The Waisman Laboratory for Brain Imaging and Behavior

University of Wisconsin SCHOOL OF MEDICINE AND PUBLIC HEALTH

Weighted Fourier Analysis and Shape Parameterization

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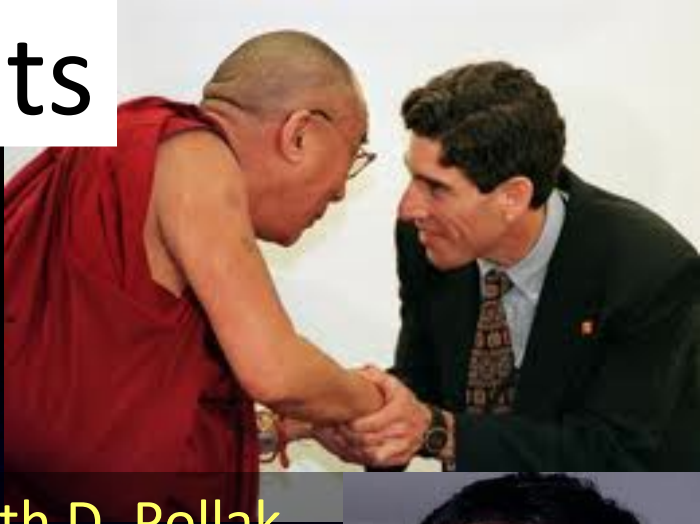
STAT768/BMI768

Statistical Methods for Medical Image Analysis

Data/Image Visualization
Multivariate Analysis
Hilbert and Fourier Methods
Fixed and Mixed-Effect Models
Logistic Regression/Classification
Multiple Comparisons/Power Analysis
Regression/Statistical Inference on Manifiolds
Everything you will see in today's lecture

Textbook: Computational Neuroanatomy: The Methods, Moo K. Chung, World Scientific Publishing 2012.

Acknowledgments



Jamie L. Hanson, Richard J. Davidson, Seth D. Pollak

University of Wisconsin-Madison

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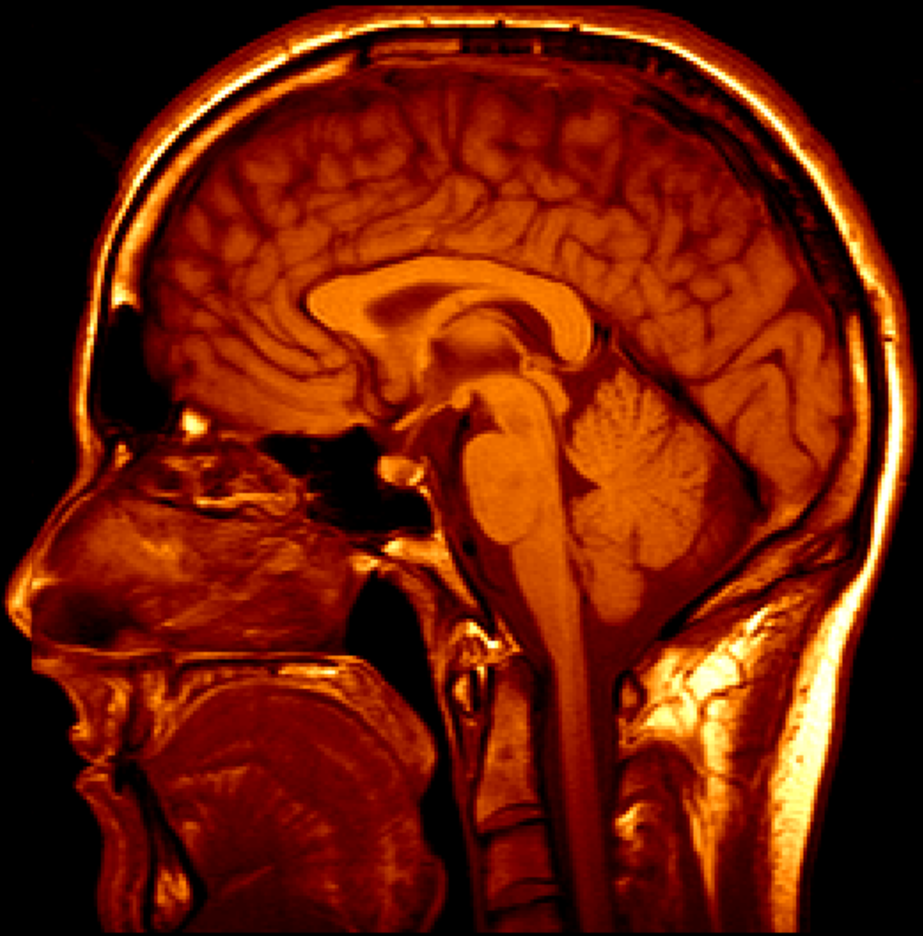
University of Wisconsin-Madison

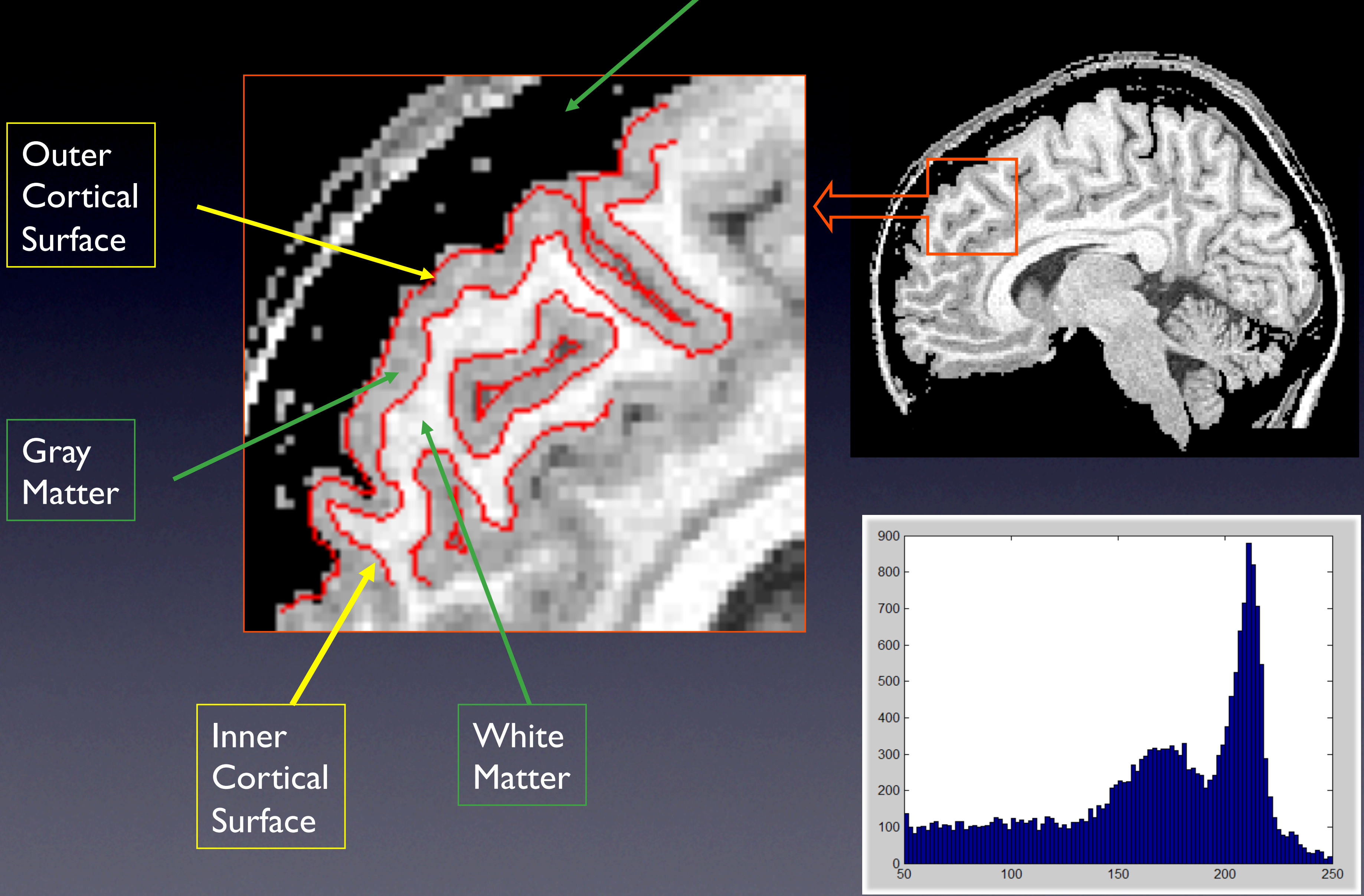
Motivation

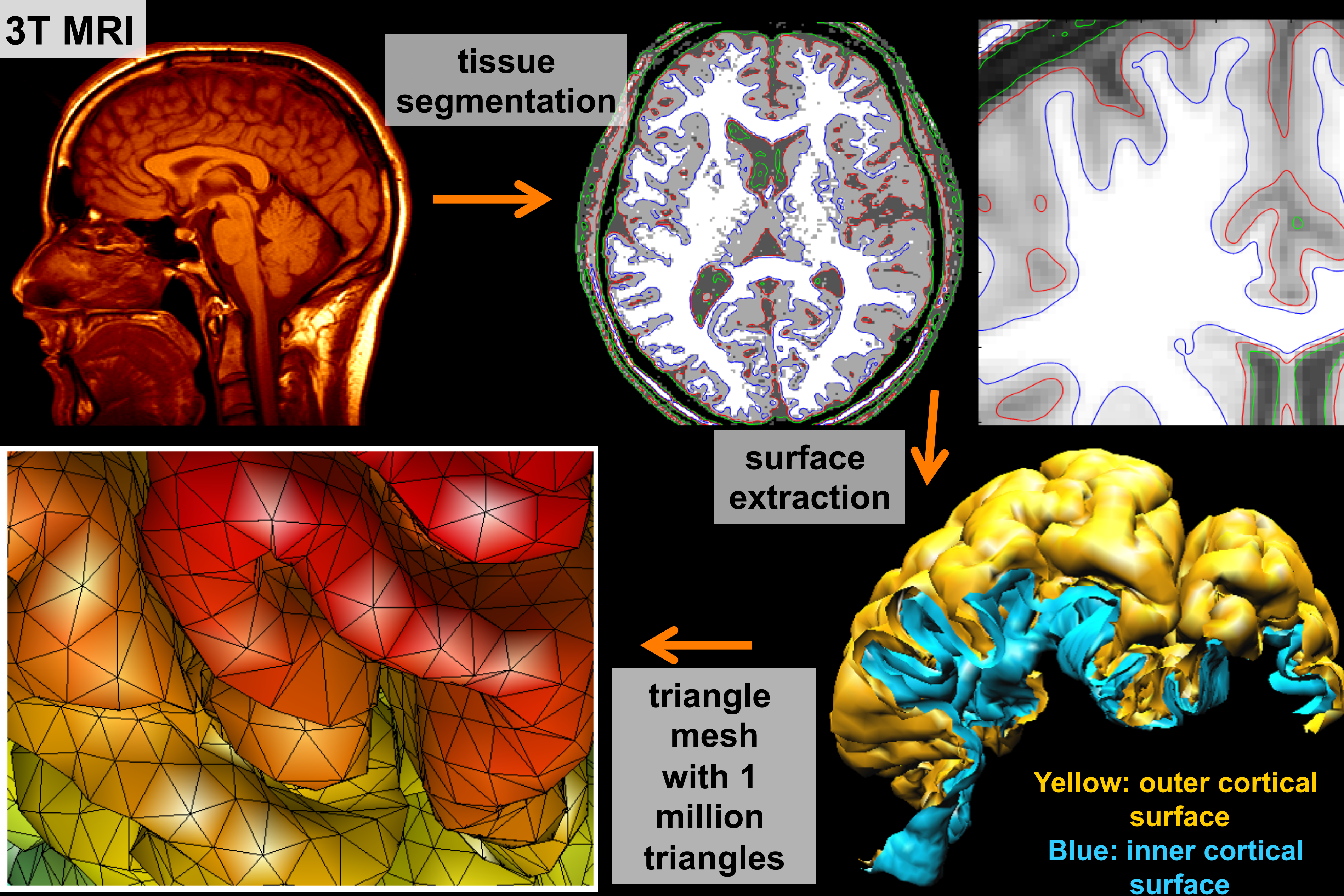
3 Tesla Magnetic Resonance Imaging



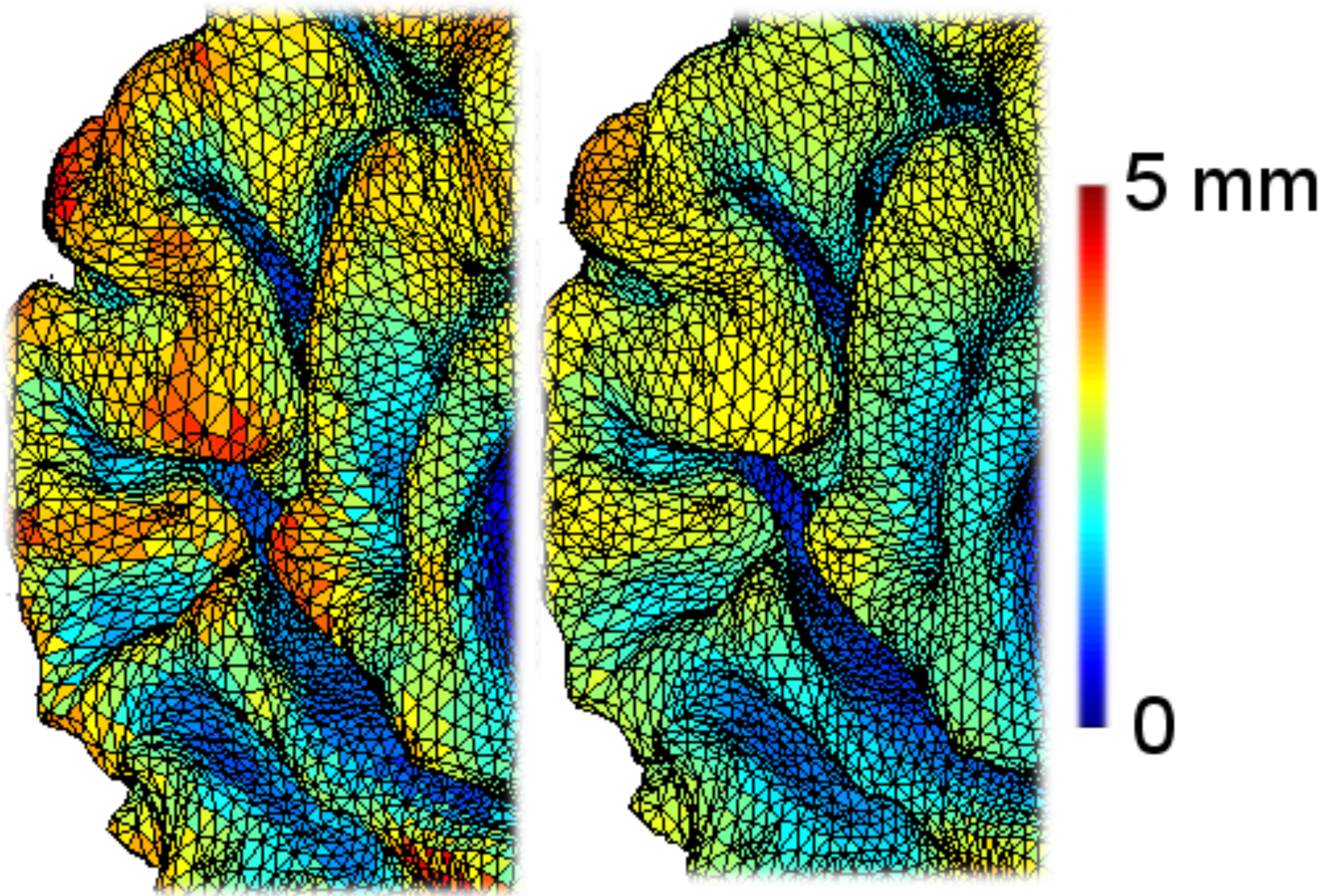
1 brain image
= 200 x 200 x 100 array
= 4million measurements

Cortical geometry




3T MRI
tissue segmentation
surface extraction
triangle mesh with 1 million triangles
Yellow: outer cortical surface
Blue: inner cortical surface

Noise in measurement



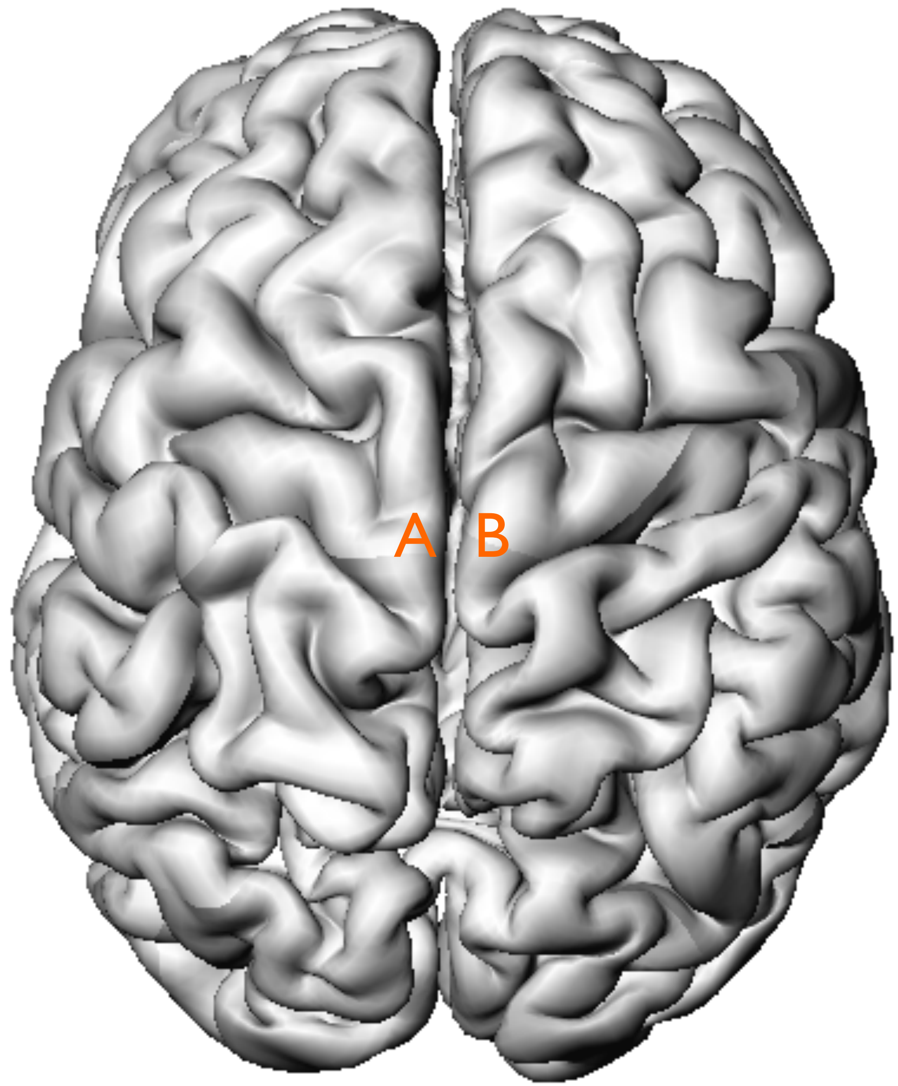
noise cortical thickness

after smoothing

3D Gaussian kernel smoothing will blur measurements between A and B.

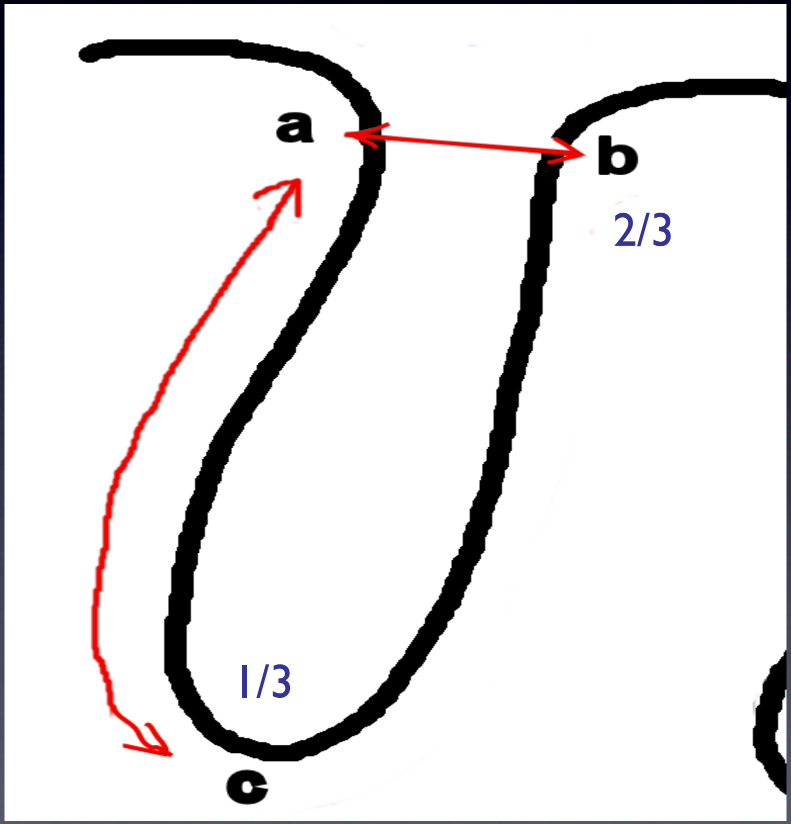
↓

Need to smooth along the surface.

