Cortical and Subcortical Neuranatomical Modeling

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Talk Outline

1. Cortical Analysis.
2. Subcortical Analysis.
3. Linking macro and microstructure.

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2. Subcortical Analysis.
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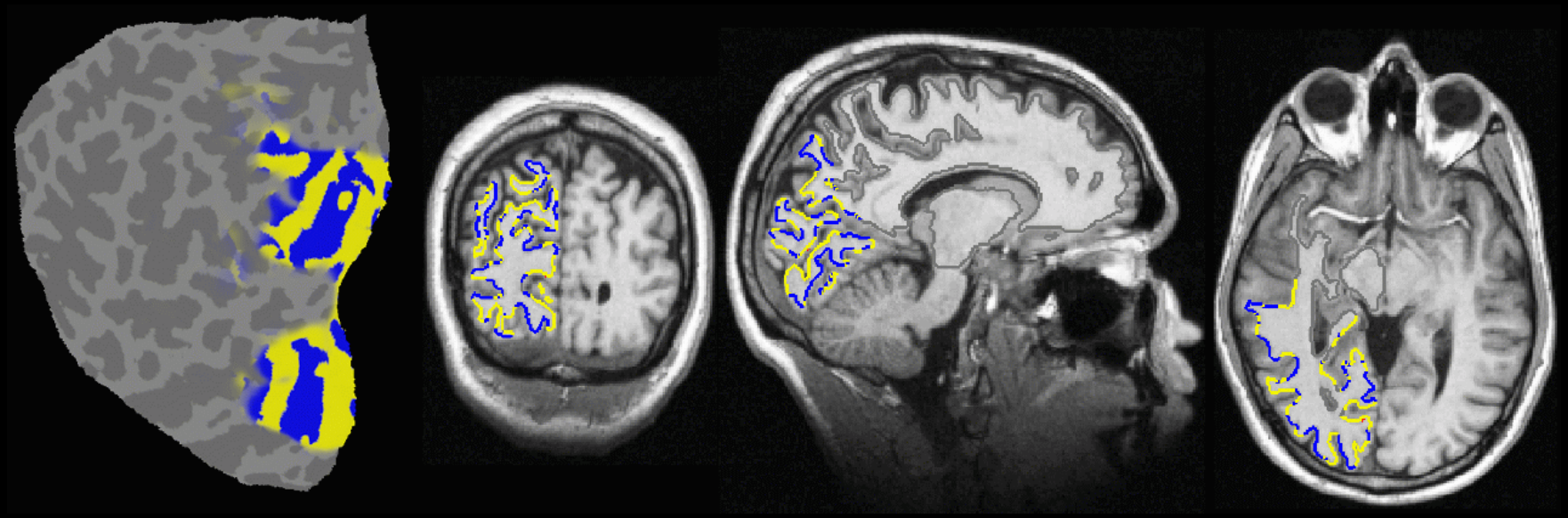
Why Is a Model of the Cortical Surface Useful?

Local functional organization of cortex is largely 2-dimensional!



From (Sereno et al, 1995, Science).

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.

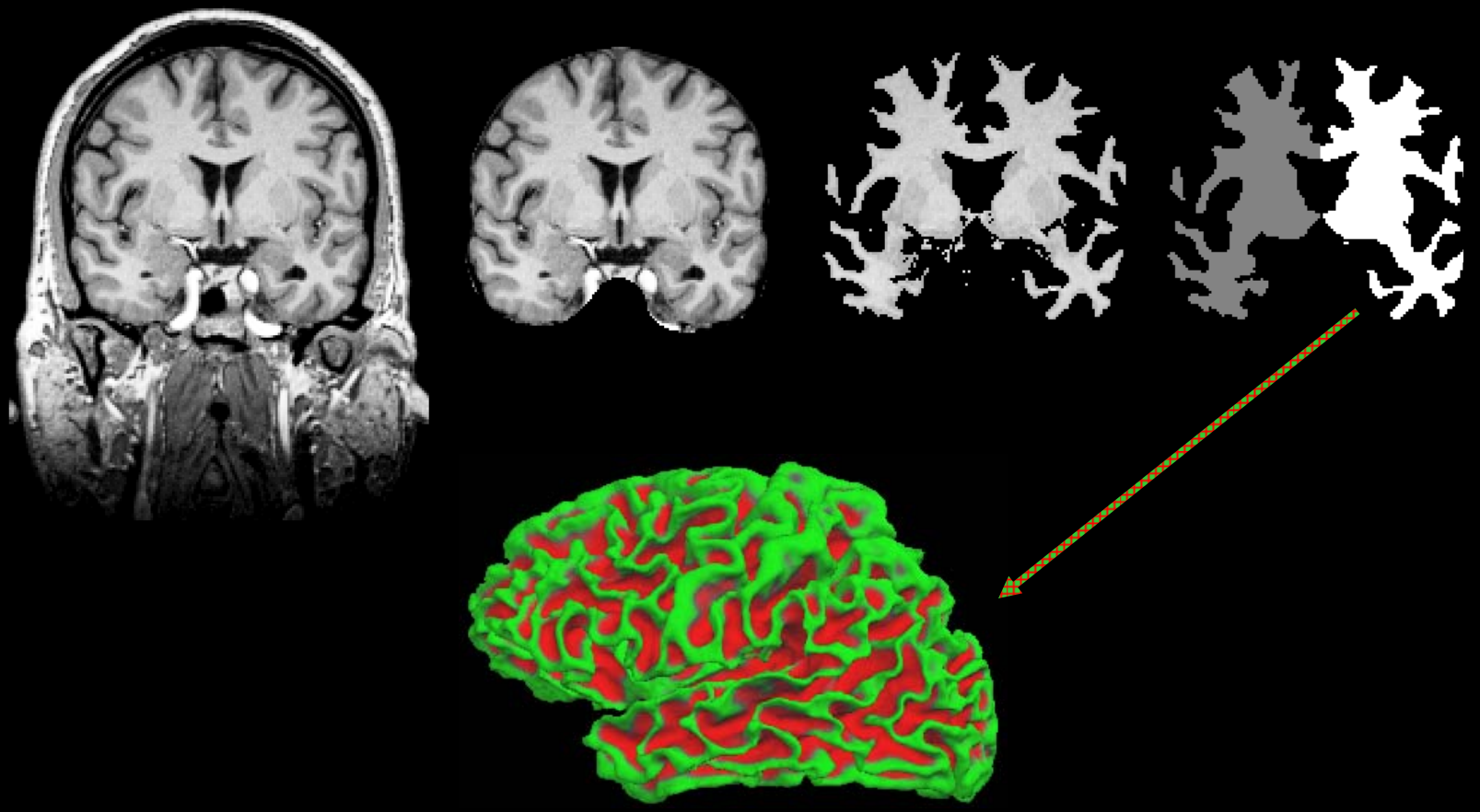
Intensity of a tissue class varies as a function of spatial location

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).

MRI Segmentation and Surface Reconstruction

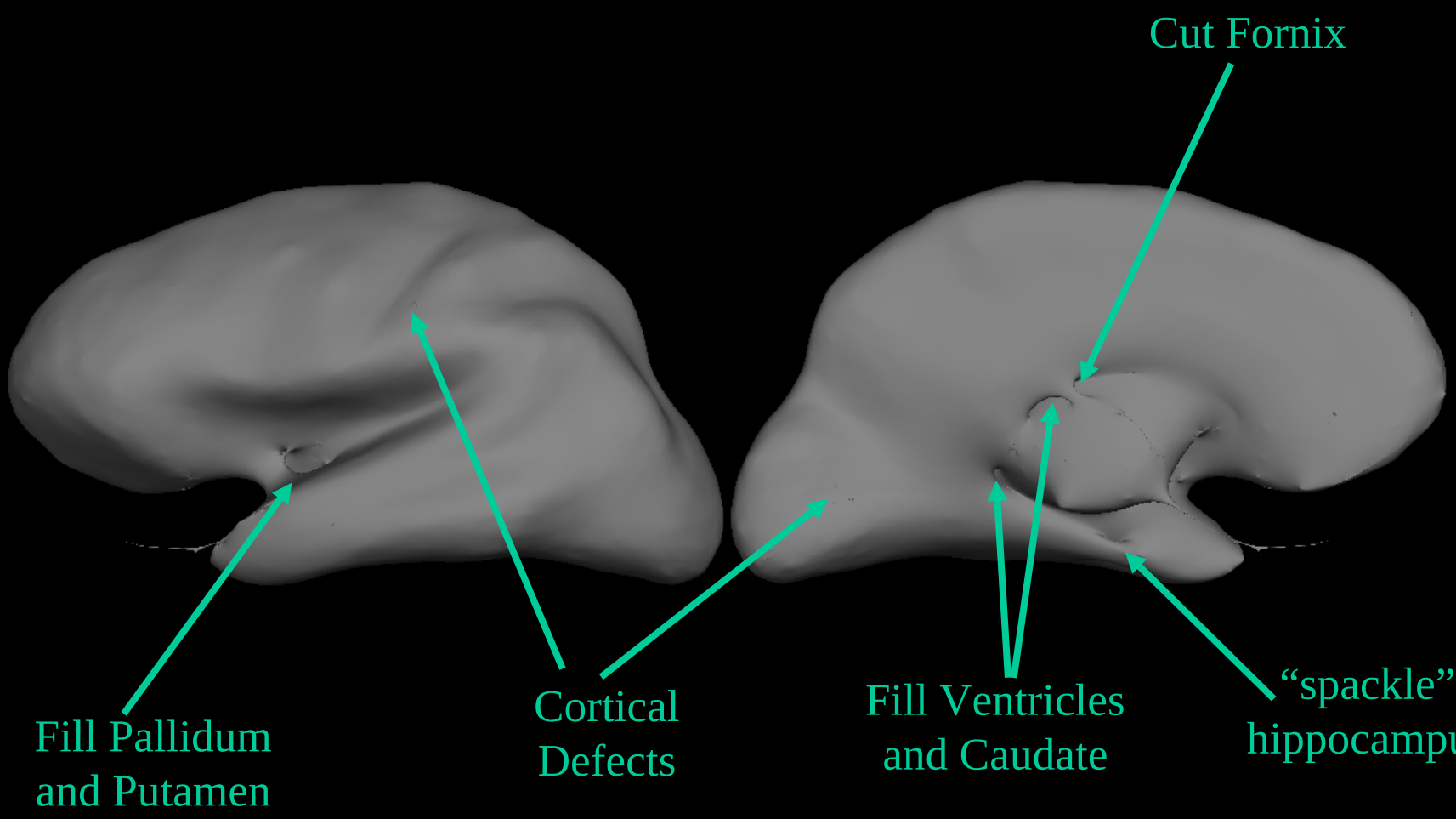


Topology Correction

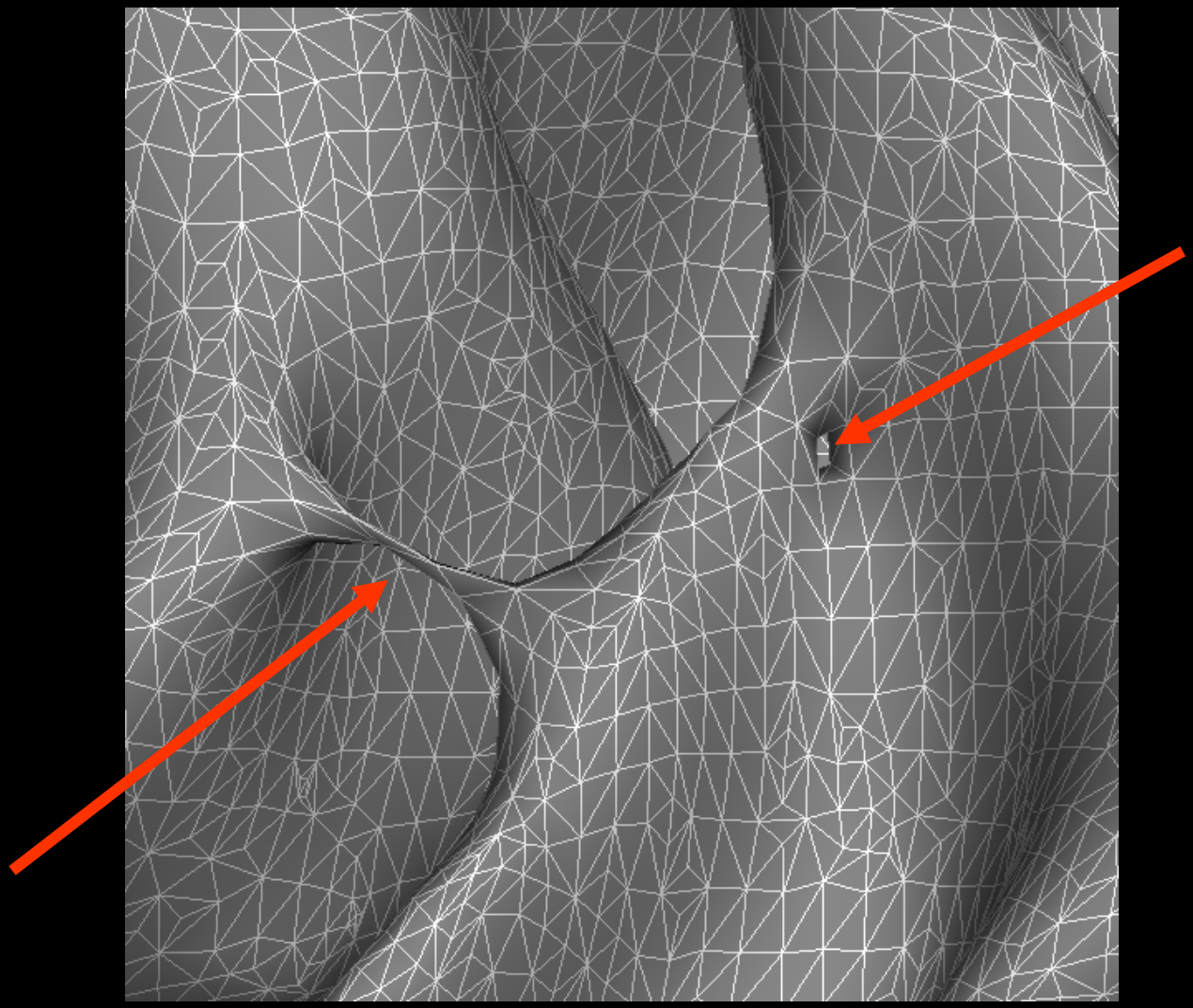
The true topology of the cortical ribbon is that of a sheet (Euler number=1).

We would like the reconstructed gray/white boundary to have spherical topology (Euler number=2), but errors in the segmentation and non-cortical anatomical features of the white matter cause departures from spherical topology (“defects”).

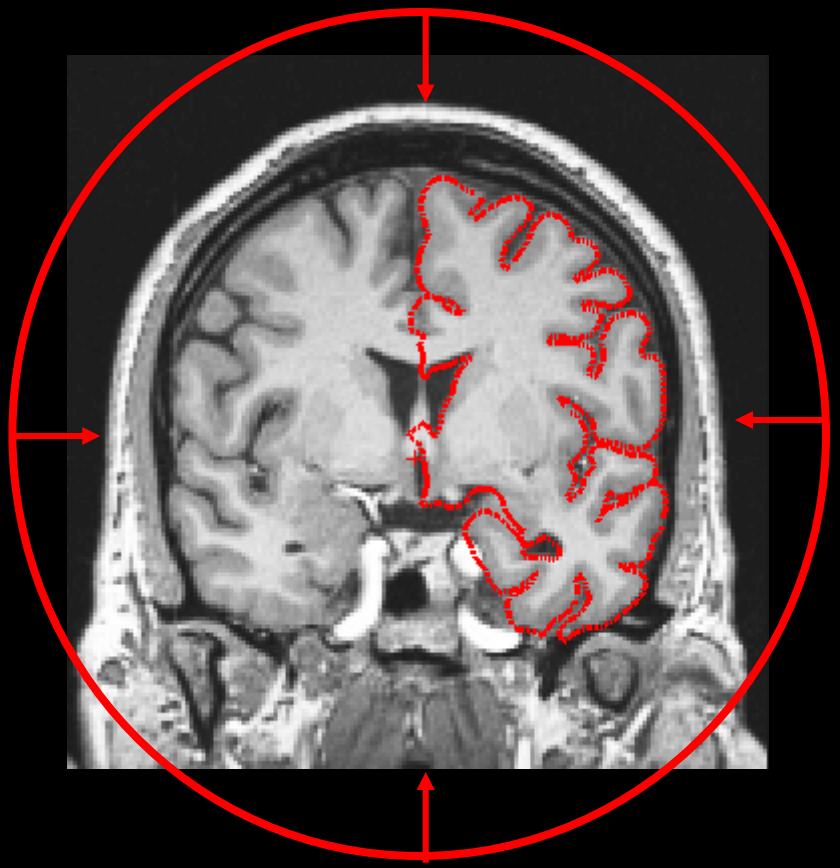
Typical “Defects”



Topological Defects



Standard method*: shrink wrapping



start with a surface S (e.g. sphere) of known topology find a mapping $M:S \mapsto C$ of it to the cortex *C* that doesn't change its topology (e.g. Davatzikos, 1996; Macdonald 2000)

*newer volumetric work (Shattuck and Leahy, 2001; Han et al., 2002)

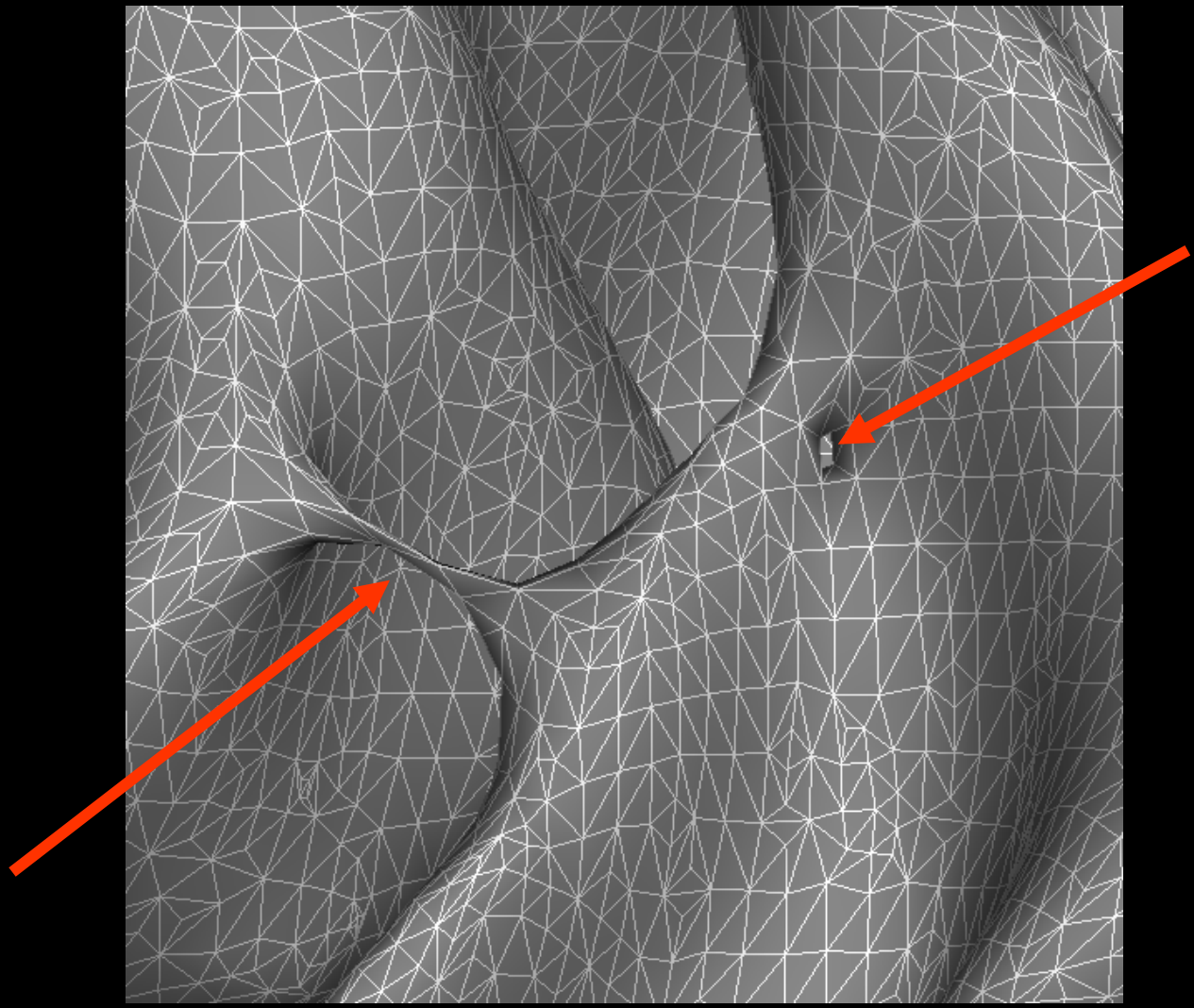
How to maintain geometric accuracy?

Problems:

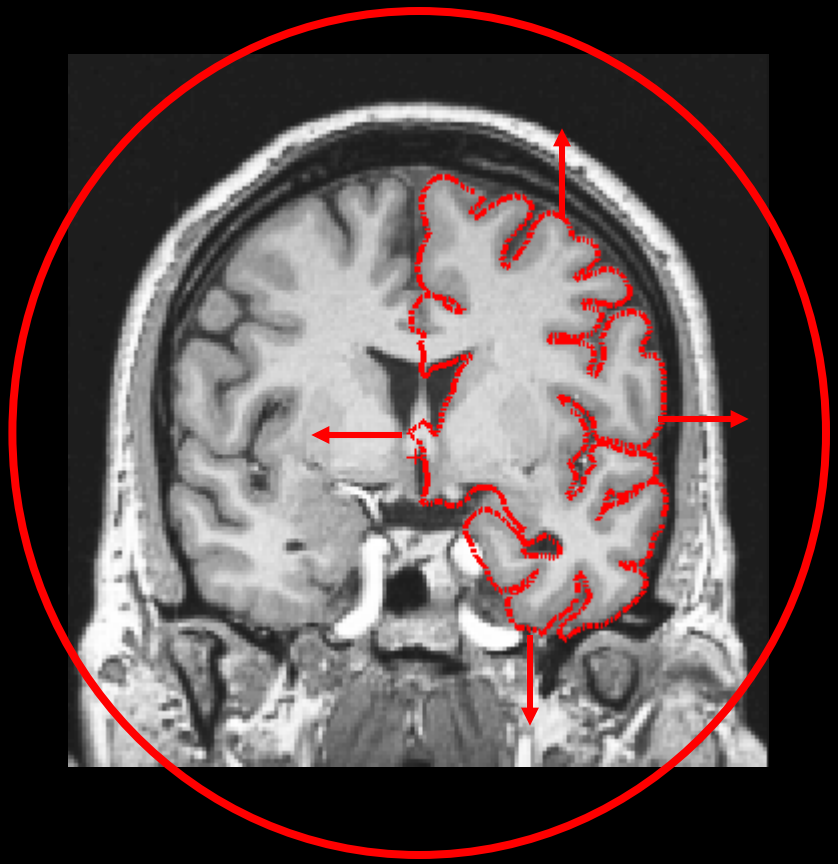
1. **The initial surface *S* is typically *much* smoother than the target surface *C*. The energy functionals for finding *M* are therefore highly non-convex.**

2. **Local errors that would have given rise to inaccurate segmentation if the topology were not constrained, can cause large scale geometric inaccuracies in the surfaces.**

What Surface Would a Shrink-Wrapping Algorithm Result in?



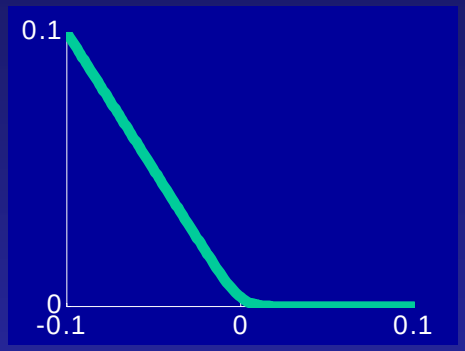
Solution: Manifold Surgery.



Generate *C'* and find a mapping M^{-1} from *C'* to *S* that is invertible over as much of *C* as possible. Noninvertible regions contain defects!

