Computational Neuroanatomy.

Bruce Fischl
MGH NMR Center

Collaborators

Anders M. Dale	MGH
Andre van der Kouwe	MGH
Marty Sereno	UCSD
David Salat	MGH
Christophe Destrieux	Tours

Thanks also to Randy Buckner, Bruce Rosen, Eric Halgren, Marilyn Albert, Gina Kuperberg, Ron Killiany, Diana Rosas, David Kennedy, Nikos Makris, Verne Caviness, Paul Raines, Chad Wissler, Roger Tootell, Doug Greve, Sean Marrett, Janine Mendola, Rahul Desikan, Kevin Teich, Chris Moore, Christian Haselgrove, Tony Harris, Evelina Busa, Maureen Glessner, and Nouchine Hadjikhani

Computational Neuroanatomy:

Definition 1:
The manner in which the neuroanatomical structure of the brain facilitates or carries out computations.

Definition 2:
The application of computational techniques to model neuroanatomical structures.

Computational Neuroanatomy:

Definition 1:

The manner in which the neuroanatomical structure of the brain facilitates or carries out computations.

Definition 2:

The application of computational techniques to model neuroanatomical structures.

Computational Neuroanatomy:

Definition 1:
The manner in which the neuroanatomical structure of the brain facilitates or carries out computations.

Definition 2:
The application of computational techniques to model neuroanatomical structures.

Warning!

There are no textbooks on computational neuroanatomy:

Much of what you hear in this lecture will be opinion!

Talk Outline

- The Spatial Structure of Retinotopic Cortex.
- Cortical Analysis.
- Subcortical Analysis.

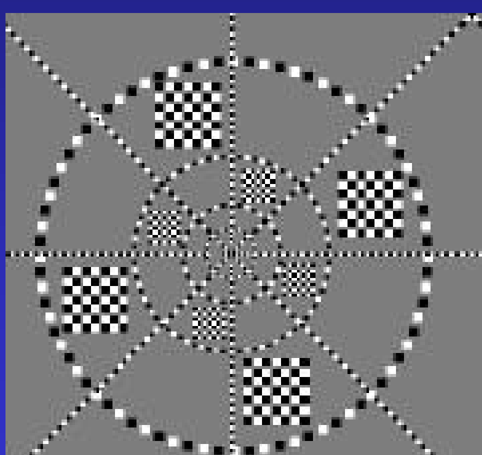
Talk Outline

- The Spatial Structure of Retinotopic Cortex.
- Cortical Analysis.
- Subcortical Analysis.

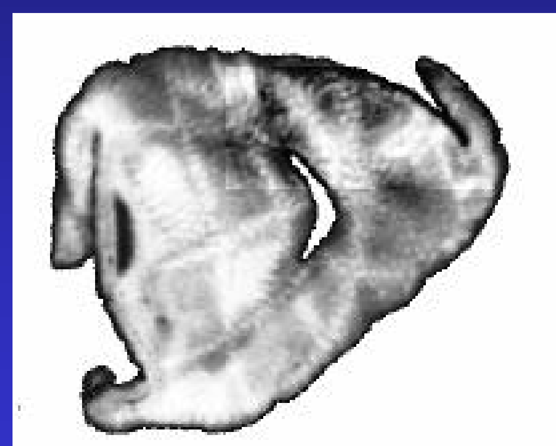
How is the Visual Field Represented in Mammalian Cortex?*

(Physically Flattened Macaque V1)

Stimulus



2-DG map of V1



*thanks to Eric Schwartz for this slide

What is the form of the retino-cortical map function?

First insight: Burkhardt Fischer (1970):

If retinal cell density/length is 1/*r*

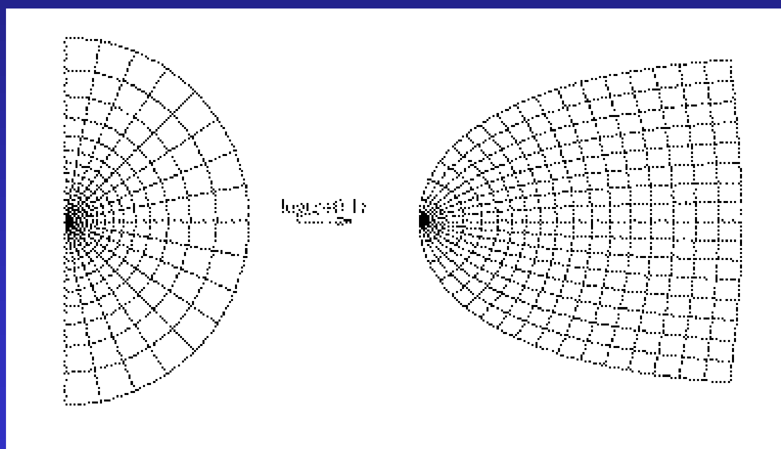
Then several possible optic tract exist maps, one of which is (*z*=retina, *w*=cortex):

Problems With Log(z) Hypothesis

- In cat, V1 not really log polar.
- Retinal cell density doesn’t necessarily determine the cortical map. This point still uncertain in both monkey and cat!
- Log(z) has a singularity at the origin – the most important place!