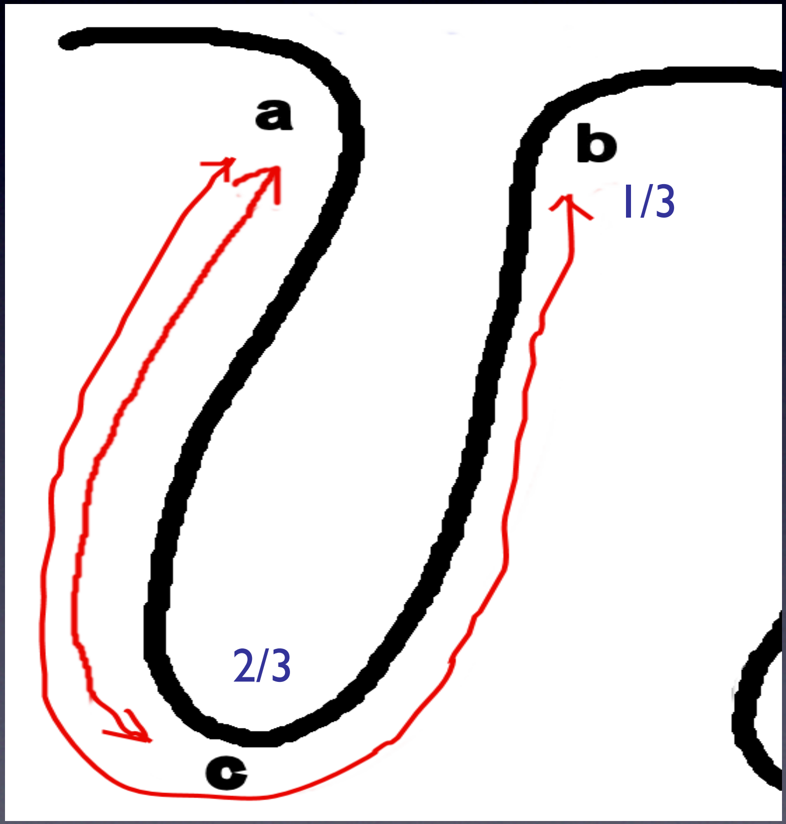


Assigning smoothing kernel weights

Due to curved geometry, the shortest distance between two points is not a straight line. So we may incorrectly assign less weights to closer observations.



3D volume based kernel weighting



2D surface based kernel weighting

Cortical surface smoothing techniques from my group

Chung et al., 2001 NeuroImage 13S:96
Chung et al., 2003 CVPR 467-473
Chung et al., 2005 NeuroImage 25:1256-65
Chung et al., 2005 IPMI 627-638
Chung et al., 2007 IEEE TMI 26:566-581
Chung et al., 2008 IEEE TMI 27:1143-1151
Seo et al., 2010 MICCAI 505-512
Kim et al., 2012 MMBIA

Diffusion smoothing

Chung et al., 2001 NeuroImage 13S:96
Chung et al., 2003 CVPR 467-473

Heat Kernel Smoothing
by approximating Gaussian kernel

Chung et al., 2005 NeuroImage 25:1256-65
Chung et al., 2005 IPMI 627-638

Weighted Fourier
requires mapping to a sphere

Chung et al., 2007 IEEE TMI 26:566-581
Chung et al., 2008 IEEE TMI 27:1143-1151

Heat Kernel Smoothing
via Laplace-Beltrami eigenfunctions

Seo et al., 2010 MICCAI 505-512
Kim et al., 2011 PSIVT 36-47

Sparse Smoothing
via Laplace-Beltrami eigenfunctions

Kim et al., 2012 MMBIA

Polynomial model for surfaces

Parameterization using polynomials

$$f(p) = \beta_0\phi_0(p) + \beta_0\phi_0(p) + \cdots + \beta_k\phi_k(p)$$

We use {1, p, p^2, p^3, p^4, …} as a basis.

Parameters are estimated using the least squares method.

Estimating Fourier coefficients

- For each point p_i , we have measurement $f(p_i)$.
- Corresponding Fourier series:

$$f(p_i) = \beta_0\phi_0(p_i) + \beta_0\phi_0(p_i) + \cdots + \beta_k\phi_k(p_i)$$

- Matrix form:

$$F = \Phi\beta$$

$$\beta = (\Phi'\Phi)^{-1}\Phi' F$$

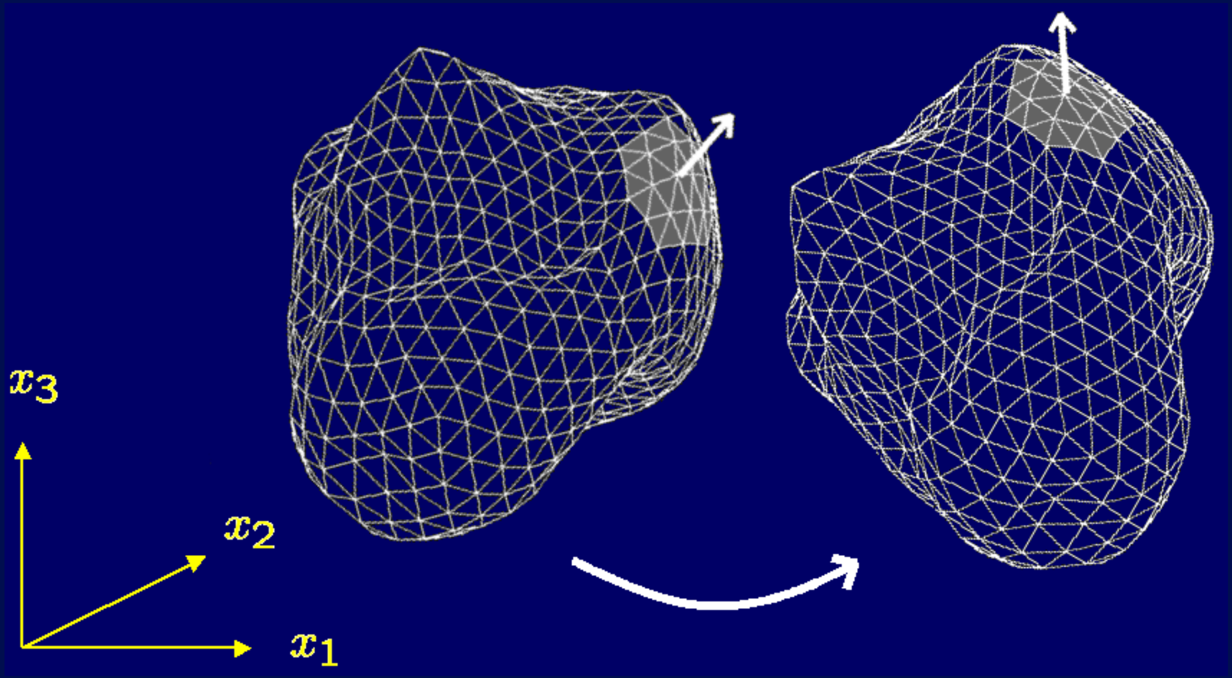
- This is a nontrivial linear problem if *k* is huge.

Exercise. Solve this problem with MATLAB when n, k > 1 million
Answer: attend BMI768

Surface Parameterization via quadratic surface

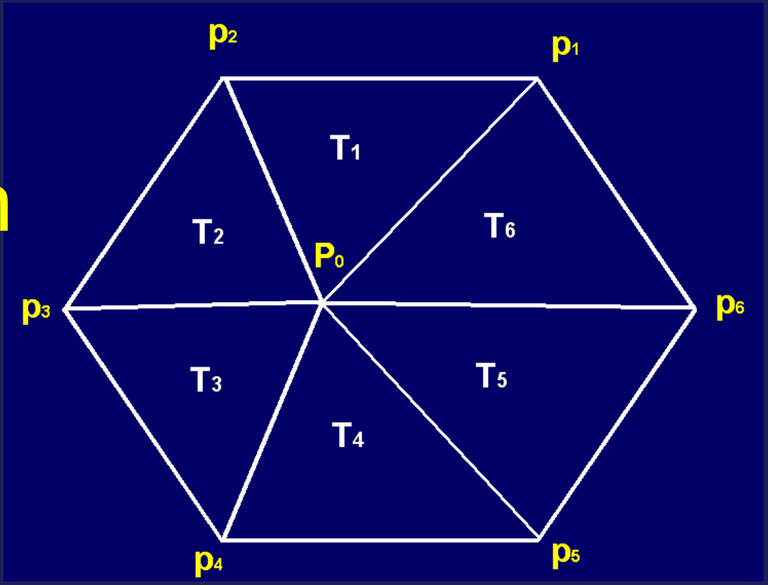
Global: tensor splines, SPHARM
Local: quadratic surface fitting

$$X(u^1, u^2) = \begin{pmatrix} x_1(u^1, u^2) \\ x_2(u^1, u^2) \\ x_3(u^1, u^2) \end{pmatrix}$$



$$s(u^1, u^2) = \beta_1 u_1 + \beta_2 u_2 + \beta_3 u_1^2 + 2\beta_4 u_1 u_2 + \beta_5 u_2^2 + \cdots$$

Polynomial regression on irregular triangular mesh

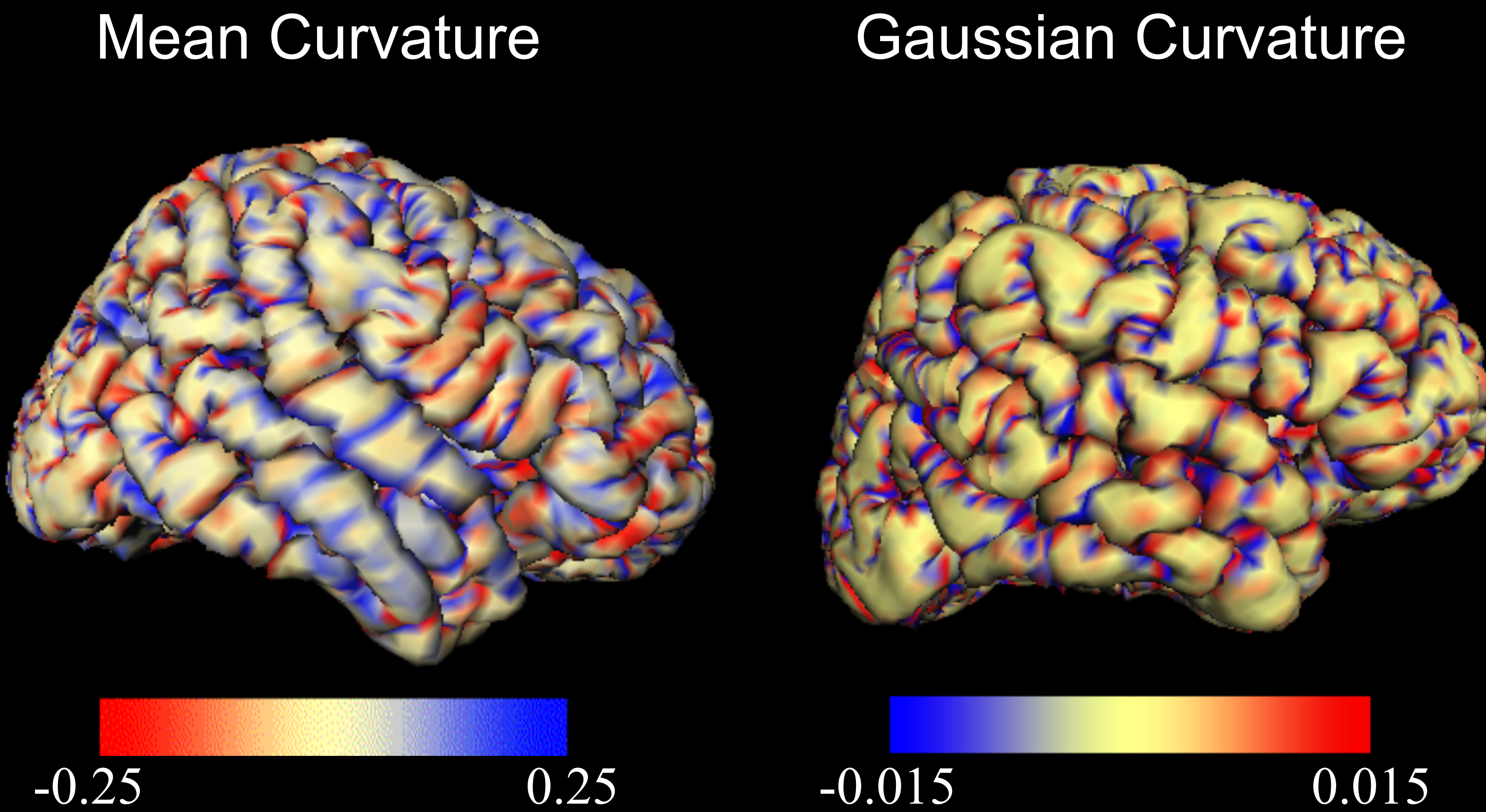


$$Y = \mathbb{X}\beta$$

$$\begin{pmatrix} u_1^3 \\ u_2^3 \\ \vdots \\ u_m^3 \end{pmatrix} = \begin{pmatrix} u_1^1 & u_1^2 & (u_1^1)^2 & u_1^1 u_1^2 & (u_1^2)^2 \\ u_2^1 & u_2^2 & (u_2^1)^2 & u_2^1 u_2^2 & (u_2^2)^2 \\ \cdots & \cdots & \cdots & \cdots & \cdots \\ u_m^1 & u_m^2 & (u_m^1)^2 & u_m^1 u_m^2 & (u_m^2)^2 \end{pmatrix} \begin{pmatrix} \beta_1 \\ \beta_2 \\ \vdots \\ \beta_m \end{pmatrix}$$

$$\hat{\beta} = (\mathbb{X}'\mathbb{X})^{-}\mathbb{X}'Y$$

Curvature estimation from polynomial fit

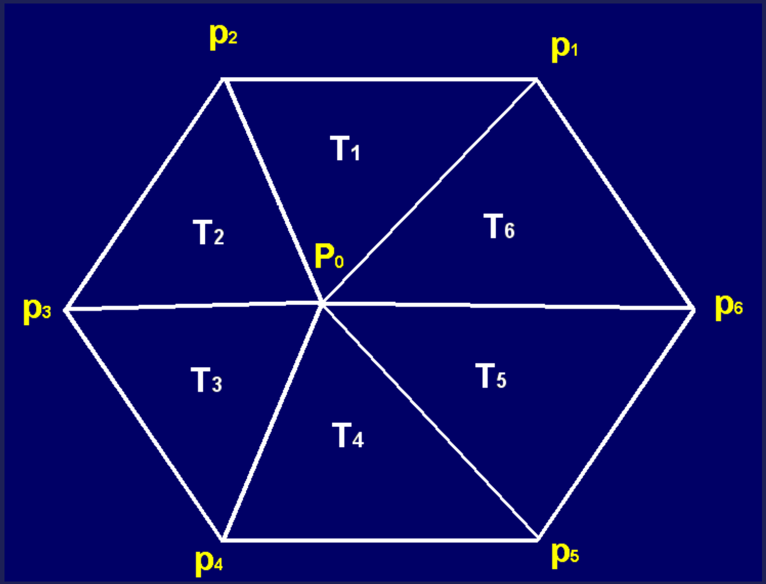


Exercise. Compute curvatures for brain surfaces. This is not an easy problem. Due to high noise, you won't be able to display this type of smooth curvature maps.

Laplace-Beltrami Operator

$$\Delta_X F = \frac{1}{|g|^{1/2}} \sum_{i,j=1}^{2} \frac{\partial}{\partial u^i}\left(|g|^{1/2} g^{ij} \frac{\partial F}{\partial u^j}\right)$$

Estimating differential operator on manifolds



$$\widehat{\Delta} F(p_0) = w_0 F(p_0) + w_1 F(p_1) + \cdots + w_m F(p_m)$$

Estimation via conformal transformation

$$s(u^1, u^2) = \beta_1 u_1 + \beta_2 u_2 + \beta_3 u_1^2 + 2\beta_4 u_1 u_2 + \beta_5 u_2^2 + \cdots$$

$$g = \begin{pmatrix} 1+\beta_1^2 & \beta_1\beta_2 \\ \beta_1\beta_2 & 1+\beta_2^2 \end{pmatrix}$$

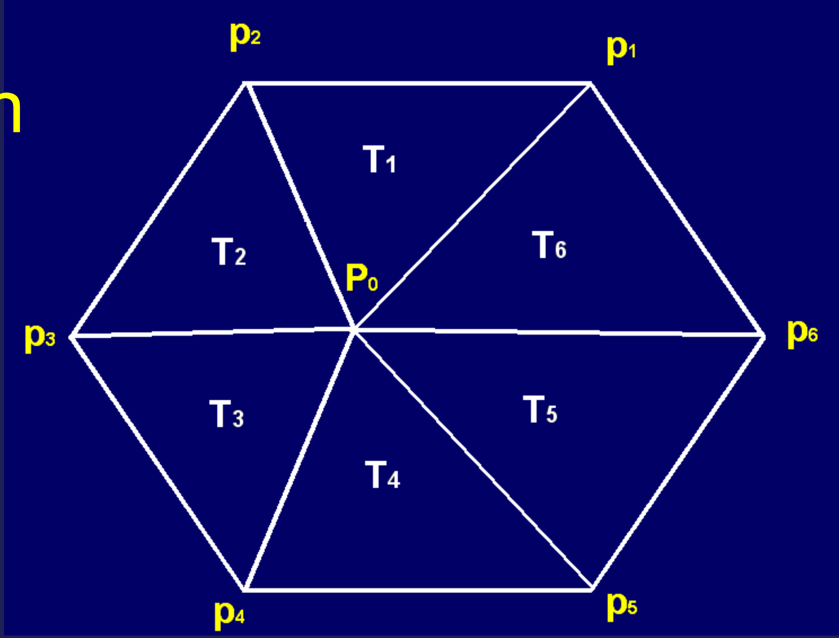
Laplace-Beltrami
operator is invariant

$$s(v^1, v^2) = \gamma_1 (v^1)^2 + \gamma_2 v^1 v^2 + \gamma_3 (v^2)^2 + \cdots$$

$$g = \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix}$$

$$\Delta_X = \frac{1}{\lambda}\left(\frac{\partial^2}{\partial^2 u^1} + \frac{\partial^2}{\partial^2 u^2}\right)$$

Estimating the planar Laplacian on irregular triangular mesh



$$Y = \mathbb{X}\beta$$

$$\begin{pmatrix} F(p_1) - F(p_0) \\ F(p_2) - F(p_0) \\ \vdots \\ F(p_m) - F(p_0) \end{pmatrix} = \begin{pmatrix} v_1^1 & v_1^2 & (v_1^1)^2 & v_1^1 v_1^2 & (v_1^2)^2 \\ v_2^1 & v_2^2 & (v_2^1)^2 & v_2^1 v_2^2 & (v_2^2)^2 \\ \cdots & \cdots & \cdots & \cdots & \cdots \\ v_m^1 & v_m^2 & (v_m^1)^2 & v_m^1 v_m^2 & (v_m^2)^2 \end{pmatrix} \begin{pmatrix} \frac{\partial F(p_0)}{\partial v^1} \\ \frac{\partial F(p_0)}{\partial v^2} \\ \frac{\partial^2 F(p_0)}{\partial (v^1)^2} \\ \frac{\partial^2 F(p_0)}{\partial v^1 \partial v^2} \\ \frac{\partial^2 F(p_0)}{\partial (v^2)^2} \end{pmatrix}$$