Manifold Surgery: Equations

Energy Functional: $$E = \sum_{i=1}^{F} \left(\frac{\log(1 + e^{-kR_i})}{k} \right)$$

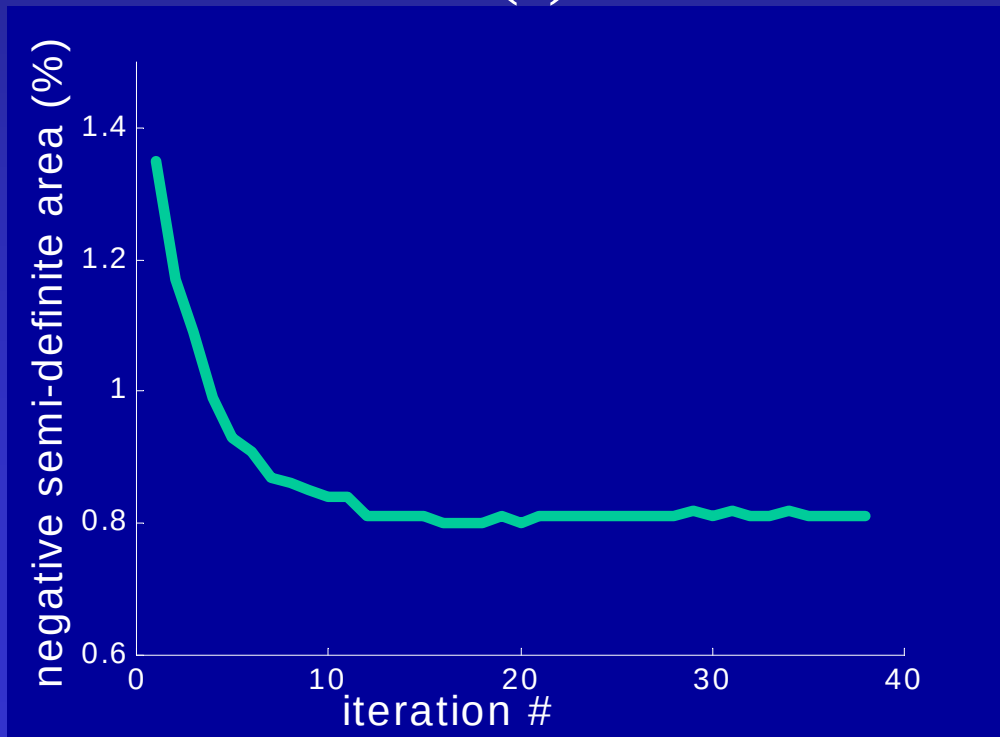


det(J)

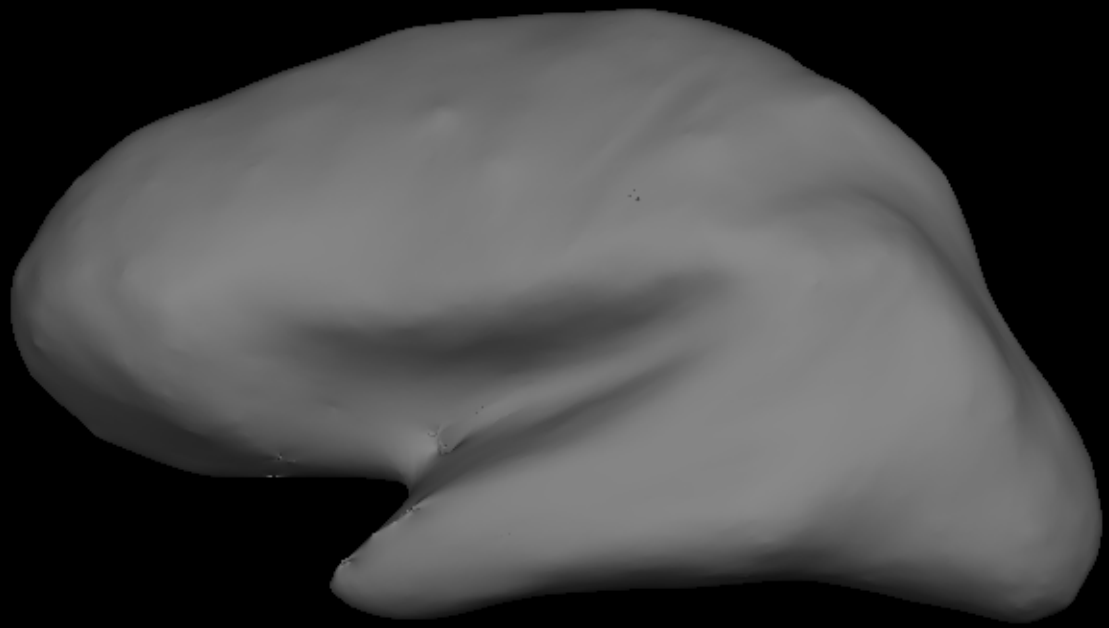
R_i – jacobian at the i^{th} face in tessellation

F – number of faces in tessellation

k – positive real constant



Detection of non-homeomorphic Regions



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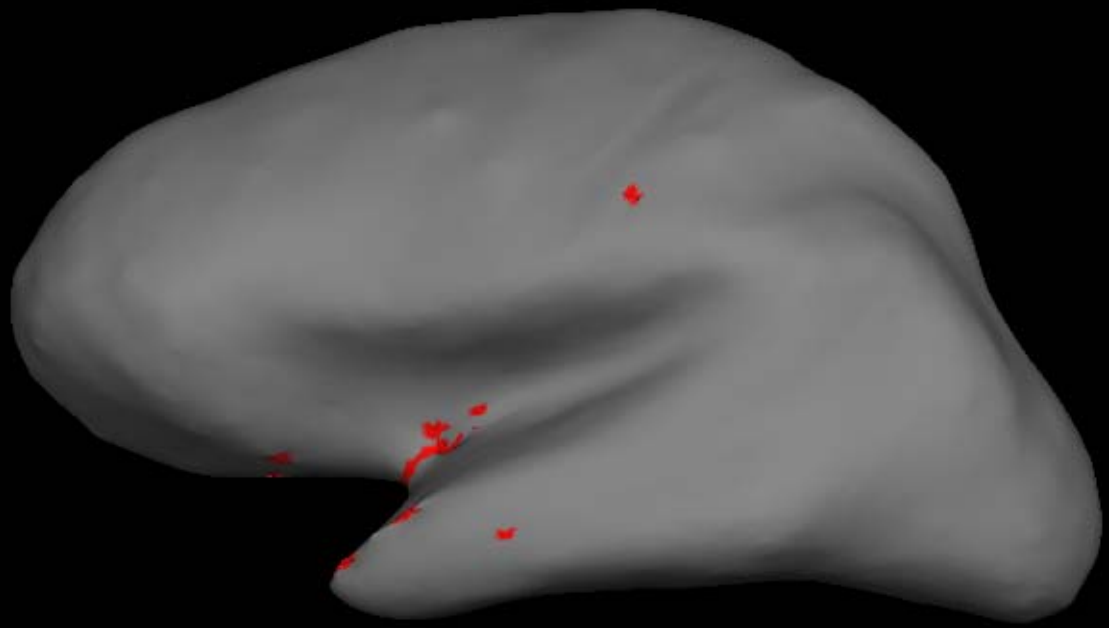

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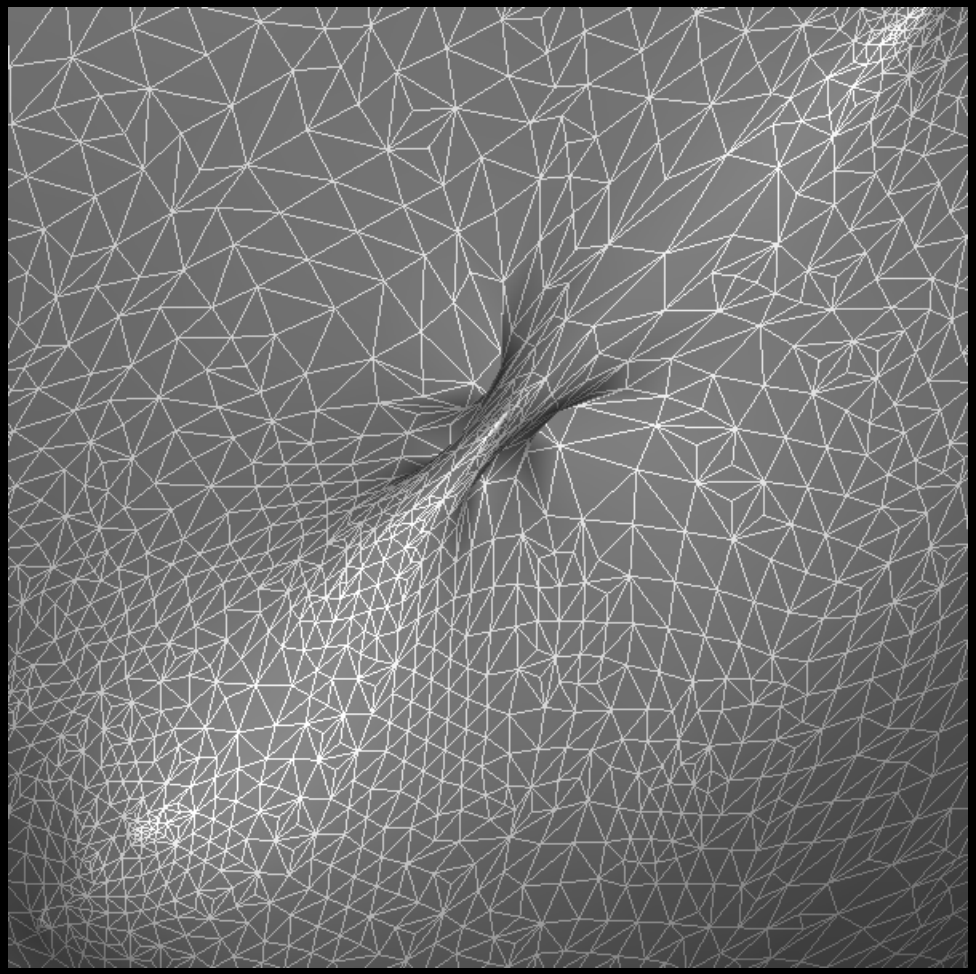
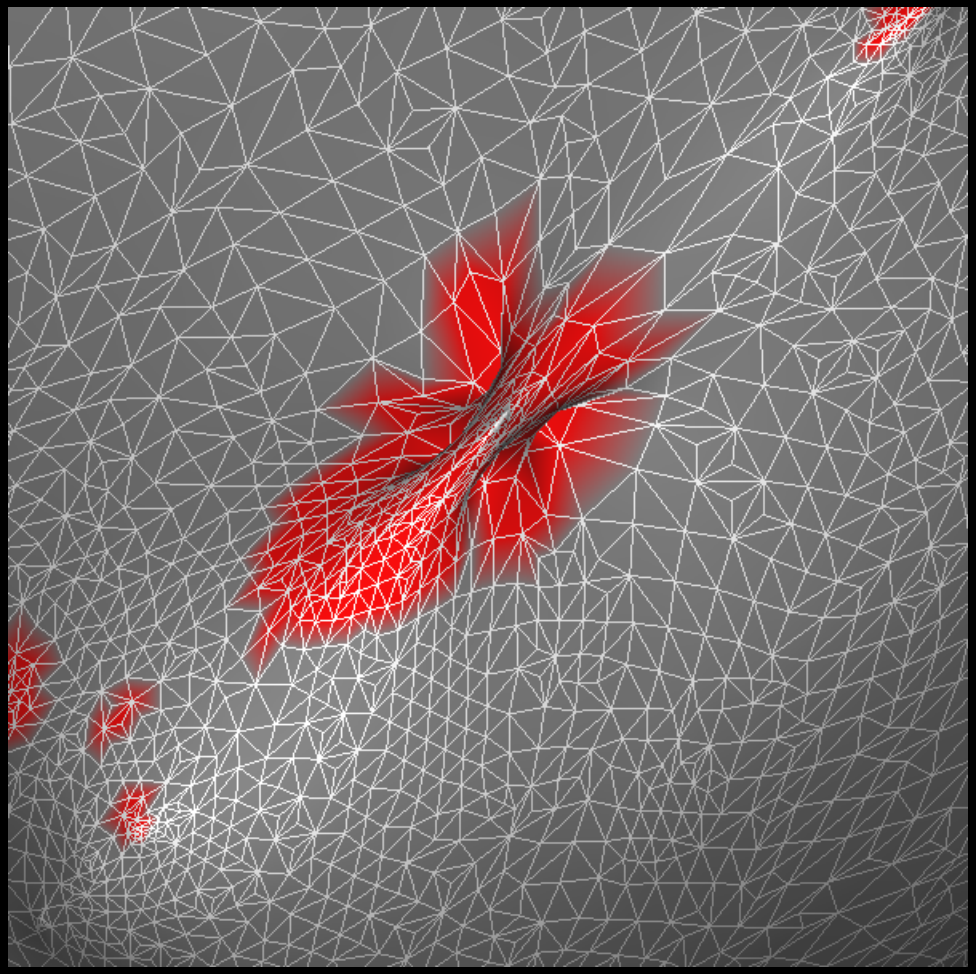


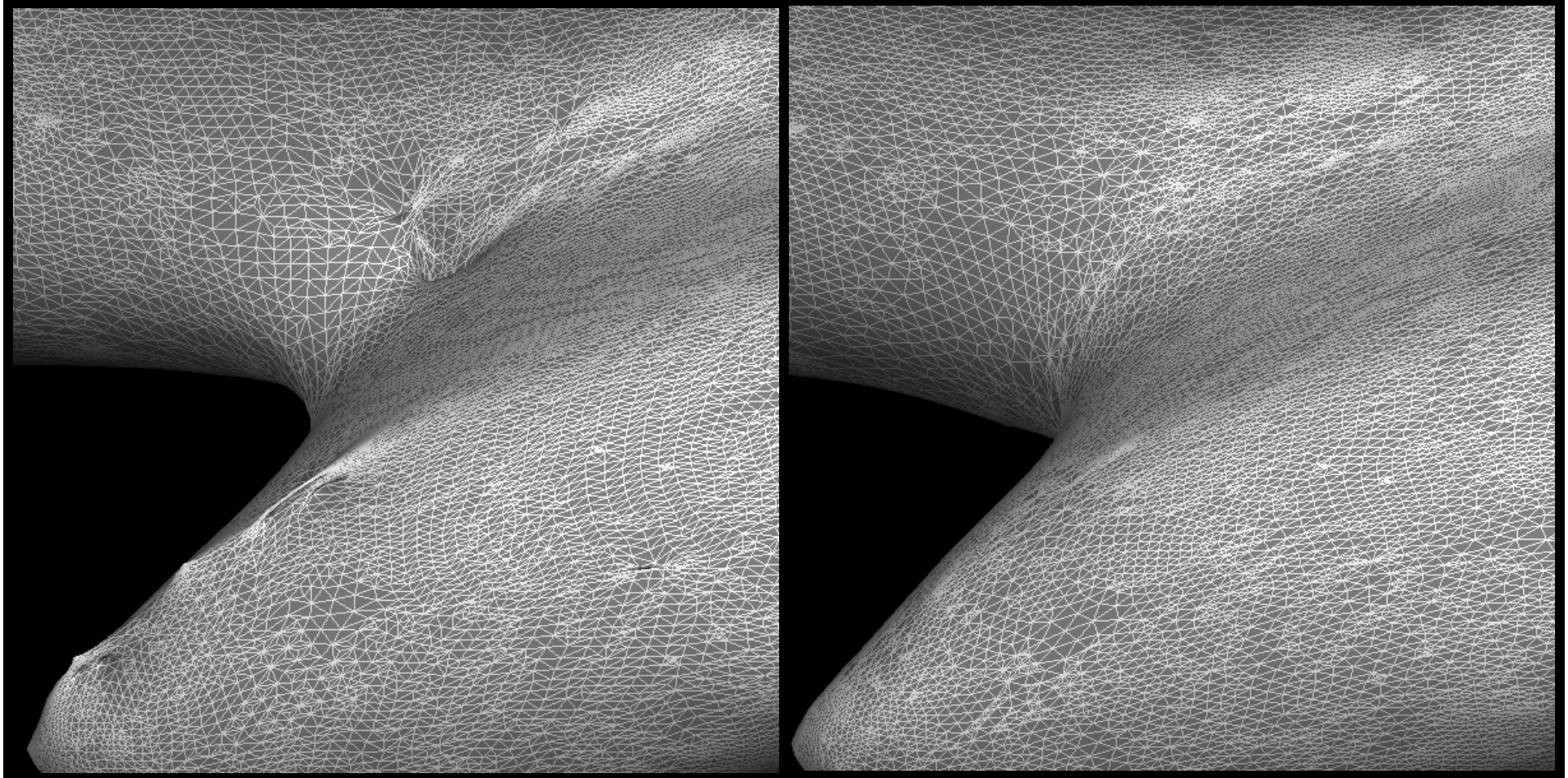
Detection of non-homeomorphic Regions



Manifold Surgery: Retessellation

1. Mark all triangles that have any edge overlapping any other edge in the tessellation.
2. Discard all faces and edges in marked triangles.
3. Use a genetic retessellation algorithm: keep adding edges between all vertices in defects until no more can be added without causing an intersection with an existing edge on the sphere or in the embedding space. Optimize p(S|I) (posterior probability of observed surface S given the MR image I).

