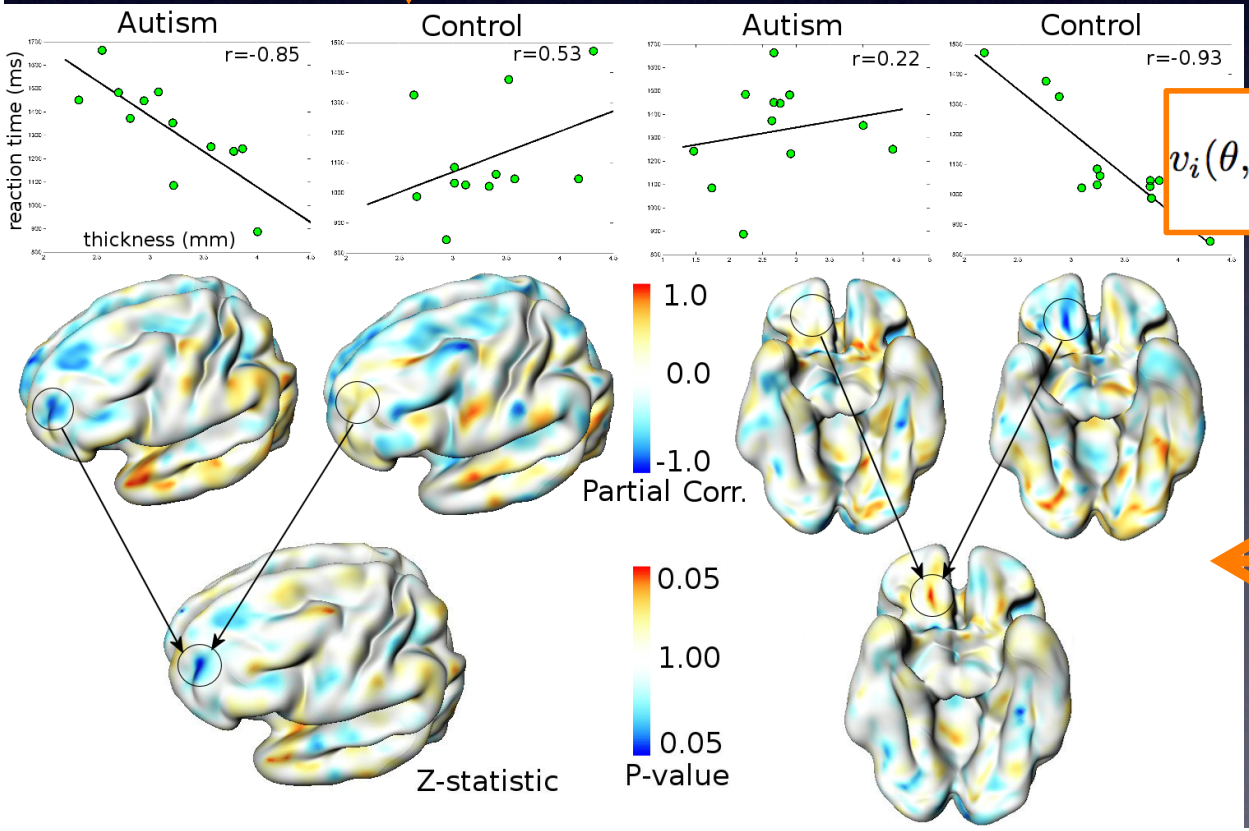
Kim M Dalton[1,2], Brendon M Nacewicz[2], Tom Johnstone[2], Hillary S Schaefer[2], Morton Ann Gernsbacher[1,3], H H Goldsmith[1,3], Andrew L Alexander[1,2,4] & Richard J Davidson[1–4]