Diffusion smoothing

Chung et al., 2001 NeuroImage 13S:96
Chung et al., 2003 CVPR 467-473

Diffusion smoothing

Diffusion equation

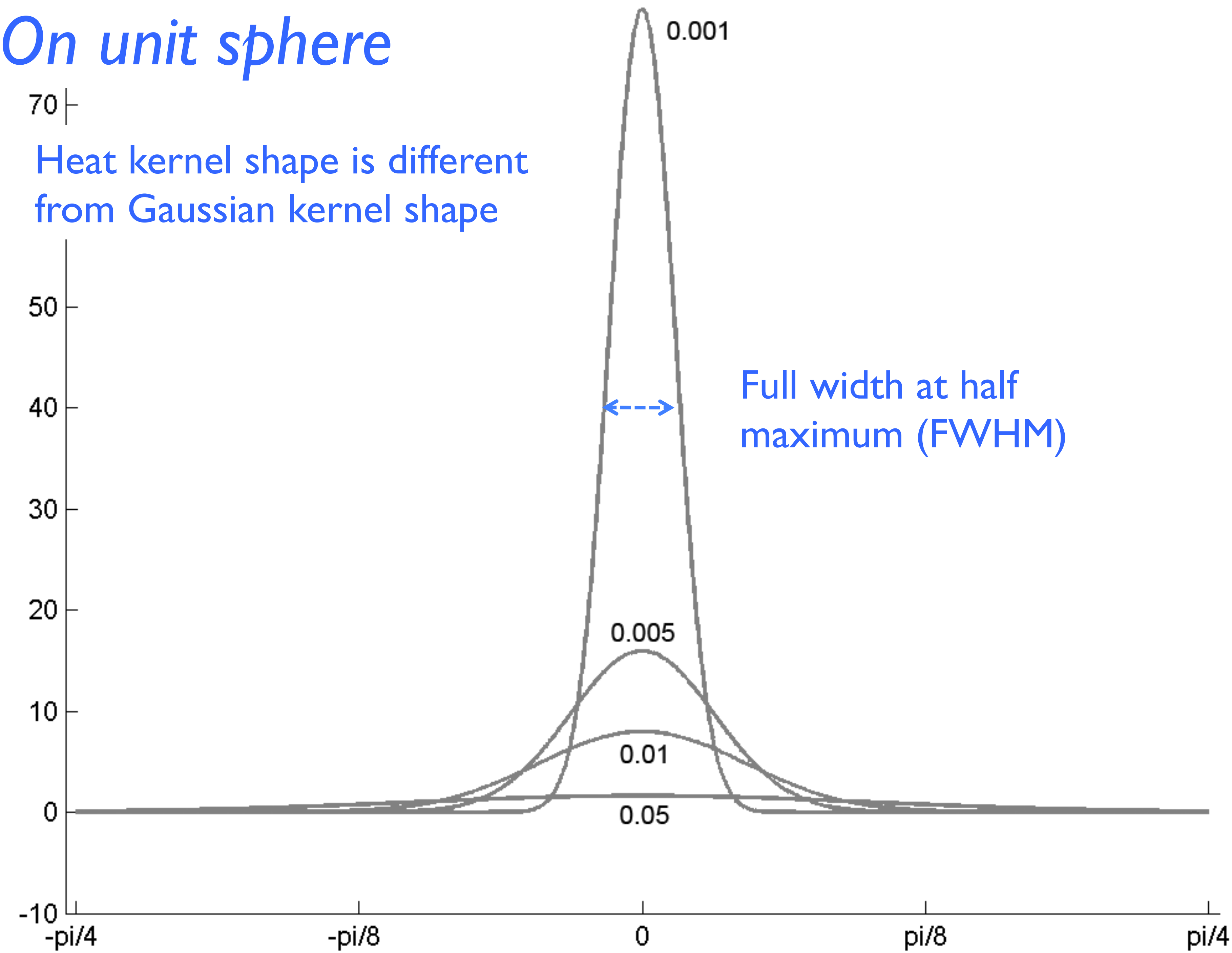
$$\frac{\partial f}{\partial t} = \Delta f, \; f(x, t = 0) = X(x)$$

$$\sigma = \sqrt{2t}$$

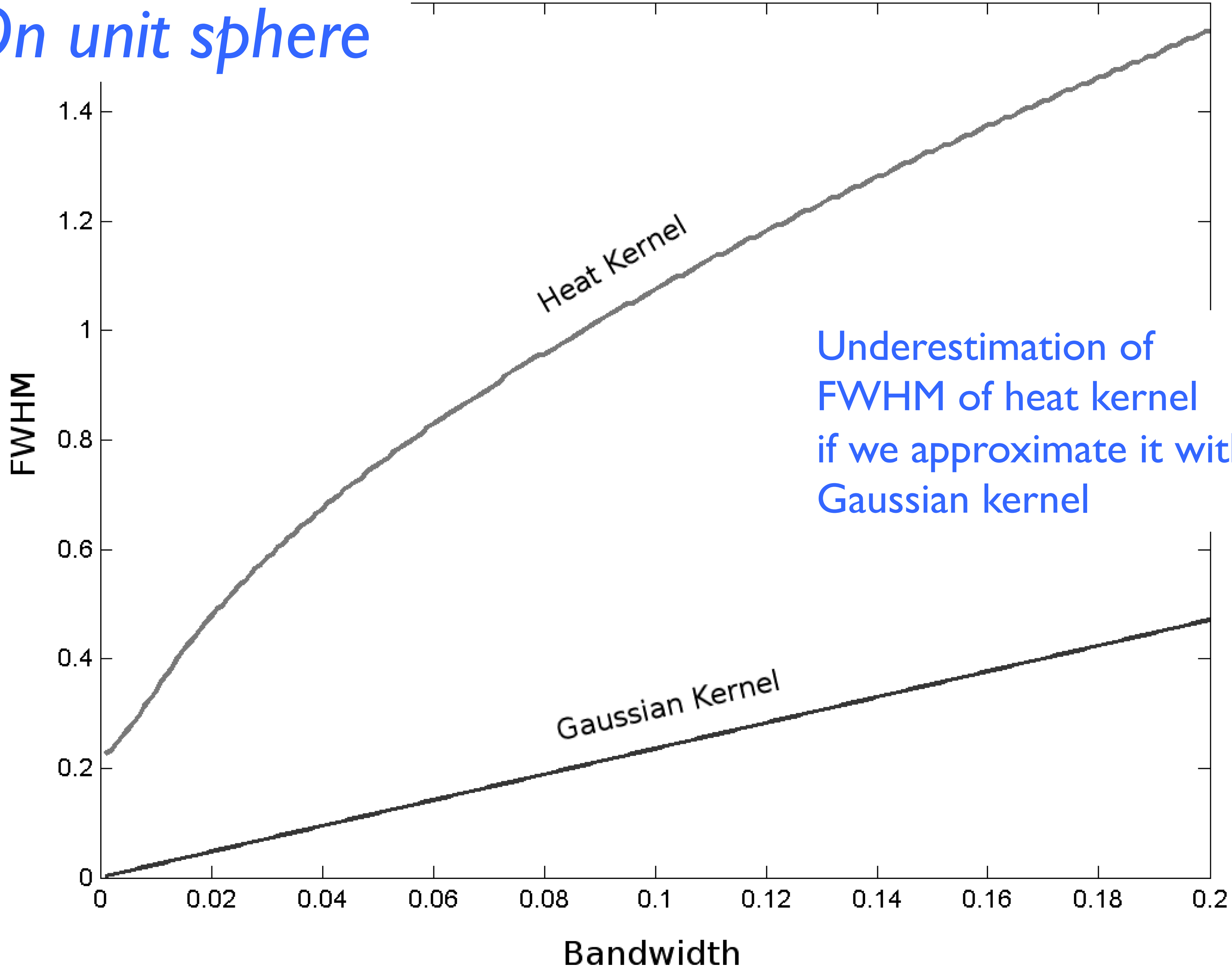
Heat kernel smoothing

$$f = K_\sigma * X$$

On unit sphere



On unit sphere



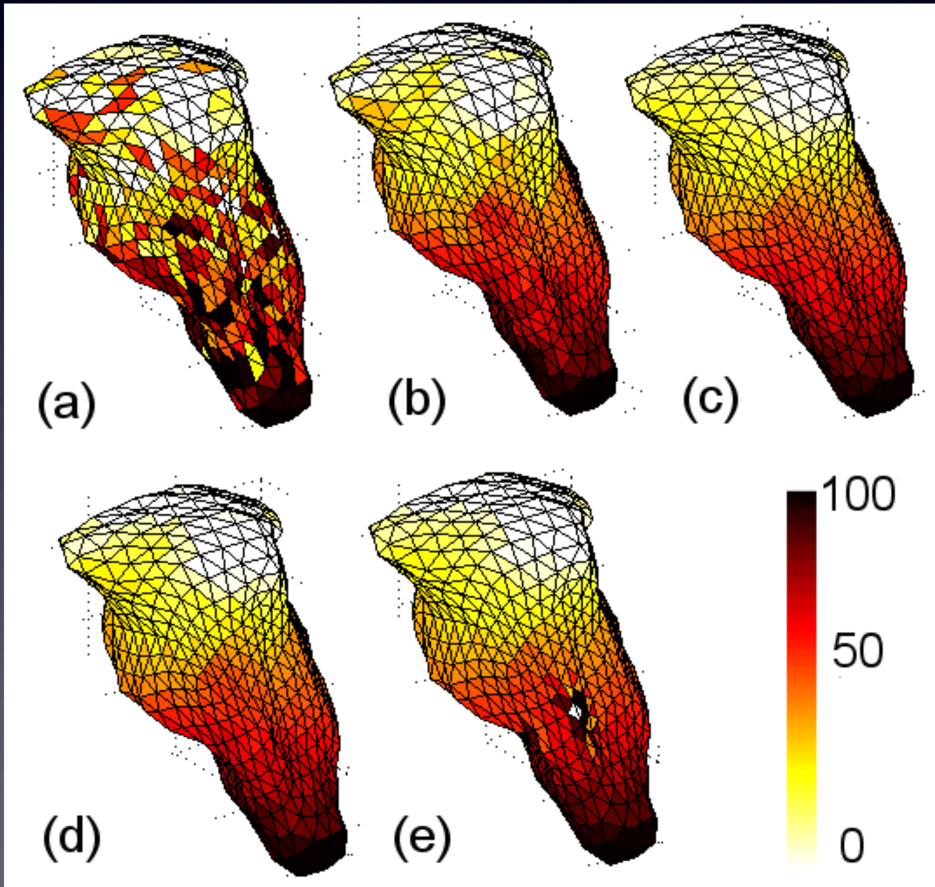
Underestimation of FWHM of heat kernel if we approximate it with Gaussian kernel

Diffusion equation approaches

Andrade et al. 2001 -- Quadratic polynomial fitting
Chung et al. 2001 -- Cotan formulation

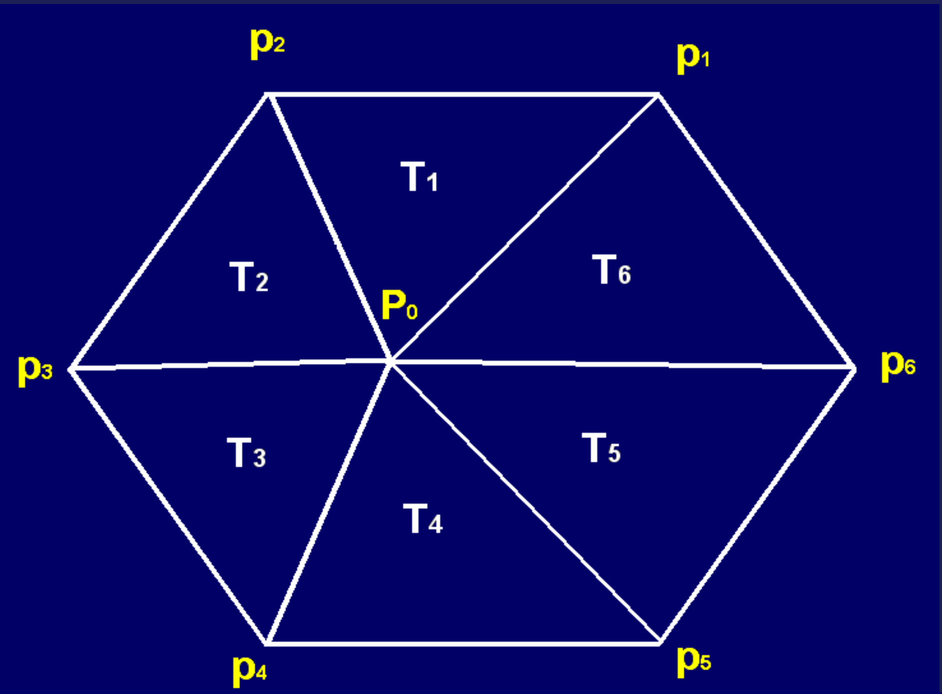
- Need to discretize PDF

- Possible numerical instability in the forward Euler scheme



FEM-based cotan formulation for LB-operator

$$\Delta_X F = \frac{1}{|g|^{1/2}} \sum_{i,j=1}^{2} \frac{\partial}{\partial u^i}\left(|g|^{1/2} g^{ij} \frac{\partial F}{\partial u^j} \right)$$



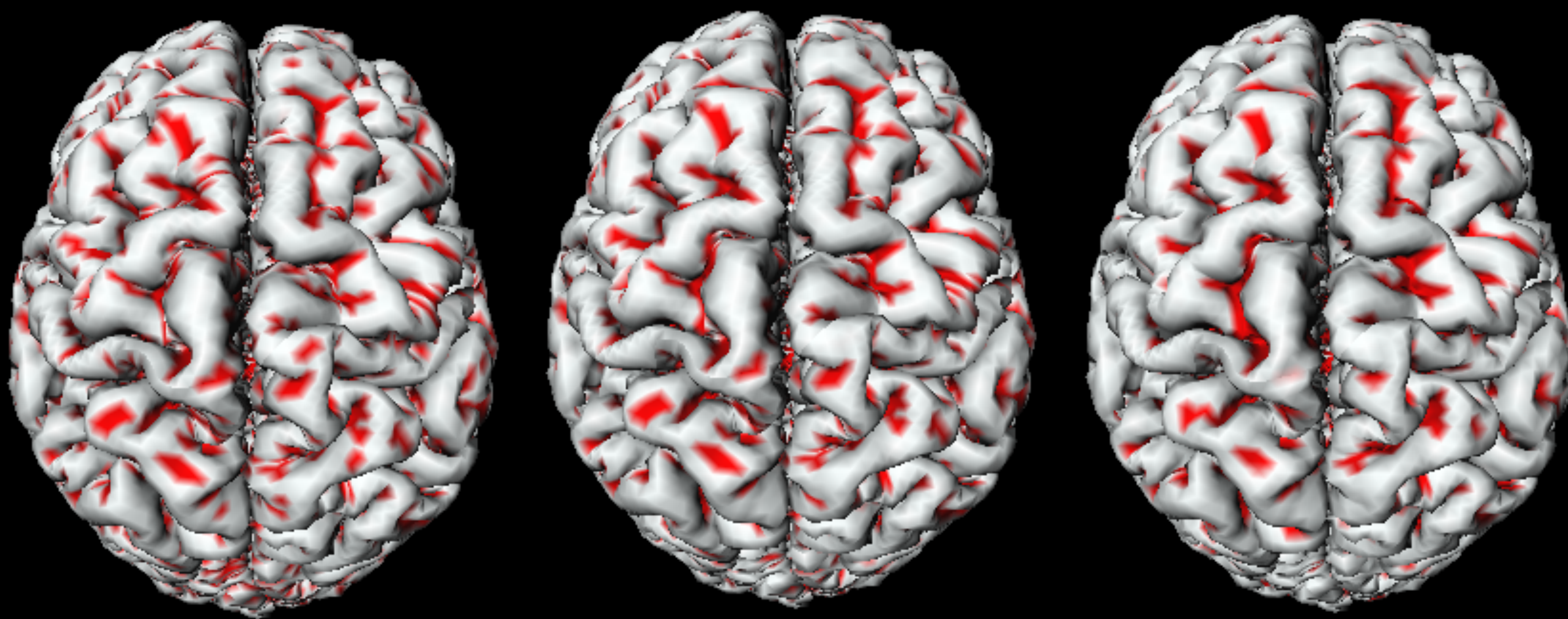
$$w_i = \frac{\cot\theta_i + \cot\phi_i}{\sum_{i=1}^{m} |T_i|}$$

$$\widehat{\Delta} F(p_0) = w_0 F(p_0) + w_1 F(p_1) + \cdots + w_m F(p_m)$$

Chung et al., 2001, OHBM, 2003 CVPR.

Lopez-Perez et al, 2004, ECCV.

5mm FWHM Diffusion Smoothing



mean curvature

20 iterations

100 iterations

Heat Kernel Smoothing
by approximating Gaussian kernel

Chung et al., 2005 NeuroImage 25:1256-65
Chung et al., 2005 IPMI 627-638

Approximating heat kernel with Gaussian kernel

Parametrix expansion (*Rosenberg, 1997*):

$$K_\sigma(p,q) \quad = \quad \frac{1}{(4\pi\sigma)^{1/2}} e^{-\frac{d^2(p,q)}{4\sigma}} \left[1 + O(\sigma^2)\right]$$

For small bandwidth and close *p* and *q*,
heat kernel collapses to Gaussian kernel.

Iterative kernel smoothing

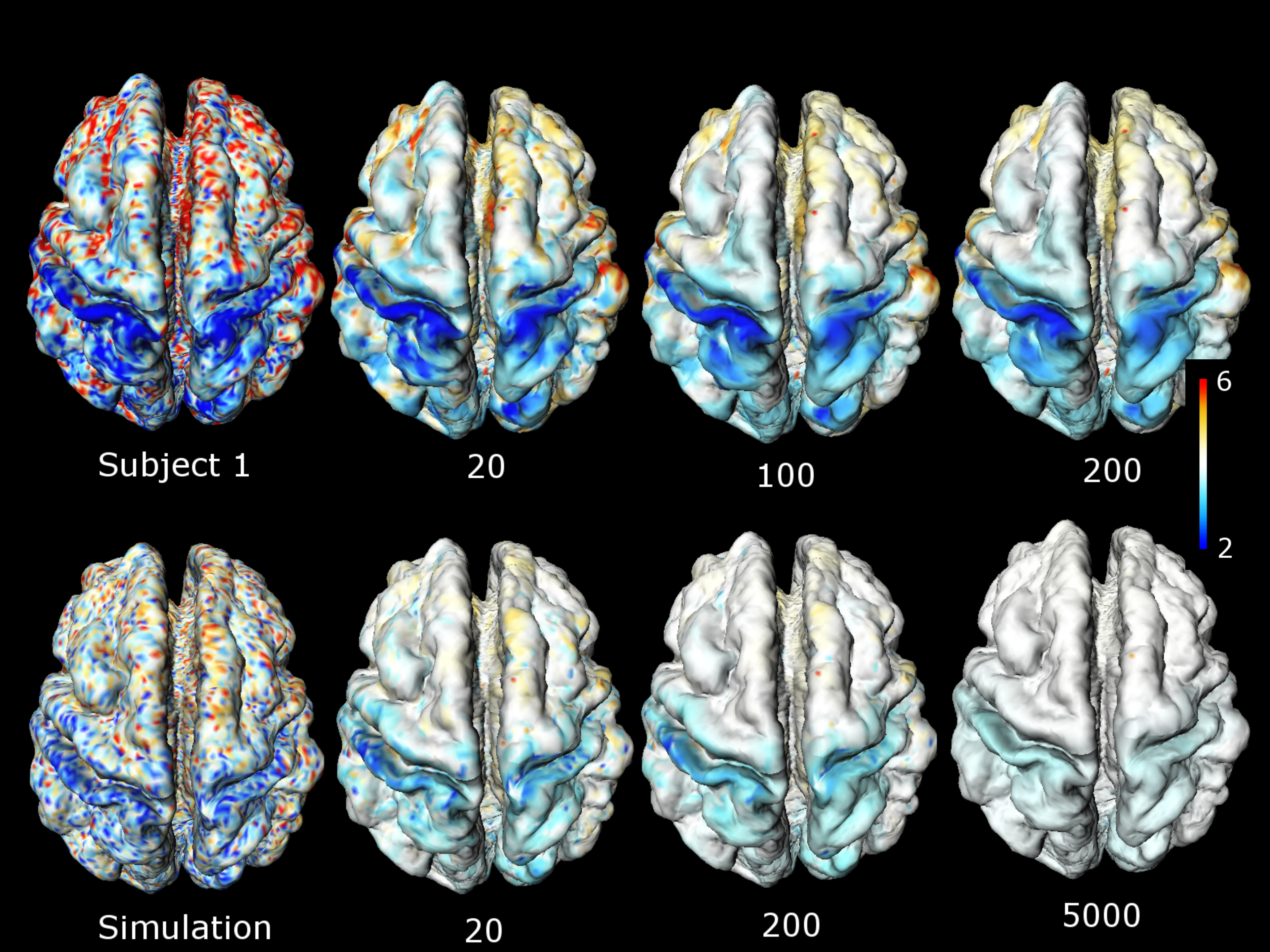
Most widely used cortical smoothing approach
Implemented in almost all brain imaging tools
SurfStat, FreeSurfer, AFNI

$$K_{k\sigma} * f = \underbrace{K_\sigma * \cdots * K_\sigma}_{k \text{ times}} * f$$