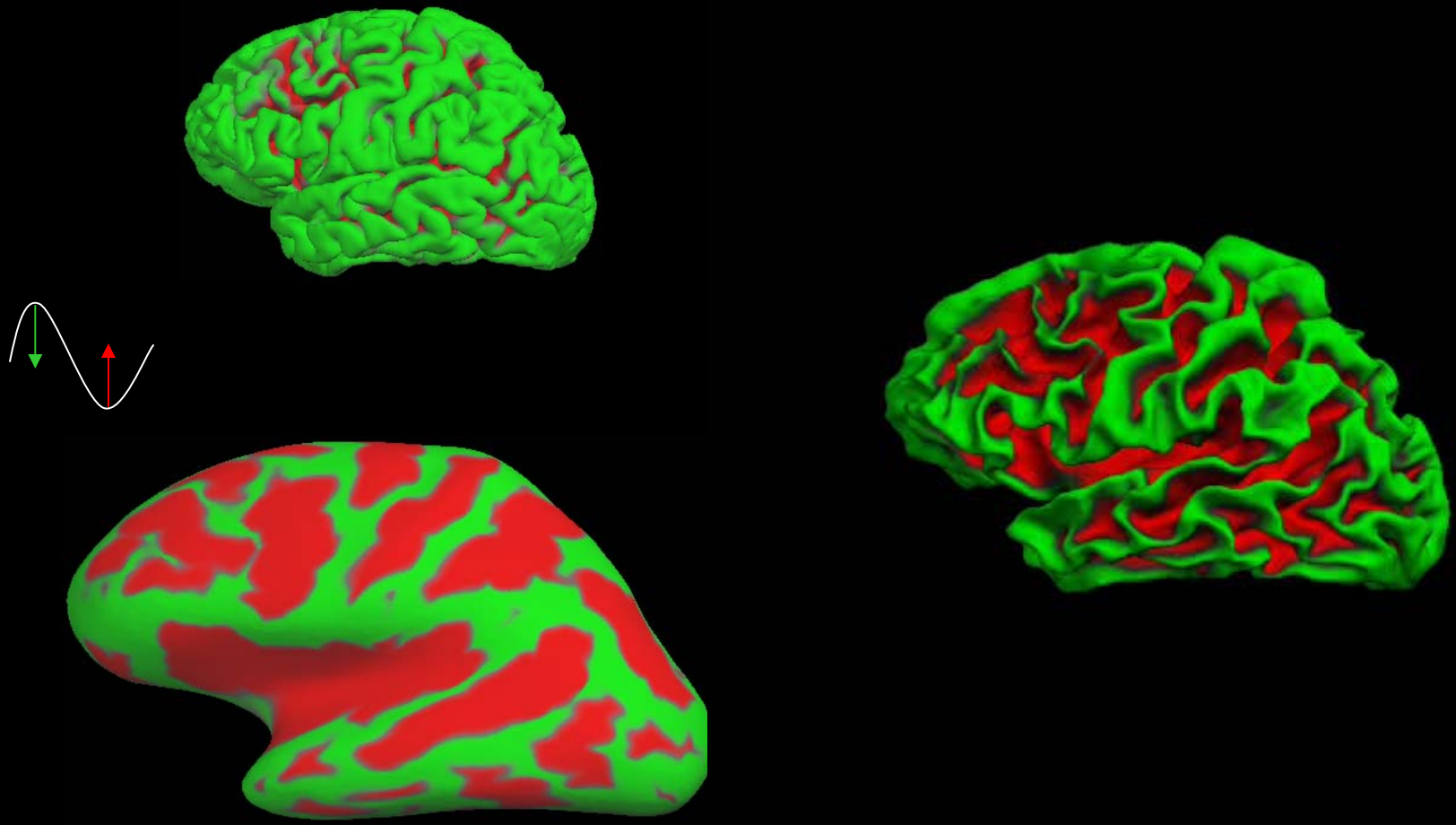
Manifold Surgery: Results



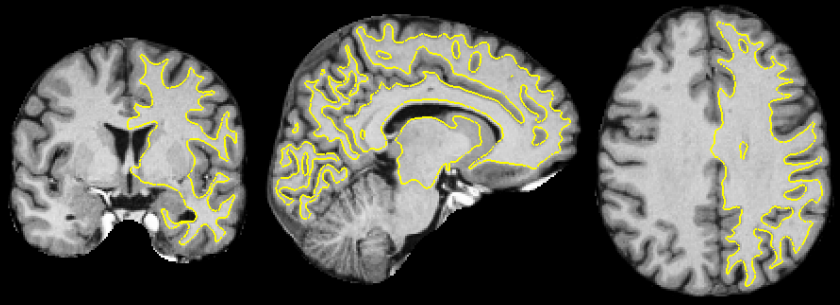
BEFORE

AFTER

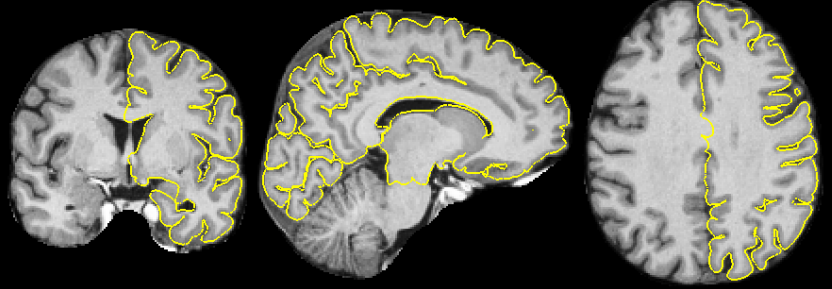
Surface Inflation



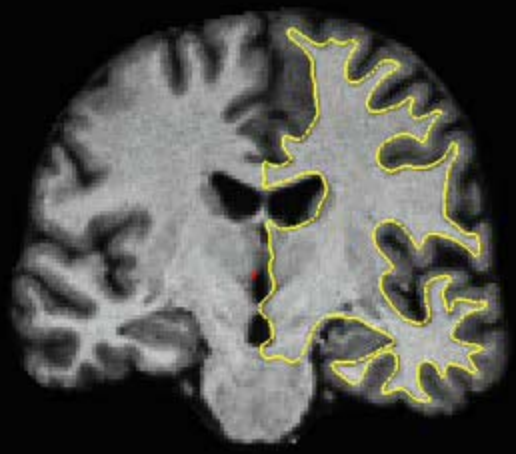
White matter and pial surfaces



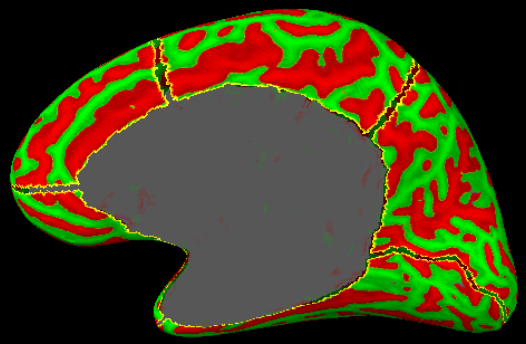
Gray-white boundary



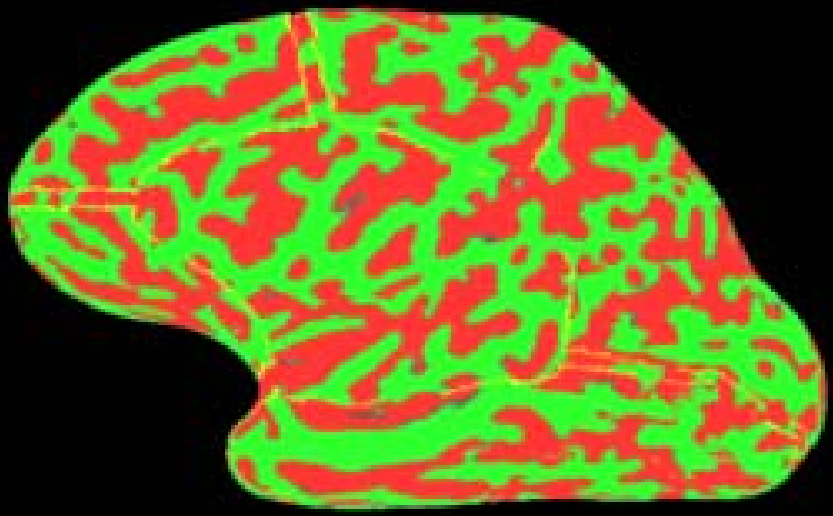
Pial surface

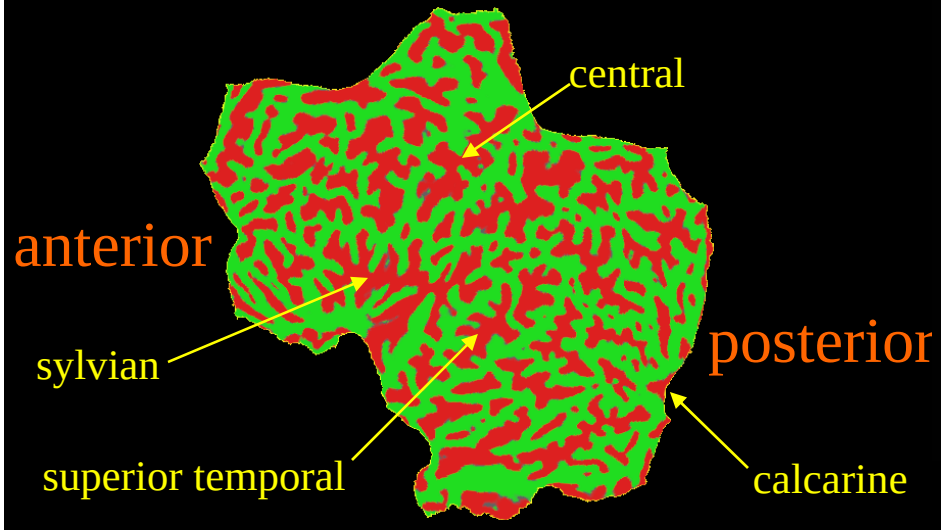


Surface Flattening – Whole Hemisphere

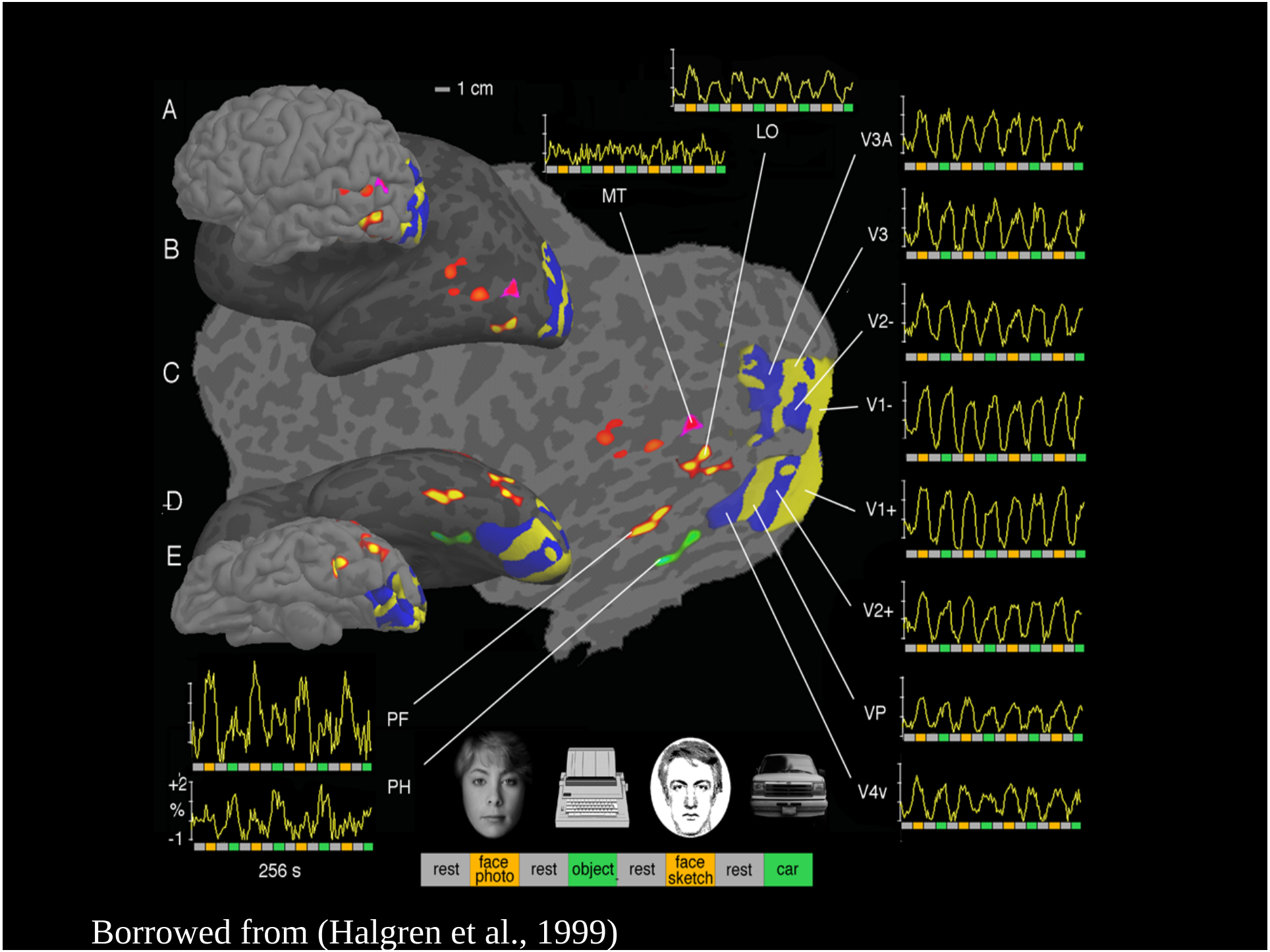


Inflated surface with cuts





Metrically optimal flat map



Borrowed from (Halgren et al., 1999)

Talairach Coordinates

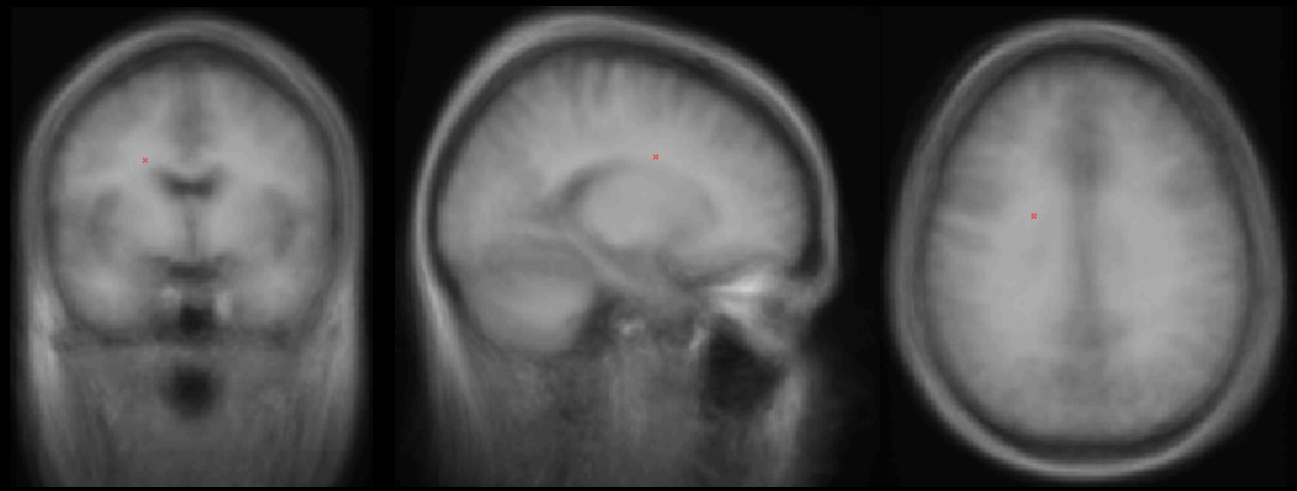
Can mean many things, but most common is linear transform to align input image with a target image that is average of many individuals aligned with the atlas of Talairach and Tournoux (1988).

Not Good For Cortex!

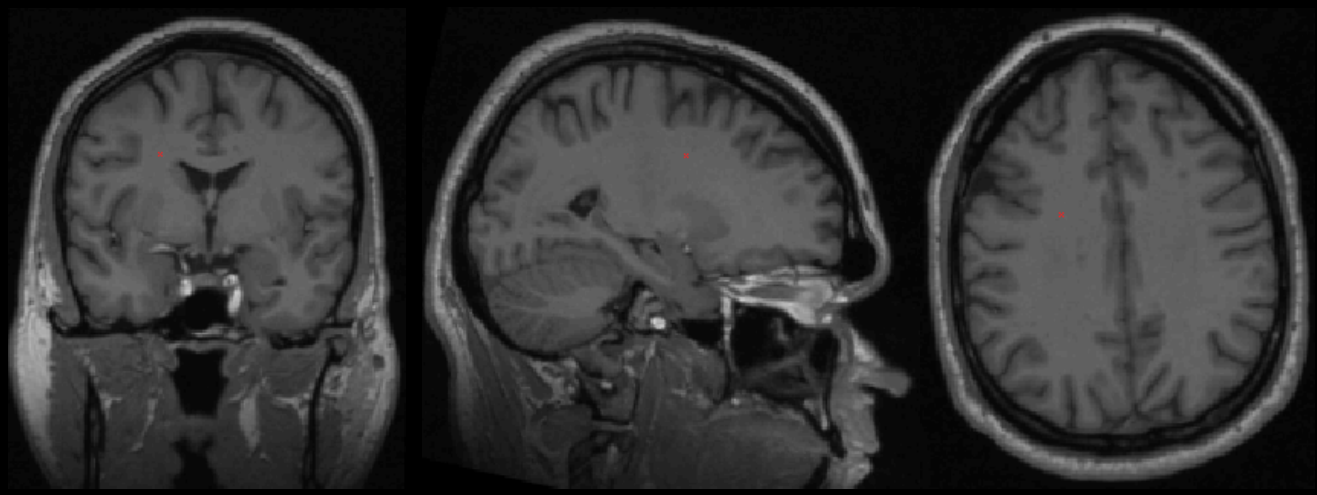
1. Typical transform is too low dimensional to account for variability in cortical folds.
2. Landmarks are subcortical (and far from much of cortex).
3. Implicit assumption that 3D metric is appropriate one.

Talairach averaging

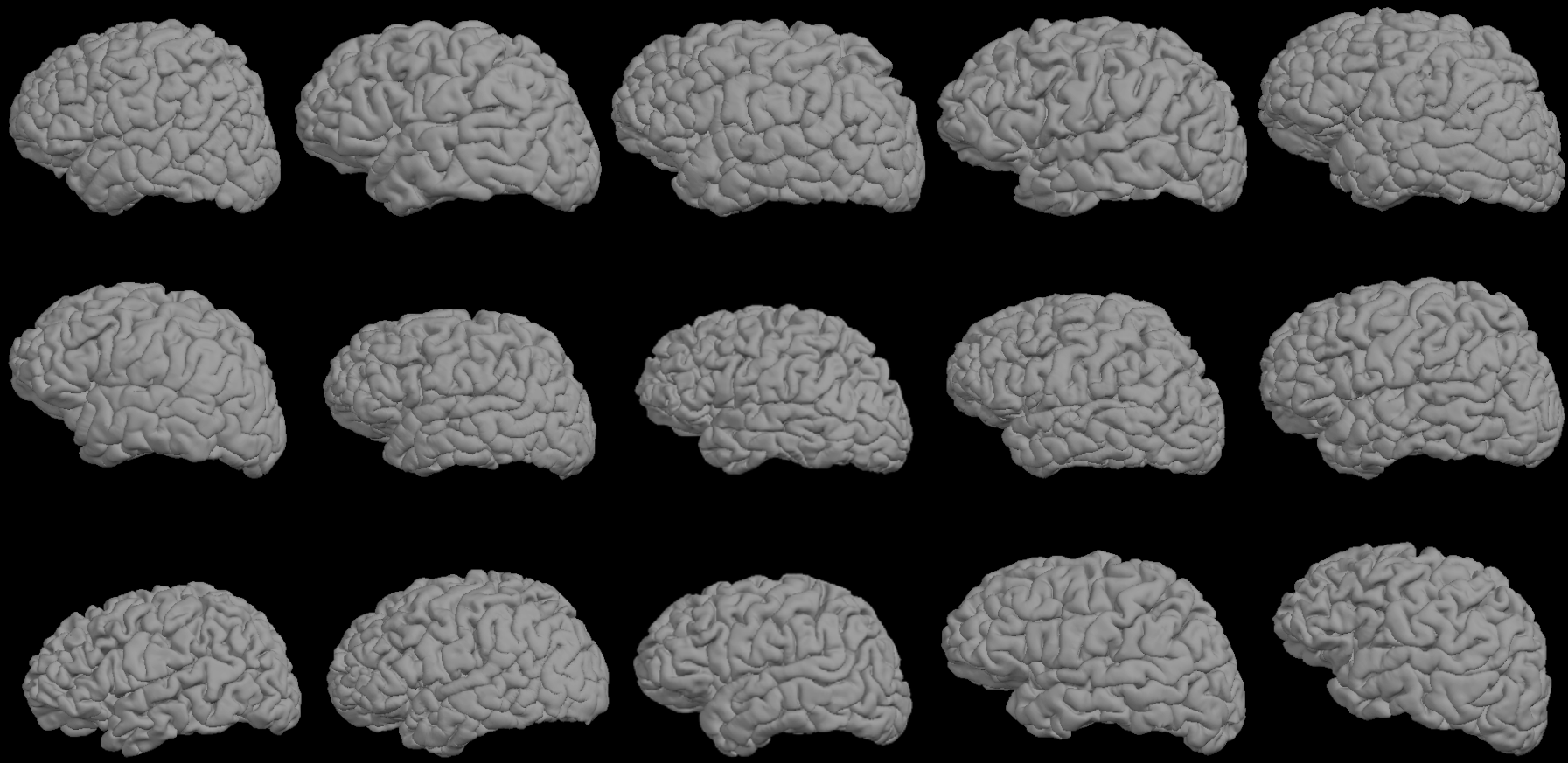
Average of 40



Single subject

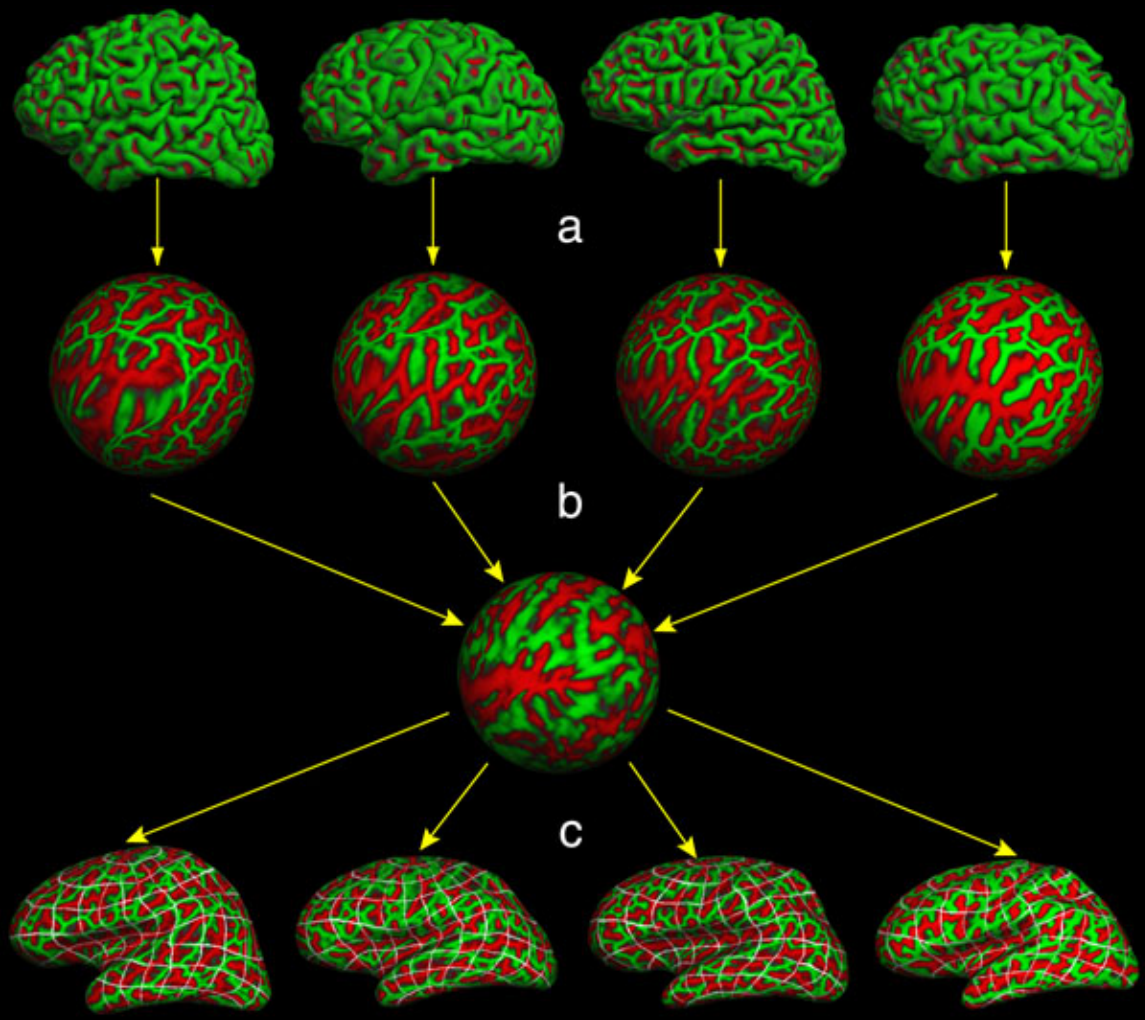


How to align different cortical surfaces?



e.g. Thompson and Toga, Drury and Van Essen, Tosun and Prince

A Surface-Based Coordinate System



Spherical Morphing: Equations

Energy Functional: $J_c+\lambda_d J_d+\lambda_T J_T$

J_c: Correlation error (aligns folding patterns)

J_d: Metric distortion (constrains allowable shape differences)

J_T: Topology term (forces mapping to be invertible)

Spherical Morphing: Equations

Average Folding Pattern:

$$\overline{C}(\varphi,\theta) = \frac{1}{N}\sum_{i=1}^{N} C_i(\varphi,\theta)$$

Variance of Folding

$$\sigma^2(\varphi,\theta) = \frac{1}{N-1}\sum_{i=1}^{N}(C_i(\varphi,\theta) - \overline{C}(\varphi,\theta))^2$$

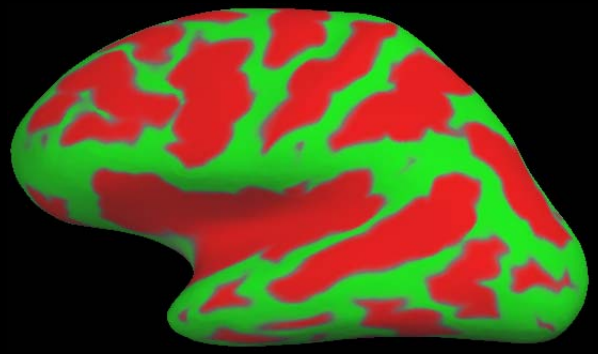
Maximum Likelihood Term:

$$J_c = \frac{1}{2V}\sum_{v=1}^{V}\left(\frac{G_\alpha * (C_v - \overline{C}(\phi(v),\theta(v)))}{\sigma(\phi(v),\theta(v))}\right)^2$$

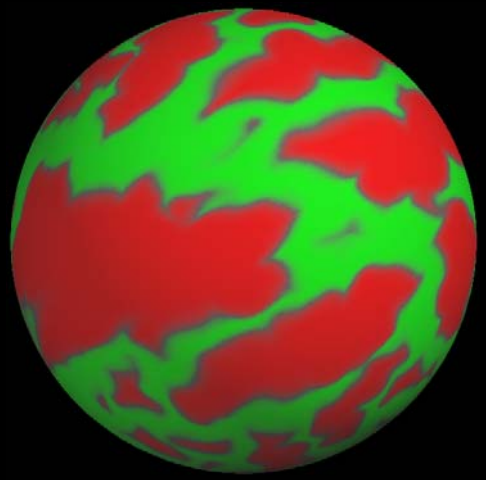
Complete Energy Functional:

