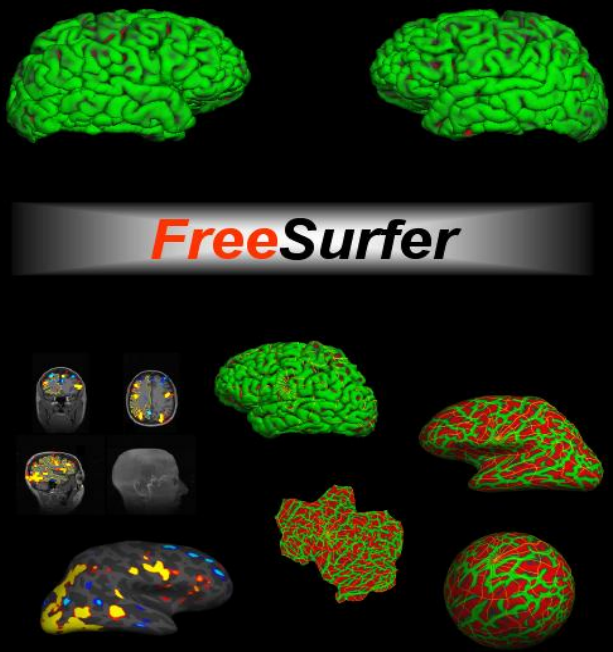
Introduction to FreeSurfer

surfer.nmr.mgh.harvard.edu



MASSACHUSETTS GENERAL HOSPITAL

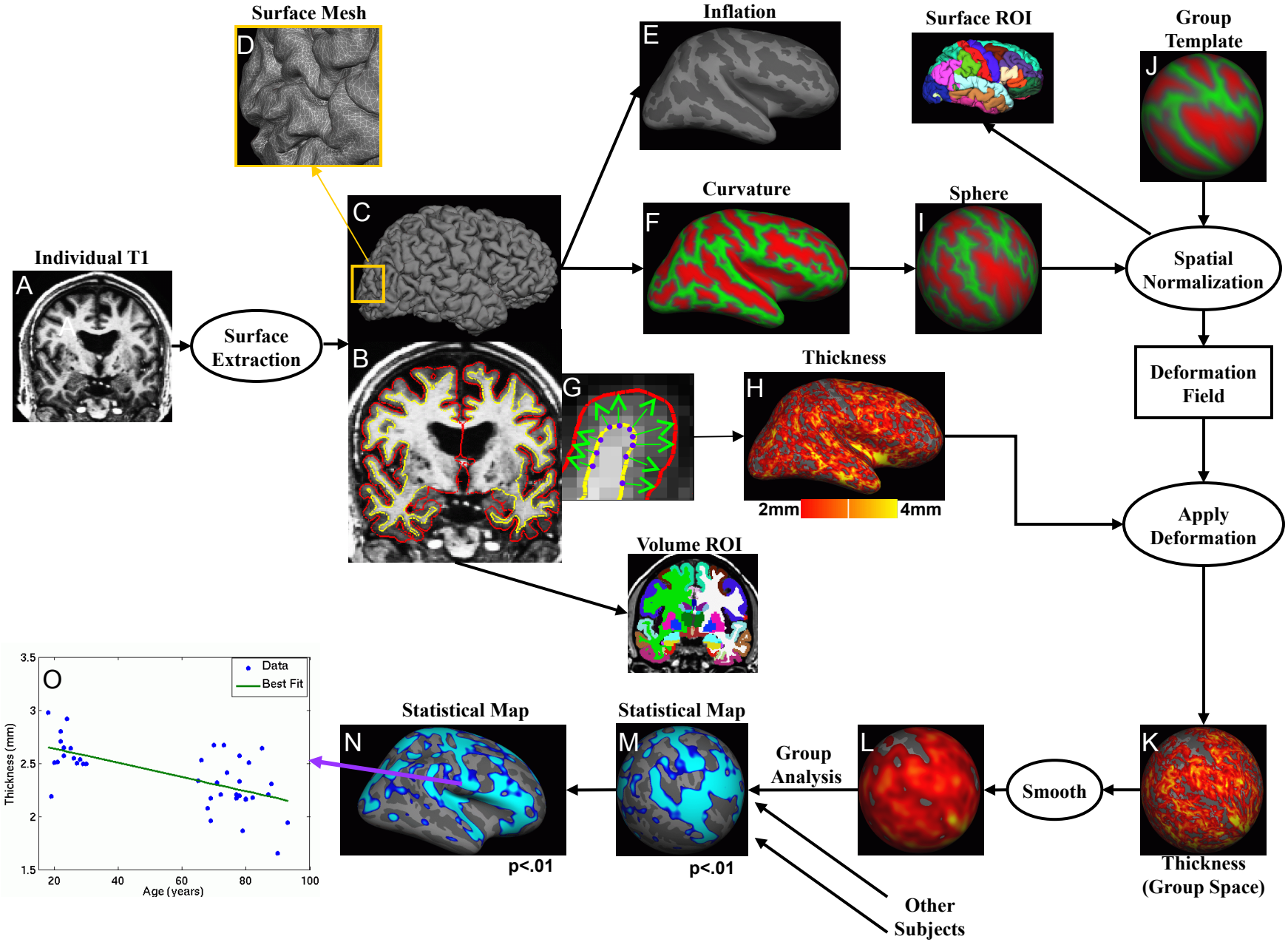
What is FreeSurfer?

- Neuroimaging analysis software package
- Fully characterizes anatomy
  - Cortex – thickness, folding patterns, ROIs
  - Subcortical – structure boundaries
- Surface-based Inter-subject Registration
- Multi-modal integration
  - fMRI (task, rest, retinotopy)
  - DTI Tractography

Outline

- Anatomical Analysis
  - Surface-based (Cortex)
  - Volume-based
- Thickness analysis
- Multi-modal integration
  - DTI/Tractography
  - fMRI

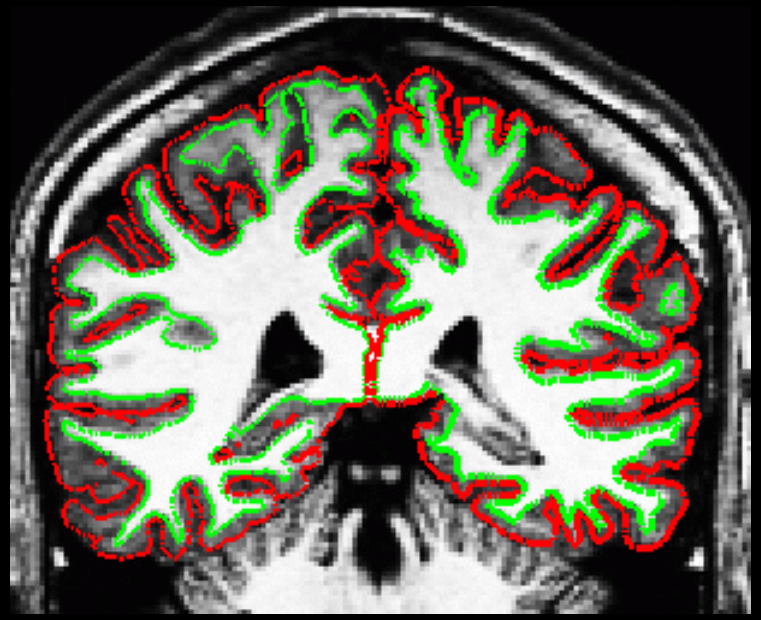
FreeSurfer Analysis Pipeline Overview



Outline

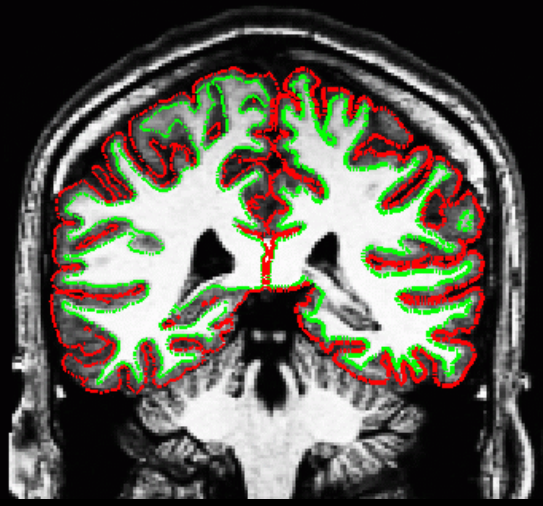
- Anatomical Analysis
  - Surface-based (Cortex)
  - Volume-based
- Thickness analysis
- Multi-modal integration
  - DTI/Tractography
  - fMRI

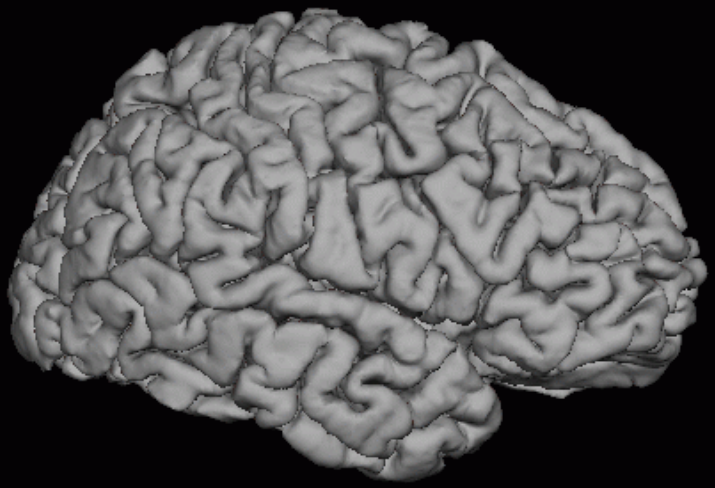
Cortex

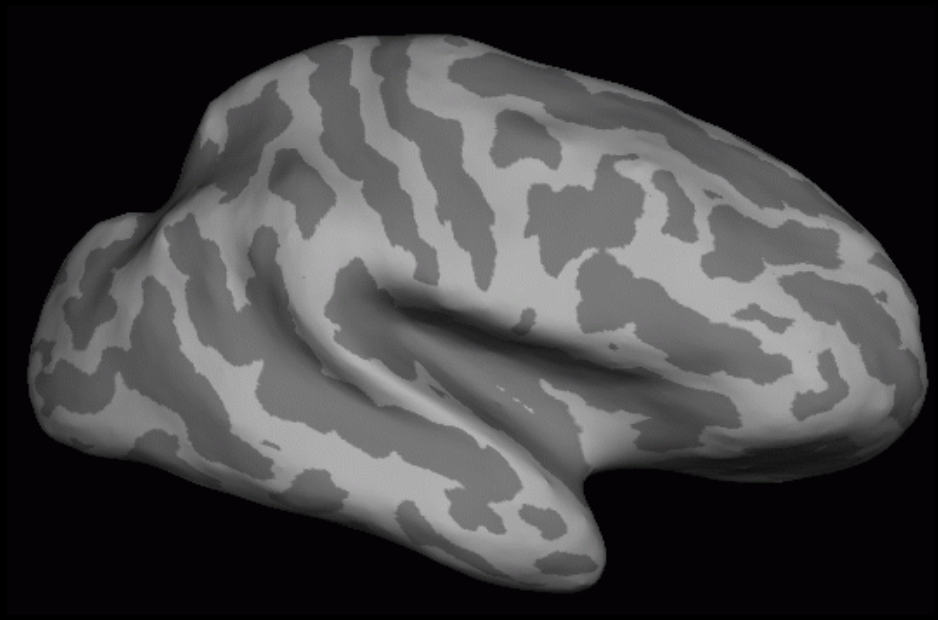


- Outer layer of gray matter
- ~70% of gray matter in brain
- 1-5mm thick
- Highly folded
- 2 Dimensional, embedded in 3D
- Function follows the surface
  - Visualization
  - Spatial Smoothing
  - Inter-subject Registration