Removal of the Foveal Singularity

Add a small constant, and map each hemifield separately: $W = \log(z + a)$



Polar Angle→

Eccentricity→

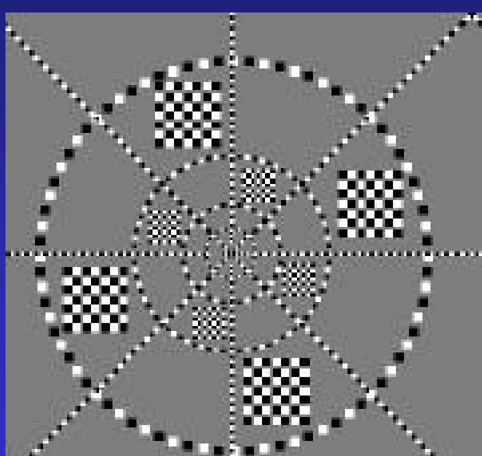
*thanks to Eric Schwartz for this slide

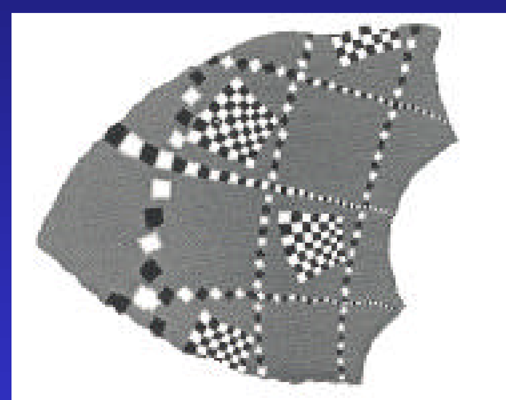
Conformal Maps

- A map function is said to be *conformal* if
  - It preserves local angles (equivalent to…)
  - The jacobian of the map function is non-singular
- Riemann map theorem: a conformal map is uniquely determined by one point correspondence, one angle, and boundary of the two domains (retina and cortex).
- Log(z) is not conformal, but Log($z+a$) is.
- Can only meaningfully talk about magnification function if the map is conformal!

Riemann fit to V1

Includes eye position regression and
geodesic brain flattening





*thanks to Eric Schwartz for this slide

What Do Images Look Like in Cortex?

Original image


“Retinal” image


“Cortical” image


*thanks to Eric Schwartz for this slide

Summary of Current Knowledge of Spatial Maps

- They exist and are strongly space-variant in cat, owl, monkey, human etc.
- They are approximately conformal (V1).
- We don’t know if they are “functional” or not.
- We don’t know how to do visual computation on SV maps in biology or in computers.

Talk Outline

- The Spatial Structure of Retinotopic Cortex.
- Cortical Analysis.
- Subcortical Analysis.

Talk Outline

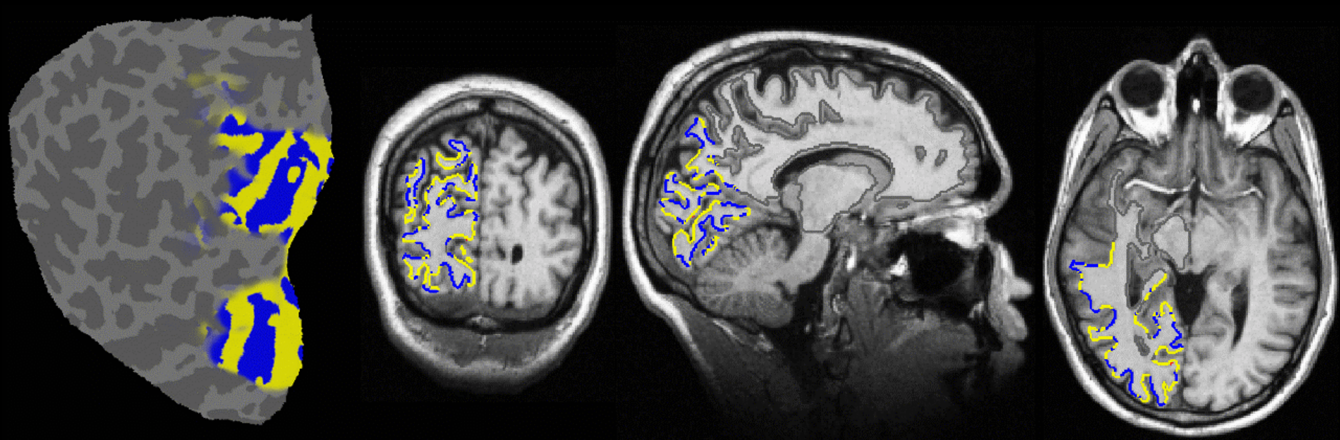
- The Spatial Structure of Retinotopic Cortex.
- Cortical Analysis.
- Subcortical Analysis.

Why Is a Model of the Cortical Surface Useful?

None of the preceding analysis of the spatial structure of the representation of the visual field in V1 could have been done without knowing the position and orientation of the cortex.

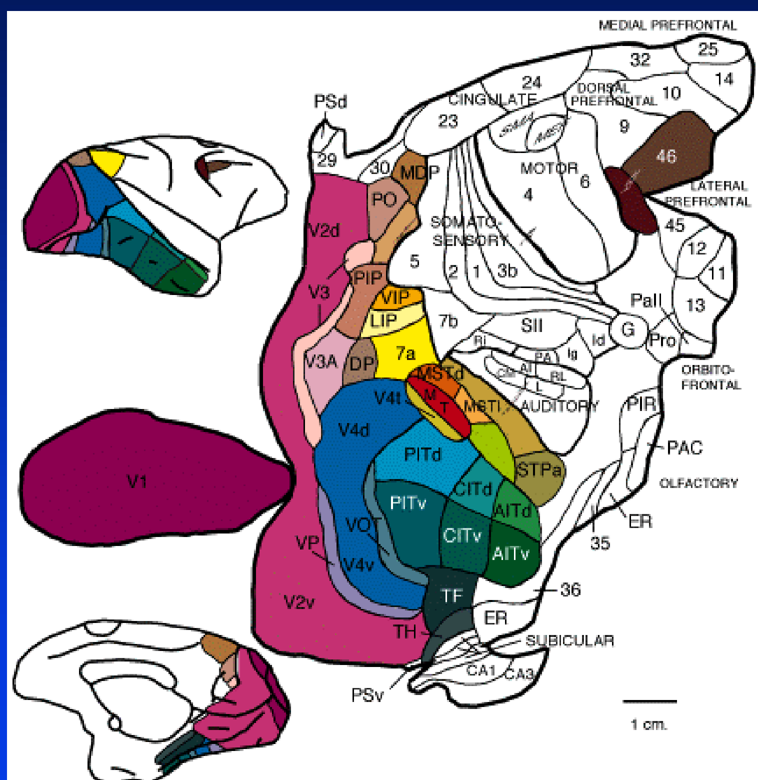
Why Is a Model of the Cortical Surface Useful?

Local functional organization of cortex is largely 2-dimensional!



From (Sereno et al, 1995, Science).

Flat Map of Monkey Visual Areas



D.J. Felleman and D.C. Van Essen, CC, 1991

Why Is Constructing a Model of The Cortical Surface Difficult?

The cortex is highly folded!