$$J = J_c + \lambda_T J_T + \lambda_d J_d$$

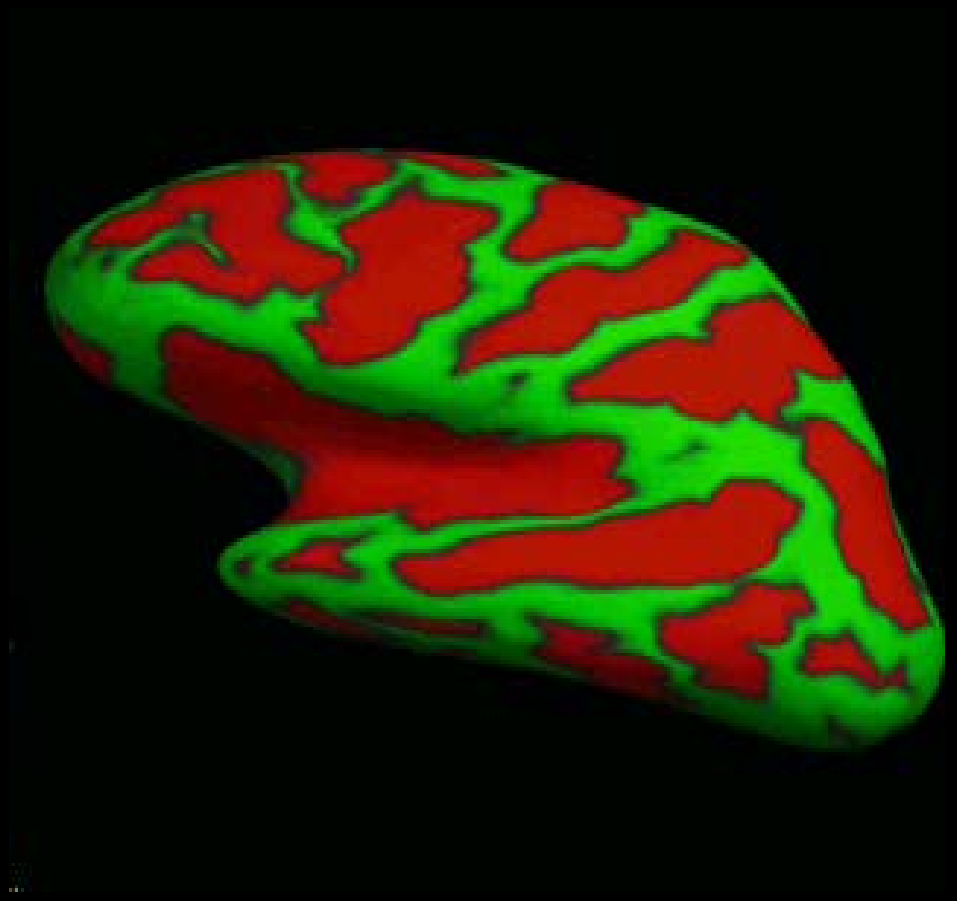
Maximally Isometric Spherical Mapping



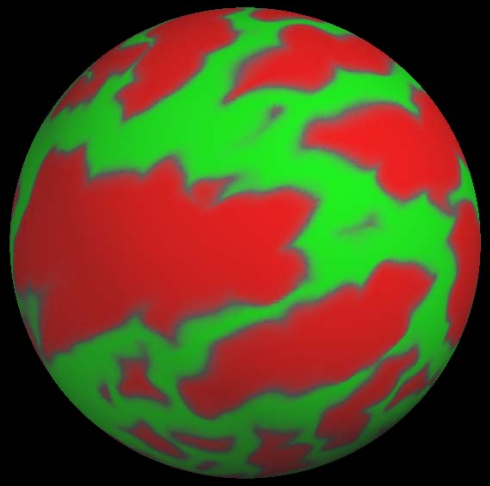
Inflated Surface



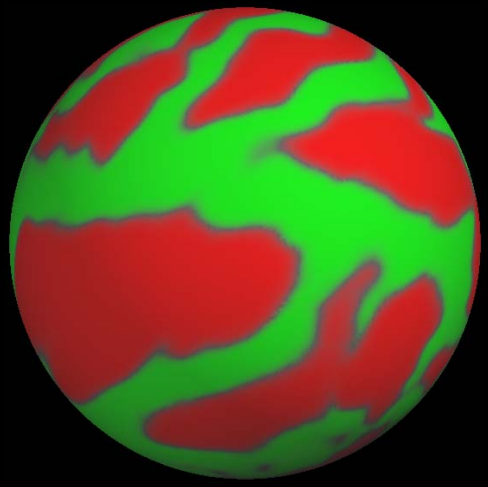
Transformed Surface



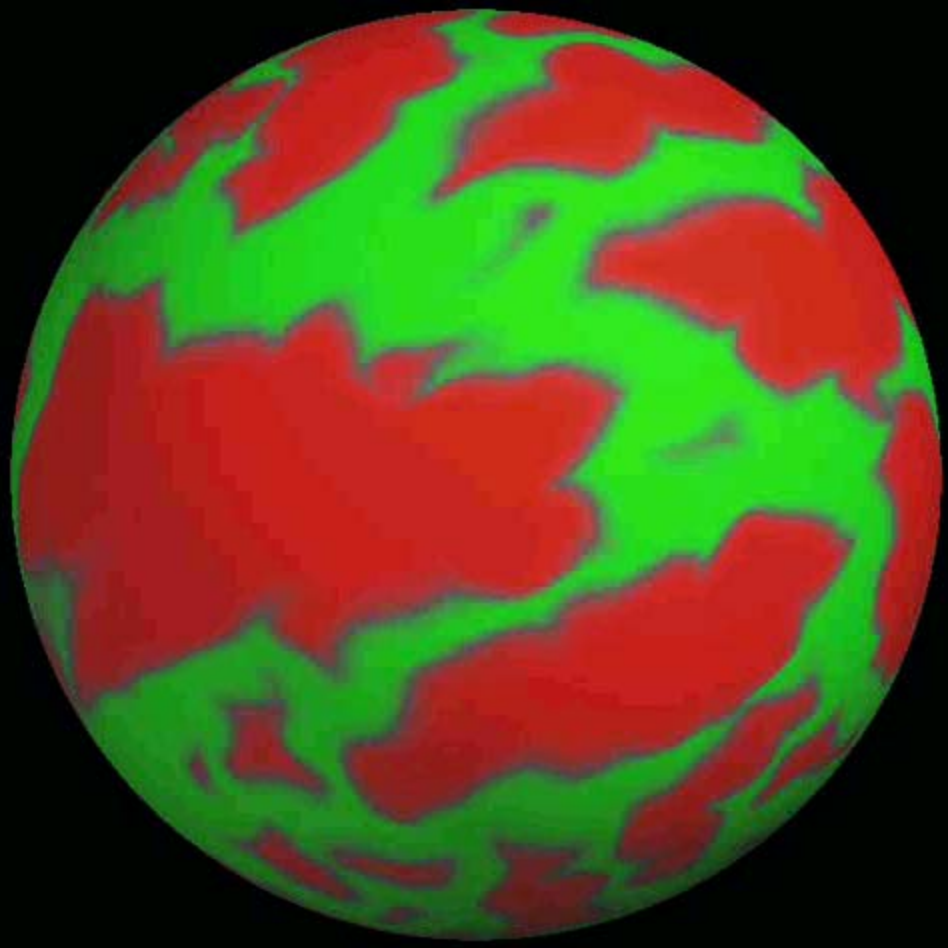
Inter-Subject Morphing



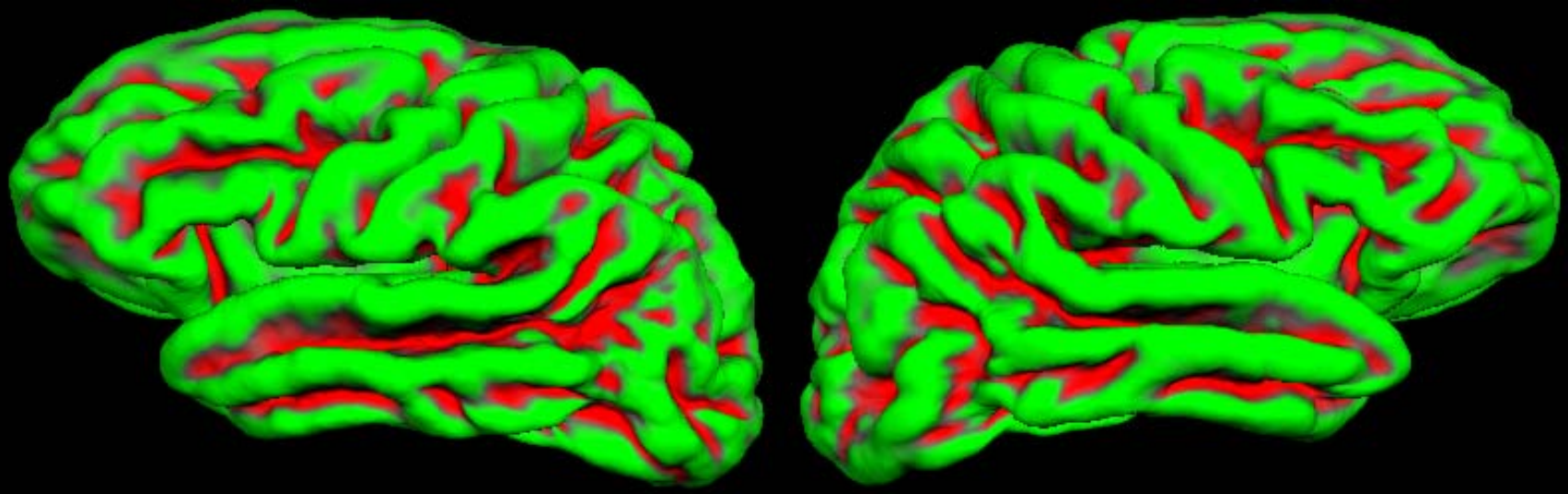
Individual Subject



Average (Target)



Surface-Based Averaging



Average surface created from 30 subjects

Applications

- Increased statistical power for inter-subject averaging
- Automatic functional/anatomical labeling
- Inter-subject averaging of morphometric properties
- Statistical analysis of morphometric properties
  - aging
  - neurodegenerative diseases
  - longitudinal studies of structural changes
  - hemispheric asymmetry
- Shape analysis of cortical folding patterns.

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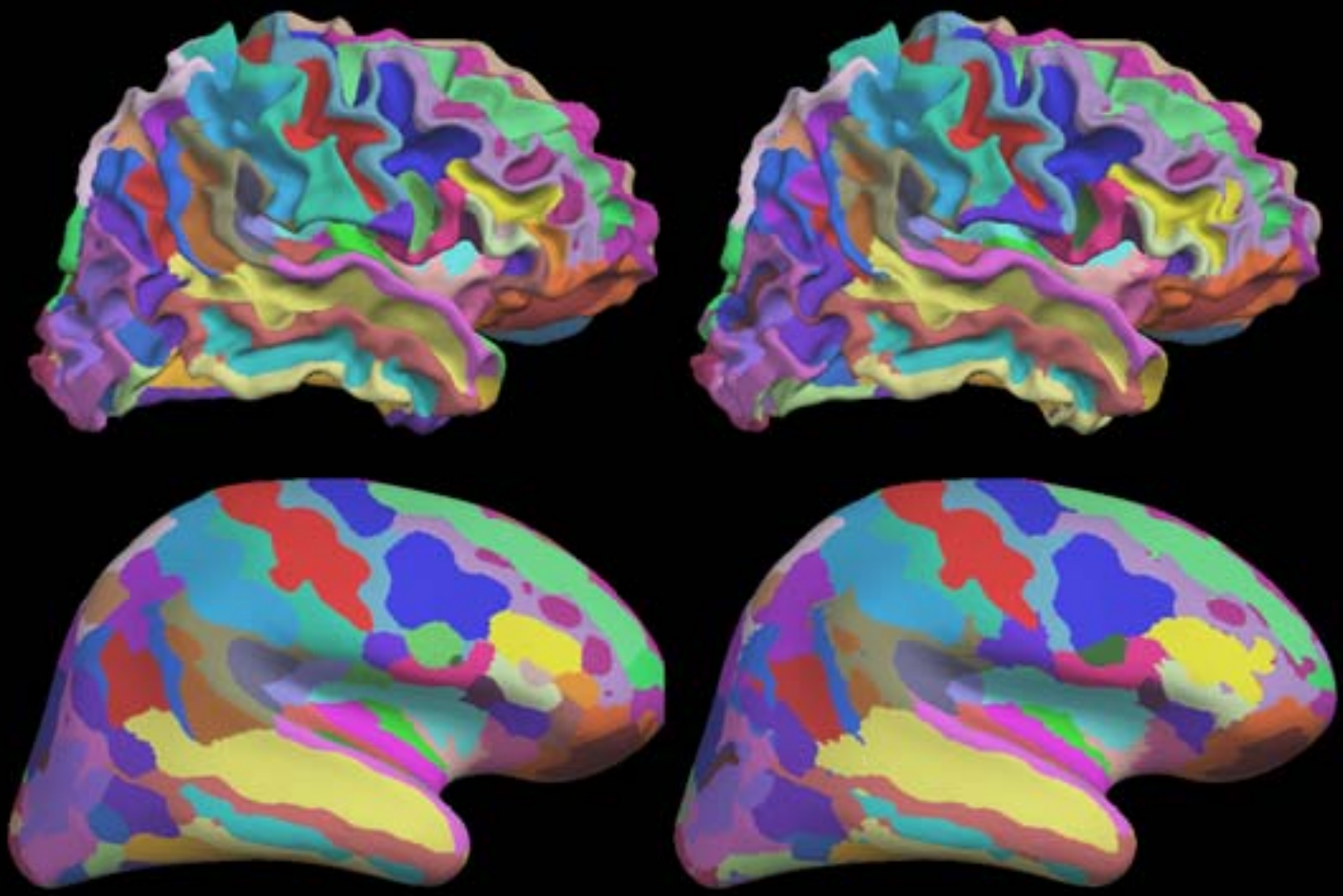
Cortical Parcellation: Manual vs. Automated



Manual Parcellation Automatic Parcellation

Thanks to Christophe Destrieux for this slide.

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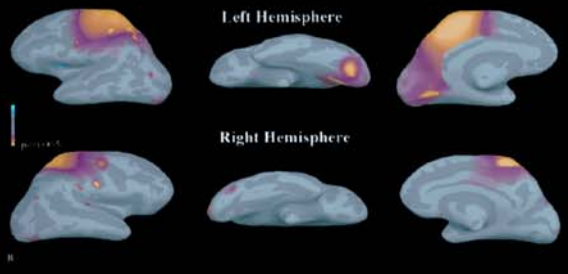
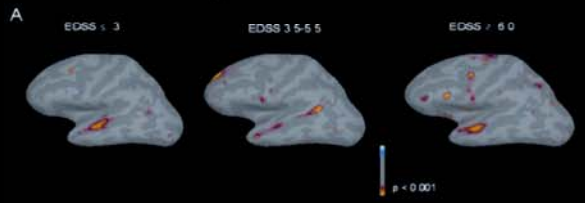
Huntington's Disease



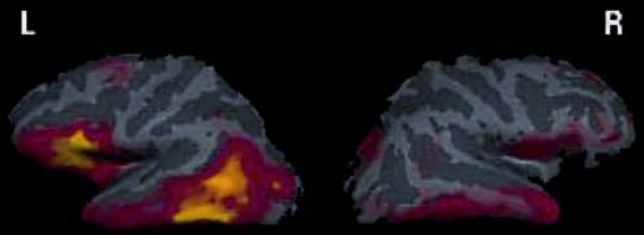
Rosas et al., 2002

Multiple Sclerosis

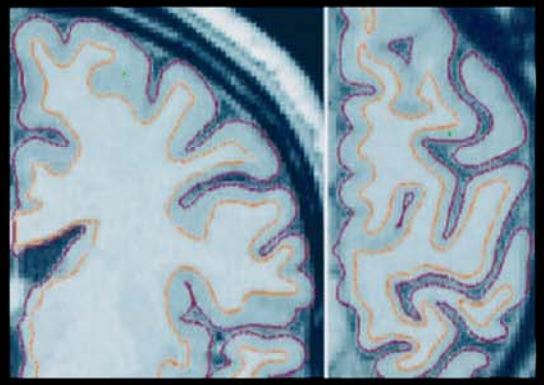


Sailer et al., 2003

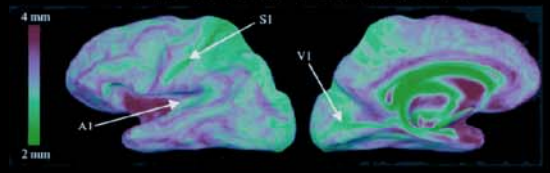
Schizophrenia



Kuperberg et al., 2003

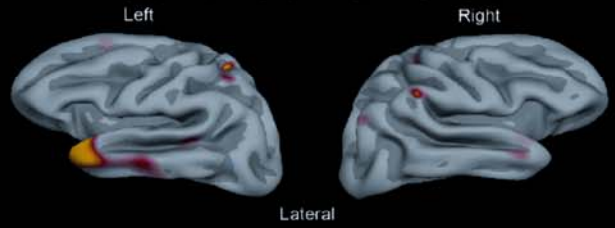


Normal Variation



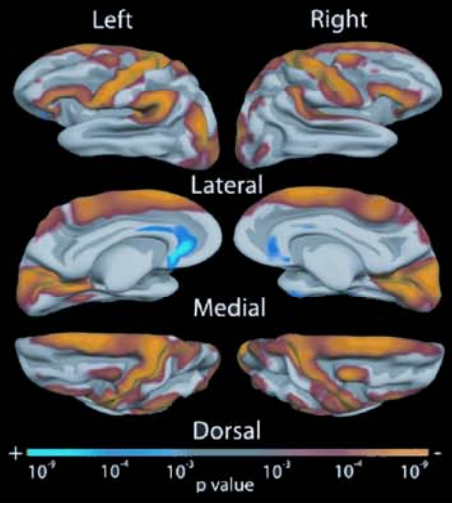
Fischl et al., 2000

Semantic Dementia



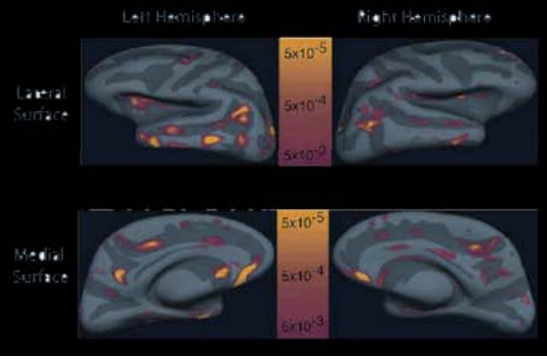
Gold et al., 2005

Aging



Salat et al., 2004

Animal Phobia



Rauch et al., 2004

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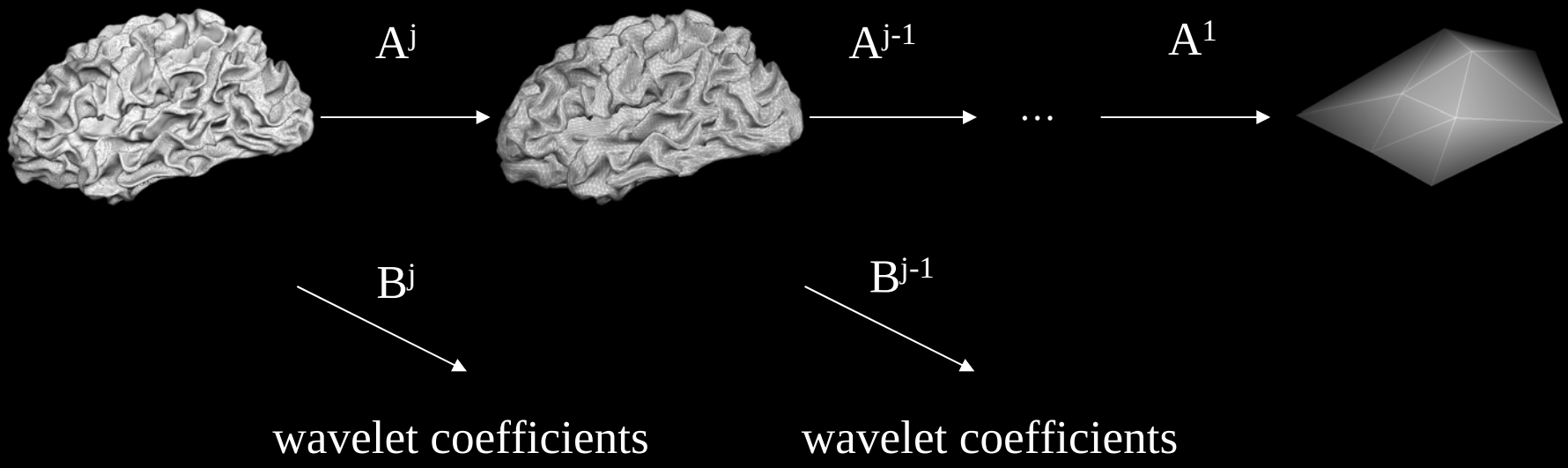
Shape Analysis: Spherical Wavelets

Biorthogonal Wavelets (c.f. Nain et al, 2008, Yu et al., 2008)



Wavelet decomposition of cortical surface

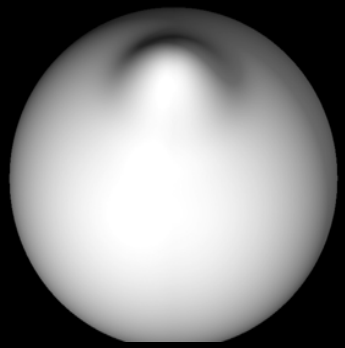
Joint work with Peng Yu, Polina Golland and B.T. Thomas Yeo

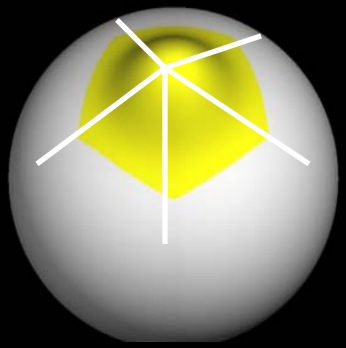
Bi-orthogonal wavelets are not rotation invariant due to aliasing

Synthetic Surface

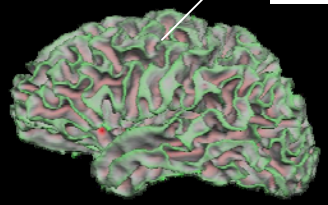
Bump aligned with the center of a wavelet basis function at low level

Rotated surface parameterization





$\{x(\theta,\varphi), y(\theta,\varphi), z(\theta,\varphi)\}$



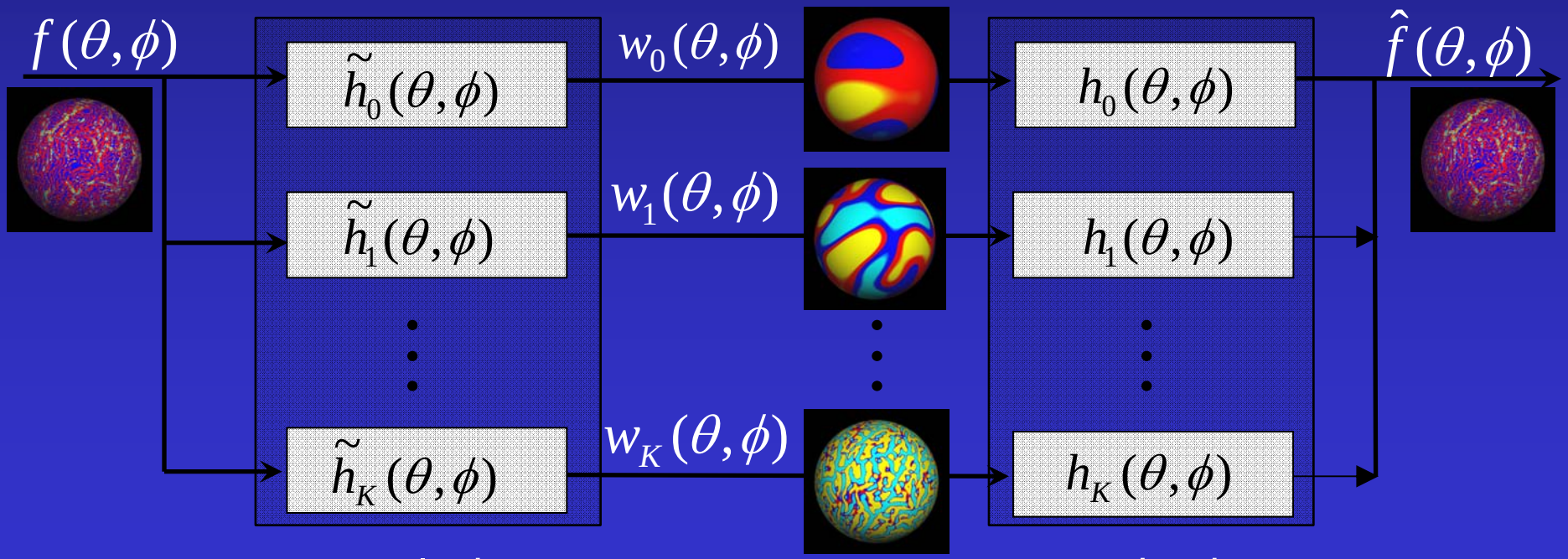
Original Surface

Surface Parameterization

No aliasing in over-complete spherical wavelet transformation (Yeo 07)

Based on continuous filter bank theory

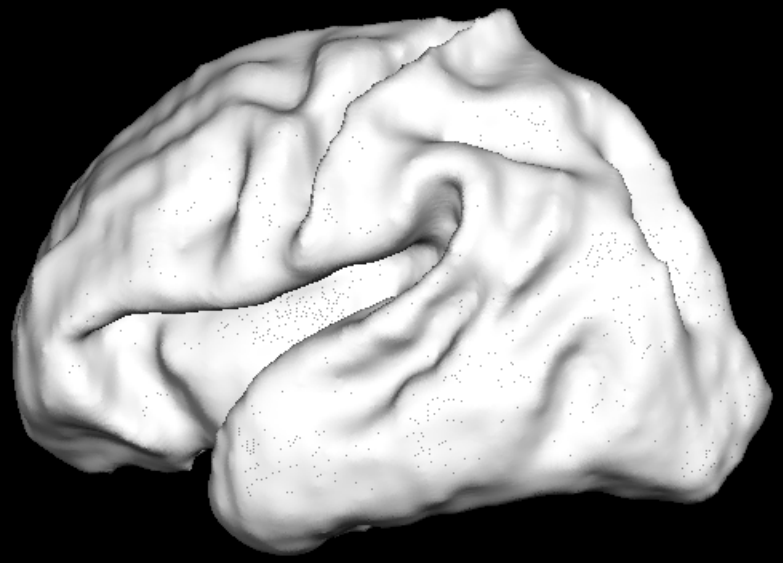
- Fast convolution in spherical harmonics space
- No aliasing



Wavelet Shape Analysis: Newborn Growth Model

Dataset:

Eight normal neonates with corrected gestational ages (cGA) of 31.1, 34, 38.1,38.4, and 39.72 weeks and 3 children. Growth model of the cortical surface using Gompertz functions in the wavelet domain