2D Surface in 3D Space



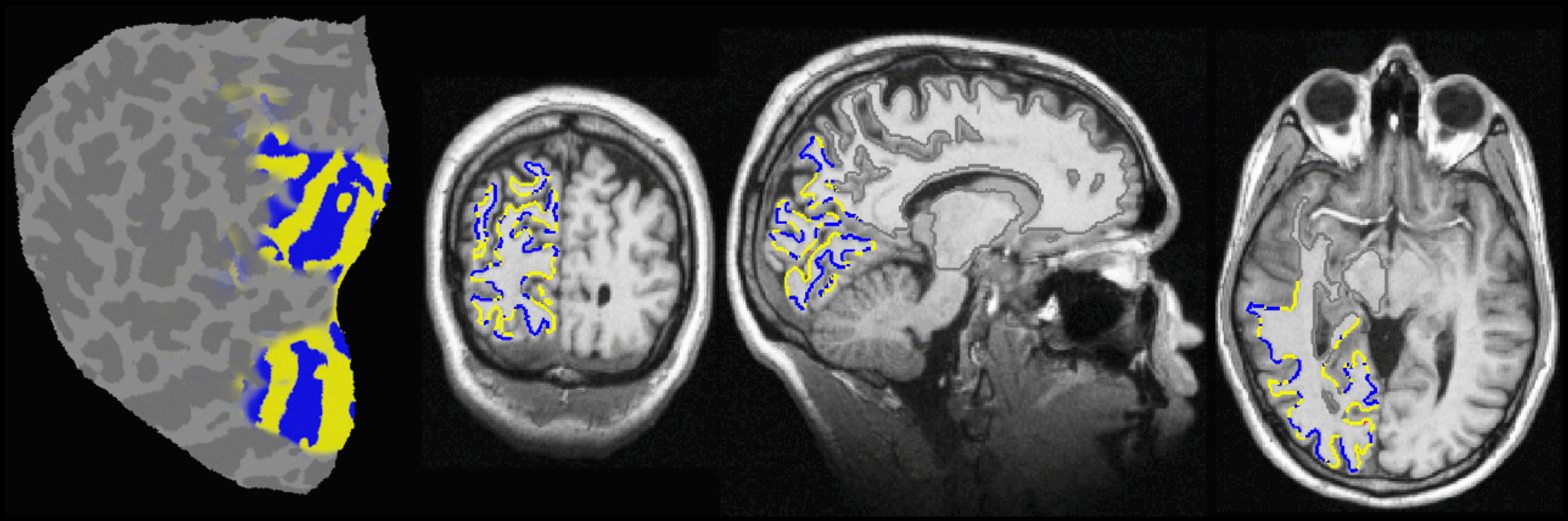




Inflation

Flattening

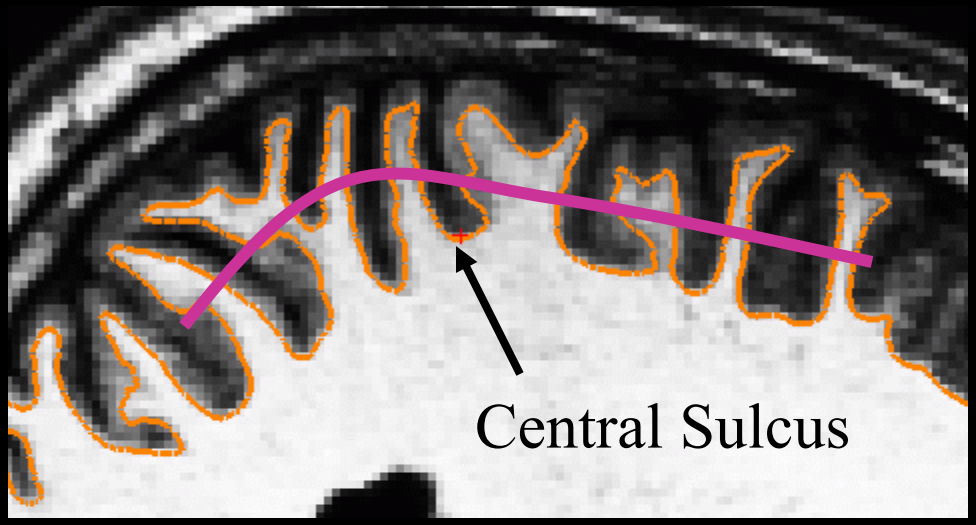
Function Follows the Surface



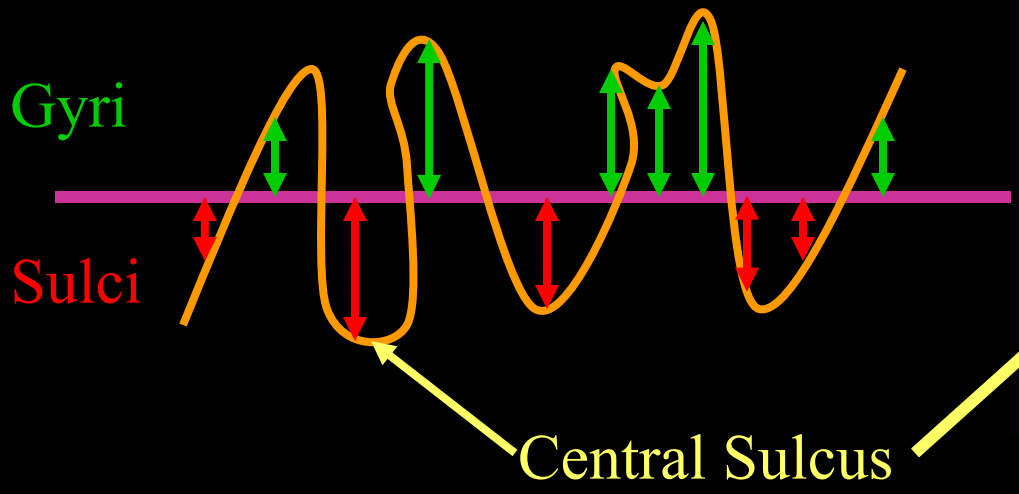
- Visual areas mapped using fMRI retinotopy
- Pattern is clear on the surface
- Pattern is lost in the volume

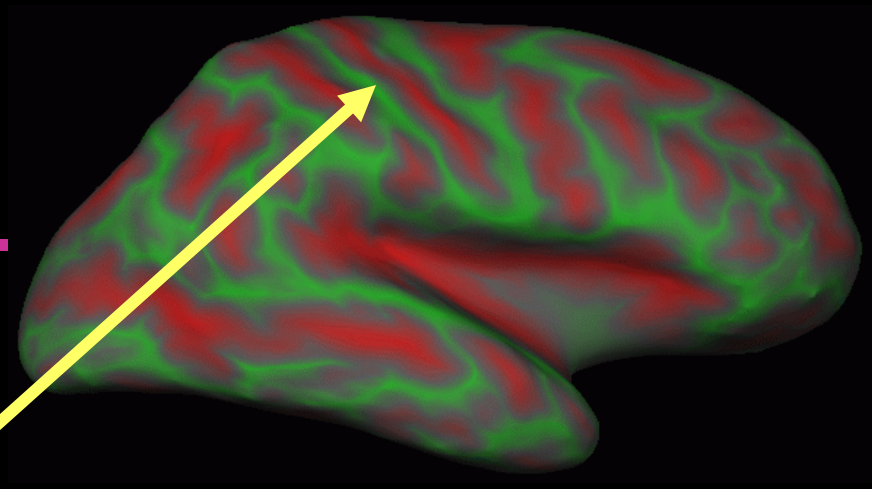
From (Sereno et al, 1995, Science).

Quantifying Folding Patterns



- Height or Depth Encodes Folding Pattern
- Every vertex has a value





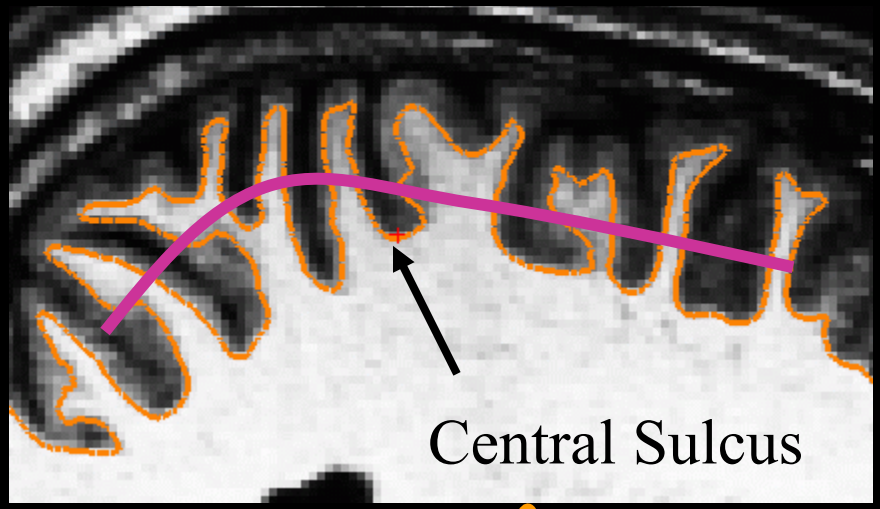
Motivation

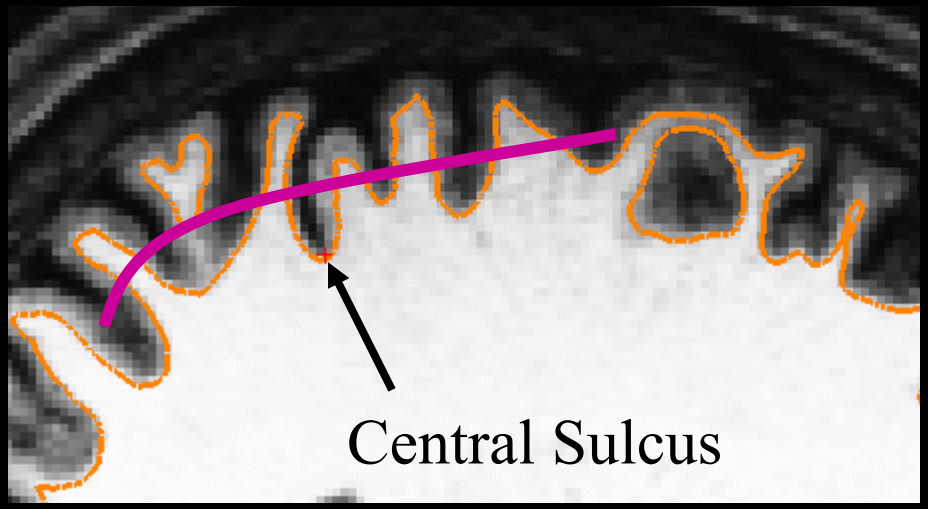
To a large degree, function follows the folding patters. So if you align the folding patterns between two subjects you will align the function.

