The Waisman Laboratory
for Brain Imaging and Behavior

University of Wisconsin
SCHOOL OF MEDICINE
AND PUBLIC HEALTH

Introduction to Brain Image Analysis and Computational Anatomy

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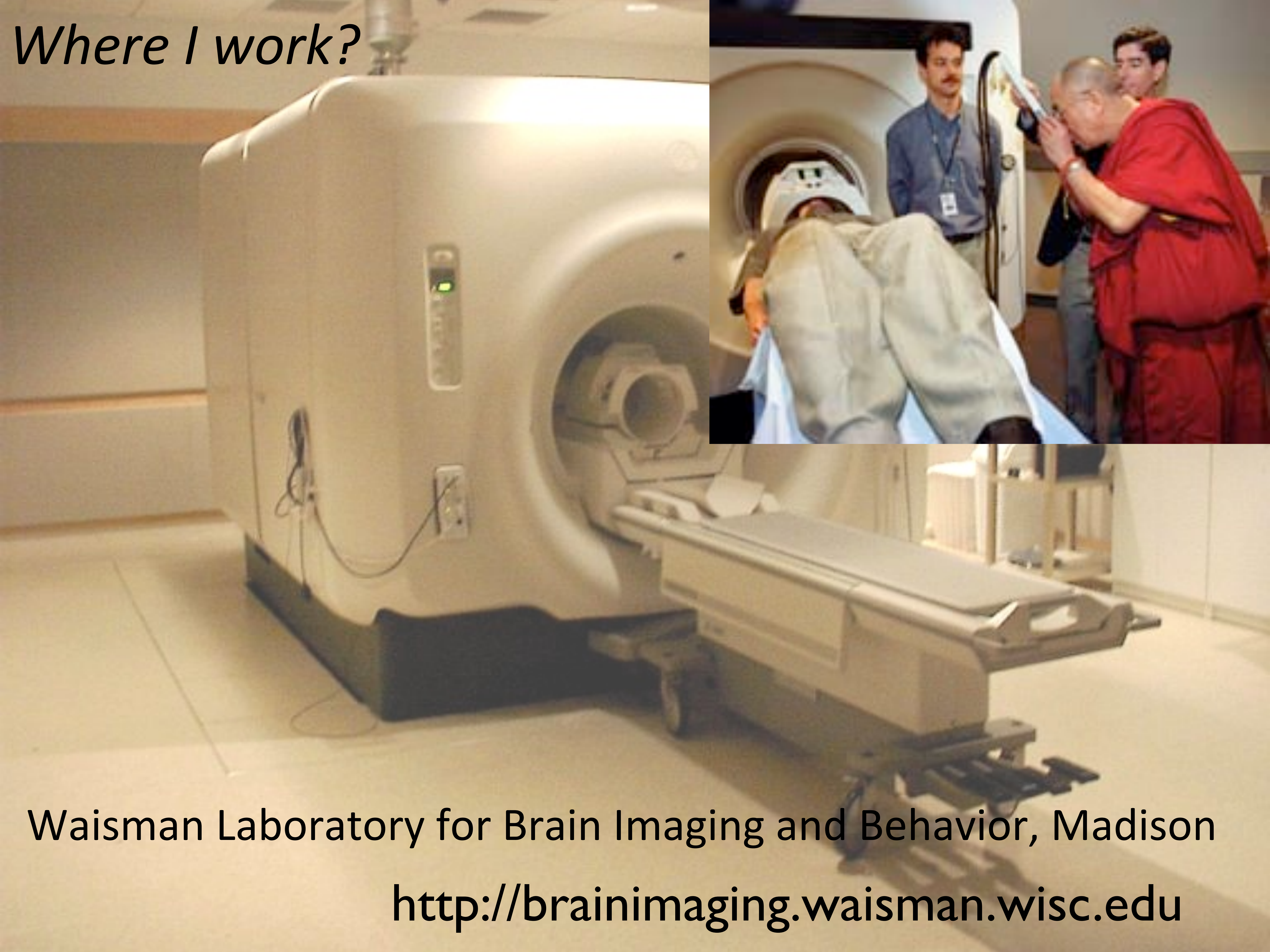
www.stat.wisc.edu/~mchung


Where I work?
Waisman Laboratory for Brain Imaging and Behavior, Madison
http://brainimaging.waisman.wisc.edu

Acknowledgement/Collaborators

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Vocal Tract Laboratory, Waisman Center

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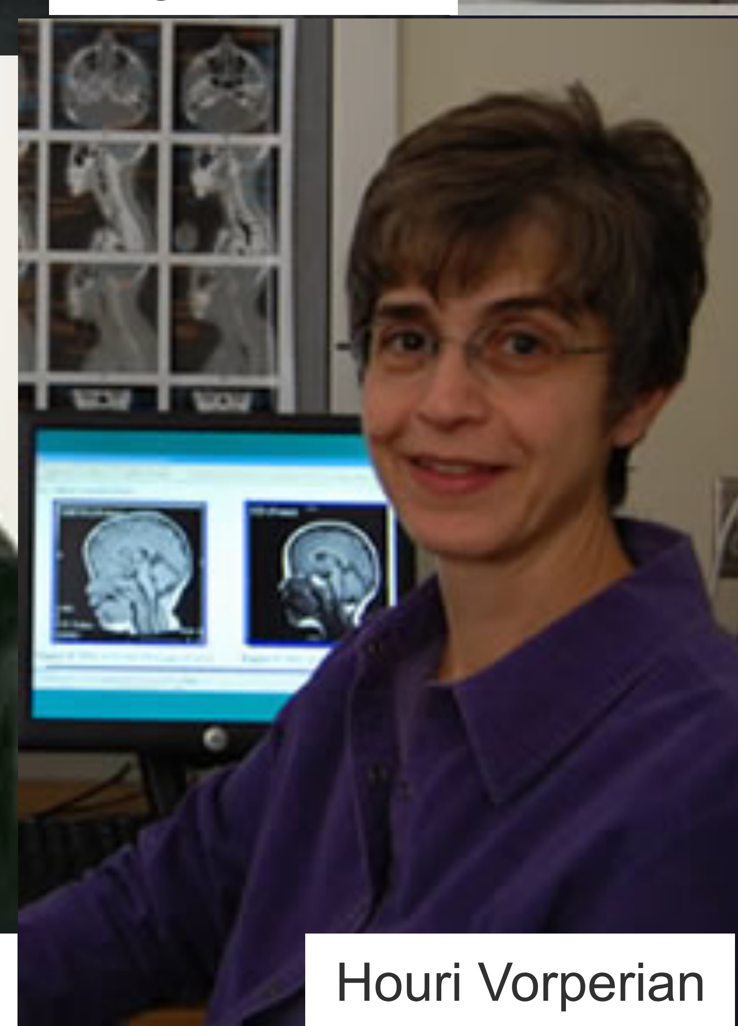
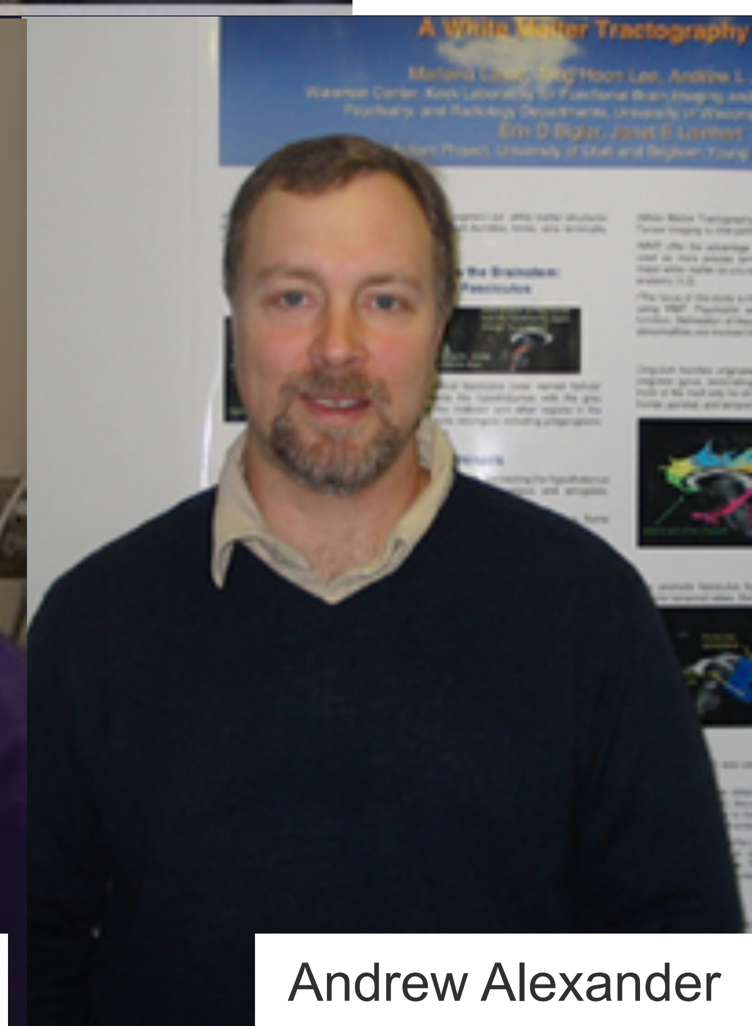
Jamie Hanson

Richard Davidson



Houri Vorperian



Andrew Alexander

References

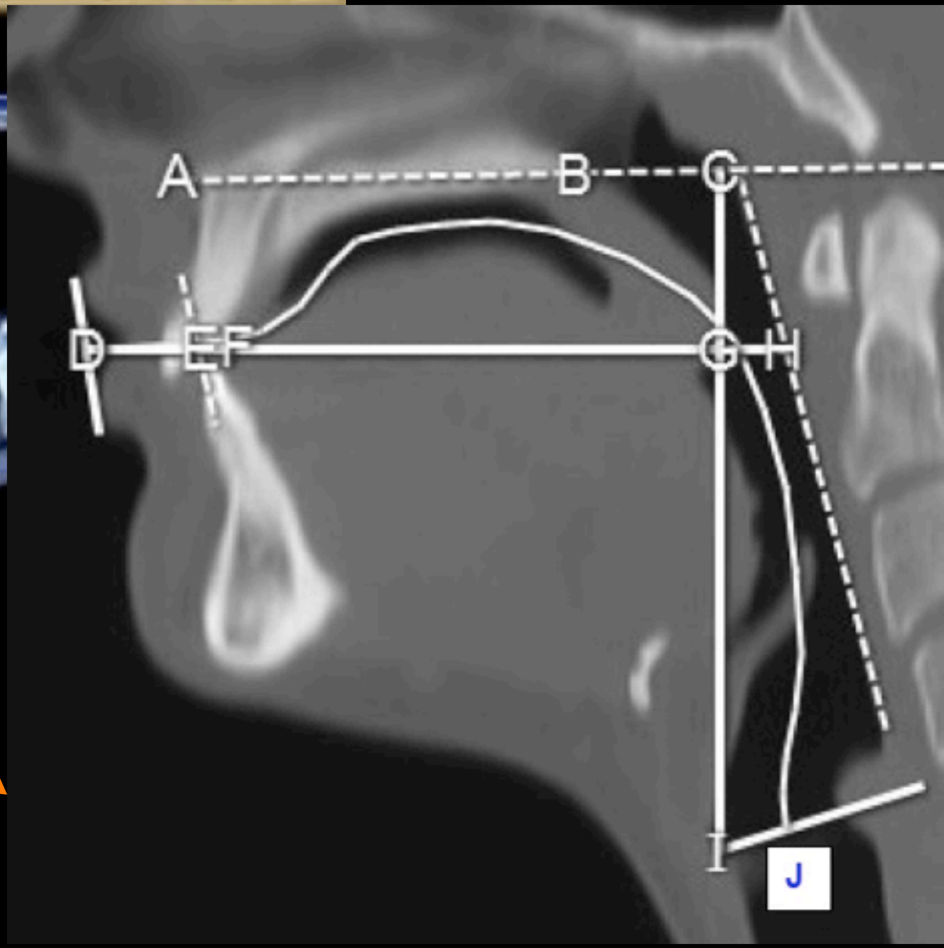
Chung, M.K., Robbins, S., Evans, A.C. 2005.Unified statistical approach to cortical thickness analysis. Lecture Notes in Computer Science (LNCS) 3565:627-638.
http://www.stat.wisc.edu/~mchung/papers/IPMI/hk.IPMI.2005.pdf

Chung, M.K., Dalton, K.M., Davidson, R.J. 2008. Tensor-based cortical surface morphometry via weighed spherical harmonic representation. *IEEE Transactions on Medical Imaging*.27:1143-1151.
http://www.stat.wisc.edu/~mchung/papers/TMI.2008.pdf

Chung, M.K., Adluru, N., Lee, J.E., Lazar, M., Lainhart, J.E., Alexander, A.L., 2010. Cosine series representation of 3D curves and its application to white matter fiber bundles in diffusion tensor imaging. *Statistics and Its Interface. 3:69-80*
http://www.stat.wisc.edu/~mchung/papers/chung.2010.SII.pdf

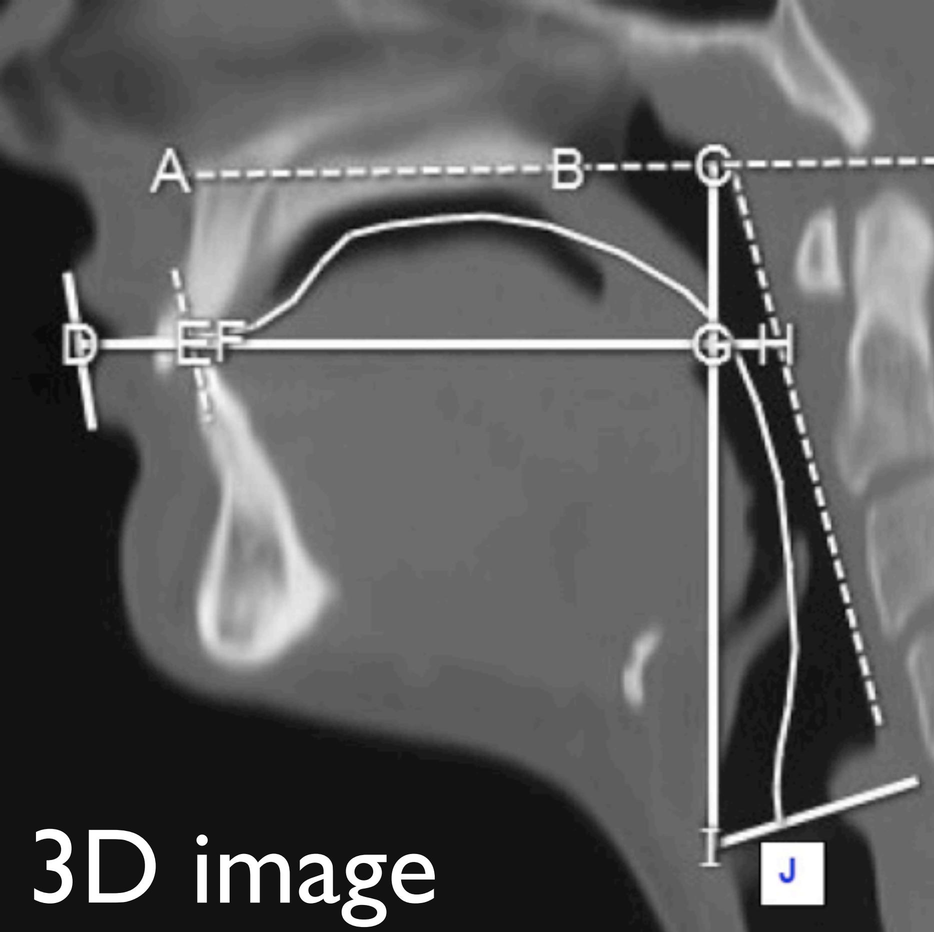
Image acquisition

Computed Tomography (CT)



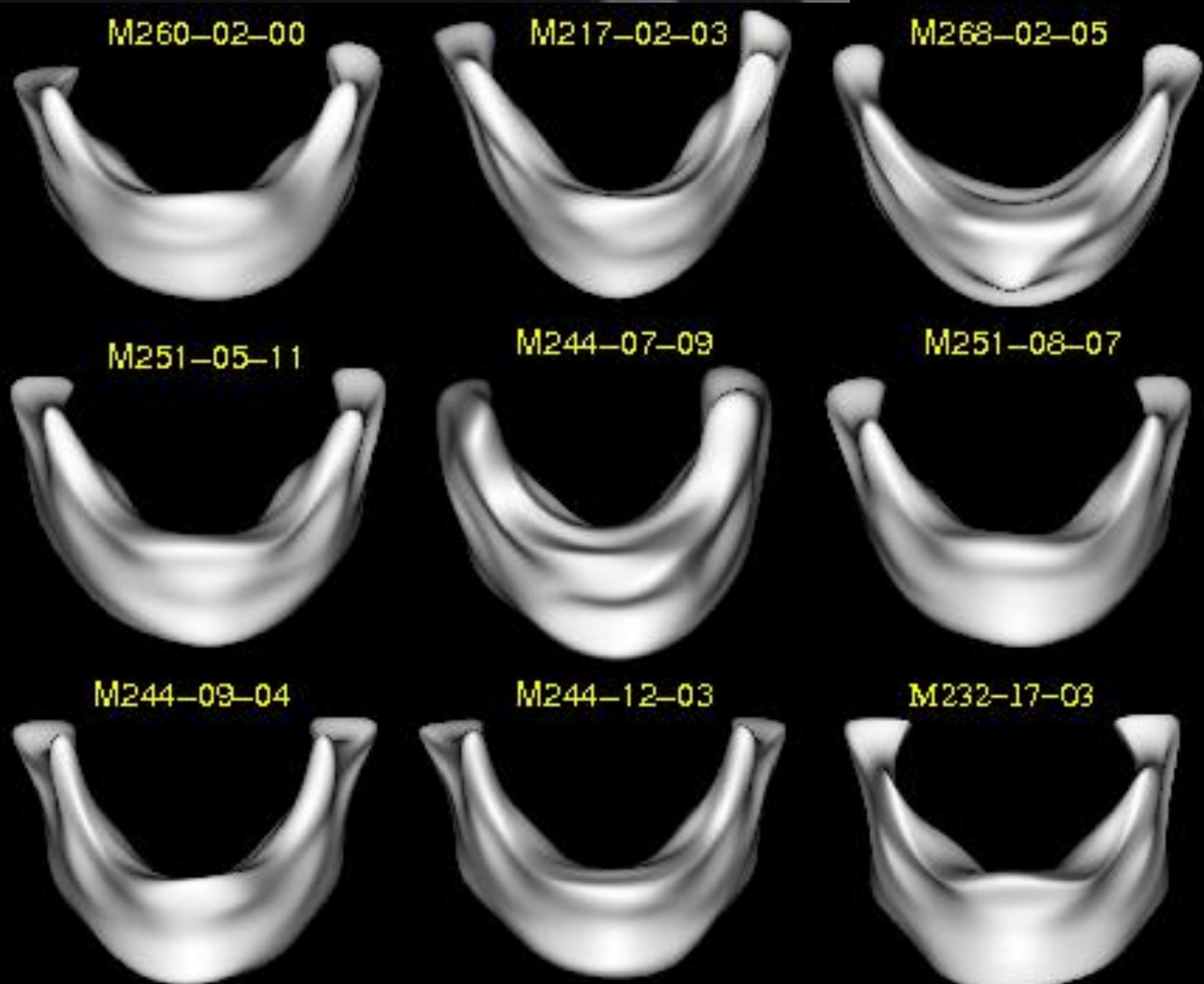
Hard tissues: bones, teeth

3D image



Binary segmentation

Surface models



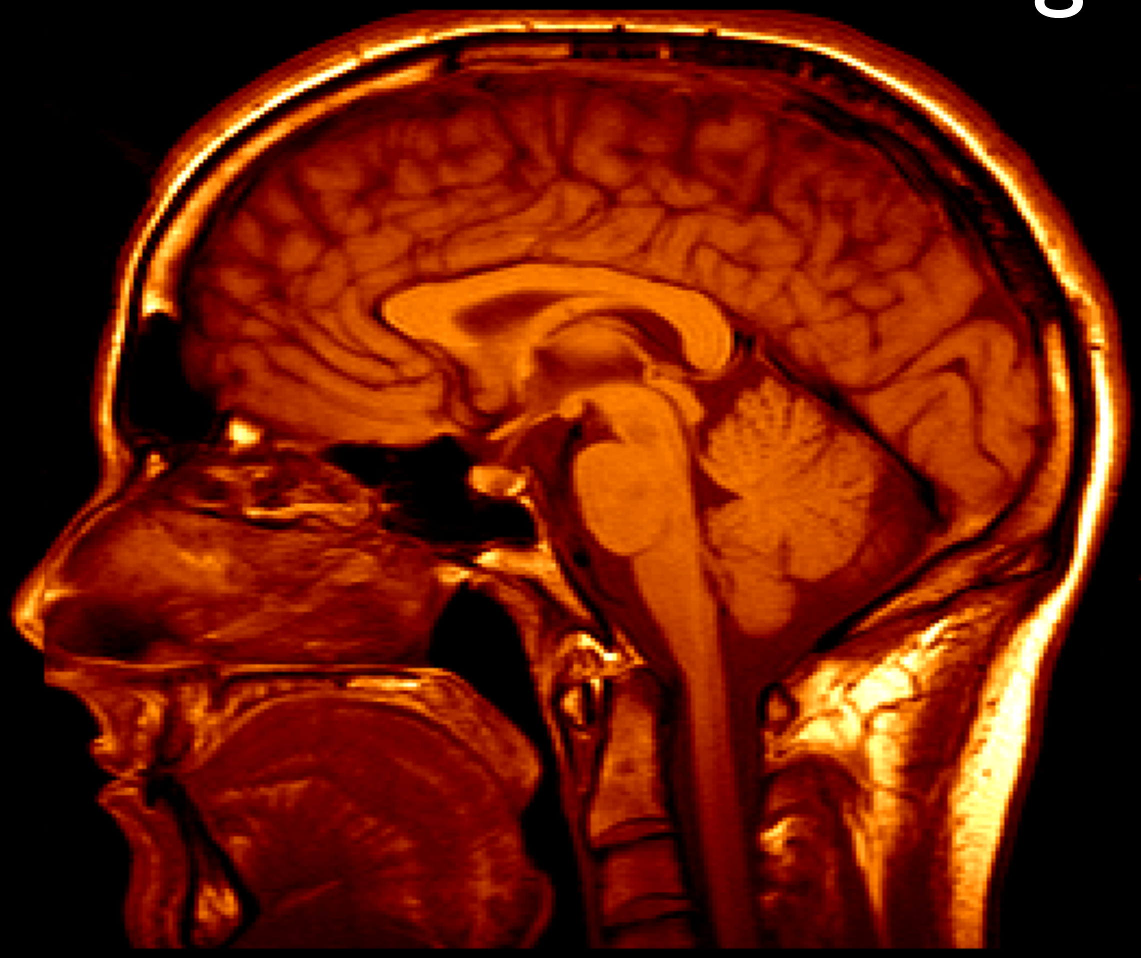
Waisman vocal tract laboratory

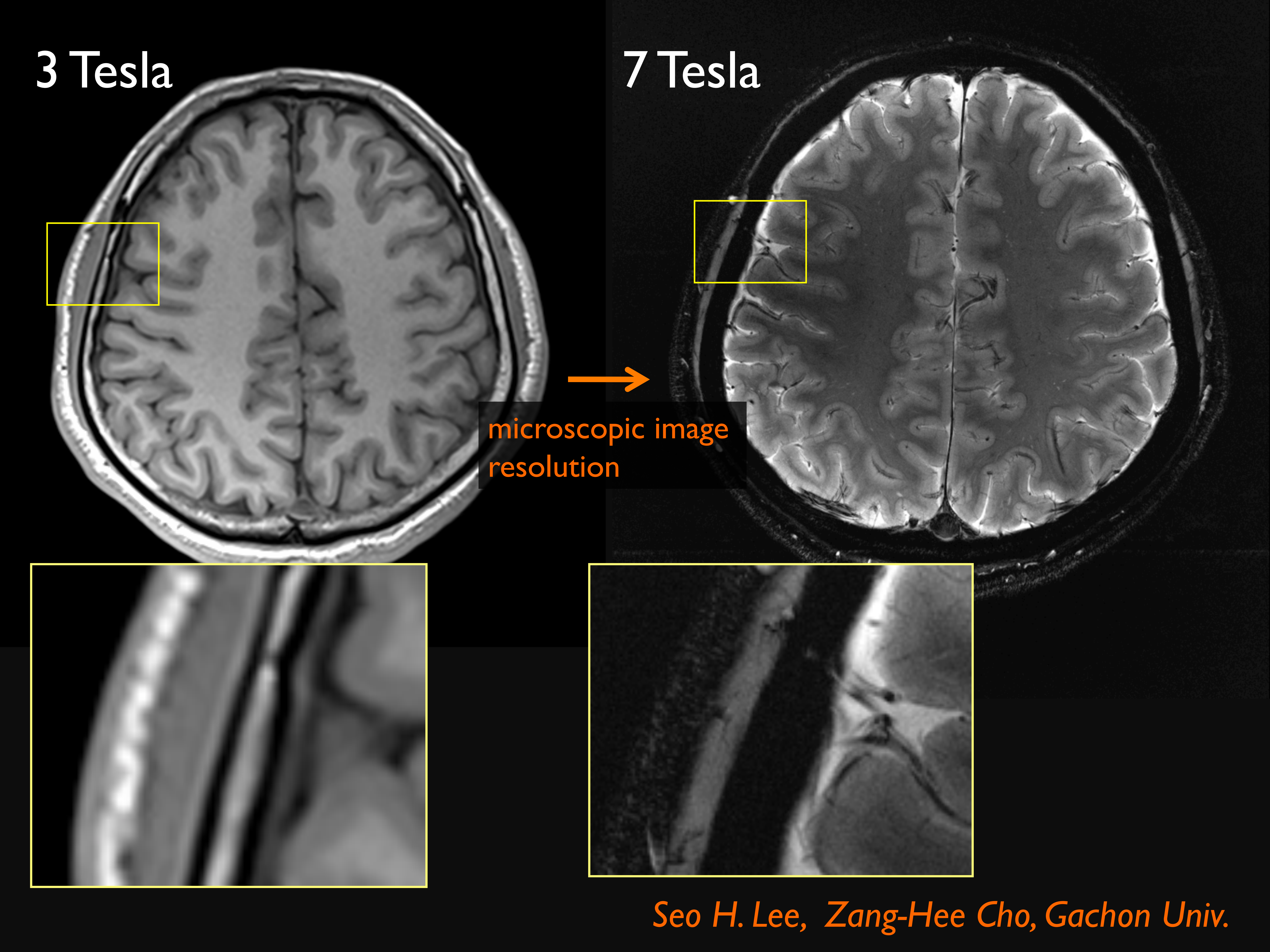
Magnetic Resonance Imaging (MRI)

3.0 Tesla GE Scanner

Soft tissues

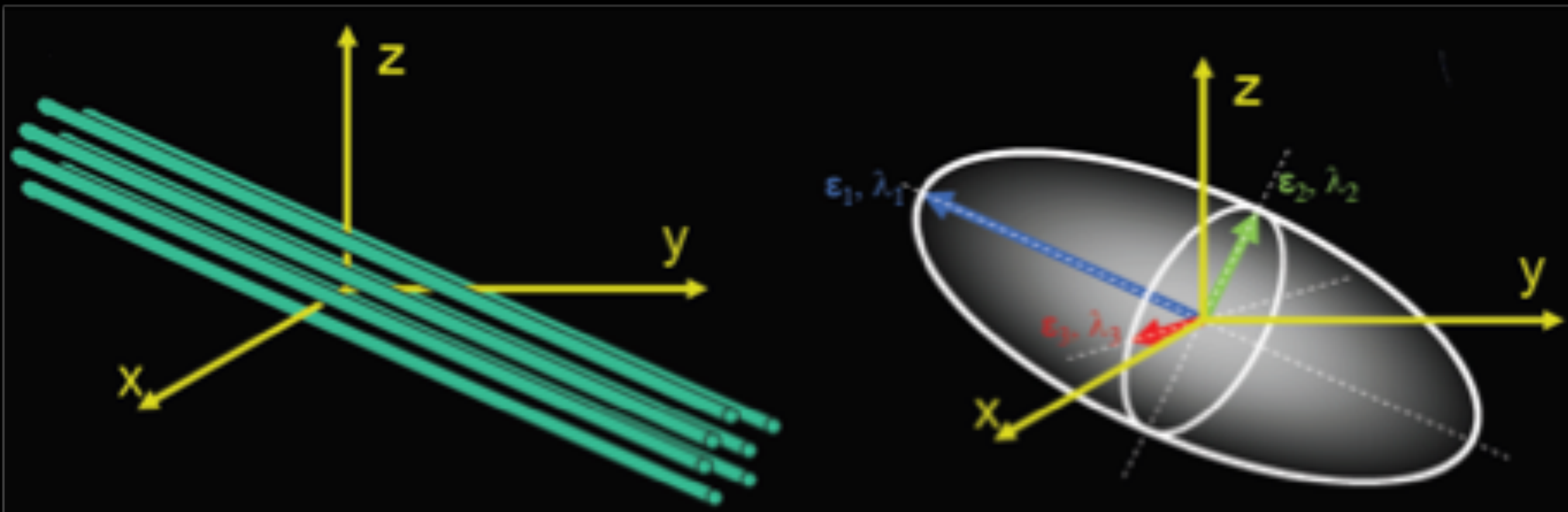
3D image



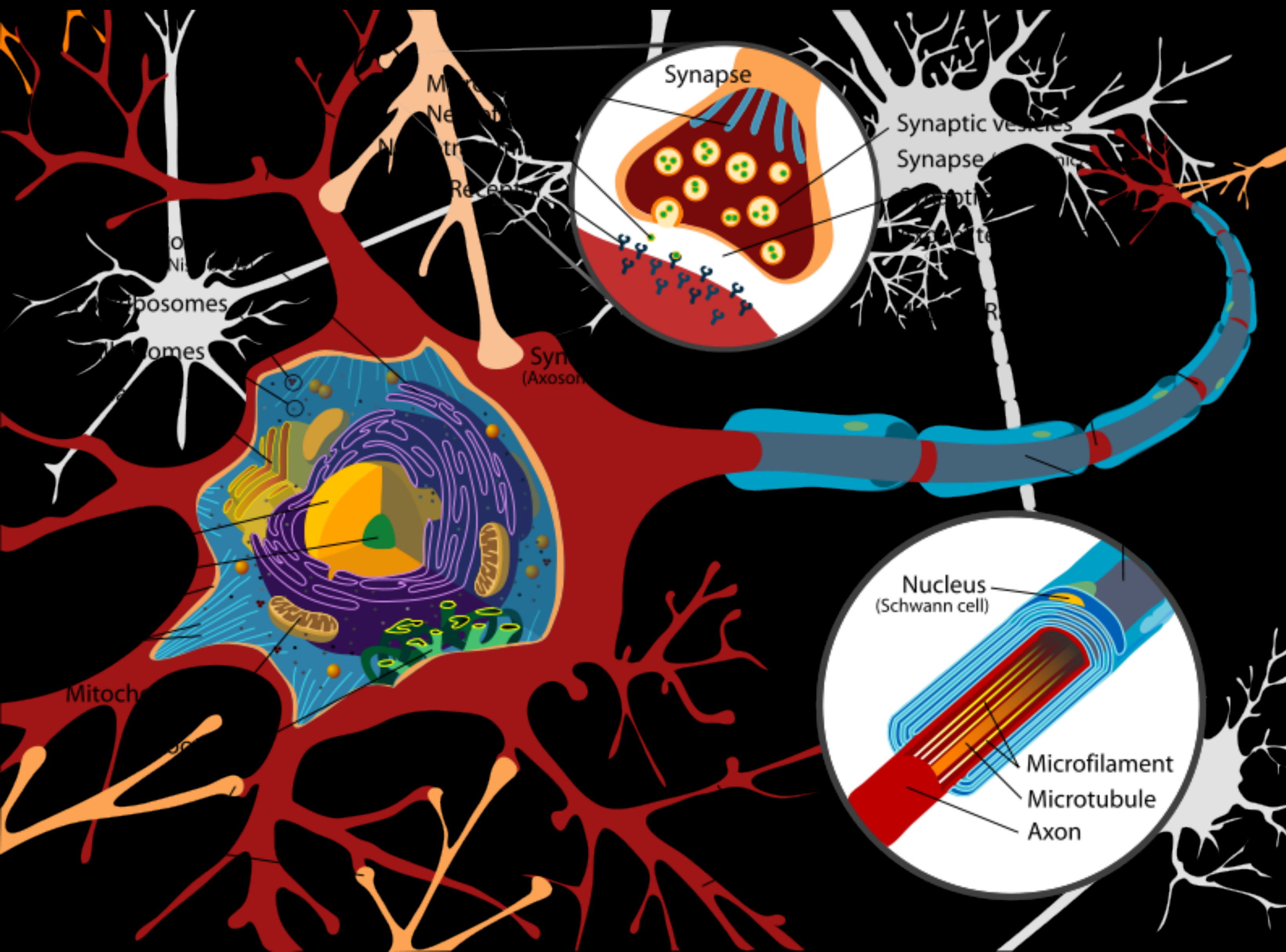

3 Tesla
7 Tesla
microscopic image
resolution
Seo H. Lee, Zang-Hee Cho, Gachon Univ.

Diffusion Tensor Imaging

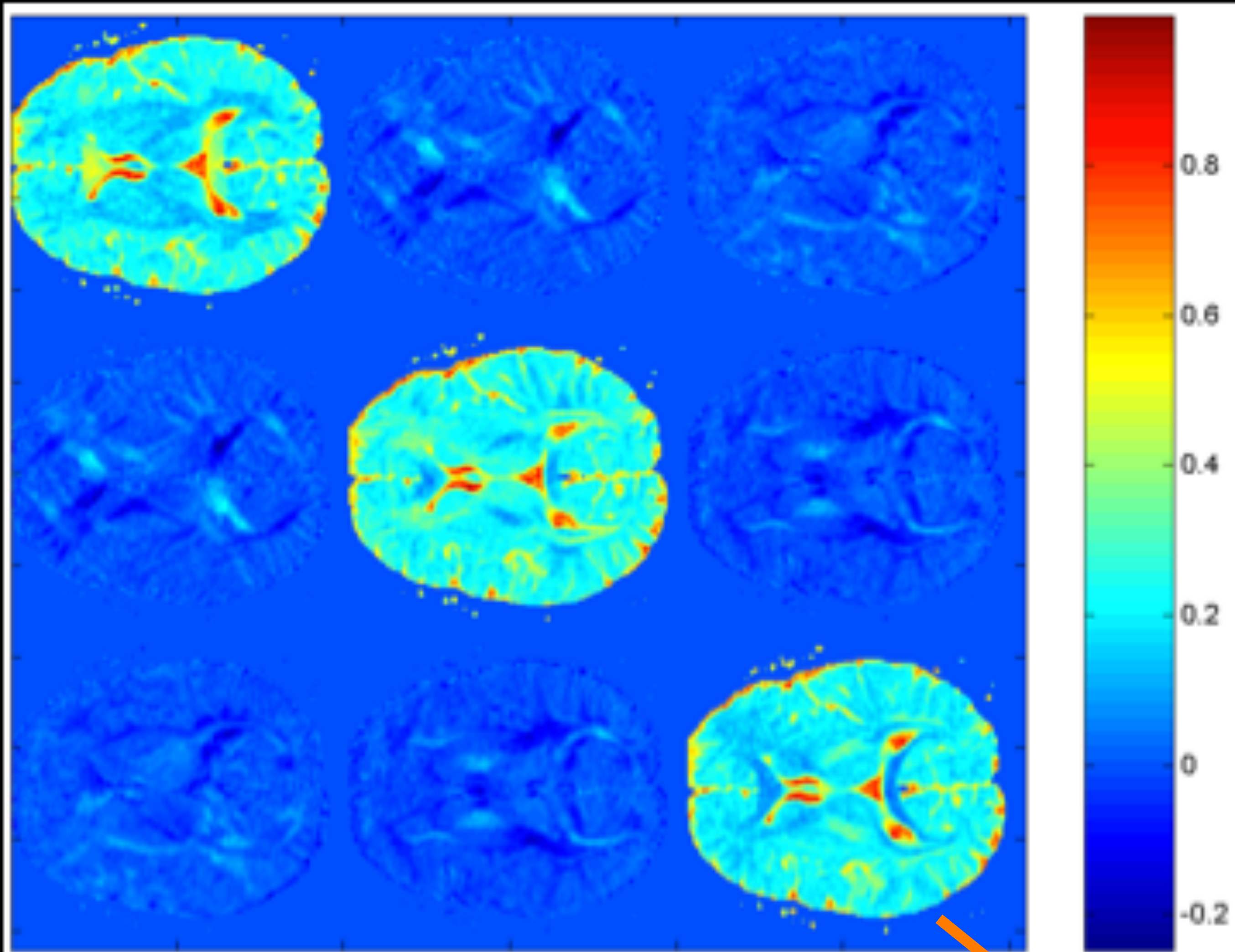
Mori and van Zijl NMR Biomed 2002



The movement of anisotropic water diffusion can be measured using DTI

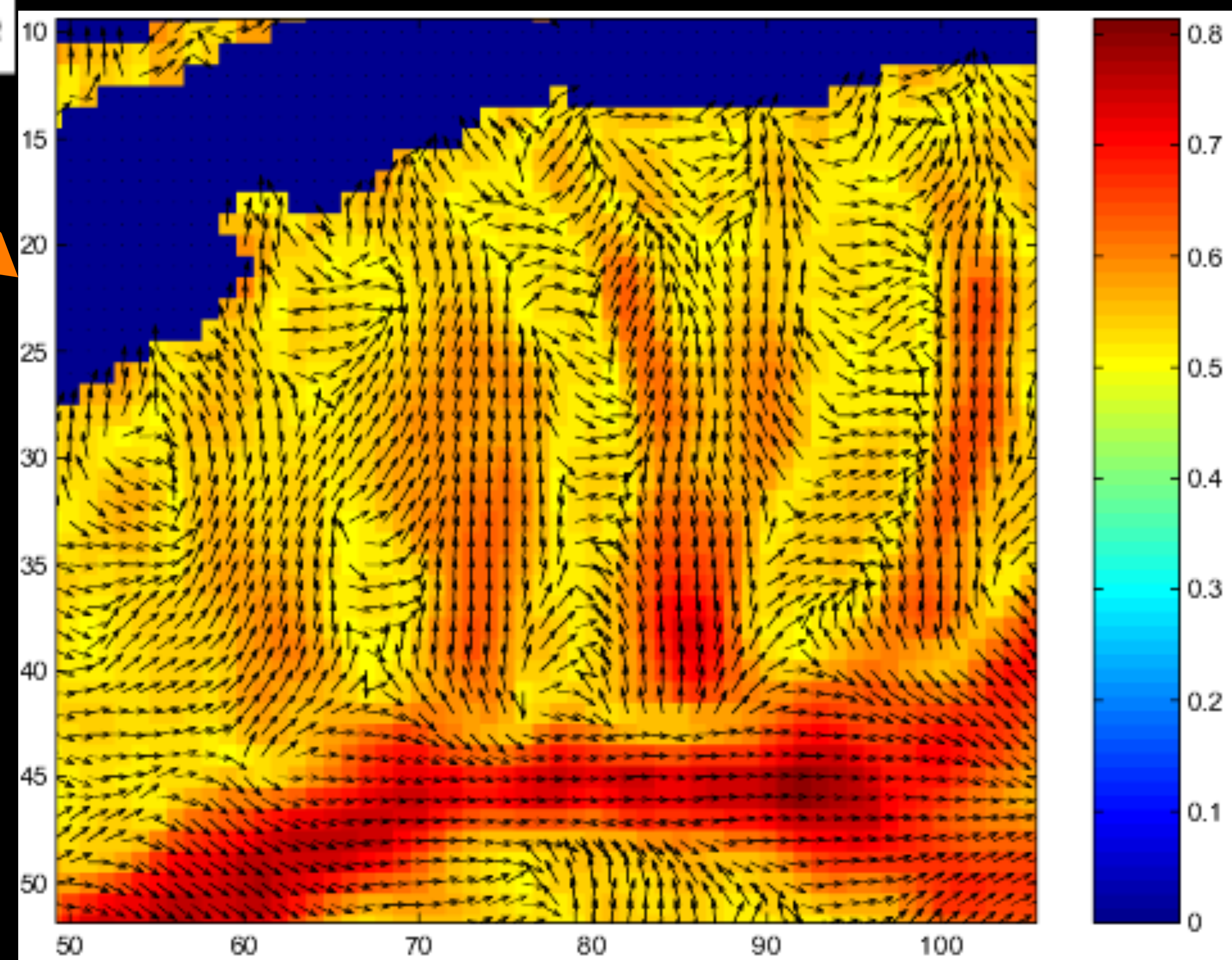


The direction of neuronal filaments in the axon dictates the movement of water diffusion.