Partial correlation mapping



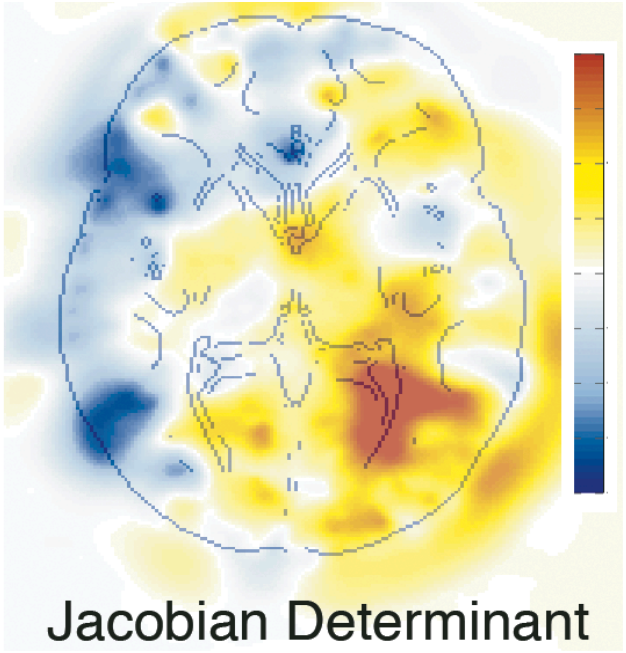
Partial correlation analysis

Weighted Fourier representation

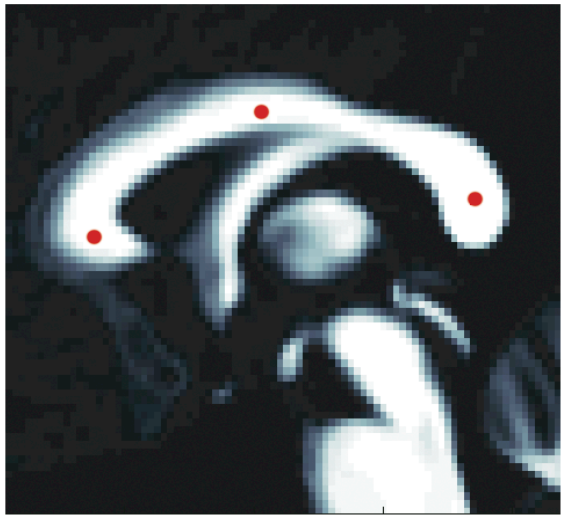


$$v_i(\theta,\varphi) = \sum_{l=0}^{k} \sum_{m=-l}^{l} e^{-l(l+1)\sigma} f_{lm}^{i} Y_{lm}(\theta,\varphi)$$

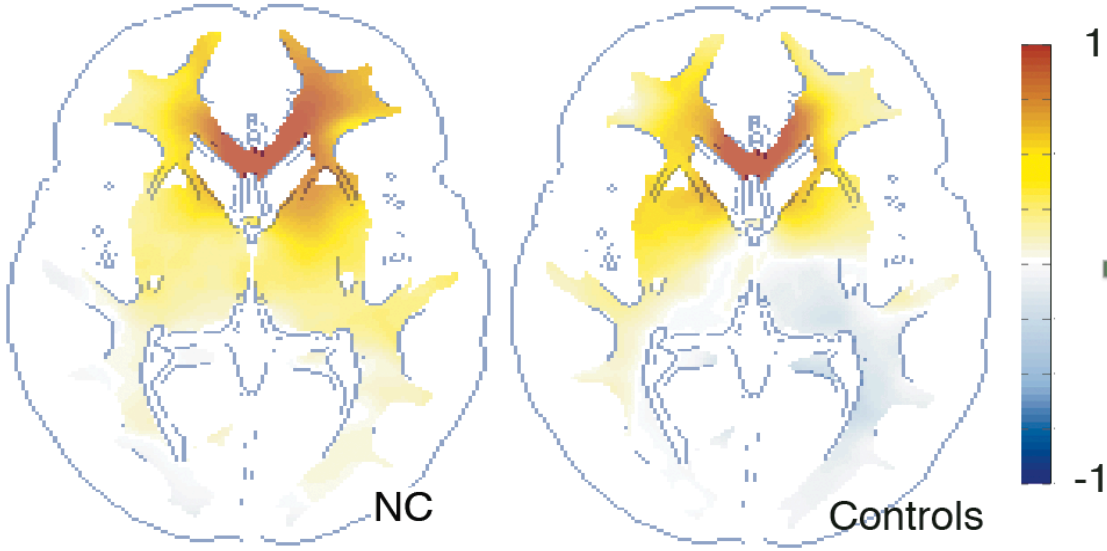
88.1799	56.6336	5.7367
-12.4775	-11.2552	-2.0791
2.4336	-15.4428	-0.4021
4.3956	2.2733	-0.9354
-0.0106	-0.0674	0.6999
2.1773	-2.4194	-0.1176
0.5808	0.8390	1.2942
0.0615	-0.1893	0.1188
-0.2629	0.7524	0.1089
0.7909	-0.7276	-0.1901
0.5458	0.6236	0.6939
.....		