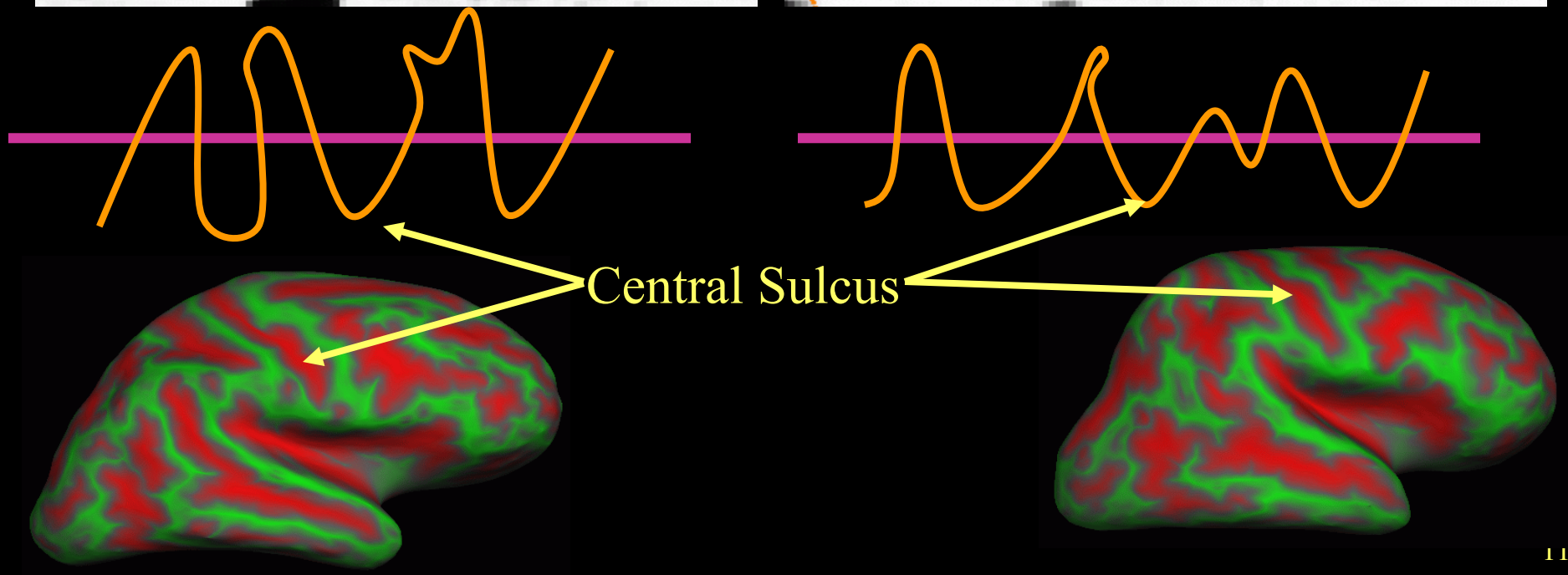
Intersubject Registration

Subject 1

Subject 2

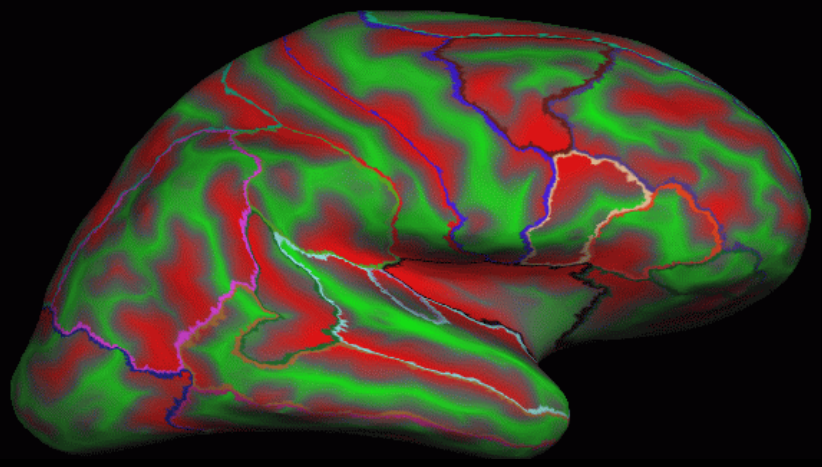




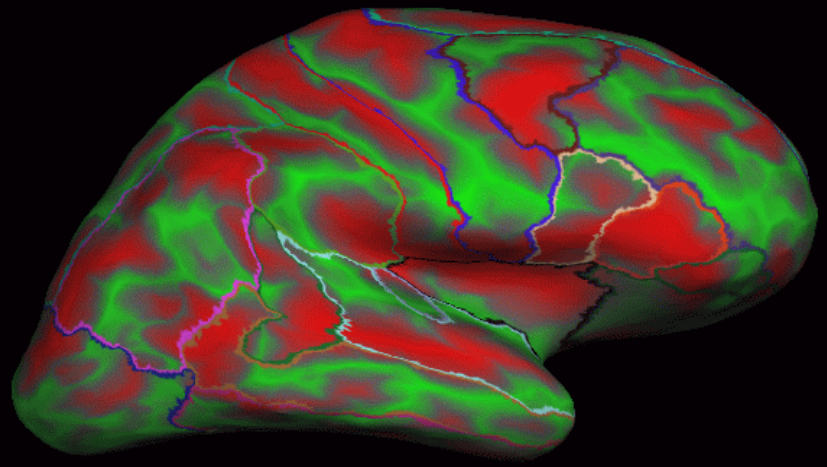


Surface Registration

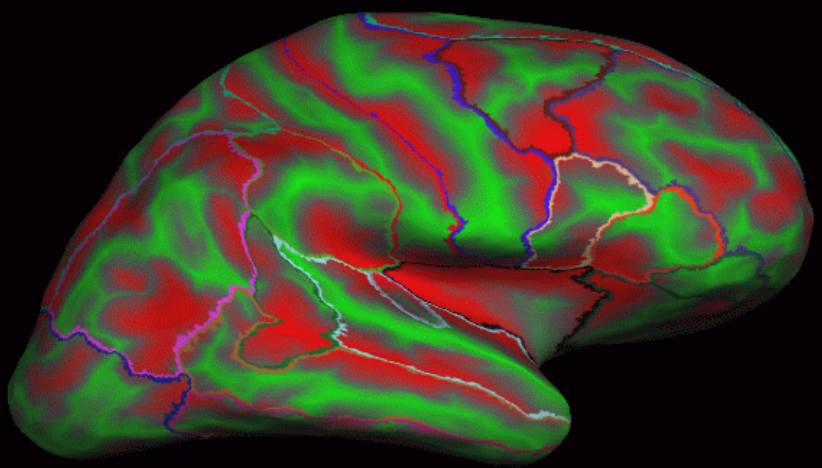
Subject 1



Subject 2 (Before)

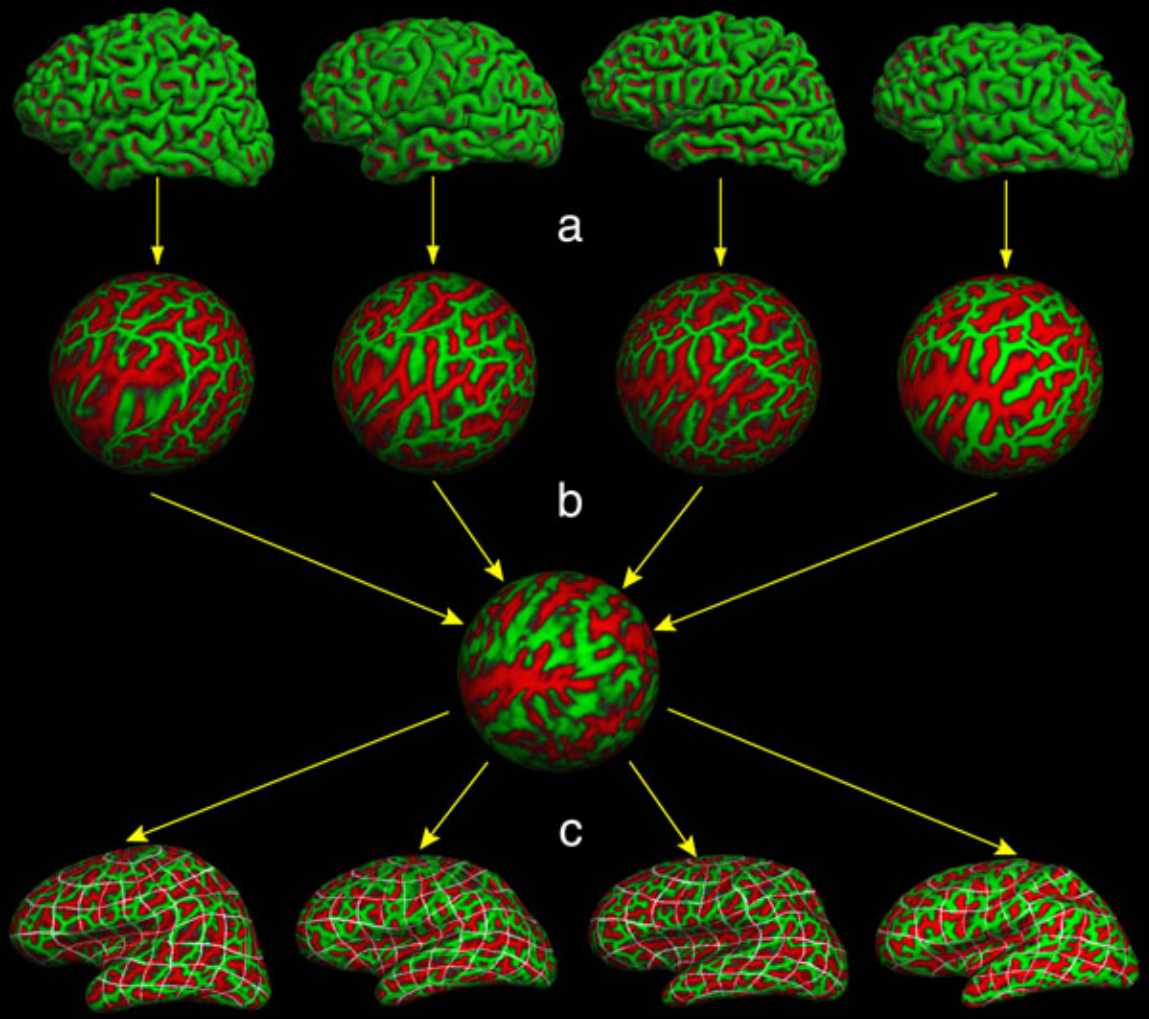


Subject 2 (After)



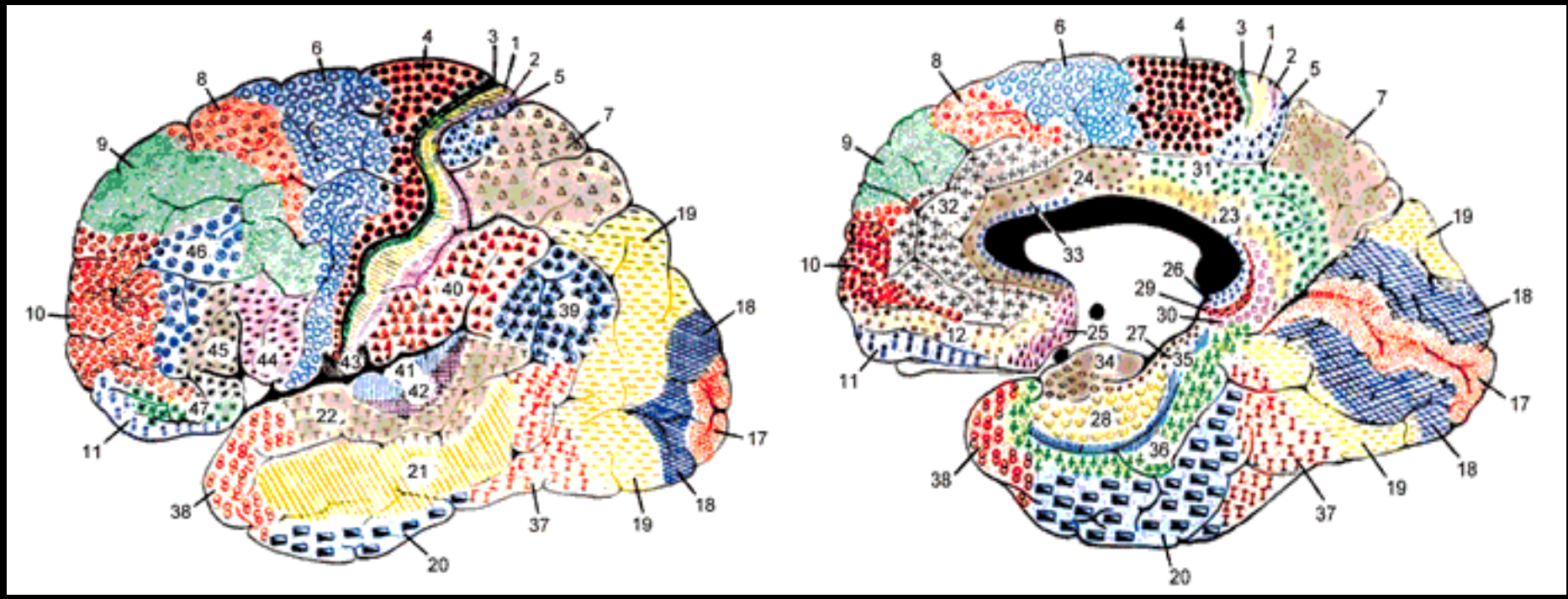
- Shift, Rotate, Stretch
- High dimensional (~500k)

A Surface-Based Coordinate System



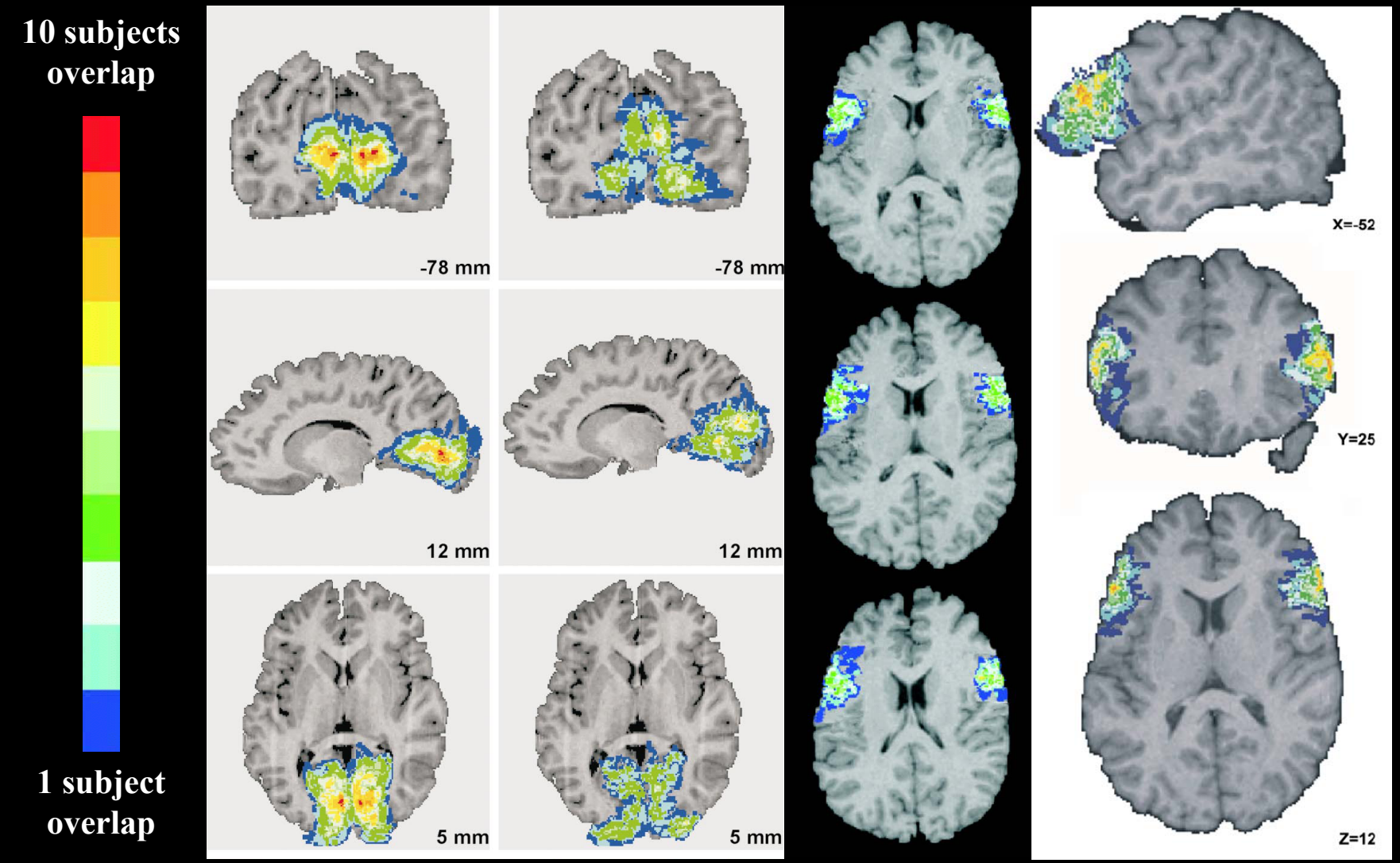
Common space for group analysis (like Talairach)