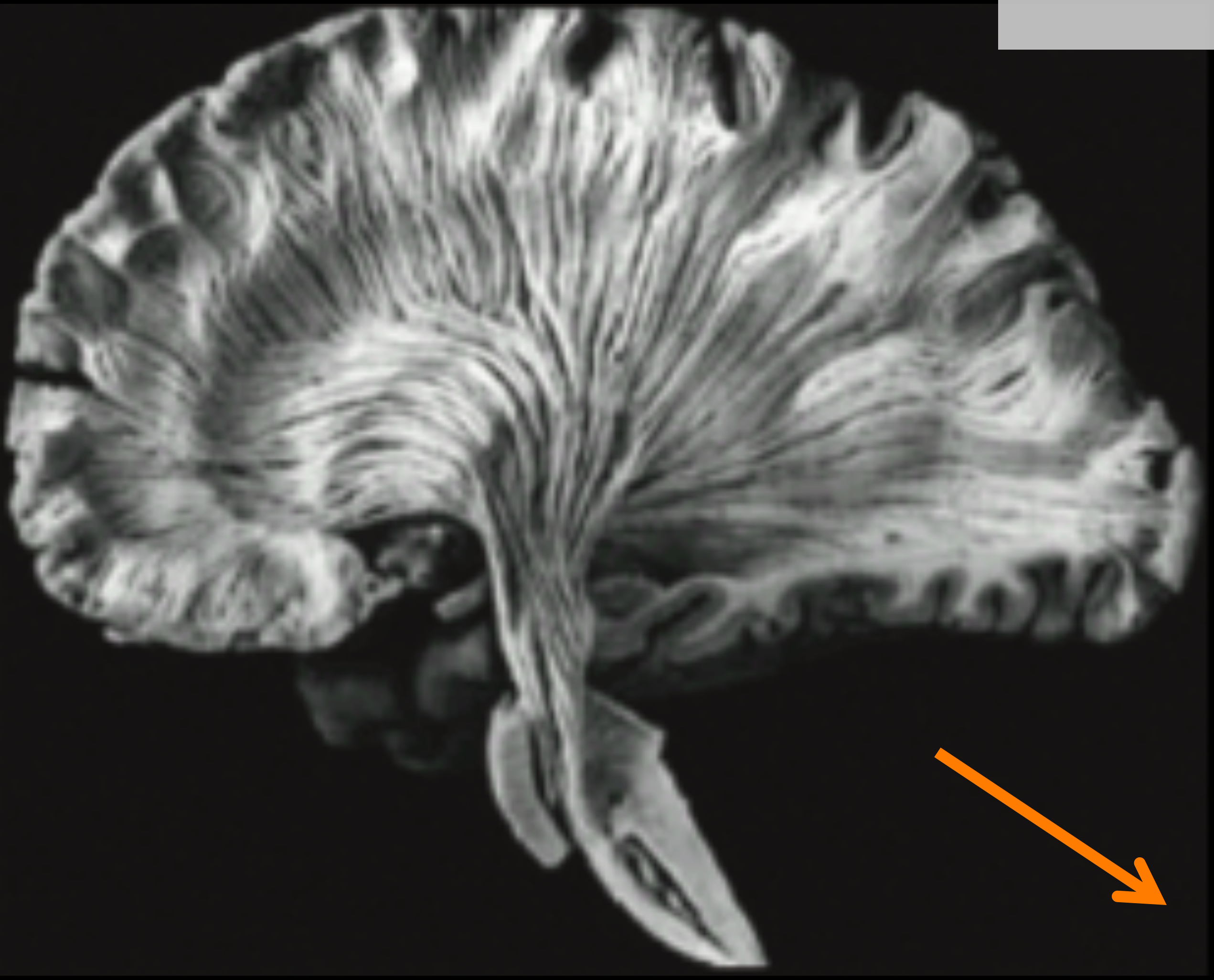


Direction of diffusion is encoded in 3x3 matrix *D* (diffusion tensor)