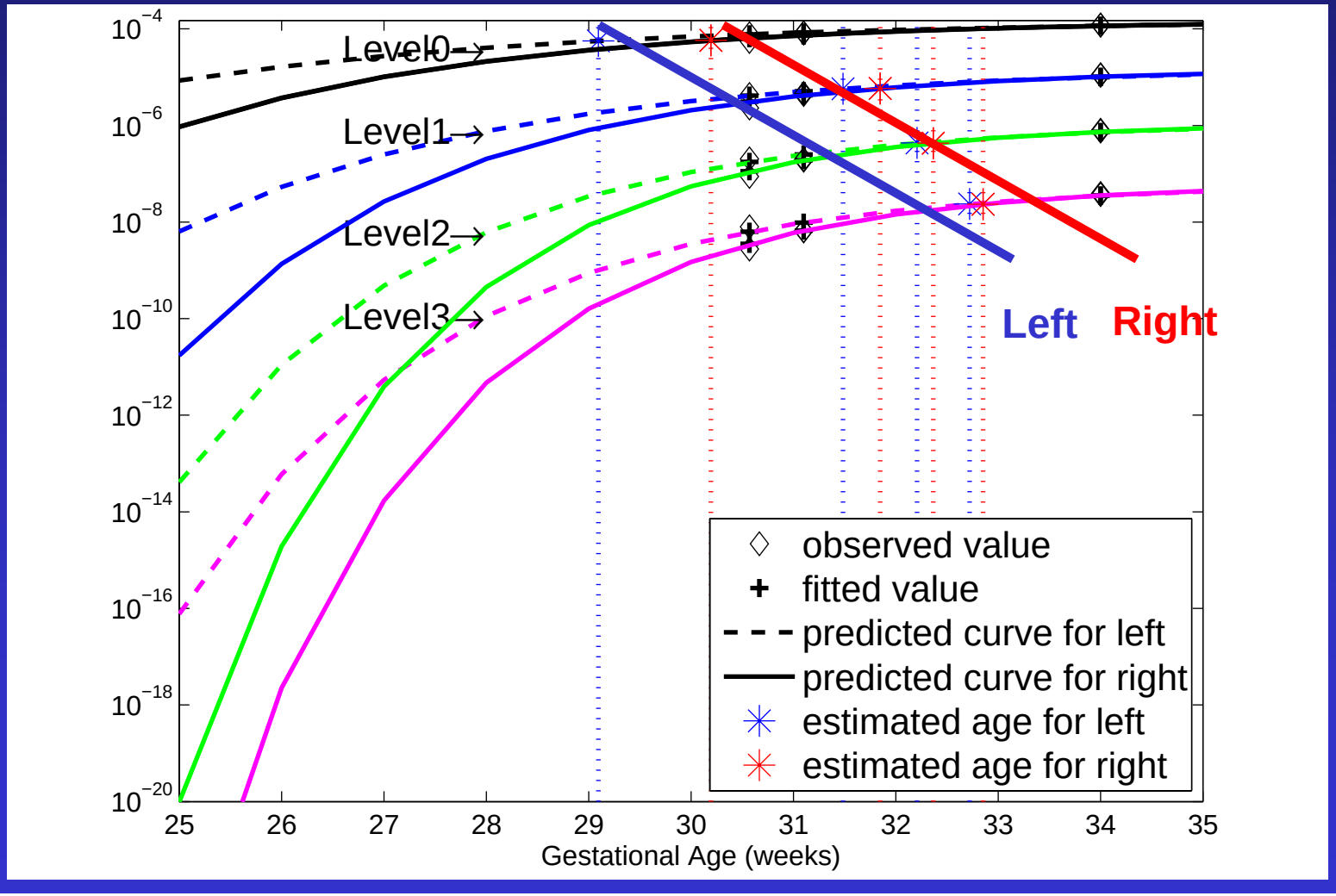
8 Newborns in gestational ages **3 kids** **Age**

30.57 31.1 34 37.71 38.1 38.4 39.72 40.43 (weeks) 2 3 7 (years)

In collaboration with Peng Yu, Polina Golland, B.T. Thomas Yeo and Ellen Grant

Over-complete wavelets: Newborn Growth Curves

Folding Development curves estimated with wavelet power of over-complete wavelets



Wavelet Shape Analysis: newborns

Joint work with Peng Yu, B.T. Thomas Yeo, Ellen Grant and Rudolph Pienaar

Talk Outline

1. Cortical Analysis.
2. Subcortical Analysis.
3. Linking macro and microstructure.

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Whole-Brain Segmentation

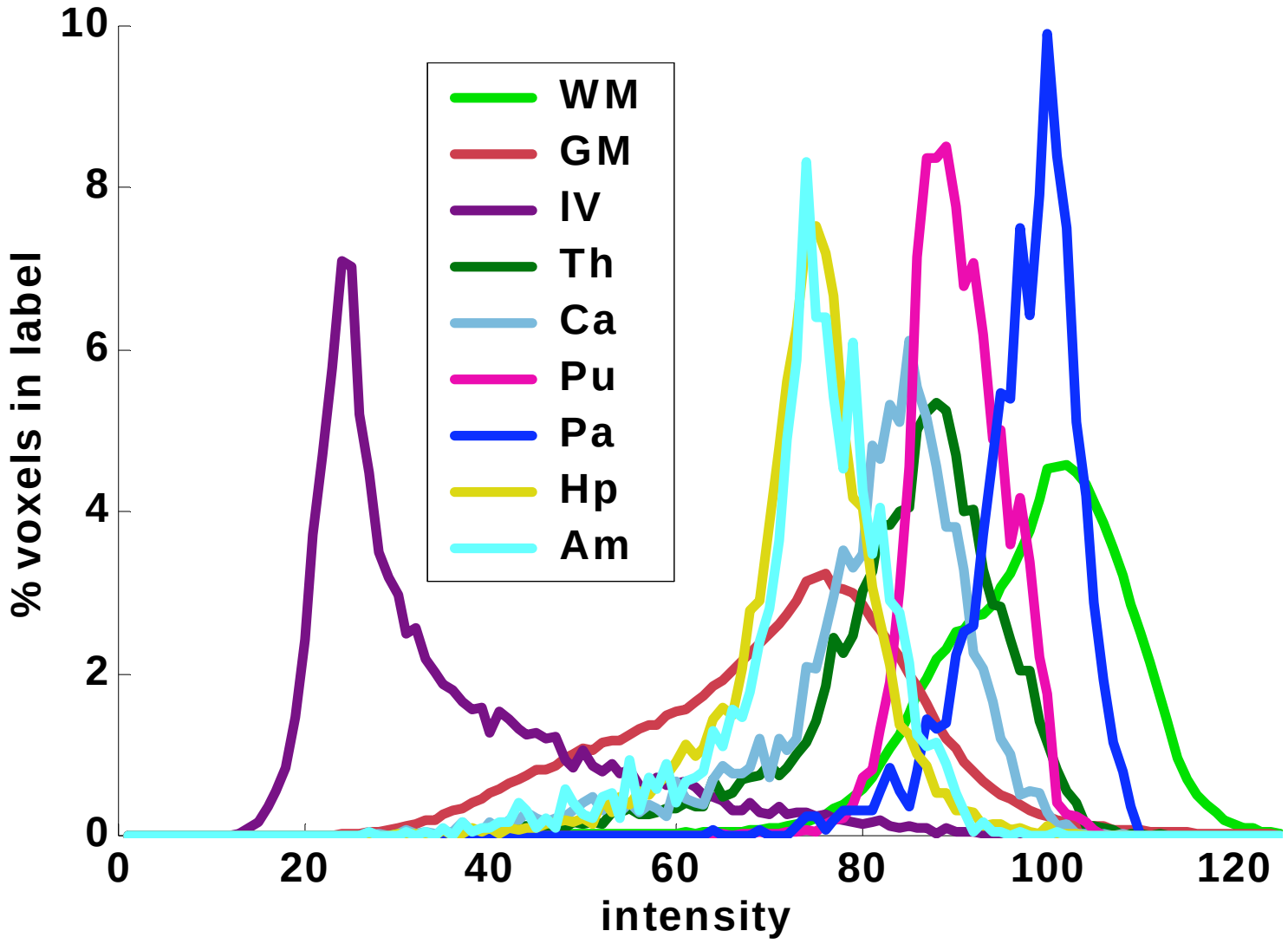
Goal: Segment T1-weighted MRI into anatomically and semantically meaningful structures (e.g. caudate, putamen, etc…).

Requirements:

- Insensitive to pathology.
- Insensitive to varying pulse sequences.

Prerequisite: registration with anatomically meaningful space (e.g. Talairach)

Why Segmentation is Hard!



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.

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

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

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

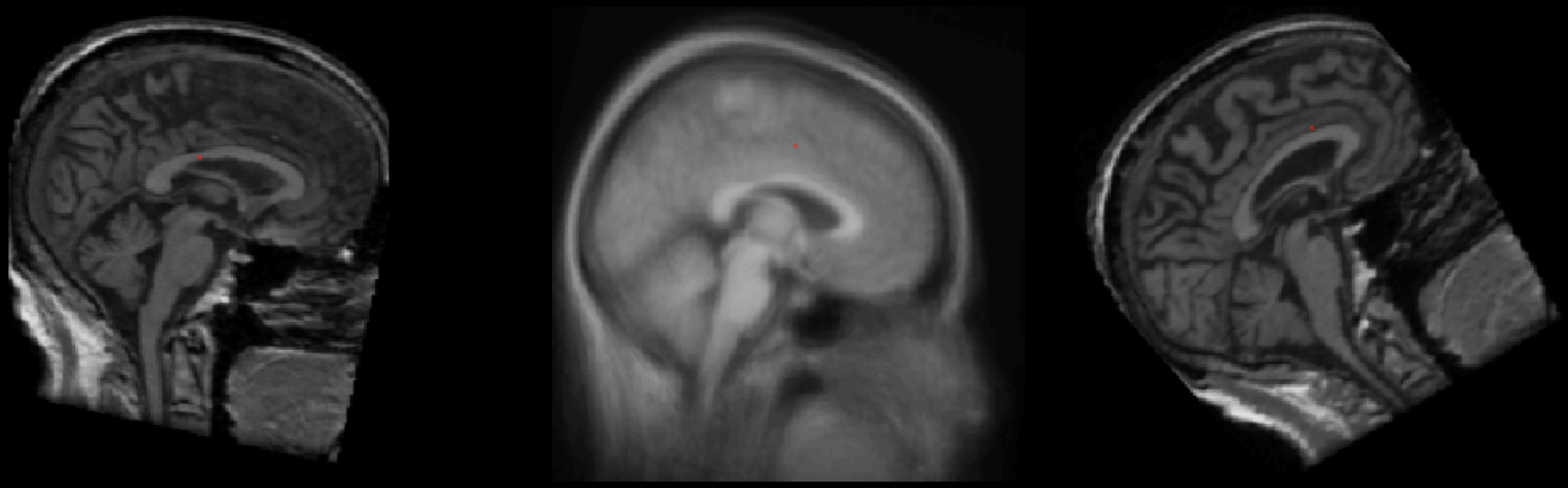
Assume $\log(p(I \mid f, T)) = \iiint -(I(f(\mathbf{r})) - T(\mathbf{r}))^2 d\mathbf{r}$

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

→ *f* is the maximum likelihood solution assuming the image noise can be modeled as a set of IID random variables with means *T(r)* and equal (unit) variances.

Mean-squared Error Registration: Low Quality Data

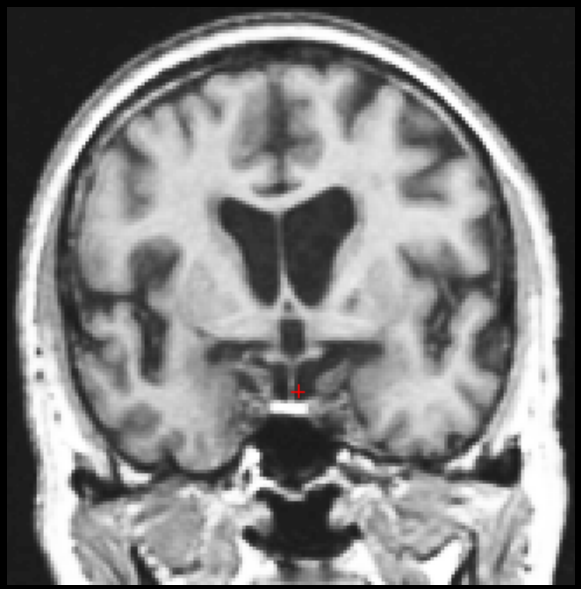
$I(\mathbf{r})$ $T(\mathbf{r})$ $I(L\mathbf{r})$



Mean-squared Error Registration

Anatomy is variable, particularly in cases of pathology*

→ *A given spatial location may contain a different tissue class in different types of subjects!*



* Thanks to Marilyn Albert and Ron Killiany for providing this data.

Segmentation-based Registration

Find the transformation that maximizes the probability that each point in the individual is drawn from *one* of the tissue classes in the template.

Find the *L* that maximizes the probability of observing image *I* given the segmentation *C*:

$$L = \arg\max\, p(I \mid L, C)$$

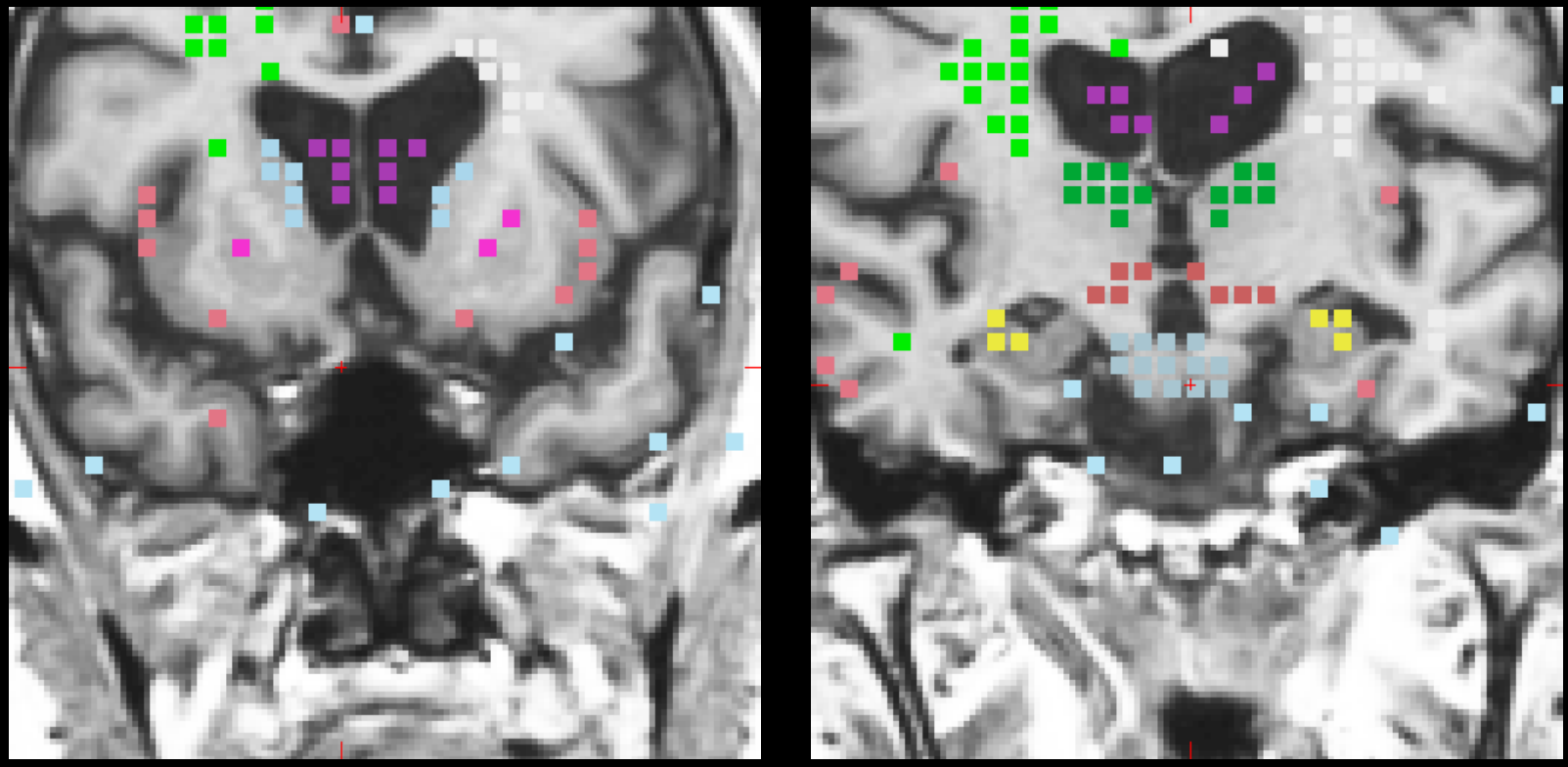
How do we find the segmentation C?

Segmentation-based Registration

Problem of finding *L* is highly overdetermined (many, many more data points than parameters to solve for).

Can assume *C* in certain atlas locations (a few thousand) where prior probabilities are high, and use them to find *L* using a *global* search (local minima/maxima not a problem).

Atlas Points After Registration

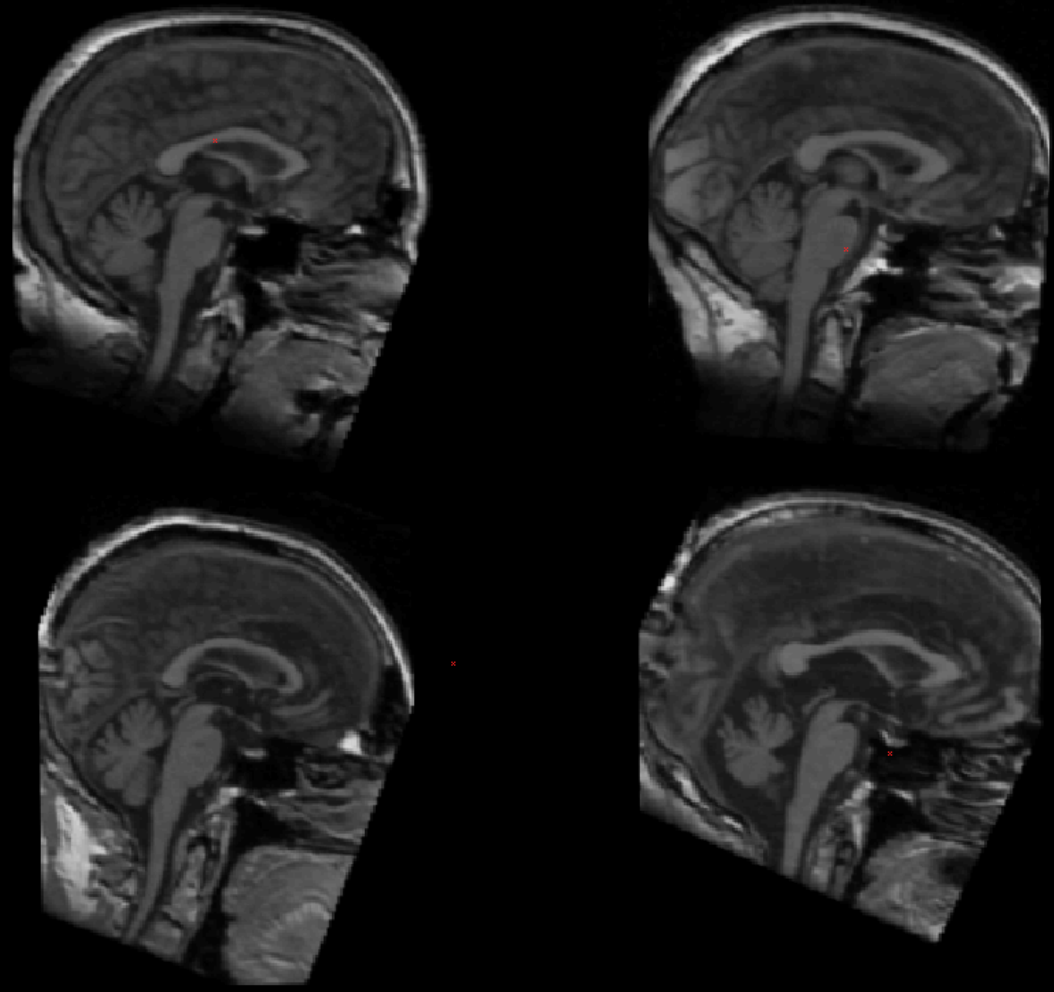


- Cerebellar cortex
- Cerebellar WM
- 4th ventricle
- RH cerebral WM
- LH cerebral WM
- Hippocampus
- LH pallidum
- Thalamus
- Cerebral cortex
- Misc.
- Lateral ventricle
- Caudate

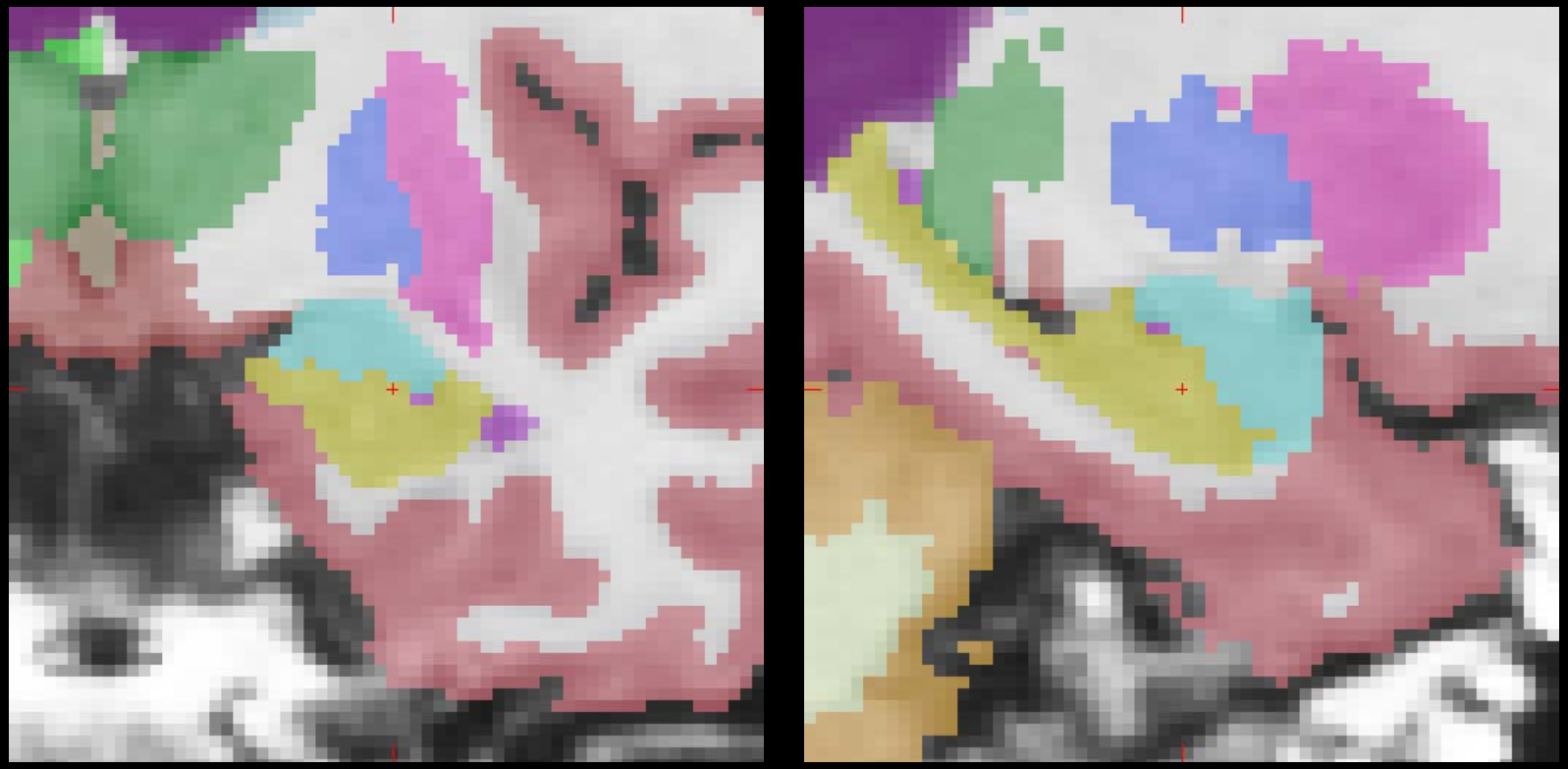
Segmentation-based Registration: Results

Normal

AD



Segmentation Results: CMA Labeling



- Cerebellar cortex
- Cerebellar WM
- 4th ventricle
- RH cerebral WM
- LH cerebral WM
- Hippocampus
- LH pallidum
- Thalamus
- Cerebral cortex
- Misc.
- Lateral ventricle
- Caudate
- Amygdala

Tissue Segmentation

Given a transform *f* into an atlas space, *C* can be estimated using a Maximum a Posteriori (MAP) approach: what is the most likely tissue classification *C* given the observed image *I* , the transformation *f*, and prior information about *C*?