Performance



Brodmann, 1909

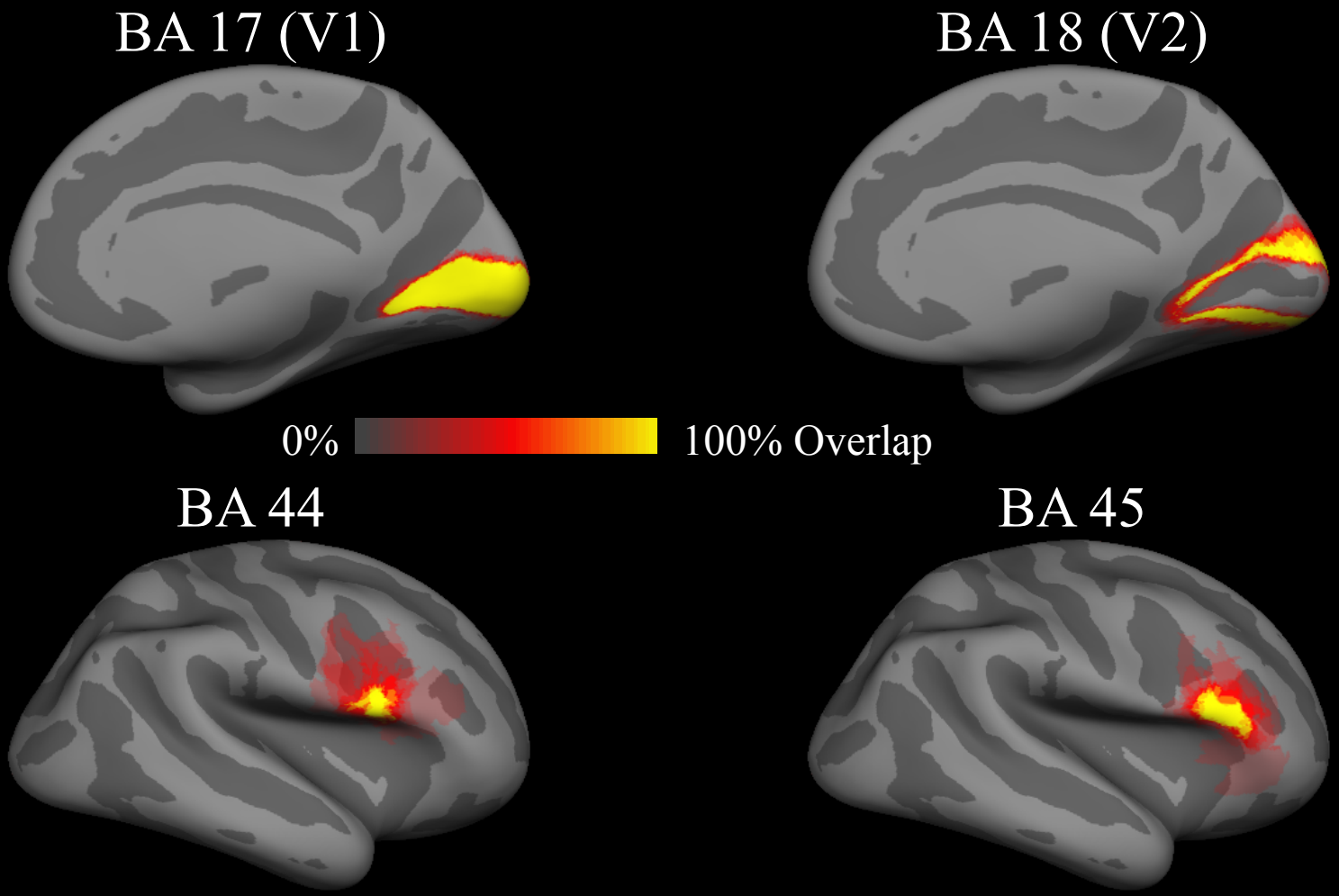
Predicting Brodmann Areas: Talairach Coordinates



BA17 (V1) BA18 (V2) BA44 (Broca's) BA45 (Broca's)

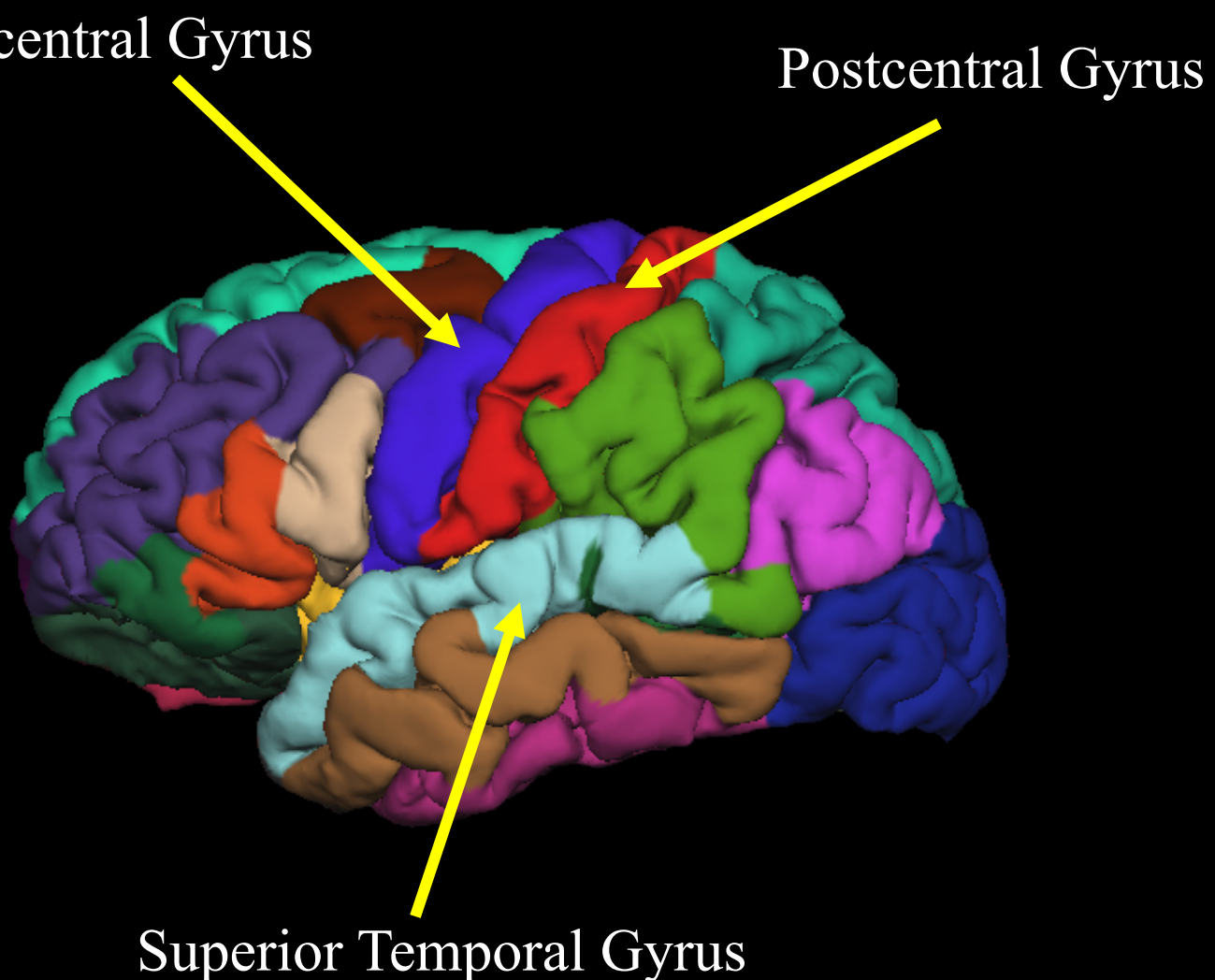
(Amunts et al, 2000, 2004)

Predicting Brodmann Areas from Folding Patterns



Fischl, et al, 2007. Thanks to Katrin Amunts, Karl Zilles and Hartmut Mohlberg for the data, and to Niranjini Rajendran and Evelina Busa for the analysis.

Automatic Gyral Segmentation

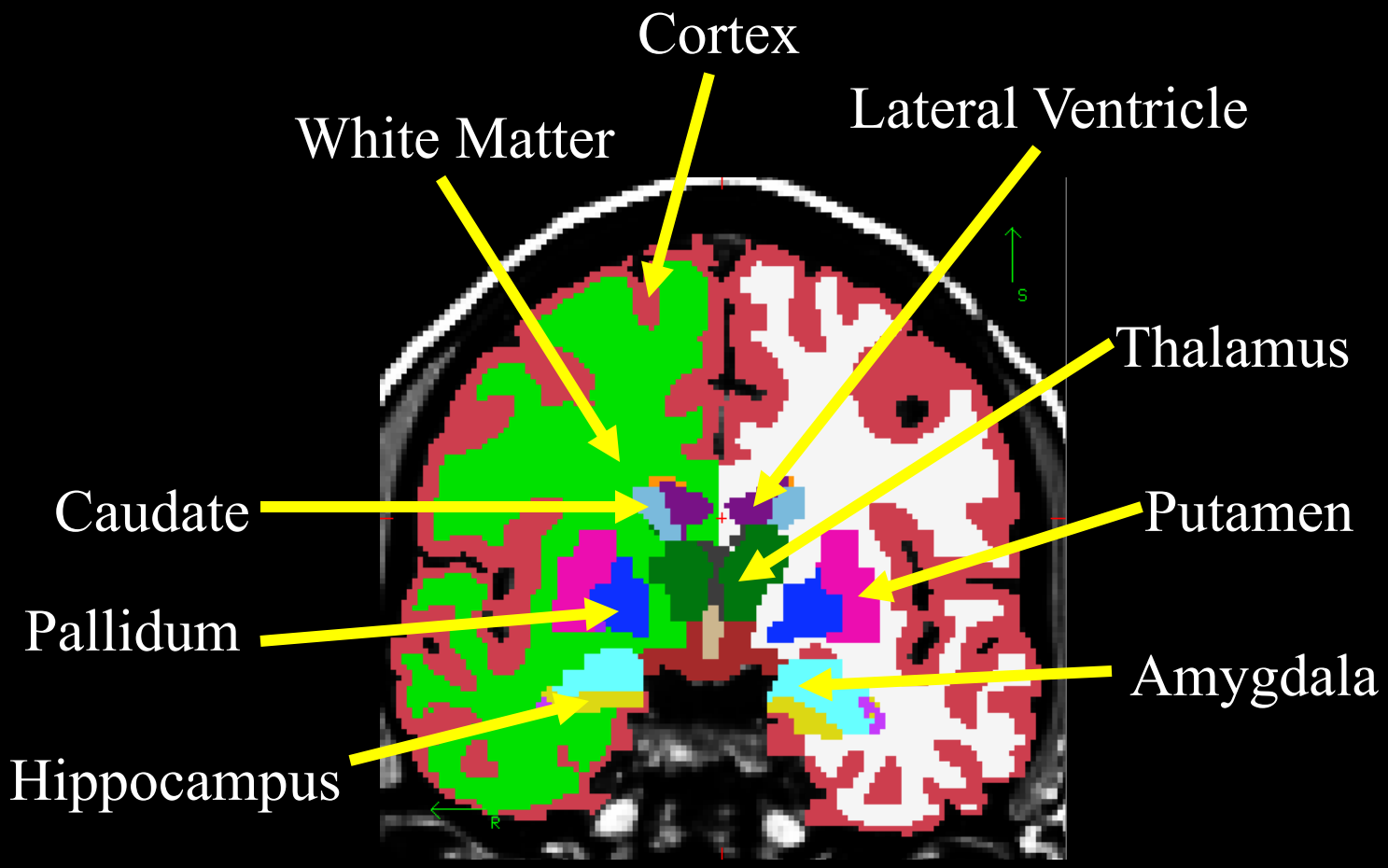


Based on individual's folding pattern

Outline

- Anatomical Analysis
  - Surface-based (Cortex)
  - Volume-based
- Thickness analysis
- Multi-modal integration
  - DTI/Tractography
  - fMRI