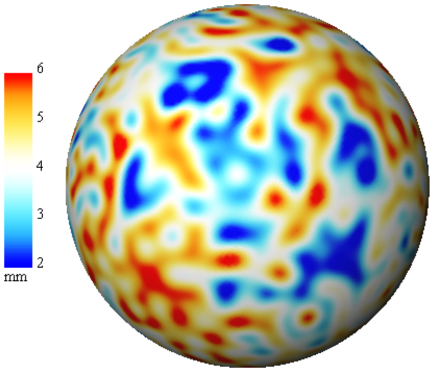
Studies that used MATLAB tools given in *Chung et al. NeuroImage (2005)*

Between 2006-2007:

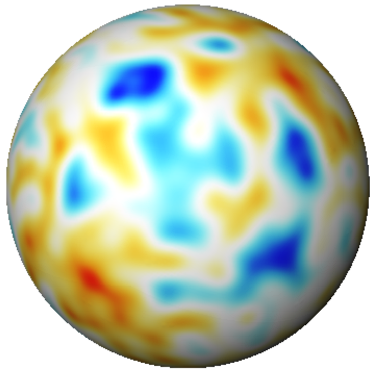
cortical curvatures (Luders, 2006; Gaser, 2006)
cortical thickness (Luders, 2006; Bernal-Rusiel, 2008)
hippocampus shape (Shen, 2006; Zhu, 2007)
magnetoencephalography (Han, 2007)
functional-MRI (Hagler, 2006; Jo, 2007)


Subject 1
20
100
200
6
2
Simulation
20
200
5000

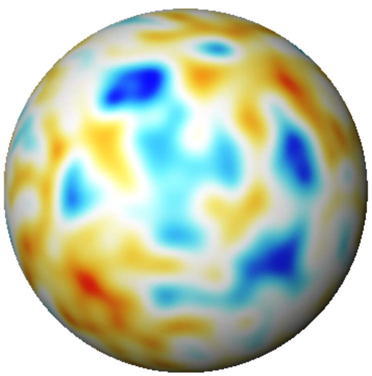
Iteration does not converge well



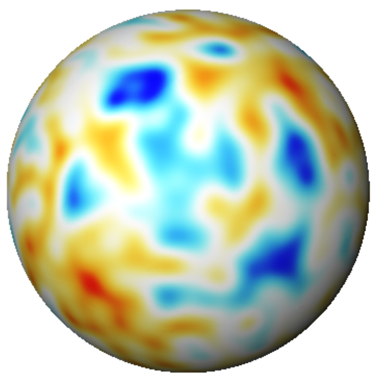
Simulated cortical thickness



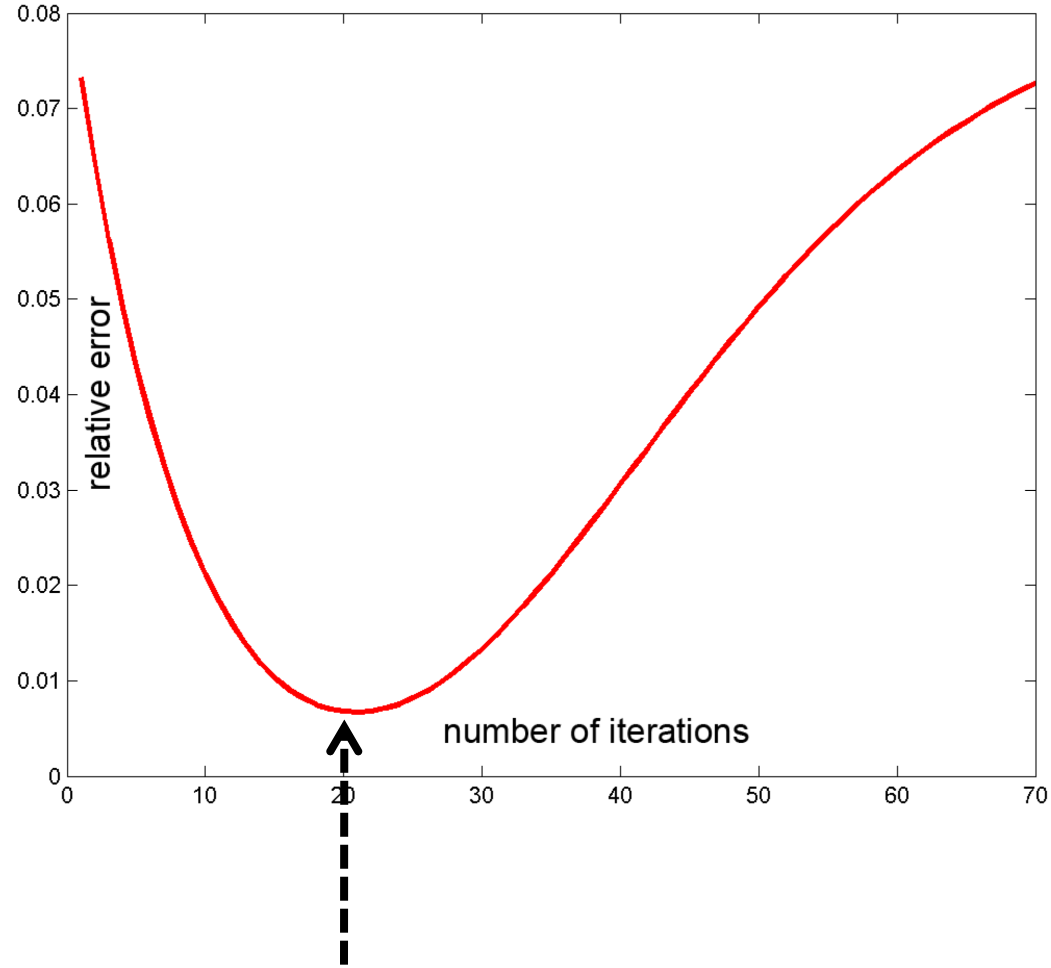
Ground truth



Analytic implementation



Iterated kernel smoothing



Iterated kernel smoothing error 0.0067

Weighted Fourier
requires mapping to a sphere

Chung et al., 2007 IEEE TMI 26:566-581
Chung et al., 2008 IEEE TMI 27:1143-1151

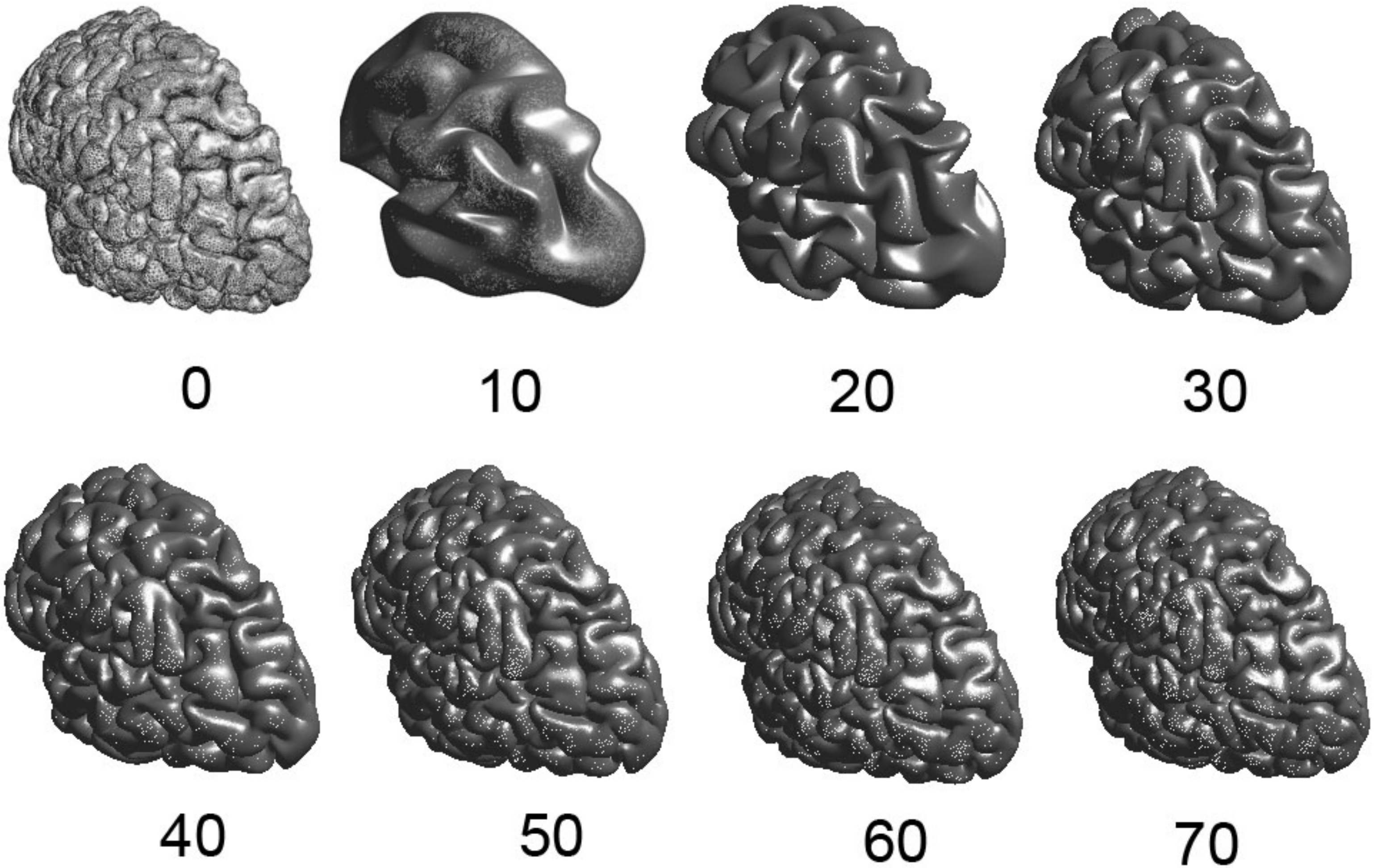
Spherical harmonic (SPHARM) representation

It is a technique for parameterizing anatomical boundaries using the spherical harmonic basis.

The surface coordinates x,y, z are expressed as a linear combination of basis functions. For instance,

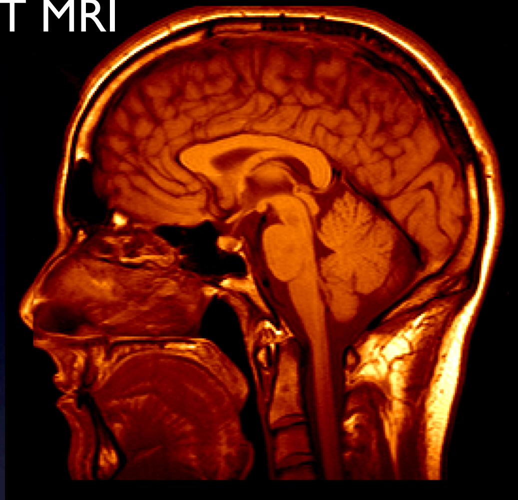
$$x(p) = \sum_{j=0}^{k} \beta_j \psi_j(p)$$

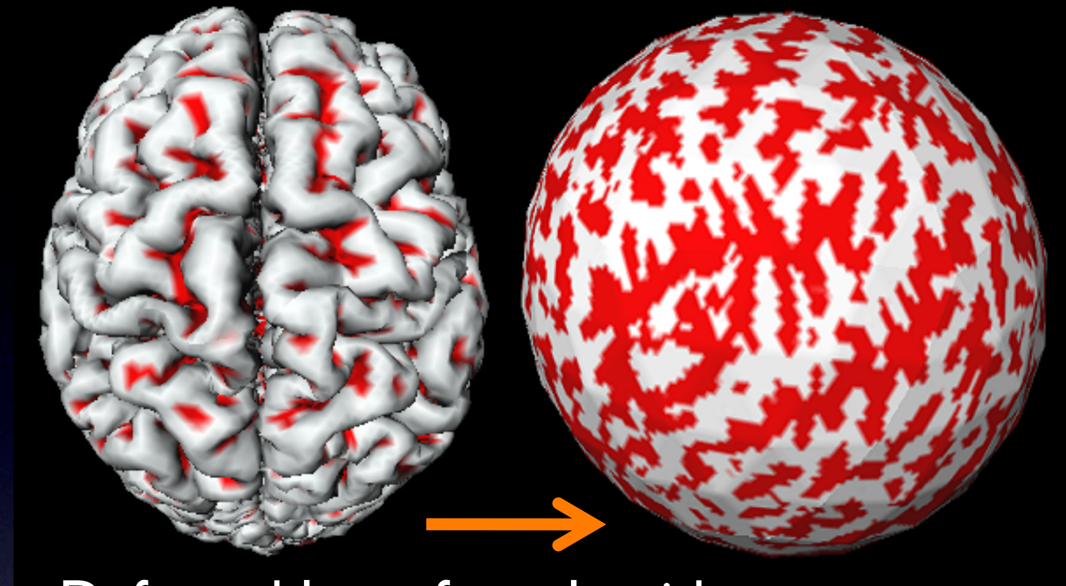
FreeSurfer results



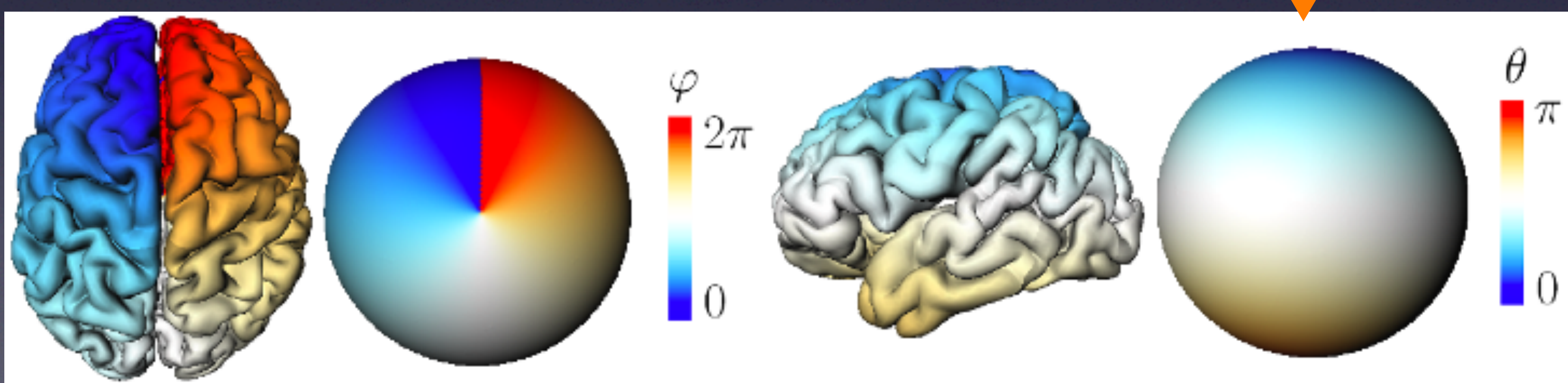
Cortical surface flattening

3T MRI



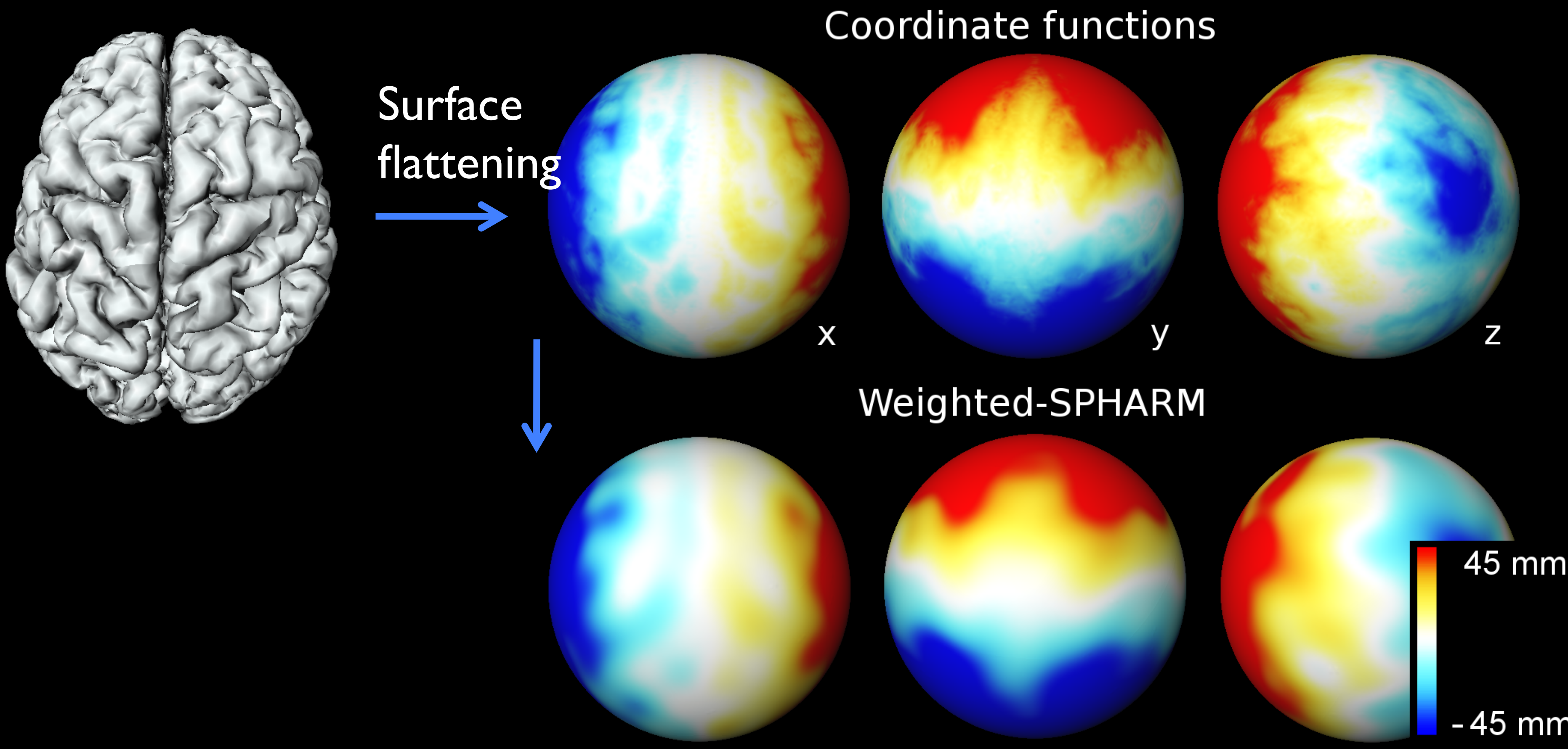


Deformable surface algorithm
(McDonalds et al., 2001)

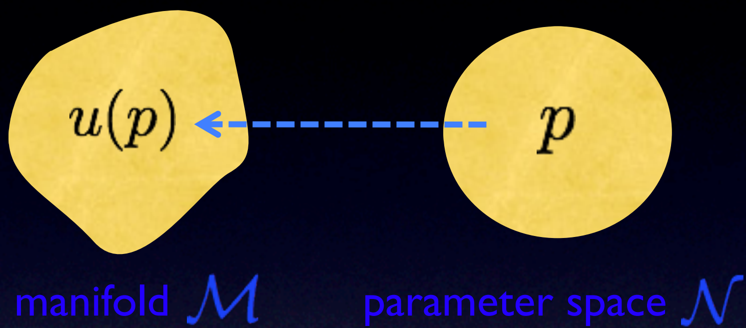


Euler angle based coordinate system

Map coordinate functions to a unit sphere



Smoothing in manifold



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

↓

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 $\mathcal{L}$

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

Basis function

PDE, series expansion, kernel smoothing

t = scale, bandwidth, diffusion time

Input signal

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

Analytic representation

Weighed eigenfunction expansion

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

Kernel smoothing

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

Chung et al., 2007. IEEE TMI

Spherical harmonics

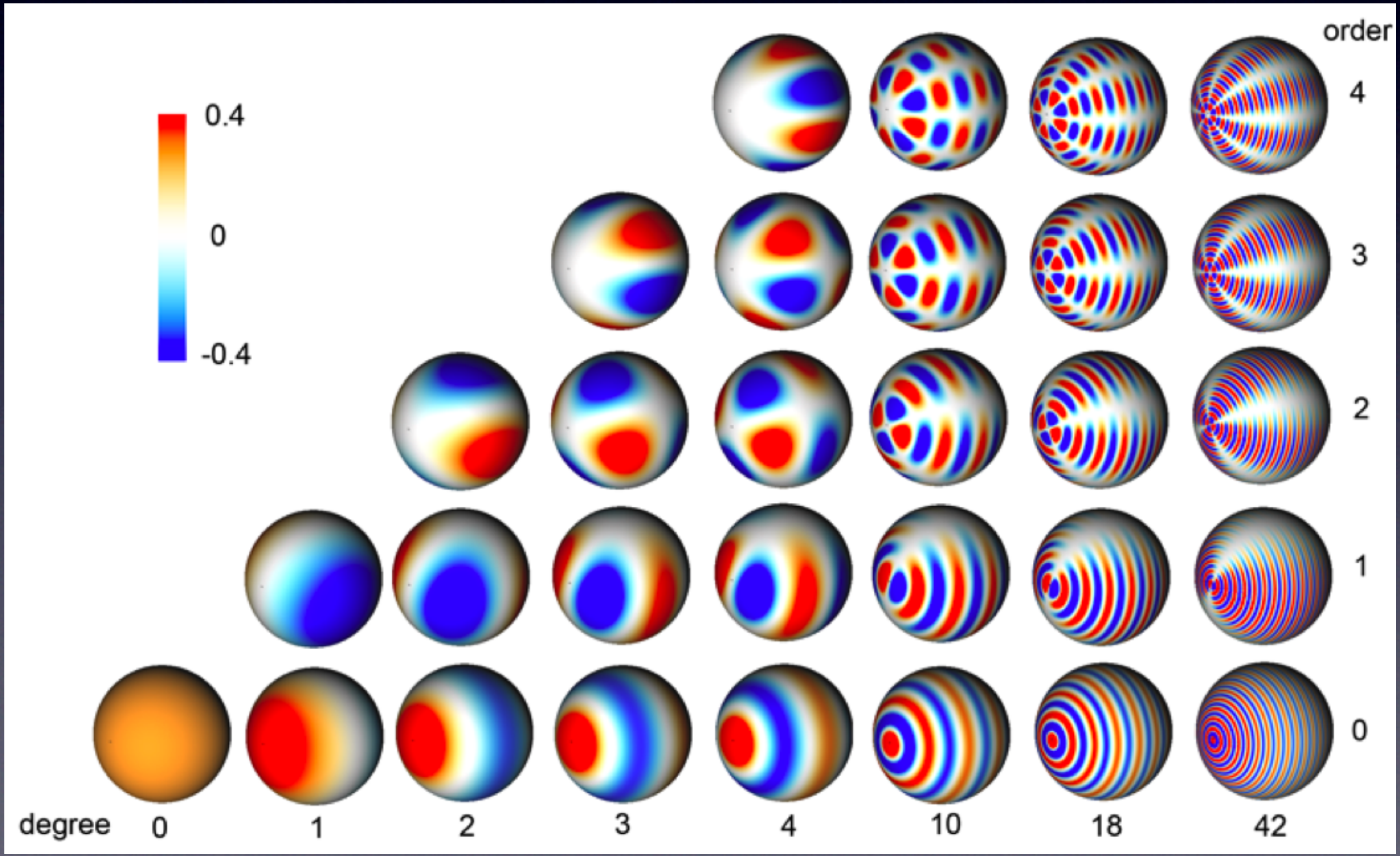
Y_{lm} is called the *spherical harmonic* of degree l and order m .