- Partial voluming.
- Subject motion.
- Susceptibility artifacts. →
- Bias field.
- Tissue inhomogeneities.

Intensity of a tissue class varies as a function of spatial location

Sources of within-class intensity variation

- Partial voluming – a single voxel may contain more than one tissue type.
- Bias field – effective flip angle or sensitivity of receive coil may vary across space.
- Tissue inhomogeneities – even within tissue type (e.g. cortical gray matter), intrinsic properties such as T1, PD can vary (up to 20%).

Contrast-to-Noise Ratio

For two classes, A and B, the contrast-to-noise ratio (CNR) is given by (one possible definition):

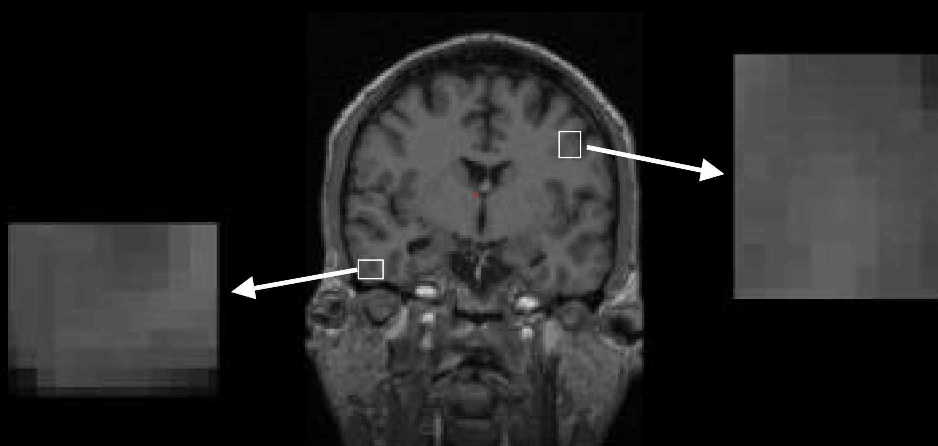
$$CNR = \frac{(\mu_A - \mu_B)^2}{\sigma_A^2 + \sigma_B^2}$$

Higher CNR values imply the class distributions overlap less.

All the previous effects reduce the CNR.

T1 weighted MR volume

Assigning tissue classes to voxels can be difficult



Goal: Reconstruction of the Cortical Surface

Generate a geometrically accurate and topologically correct model of the cerebral cortex.

Uses of the surface reconstruction include:

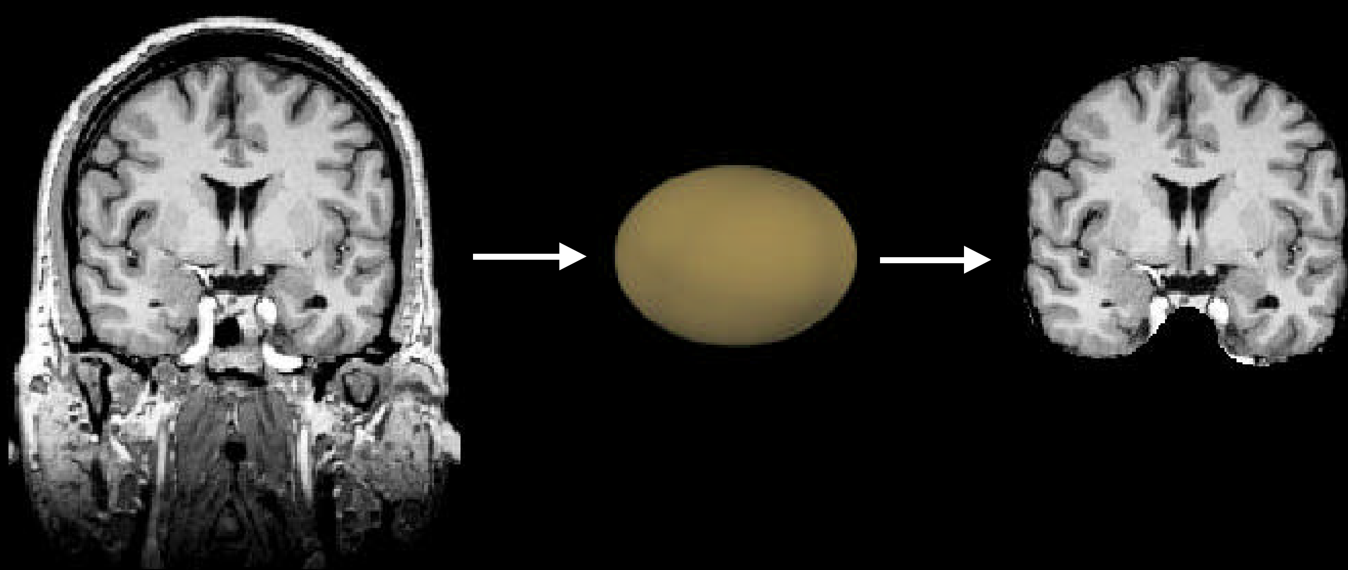
- Visualization of functional and structural neuroimaging data.
- Calculation of morphometric properties of the cortex.
- High-resolution averaging of cortical data across subjects.
- Increasing spatial resolution of EEG/MEG data.

Which Surface to Reconstruct?