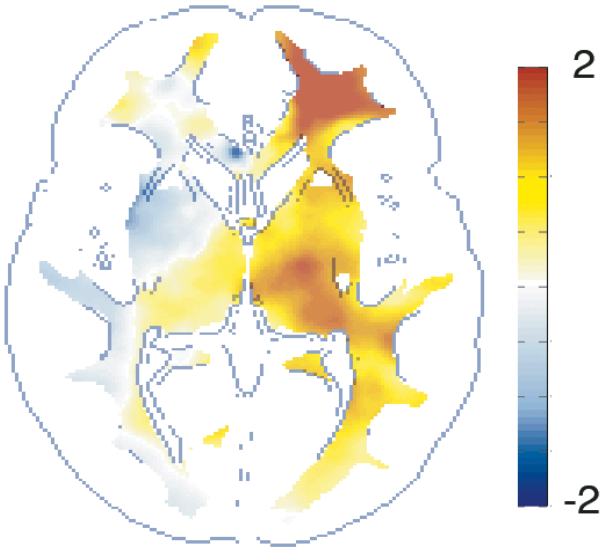
Jacobian Determinant



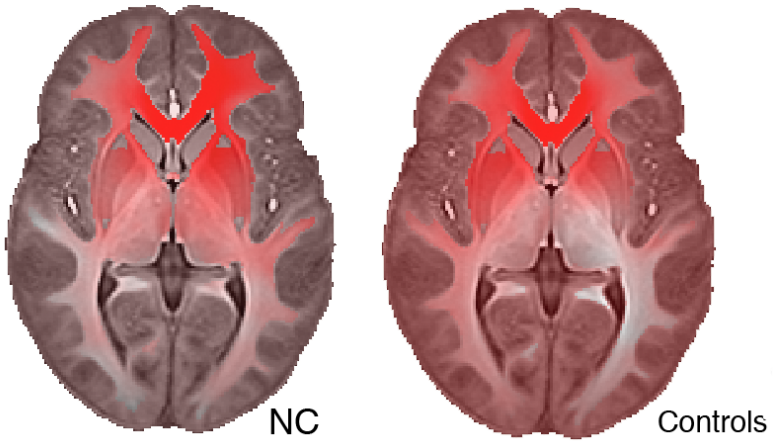
Seed voxels



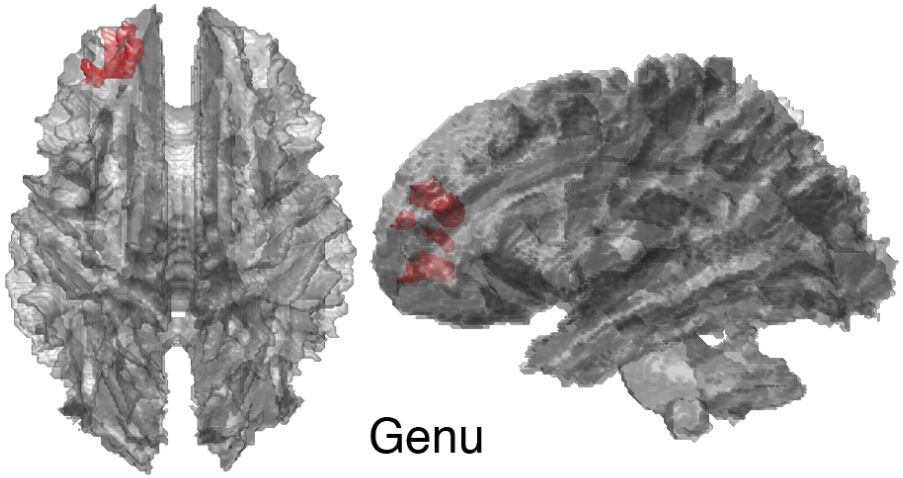
Connectivty Maps



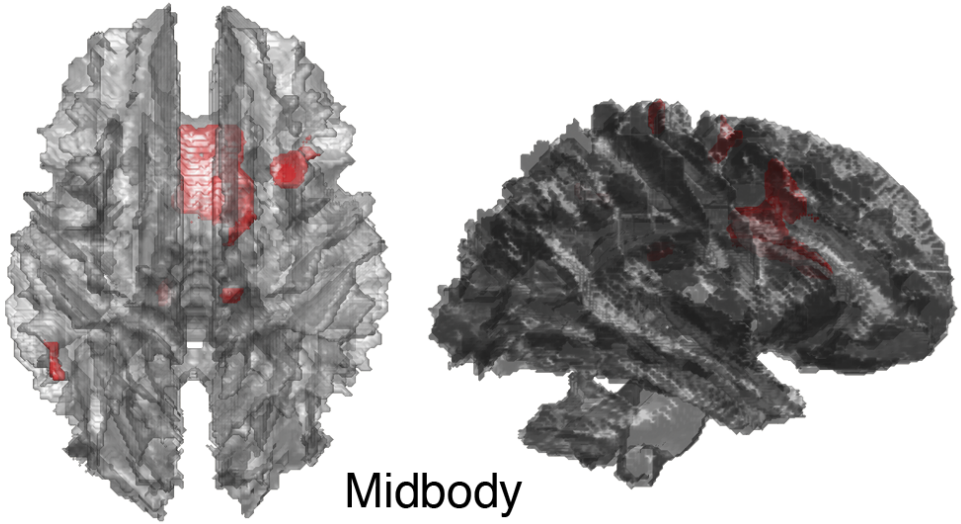
Z-statistic