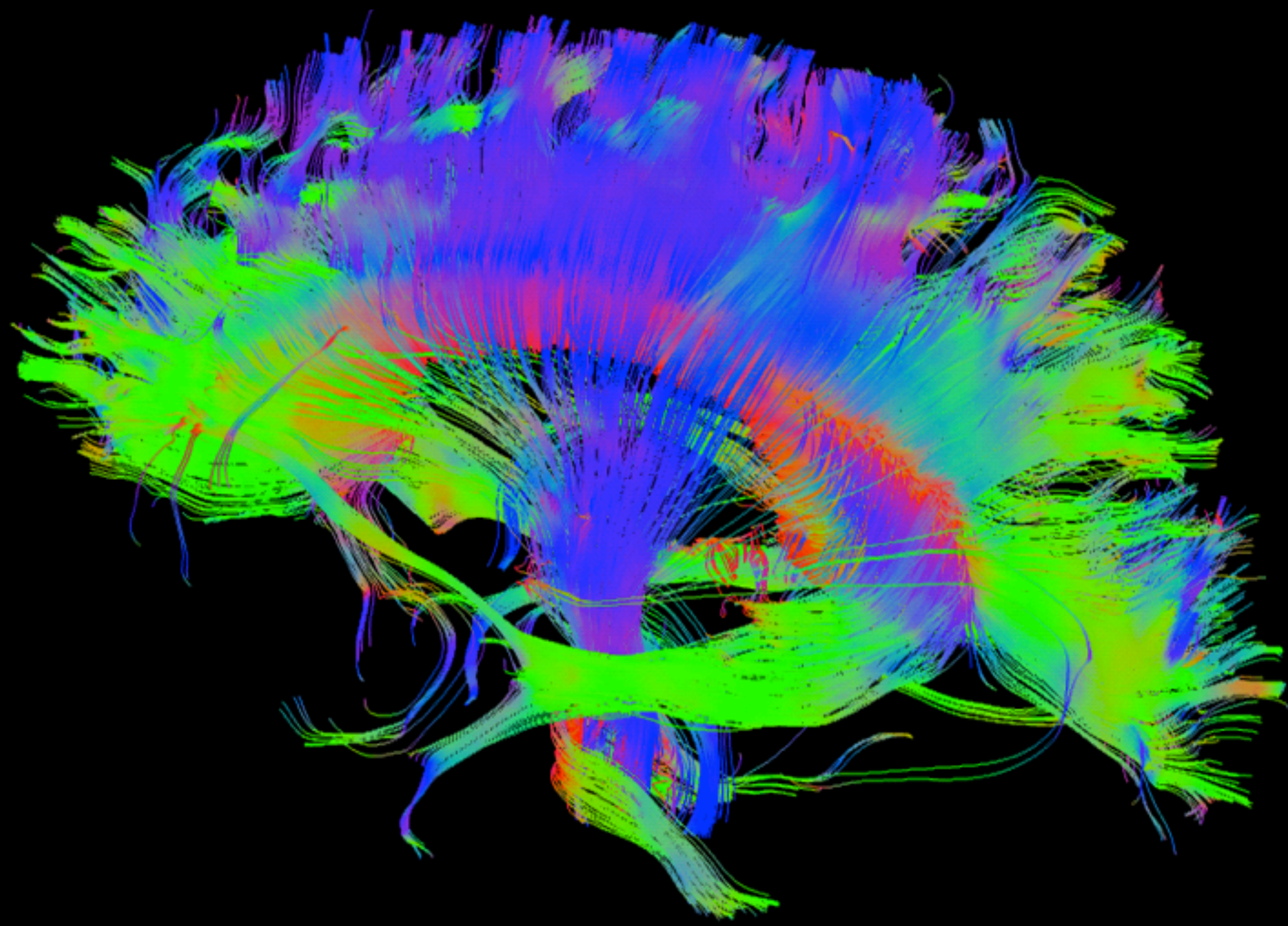
Principal eigenvectors of D



White Matter Fiber Tractography



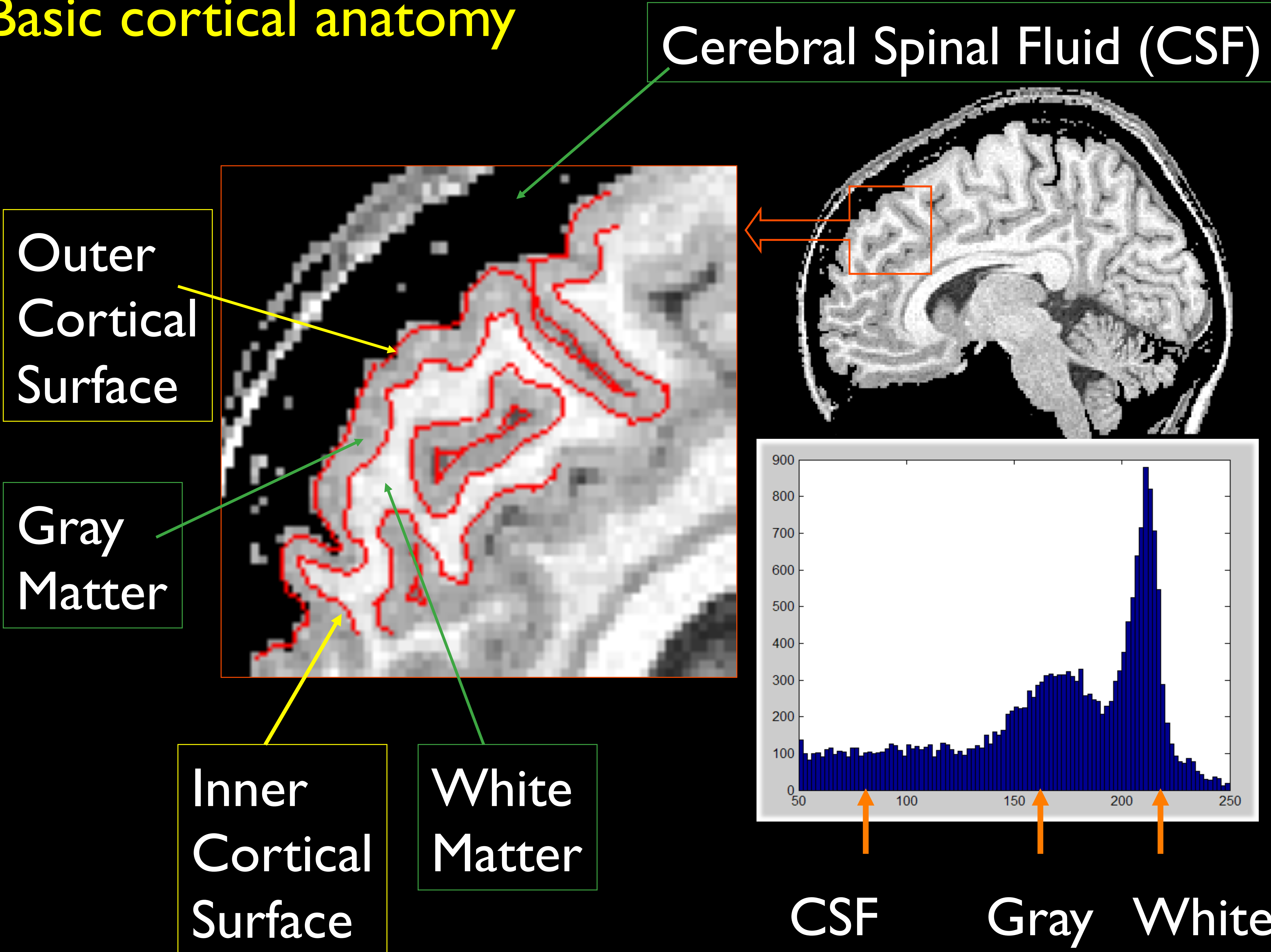
Postmortem



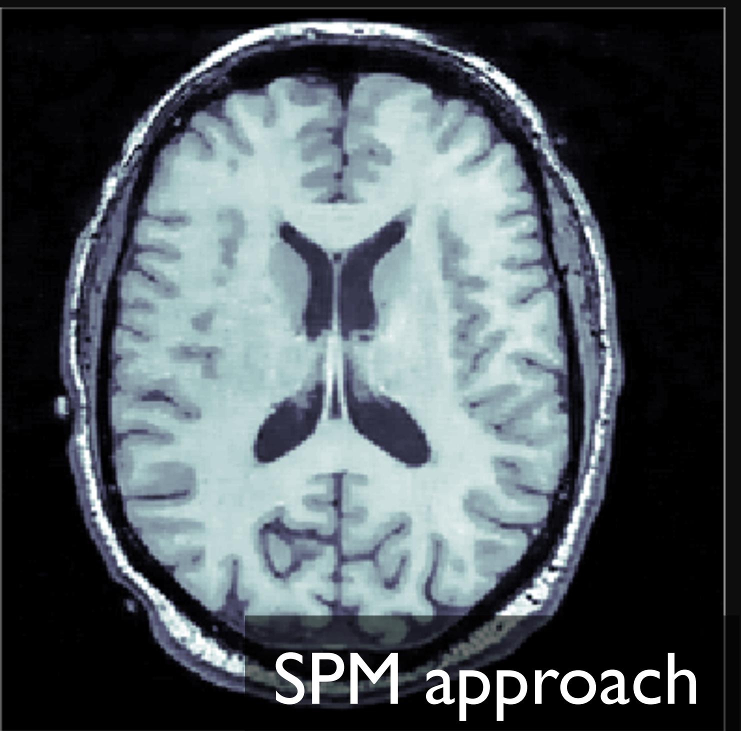
Reconstructed
0.5 million tracts

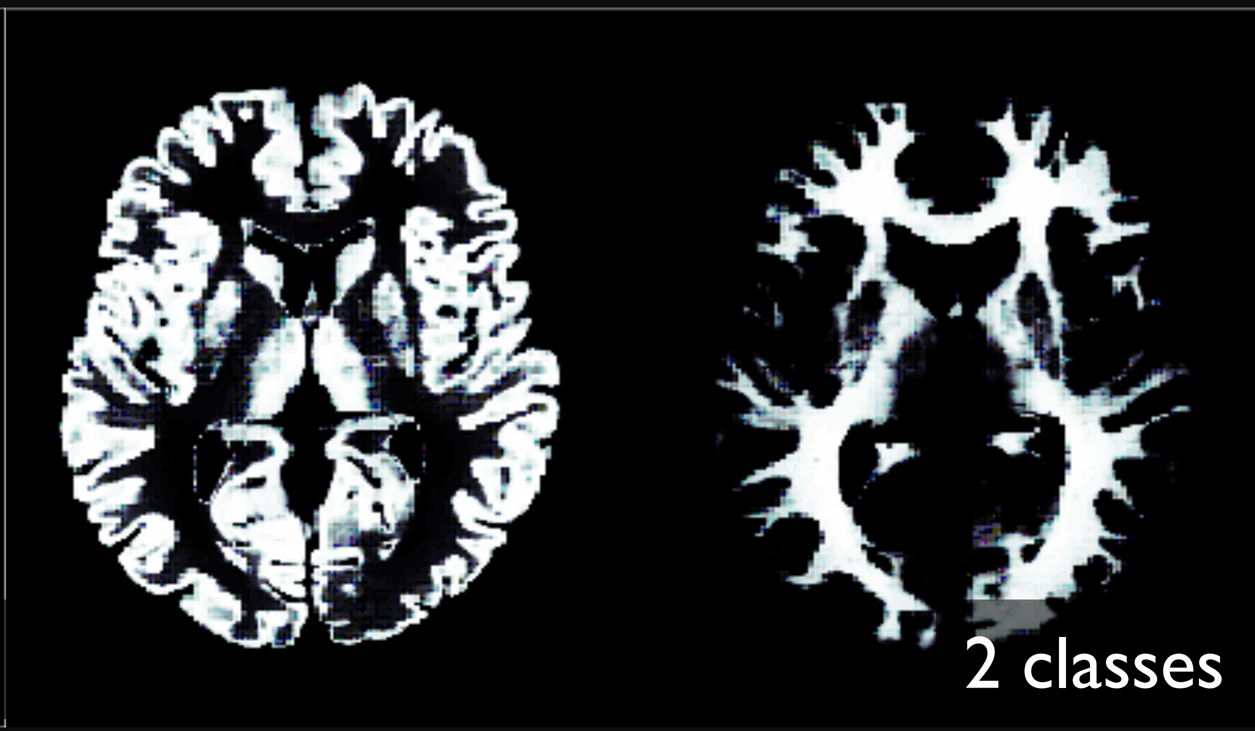
Image segmentation

Basic cortical anatomy

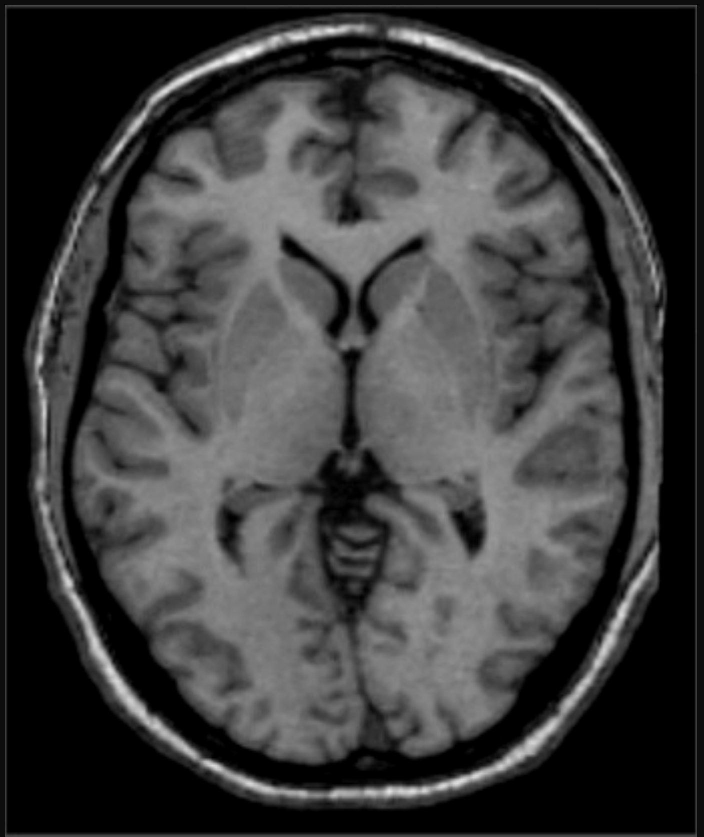


Gaussian mixture modeling with EM algorithm



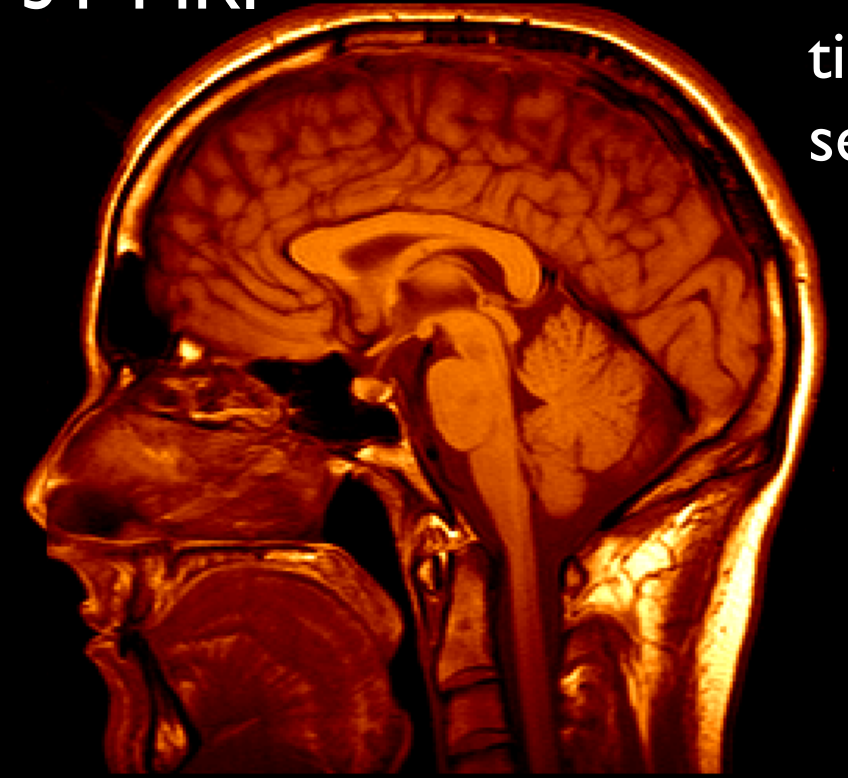


MNI Neural network classifier

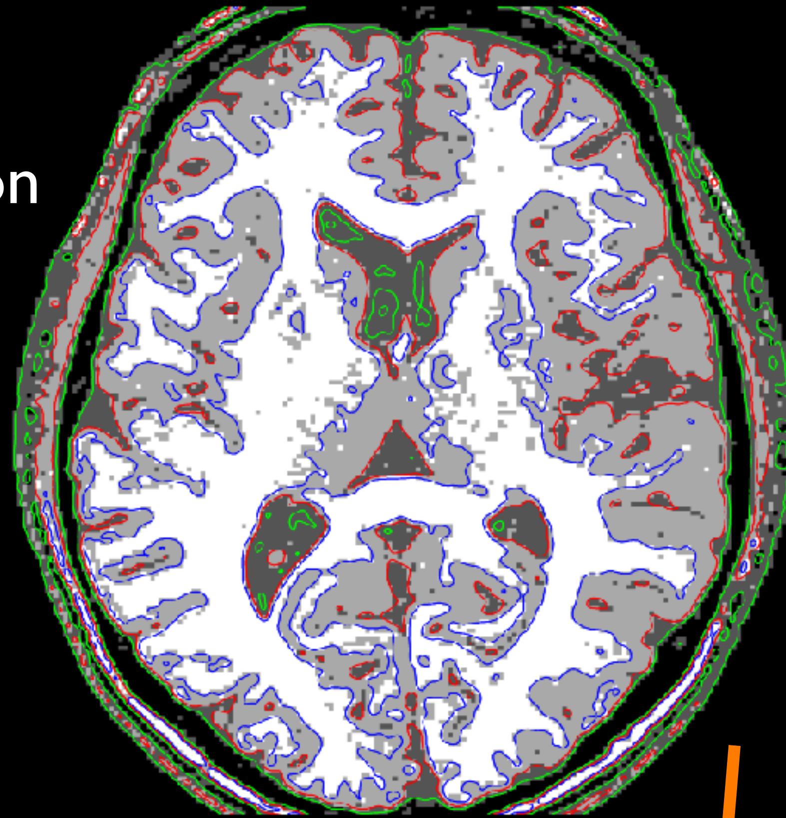


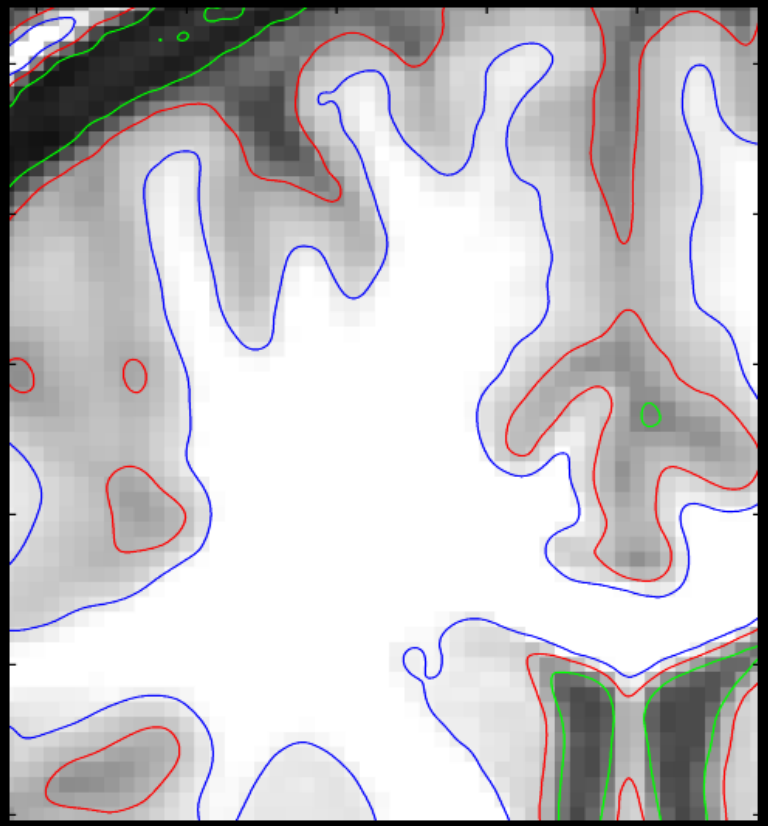
3 classes

3T MRI

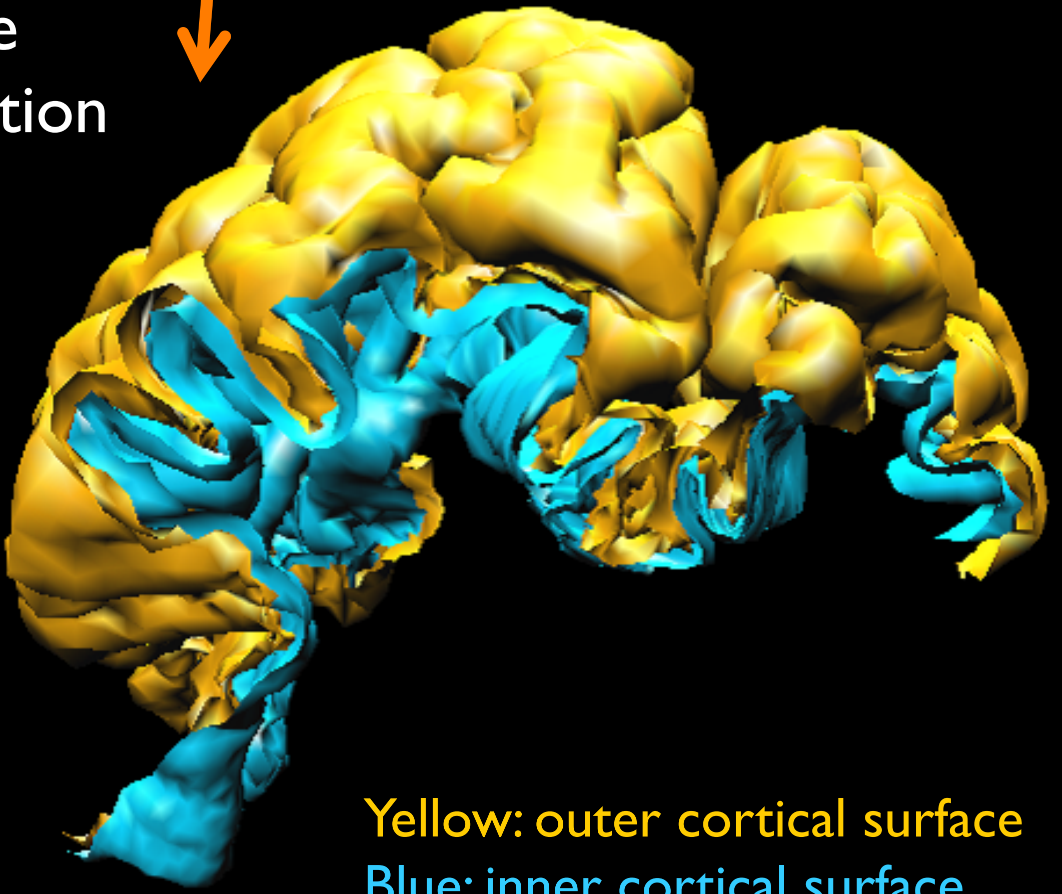


tissue segmentation



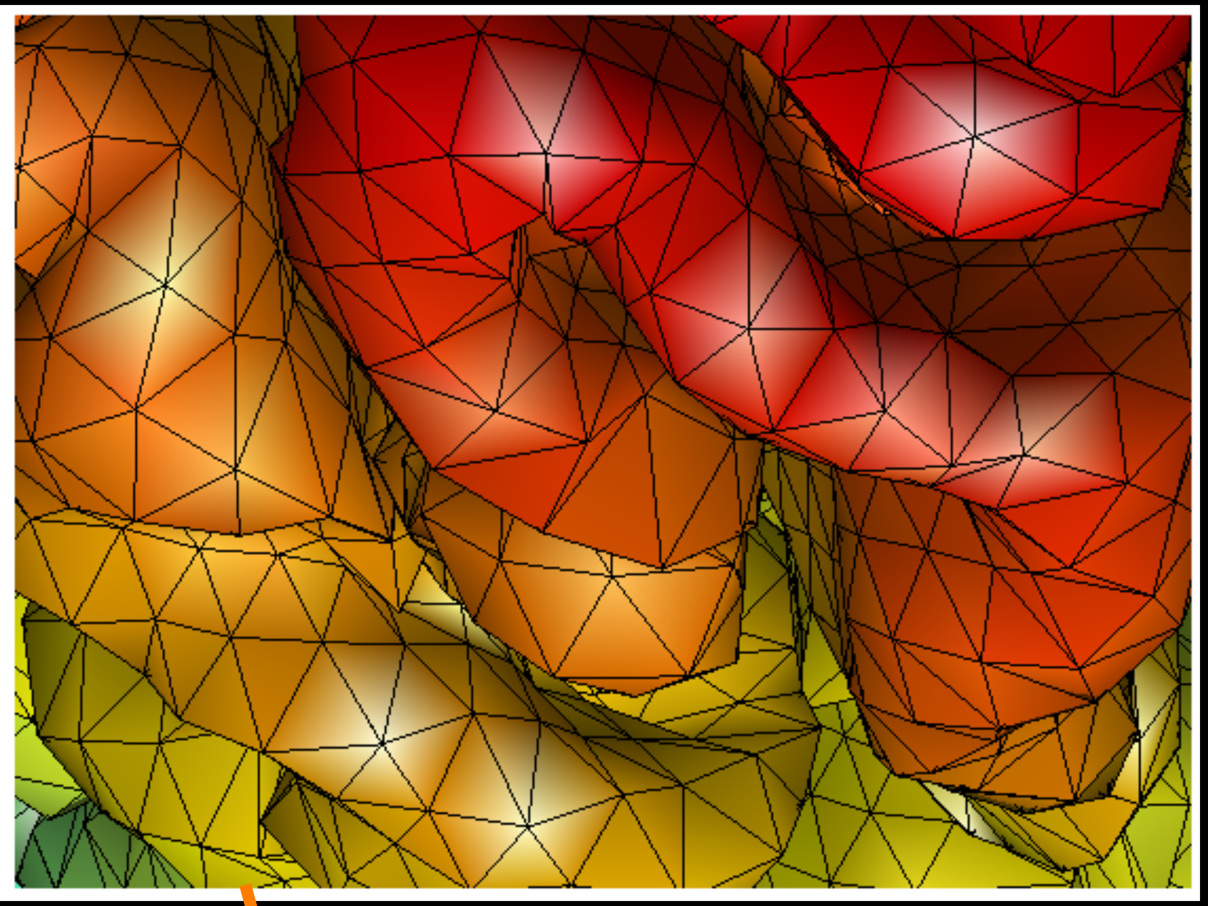


surface extraction



Yellow: outer cortical surface
Blue: inner cortical surface

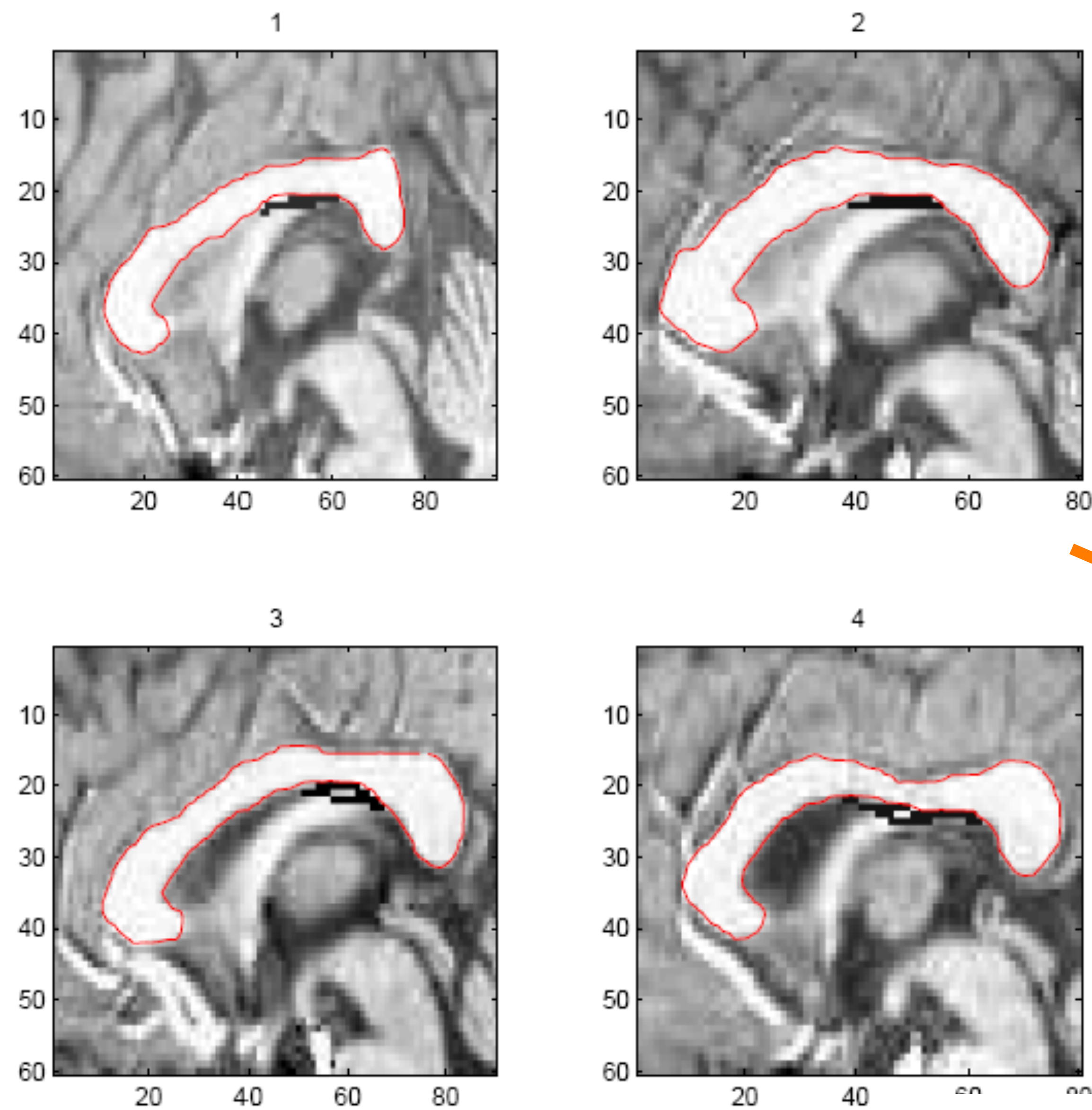
triangle mesh with 1 million triangles

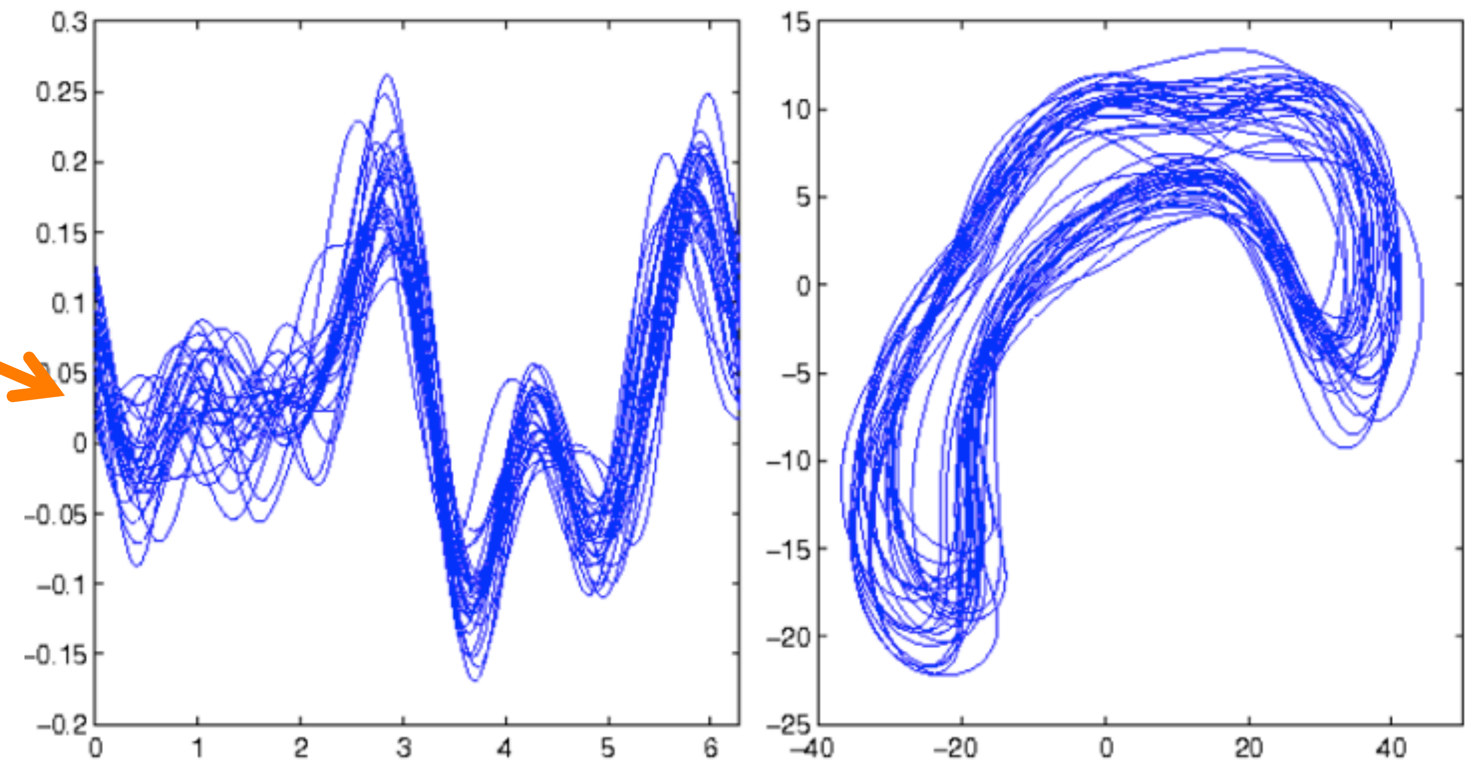


A massive 3D graph with 1 million nodes

Corpus callosum modeling

Active contour (snake) segmentation

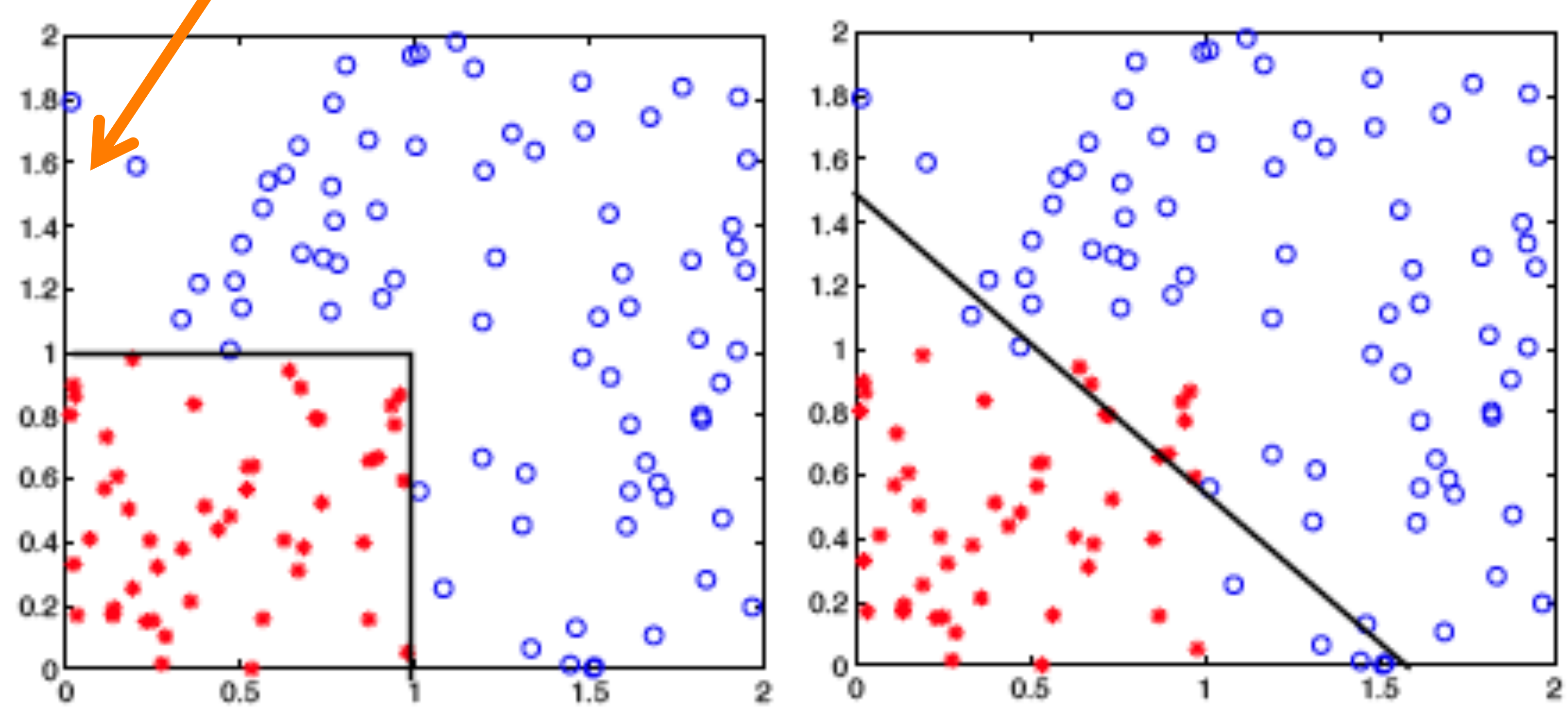




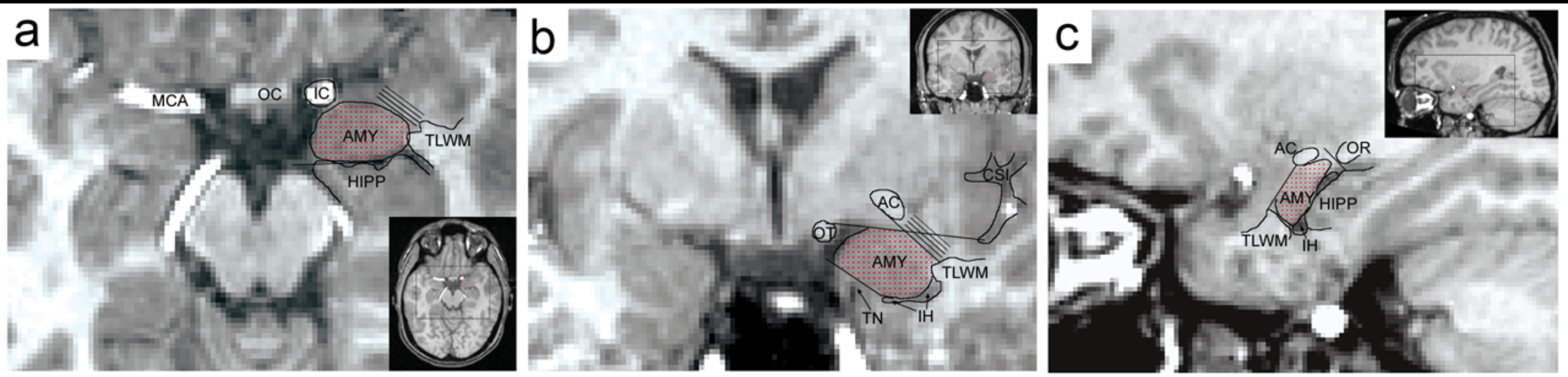
Curve registration/alignment

Classification

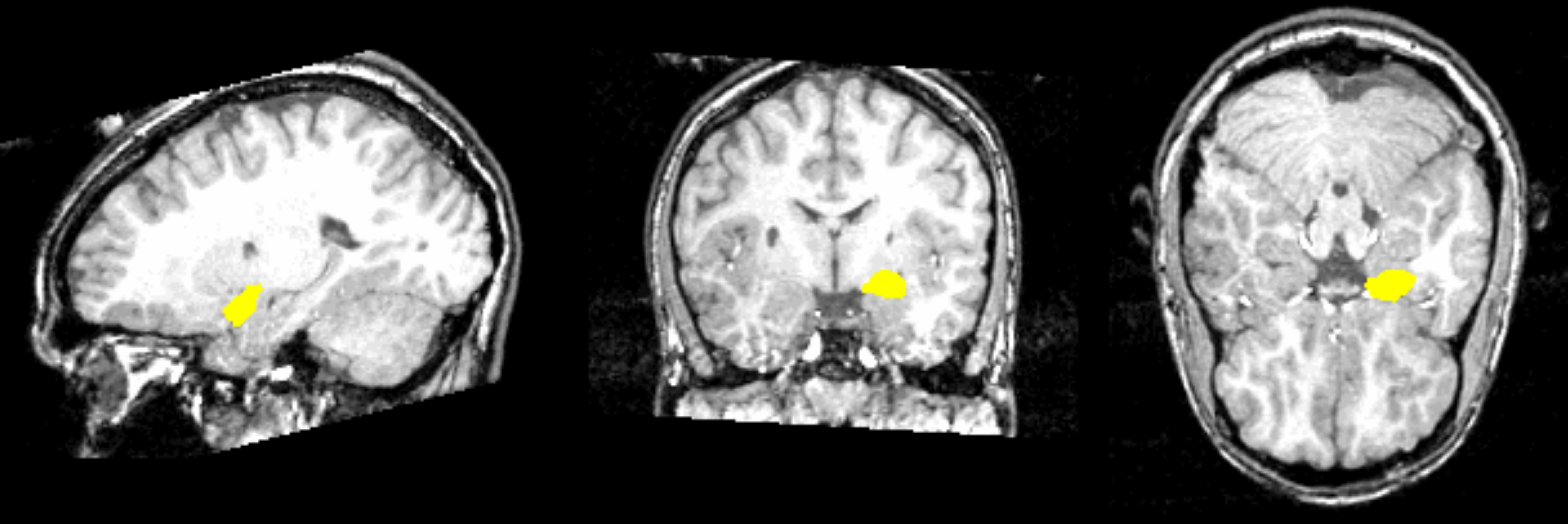
Linear discriminant analysis (LDA) 75%
Regression tree 85%



Manual segmentation



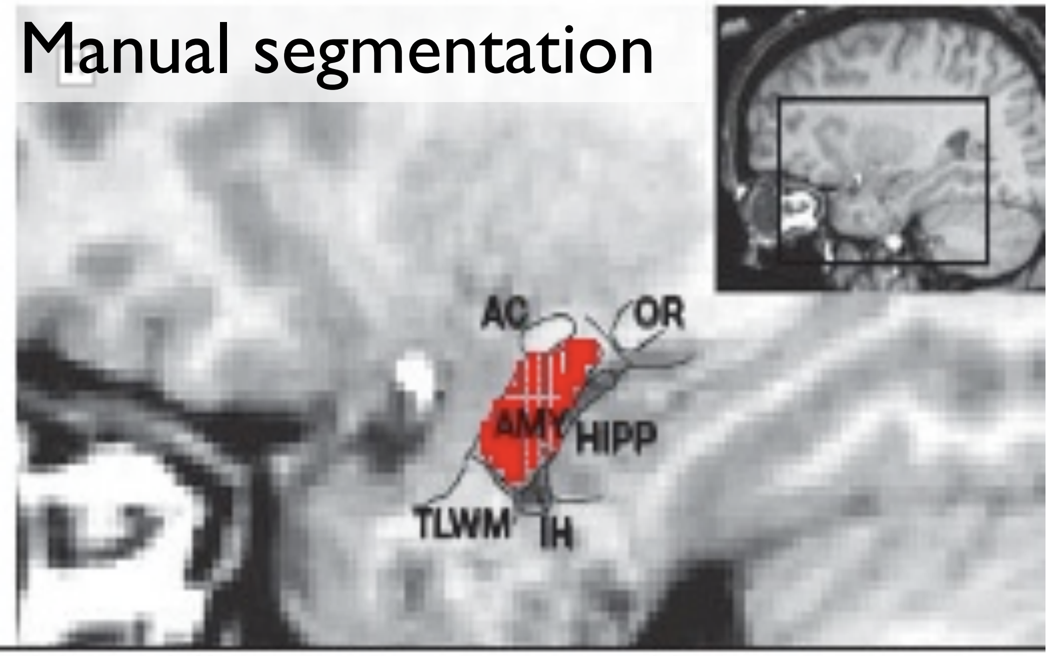
Left amygdala



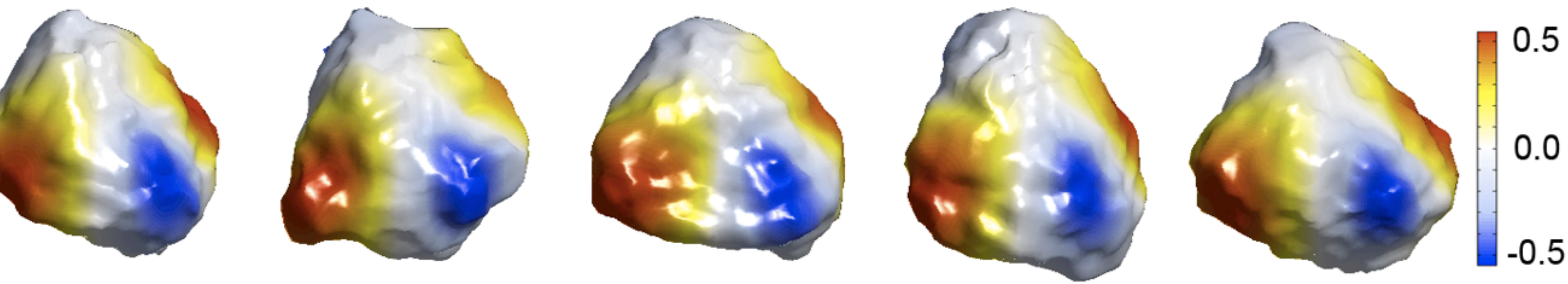
Amygdala shape modeling

Chung et al. 2010, NeuroImage

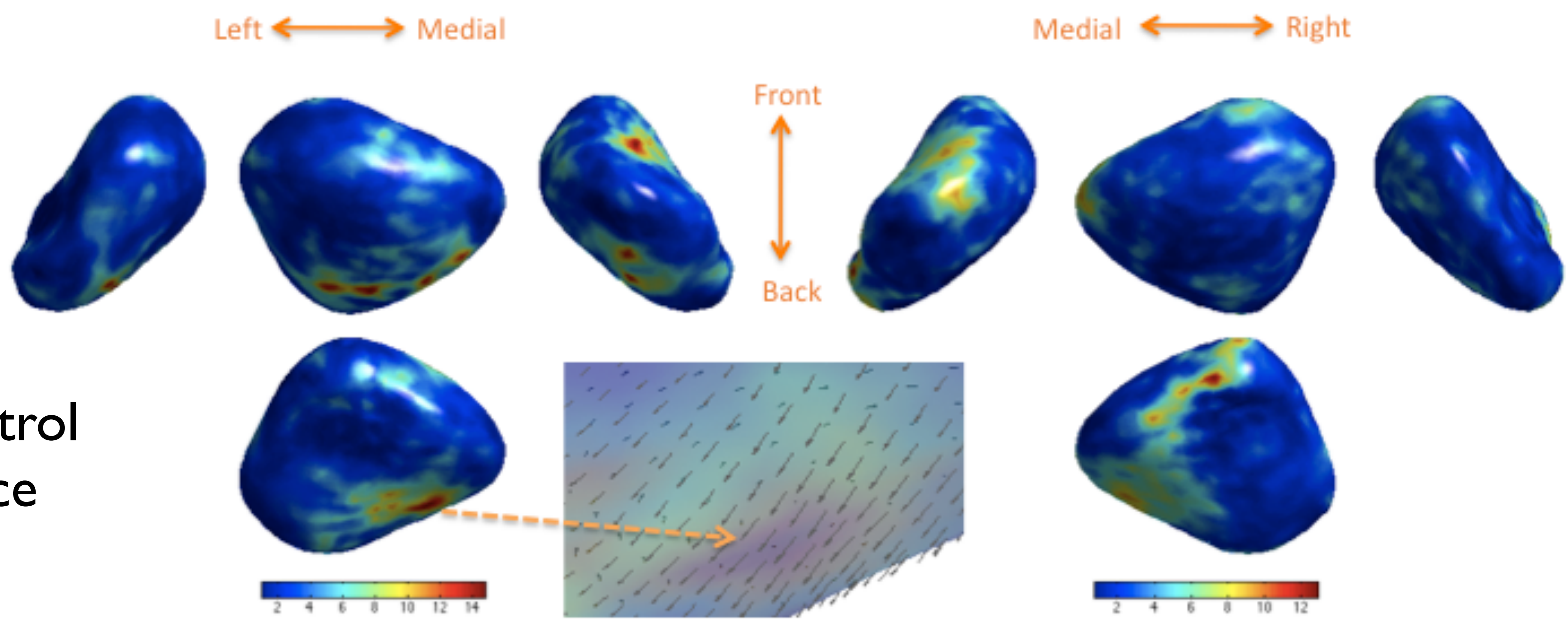
Manual segmentation



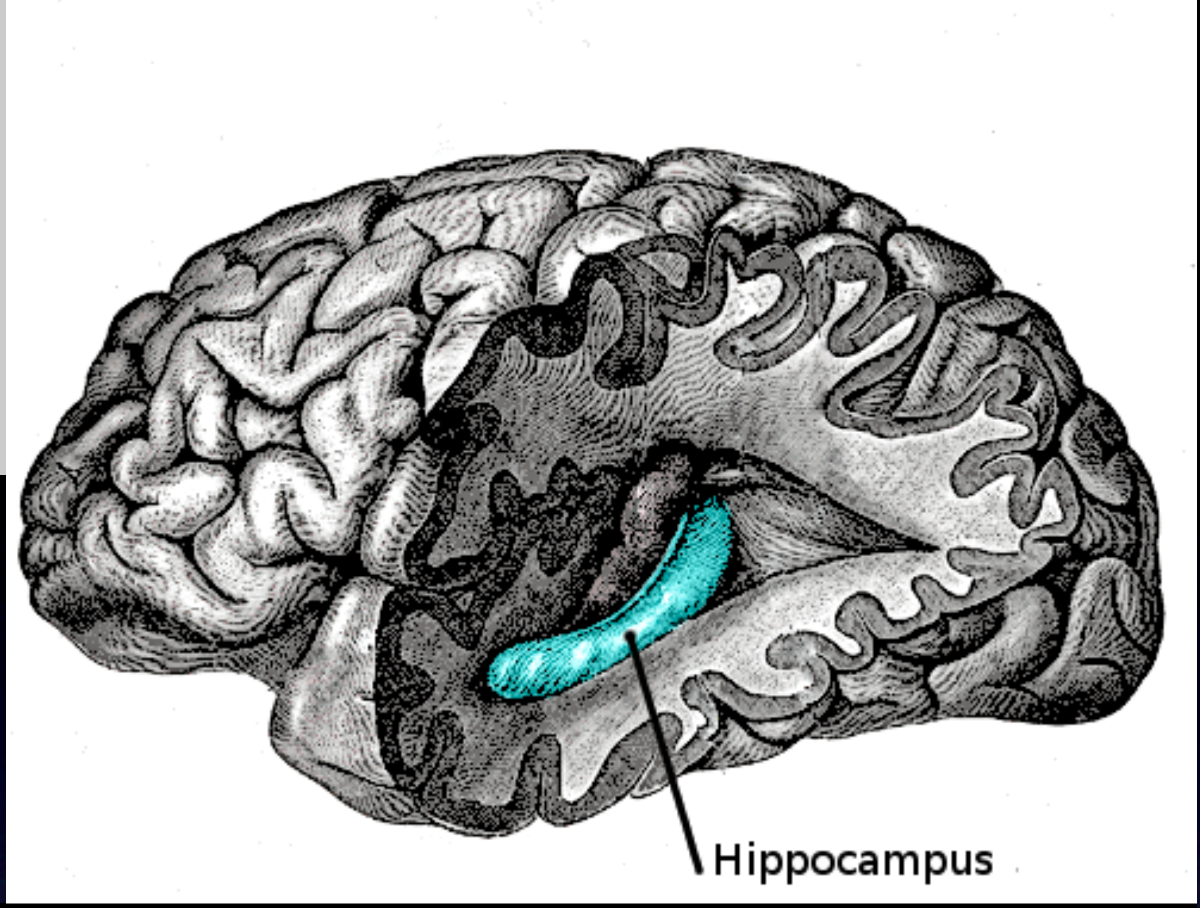
Amygdala registration via spherical harmonic representation