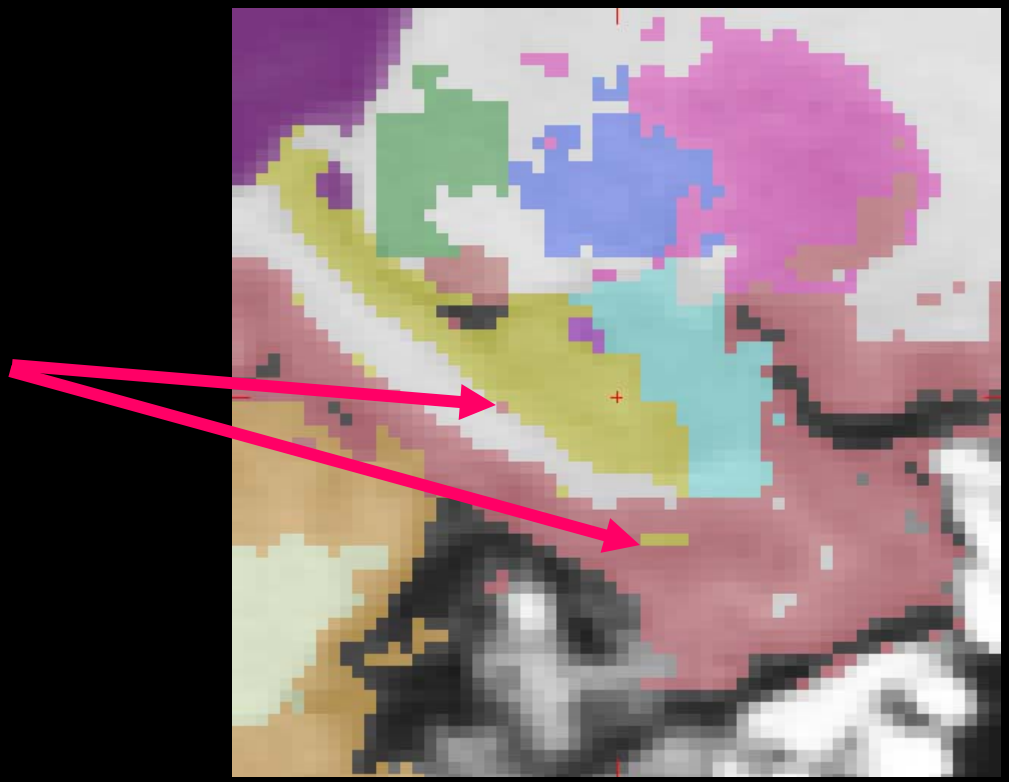
$$C = \arg\max_{C'} p(C' \mid I, f)$$

$$p(C' \mid I, f) \sim p(I \mid C', f)\, p(C')$$

What prior information *p(C)* can we use to constrain the allowable segmentations?

Gibbs Priors: Motivation

What is the probability that cortical gray matter occurs inferior to hippocampus?



Markov Random Fields

Modeling the segmentation as a *Markov Random Field (MRF)* means:

$p(C(\mathbf{r})|\text{the rest of the labels}) = p(C(\mathbf{r})|\text{labels in a neighborhood around } \mathbf{r})$

Segmentation: MRF

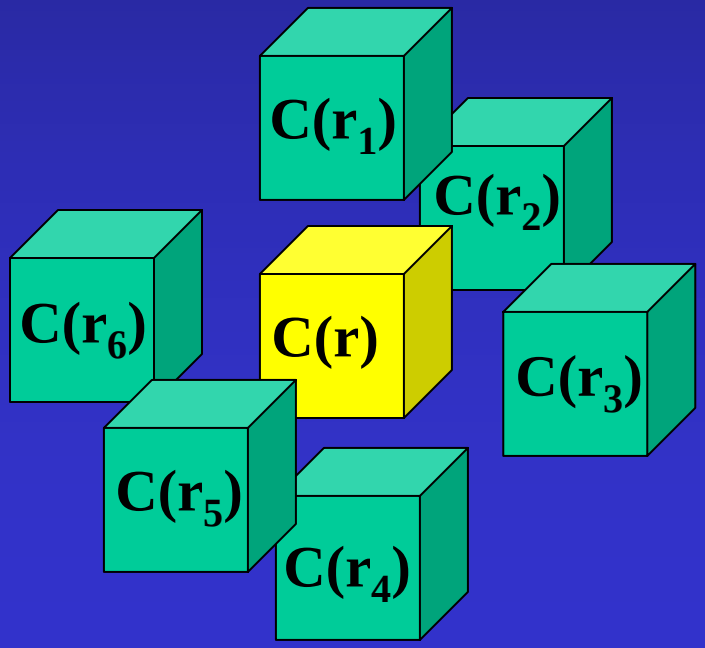
Problem: the segmentation is fractured because no spatial smoothness constraints are encoded in model.

Solution: incorporate prior probability of one tissue class being the neighbor of another into model:

$$p(C) \propto \prod_{\mathbf{r} \in R} p(C(\mathbf{r}) \mid \mathbf{r}) \prod_{\mathbf{r}_i \in N(\mathbf{r})} p(C(\mathbf{r}_i) \mid C(\mathbf{r}), i, \mathbf{r}, \mathbf{r}_i)$$

Segmentation: MRF

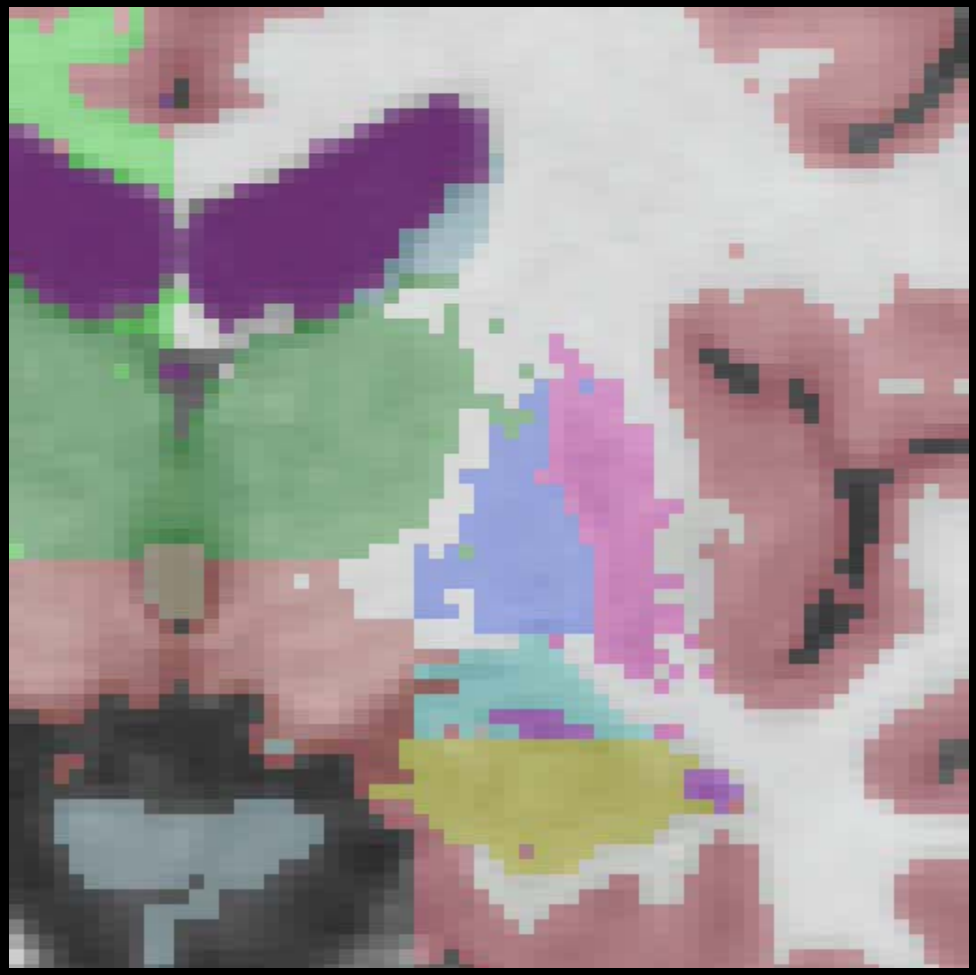
$p(\mathrm{C}(\boldsymbol{r}_i)|C(\boldsymbol{r}), I, \boldsymbol{r},\boldsymbol{r}_i)$ encodes the probability that tissue class $\mathrm{C}(\boldsymbol{r}_i)$ occurs at spatial location r_i when tissue class $C(\boldsymbol{r})$ occurred at $\boldsymbol{r}$. The segmentation is thus modeled as an *anisotropic* nonstationary *MRF*.



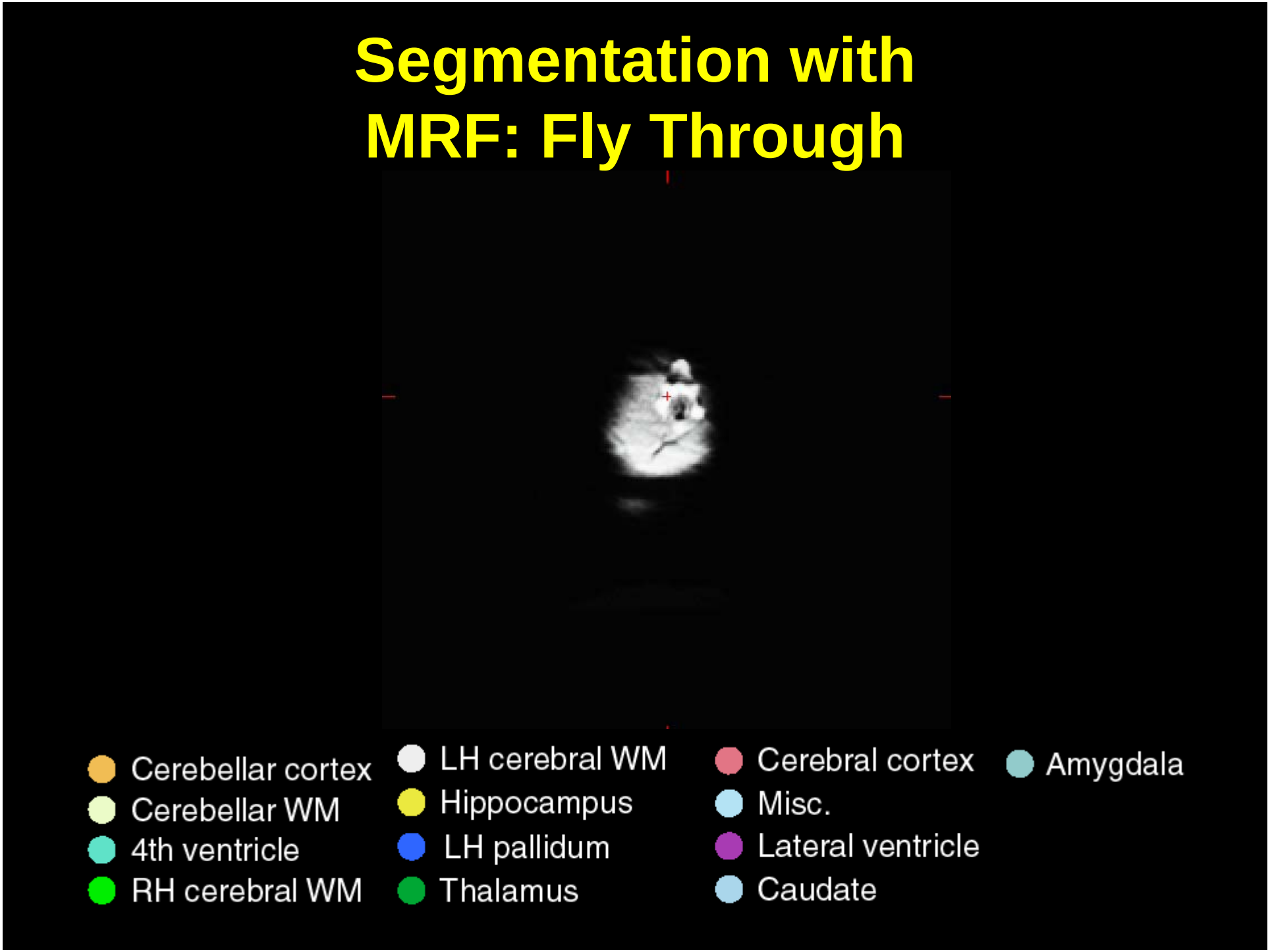
Segmentation: MRF

Preliminary Segmentation

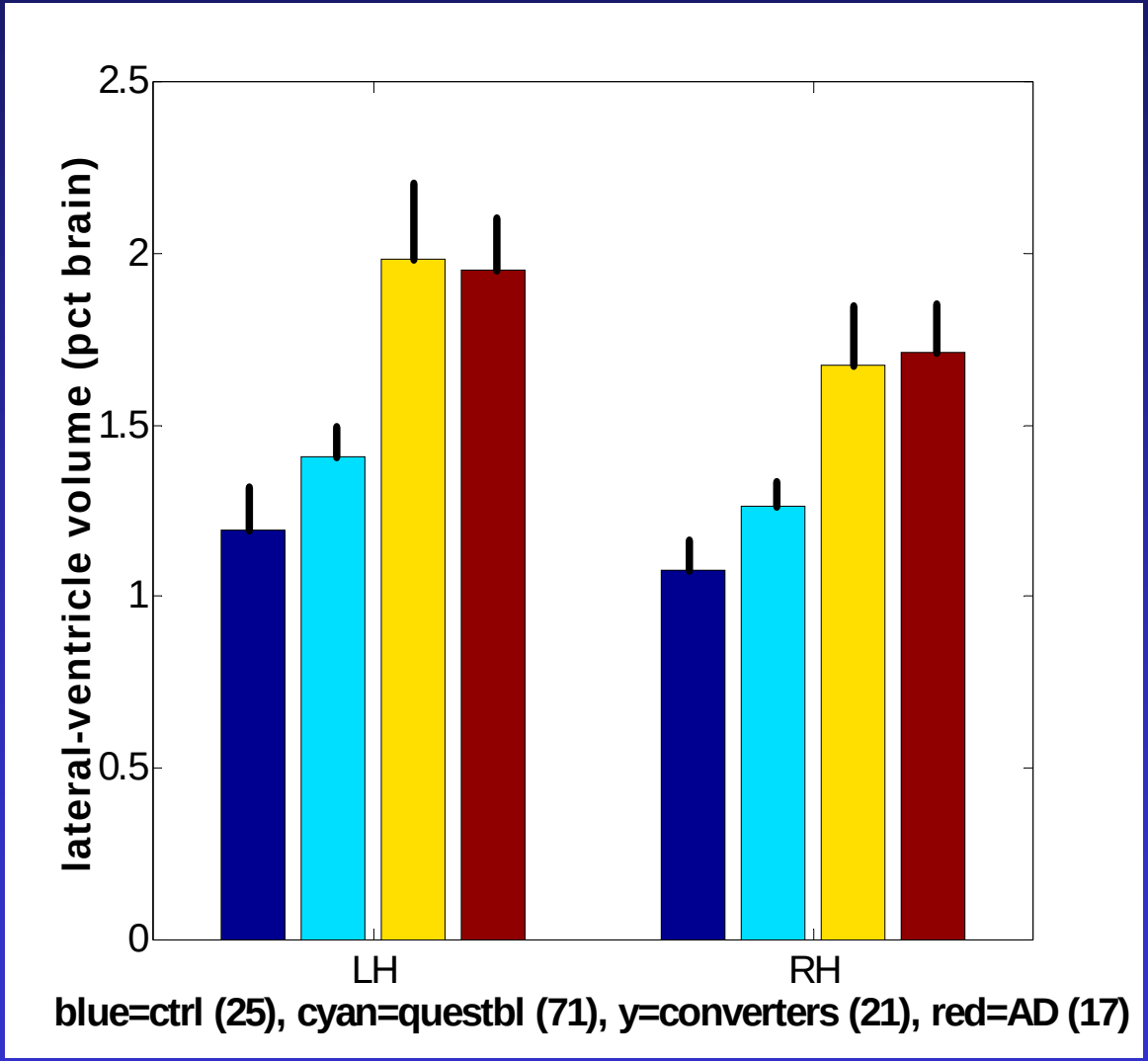
Final Segmentation



Segmentation with MRF: Fly Through



Volume Differences Predictive of AD



Data courtesy of Drs Marilyn Albert Ron Killiany

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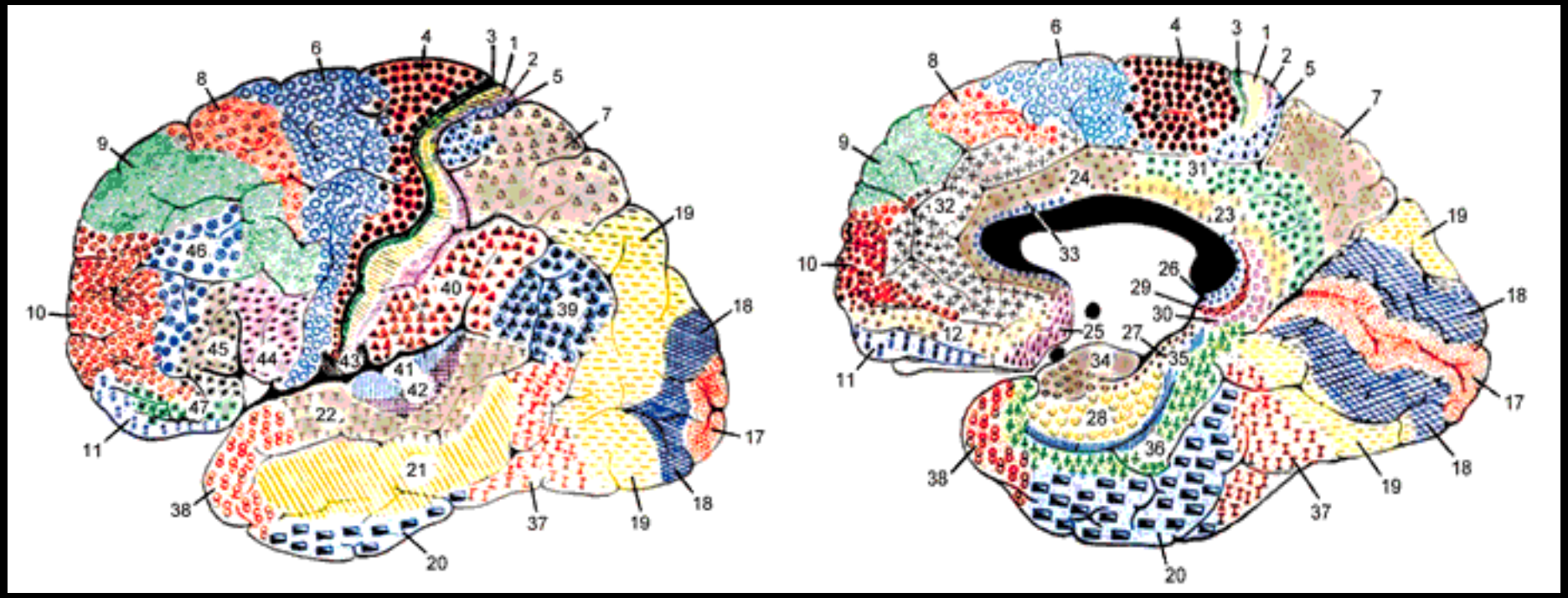
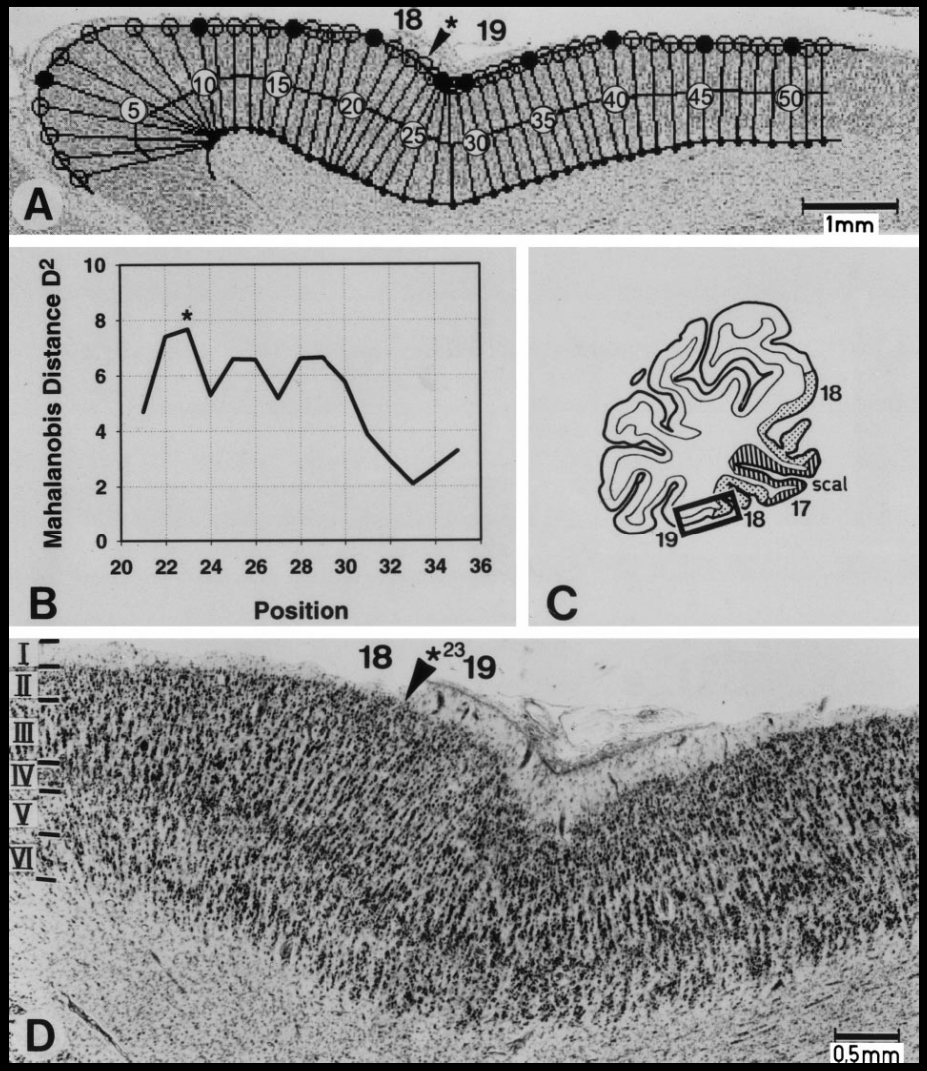
Can we do better than this?