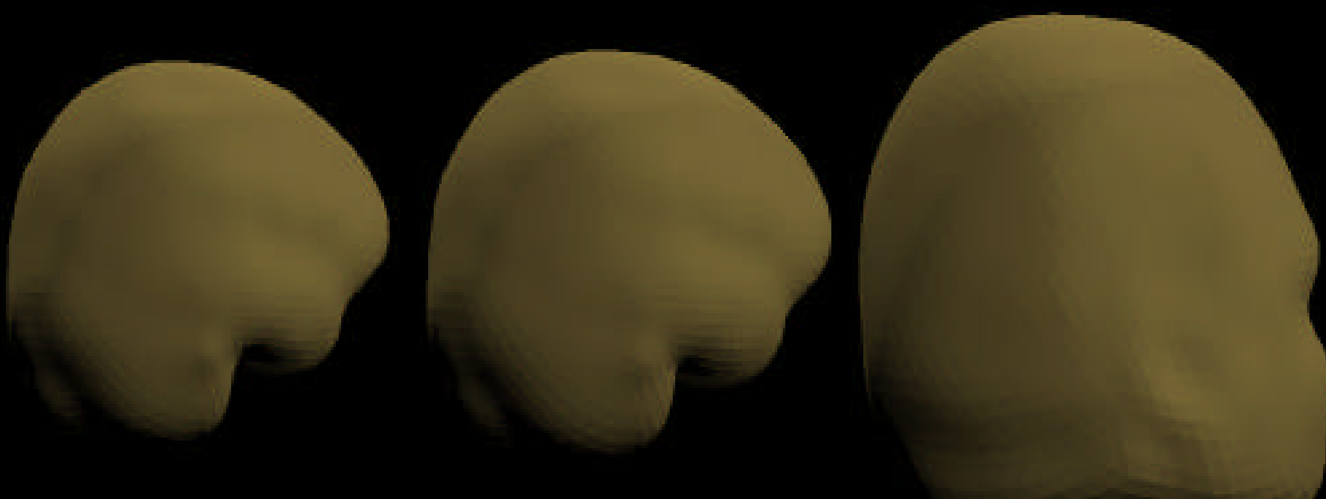
Pial surface is ultimate goal, but pretty much impossible to directly generate a representation of from MRI images (many have tried!).

Alternative: construct an interim representation of the interface between gray matter and white matter, and use it to infer the location of the true cortical surface (Dale and Sereno, 1993).

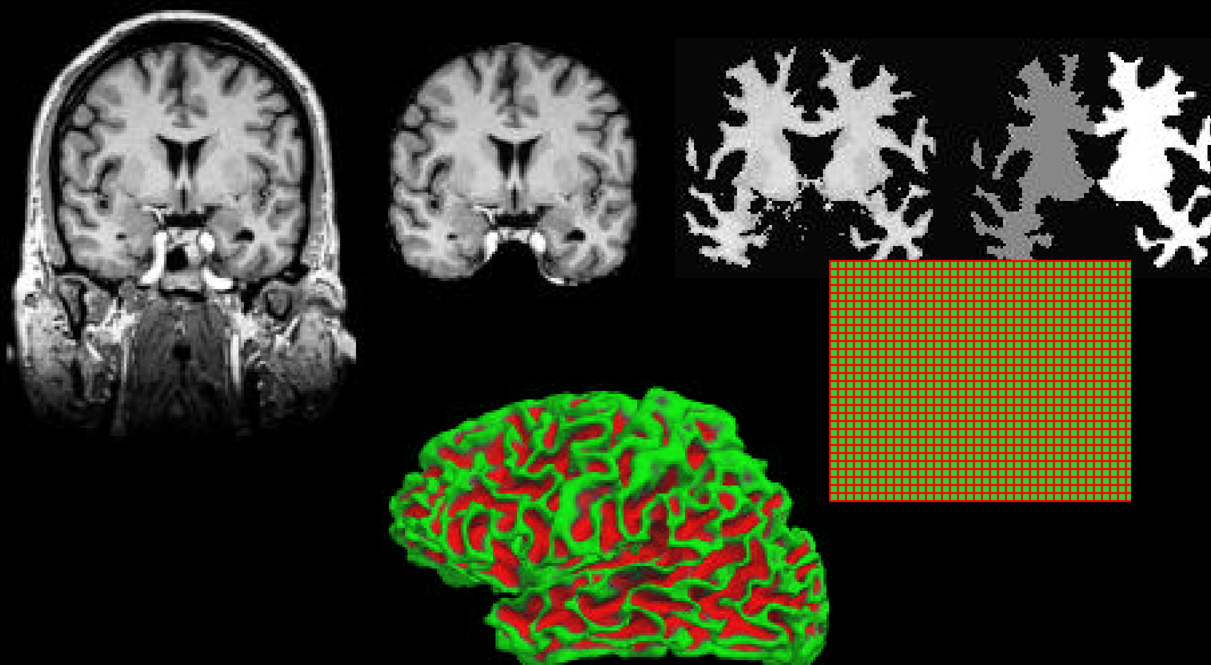
Skull Stripping and building of Boundary Element Models



Conductivity Boundaries for BEM



MRI Segmentation and Surface Reconstruction



Surface Representations

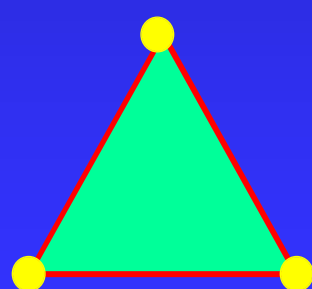
Two Choices:

- **Lagrangian** – generate an explicit representation of the surface through a ***tessellation***. Surface deformations are then carried out by computing the movement of points (vertices) on the surface.
- **Eulerian** – represent the surface by embedding it in a higher-dimensional space. The surface is represented implicitly as the set of points with constant value in the higher dimensional function (the “level-set” approach of Osher and Sethian).