Connectivity Maps

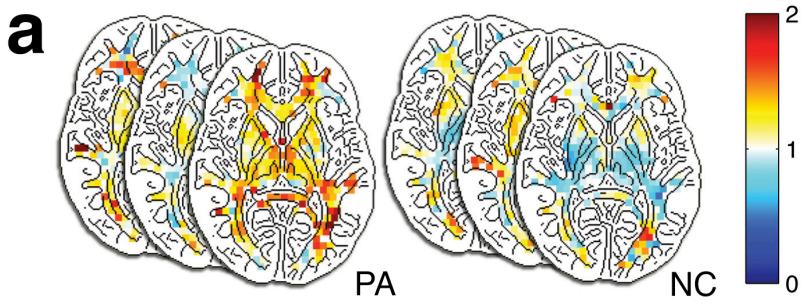


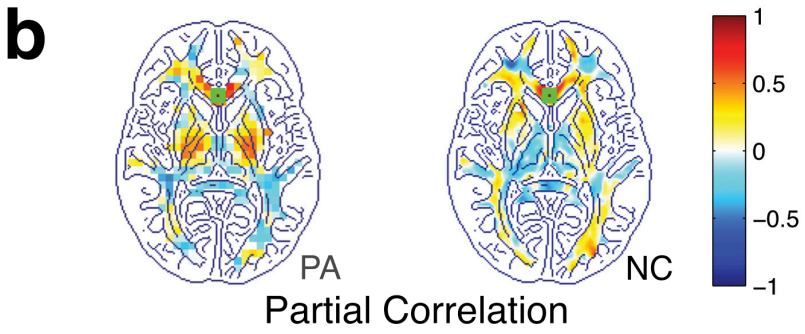
Genu

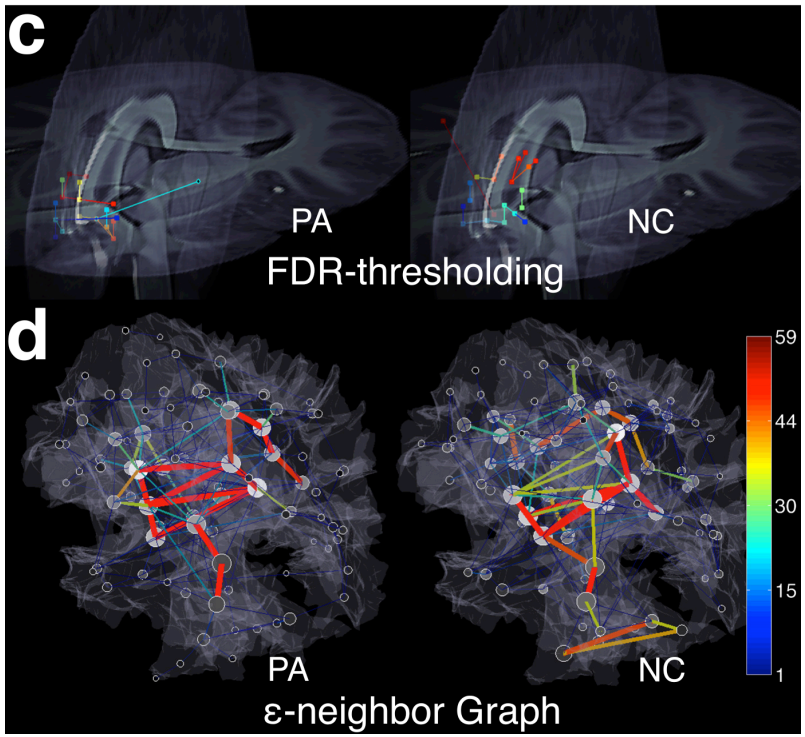


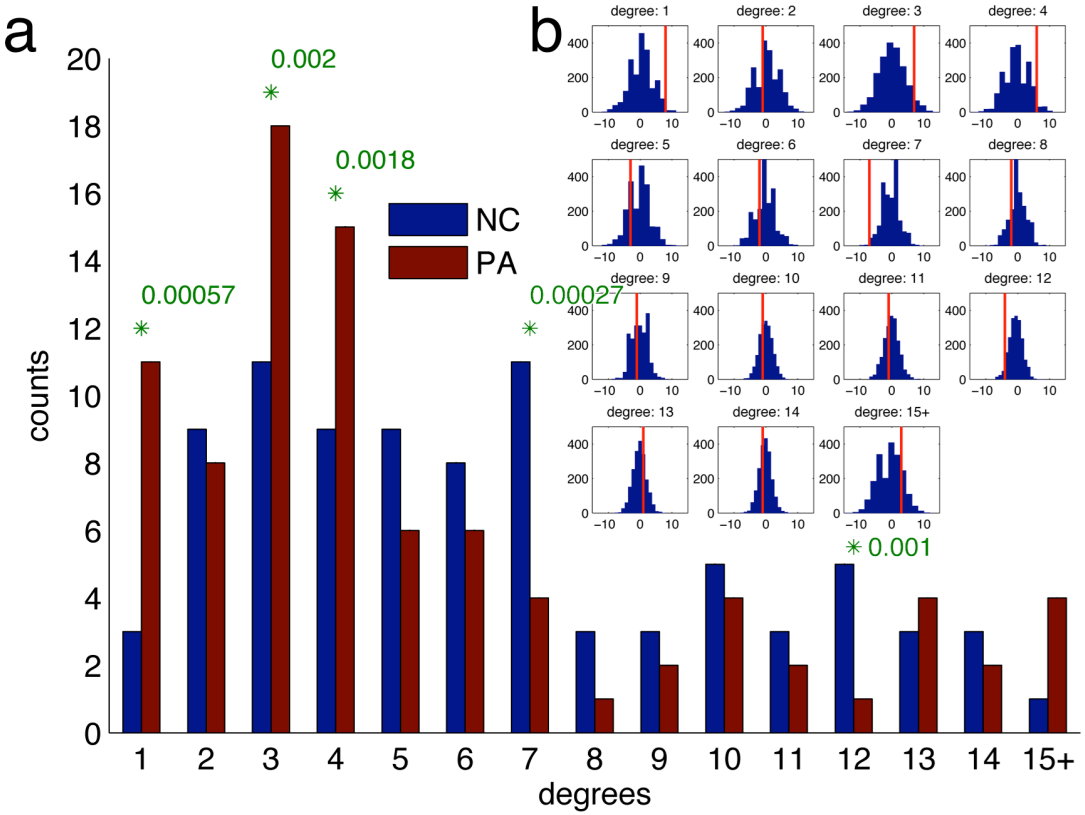
Midbody

Kim et al. ISBI 2011