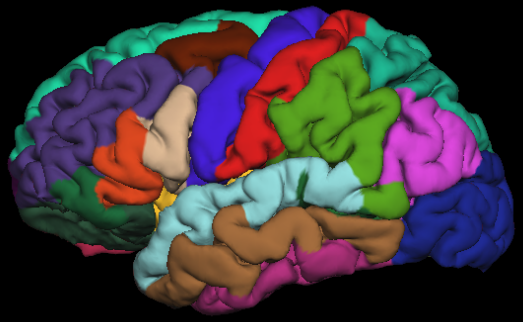
Volumetric Segmentation (aseg)



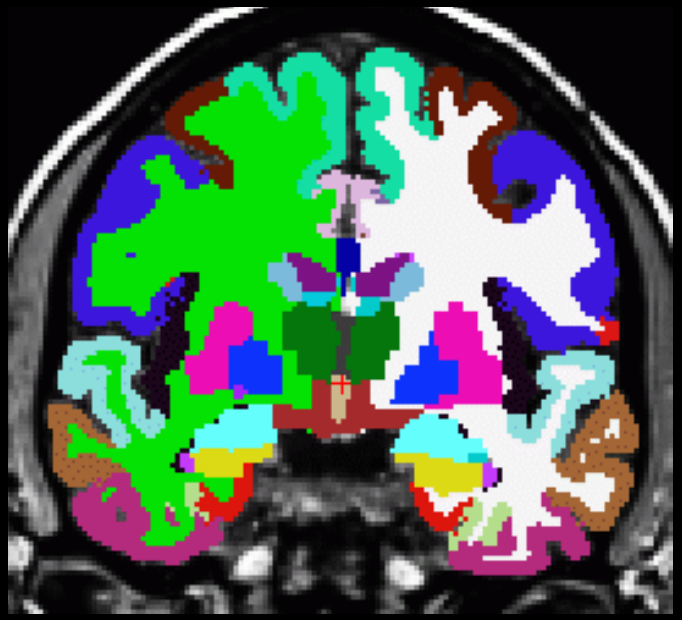
Not Shown:
Nucleus Accumbens
Cerebellum

Combined Segmentation

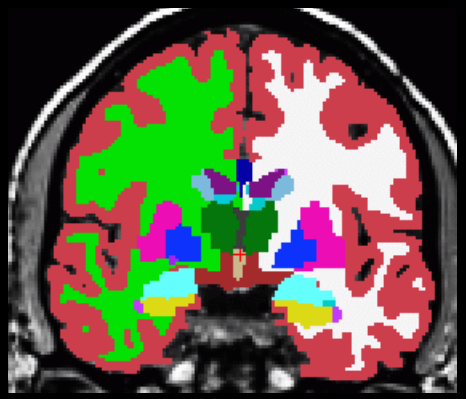
aparc



aparc+aseg



aseg

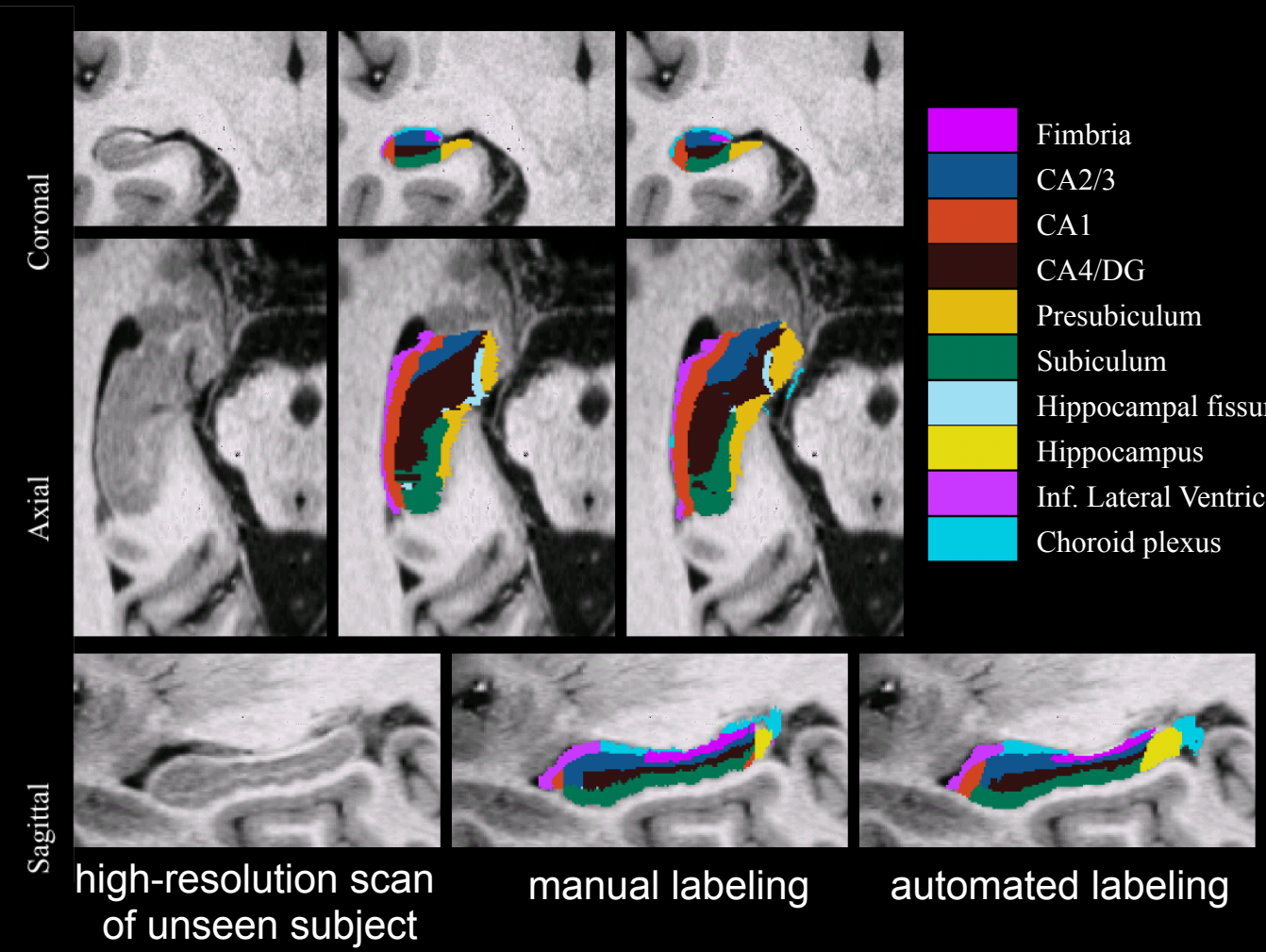


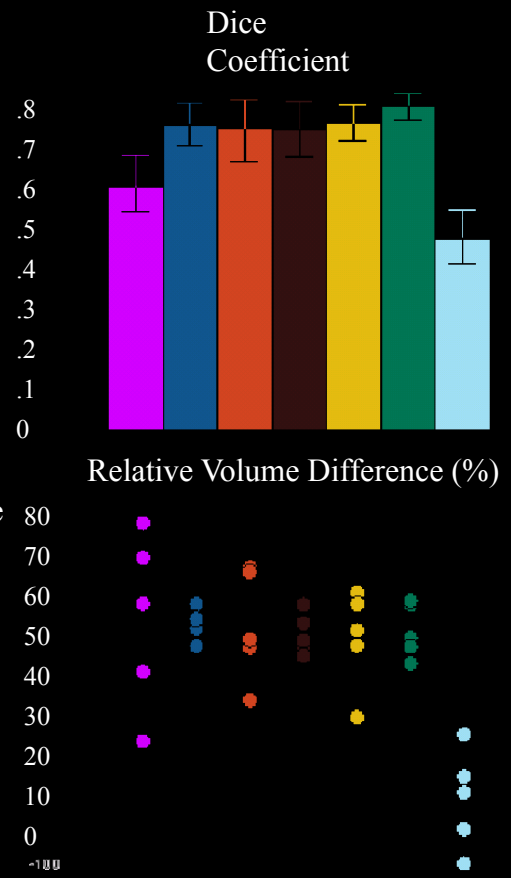
wmparc

Nearest Cortical Label to point in White Matter

Automated Subfield Segmentation

- Leave-one-out cross-validation with 5 subjects





Collaboration with Koen van Leemput, Polina Golland, Brad Dickerson and Akram Bakkour

Longitudinal Analysis: Robust Registration

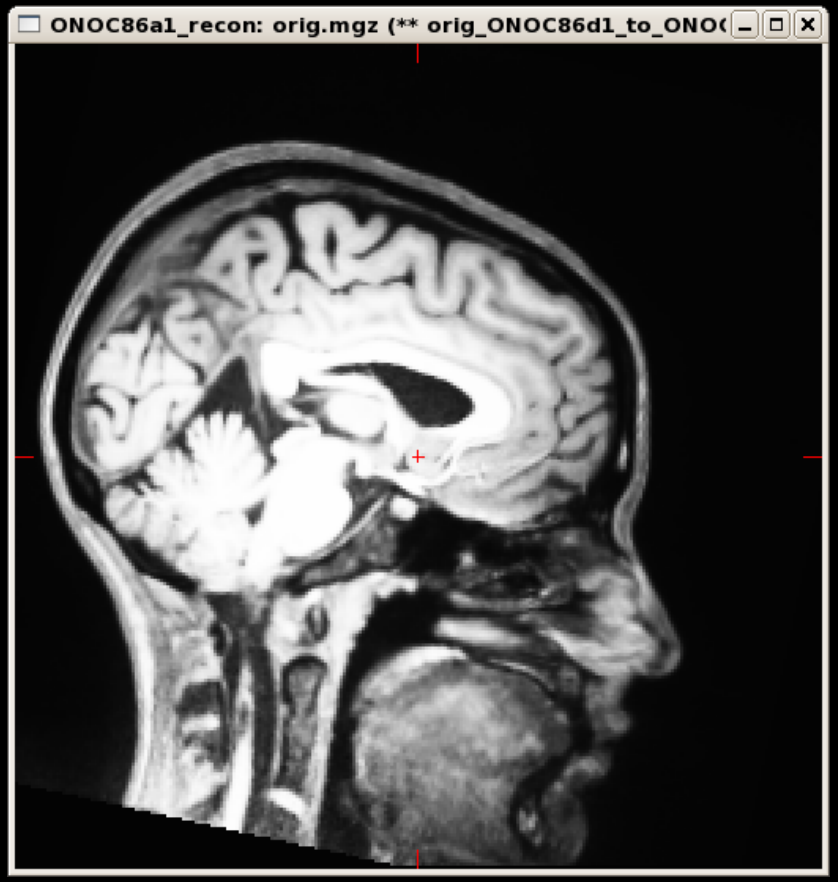
Target

Target

Collaboration with Martin Reuter and Diana Rosas

Longitudinal Analysis: Robust Registration

Registered Src
(correlation ratio)



Registered Src
(Robust)