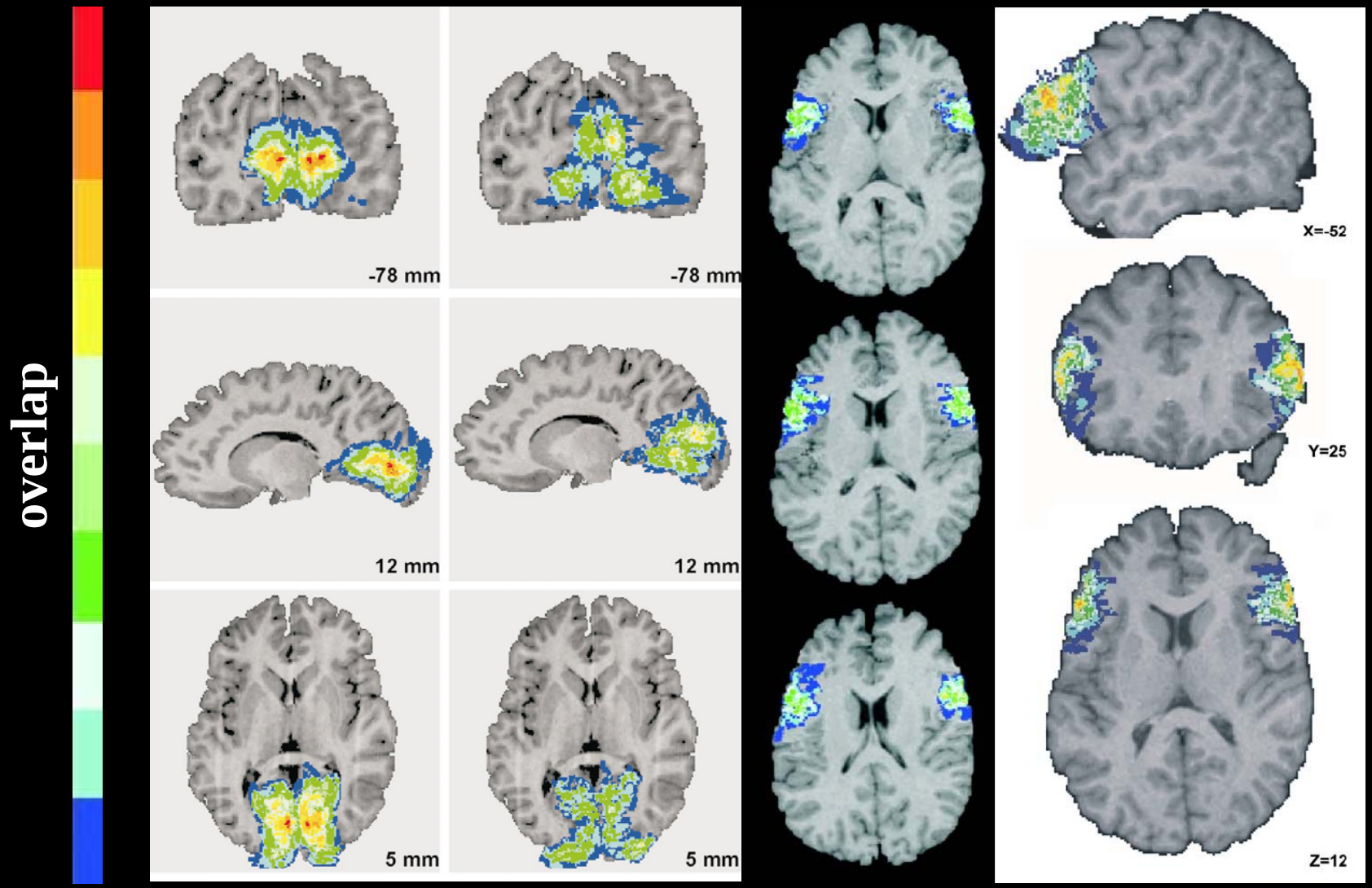
Brodmann, 1909

Automated Detection of Architectonic Boundaries



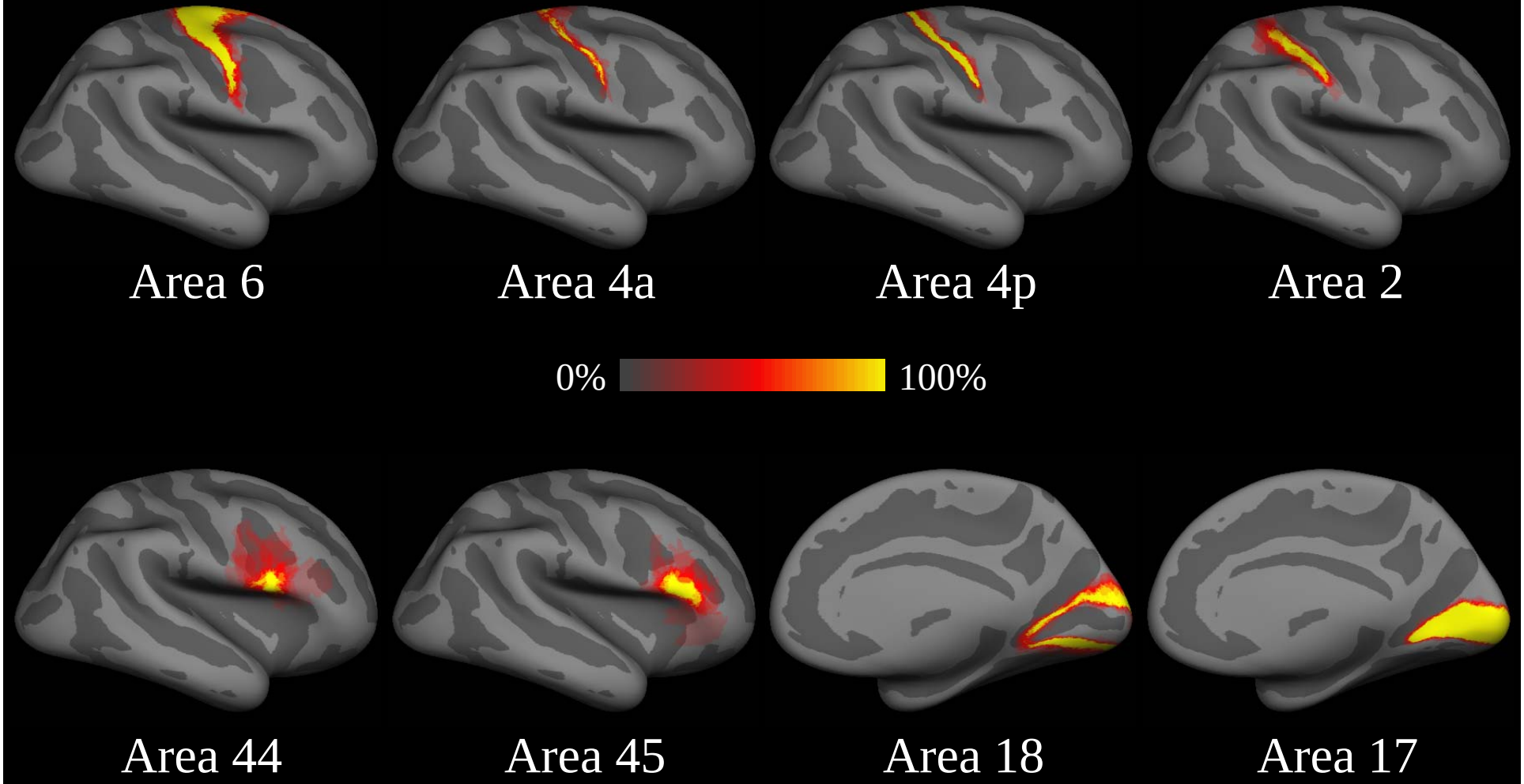
From (Amunts, et al, 2000)

Predicting Brodmann Areas: Talairach Coordinates



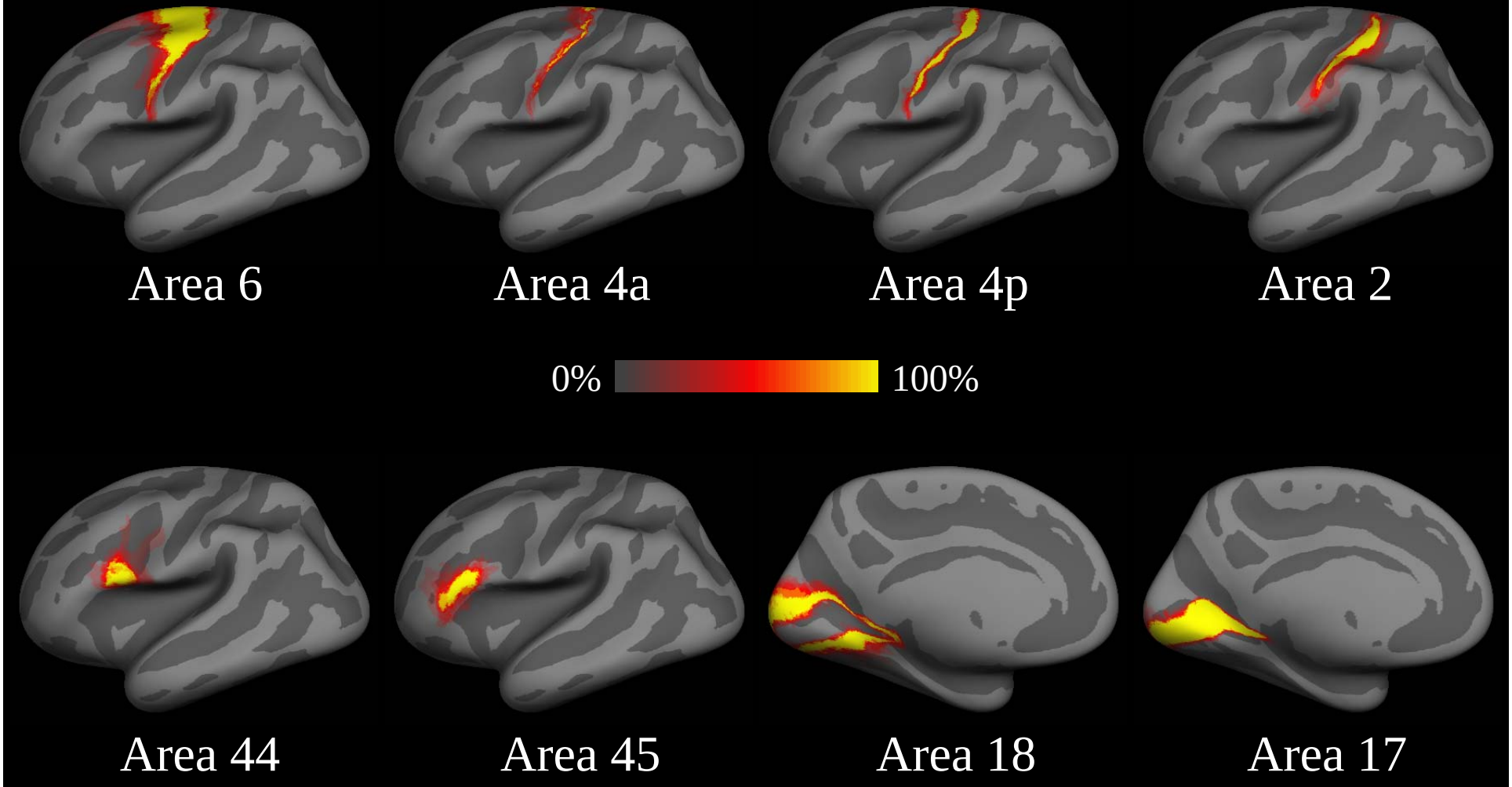
(Amunts et al, 2000, 2004)

Predicting Brodmann Areas from Cortical Geometry



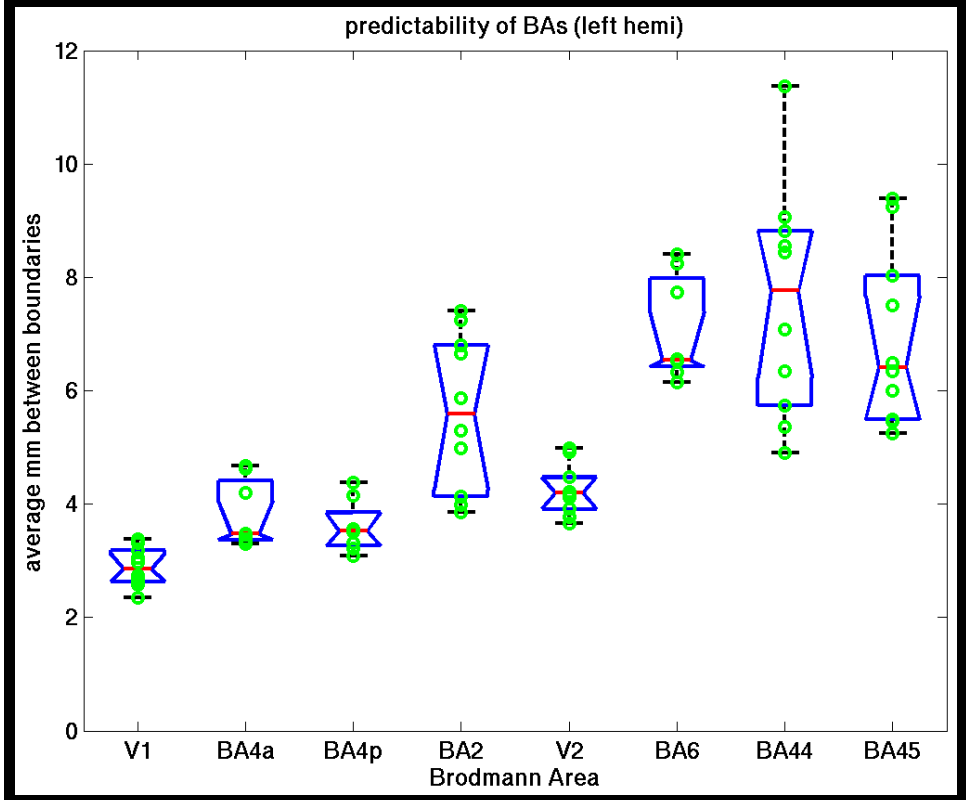
Thanks to Katrin Amunts, Karl Zilles and Hartmut Mohlberg for the data, and to Niranjini Rajendran and Evelina Busa for the analysis

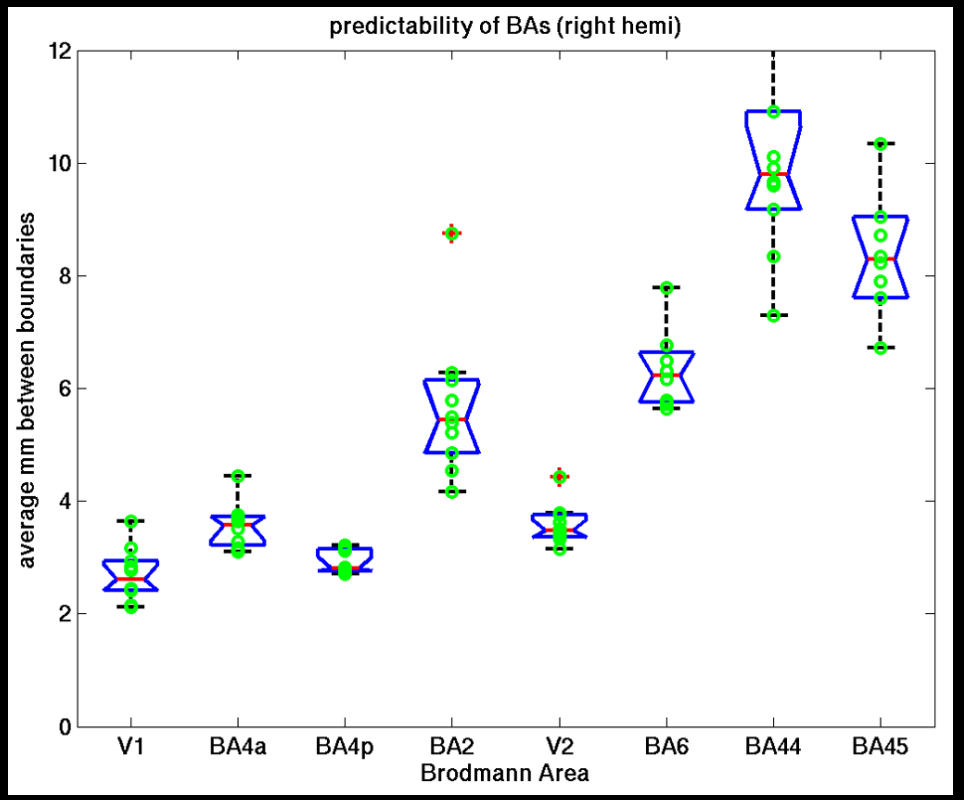
Predicting Brodmann Areas from Cortical Geometry



Thanks to Katrin Amunts, Karl Zilles and Hartmut Mohlberg for the data, and to Niranjini Rajendran and Evelina Busa for the analysis

Brodmann Area Predictability





Thanks to Katrin Amunts, Karl Zilles and H. Mohlberg for the data, to B.T. Thomas Yeo, Niranjini Rajendran and Evelina Busa for the analysis, and to Kilian Pohl for suggesting the distance measure.

What Features To Use?

Average Folding Pattern: $$\overline{C}(\varphi,\theta)=\frac{1}{N}\sum_{i=1}^{N}C_i(\varphi,\theta)$$

Variance of Folding: $$\sigma^2(\varphi,\theta)=\frac{1}{N-1}\sum_{i=1}^{N}(C_i(\varphi,\theta)-\overline{C}(\varphi,\theta))^2$$

Likelihood Term: $$J_P=\frac{1}{2V}\sum_{v=1}^{V}\left(\frac{G_\alpha * (C_v-\overline{C}(\phi(v),\theta(v)))}{\sigma(\phi(v),\theta(v))}\right)^2$$

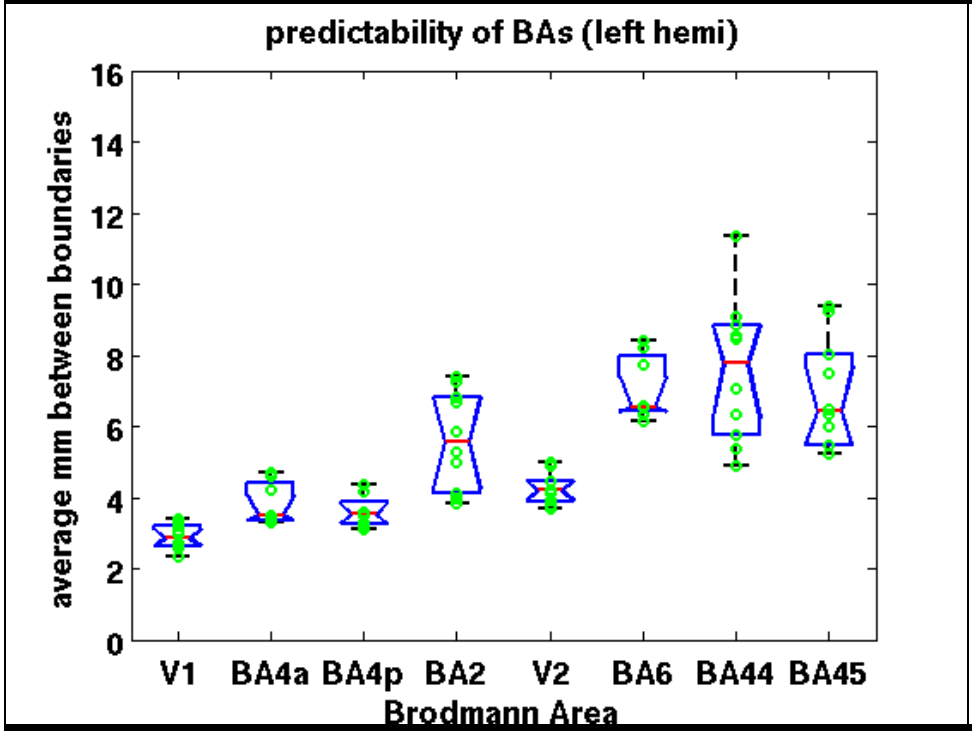
What space should mean and variance be computed in?

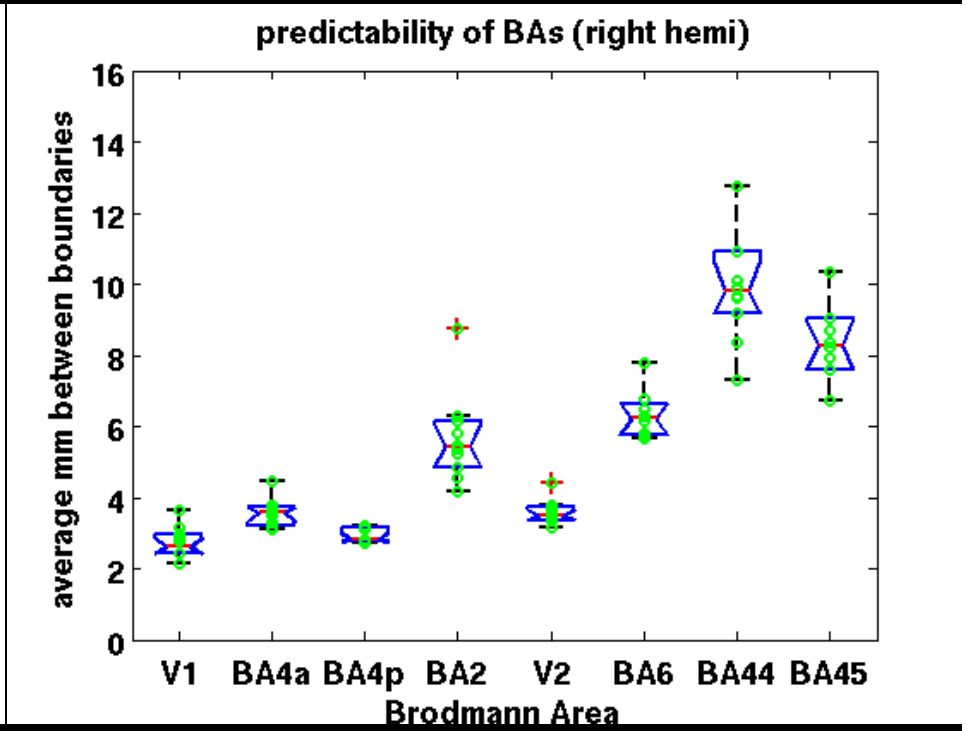
What if we align labels (instead of geometry) and compute statistics in label-aligned space?

Variance becomes natural weighting of predictive features!

Joint work with Thomas Yeo and Mert Sabuncu

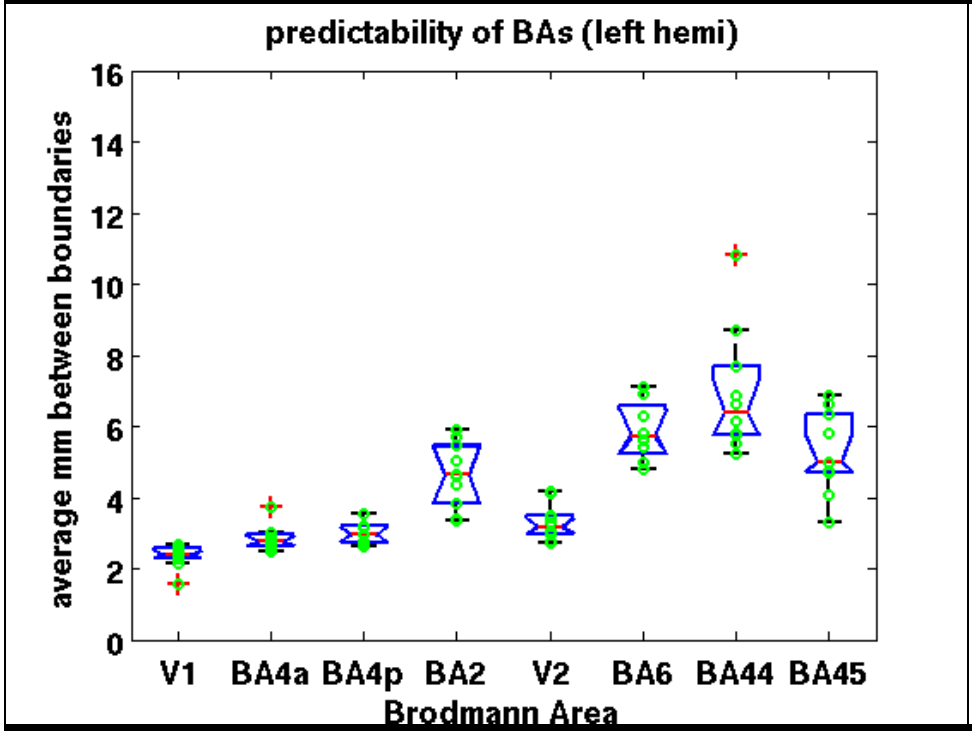
Brodmann Area Predictability (geometry)

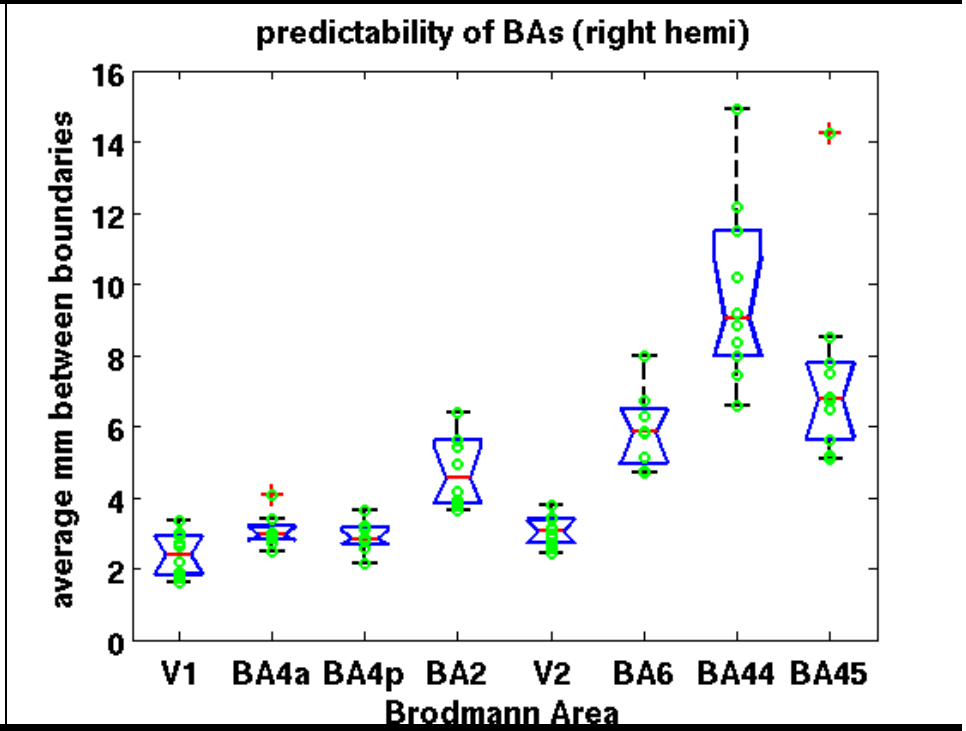




Joint work with B.T. Thomas Yeo and Mert Sabuncu

Brodmann Area Predictability (labels)