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

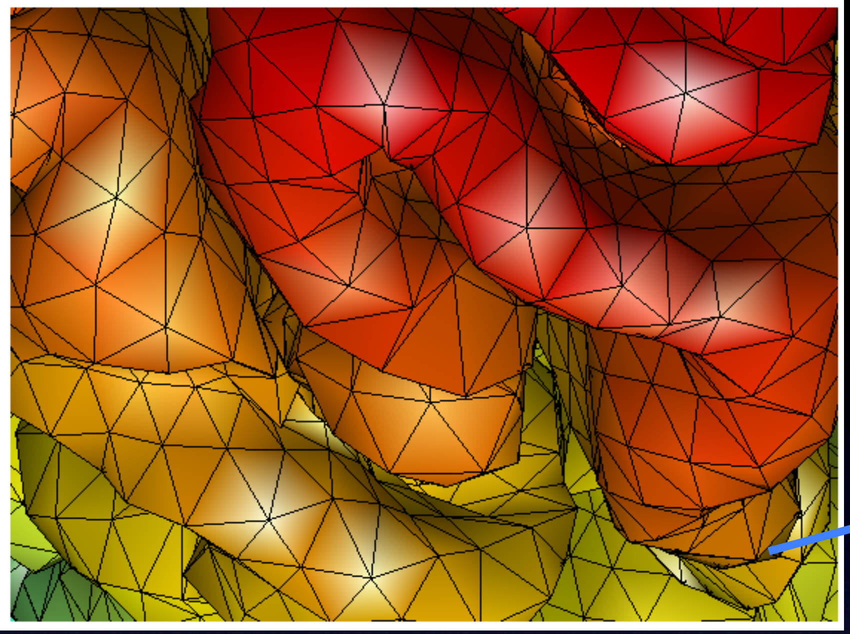
where $c_{lm} = \sqrt{\frac{2l+1}{2\pi}\frac{(l-|m|)!}{(l+|m|)!}}$ and P_l^m is the associated Legendre polynomials of order m.

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

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



Least squares estimation of Fourier coefficients



i-th vertex

$$f(p_i) = \sum_{j=0}^{k} \beta_j \psi_j(p_i)$$

$$\mathbf{f} = (f(p_1), \cdots, f(p_n))'$$

$$\beta = (\beta_0, \cdots, \beta_k)'$$

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

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

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

- For measurements $f(p_1), f(p_2), \cdots, f(p_n)$, $(n > 46,000)$, we set up normal equations:

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

***i*-th mesh vertex**

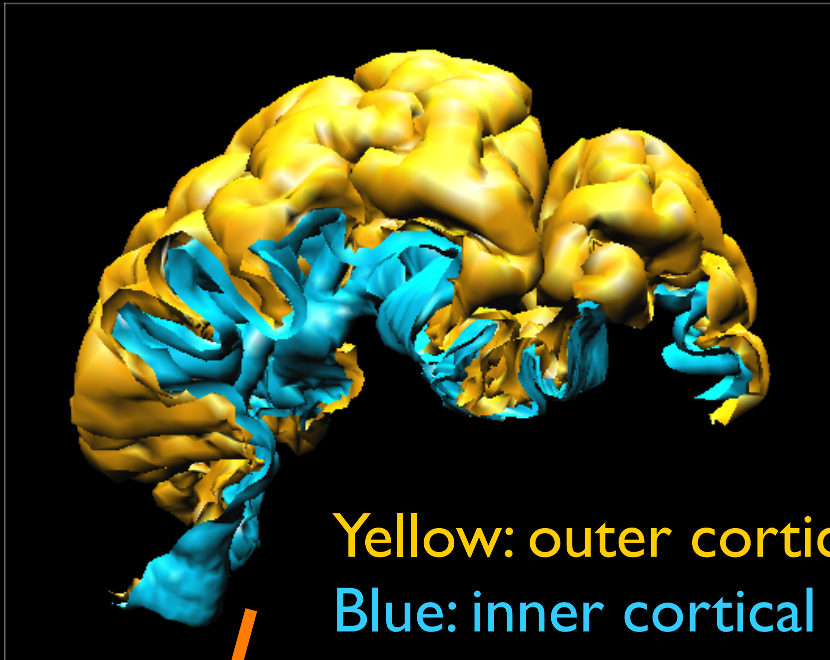
- Matrix form:

$$\underbrace{\begin{pmatrix} f(p_1) \\ f(p_2) \\ \vdots \\ f(p_n) \end{pmatrix}}_{\mathbf{F}} = \underbrace{\begin{pmatrix} Y_{00}(p_1) & Y_{1-1}(p_1) & Y_{10}(p_1) & \cdots & Y_{kk}(p_1) \\ Y_{00}(p_2) & Y_{1-1}(p_2) & Y_{10}(p_2) & \cdots & Y_{kk}(p_2) \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ Y_{00}(p_n) & Y_{1-1}(p_n) & Y_{10}(p_n) & \cdots & Y_{kk}(p_n) \end{pmatrix}}_{\mathbf{Y}} \underbrace{\begin{pmatrix} \beta_{00} \\ \beta_{1-1} \\ \vdots \\ \beta_{kk} \end{pmatrix}}_{\beta}$$

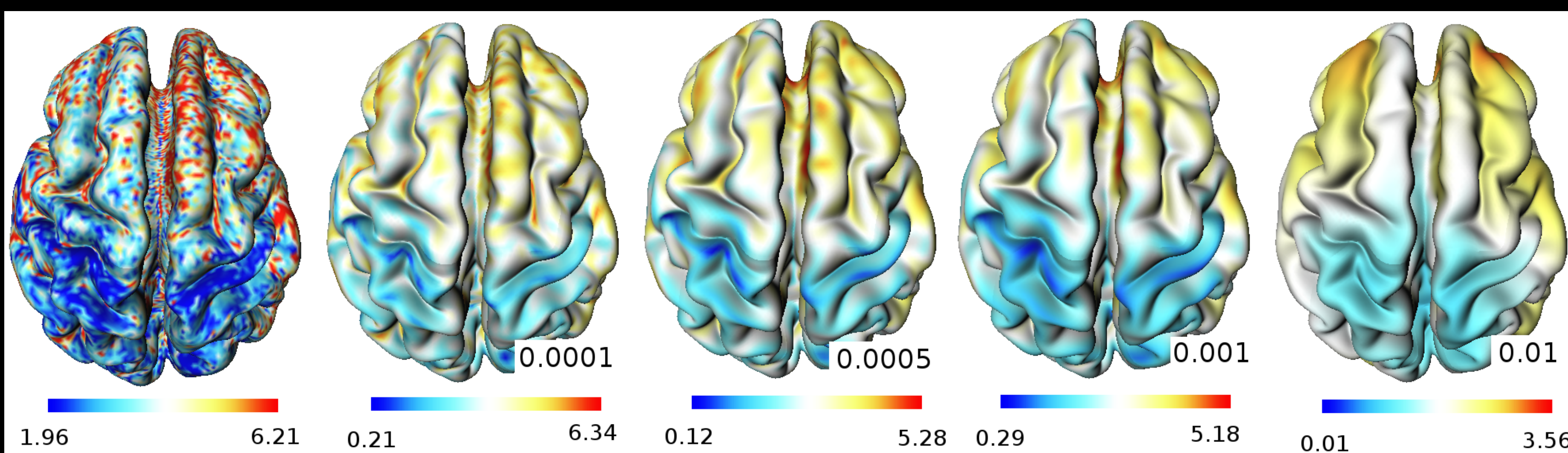
40962 x 7000

Estimation: $\widehat{\beta} = (\mathbf{Y}'\mathbf{Y})^{-1}\mathbf{Y}'\mathbf{F}$.

Weighted-SPHARM of cortical thickness



Yellow: outer cortical surface
Blue: inner cortical surface



Determining the optimal degree via stepwise forward model selection framework

Consider the following $(k-1)$-th degree model

$$f(p_i) = \sum_{l=0}^{k-1} \sum_{m=-l}^{l} e^{-\lambda(l+1)\sigma} f_{lm} Y_{lm}(p_i) + \epsilon(p_i), \ i = 1, \cdots, n$$

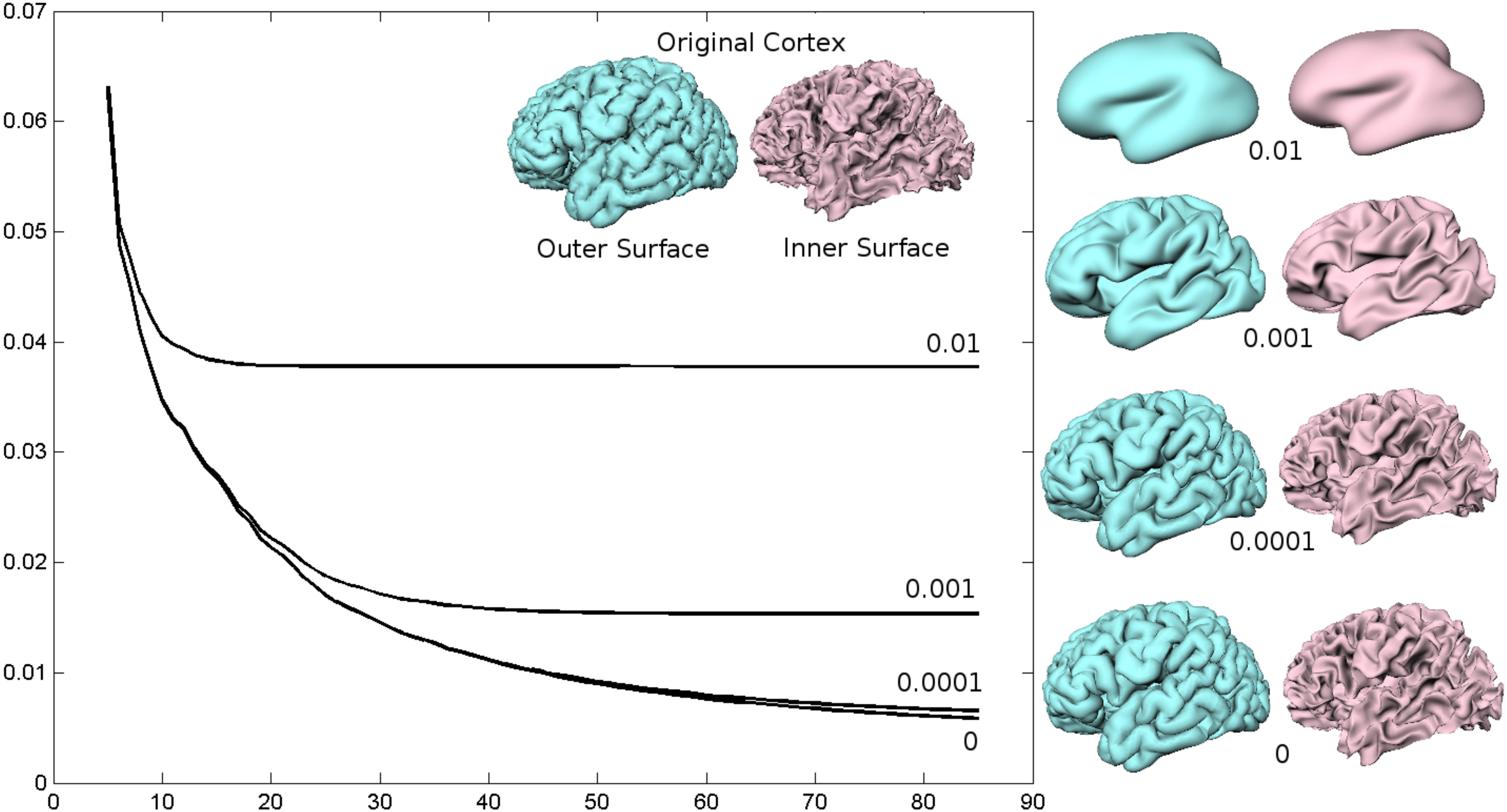
where ϵ are Gaussian random variables. Testing if the k-th degree model is better than the previous $(k-1)$-th degree model can be done by testing

$$H_0 : f_{km} = 0 \text{ for all } -k \leq m \leq k.$$

Then under the null hypothesis, the test statistic is

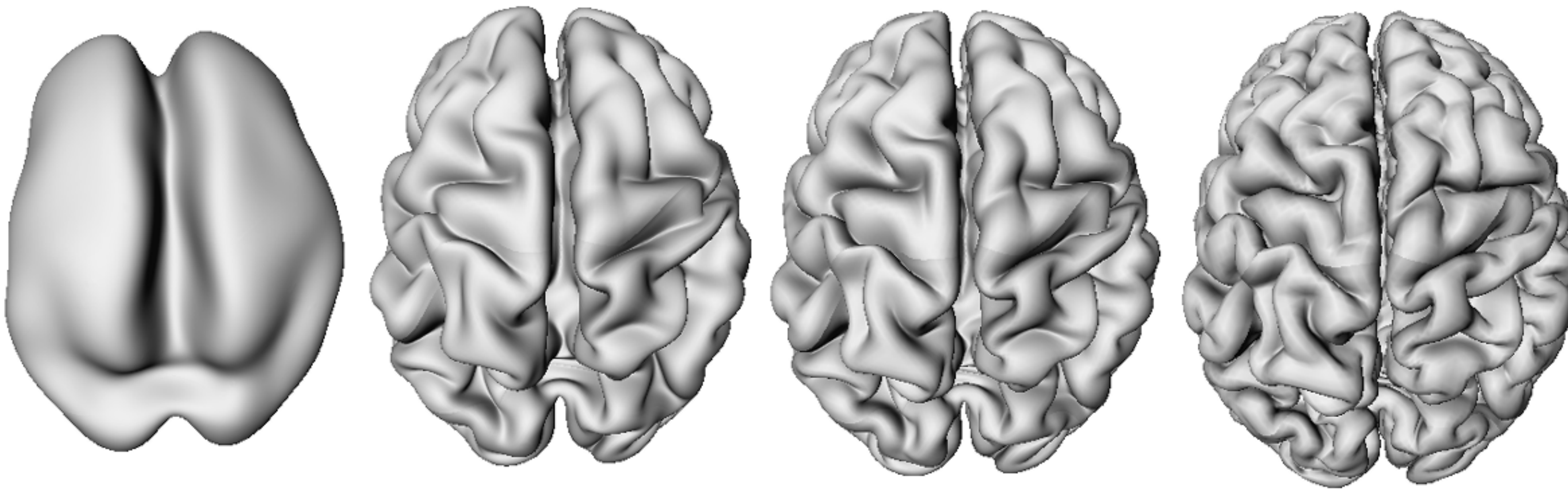
$$F = \frac{(\text{SSE}_{k-1} - \text{SSE}_k)/(2k+1)}{\text{SSE}_{k-1}/(n-(k+1)^2)} \sim F_{2k+1, n-(k+1)^2}$$

Weighted-SPHARM at the 80th degree for different bandwidth



Root mean squared error (RMSE)
= error between original surface and weighted-SPHARM

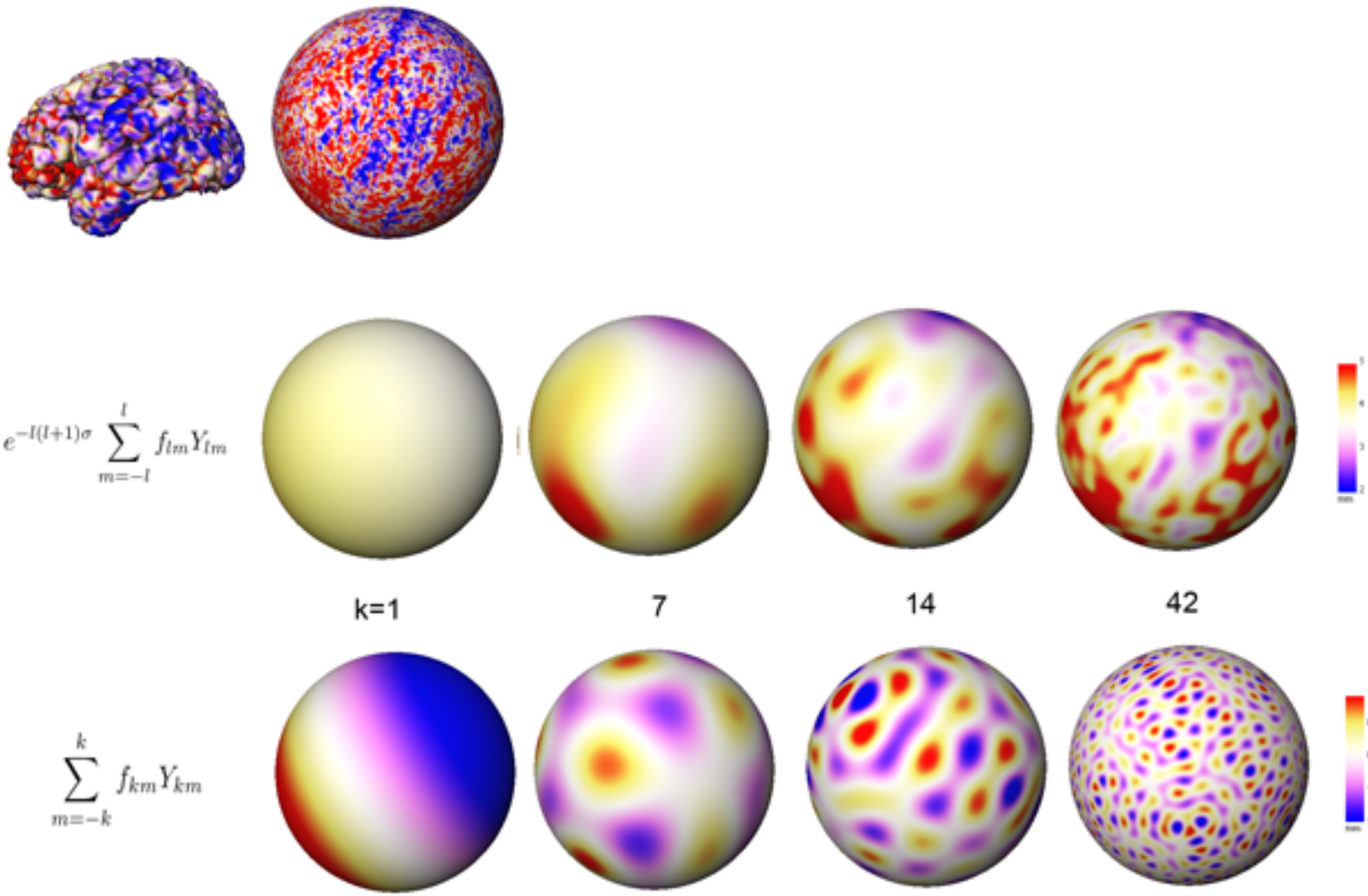
Weighted-SPHARM at different bandwidth



0.01 0.001 0.0005 0.0001

- The degree is selected automatically.
- The only free parameter in the model is the bandwidth.