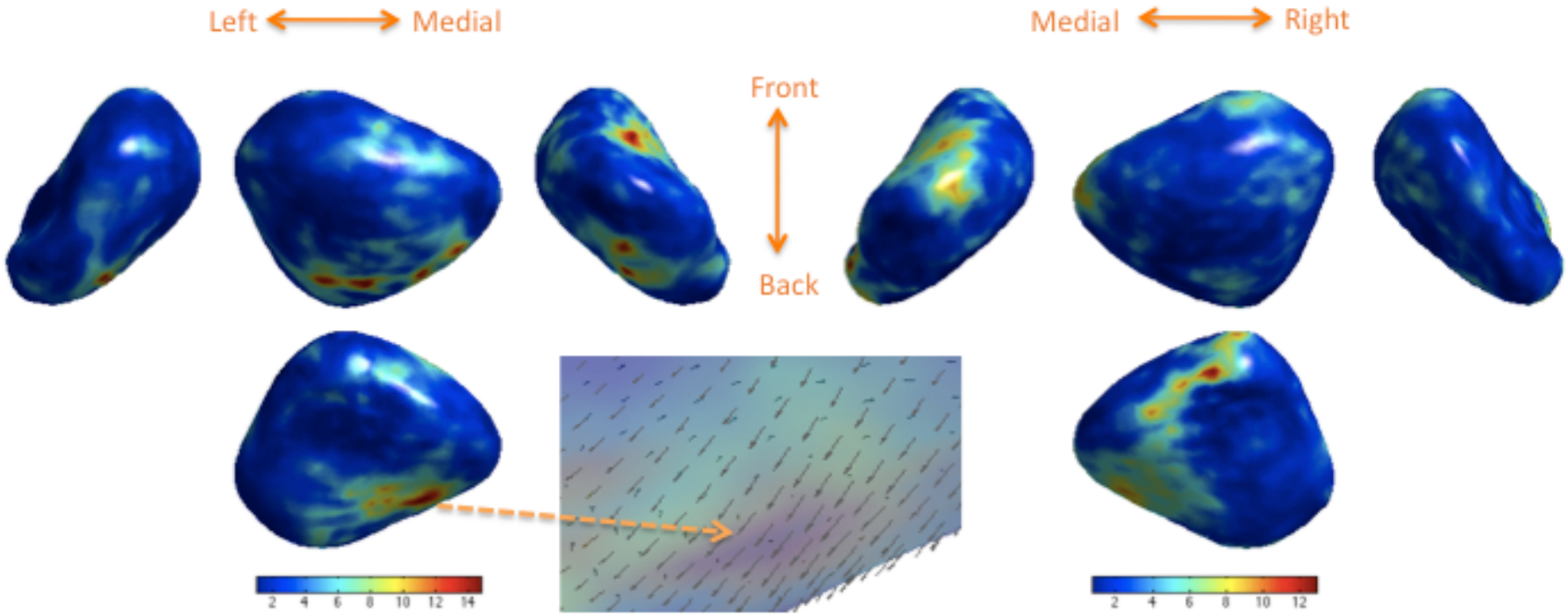








Abnormal amygdala shape difference in autism



Multivariate linear model + Worsley's random field theory

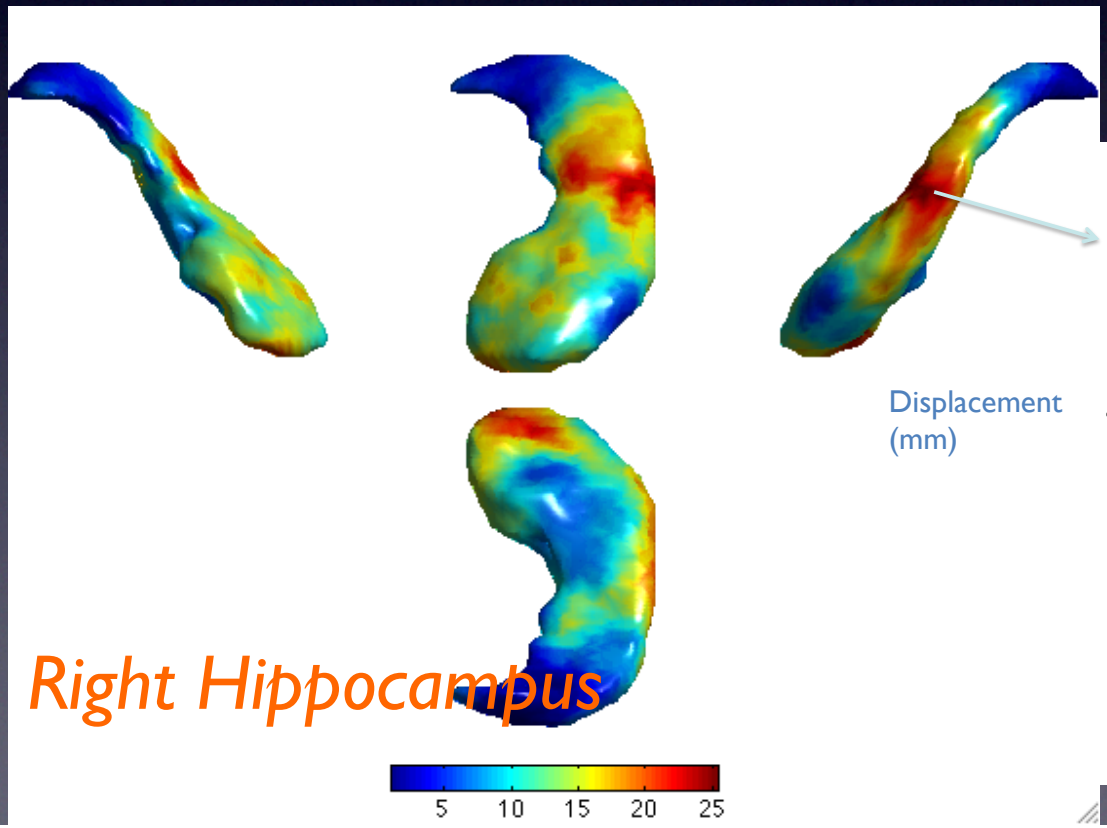
$$P_{n\times 3} = X_{n\times p}B_{p\times 