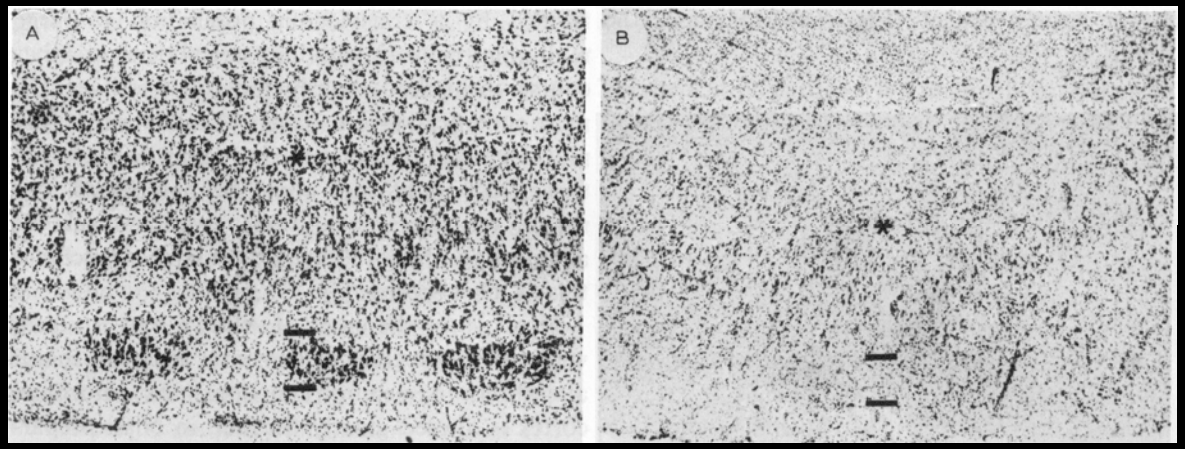




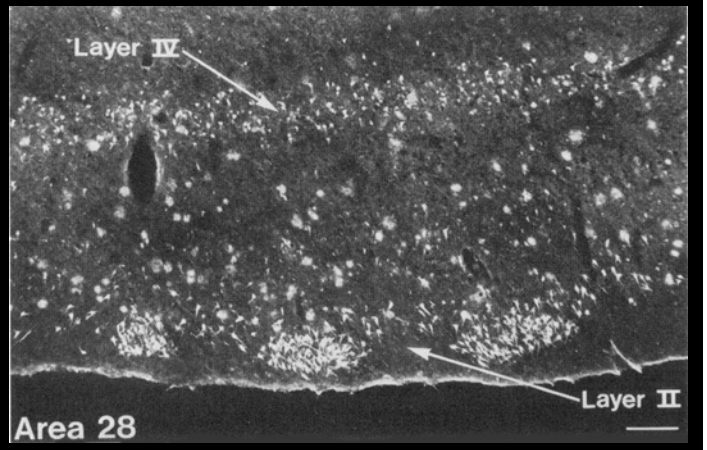
Joint work with B.T. Thomas Yeo and Mert Sabuncu

Histology
(can we do it with MRI?)

CONTROL AD



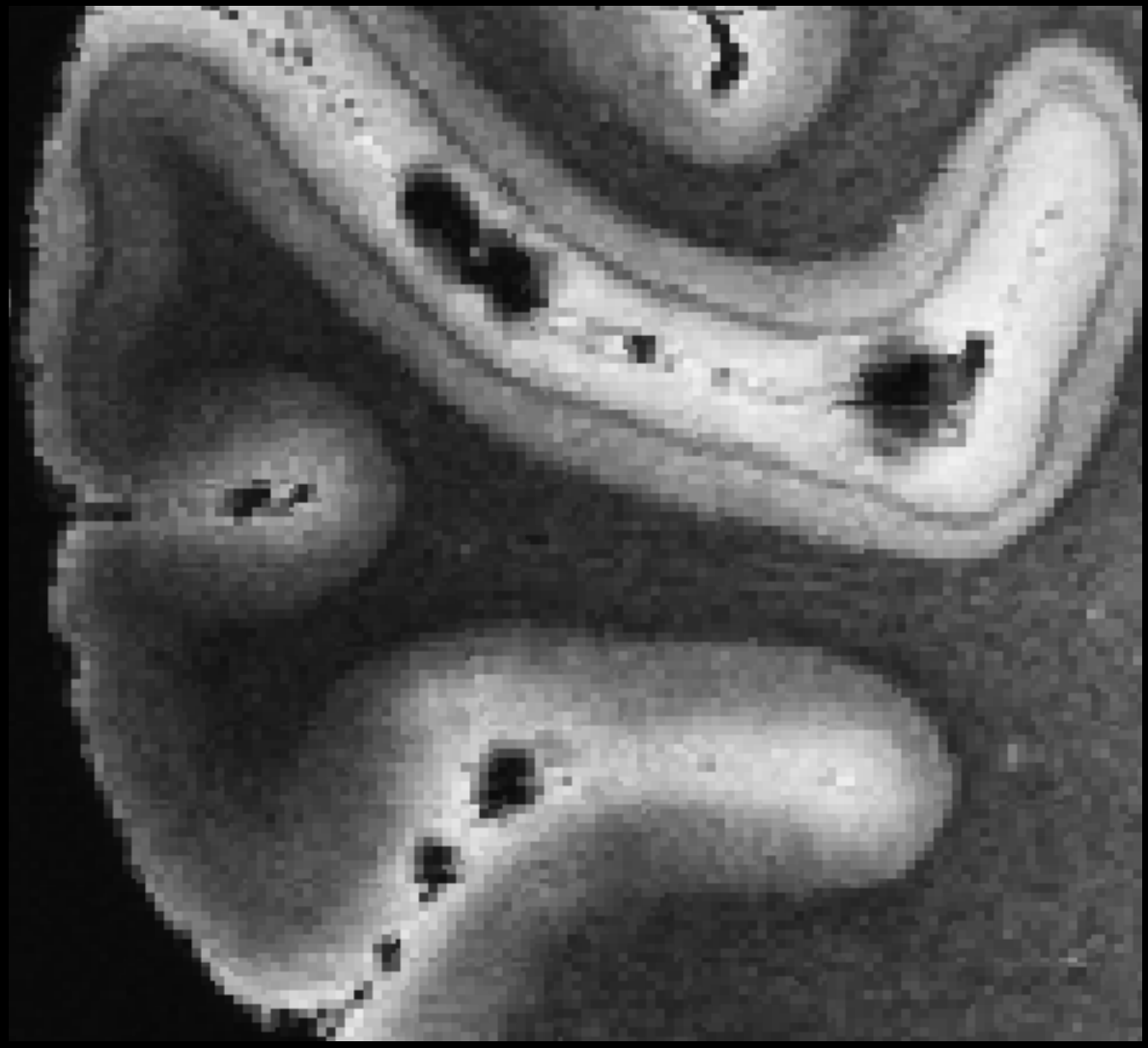
Nissl Stain



thioflavin S
(neurofibrillary tangles
and neuritic plaques)

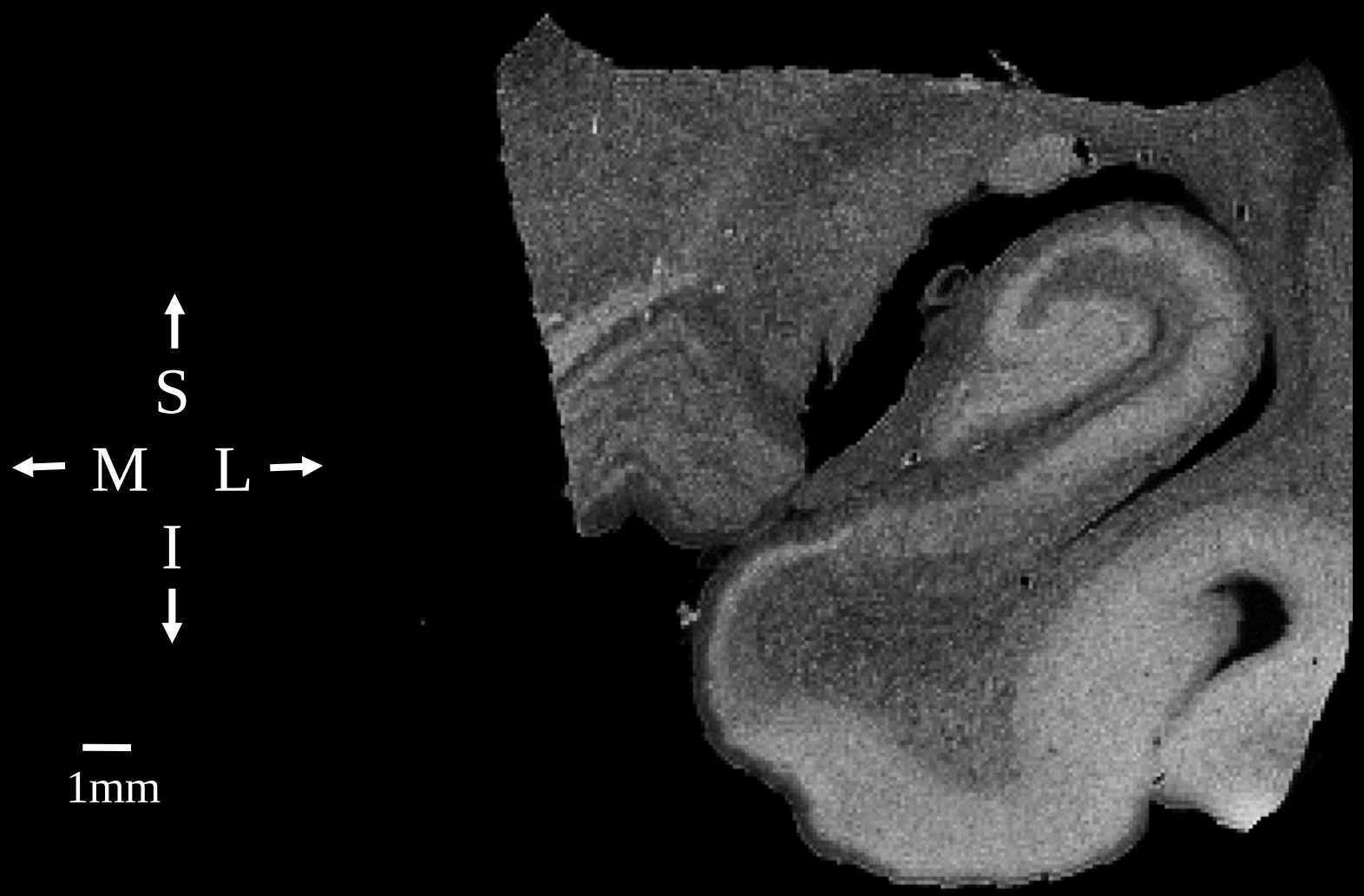
Thanks to Brad Hyman and Jean Augustinack for this slide.

Delineating Area 17



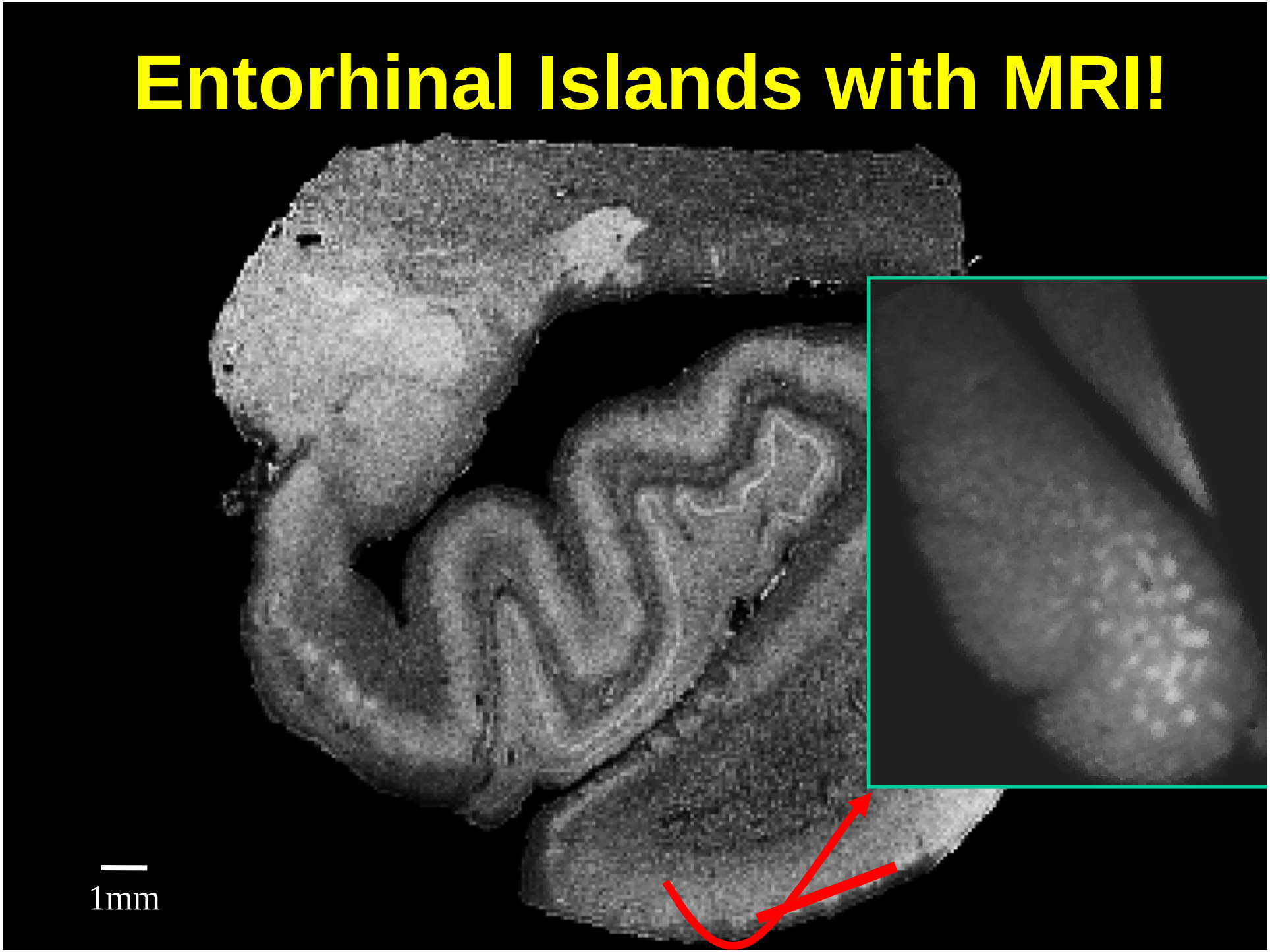
7T, 160μm isotropic, NEX=2, 4 echos, TR=55 ms, esp 13ms, $\alpha=10^{o}$

Temporal Lobe Fly-Through

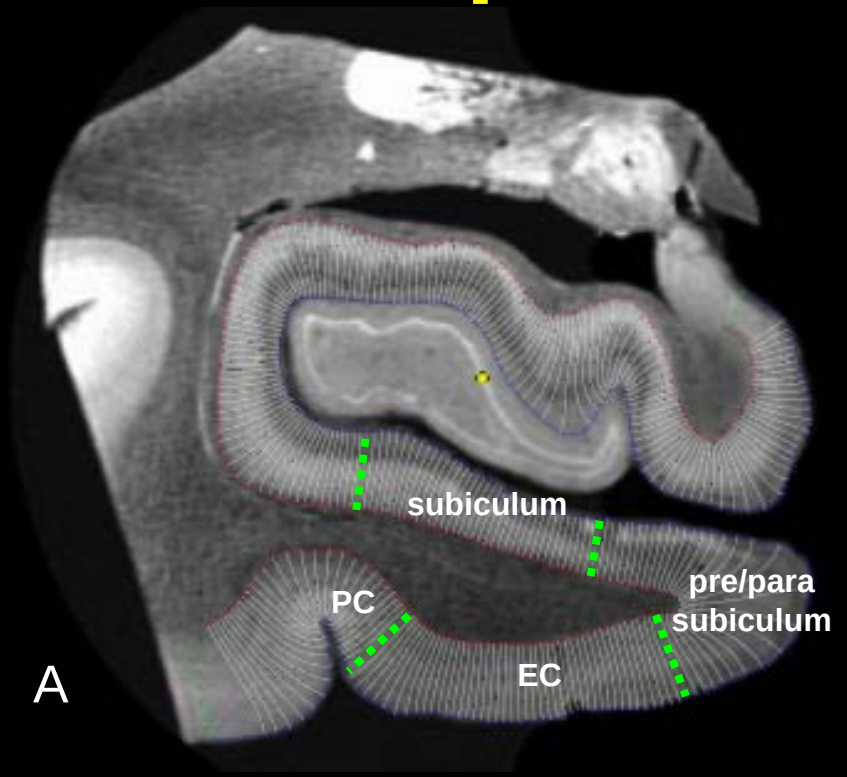


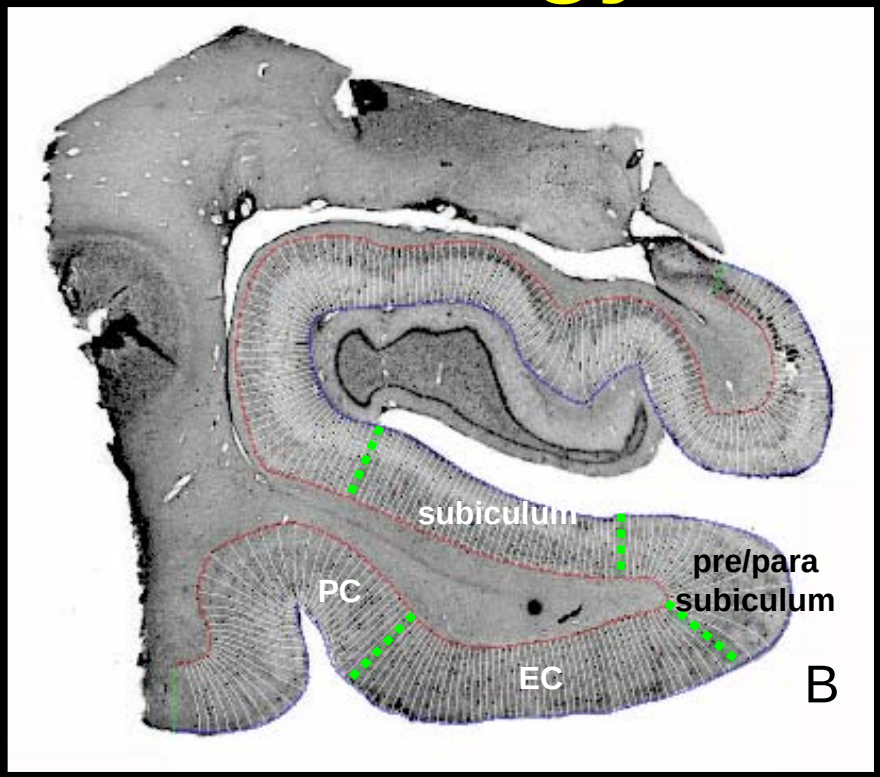
100μm isotropic MR, 7T, TR=20msec, TE=7.8msec, α=23º (synthesized)

Entorhinal Islands with MRI!



Automated Areal Border Detection: Comparison with Histology



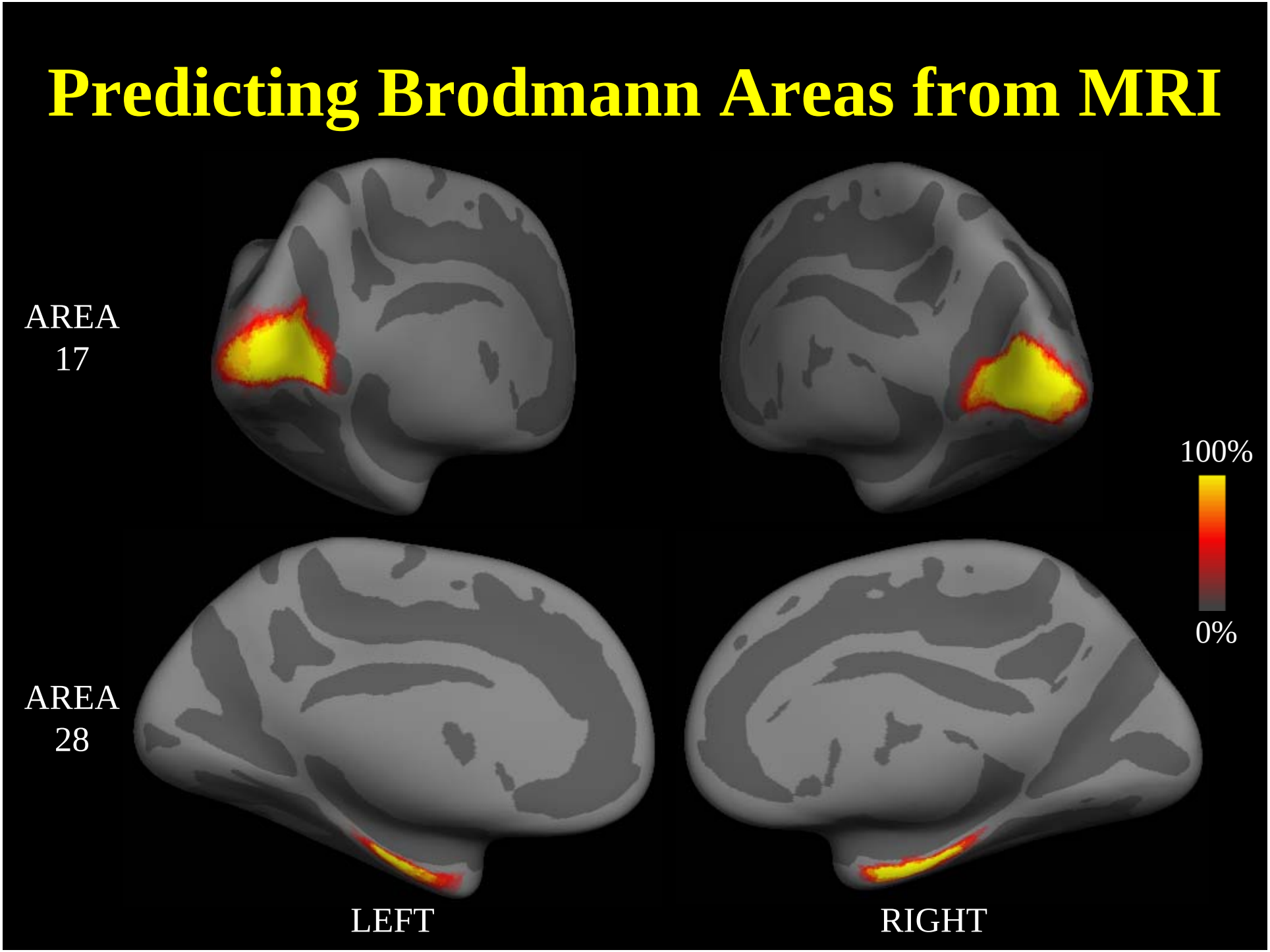


Coronal sections of the hippocampus at identical level on 7T MRI (A) and Nissl-stained histology (B). Significant maxima distinguishing cytoarchitectonic areas within the parahippocampal region are found in the same location for both modalities.

Abbreviations: EC=entorhinal cortex; PC=perirhinal cortex; para-sub=parasubiculum; pre-sub=presubiculum

Joint work with Neda Bernasconi, Gheorghe Postelnicu and Jean Augustinack

Predicting Brodmann Areas from MRI



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Marty Sereno

MIT

B.T. Thomas Yeo
Mert Sabuncu
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