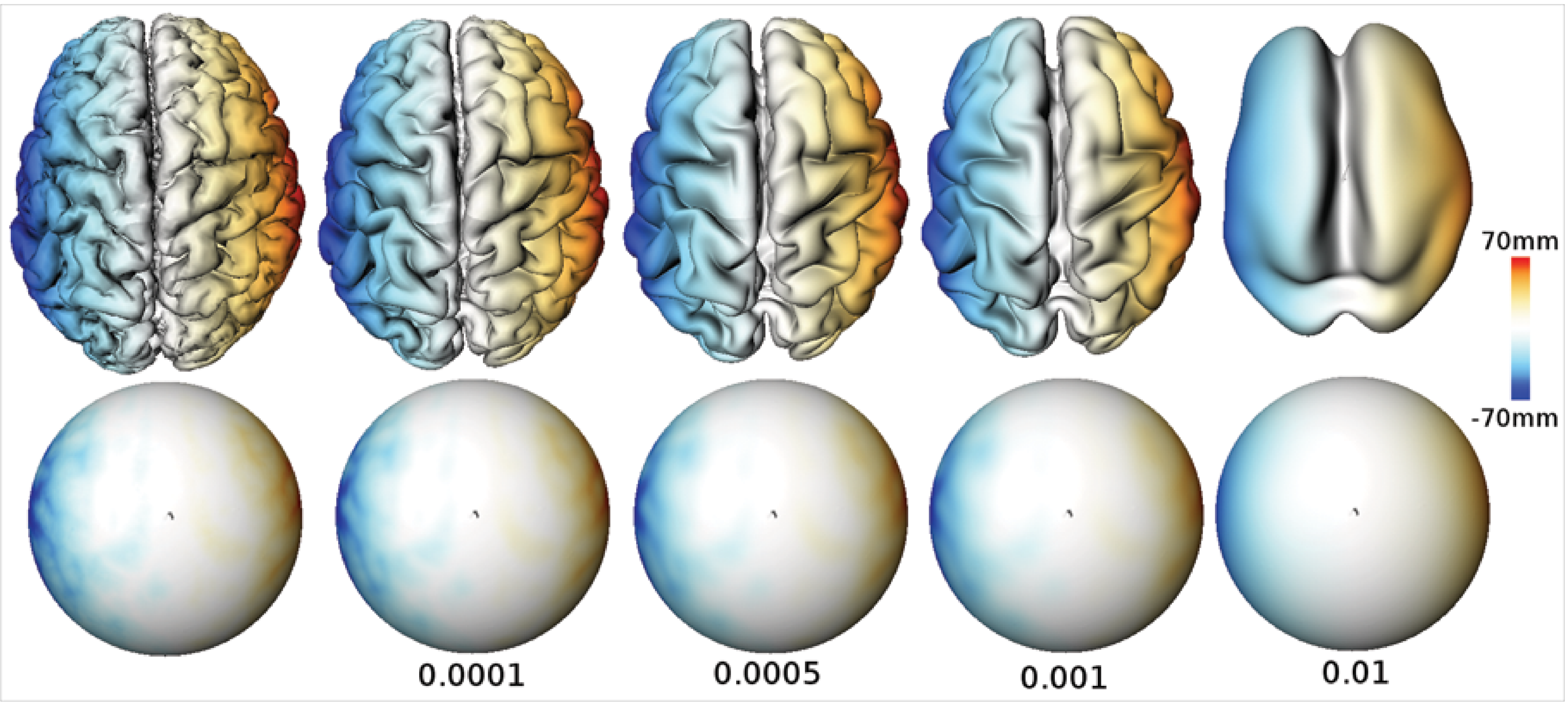
Weighted-SPHARM of cortical thickness



$$\sum_{l=1}^{k} e^{-l(l+1)\sigma} \sum_{m=-l}^{l} f_{lm} Y_{lm}$$

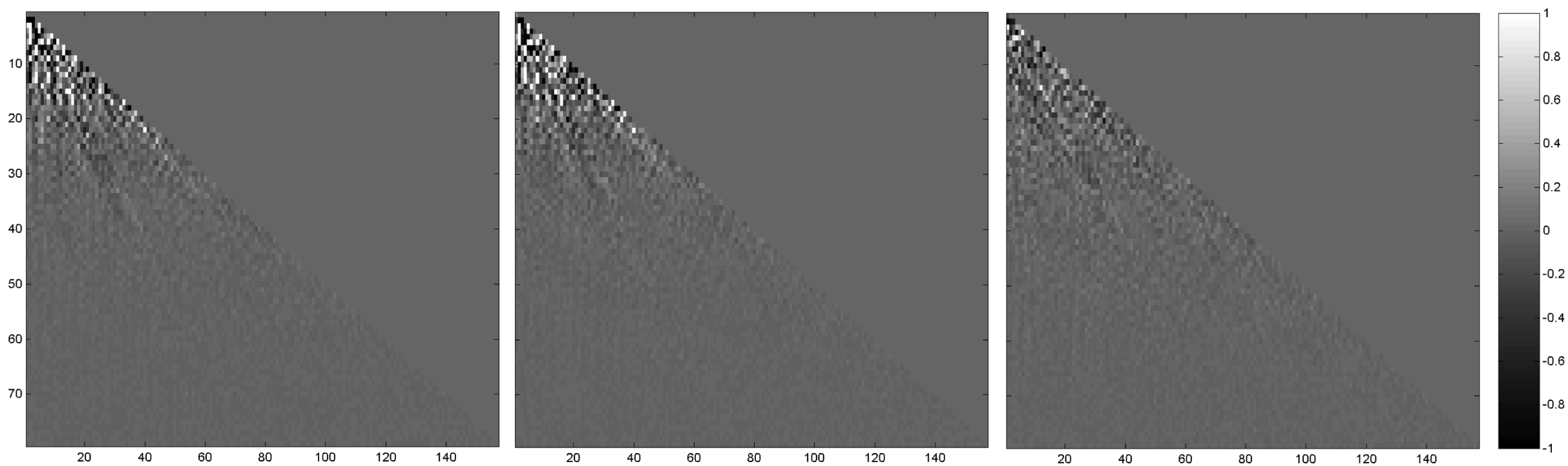
$$\sum_{m=-k}^{k} f_{km} Y_{km}$$

Weighted spherical harmonic representation of cortical surface



Color scale: X-coordinate function

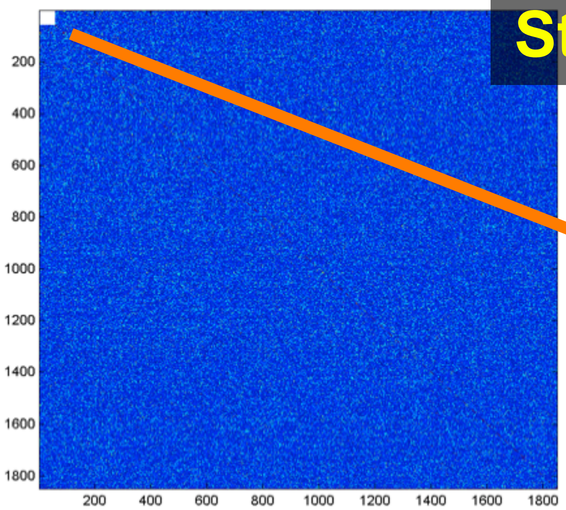
78th degree SPHARM representation

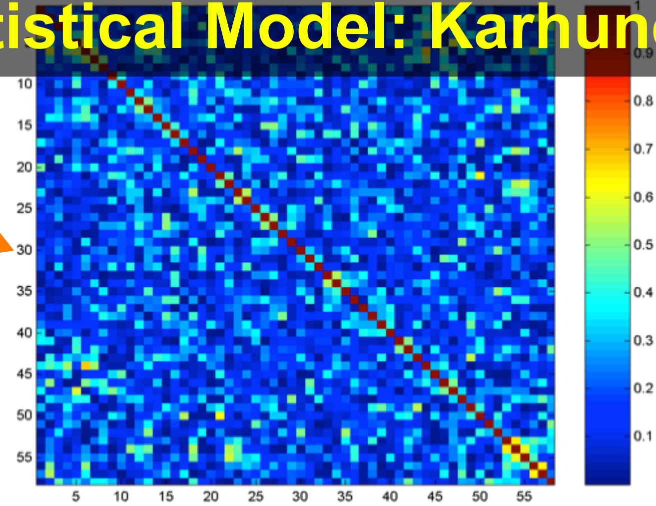


autism **control** **difference**

The coefficients are treated as a multivariate measure and feed into classification techniques.

Statistical Model: Karhunen-Loeve expansion

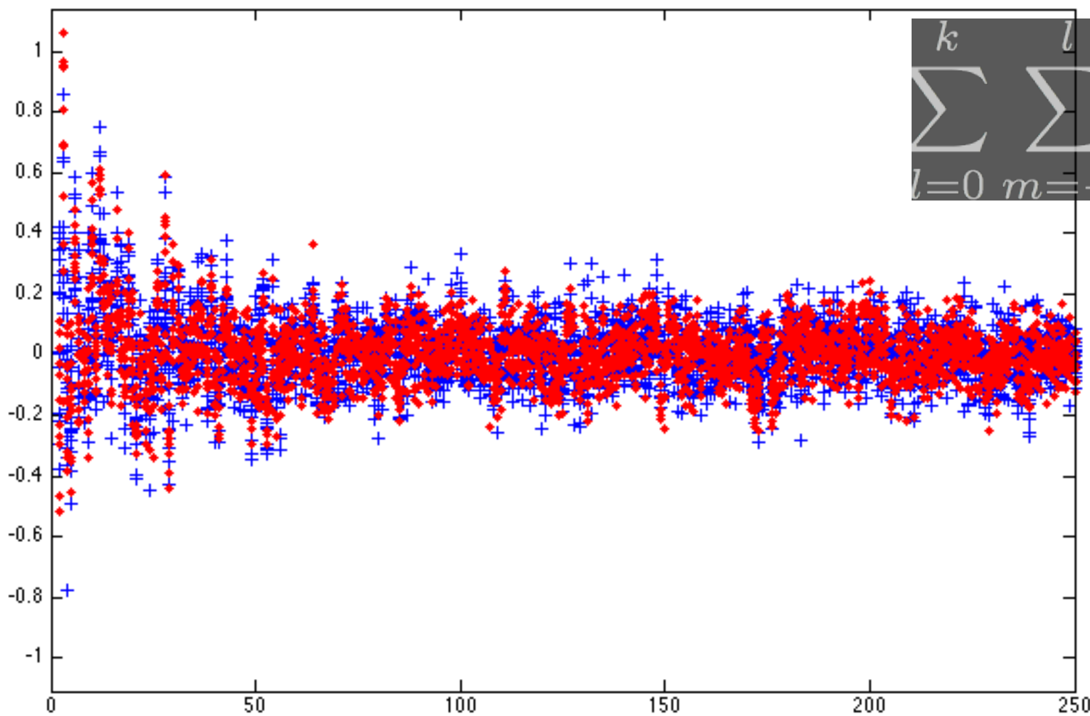




Cross correlations

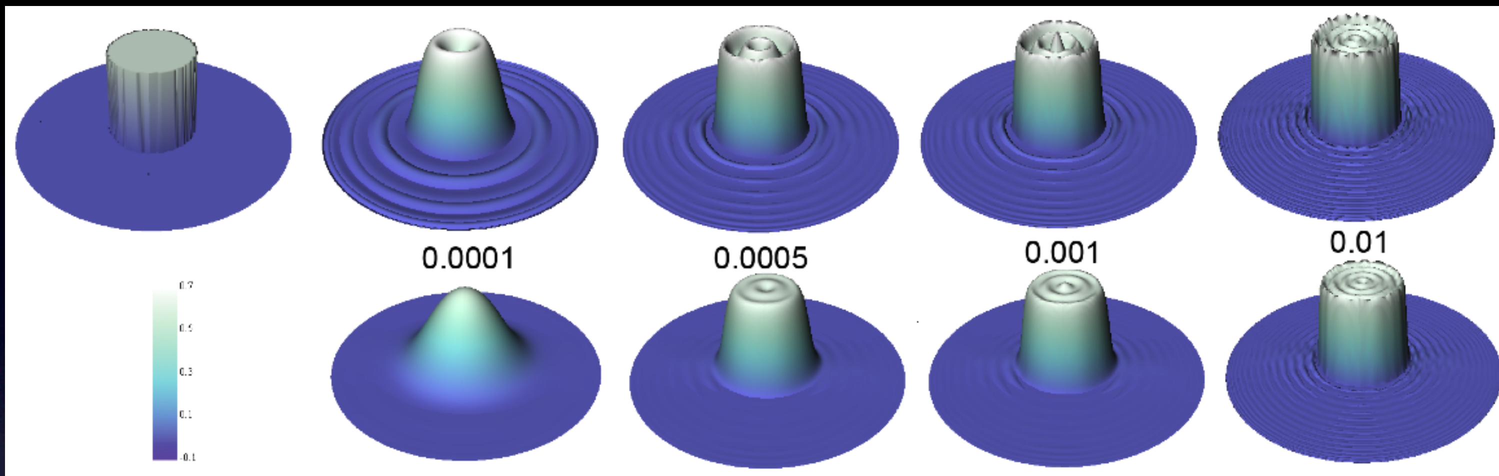
uncorrelated normal

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



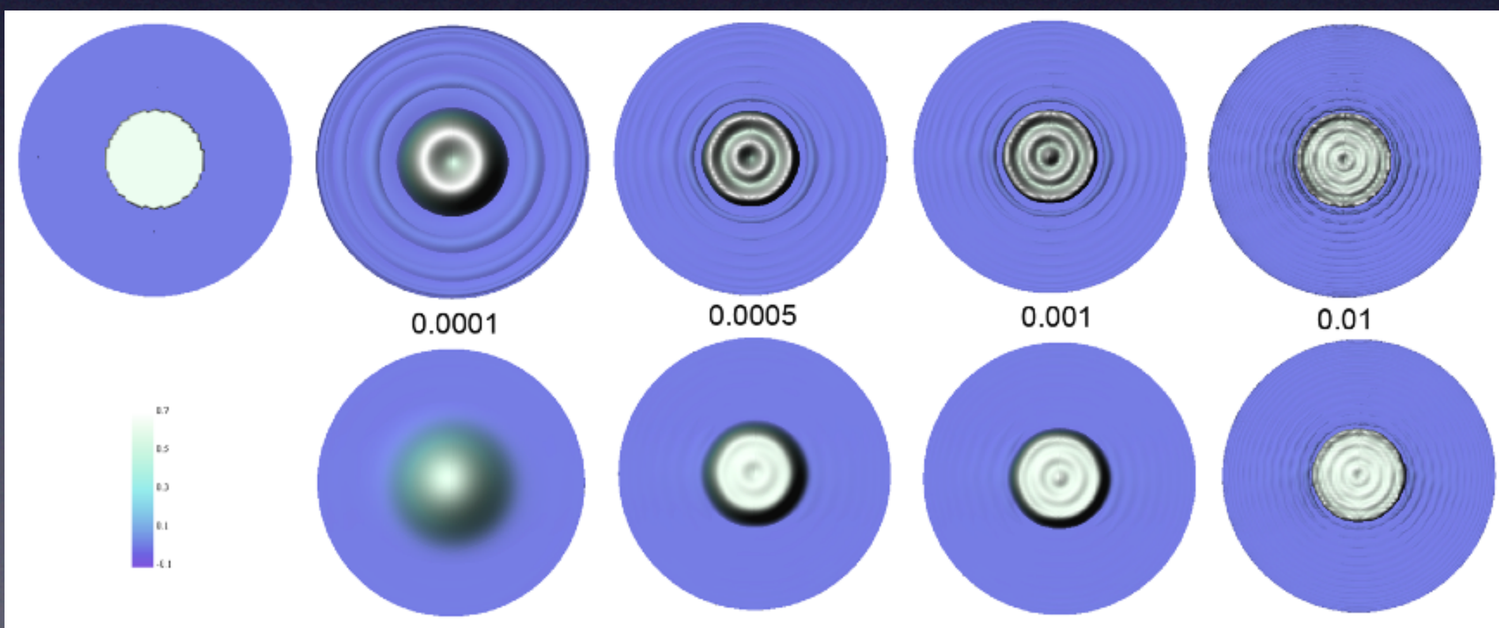
Classification ?
Discrimination?