3} + Z_{n\times r}G_{r\times 3} + U_{n\times 3}\Sigma_{3\times 3}$$

Coordinates = Group + Brain + Age + Noise

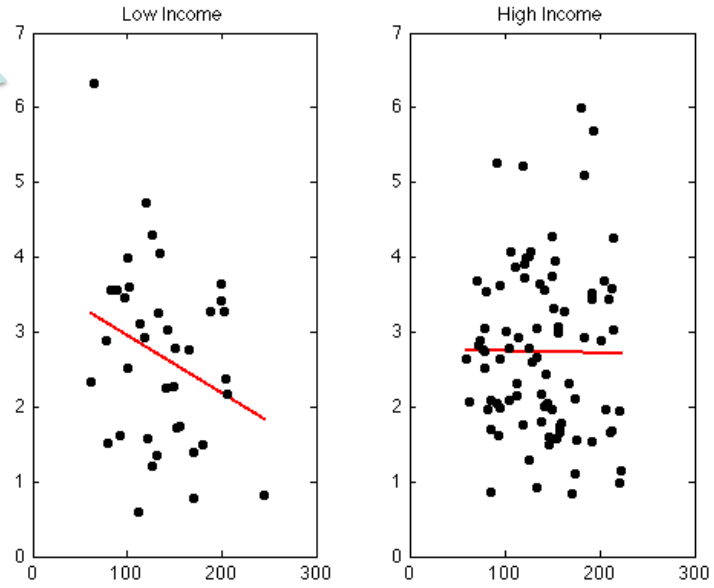
Fixed effect model accounting treating multiple scans within a subject as independent