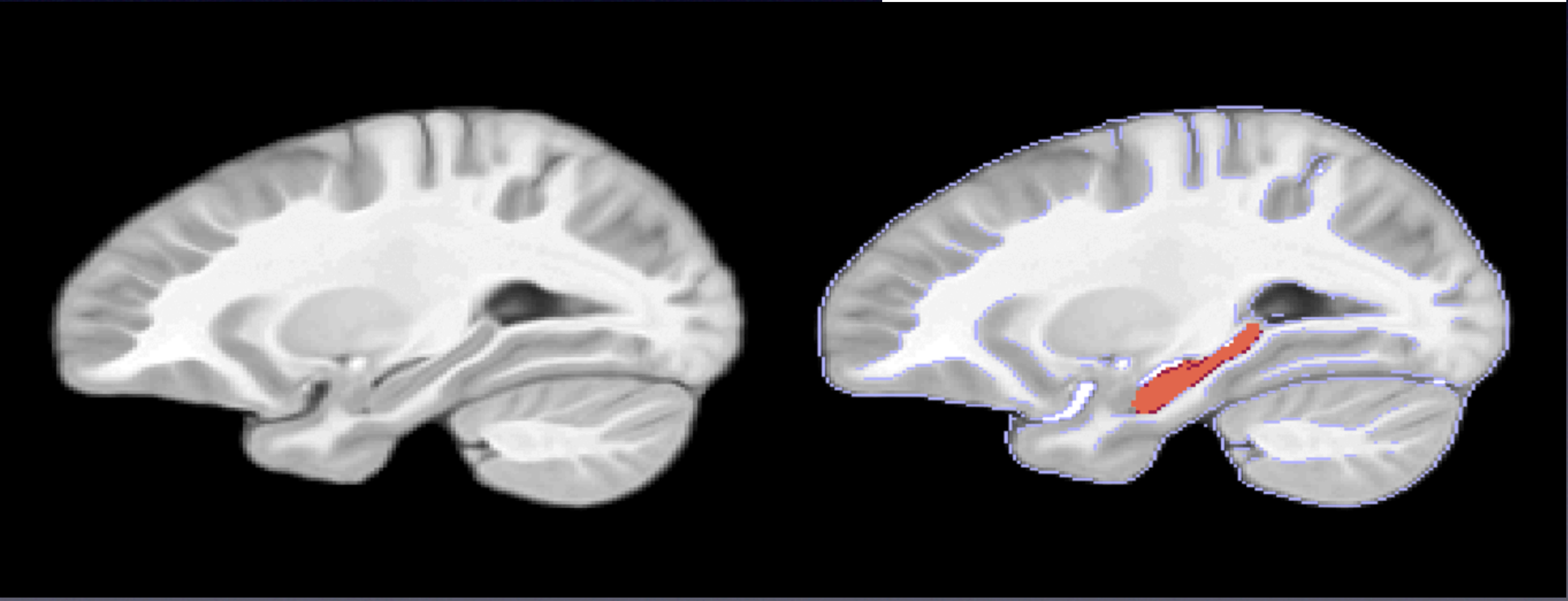


Autism vs. control group difference

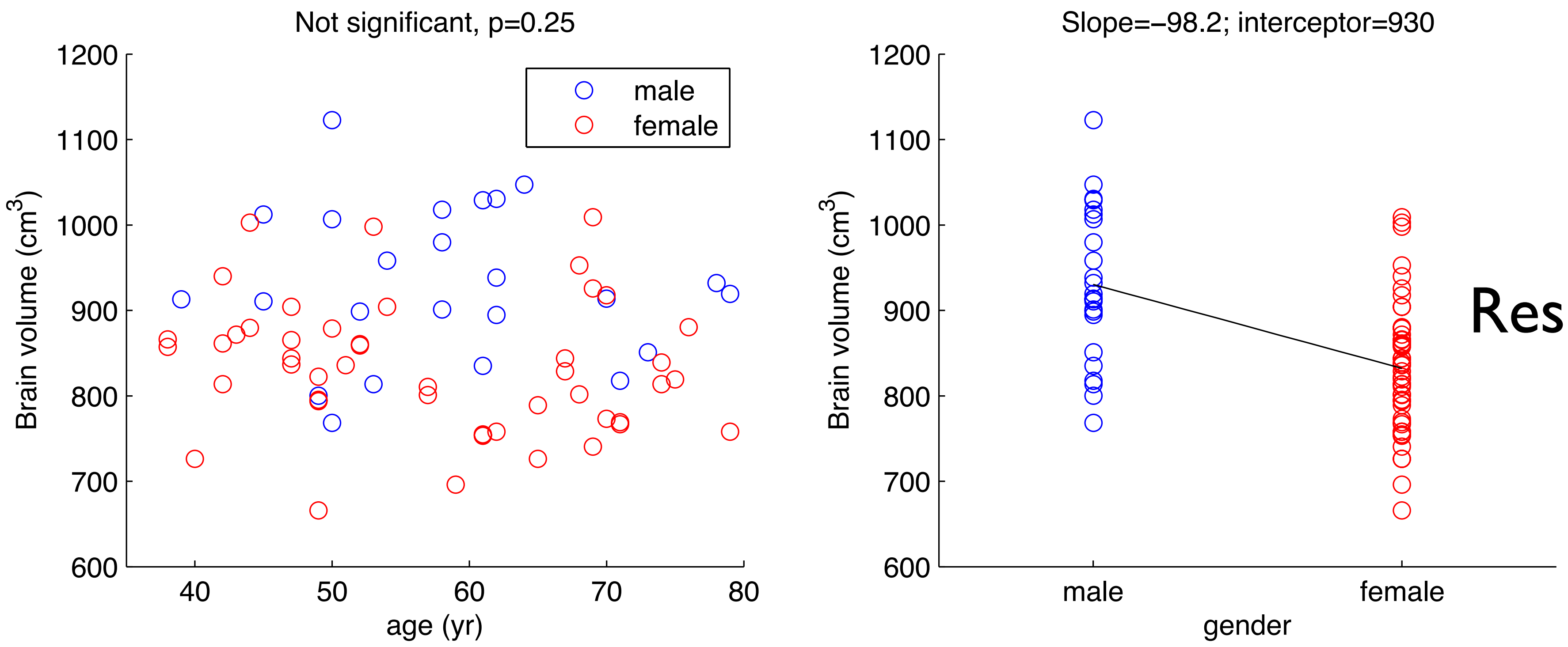


Manual hippocampus segmentation on MRI template

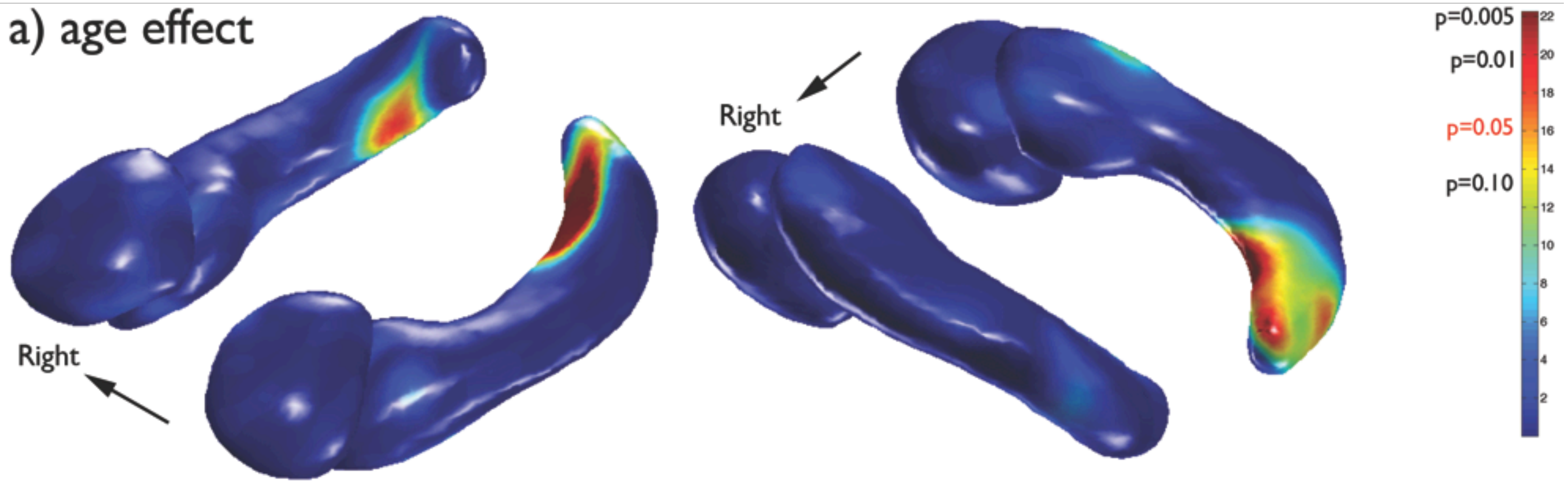




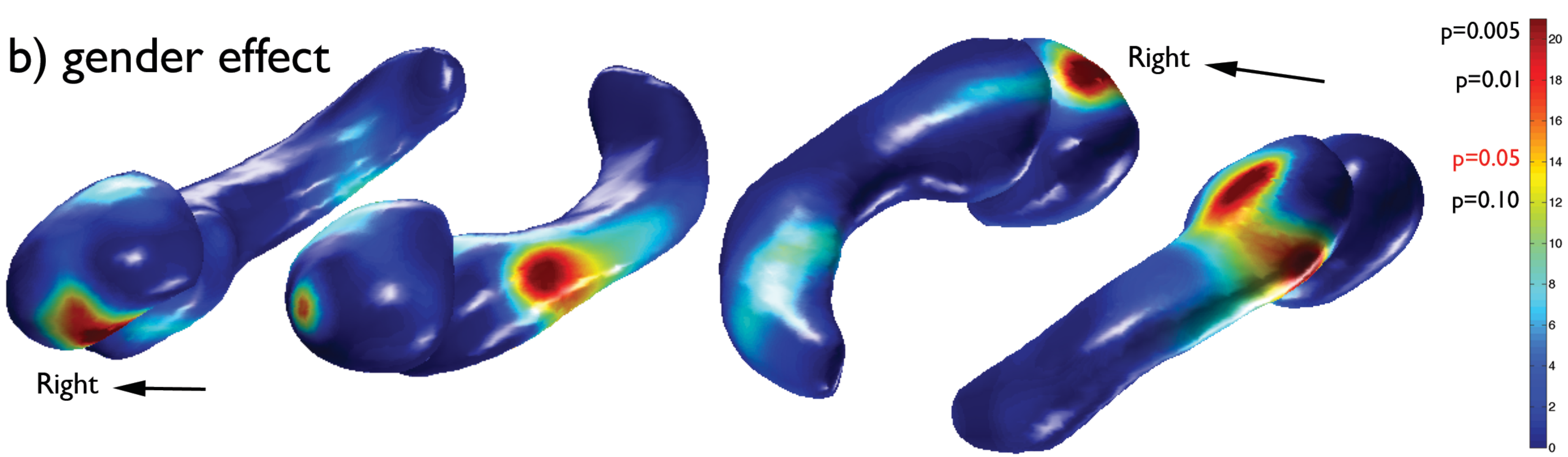
General linier mode



Response = age + gender + error



Normal subjects between 38 and 79 years

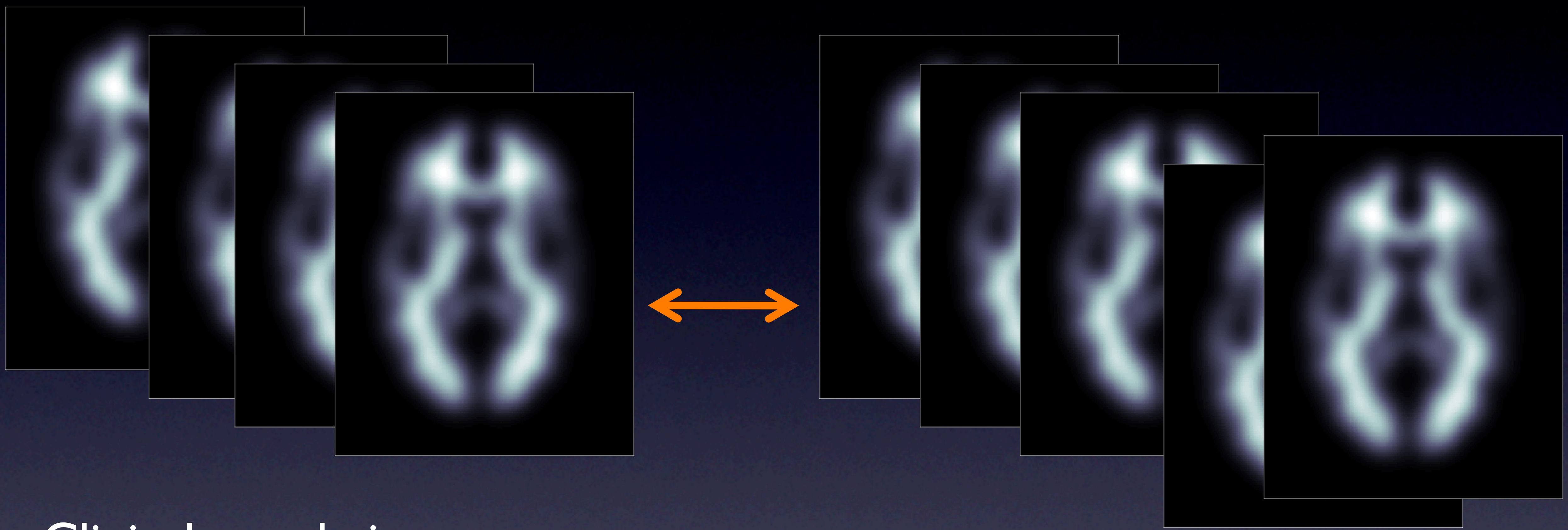


Kim et al, 2011 PISVT

Image registration

Typical question in computational neuroanatomy

Given a collection of images

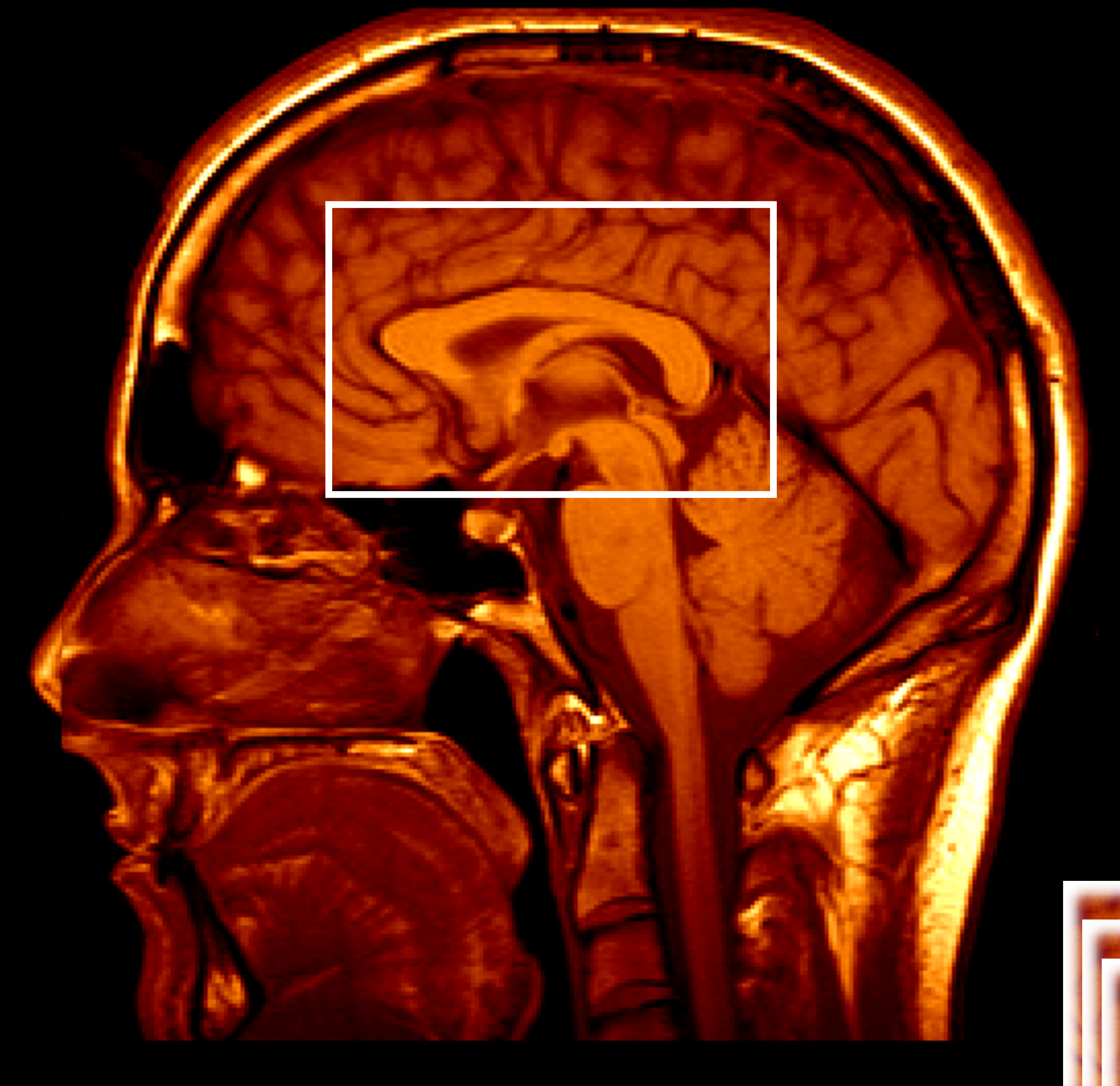


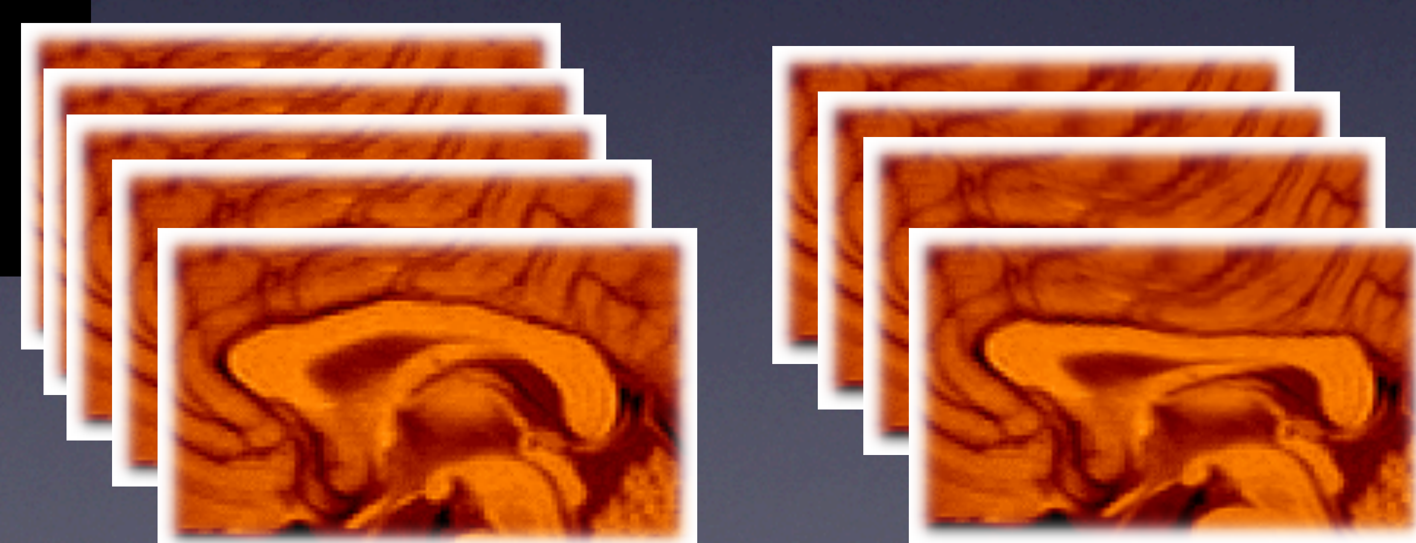
Clinical population:
autism, Parkinson's decease

Normal controls

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

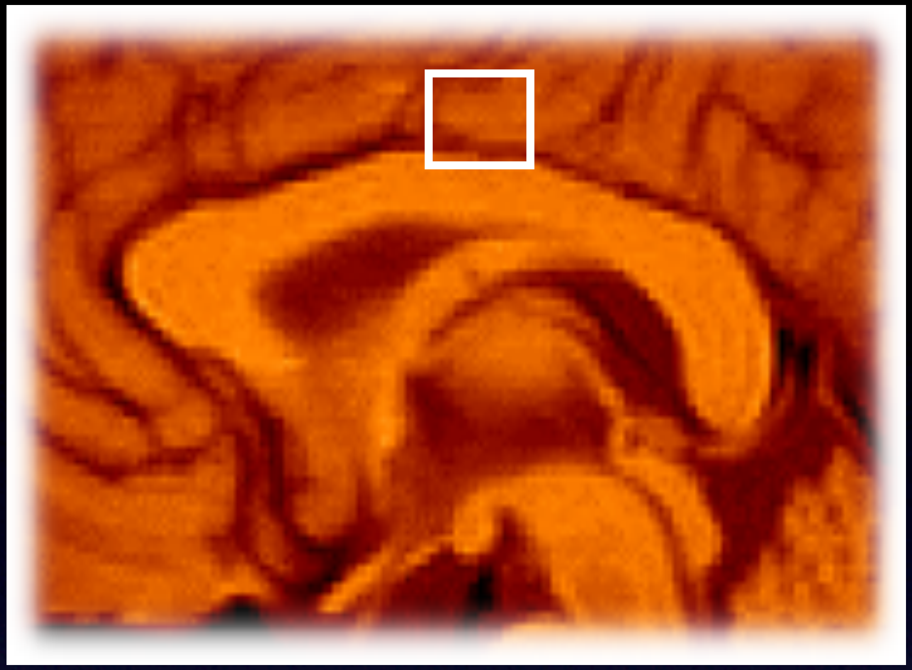
Each subject has different brain shape. So how do we compare shape difference across subjects?

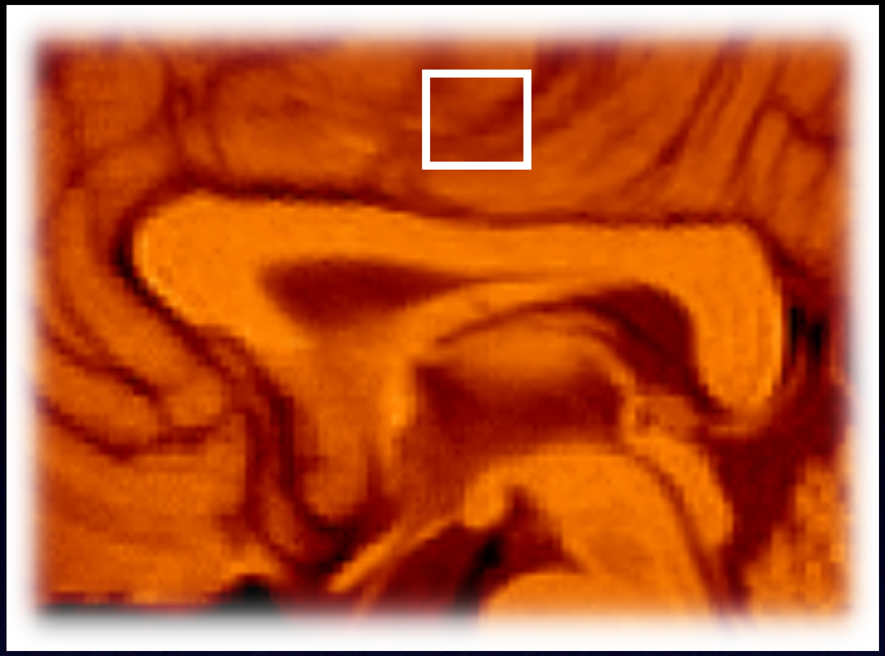




Group 1

Group 2

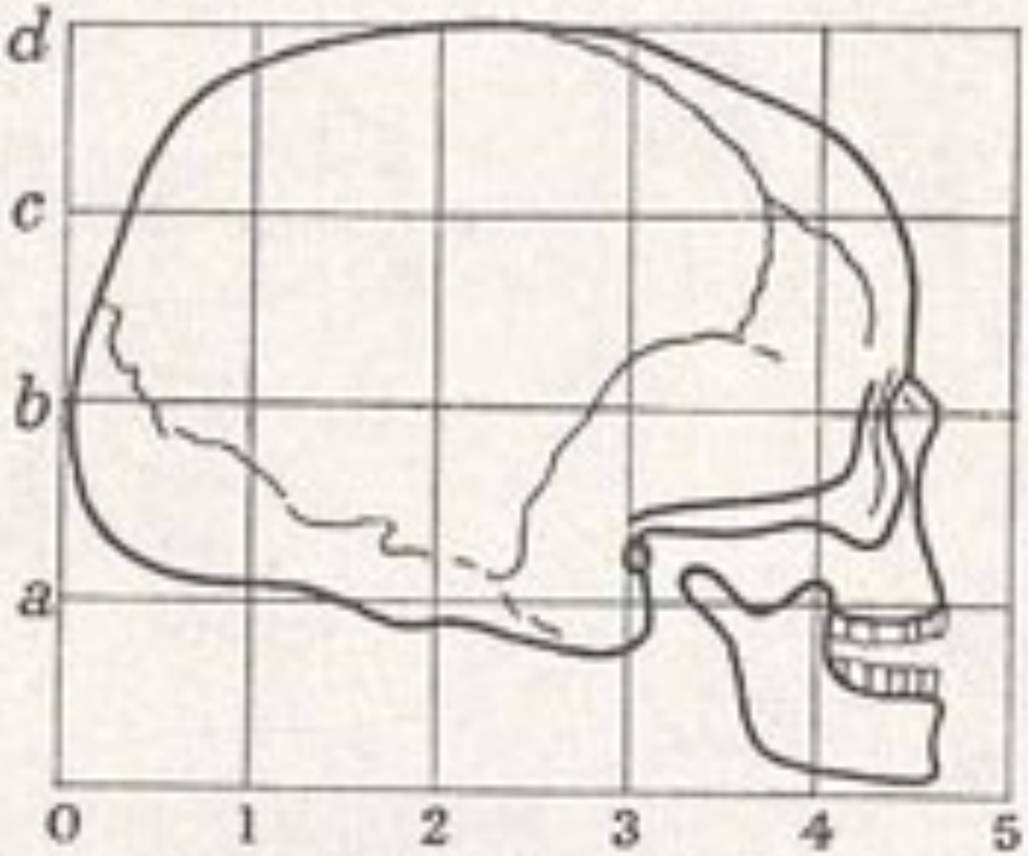


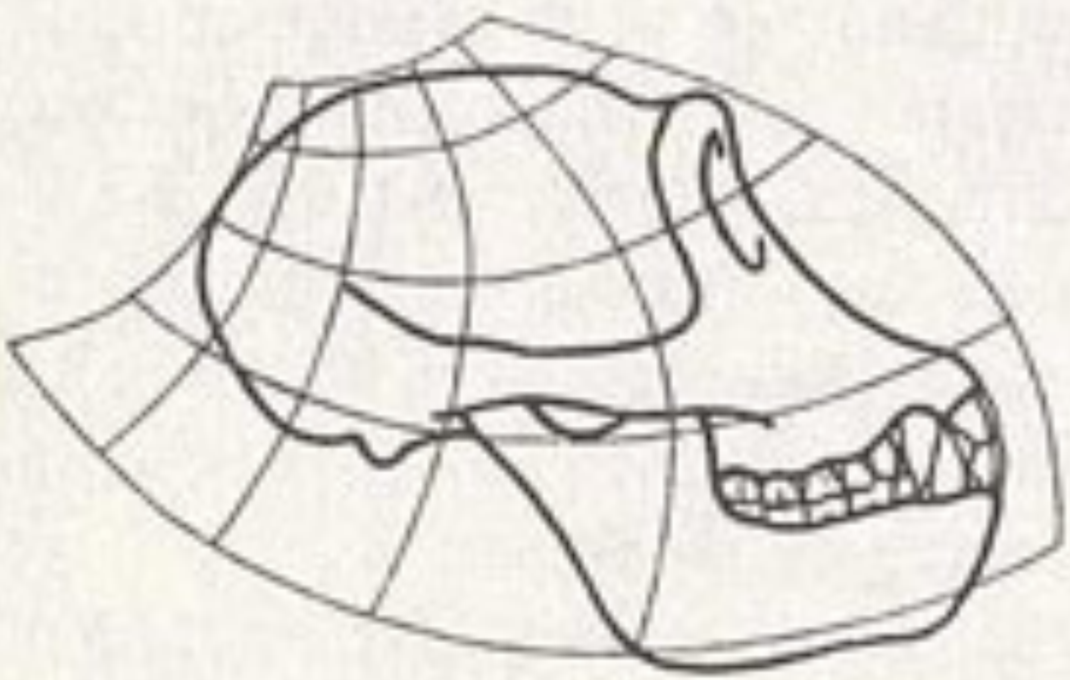


Direct voxel-to-voxel comparison causes anatomical mismatching.

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 ‘

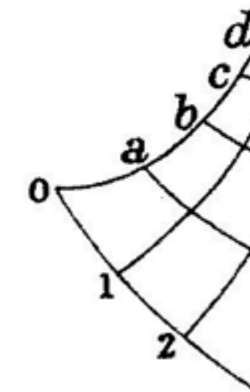
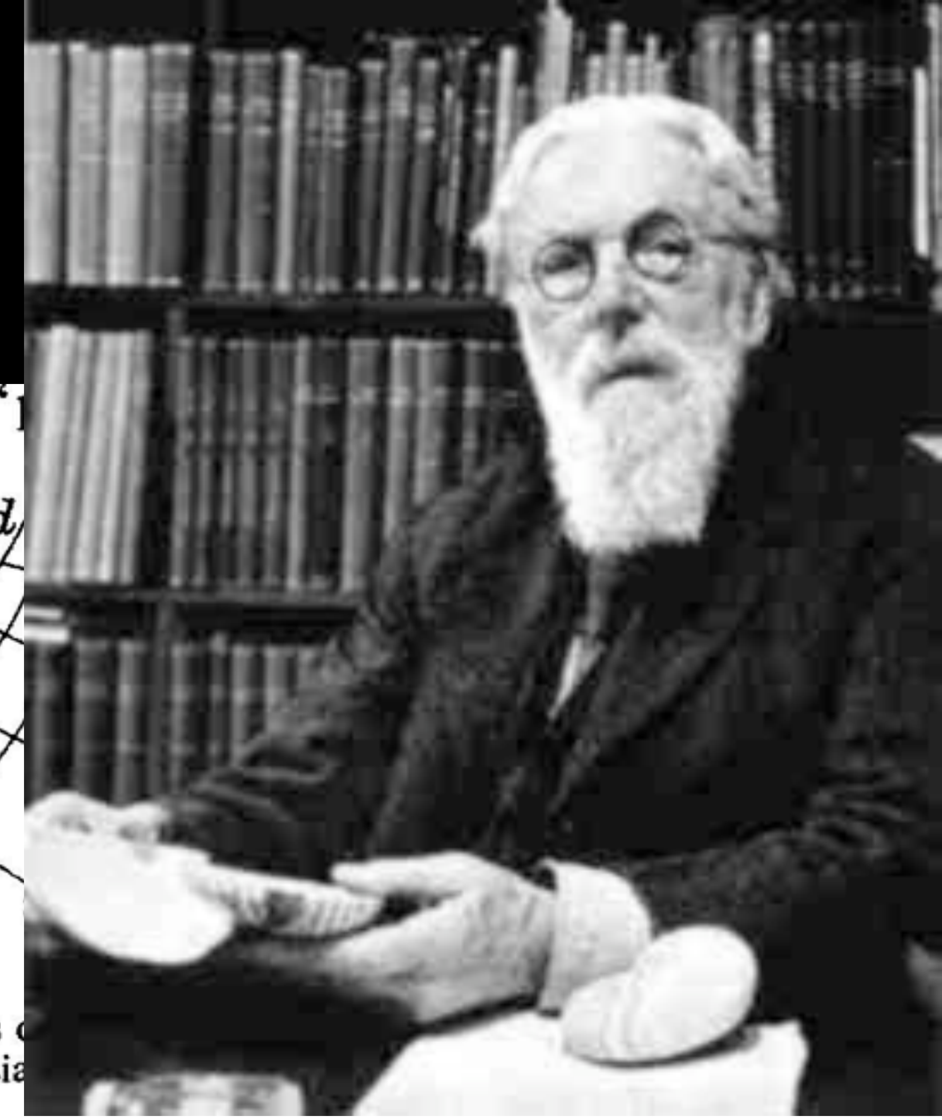


Fig. 178. Co-ordinates
the Cartesia



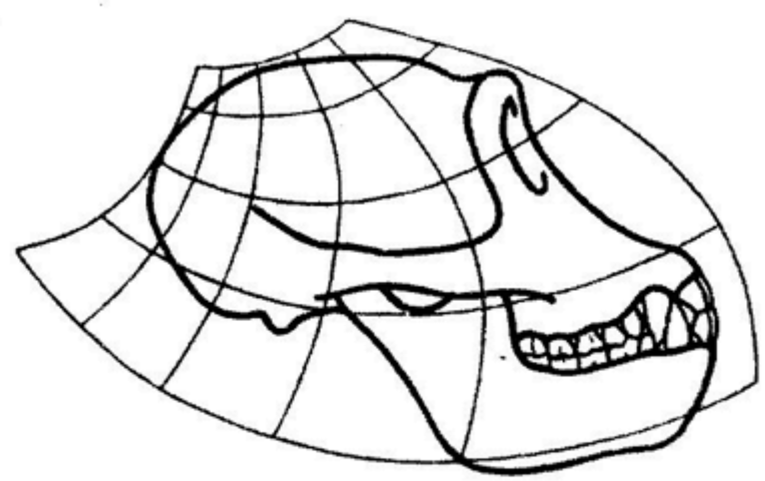


Fig. 179. Skull of chimpanzee.

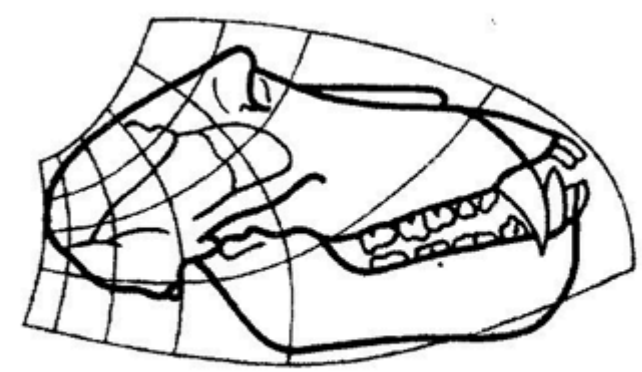
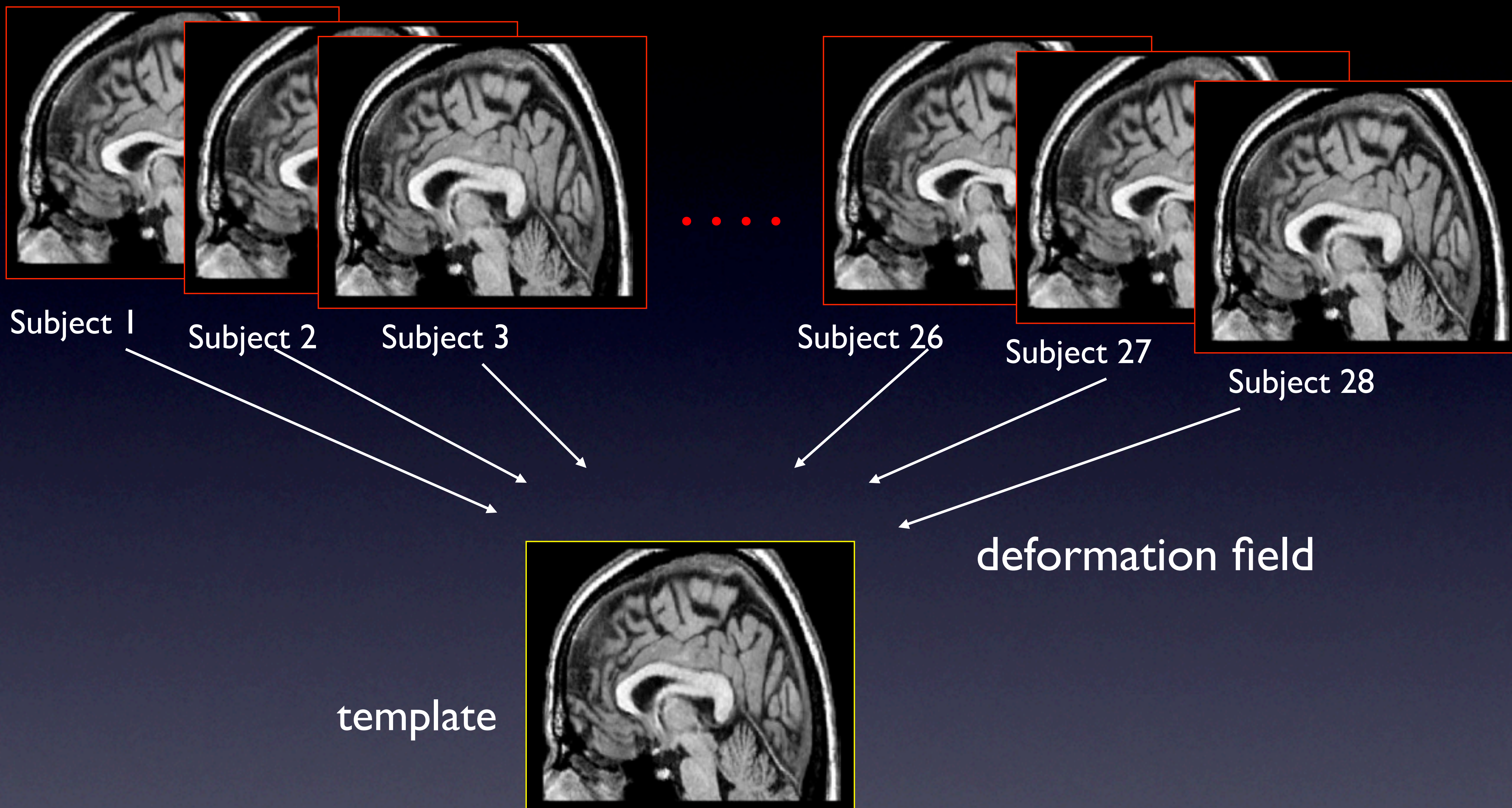


Fig. 180. Skull of baboon.

diagram … n Fig. 180
I have sh … oon, and it
is obviou … order, and
differs o … ion.[1] These
anthrop … another by

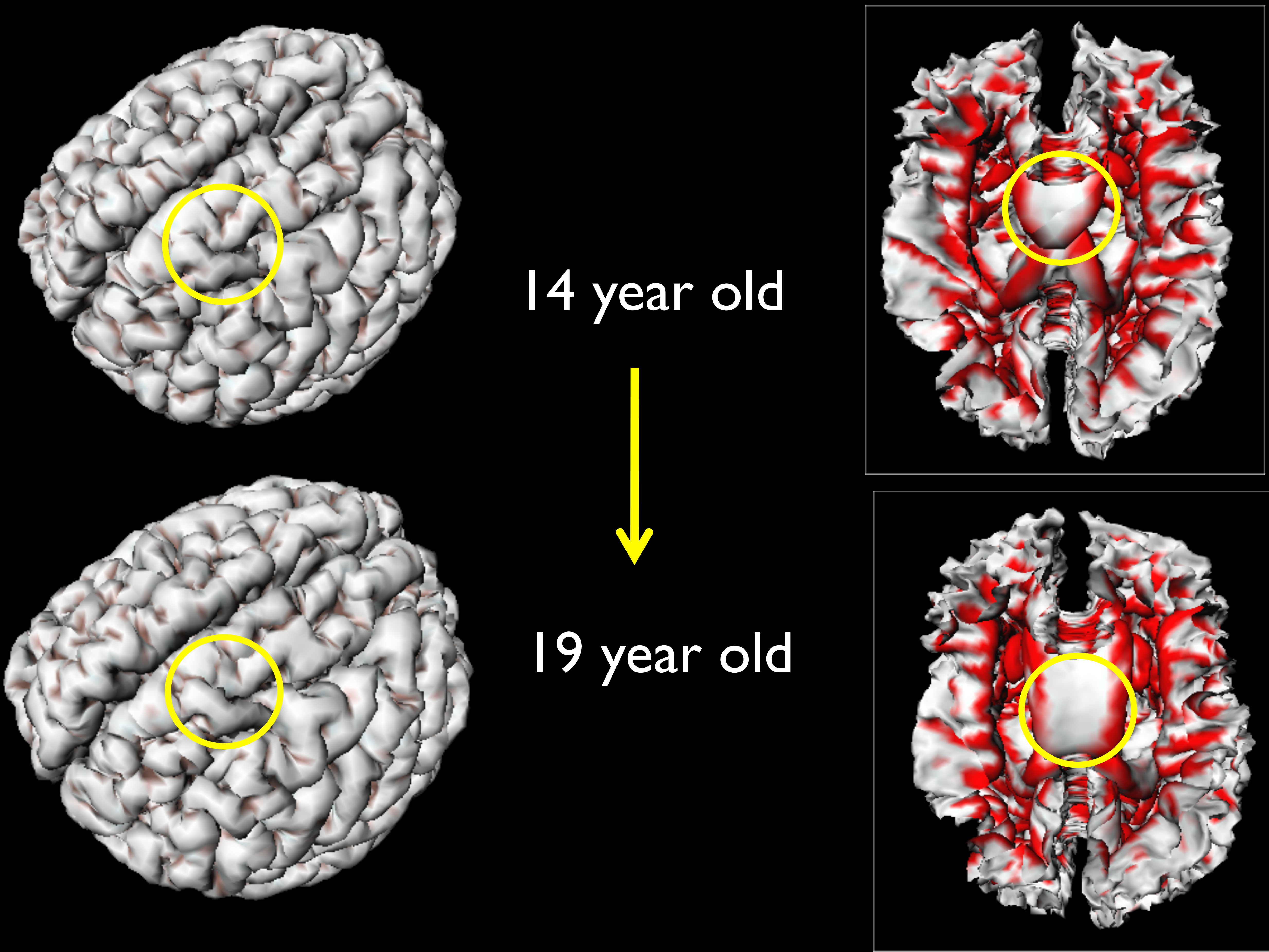
On Growth and Form
D’Arcy Thompson

Deformable template framework

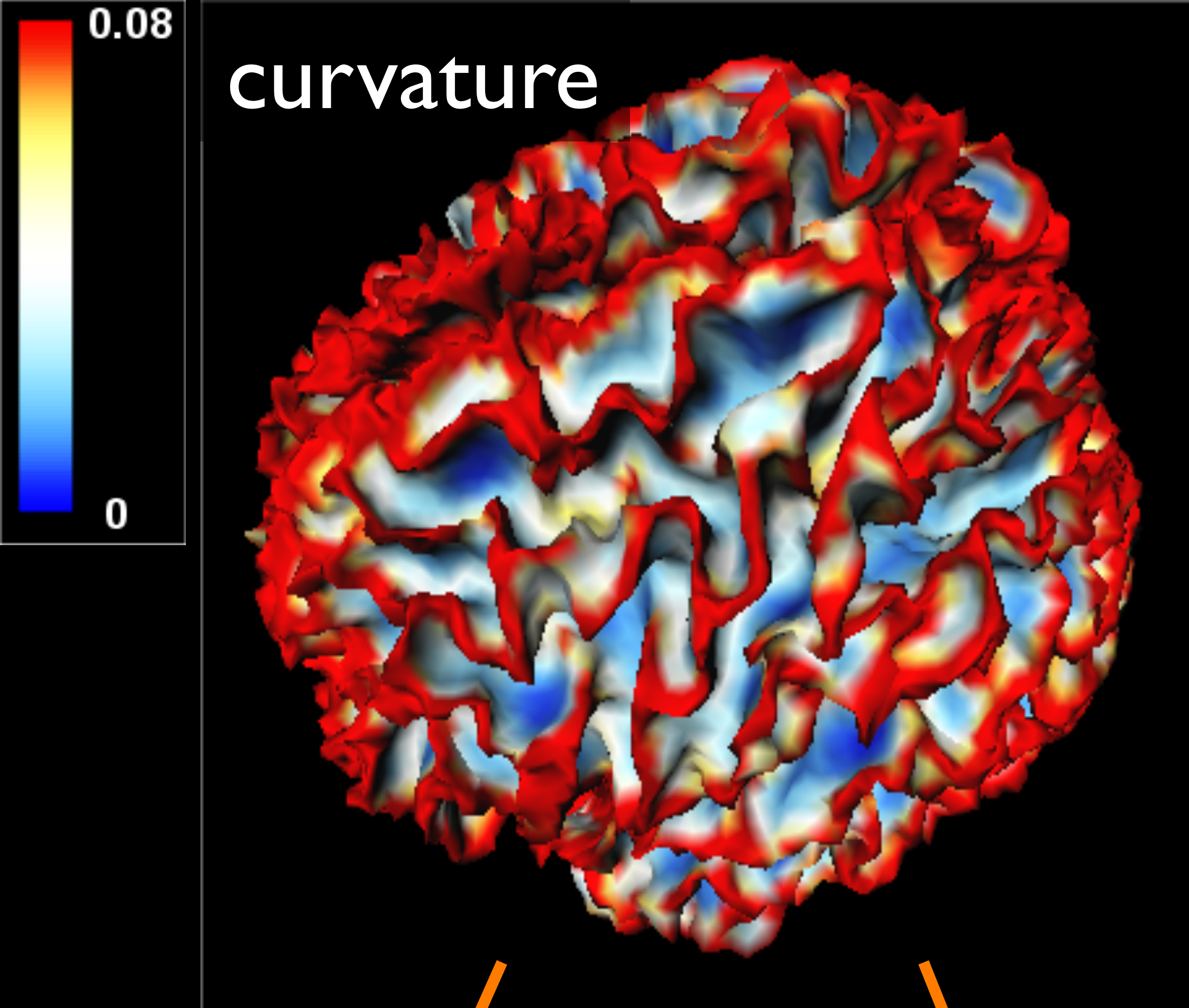


MRIs will be warped into a template and anatomical differences can be compared at a common reference frame.