Gibbs phenomenon on hat shaped surface



SPHARM

Weighted SPHARM

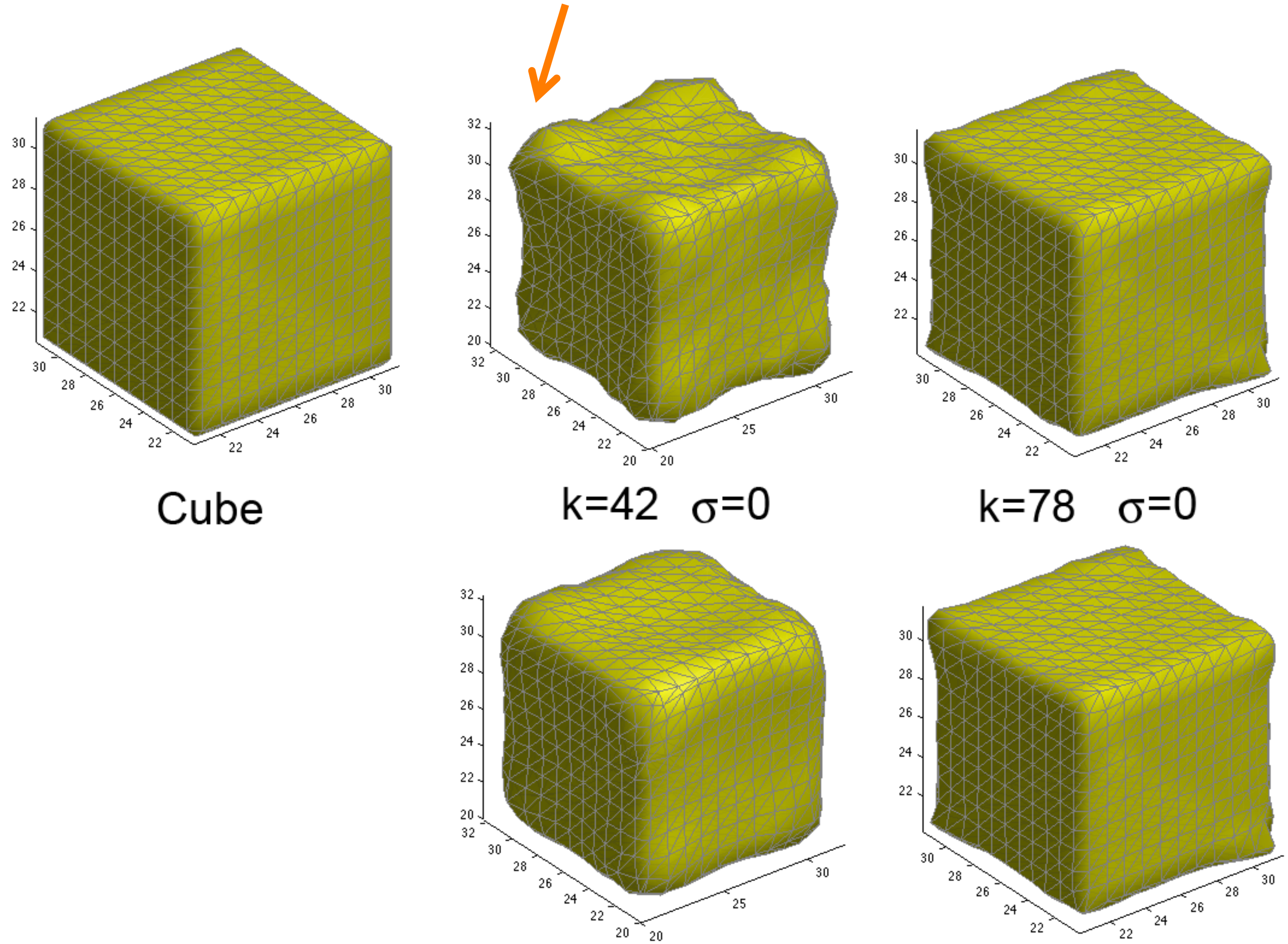


SPHARM

Weighted SPHARM

Gibbs phenomenon (ringing artifacts) on surface

Severe distortion at low degree



Cube

k=42 σ=0

k=78 σ=0

SPHARM

k=42 σ= 0.001

k=78 σ= 0.0001

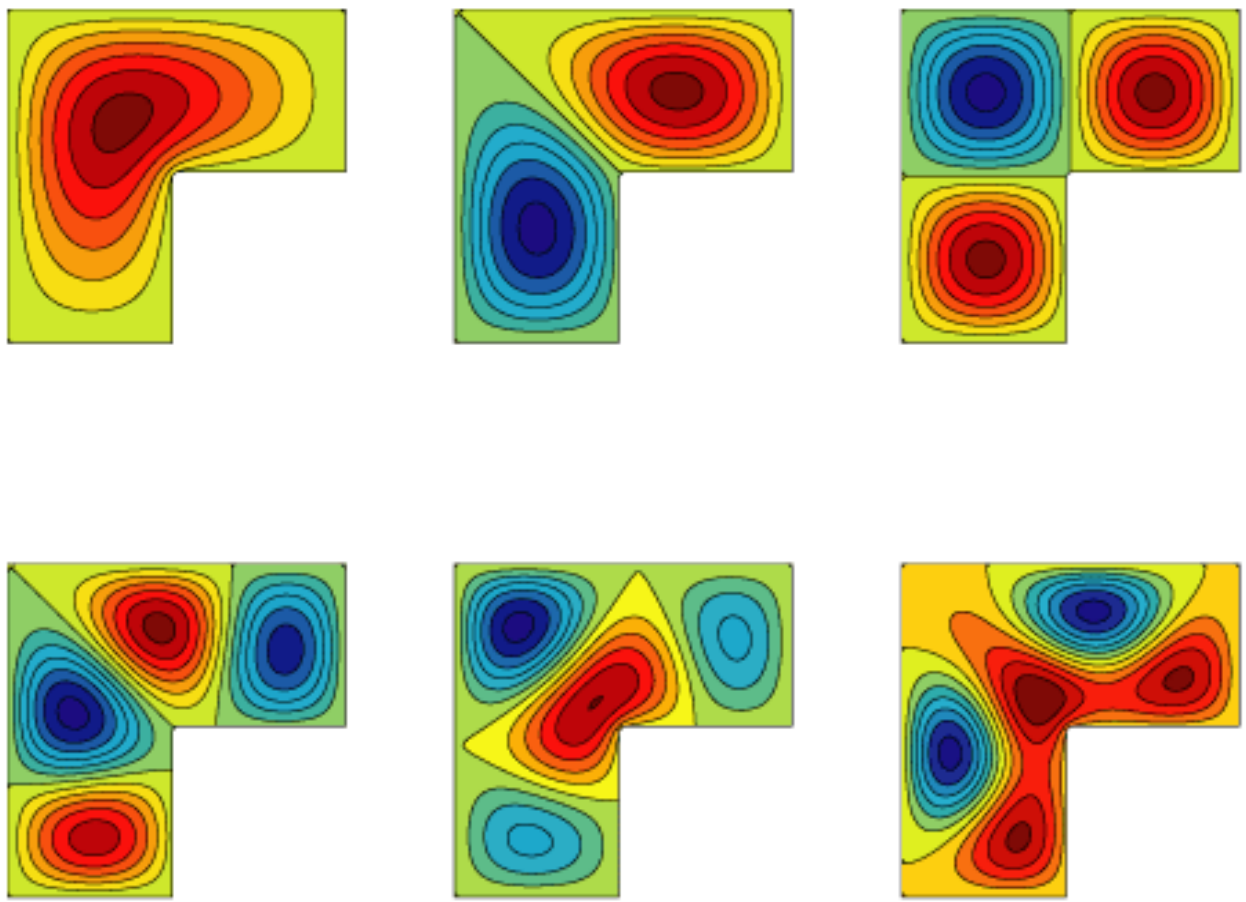
Exponentially Weighted SPHARM

Heat Kernel Smoothing
via Laplace-Beltrami eigenfunctions

Seo et al., 2010 MICCAI 505-512
Kim et al., 2011 PSIVT 36-47

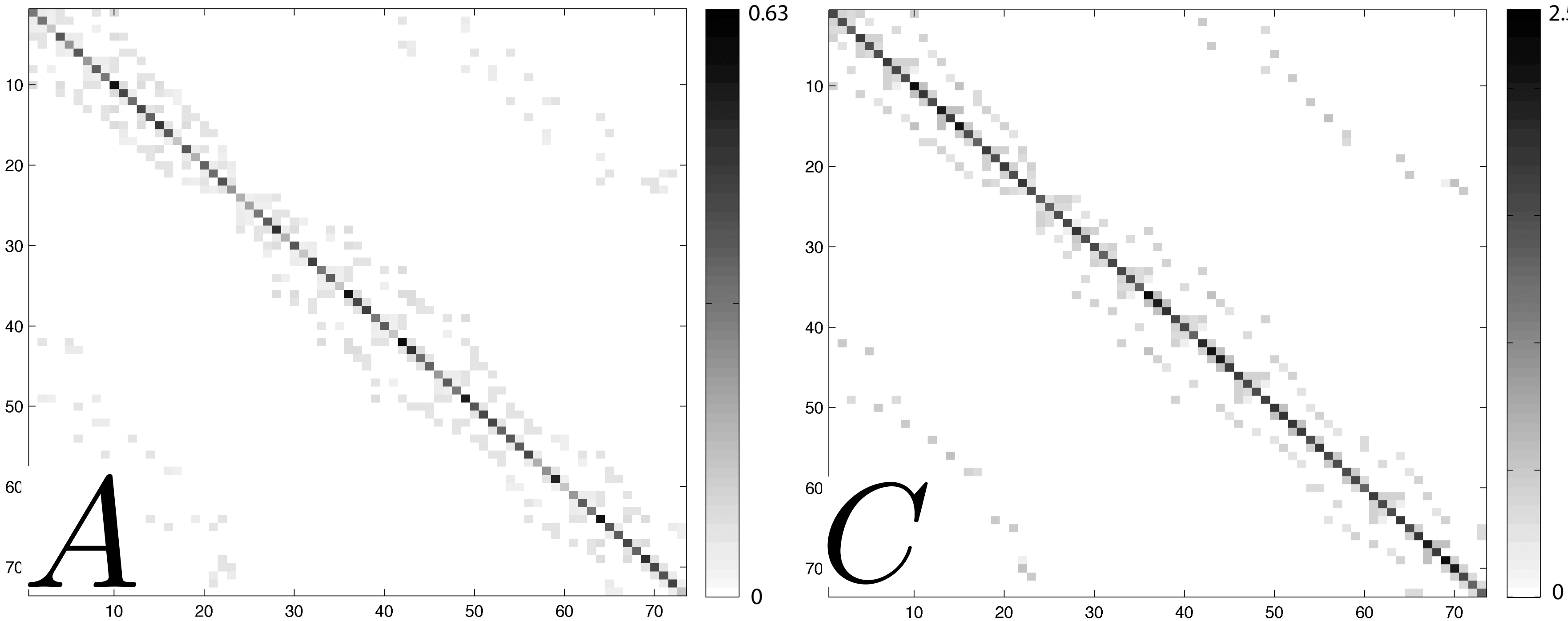
Eigenfunctions of Laplace-Beltrami operator

Helmholtz equation $$\Delta \psi_j = \lambda_j \psi_j$$



Generalized eigenvalue problem via cotan discretization

Qiu et al., 2006, TMI

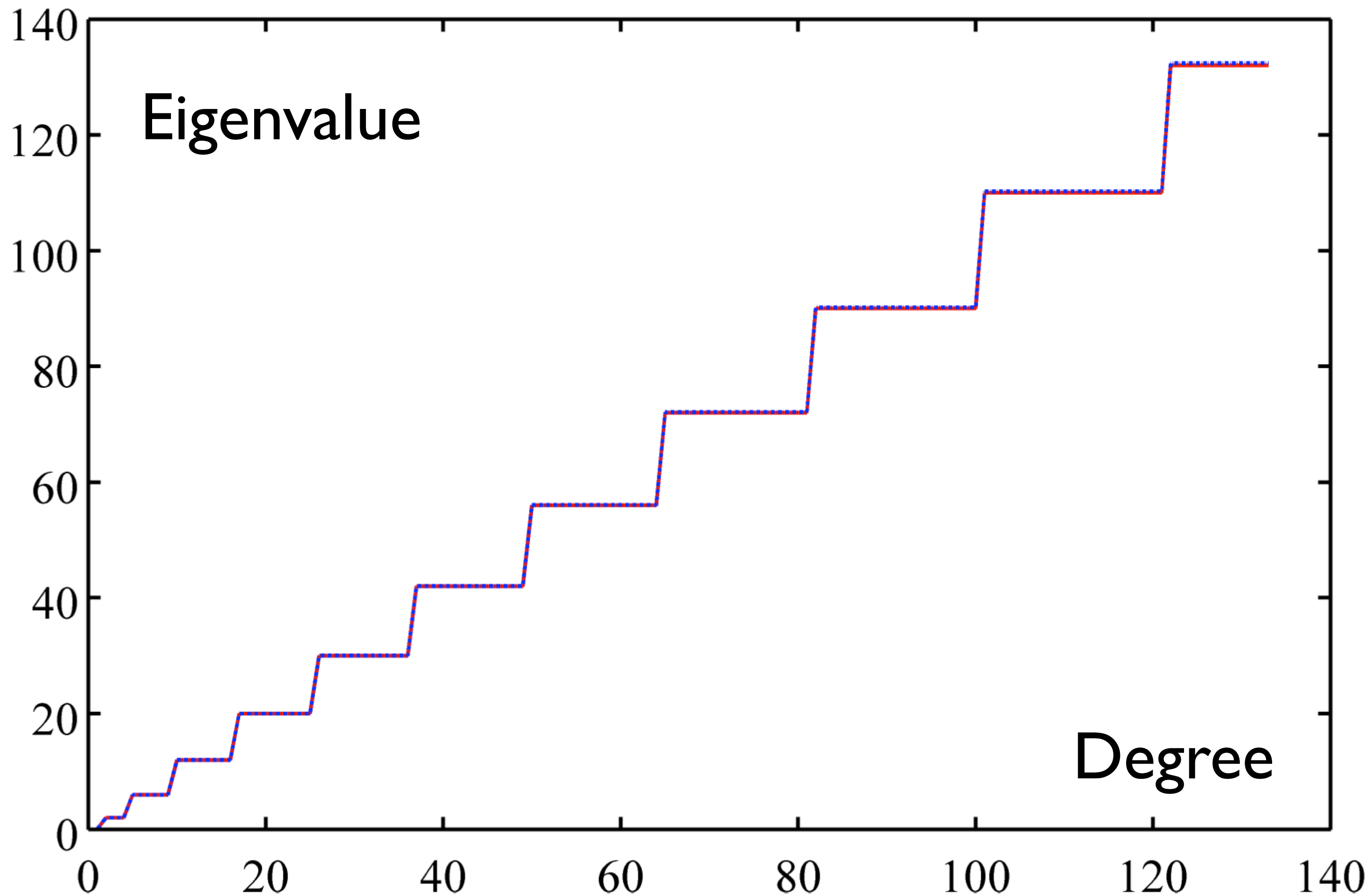


$$\Delta f = \lambda f \longrightarrow C\psi = \lambda A \psi$$

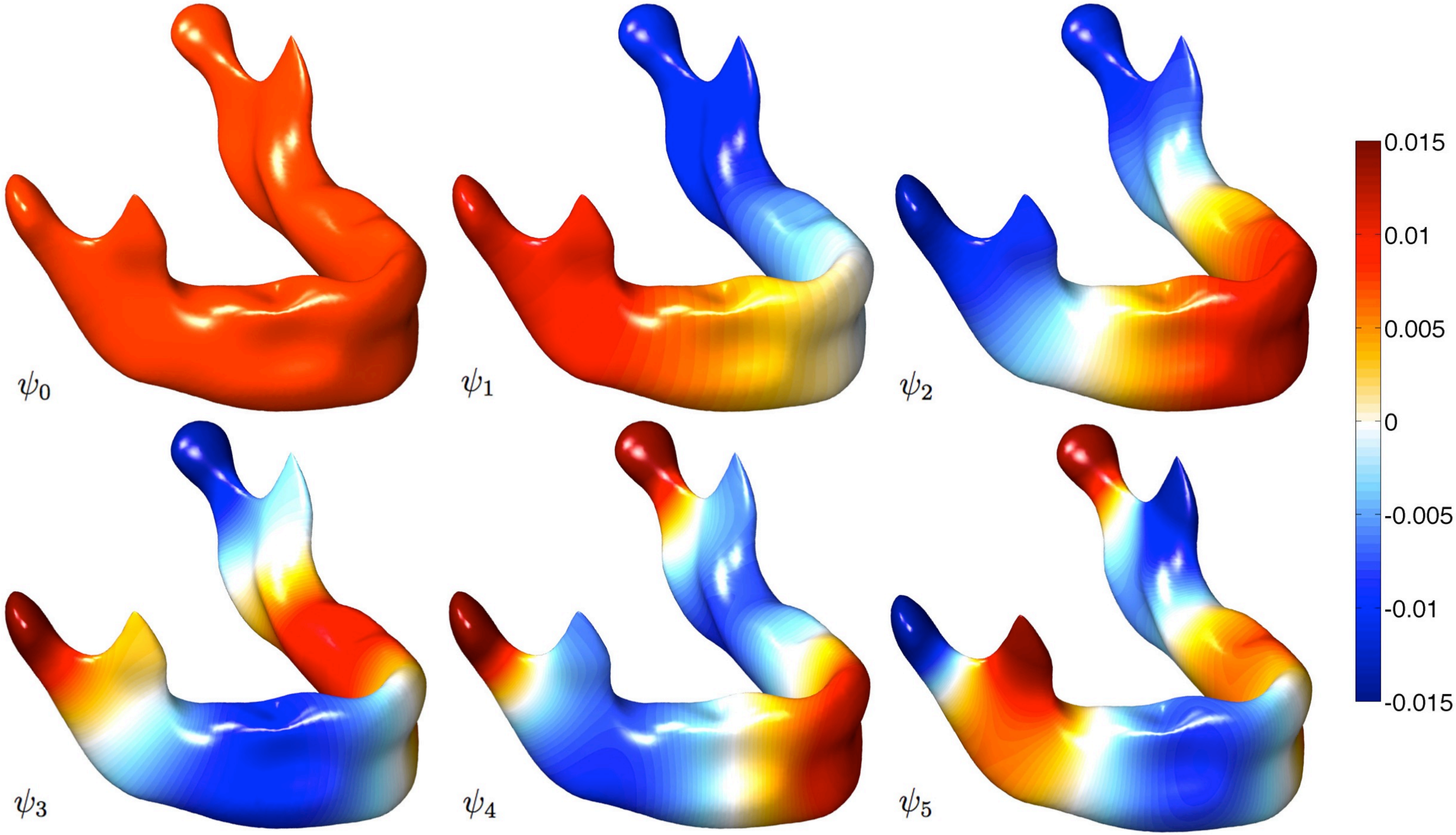
MATLAB code:

http://brainimaging.waisman.wisc.edu/~chung/lb

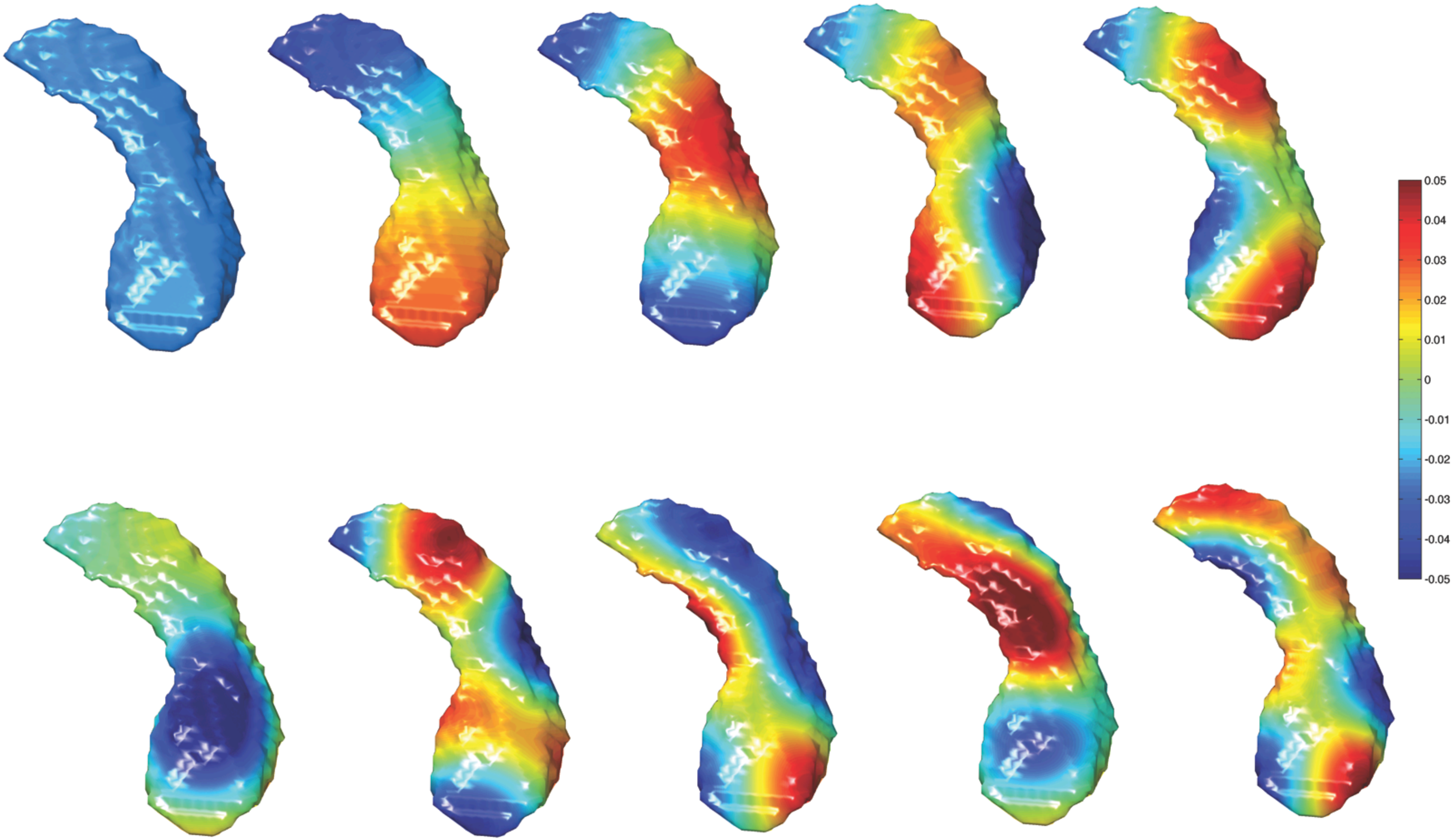
Validation on a unit sphere



Orthonormal basis on mandible



First 10 orthonormal basis on left hippocampus



Diffusion via heat kernel smoothing

Diffusion equation $$\frac{\partial f}{\partial t} = \Delta f, \; f(x, t = 0) = X(x)$$

$$\sigma = \sqrt{2t}$$

Heat kernel smoothing $$f = K_\sigma * X$$

$$K_\sigma(p, q) = \sum_{j=0}^{\infty} e^{-\lambda_j \sigma} \psi_j(p) \psi_j(q)$$

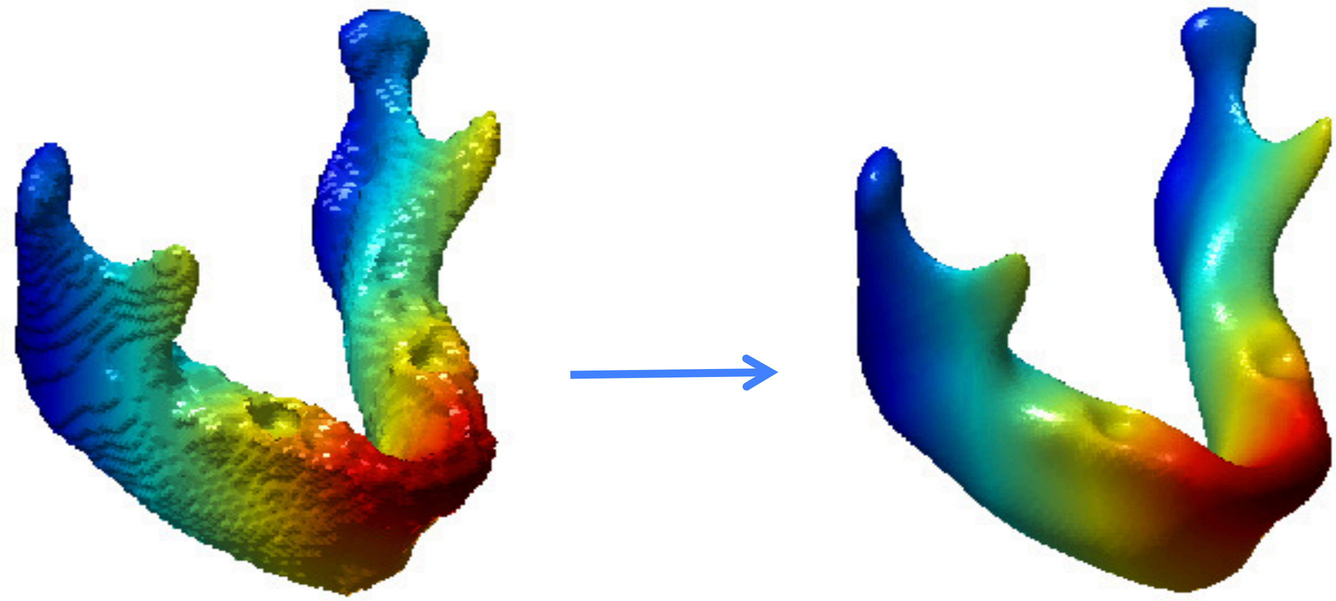
Chung et al., 2005 NeuroImage
Seo et al., 2010 MICCAI