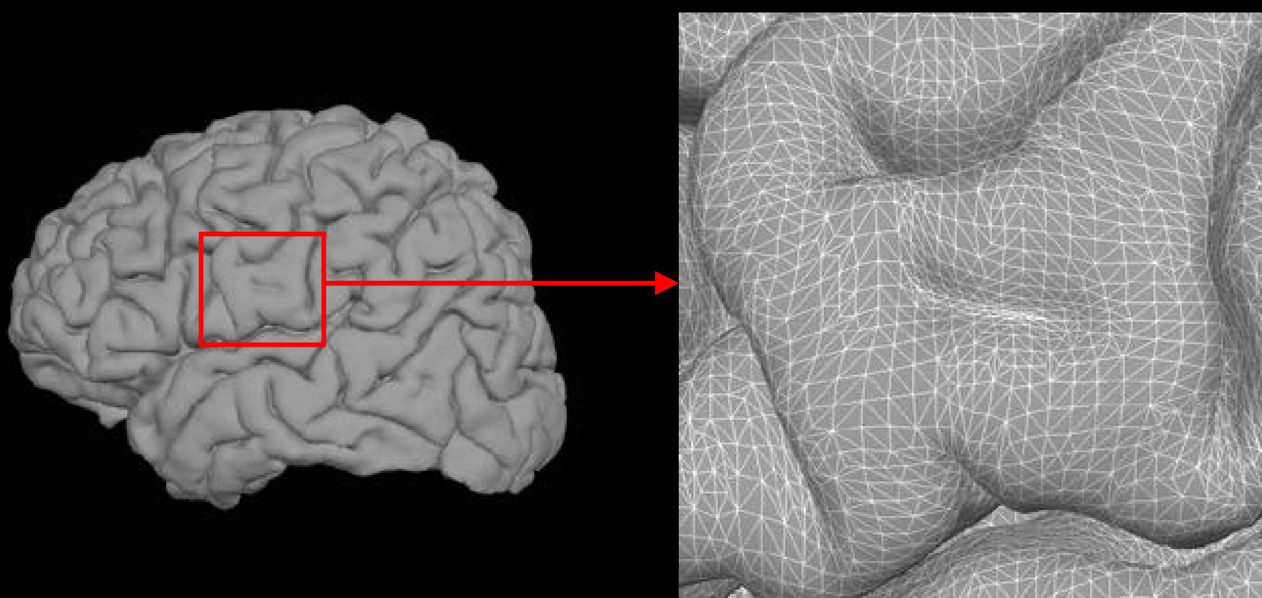
Tessellation

Tessellation - a covering of a space with a pattern such that the elements of the pattern do not overlap.

In our case (and typically), we cover the cortex with triangles. The tessellation is thus made up of ***vertices (points)***, ***faces*** (***triangles)*** and ***edges*** ***(line segments)***.



Tessellation: example



Surface Inflation: Equations

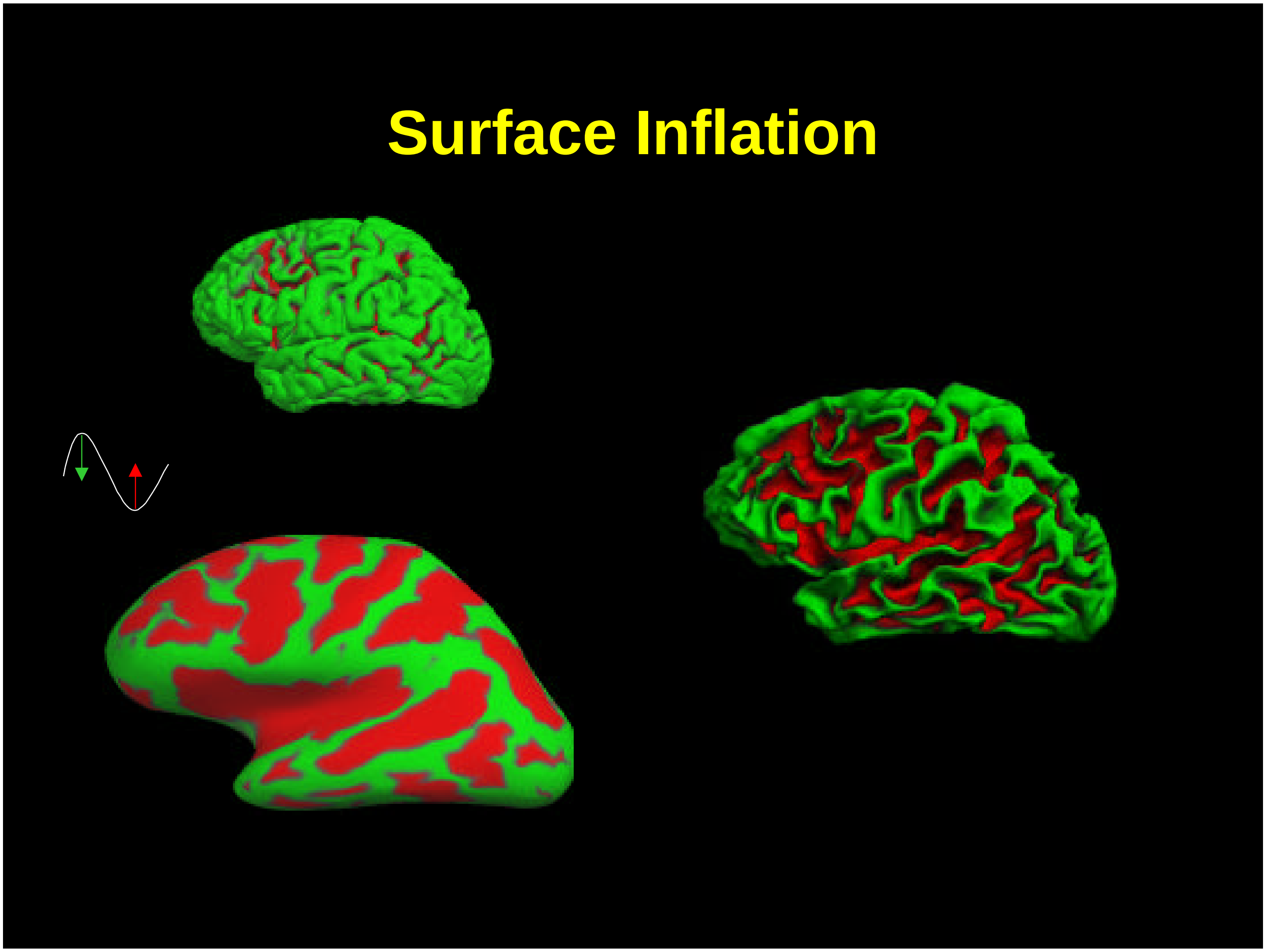
Metric Distortion Term: $$J_d = \frac{1}{4V} \sum_{i=1}^{V} \sum_{n \in N(i)} (d_{in}^{t} - d_{in}^{0})^2 \qquad d_{in}^{t} = \left\| \mathbf{x}_i^t - \mathbf{x}_n^t \right\|$$

Smoothness Term: $$J_S = \sum_{i=1}^{V} \frac{1}{\# N(i)} \sum_{n \in N(i)} \left\| (\mathbf{x}_i - \mathbf{x}_n) \right\|^2$$

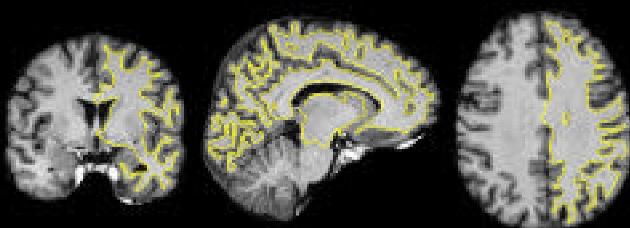
Where *N(i)* is a *neighborhood* function that returns the set of neighbors of the *i*th vertex.