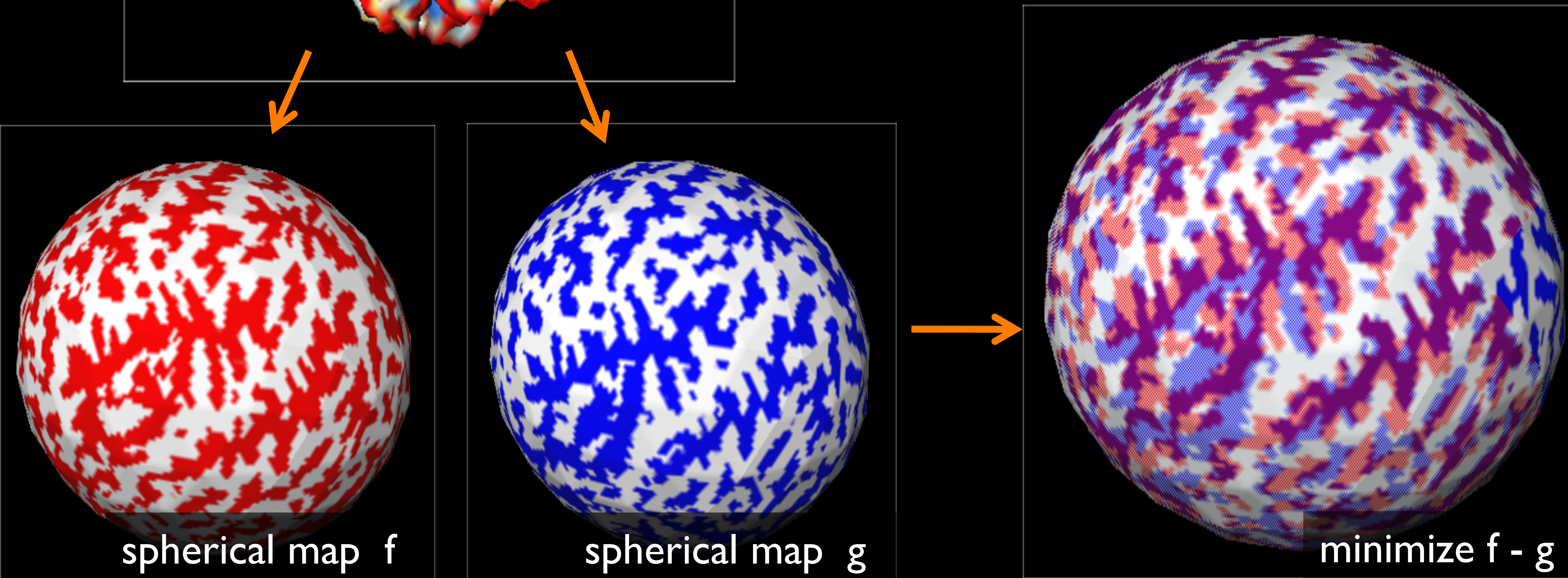
Motivation for 2D cortical surface matching



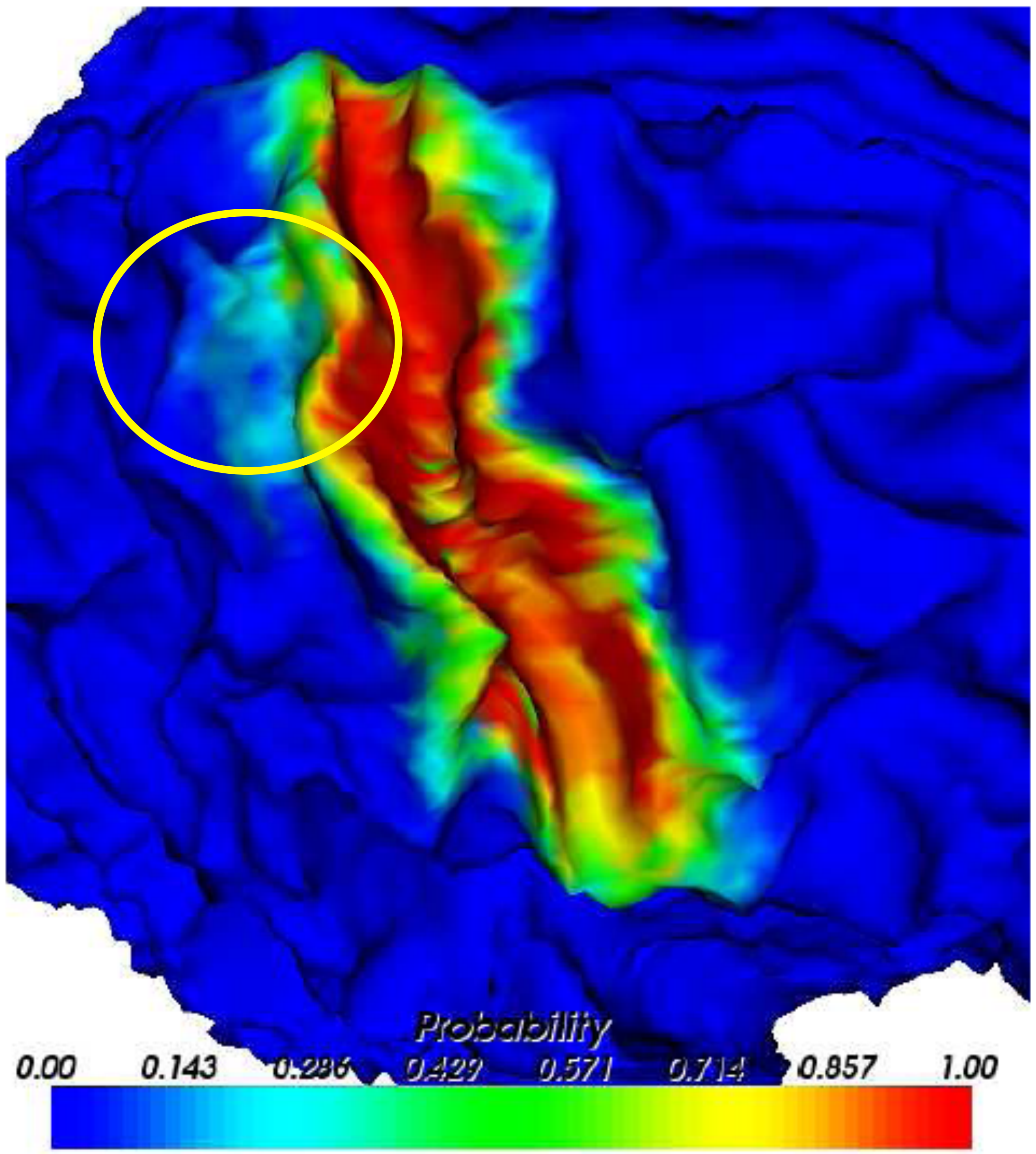
Surface-to-surface registration



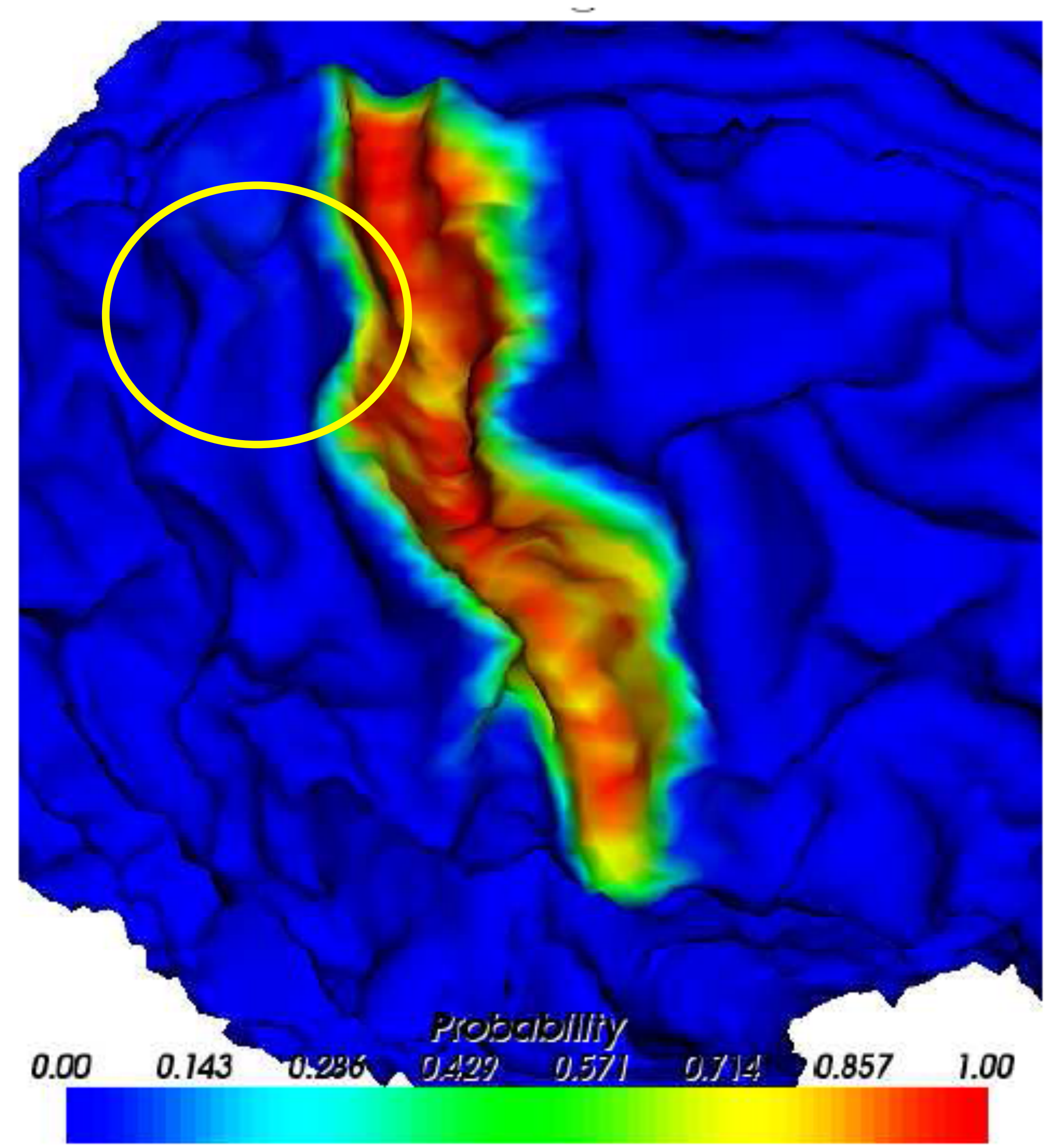
Find smooth deformation that minimizes the goodness-of-fit



Probability of matching in right central sulcus



3D volume registration

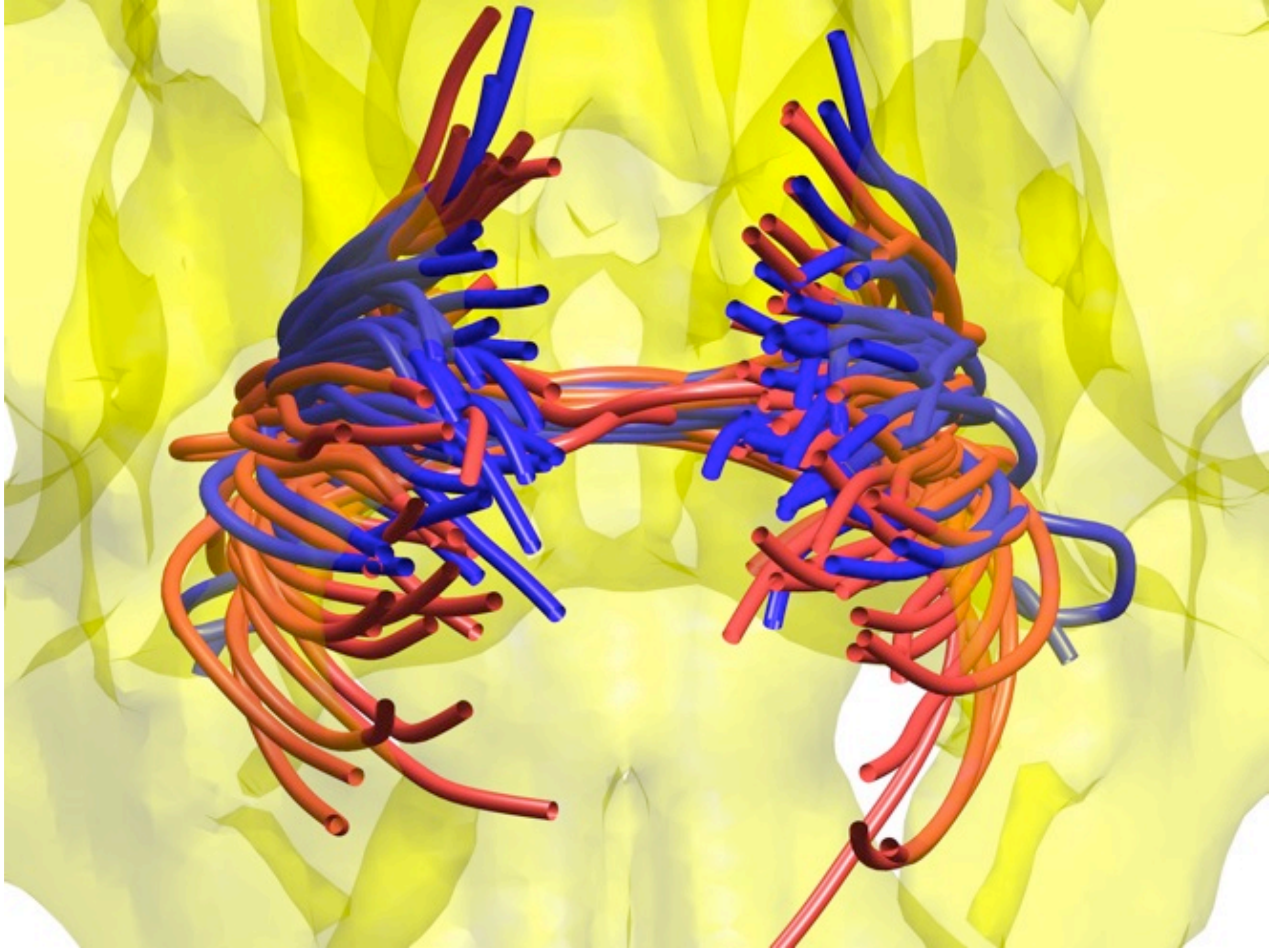


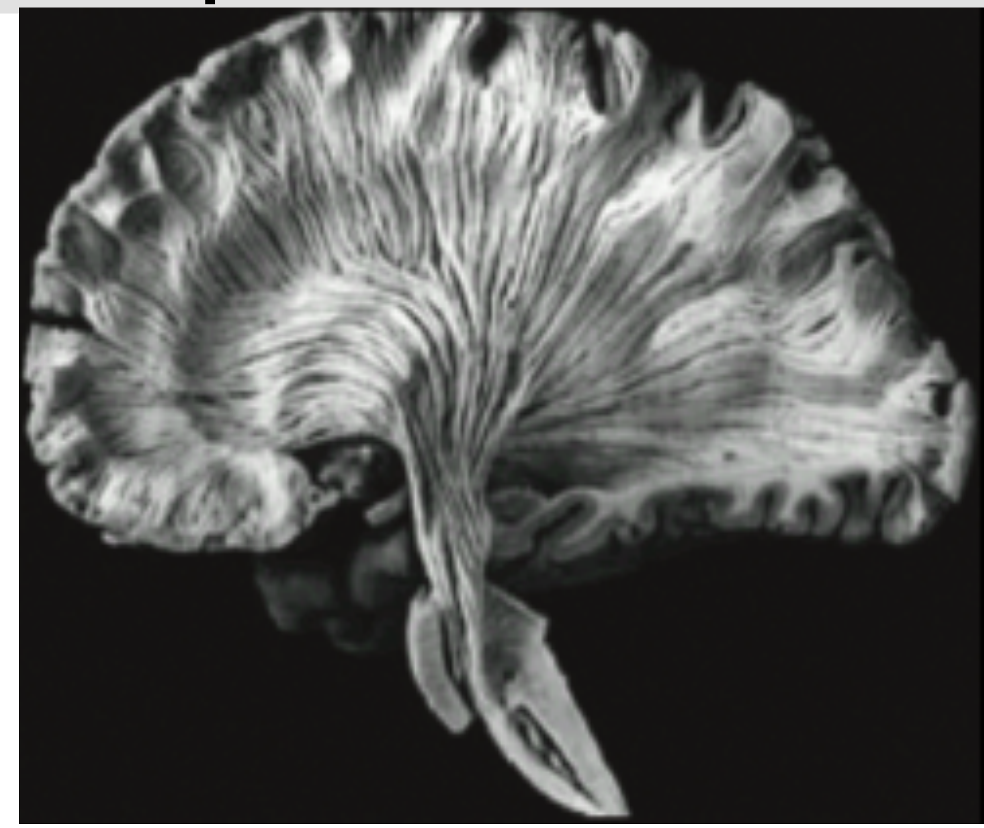
2D surface registration

Chung et al., 2005 NeuroImage

Shape representation

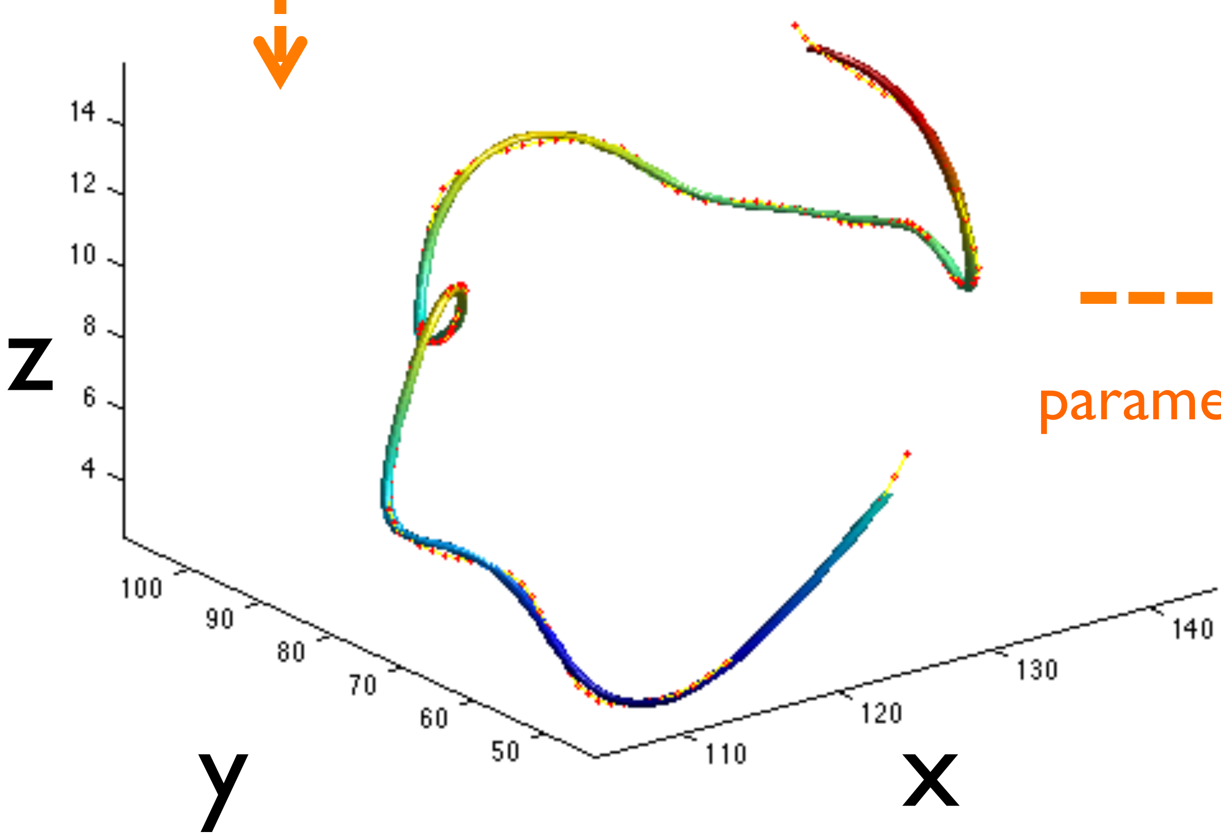
DTI white matter fiber tract representation



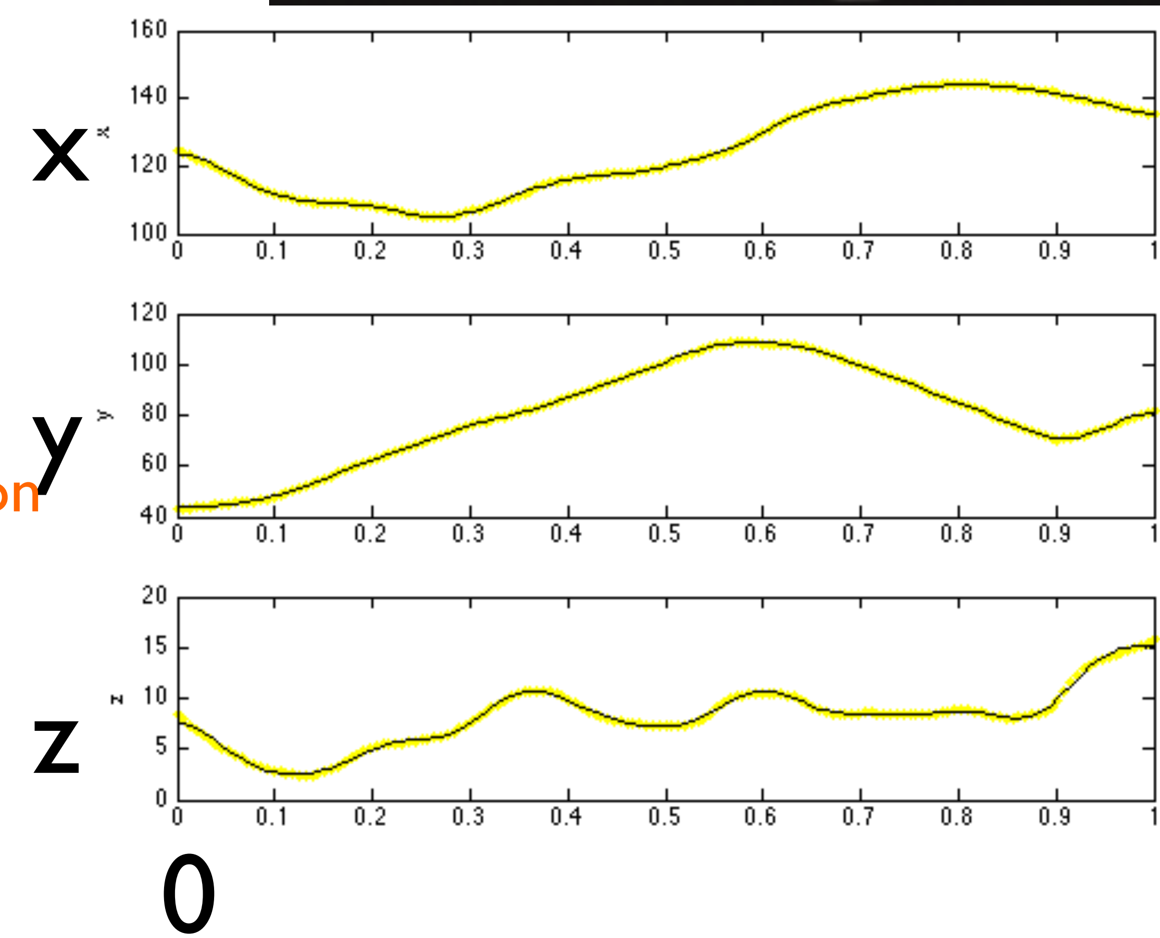


Tractography

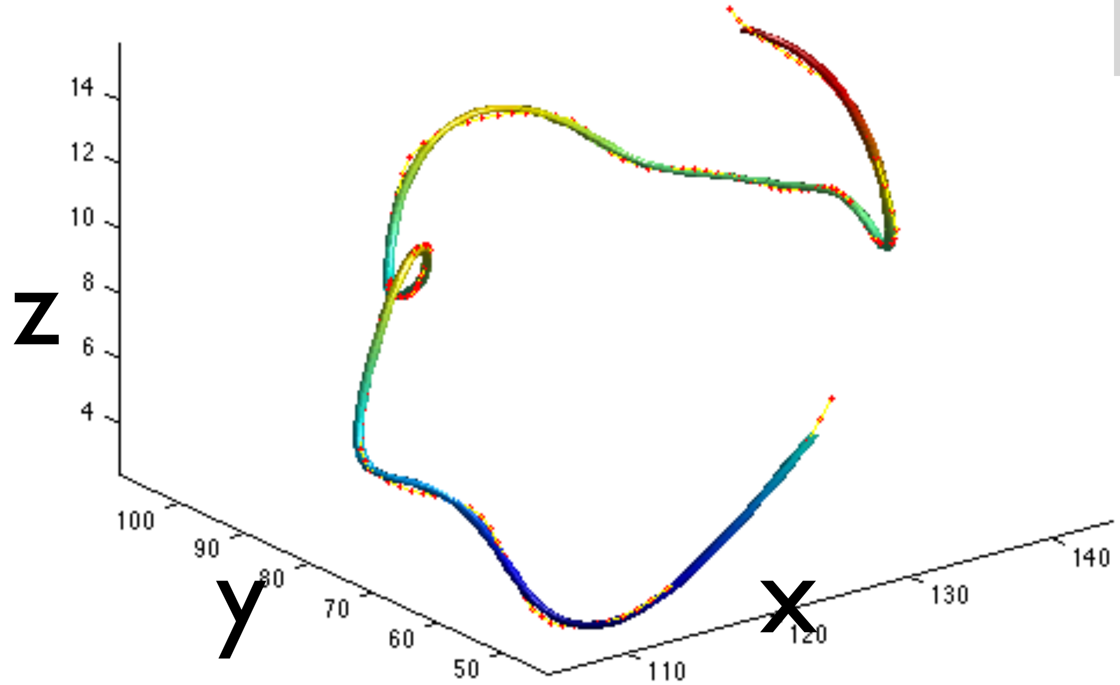
Extract single tract



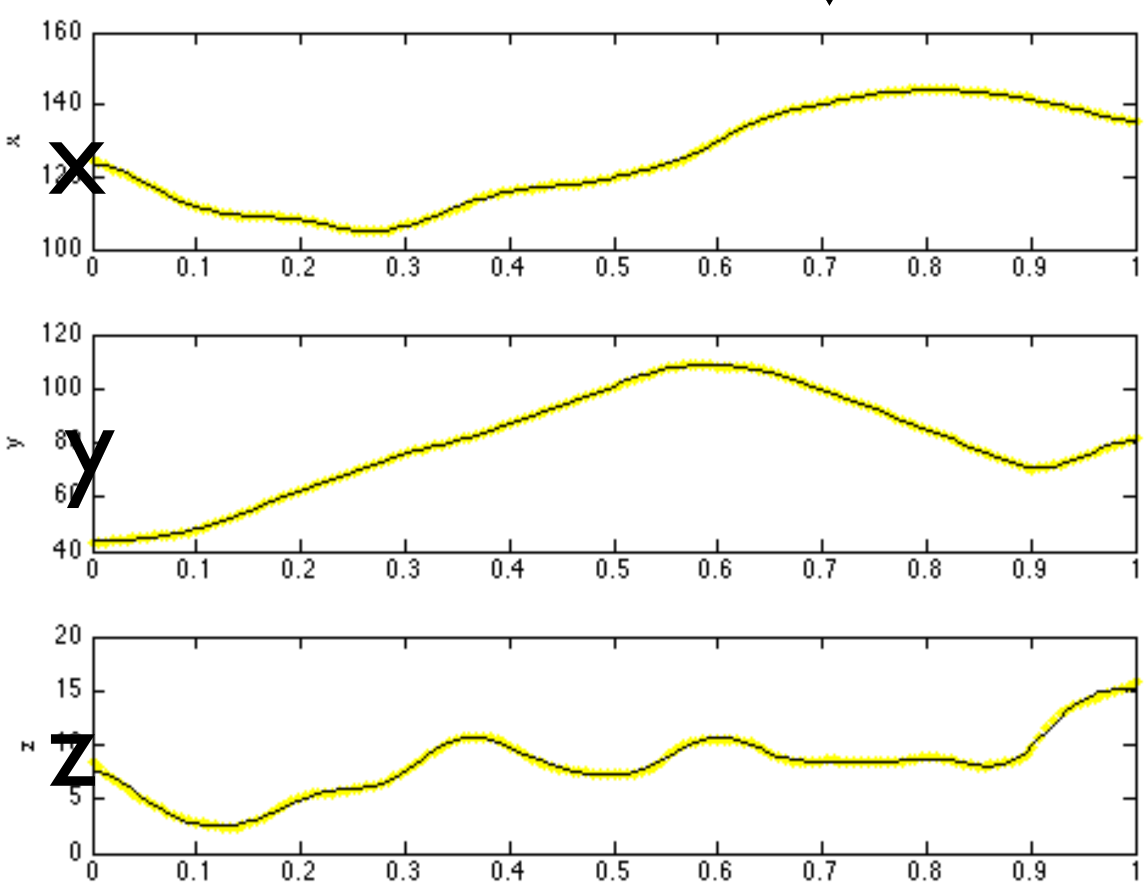
parameterization



Cosine series representation



parameterization



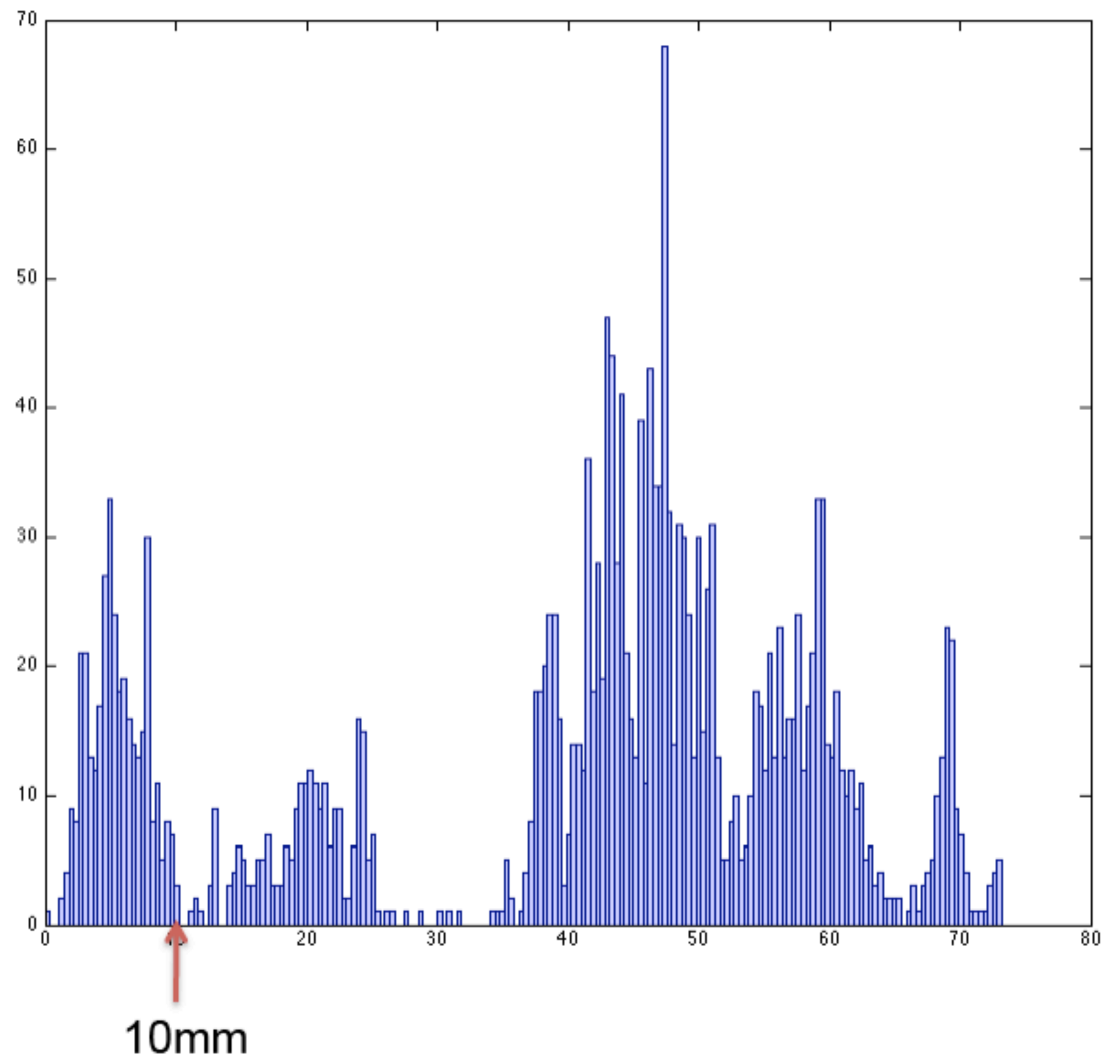
basis expansion

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.

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

Fiber tract clustering

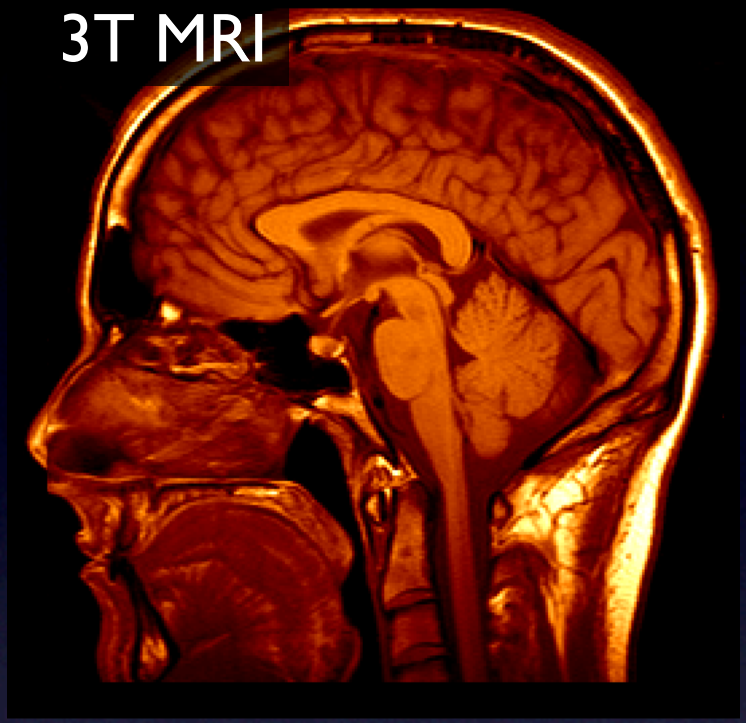


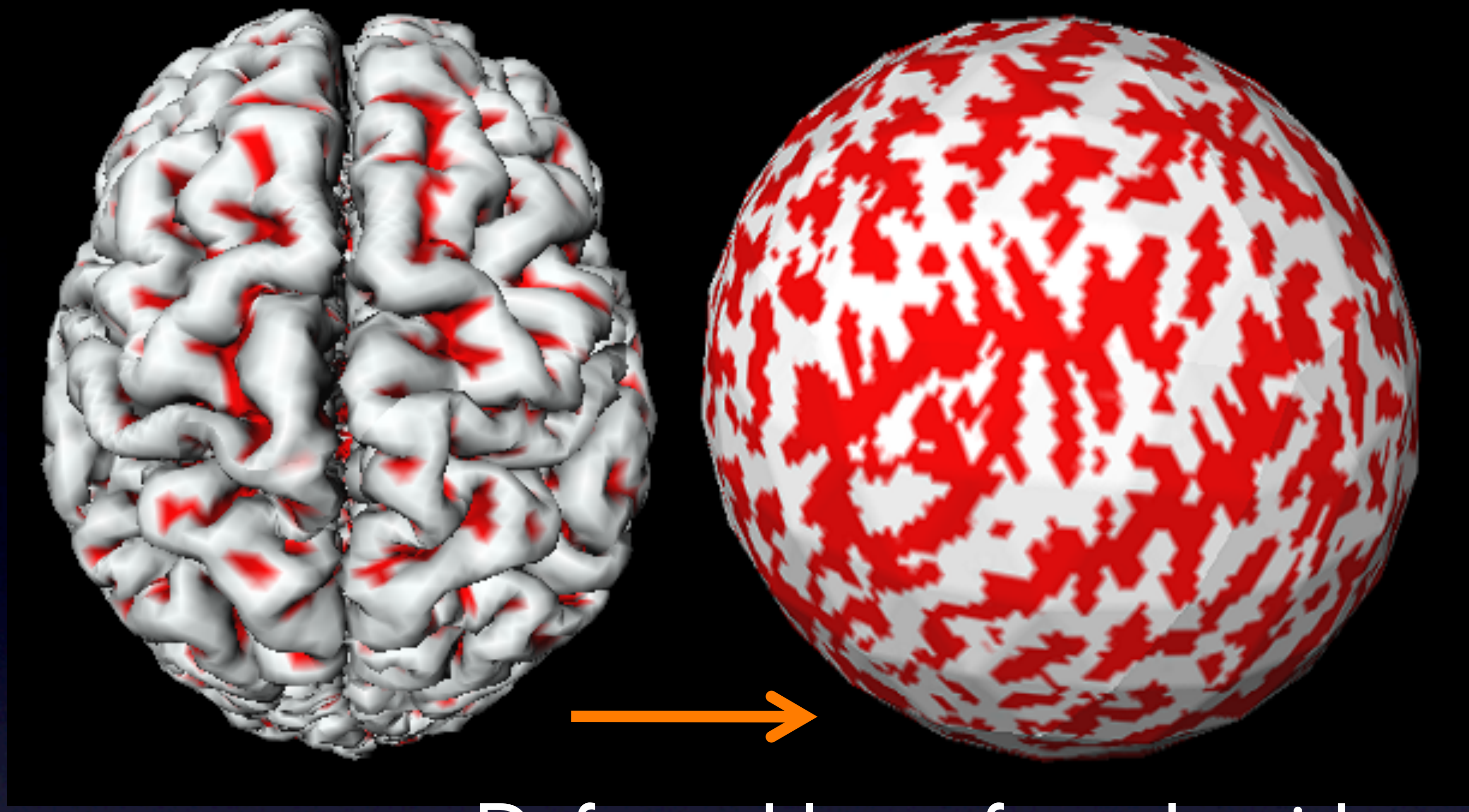
Histogram of discrepancy measure

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

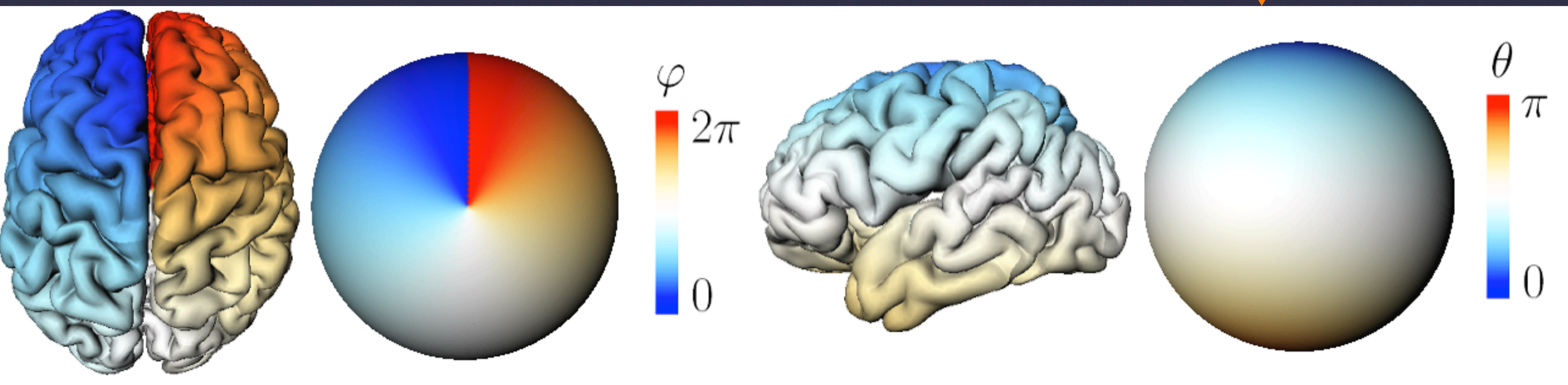
$$= \int_0^1 \sum_{j=1}^{3} \left[\sum_{l=0}^{k} (\zeta_{lj} - \eta_{lj}) \psi_l(t) \right]^2 dt \;\; = \sum_{j=1}^{3} \sum_{l=0}^{k} (\zeta_{lj} - \eta_{lj})^2$$