Heat kernel smoothing on manifold

Heat kernel:

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

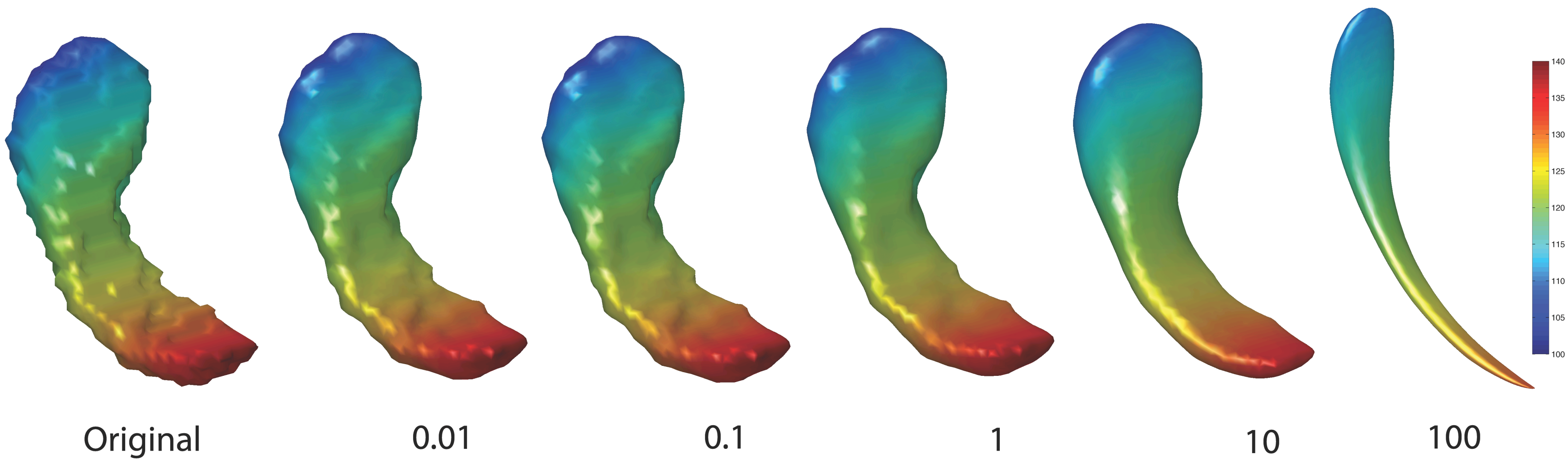
$$K_t * f = \int_{\mathcal{M}} K_t(p,q) f(q) \, dq$$



X-coordinate on mandible surface

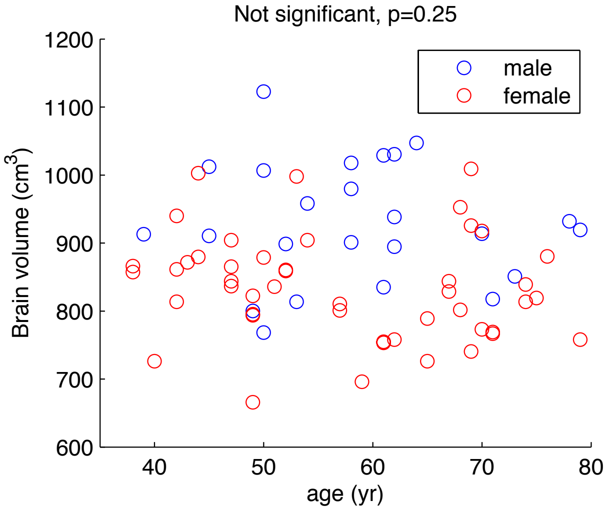
smoothed with bandwidth 10 and 1269 eigenfunctions

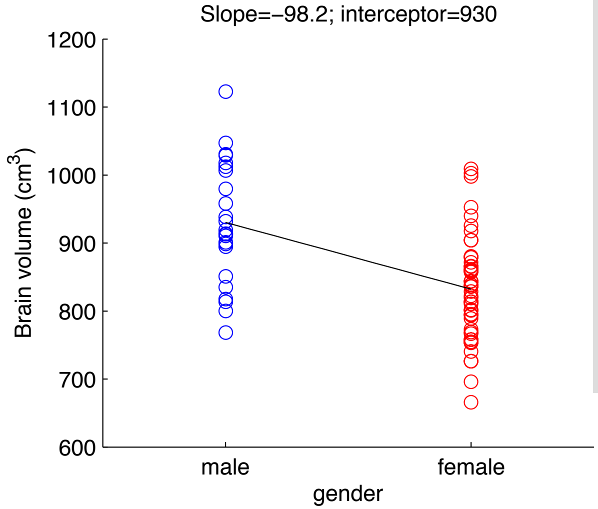
Heat kernel smoothing of hippocampus



Applications

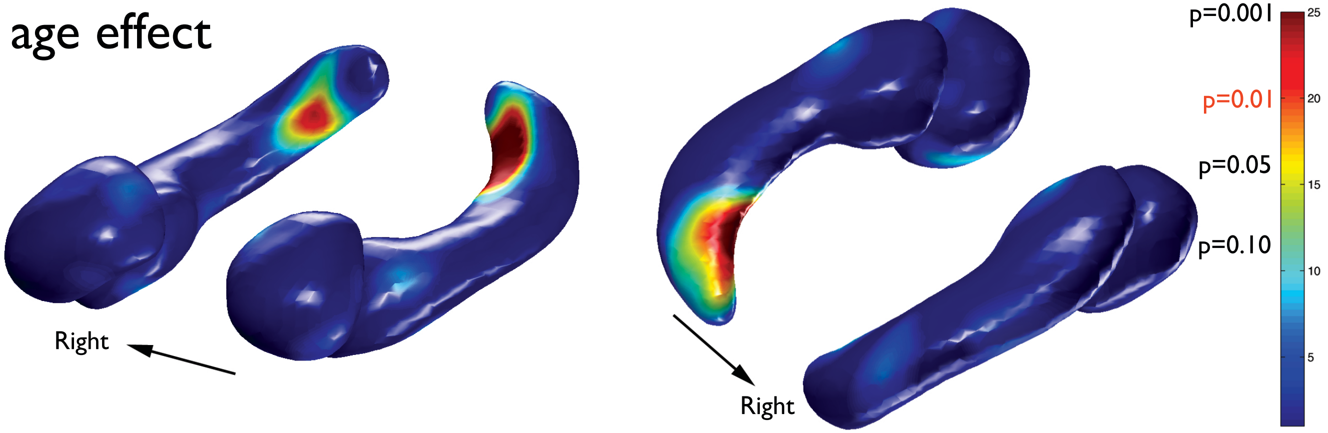
Heat kernel smoothing applied in testing the effect of age and gender on hippocampus and amygdala shape



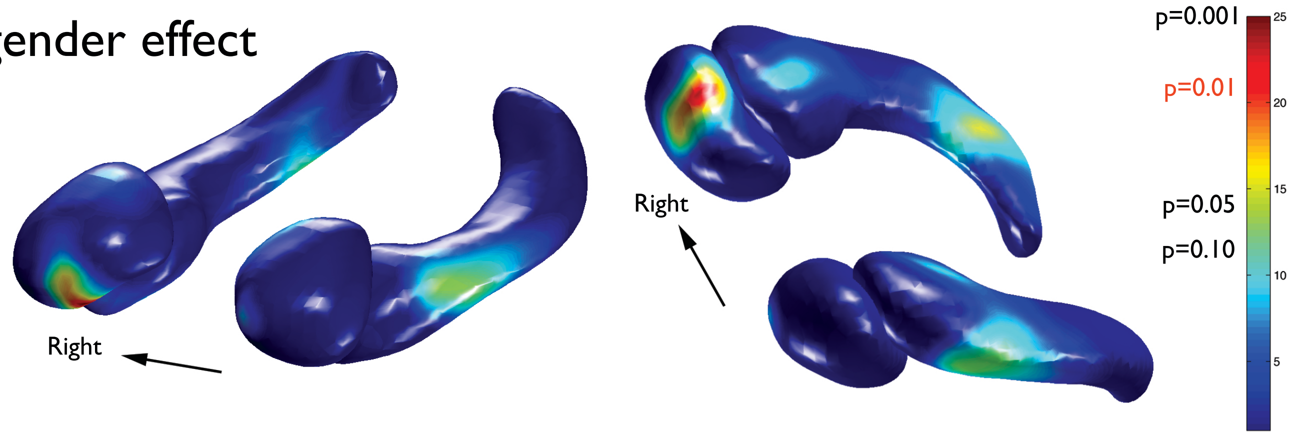


Normal subjects between 38 and 79 years

a) age effect



b) gender effect

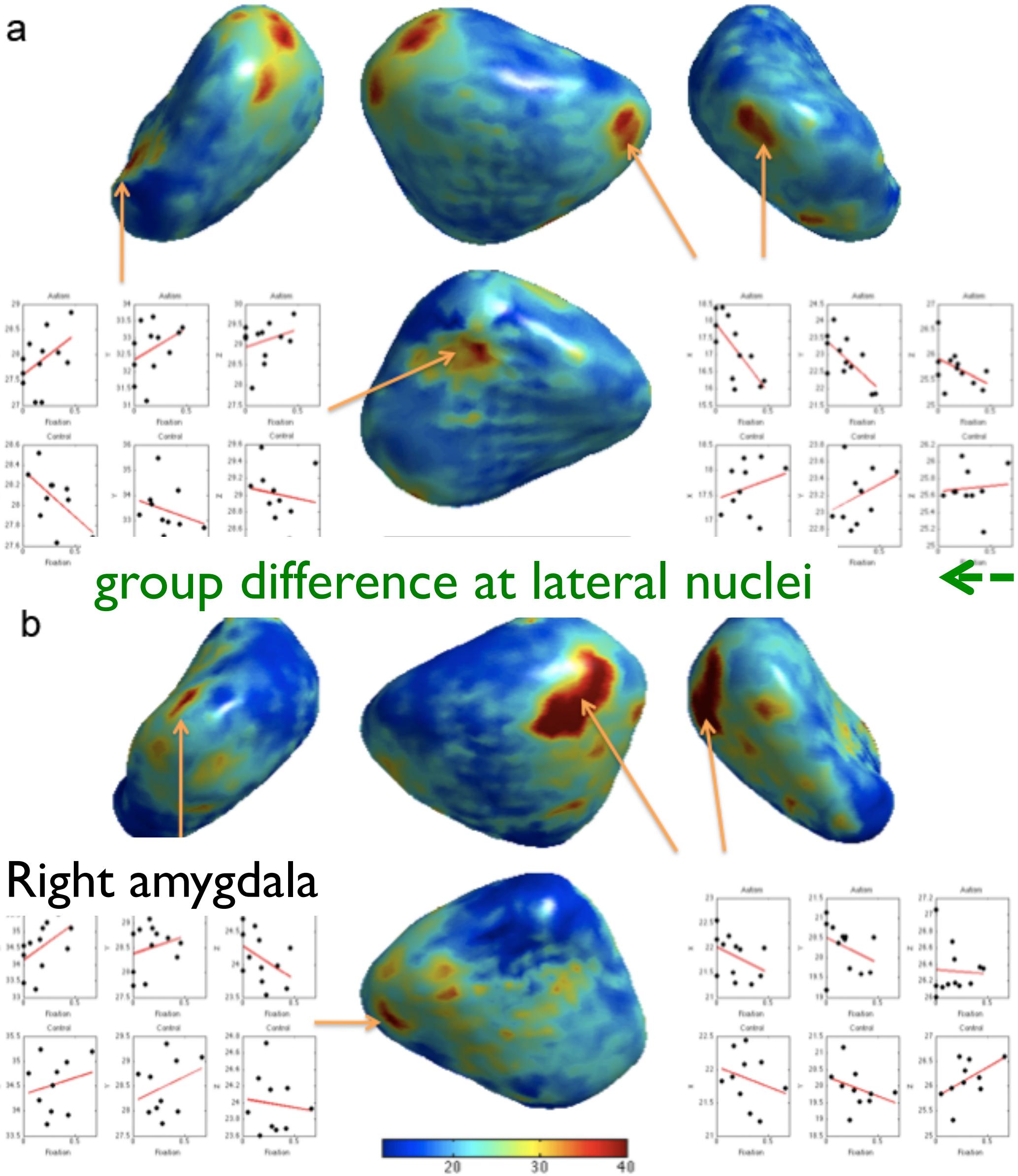


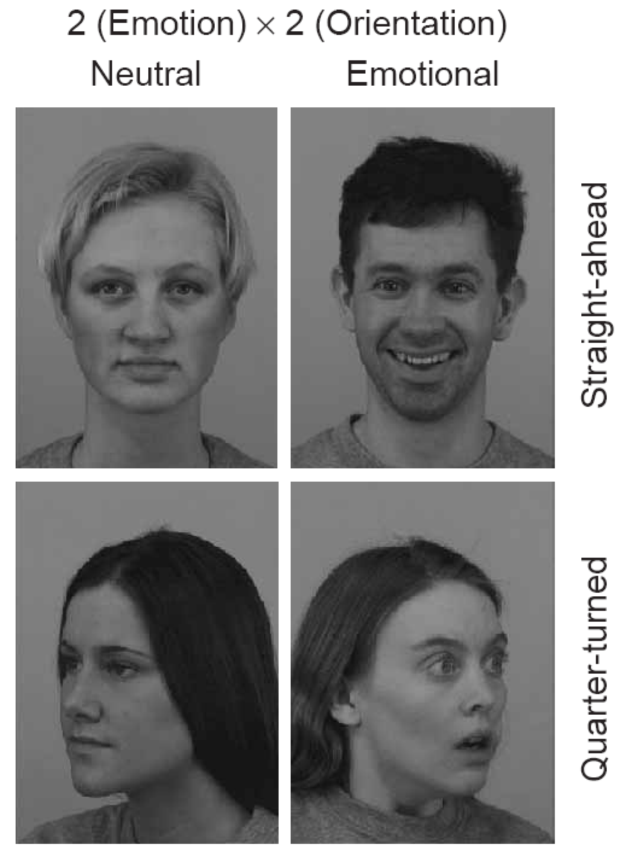
Kim et al, 2011 PISVT

Amygdala surface model in autism

Chung et al., Neuroimage 2010

Left amygdala



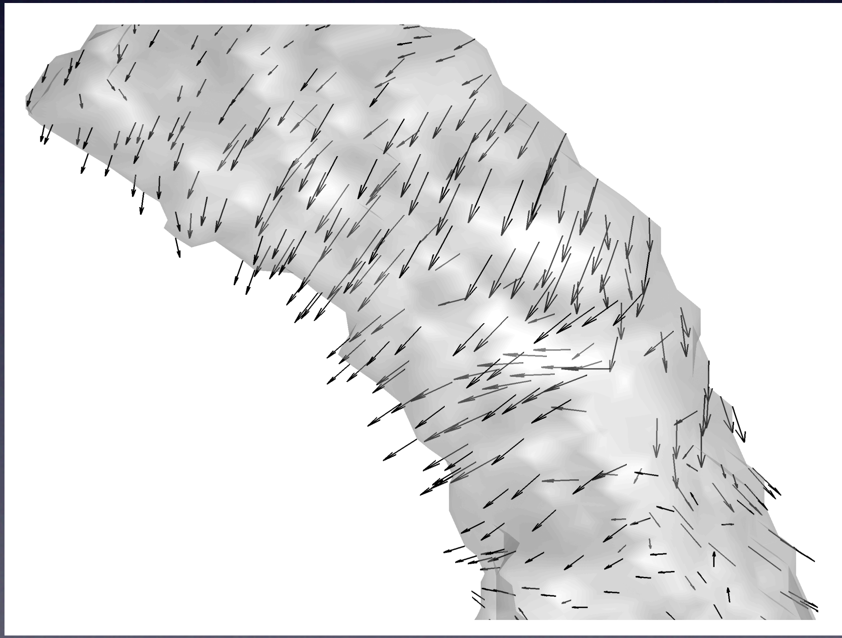


Correlating facial emotion discrimination task response and amygdala shape in autism

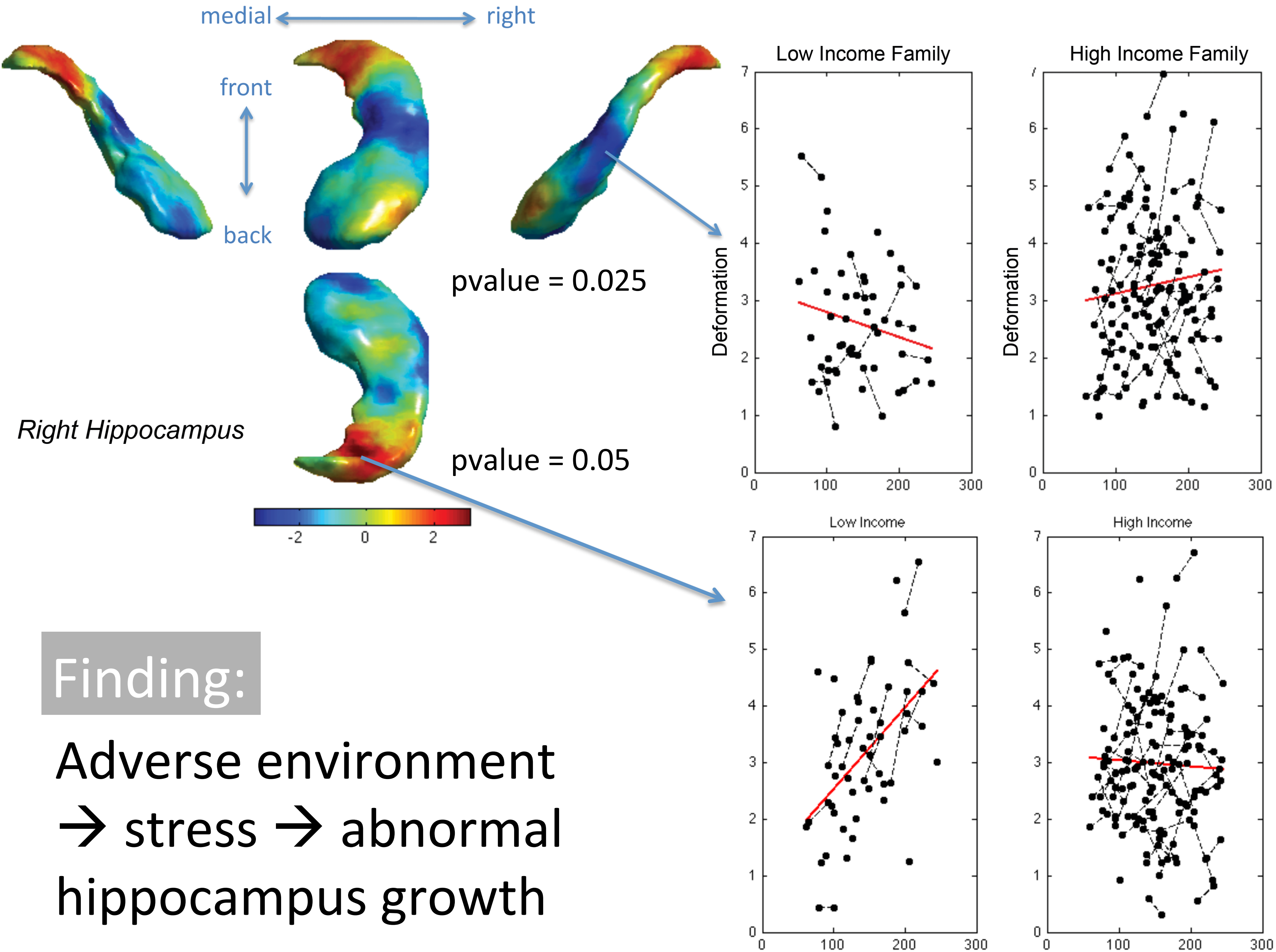
Effect of family income on hippocampus growth

86 teens from high income family (> $75000)
mean age = 12+/- 4 years
38 teens from low income family (< $35000)
mean age= 12 +/- 4 years old

Each subject has multiple scans



Mixed effect longitudinal model:
displacement = age + gender + group + <u>age*group</u>



Finding:

Adverse environment → stress → abnormal hippocampus growth

Thank you

Papers & MATLAB codes (computation, visualization etc.) can be downloaded from

www.stat.wisc.edu/~mchung