Complete Energy Functional: $J = J_d + \lambda_S J_S$

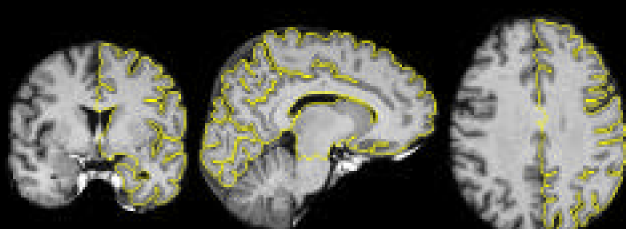
To "inflate" surface model: compute gradient of *J* with respect to the coordinates of each vertex $\boldsymbol{x}_i$, and move vertex in opposite direction (gradient descent), while constraining the total surface area to be constant.


Surface Inflation

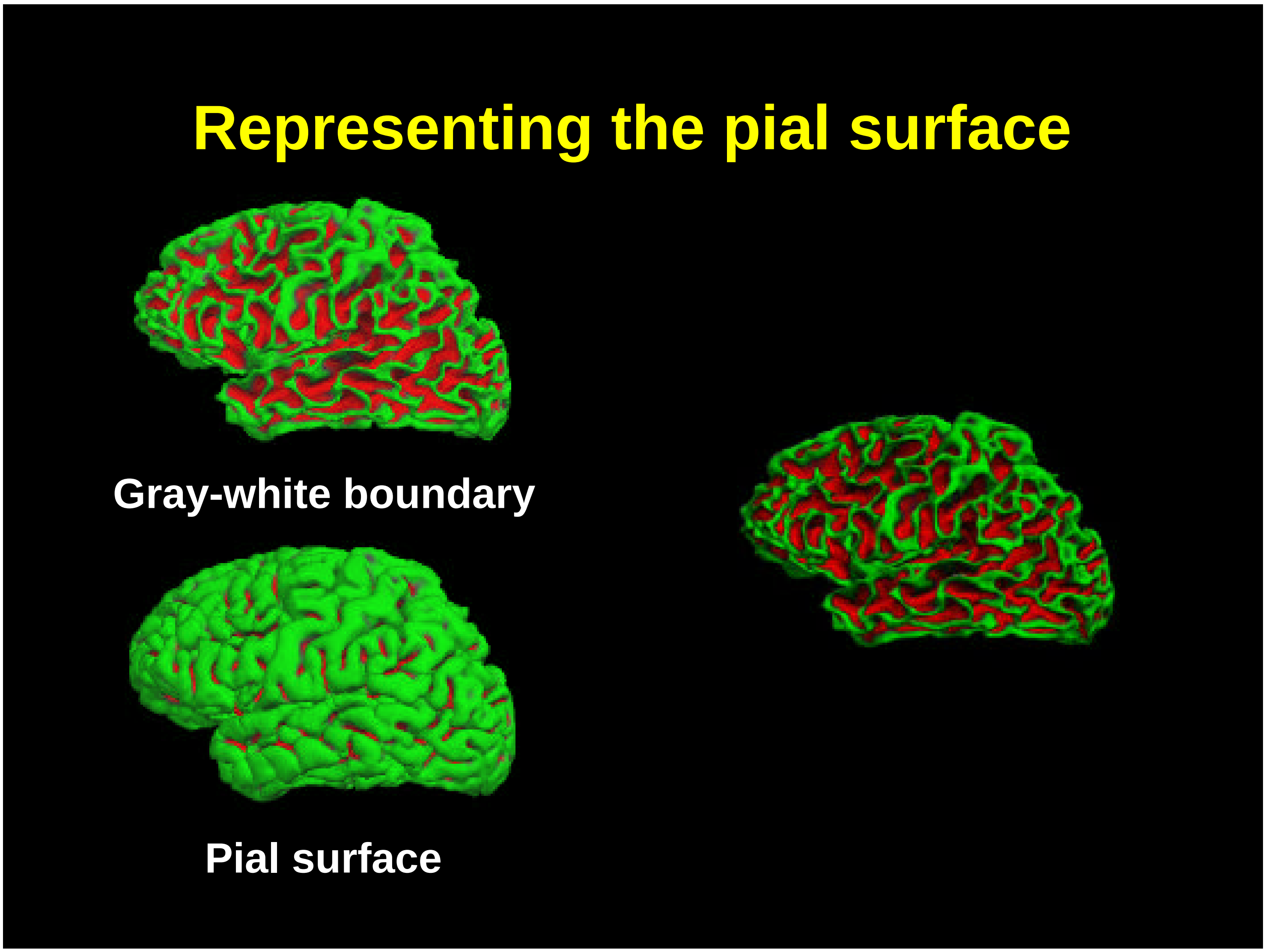
White matter and pial surfaces



Gray-white boundary



Pial surface


Representing the pial surface
Gray-white boundary
Pial surface

Quasi-Isometric Flattening: Equations

Metric Distortion Term: $$J_d = \frac{1}{4V} \sum_{i=1}^{V} \sum_{n \in B_r(i)} (d_{in}^t - d_{in}^0)^2 \qquad d_{in}^t = \left\| \mathbf{x}_i^t - \mathbf{x}_n^t \right\|$$

Topology Term: $$J_T = \frac{1}{F} \sum_{i=1}^{F} \left\{ \frac{\log(1 + e^{kR_i})}{k} - R_i \right\} \qquad R_i = \frac{A_i^t}{A_i^0}$$

Complete Energy Functional: $$J = J_d + \lambda_T J_T$$

Note: distances d_{in} are for macroscopic geodesics: vertices i and n are not necessarily neighbors.