Cortical Surface Modeling





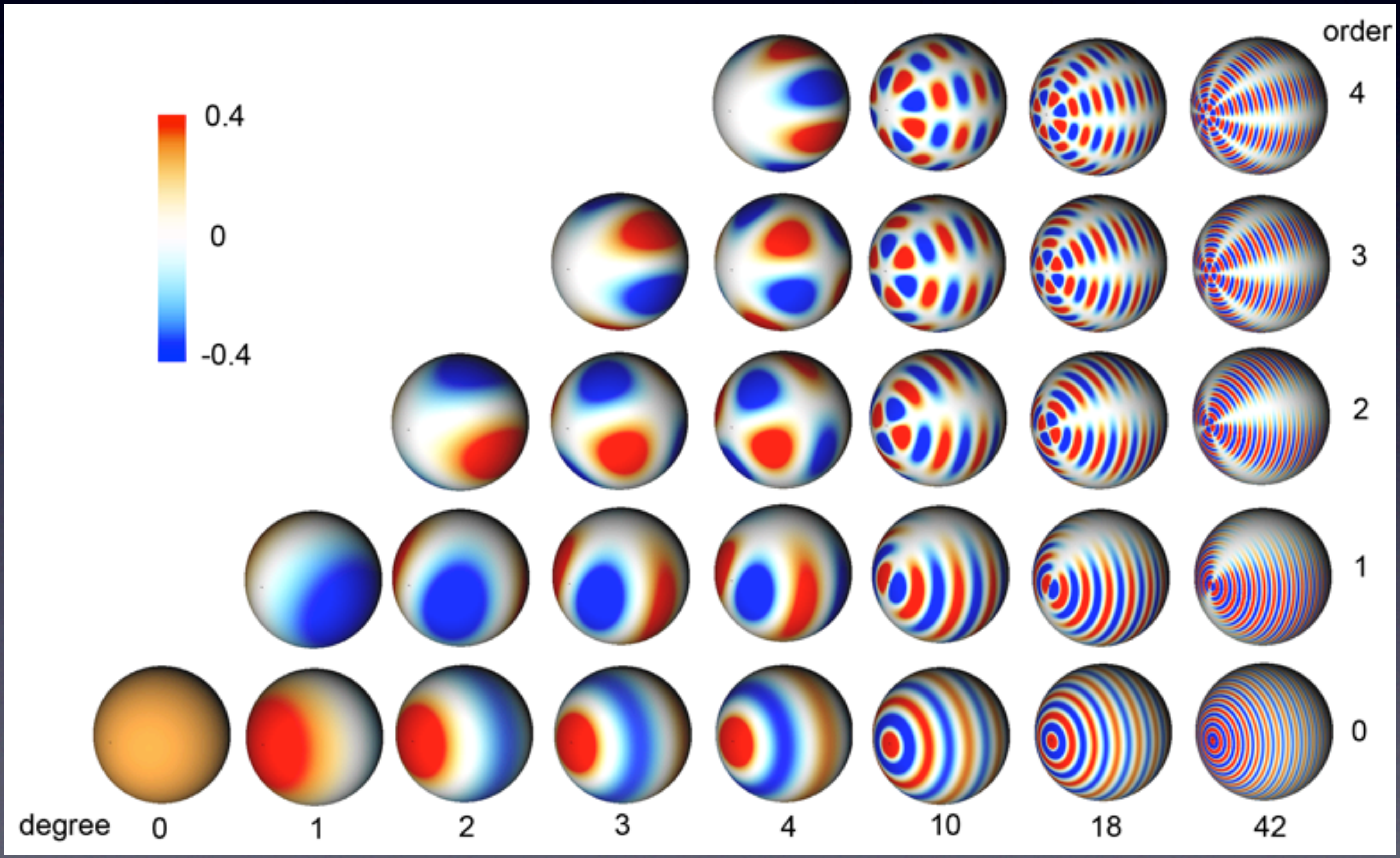
Deformable surface algorithm



Spherical angle based coordinate system

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

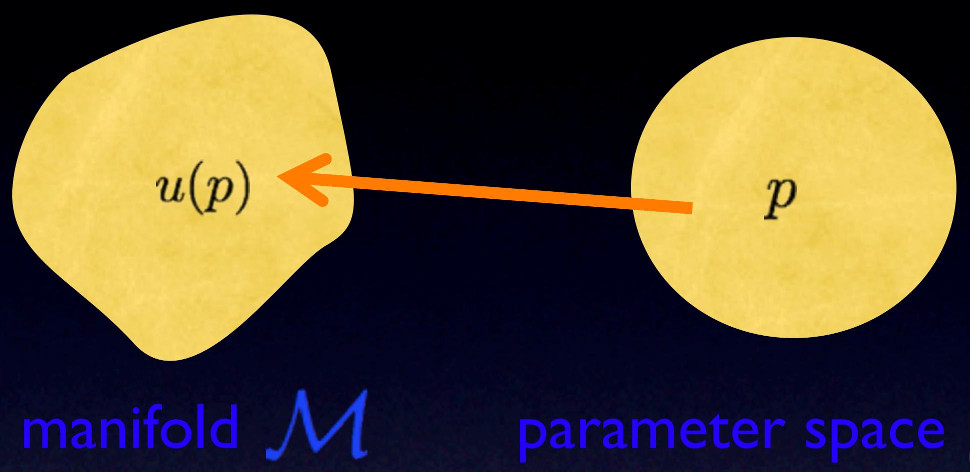
$$Y_{lm} = \begin{cases} c_{lm} P_l^{|m|}(\cos\theta)\sin(|m|\varphi), & -l \le m \le -1, \\ \frac{c_{lm}}{\sqrt{2}} P_l^0(\cos\theta), & m = 0, \\ c_{lm} P_l^{|m|}(\cos\theta)\cos(|m|\varphi), & 1 \le m \le l, \end{cases}$$



Coarse detail

Fine detail

Cortical manifold and function defined on the manifold



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

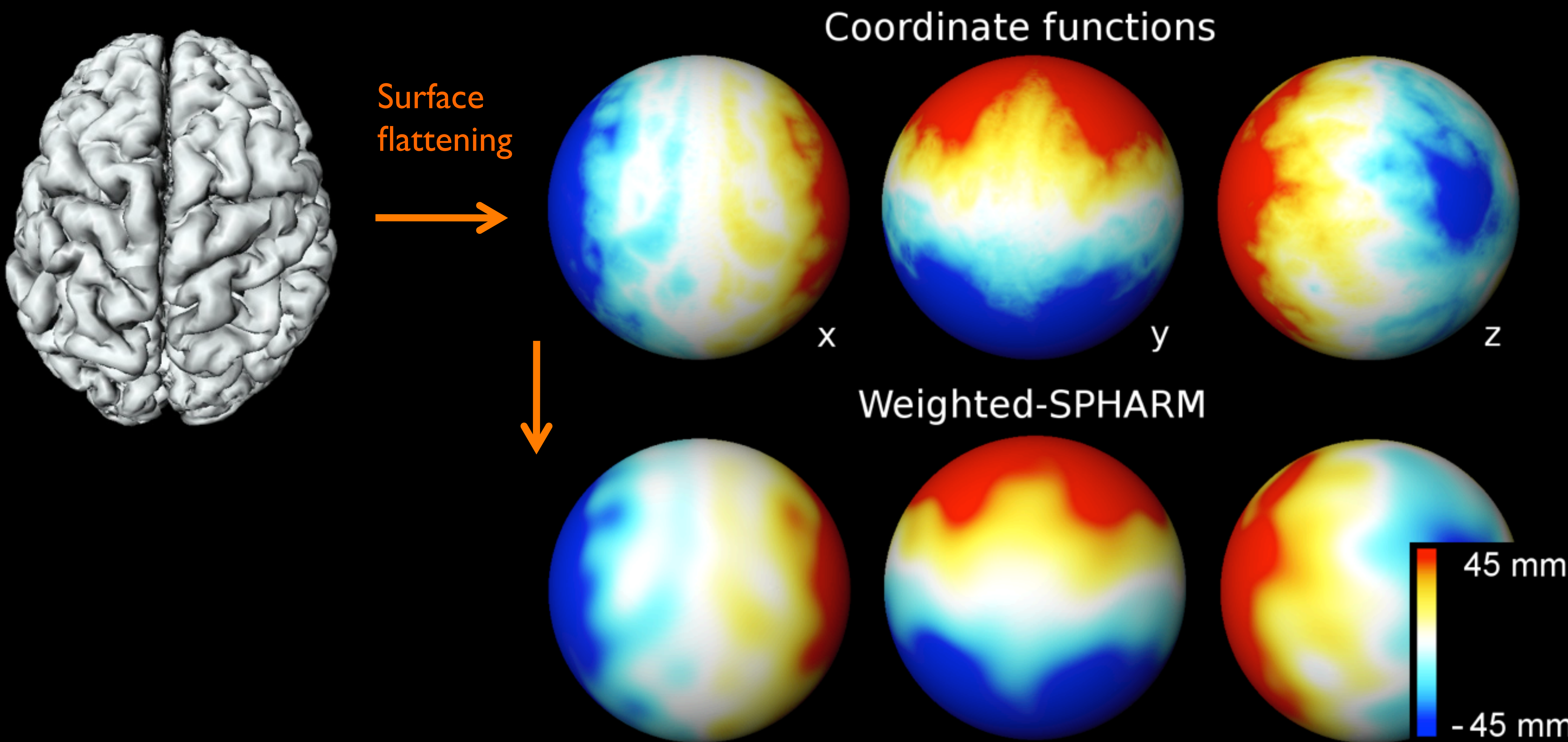
PDE: $$\partial_t g + \mathcal{L} g = 0, g(p, t=0) = f(p)$$

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

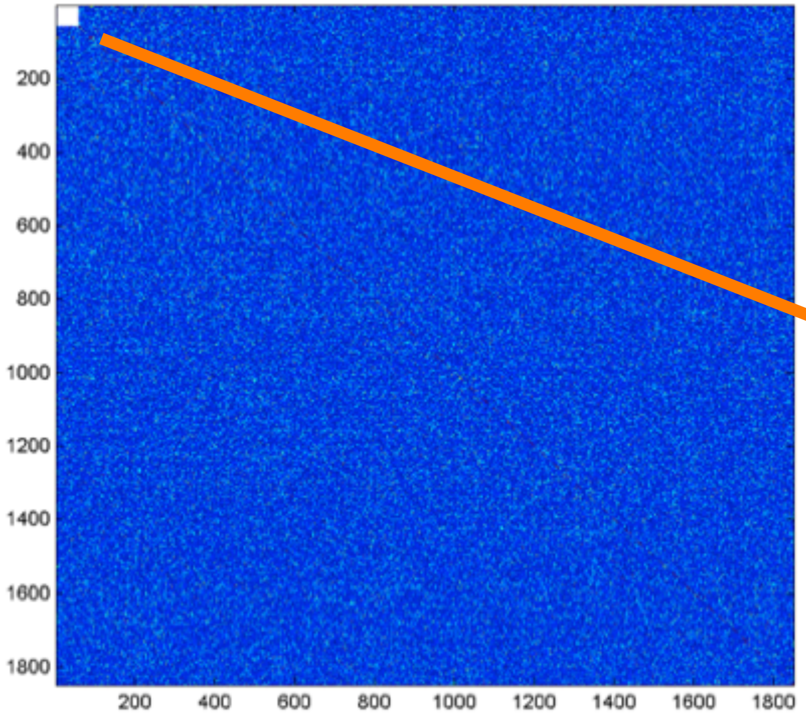
Spherical harmonic representation

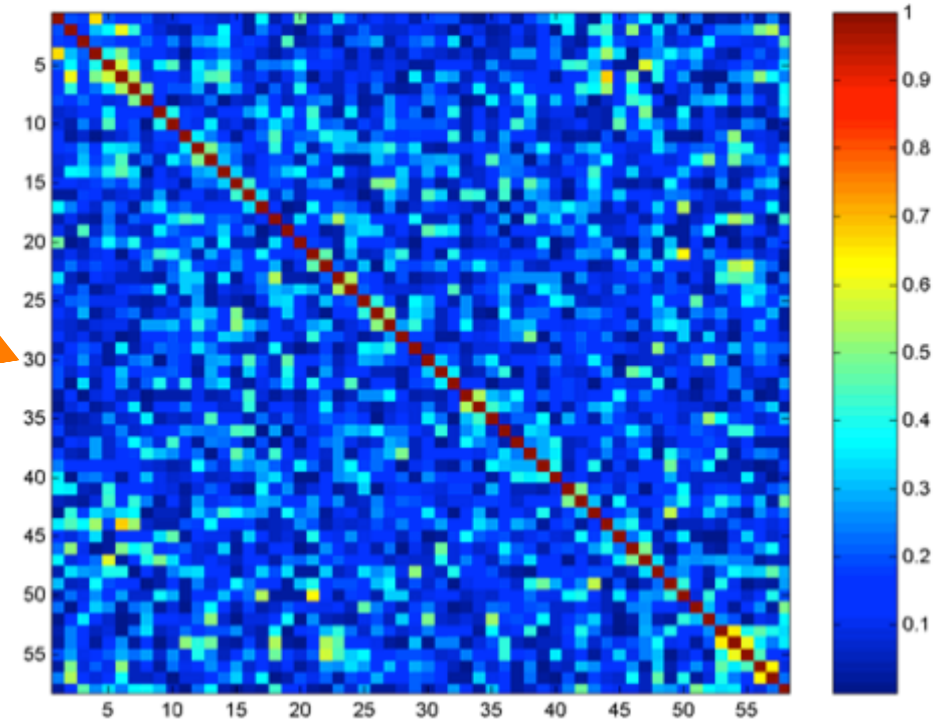


Coordinates are represented in a functional form:

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

Statistical Model: Karhunen-Loeve expansion

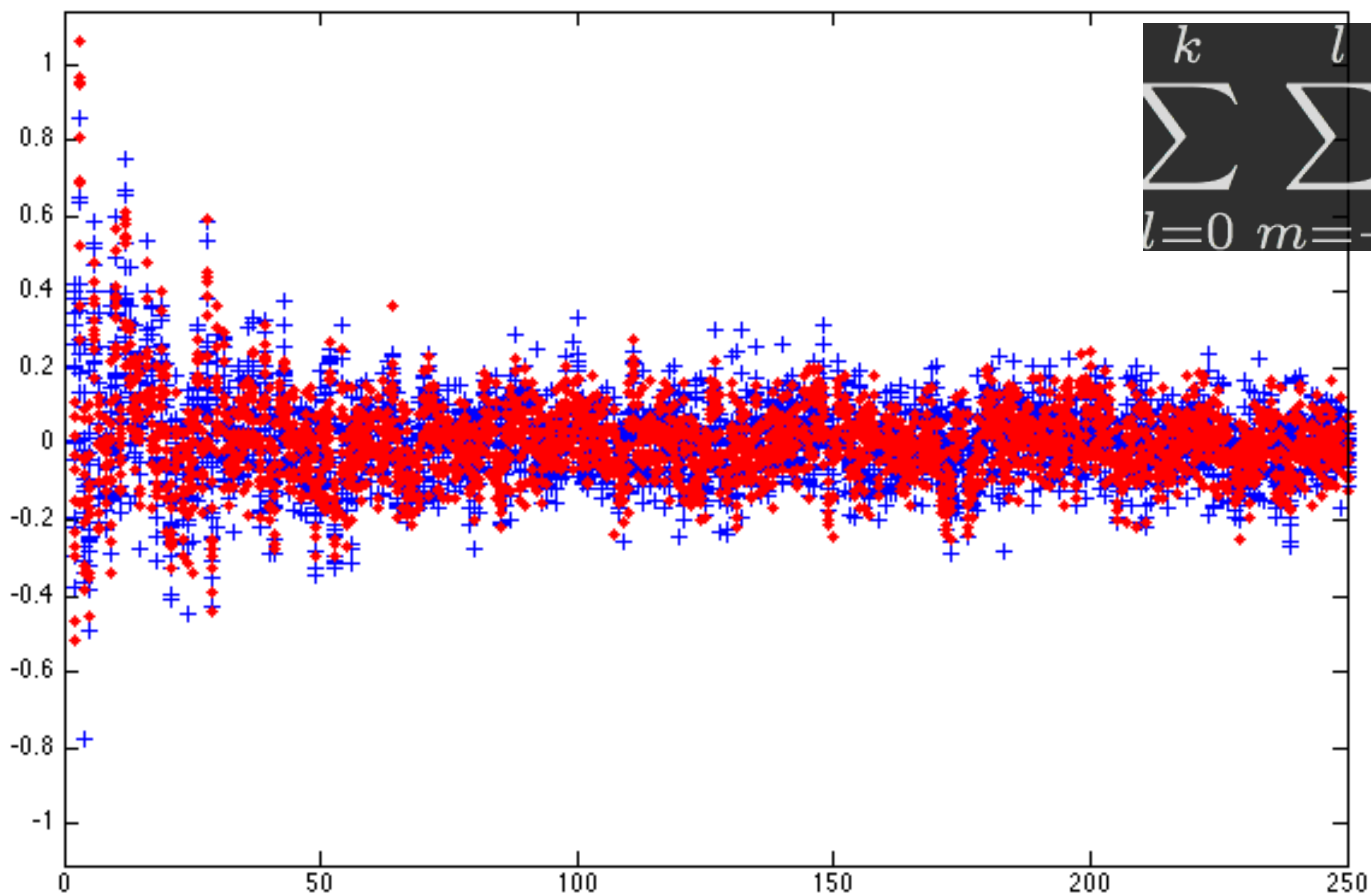




Cross correlations

uncorrelated normal

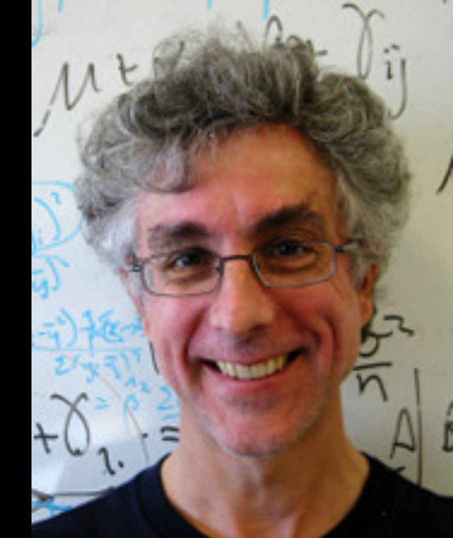
$$\sum_{l=0}^{k}\sum_{m=-l}^{l} e^{-l(l+1)t}\langle f, Y_{lm}\rangle Y_{lm}(\theta,\varphi)$$

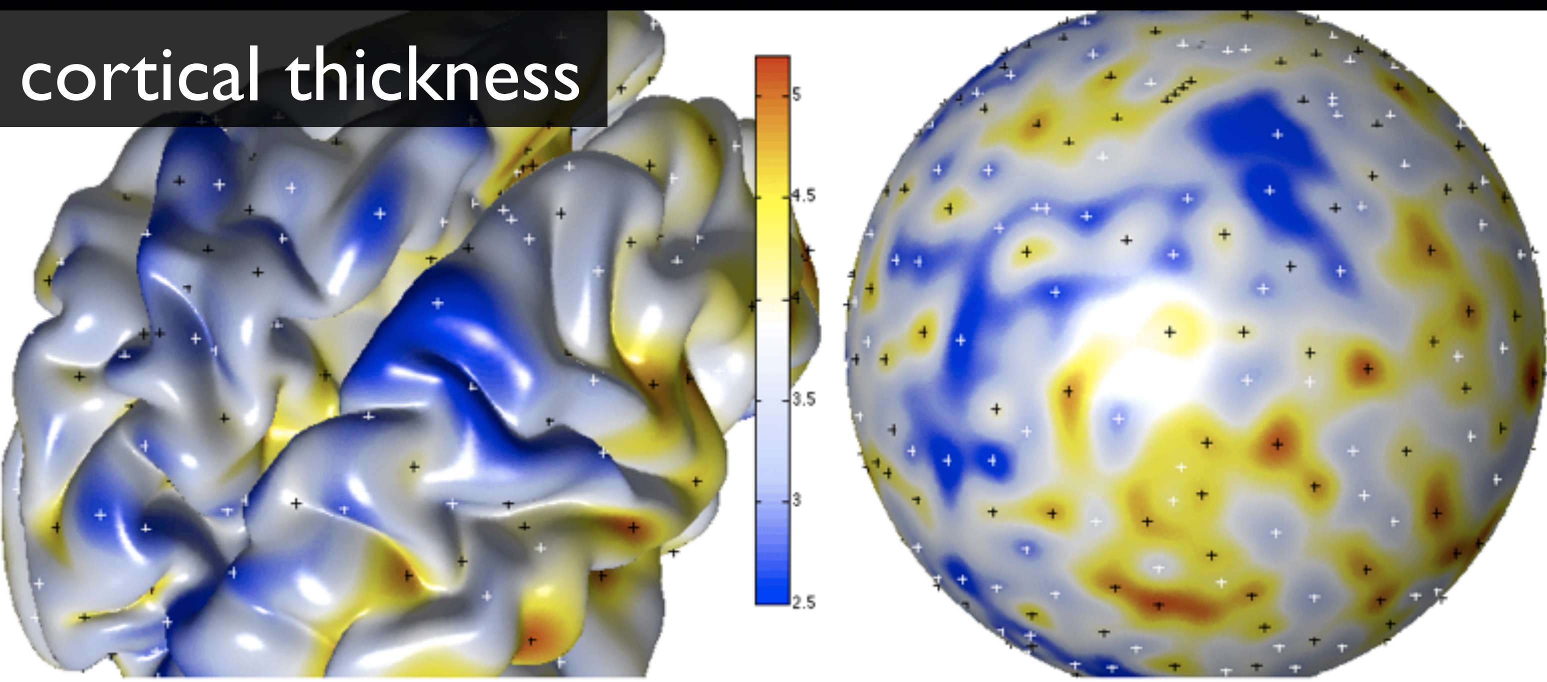


Classification ?

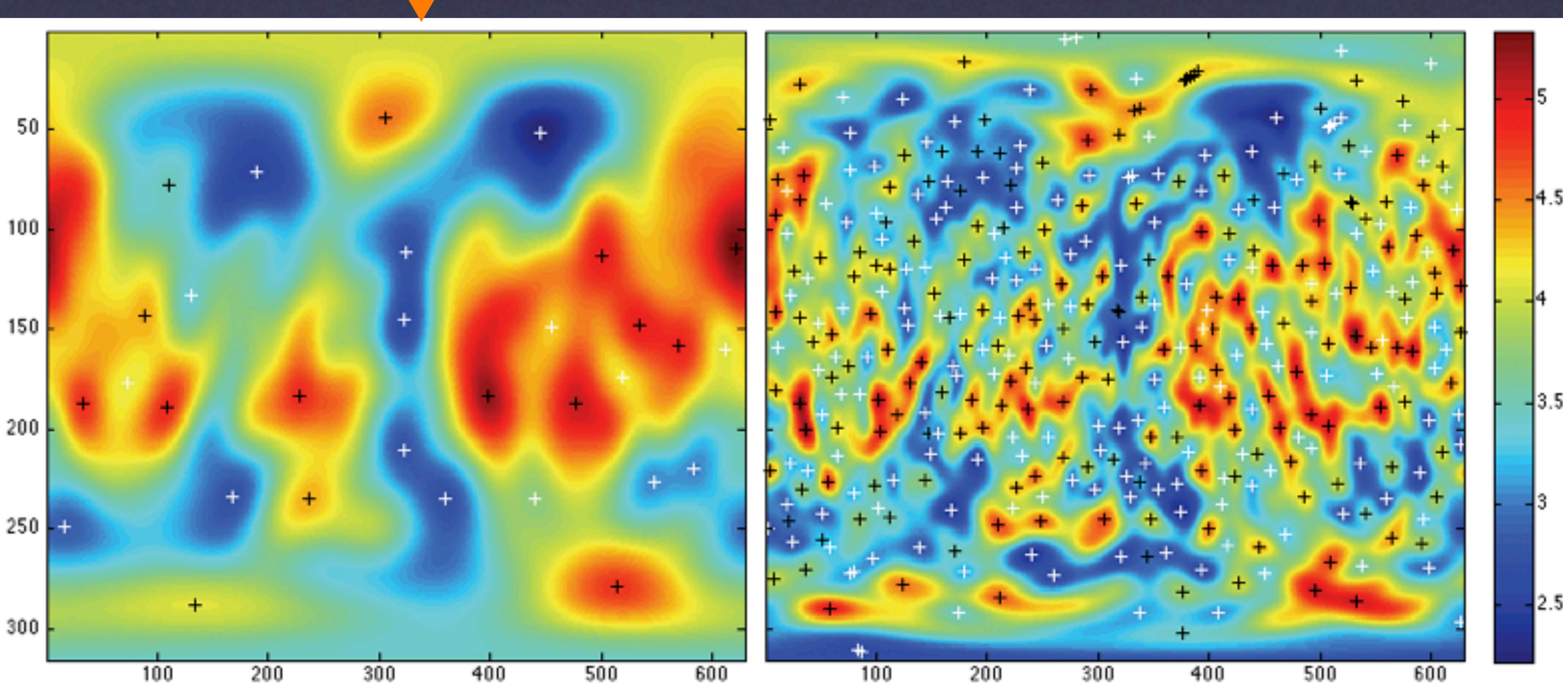
Persistent homology based signal detection (IPMI, 2009)

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



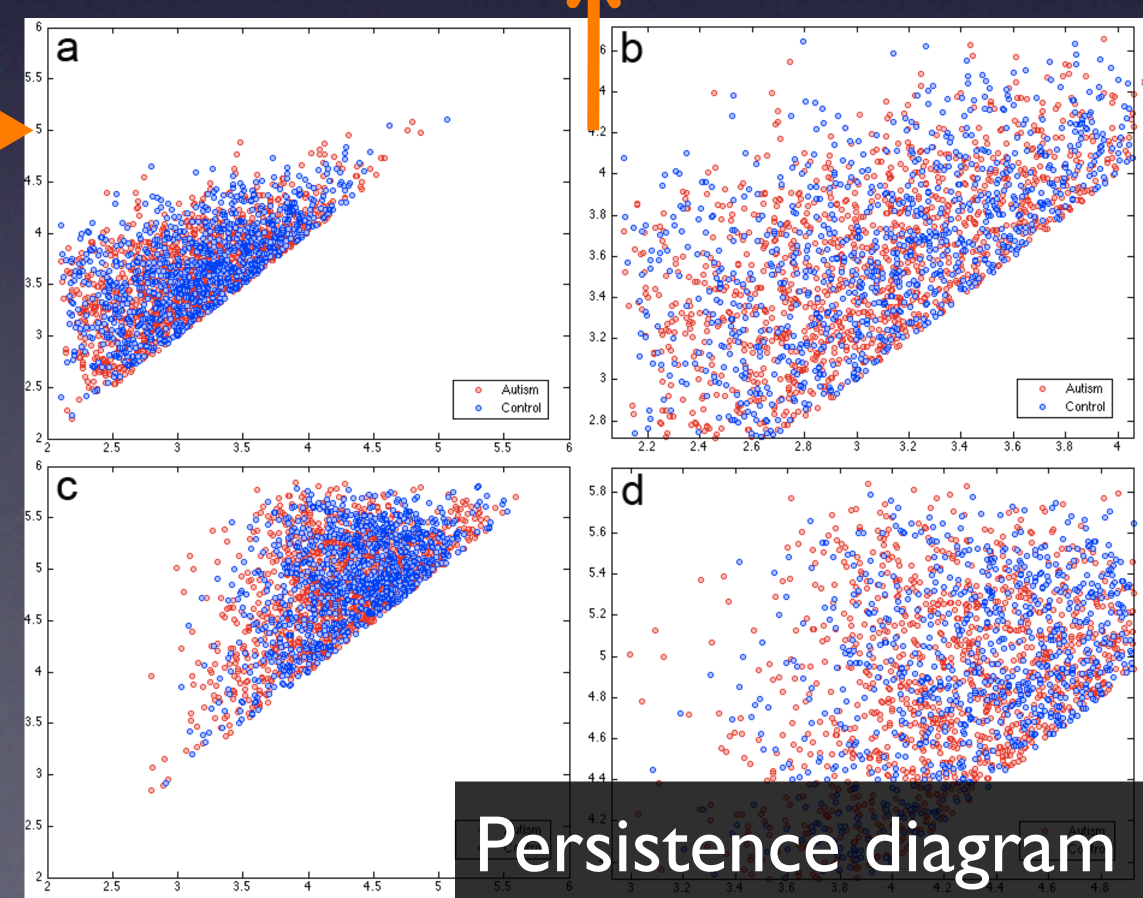


cortical flattening



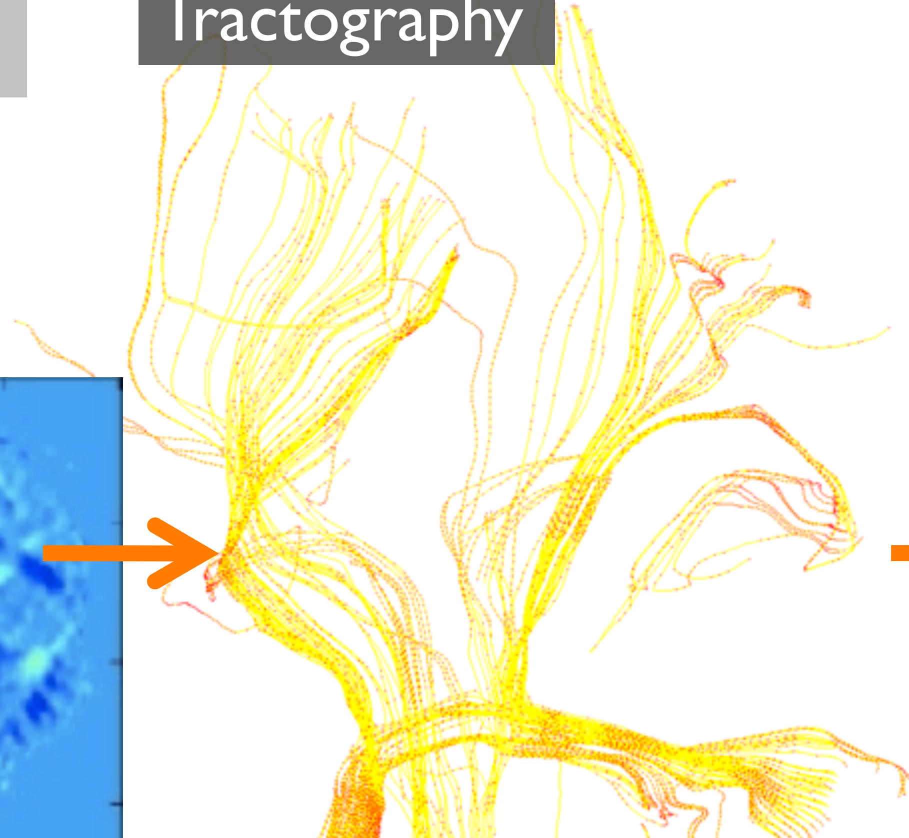
Classification accuracy of 96% using a simple support vector machine