Collaboration with Martin Reuter and Diana Rosas

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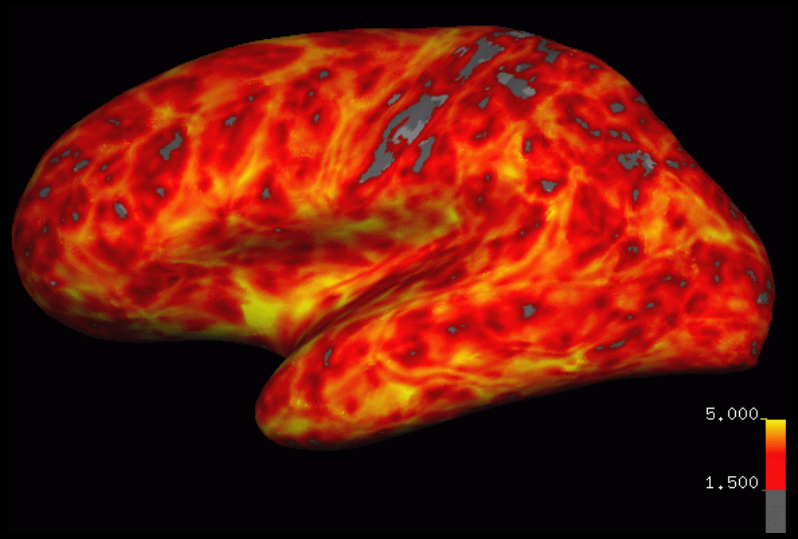
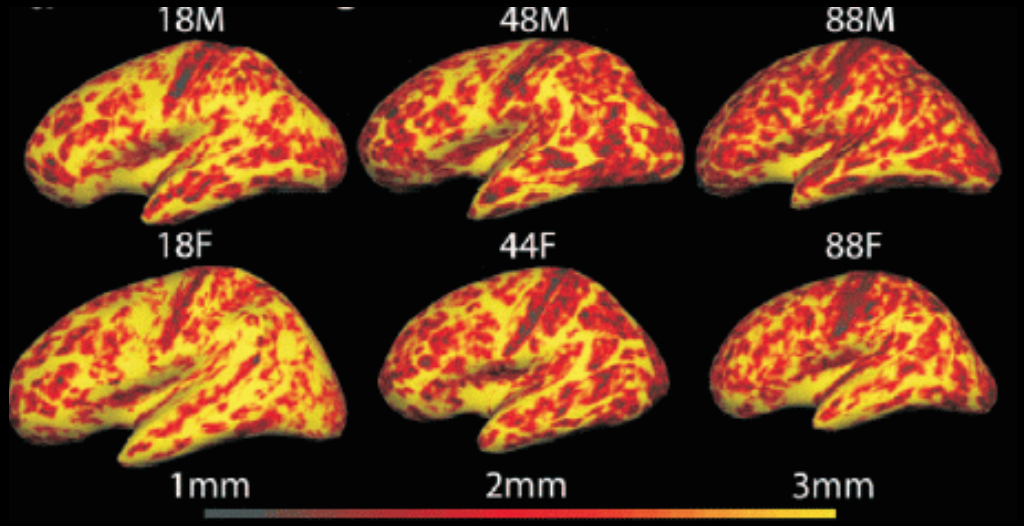
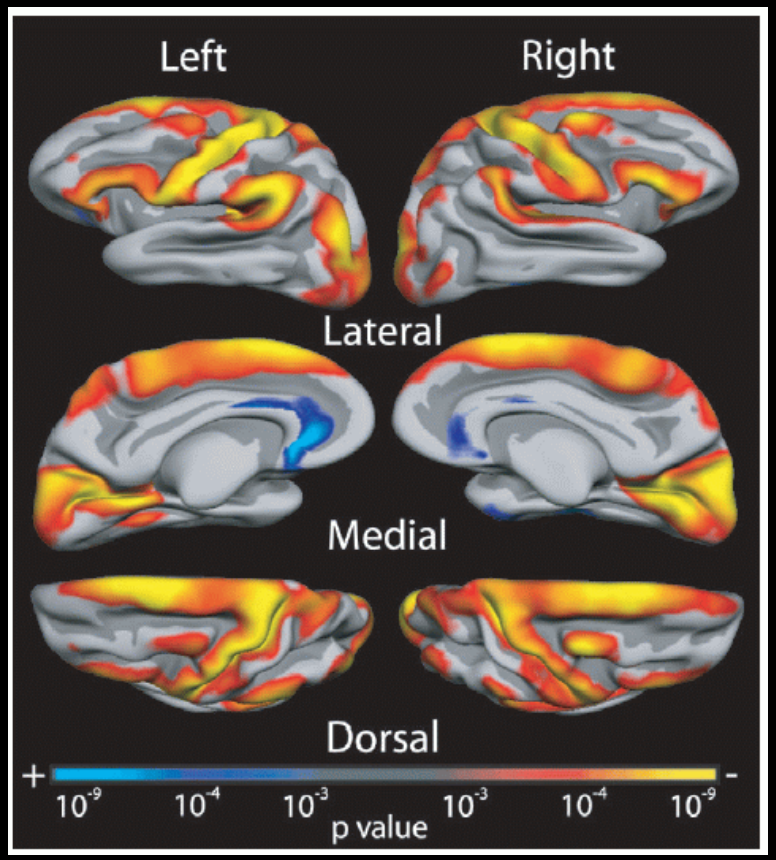
Cortical Thickness

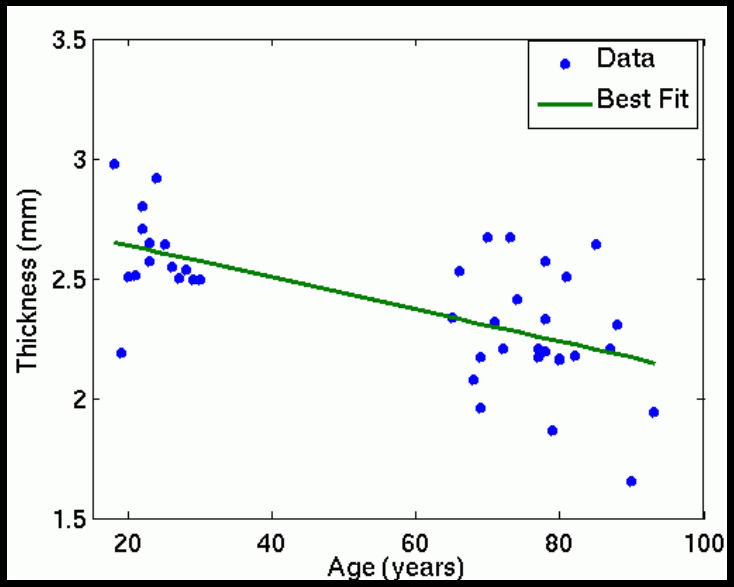
- Distance between white and pial surfaces along normal vector.
- 1-5mm



Aging







Salat, et al, 2004, Cerebral Cortex

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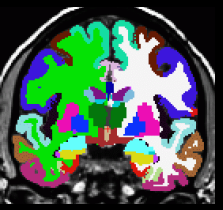
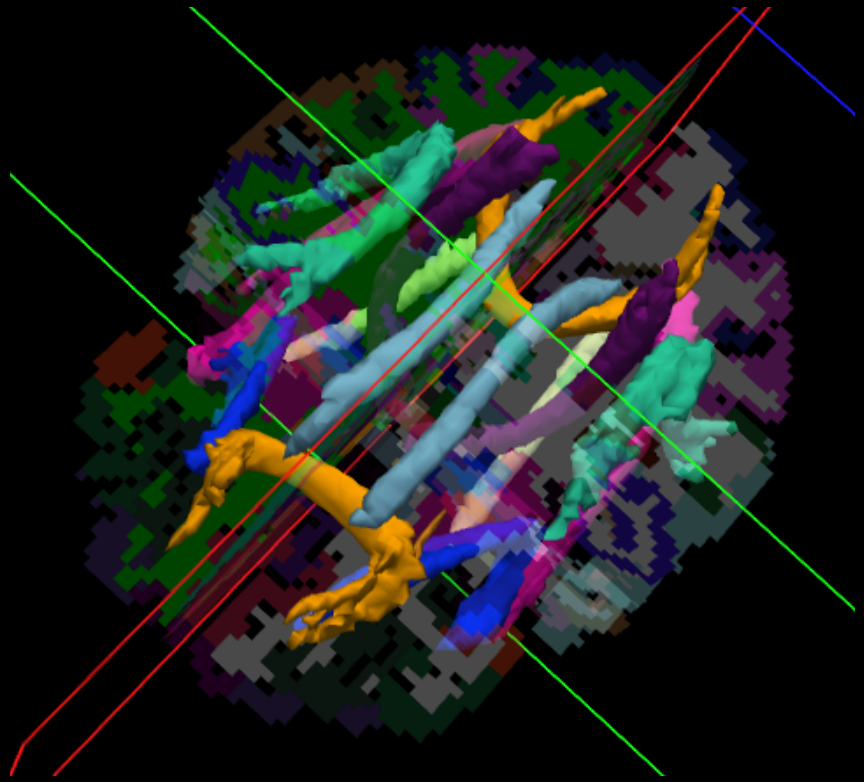
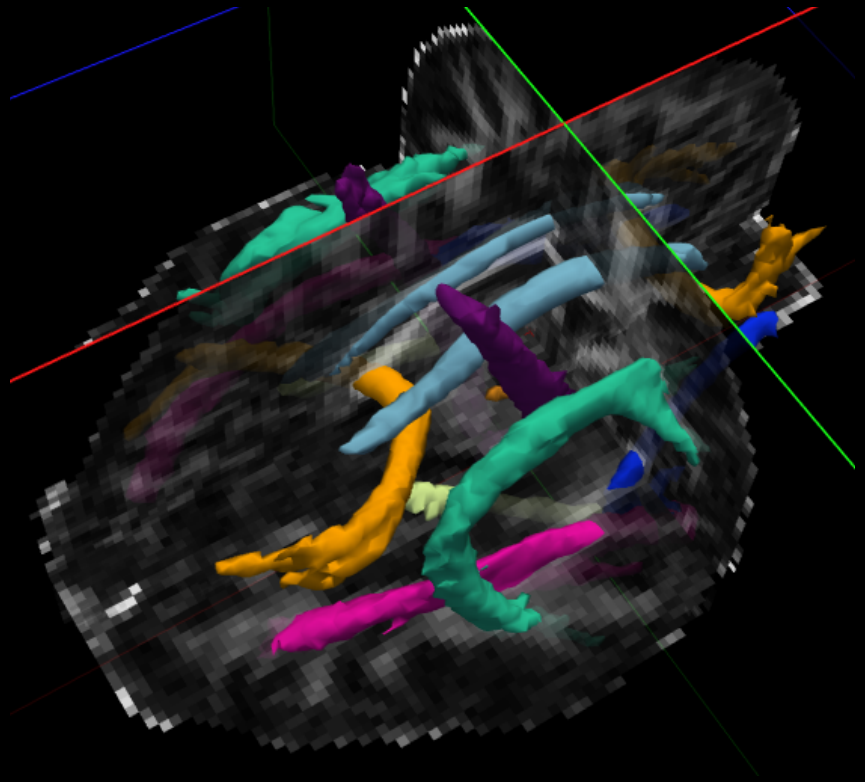


Tractography with TRACULA

(TRActs Constrained by the Underlying Anatomy)





- Completely automated modeling of 17 major fascicles
- Uses FSL DTI Analysis

Collaboration with Anastasia Yendiki, Lilla Zöllei, Saad Jbabdi, Tim Behrens and Jean Augustinack

Outline

- Anatomical Analysis
  - Surface-based (Cortex)
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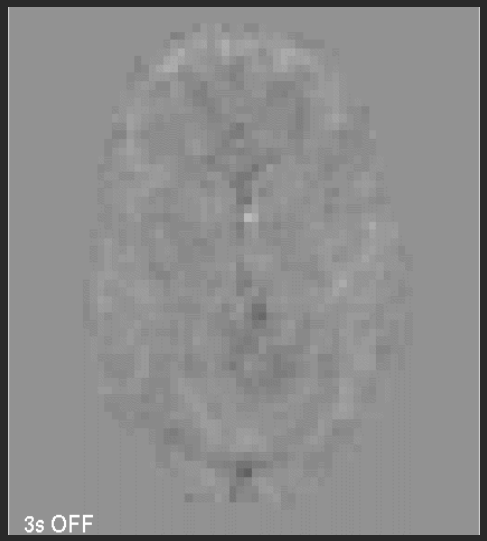
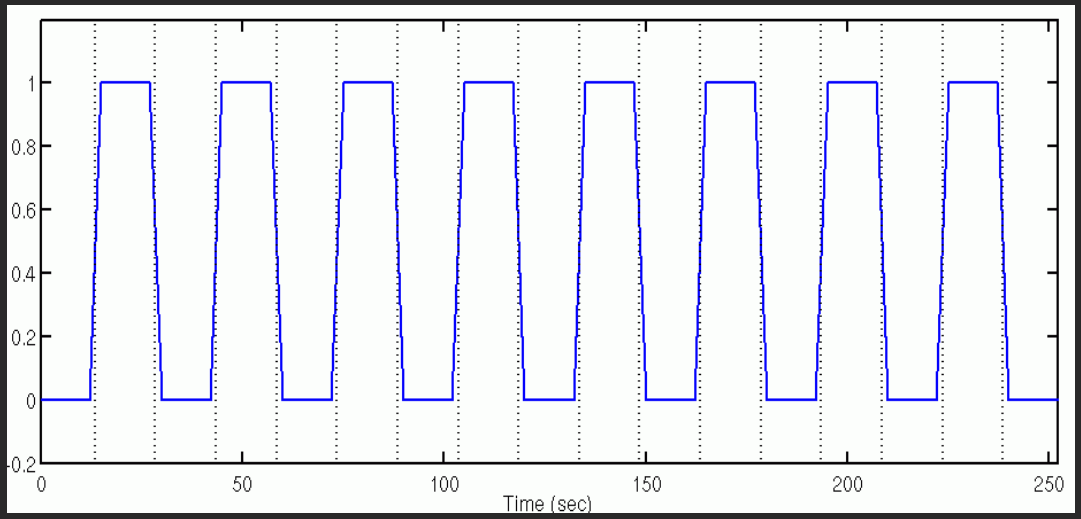
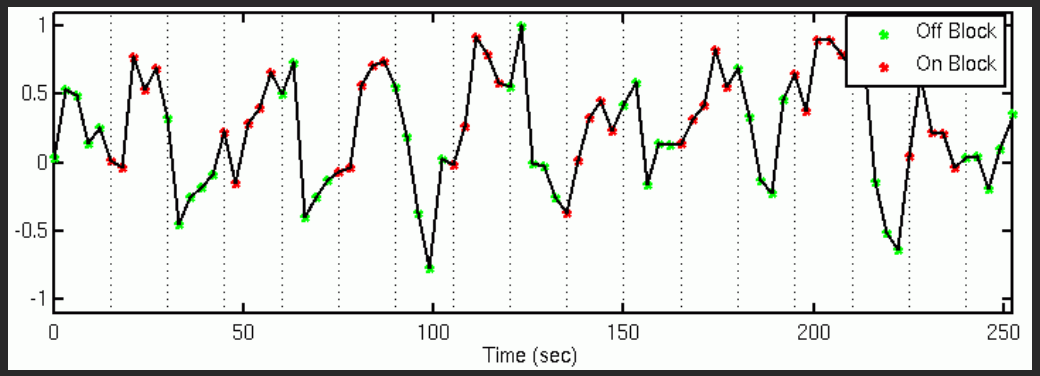
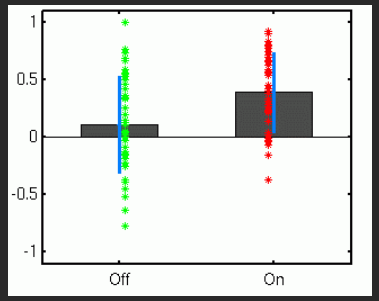
- Multi-modal integration
  - DTI/Tractography
  - fMRI – task