Quasi-Isometric Flattening: Equations (cont)

Topology Term:

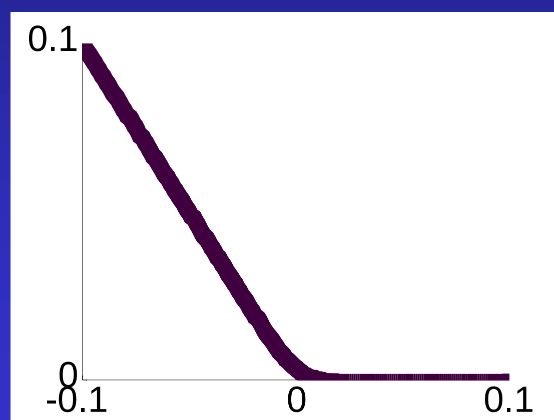
$$J_T = \frac{1}{F}\sum_{i=1}^{F}\left(\frac{\log(1+e^{kR_i})}{k} - R_i\right) \qquad R_i = \frac{A_i^t}{A_i^0}$$

Where:

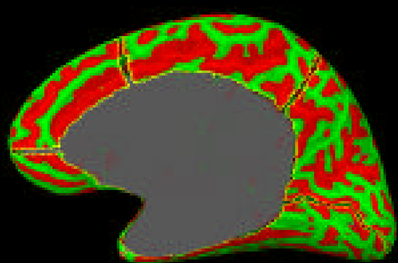
A_i^t – oriented area of i^{th} face in tessellation

F – number of faces in tessellation

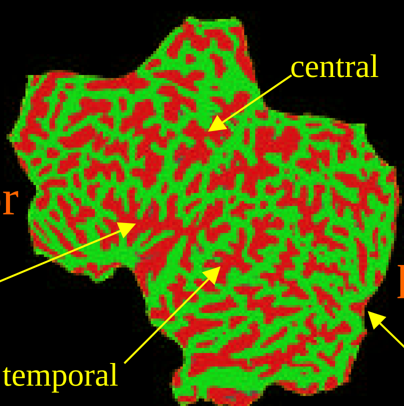
k – positive real constant



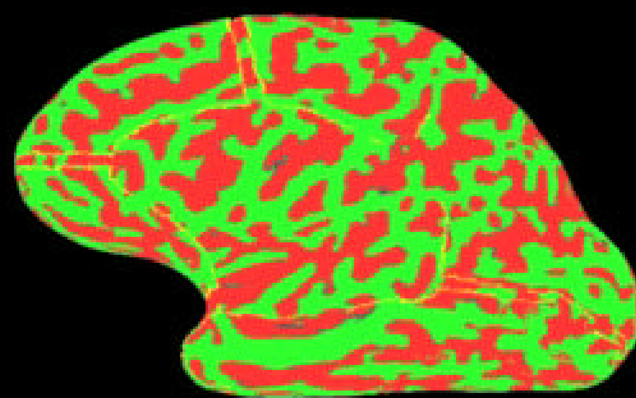
Surface Flattening – Whole Hemisphere

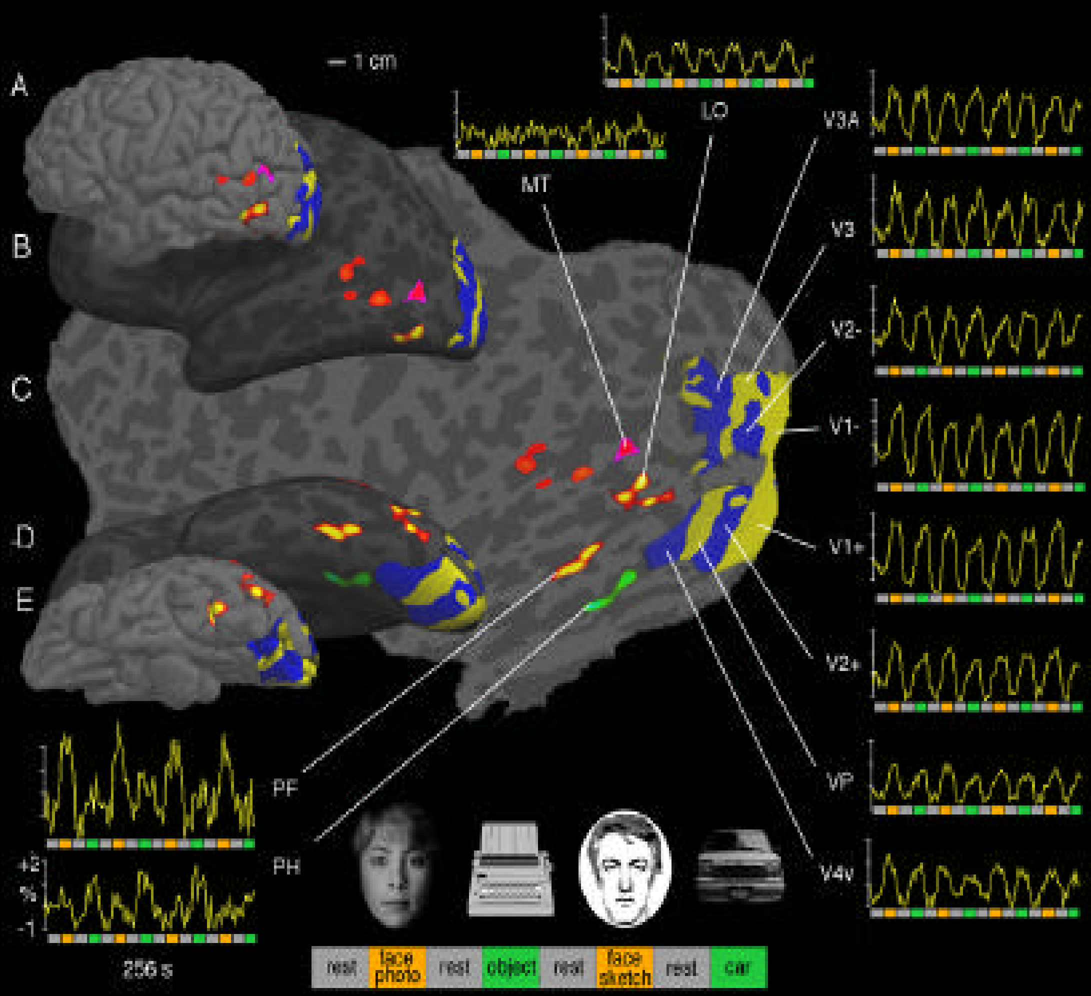


Inflated surface with cuts



Metrically optimal flat map





Borrowed from (Halgren et al., 1999)

Inter-subject Registration

Goal: align functionally homologous points across subjects (e.g. hippocampus with hippocampus, amygdala with amygdala, etc…).