Best available thickness analysis technique with Ada-boost 90%

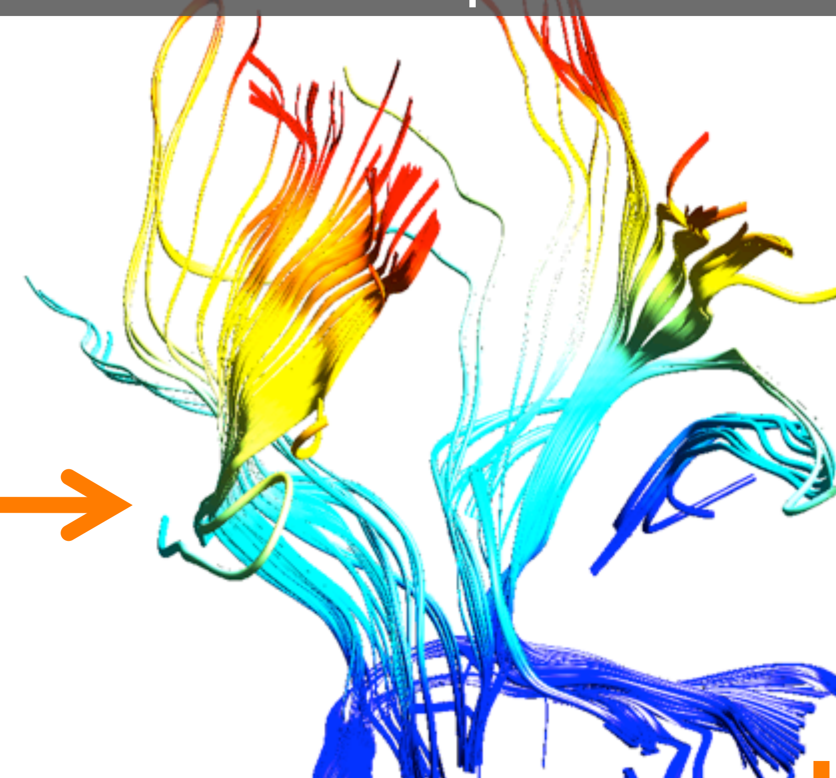


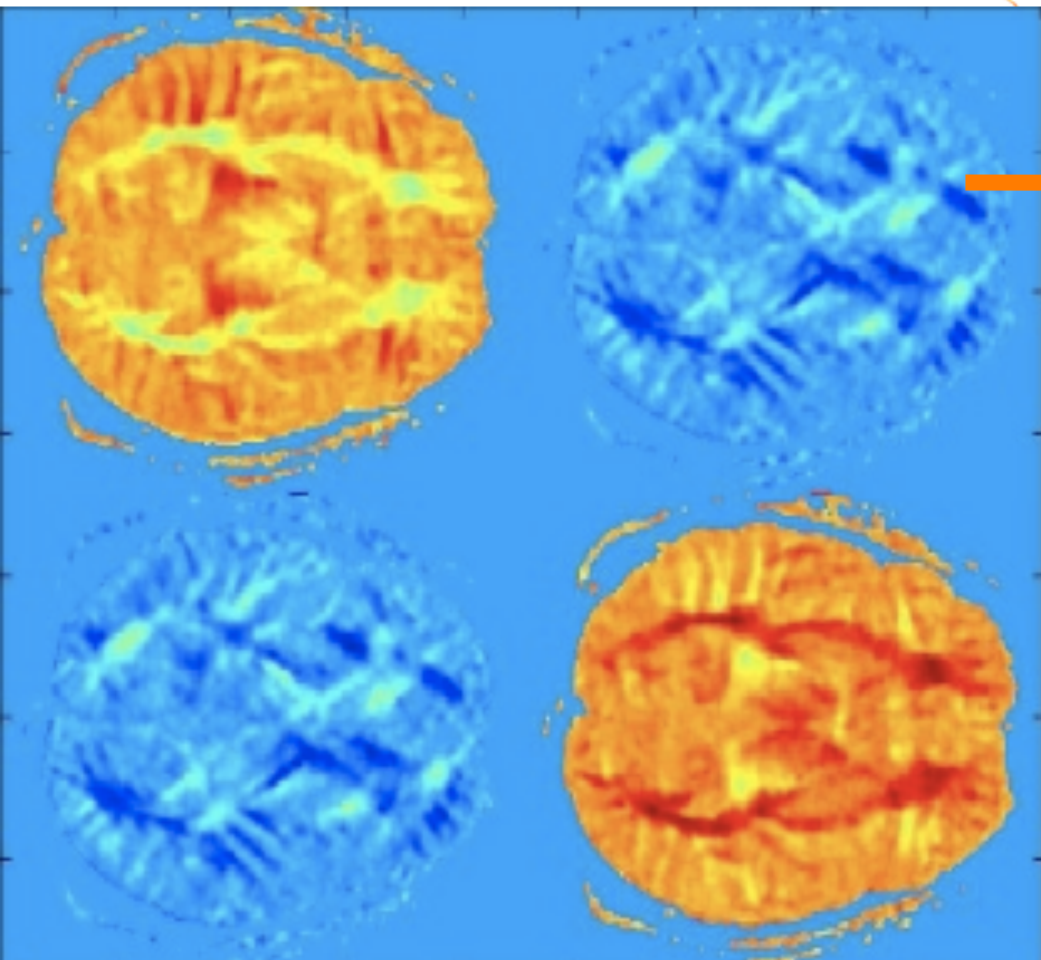
Brain network models

Tractography

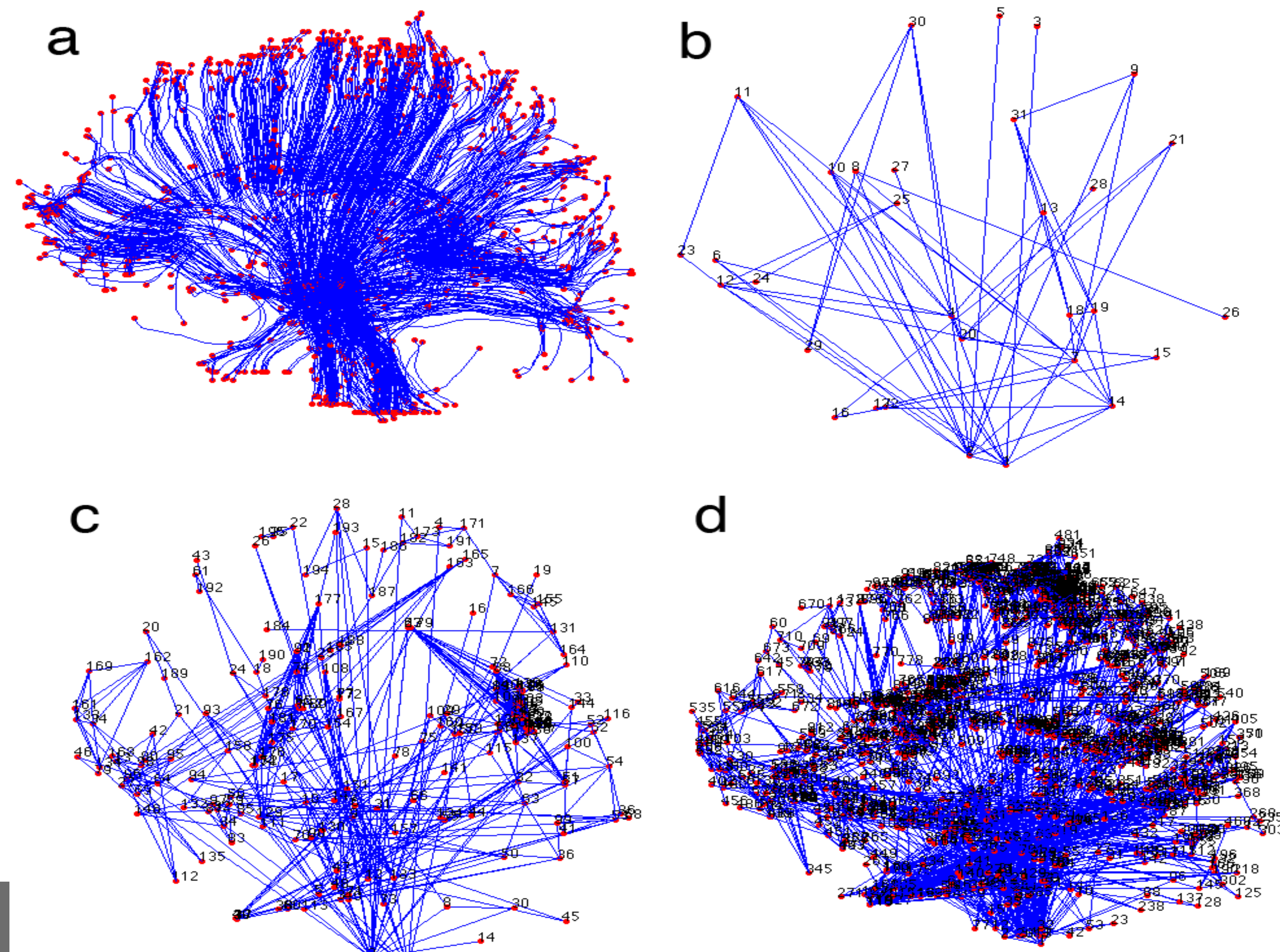


Cosine series representation





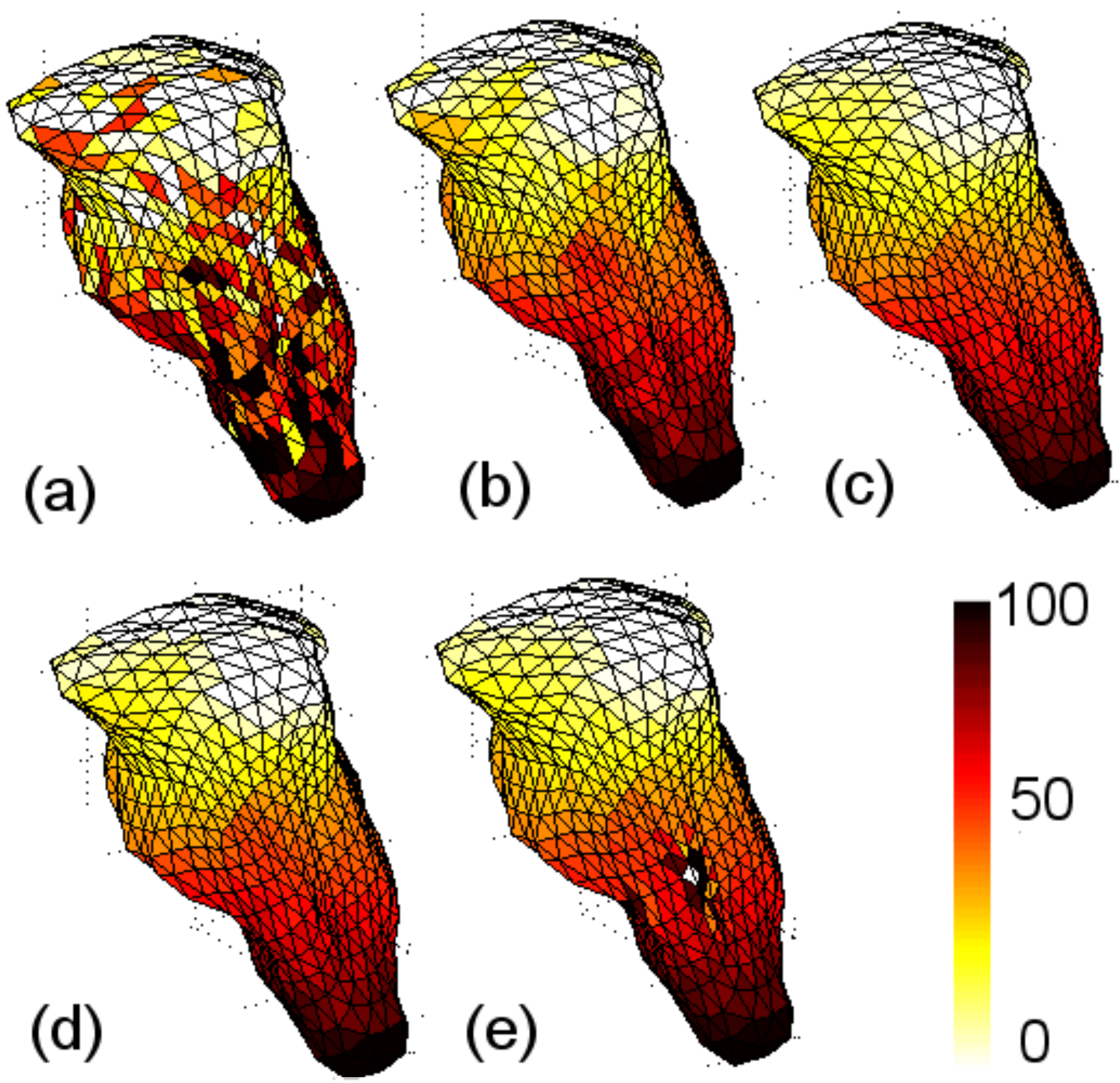
Diffusion tensor imaging (DTI)



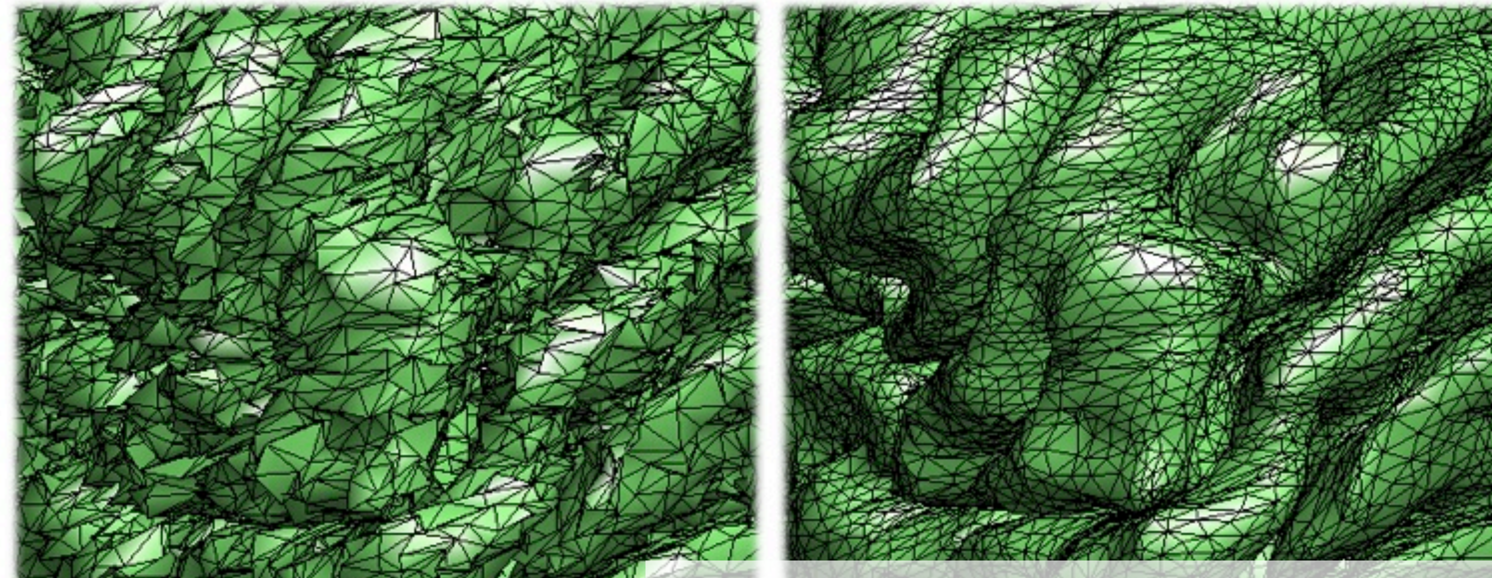
3D networks

Image smoothing

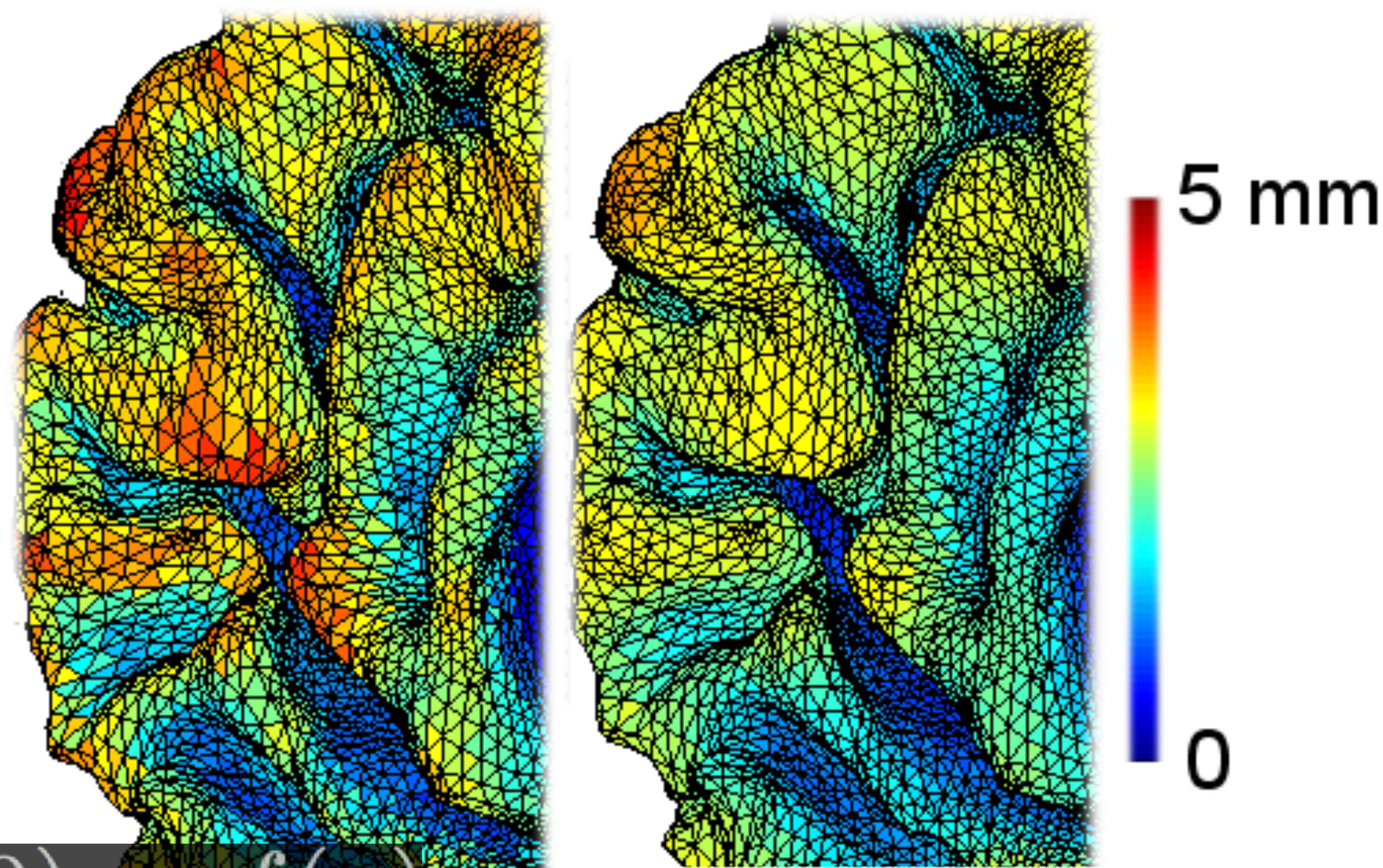
Smoothing on anatomical boundary



Diffusion smoothing on brain stem



Geometric noise smoothing



Cortical thickness smoothing

Diffusion equation

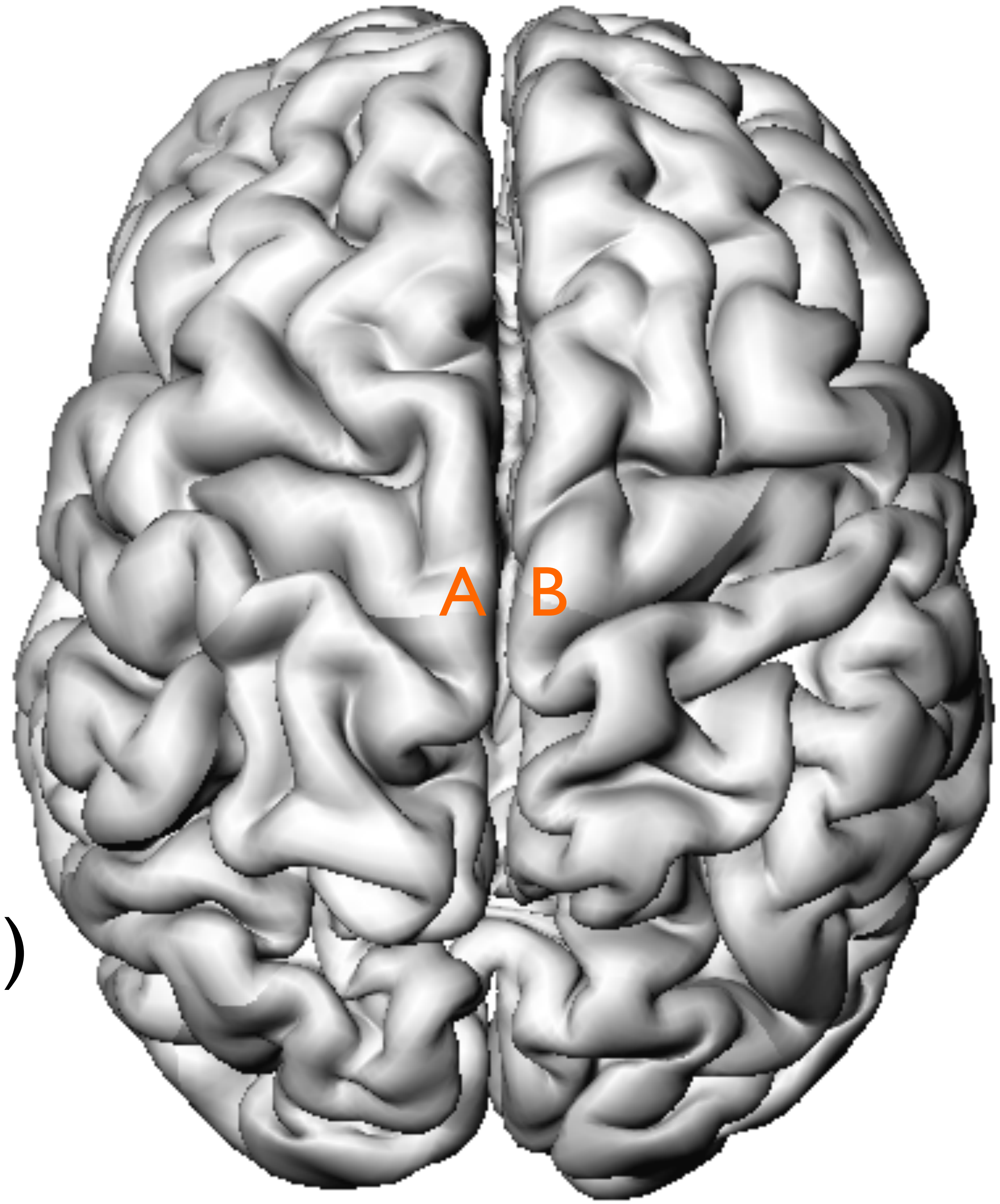
$$\partial_t g + \mathcal{L} g = 0, g(p, t = 0) = f(p)$$

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

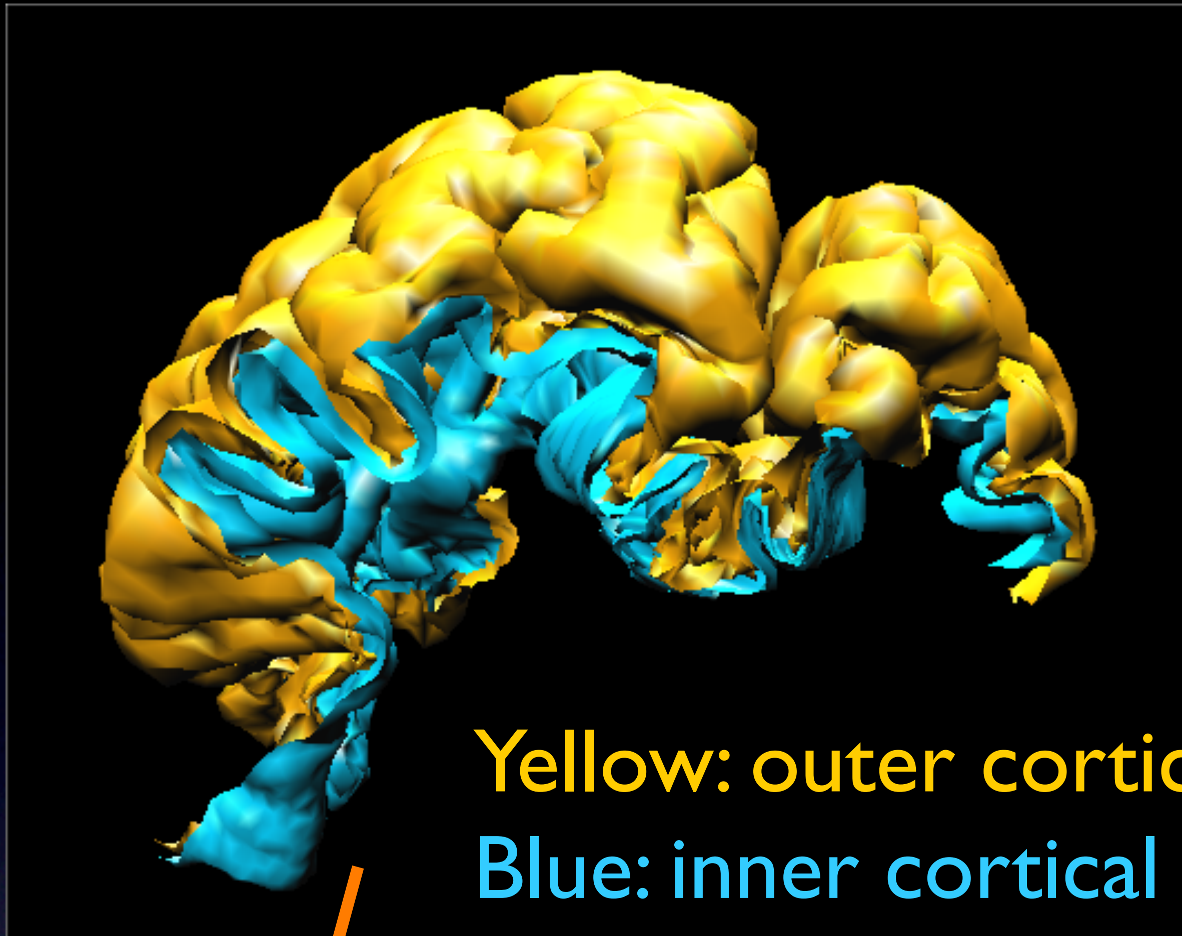
Need to smooth along the surface

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

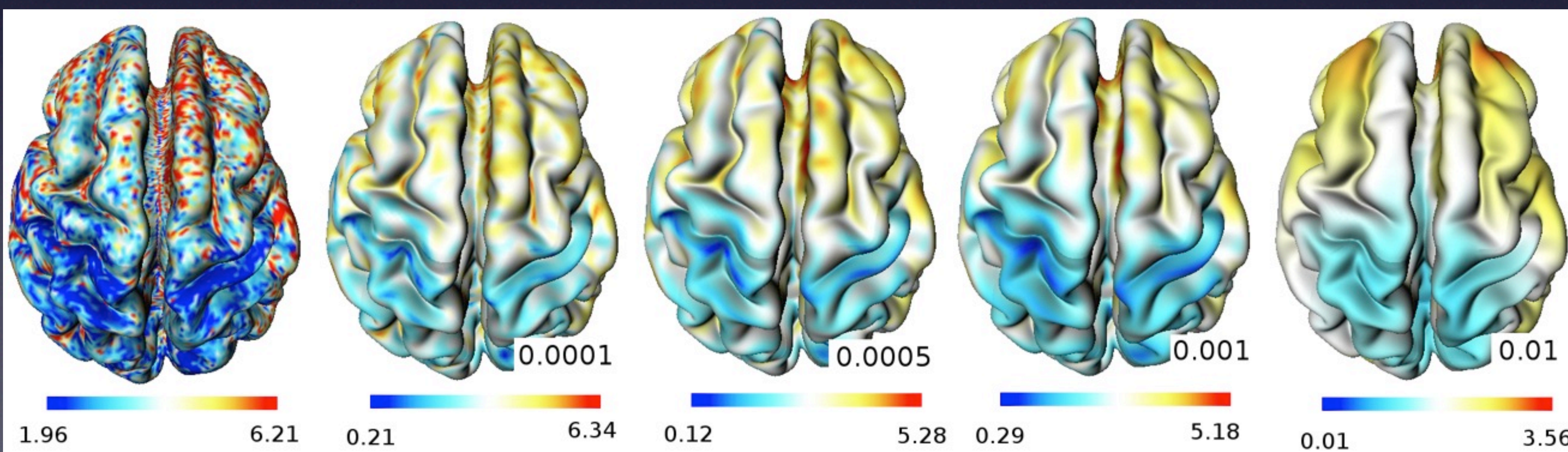
Most widely used cortical smoothing techniques



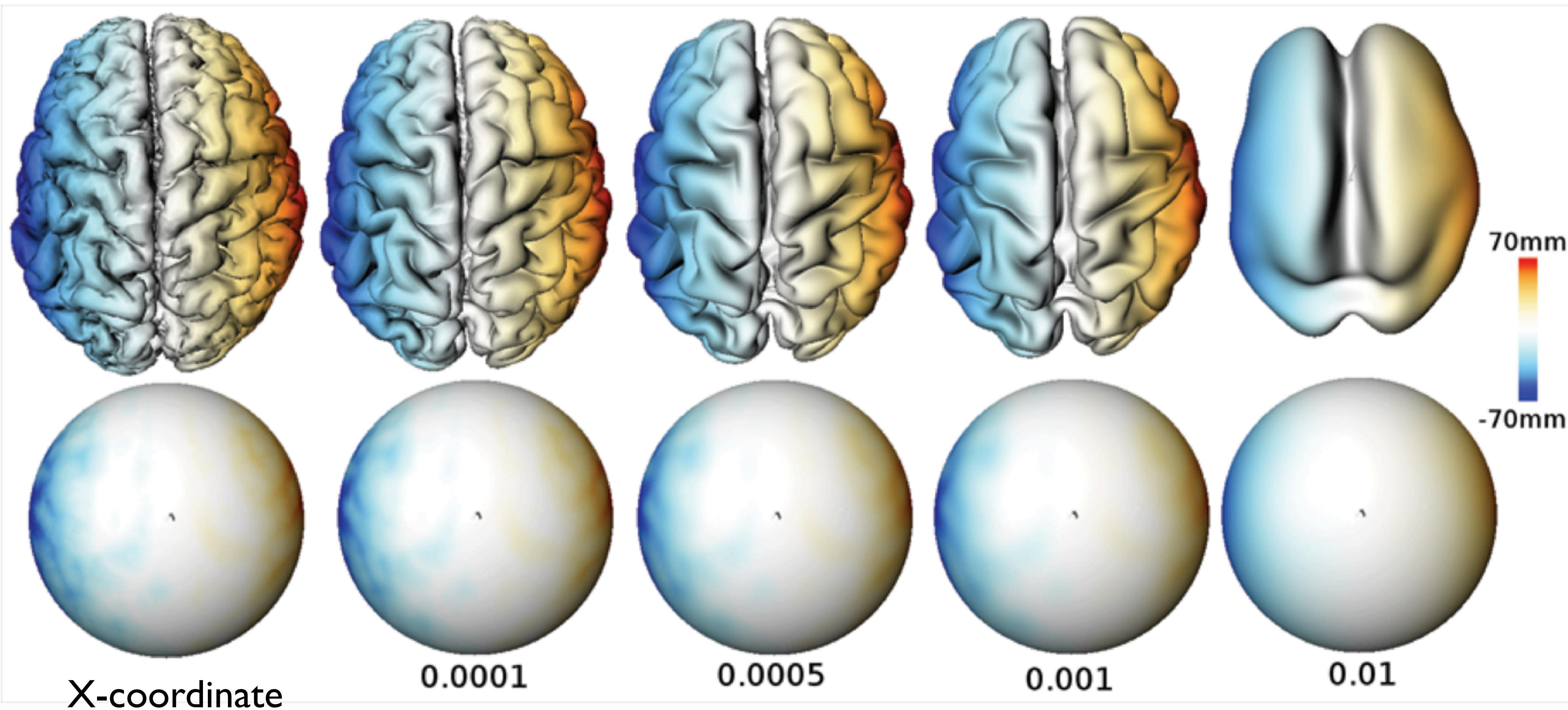
Weighted Fourier representation of cortical thickness



Yellow: outer cortical surface
Blue: inner cortical surface



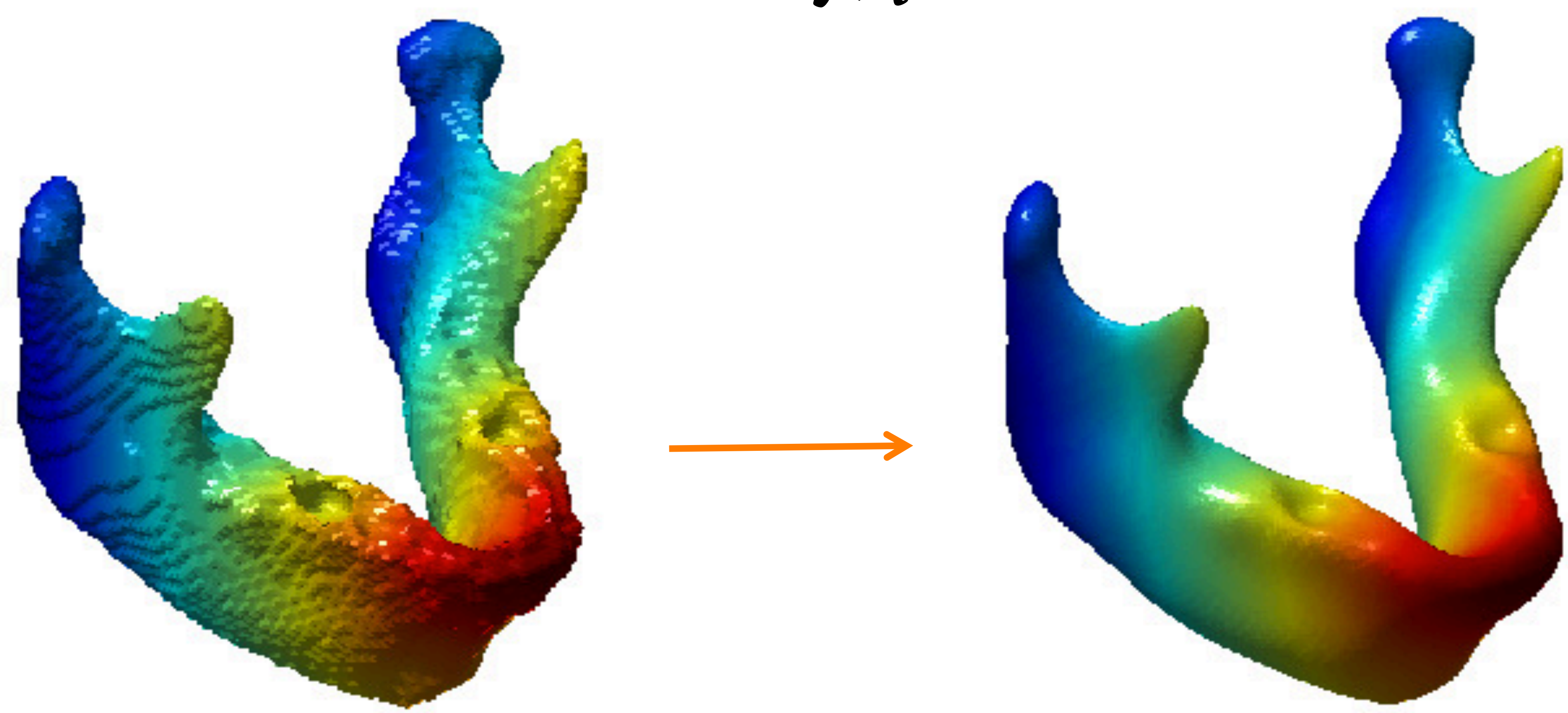
Multiscale representation of anatomy via weighted-SPHARM



Heat kernel smoothing on surface

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

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

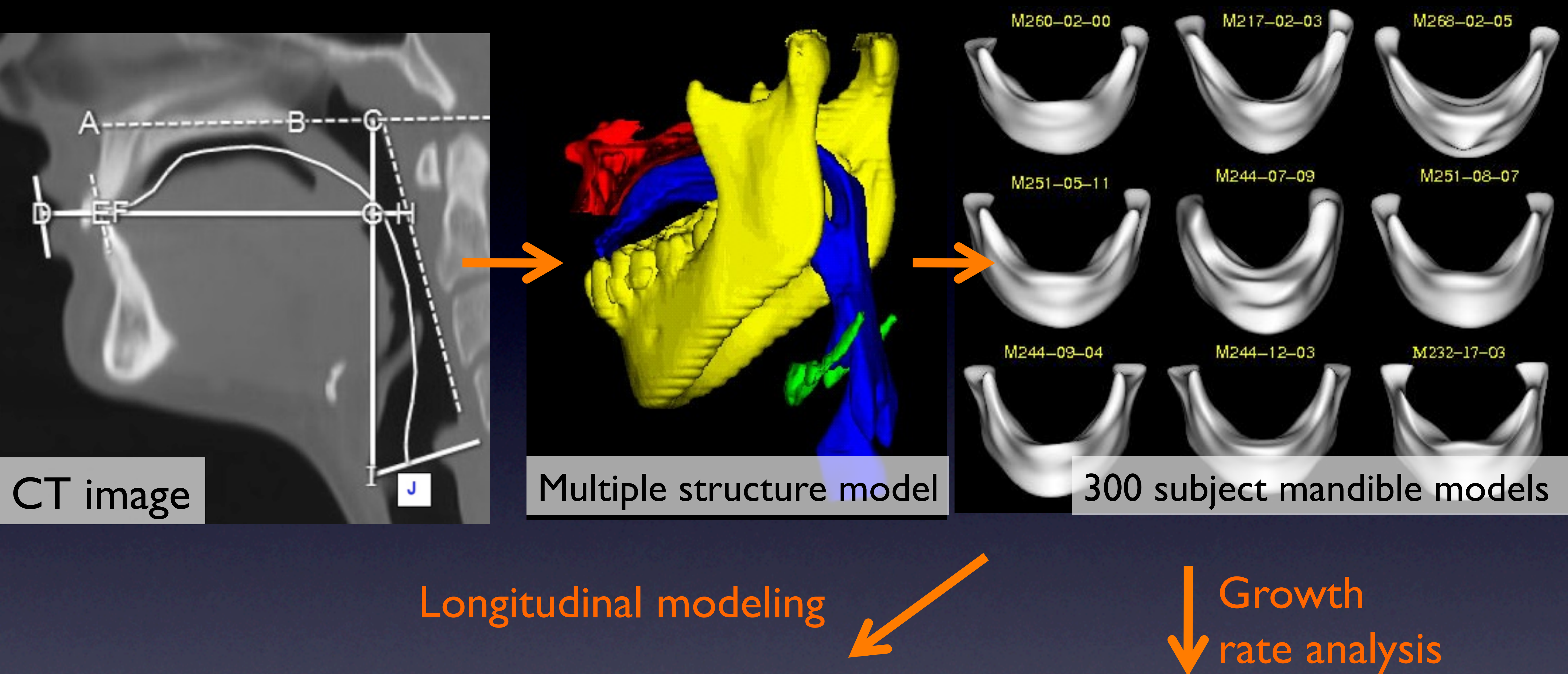


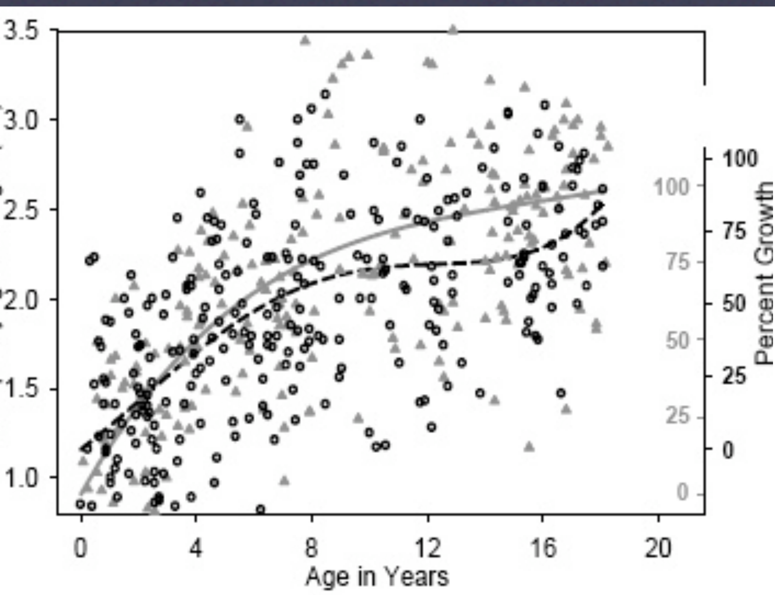
X-coordinate on mandible surface

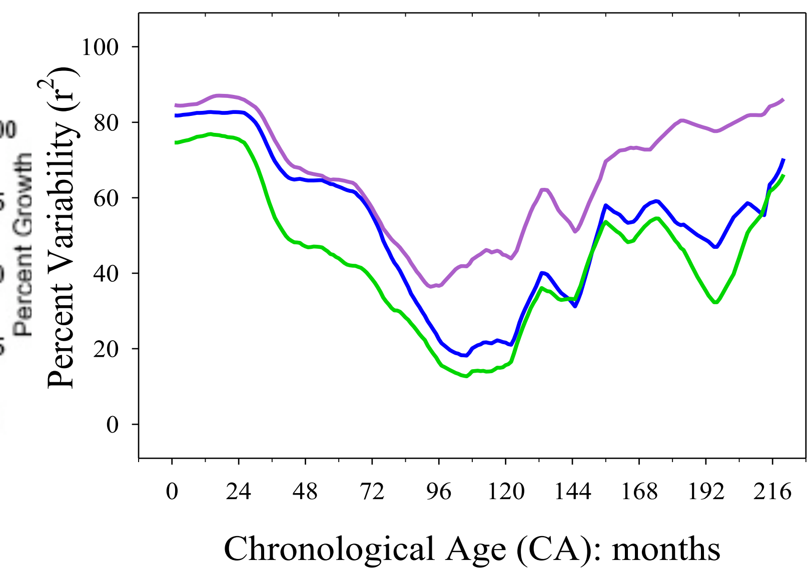
smoothed with bandwidth 10 and 1269 eigenfunctions