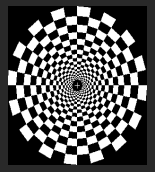
Visual/Auditory/Motor Activation Paradigm







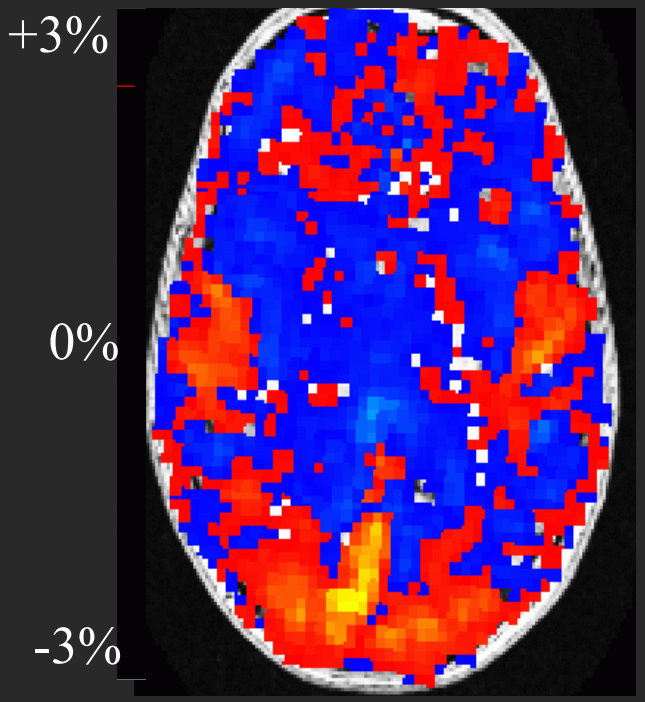




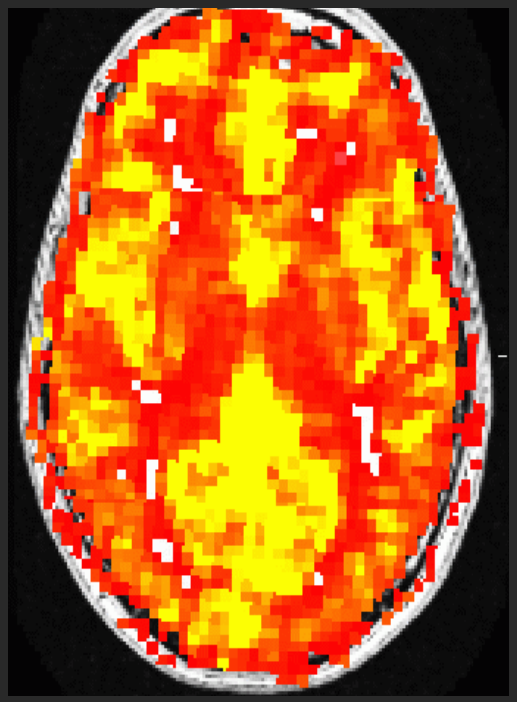
15 sec 'ON', 15 sec 'OFF'

- **Flickering Checkerboard**
- **Auditory Tone**
- **Finger Tapping**

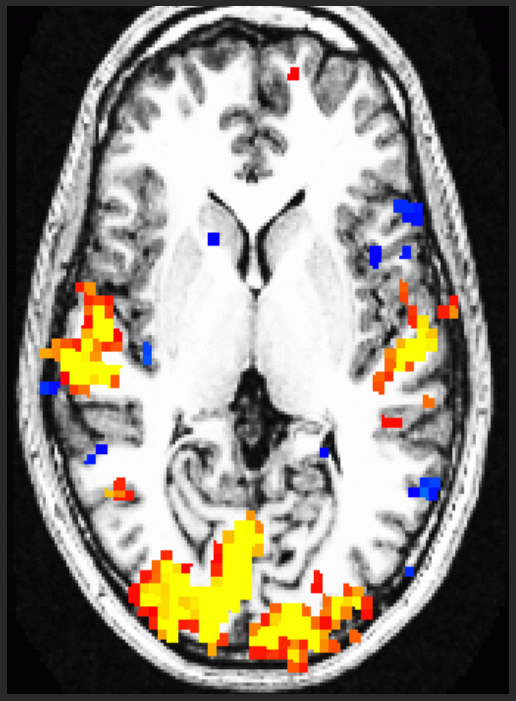
On-vs-Off SPMs



Contrast Amplitude
CON, COPE, CES

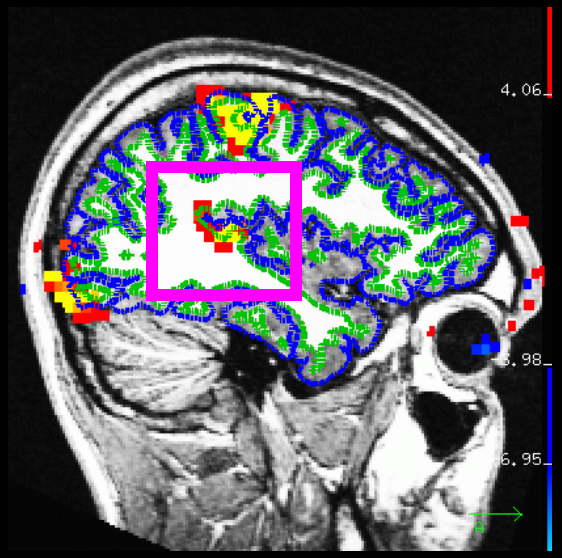


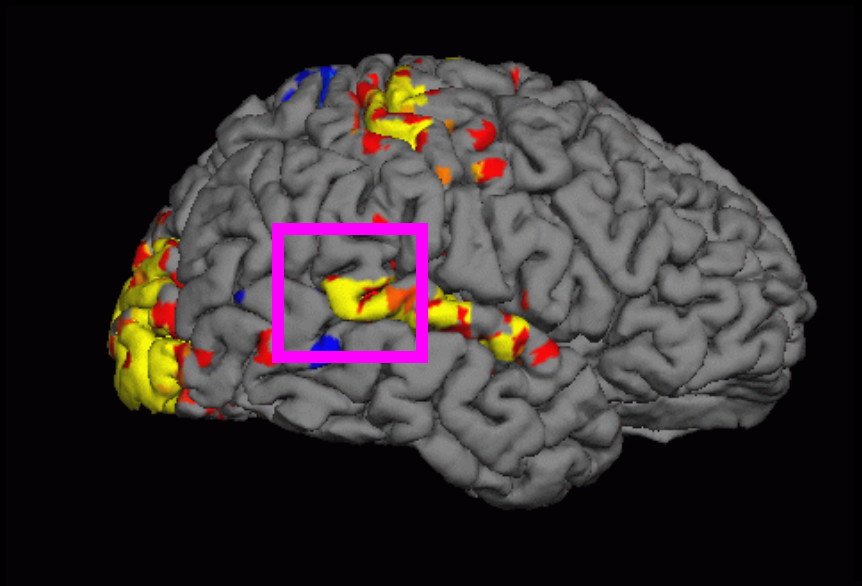
Contrast Amplitude Variance
(Error Bars)
VARCOPE, CESVAR

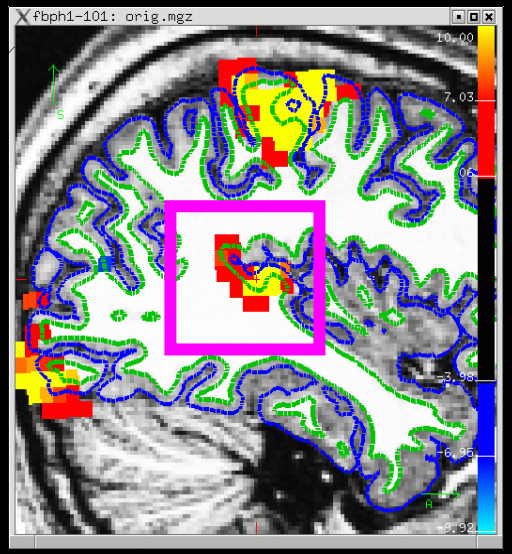


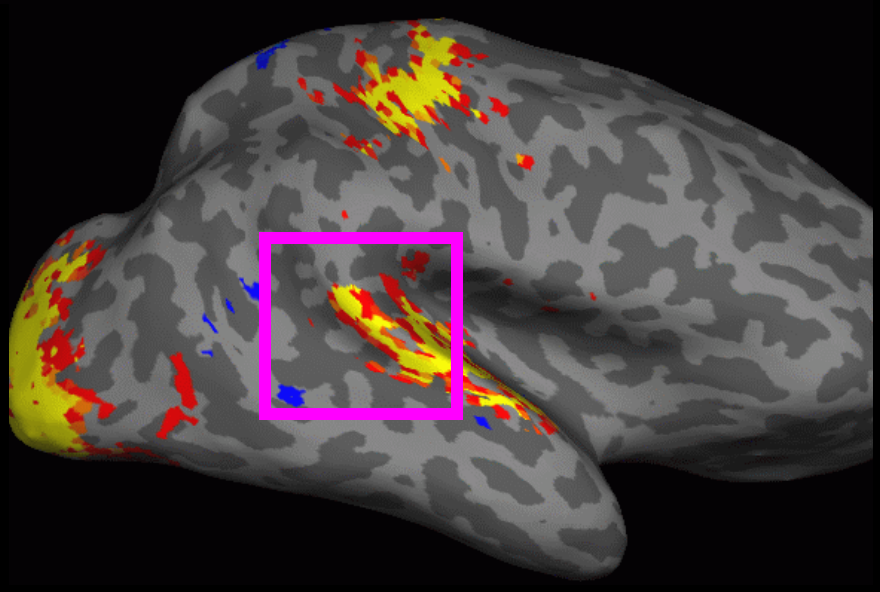
Significance t-Map (p,z,F)
(Thresholded p<.01)