Problem: this information is in general unavailable

Typical solution: align image intensities and hope this results in alignment of function/structure as well.

Inter-Subject Registration: Standard Formulation

Find *f* that minimizes $\int (I(f(\mathbf{r})) - T(\mathbf{r}))^2 d\mathbf{r}$

(*T* is target image, *I* is input image, *r* is spatial coordinate)

Some typical forms for *f*:

- **-Linear/Affine (many groups)**
- **-Polynomial (Woods et al. AIR)**
- **-Discrete Cosine Transform (Ashburner and Friston, SPM)**
- **-Navier Stokes (Miller)**

Some Definitions

p(A|B) is called the ***likelihood*** of A given B. If ***p(A|B)*** is exponential (e.g. Gaussian) in form, the log of the likelihood is much easier to work with. Usually ***A*** is some observed data and ***B*** is a set of model parameters that we want to estimate.

The ***B*** that maximizes ***p(A|B)*** is called the ***maximum likelihood*** estimate (MLE) of ***B***.

The value of ***B*** that maximizes ***p(B|A)*** is called the ***maximum a posteriori*** (MAP) estimate of B (more on this later).

What does Mean-Squared Error Estimation mean from a Probabilistic Perspective?

Assume $\log(p(I \mid f, T)) = \quad (I(f(\mathbf{r})) - T(\mathbf{r}))^2 d\mathbf{r}$

Then: $p(I \mid f, T) = \quad e^{(I(f(\mathbf{r})) - T(\mathbf{r}))^2}$

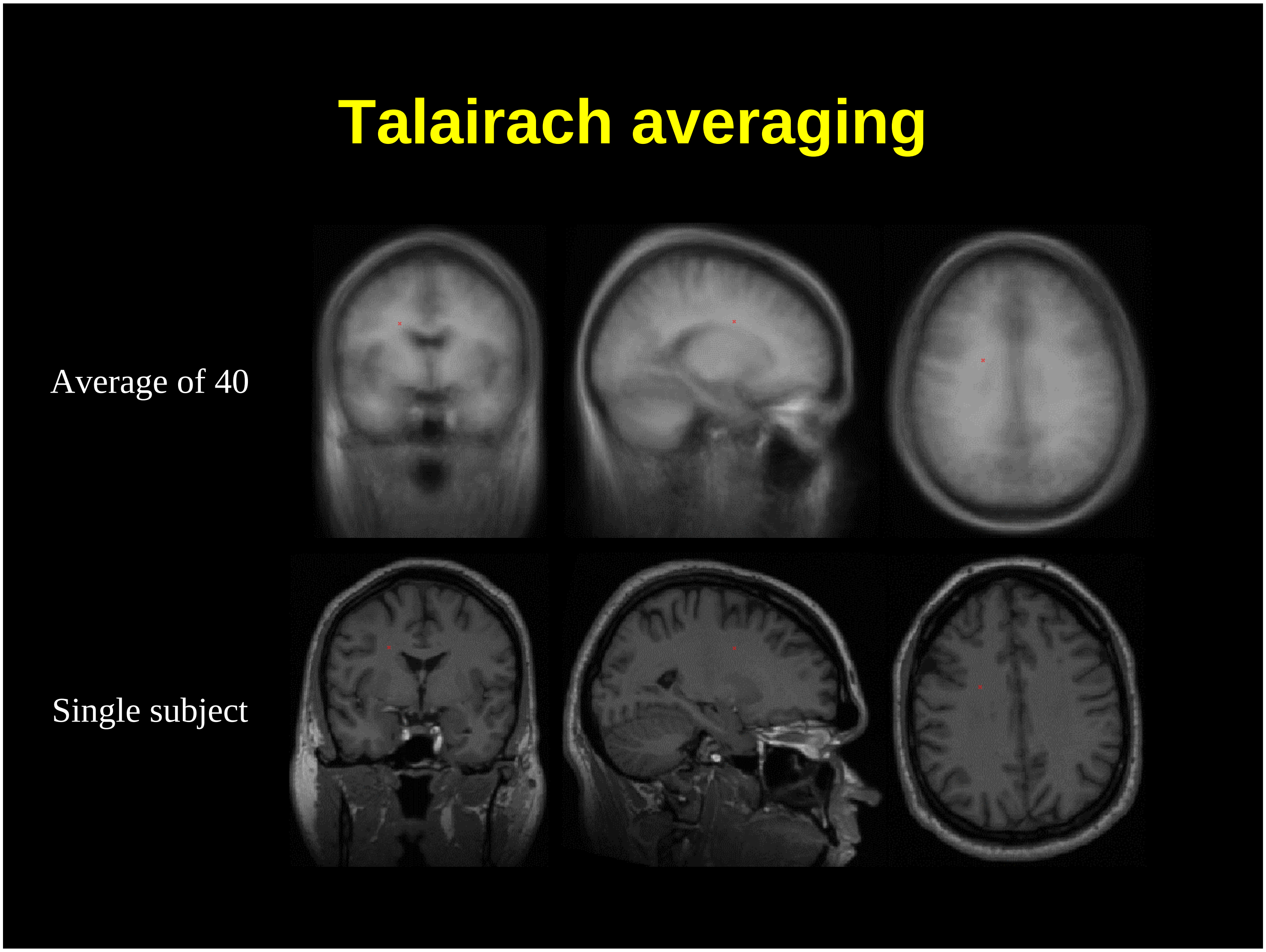
$\hat{f}$ is the maximum likelihood solution assuming the image can be modeled as a set of random variables with means *T(r)* and equal variances.

Talairach Coordinates

Can mean many things, but most common is linear transform to align input image with a target image that is average of many individuals aligned with the atlas of Talairach and Tournoux (1988).

Not Good For Cortex!

- Typical transform is too low dimensional to account for variability in cortical folds.
- Landmarks are subcortical (and far from much of cortex).
- Implicit assumption that 3D metric is appropriate one.


Talairach averaging
Average of 40
Single subject

How to align different cortical surfaces?