displacement = age + gender + group + age*group

max F = 25.4
corrected pvalue < 0.001
it inflates statistical significance



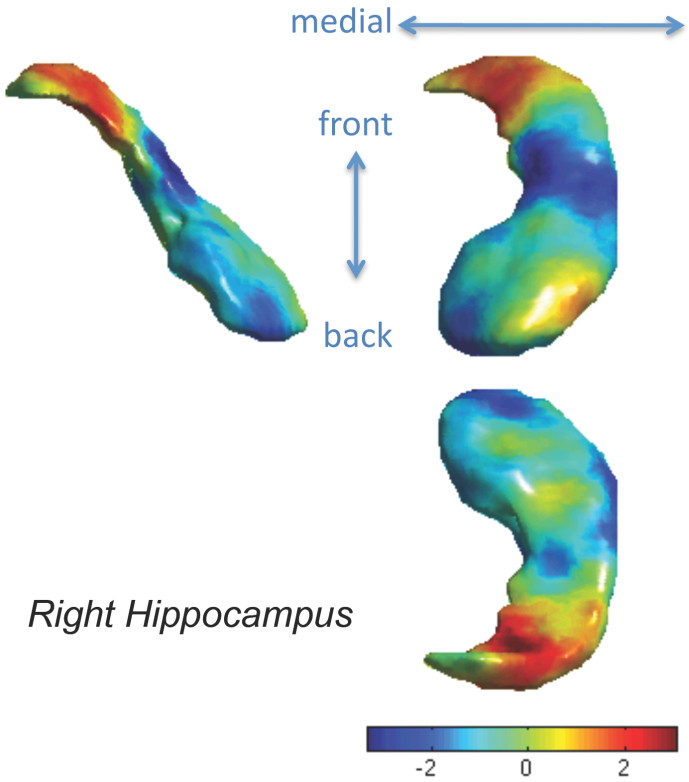
Right Hippocampus



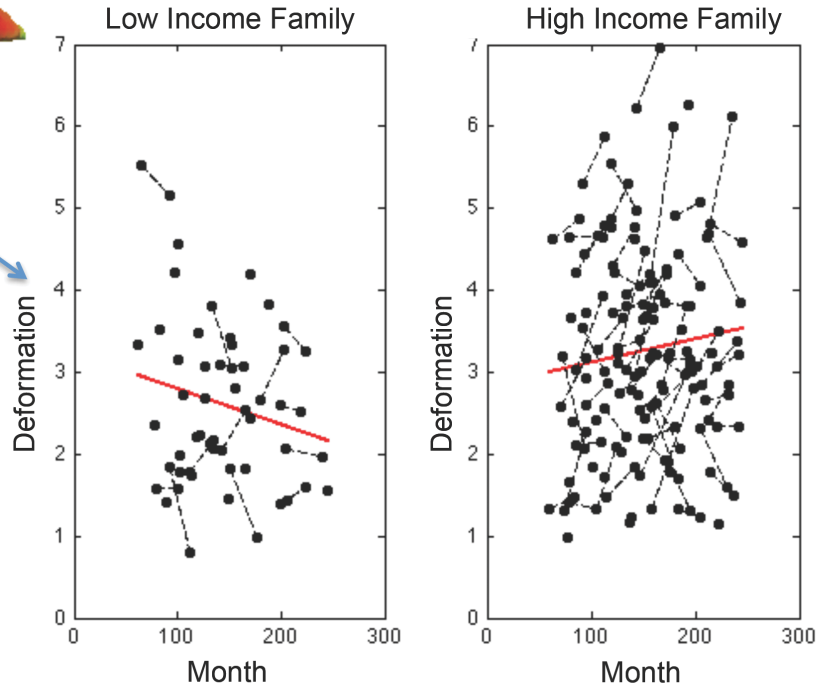
Linear mixed effect model accounting for inter-correlation of multiple scans within a subject

displacement = age + gender + group + age*group

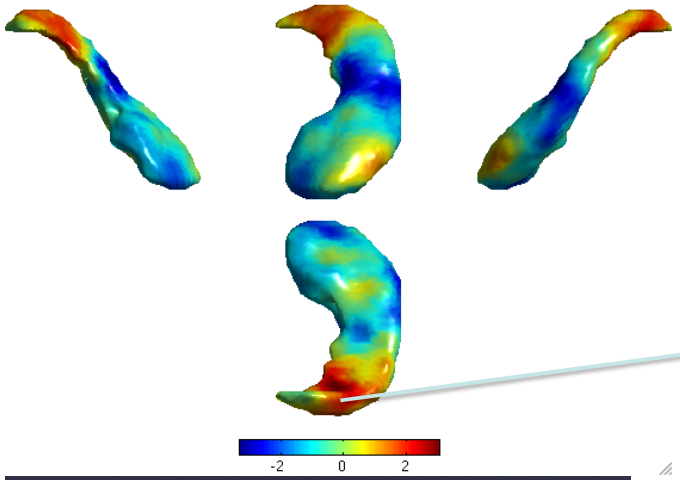
min t = -3.3398,
corrected pvalue = 0.025