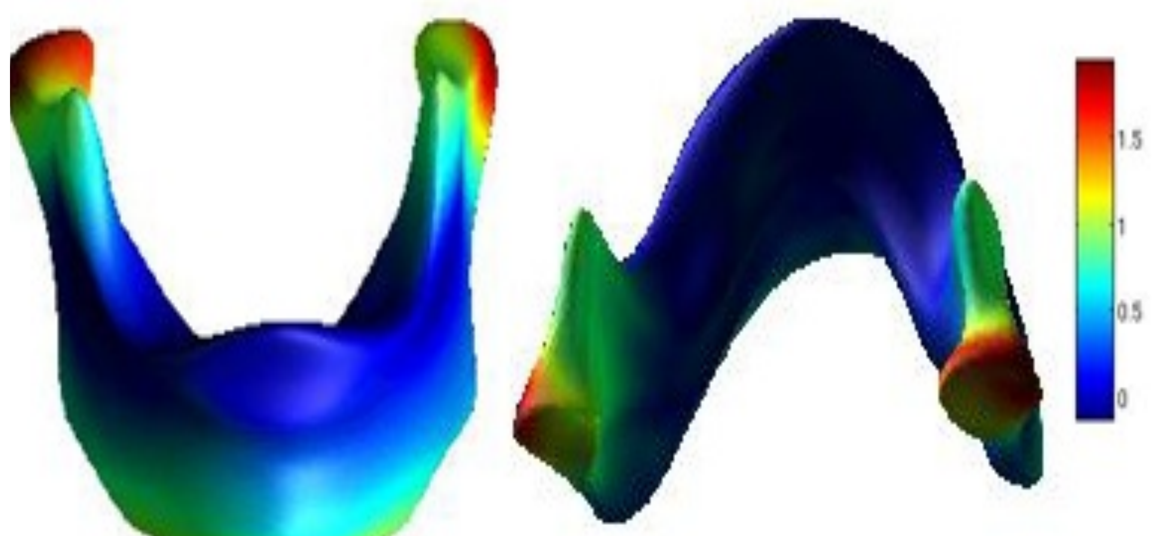
Statistical inferences

Longitudinal fixed effect growth modeling









Fixed effect model

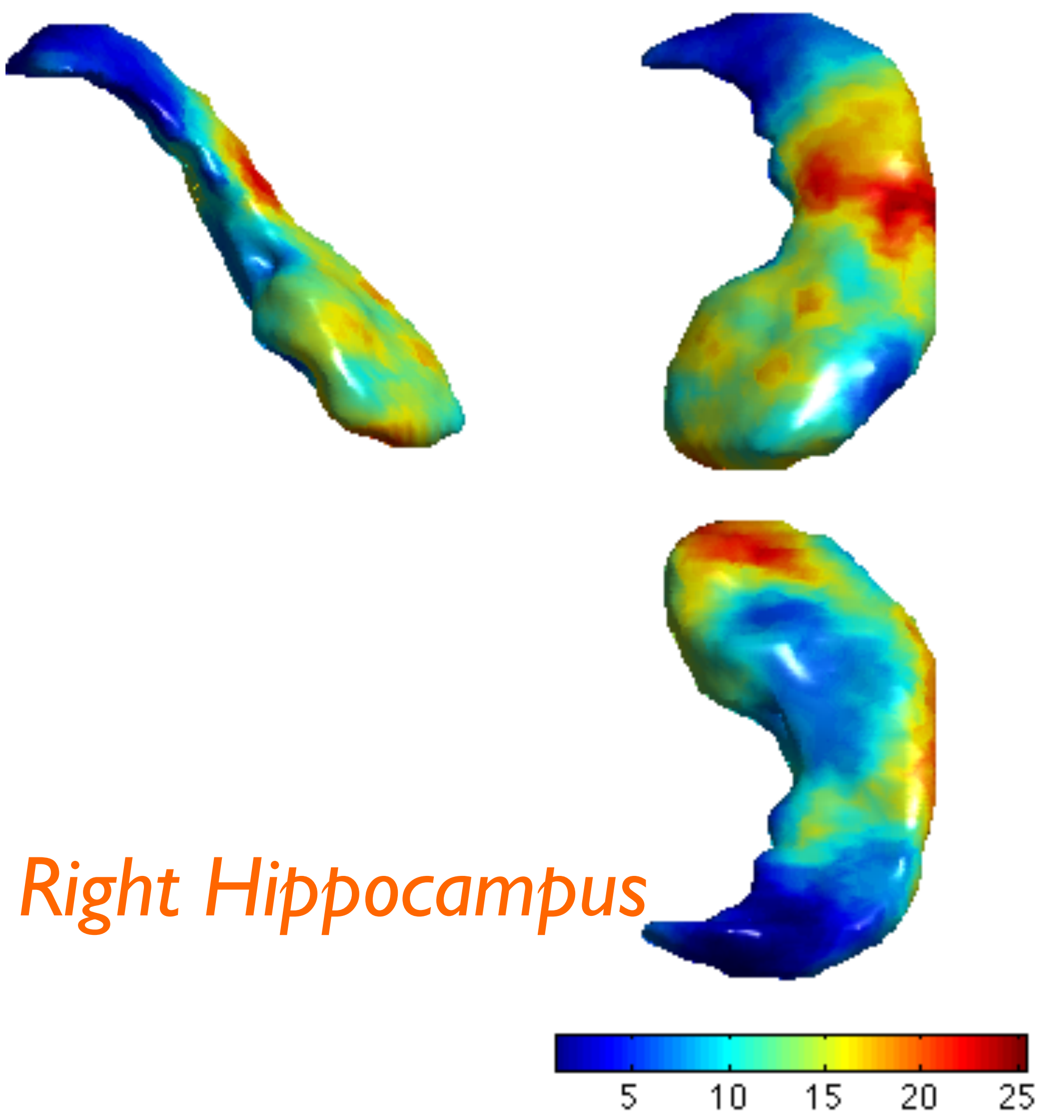
treating multiple scans within a subject as independent

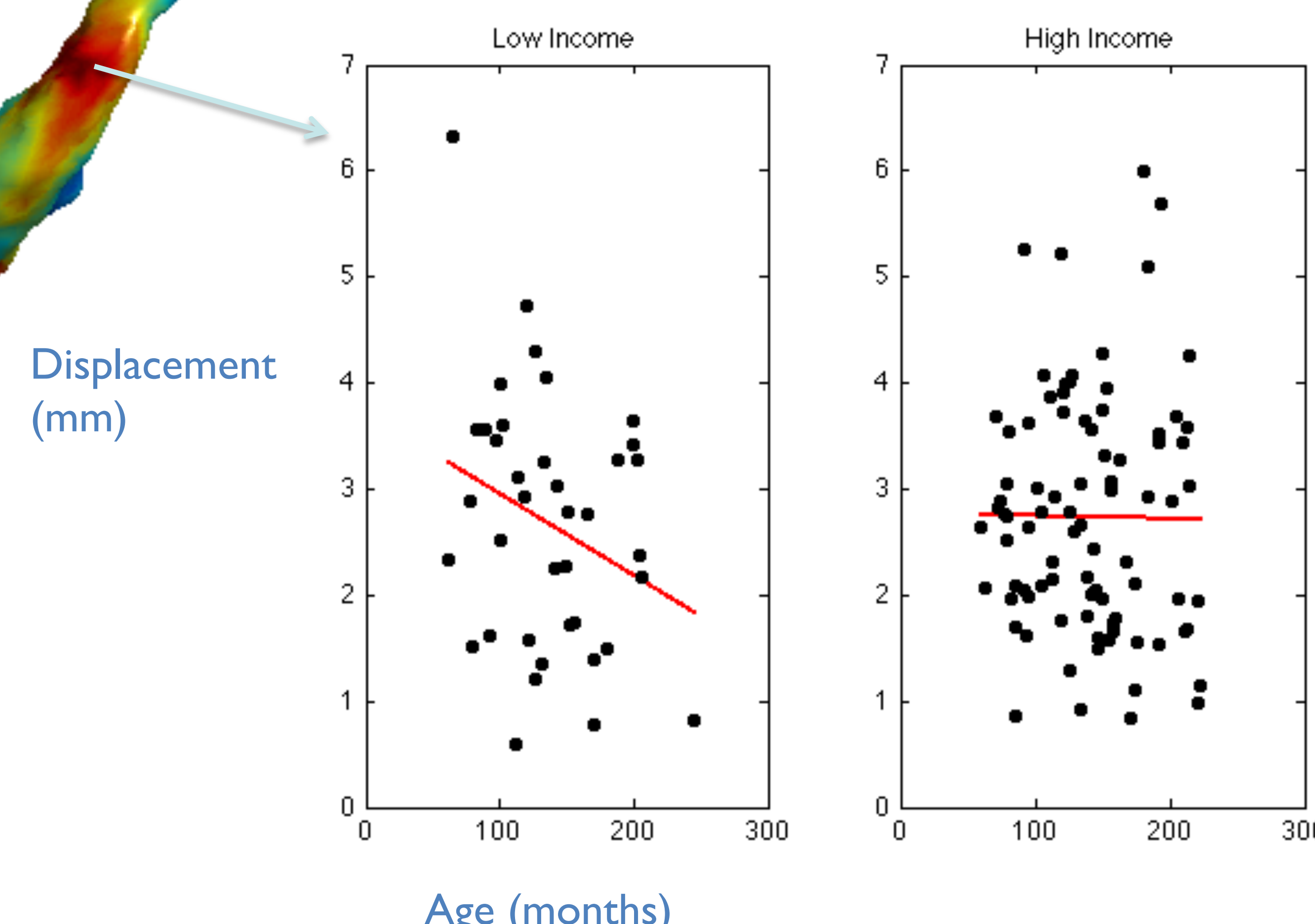
displacement = age + gender + group + age*group

max F = 25.4

corrected pvalue < 0.001

it inflates statistical significance



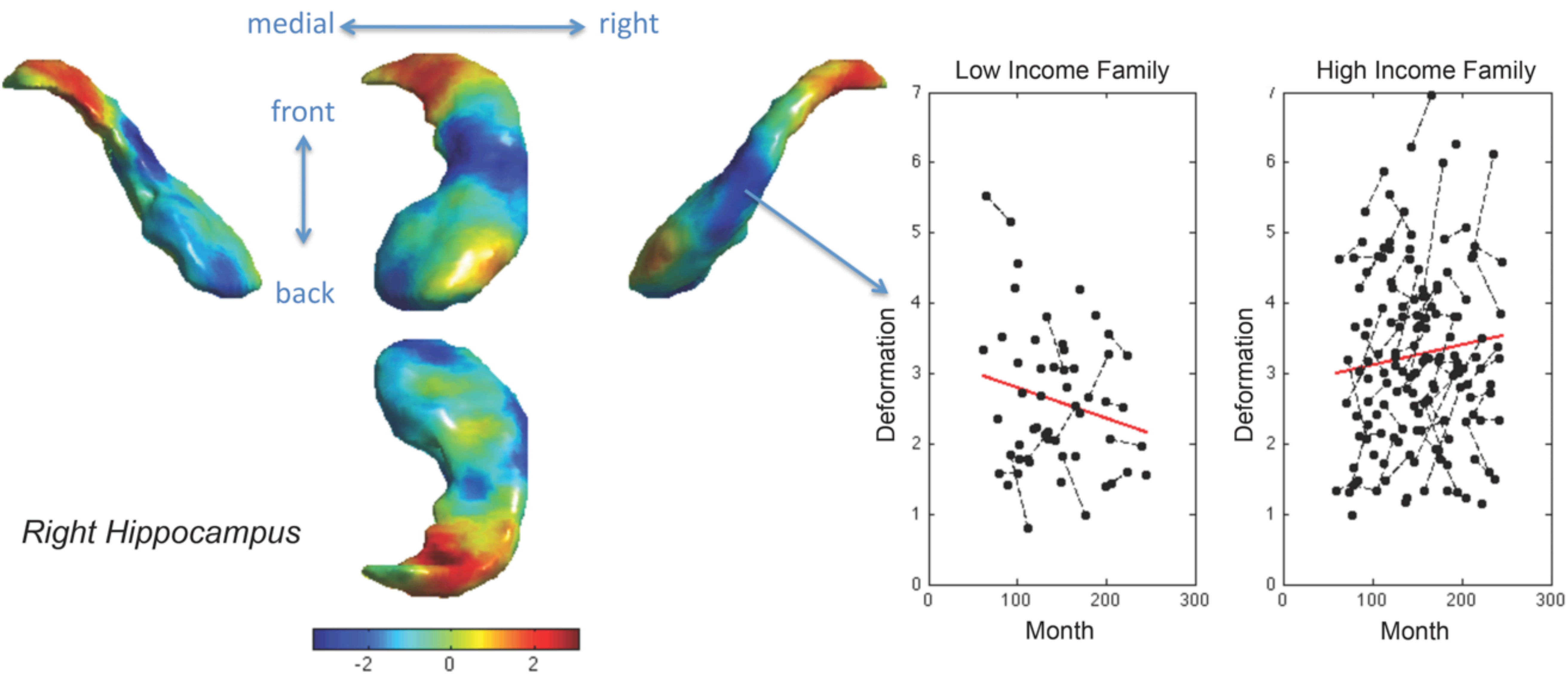


Linear mixed effect model

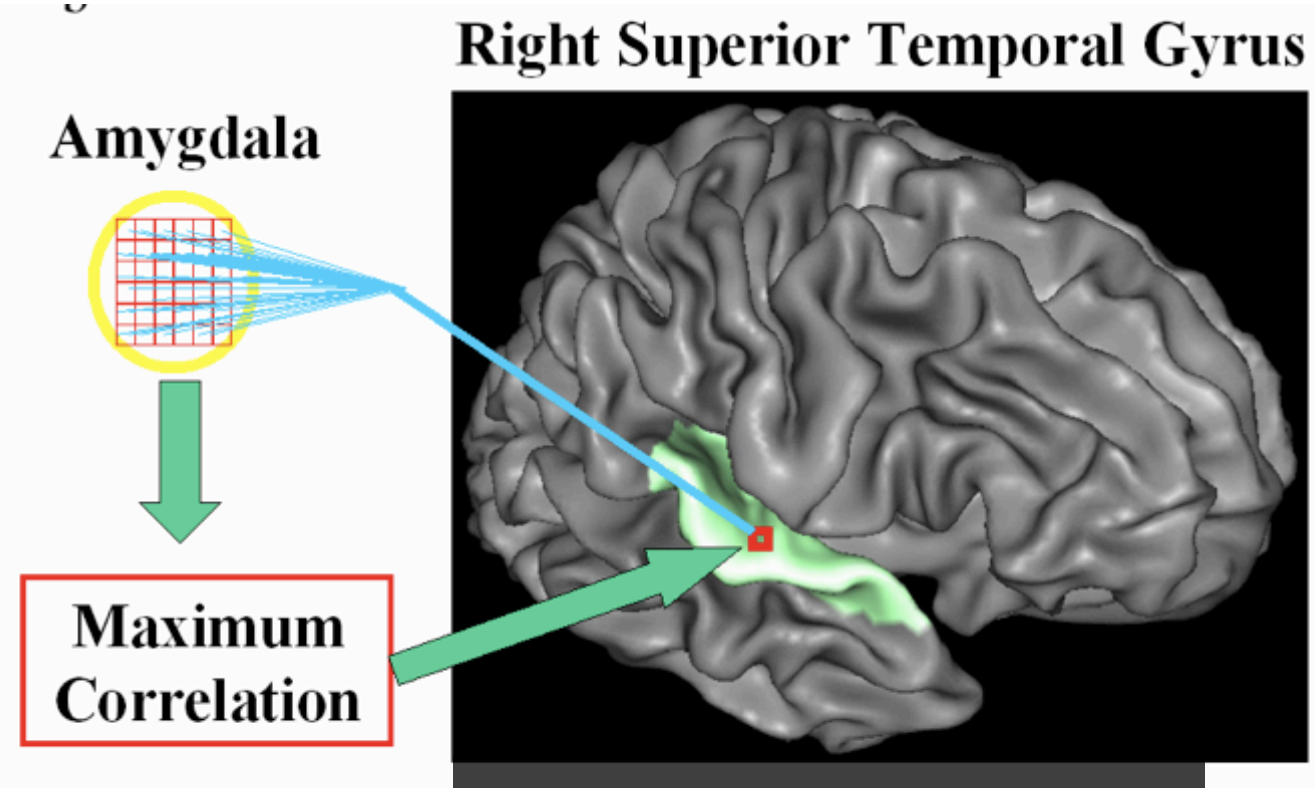
accounting for dependency of multiple scans within a subject

displacement = age + gender + group + <u>age*group</u>

min t = -3.3398,
corrected pvalue = 0.025

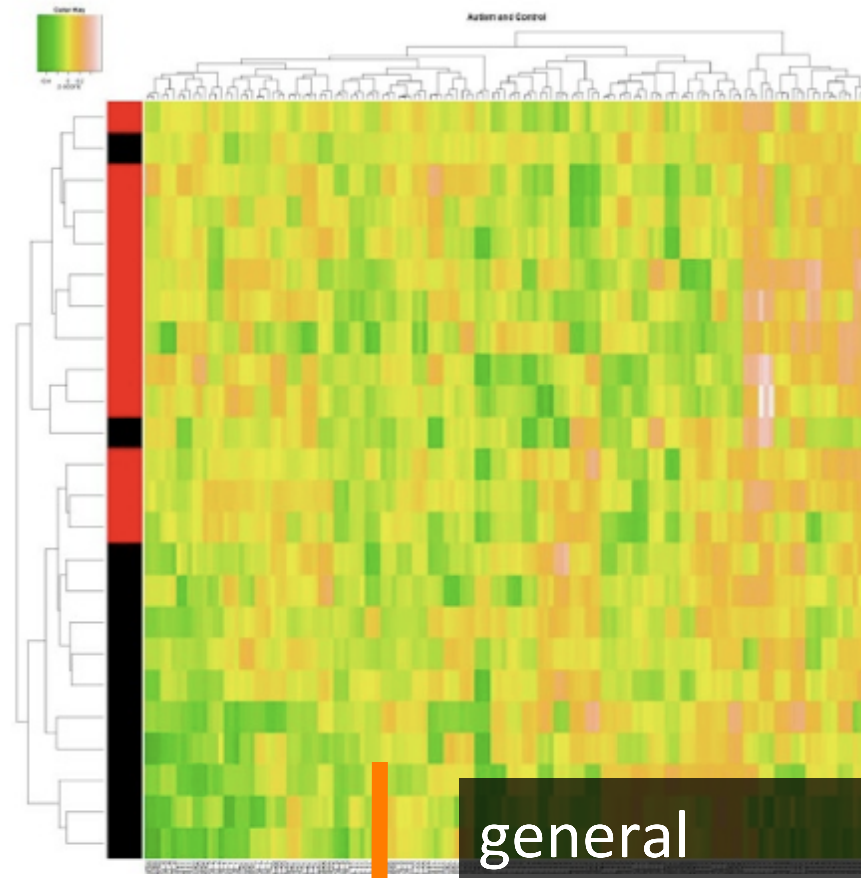


Effective fMRI connectivity D. J. Kelley

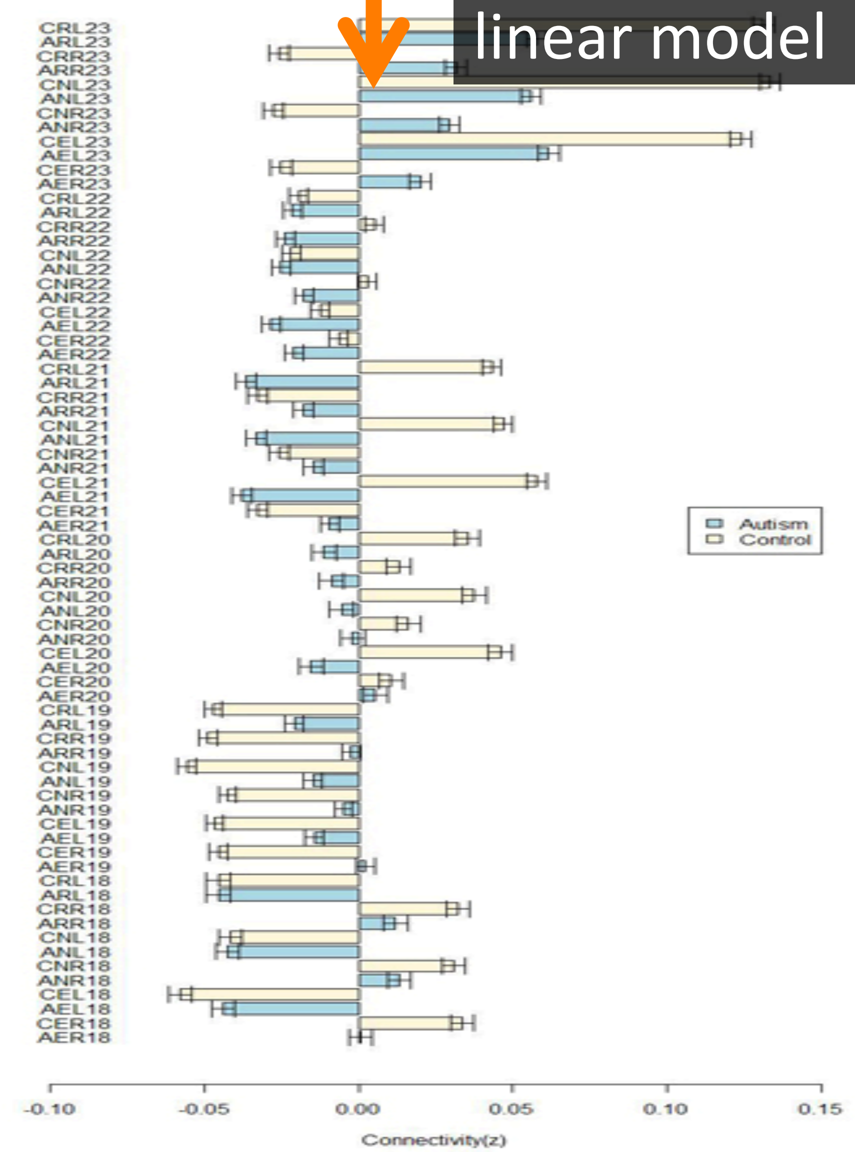


functional connectivity from amygdala seed voxel

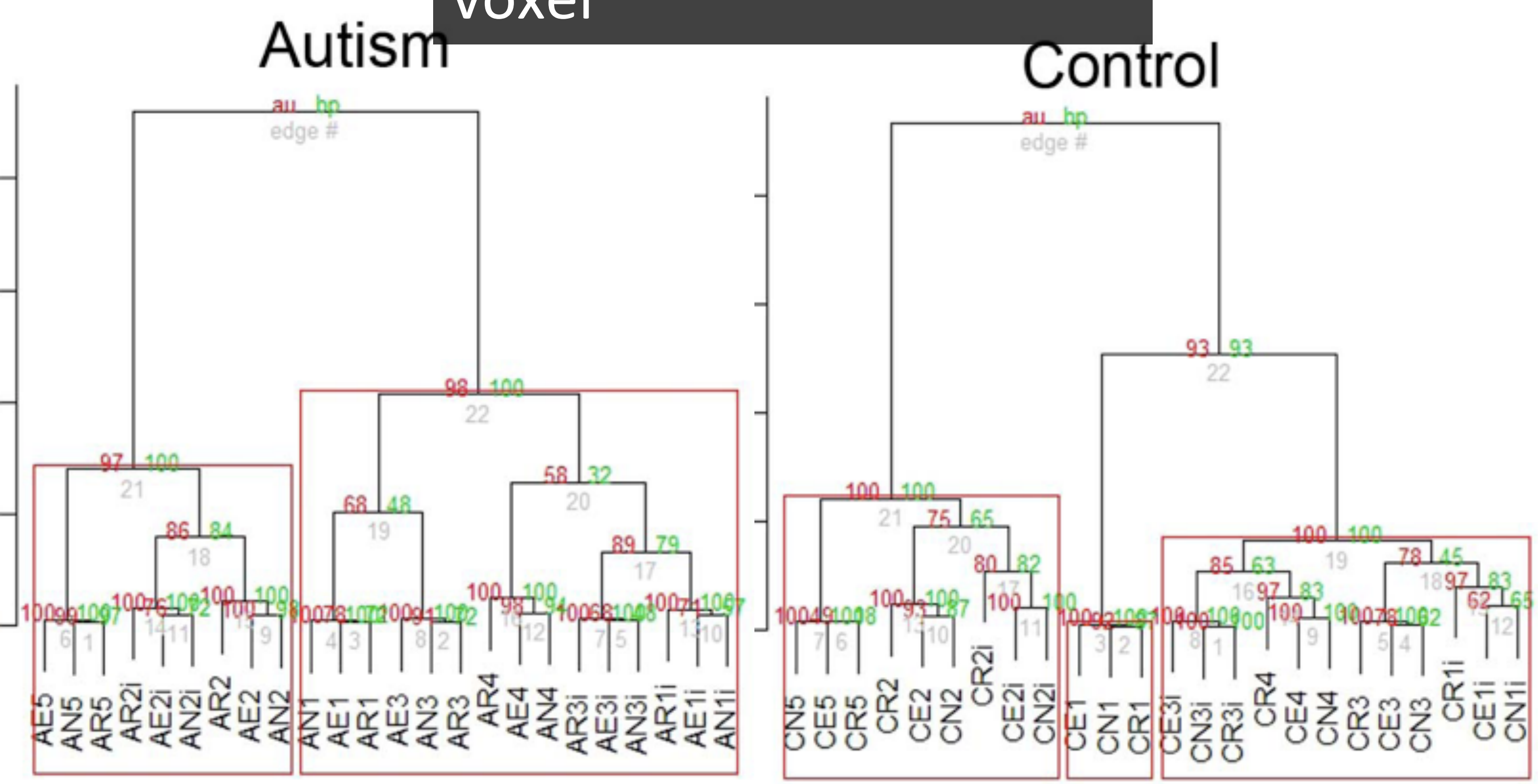
distance on correlation



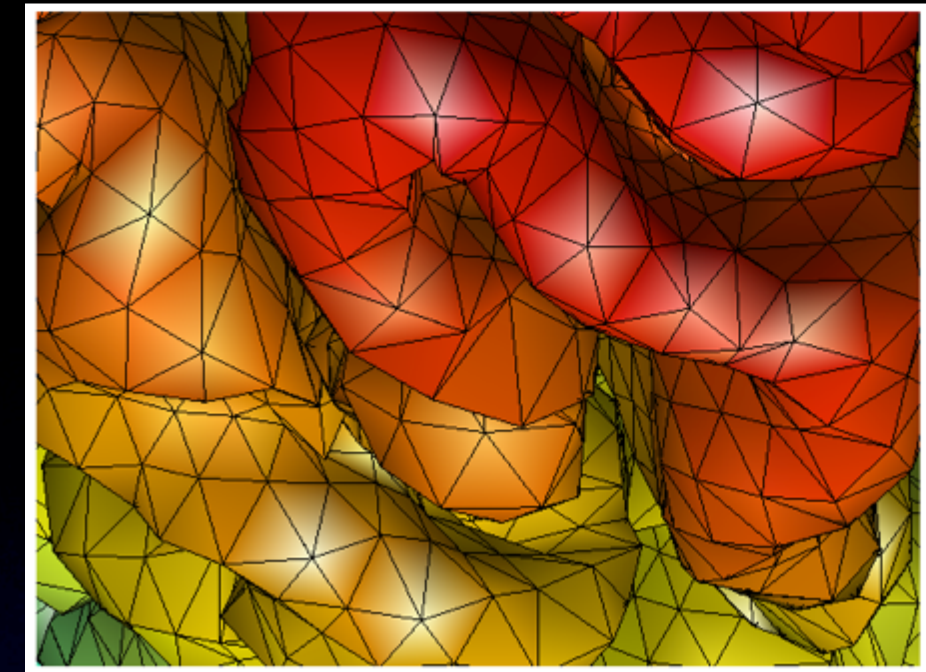
general linear model



hieratical clustering



Partial correlation mapping



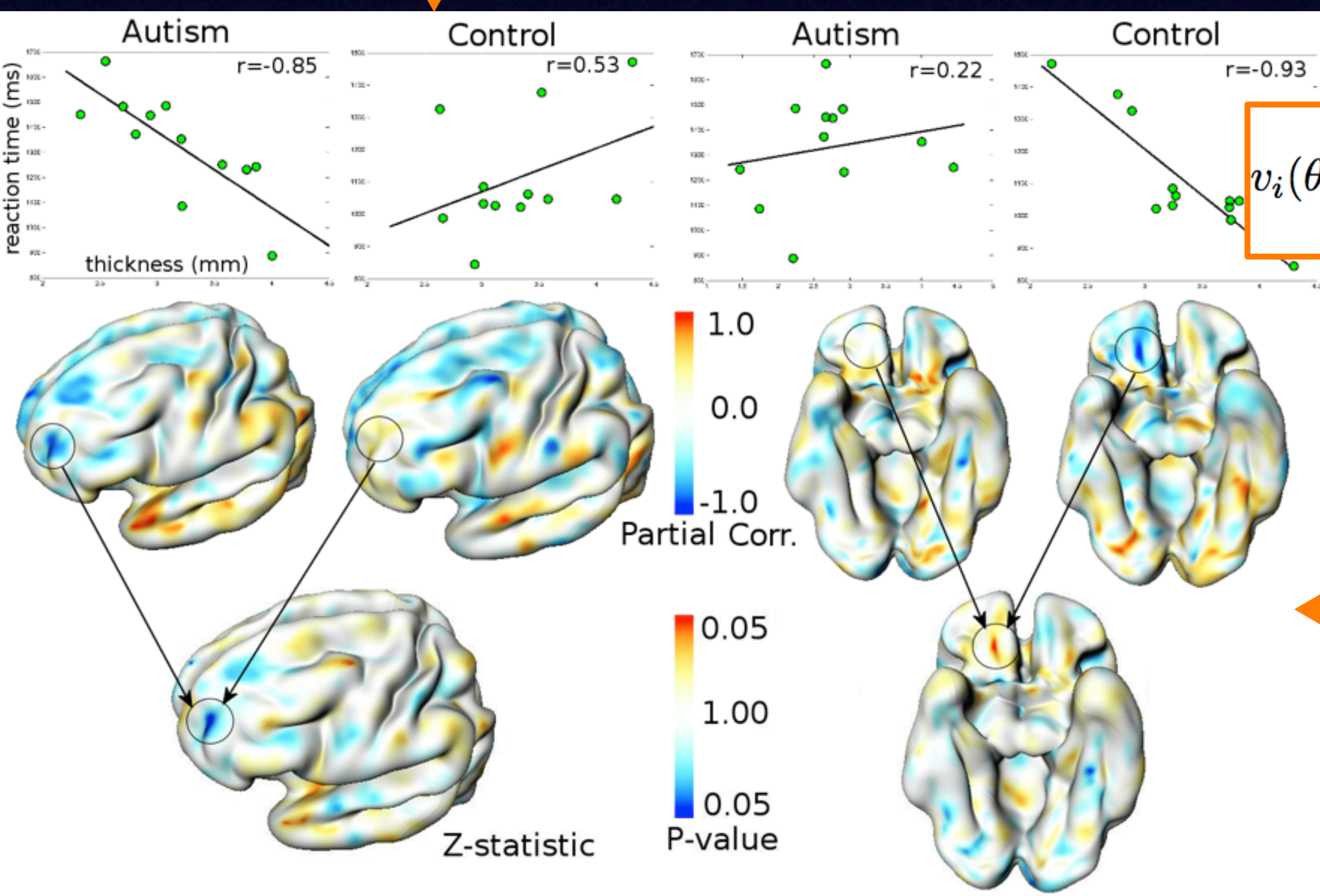
Partial correlation analysis

Weighted Fourier representation

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

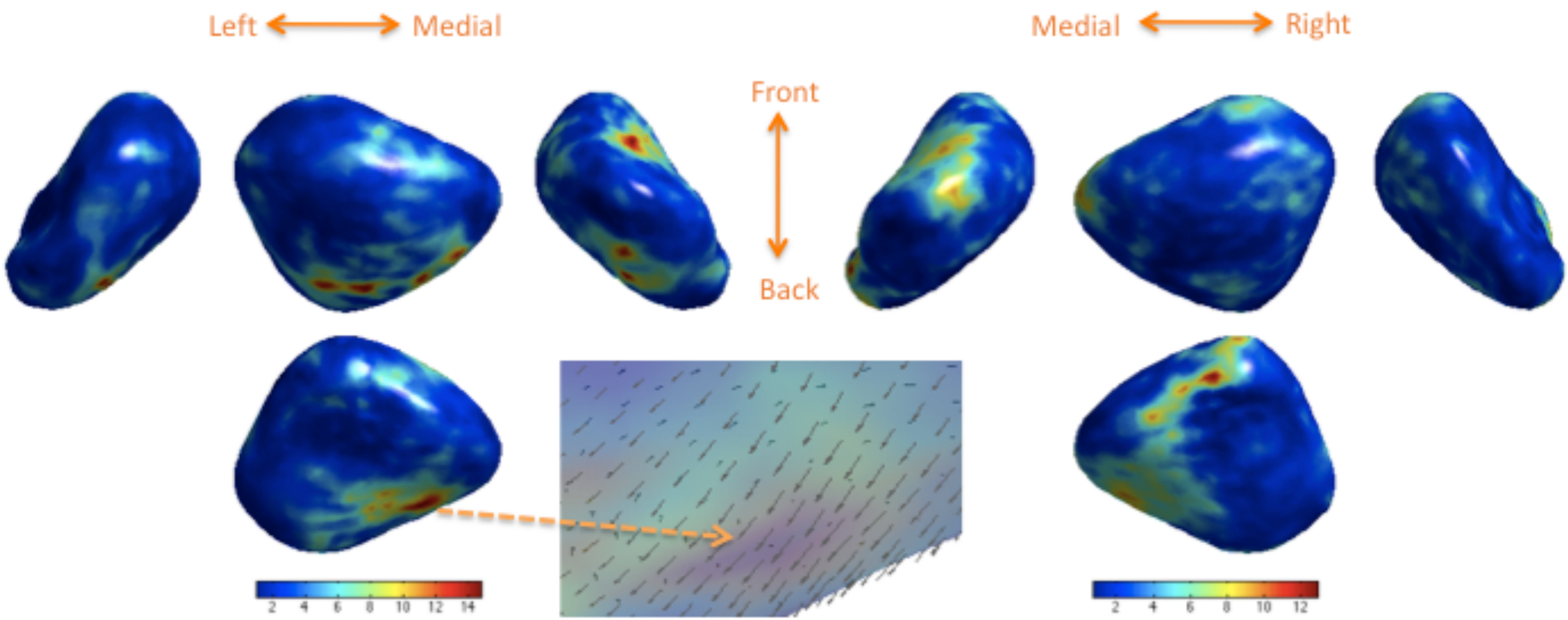
88.1799	56.6336	5.7367
-12.4775	-11.2552	-2.0791
2.4336	-15.4428	-0.4021
4.3956	2.2733	-0.9354
-0.0106	-0.0674	0.6999
2.1773	-2.4194	-0.1176
0.5808	0.8390	1.2942
0.0615	-0.1893	0.1188
-0.2629	0.7524	0.1089
0.7909	-0.7276	-0.1901
0.5458	0.6236	0.6939

....



Multivariate General Linear Models (MGLM)

Abnormal amygdala shape difference in autism



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

Coordinates = <u>Group</u> + Brain + Age + Noise

Thank you

send email for whatever questions and collaborative/consulting request to mkchung@wisc.edu