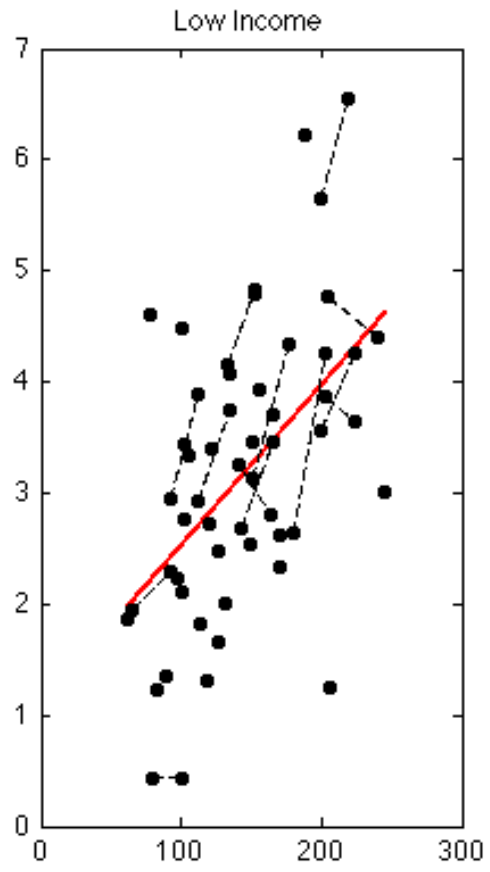


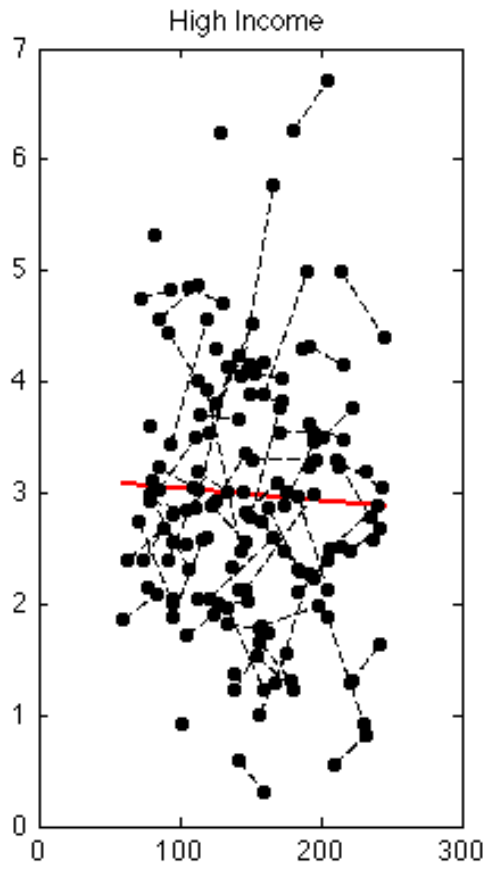
Right Hippocampus



Right hippocampus



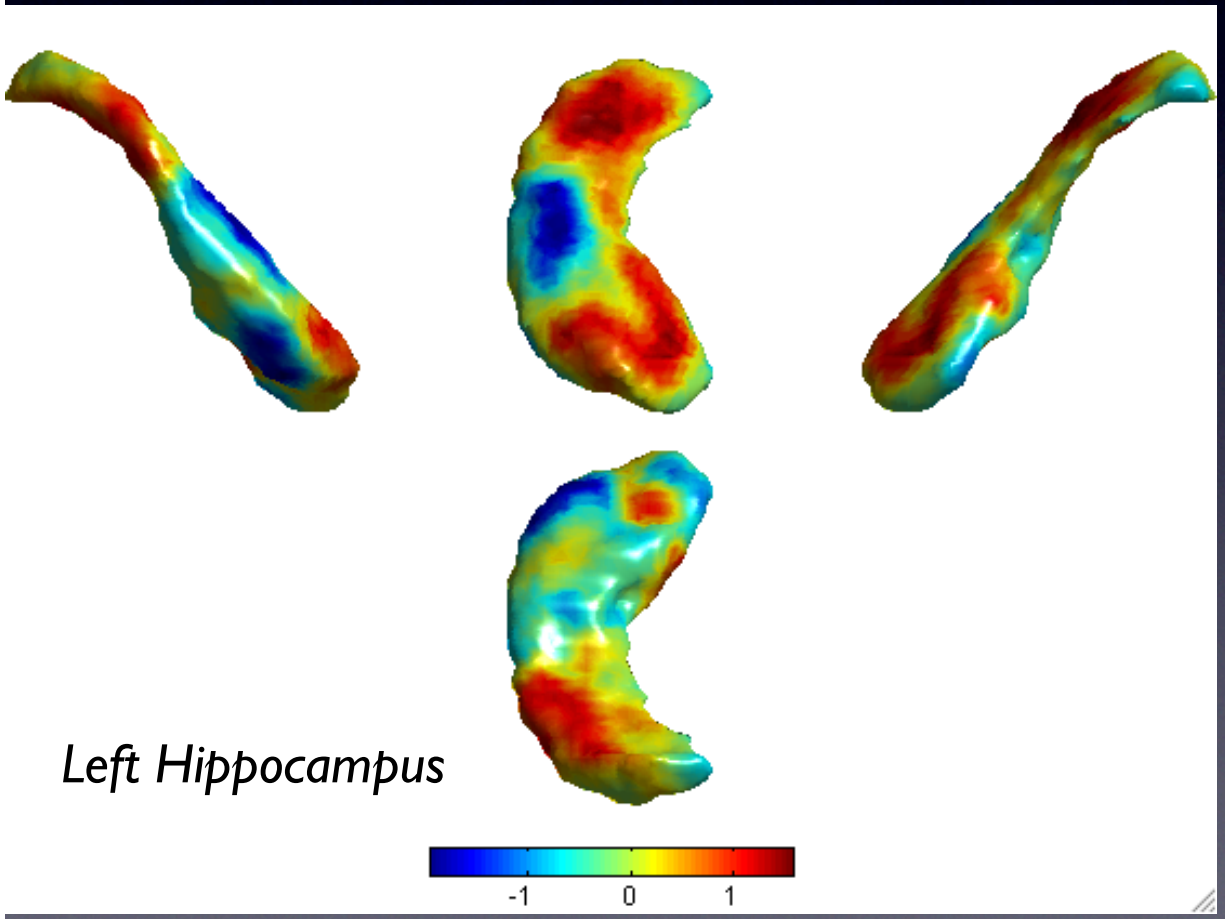




max t = 3.0531
corrected pvalue = 0.05

Linear mixed effect model on left hippocampus

displacement = age + gender + group + age*group



min t = -1.9589,
corrected pvalue > 0.4
Not significant

Thank you. Lunch time!

send email for whatever questions you have mkchung@wisc.edu