Sampling on the Surface

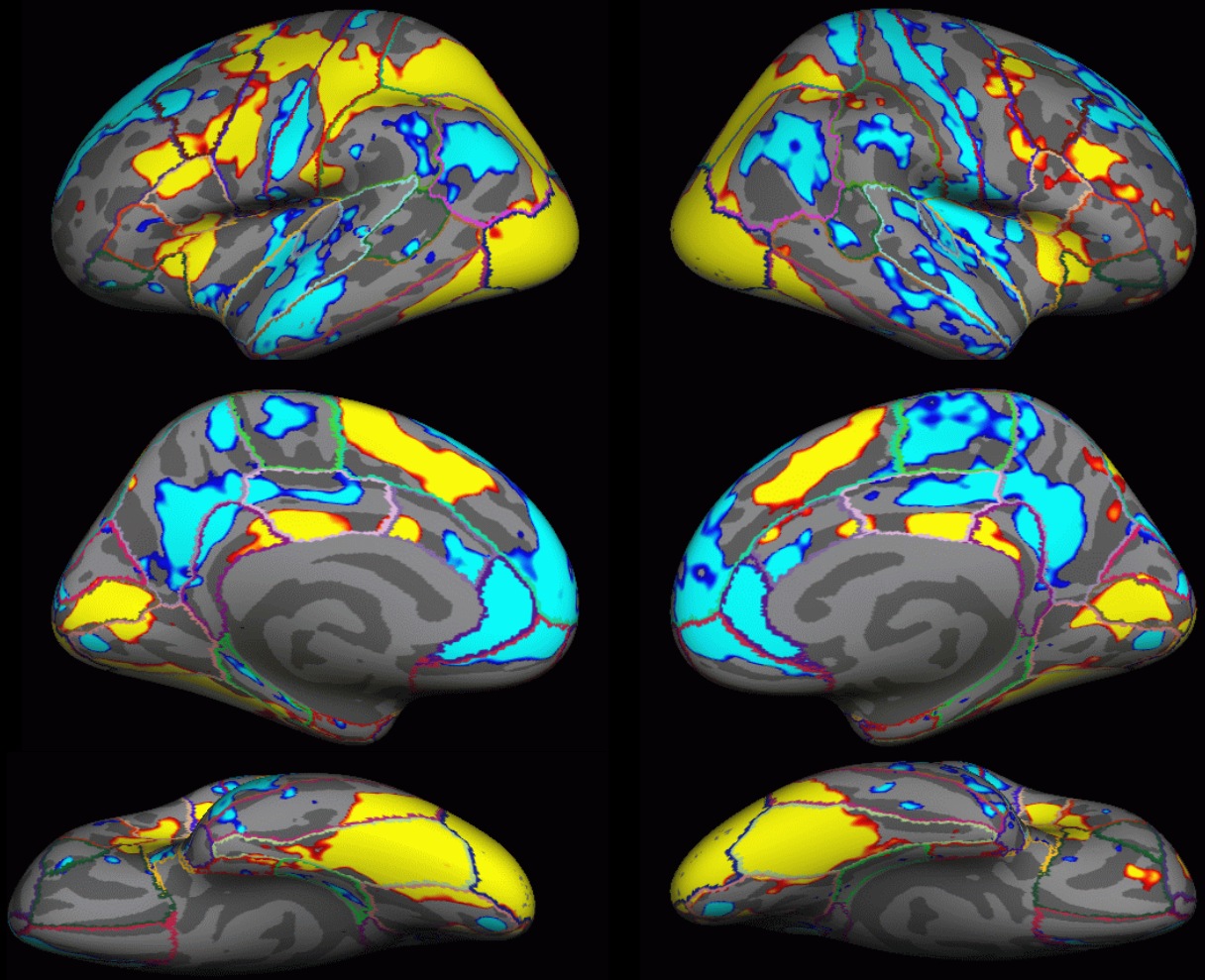






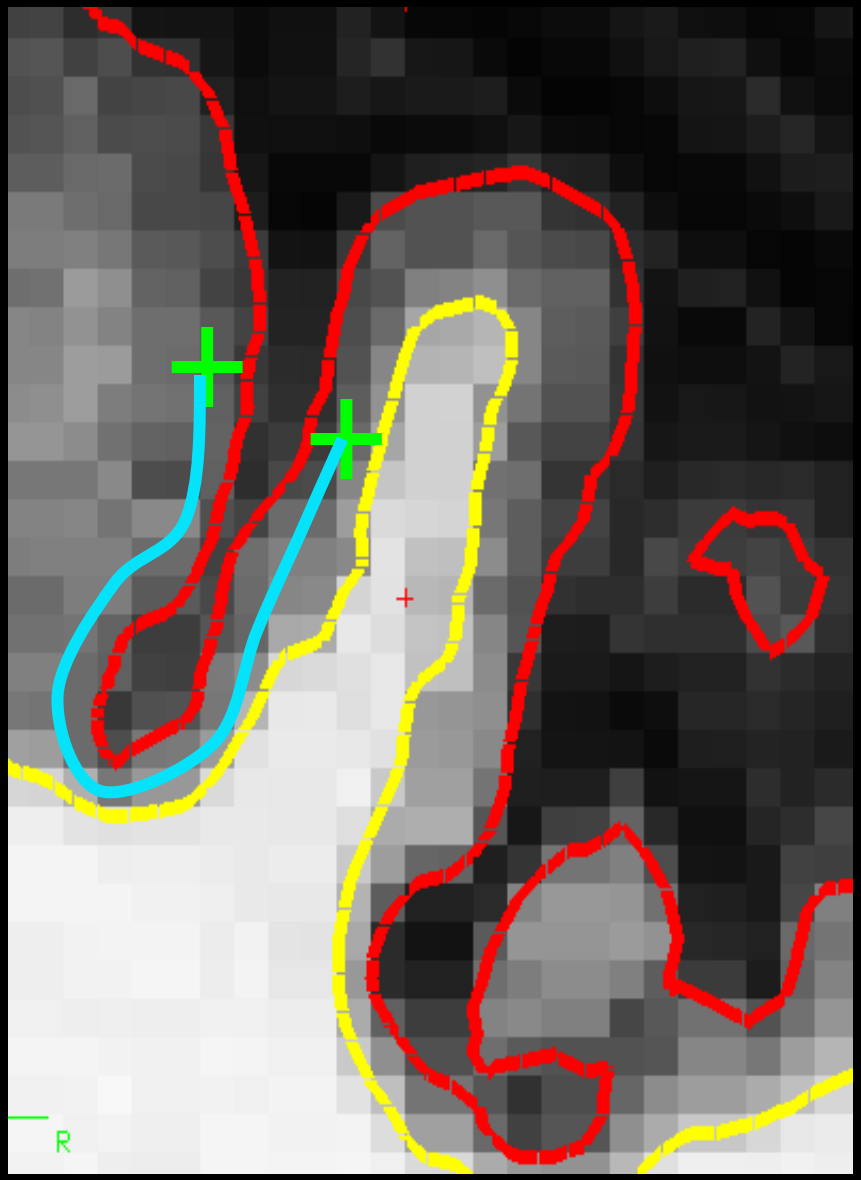


fMRI Working Memory Paradigm Group Analysis

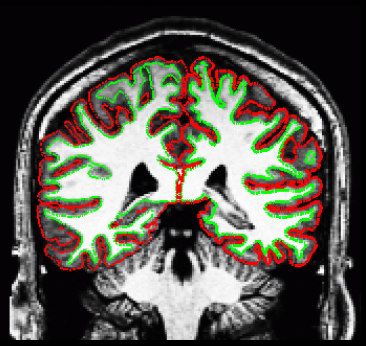


Probe-vs-Fixation. Data Functional Biomedical Informatics Research Network (fBIRN)

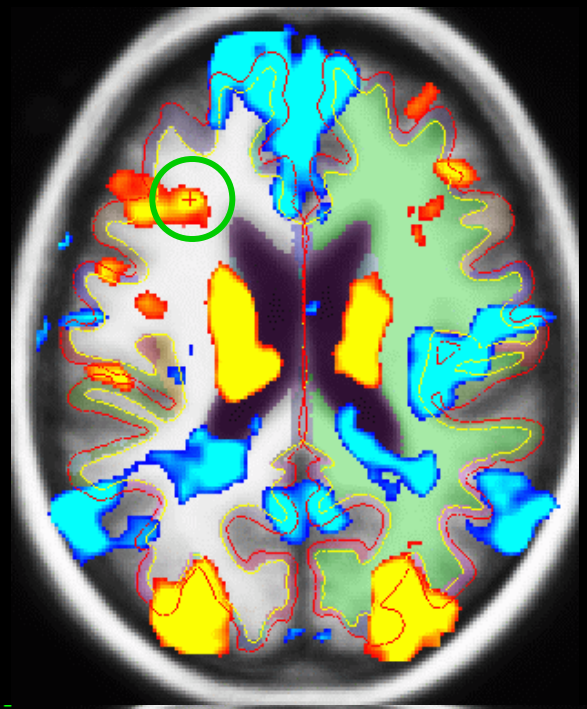
Spatial Smoothing

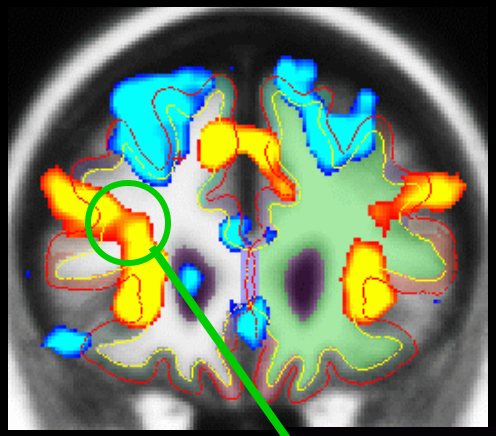


- 5 mm apart in 3D
- 25 mm apart on surface!
- Kernel much larger
- Averaging with other tissue types (WM, CSF)
- Averaging with other functional areas

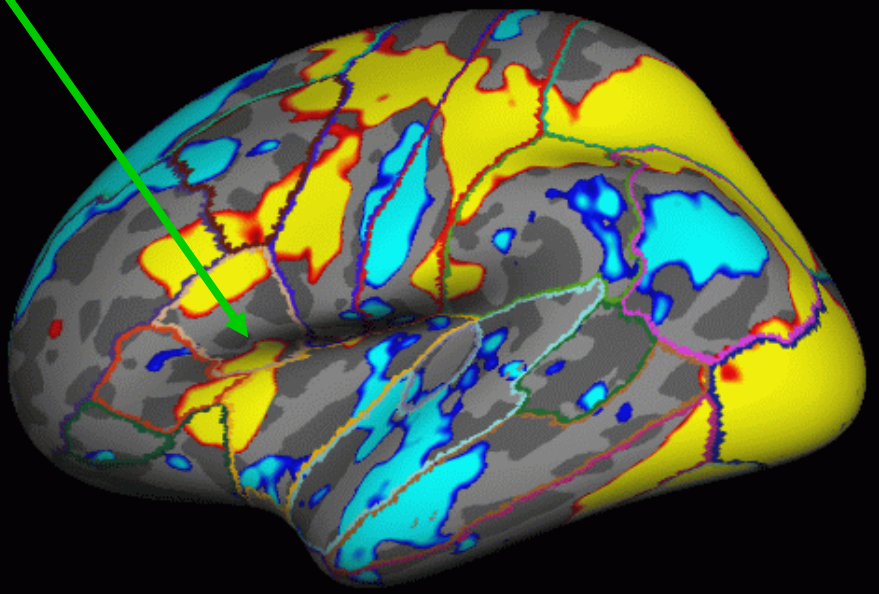


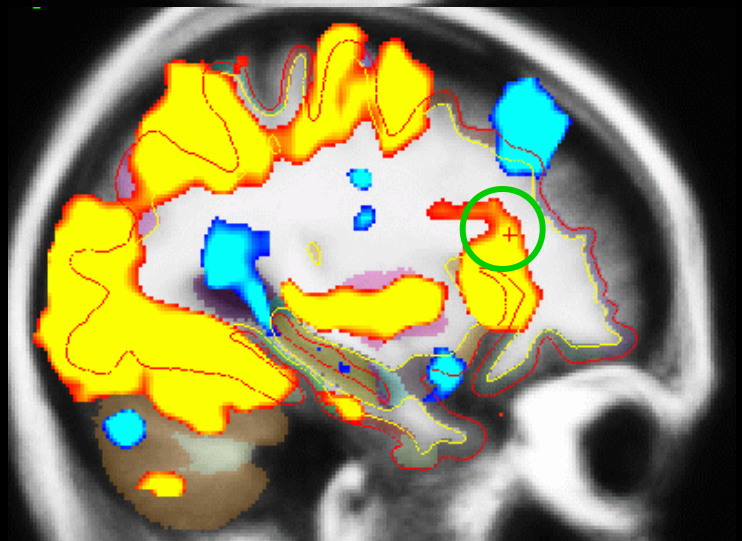
Group fMRI Analysis: Volume vs Surface





Affine registration to MNI305

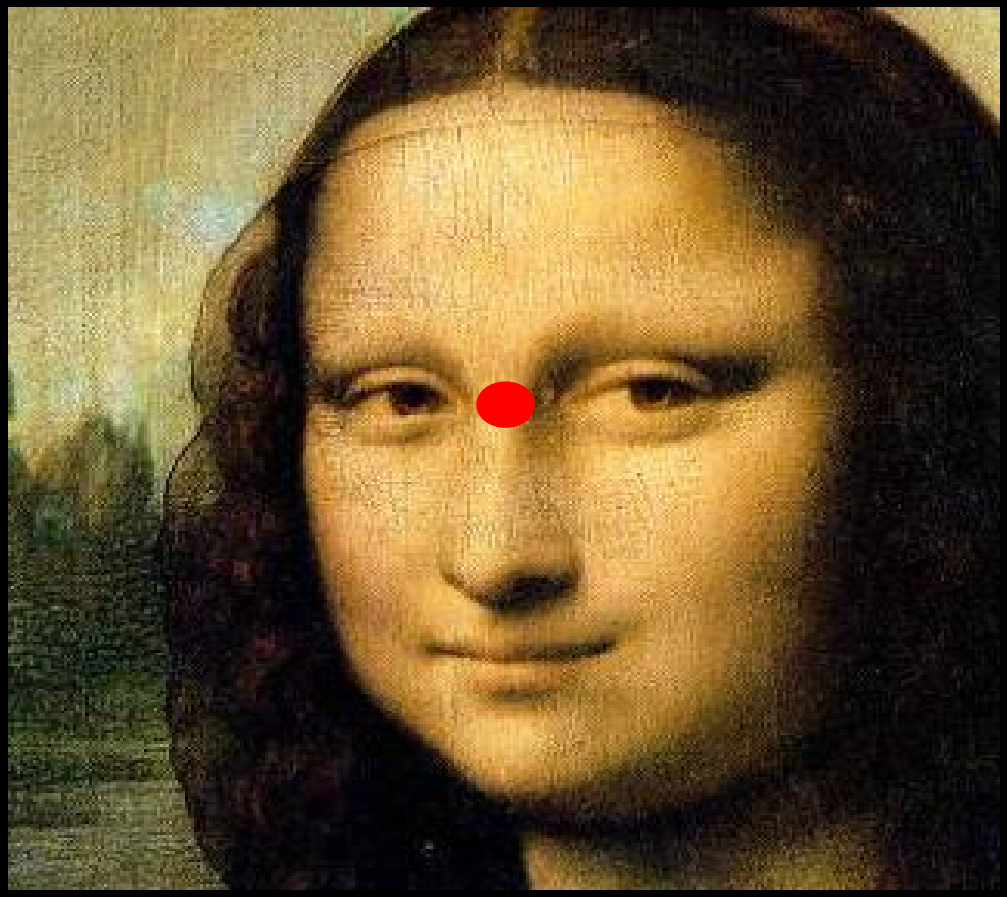


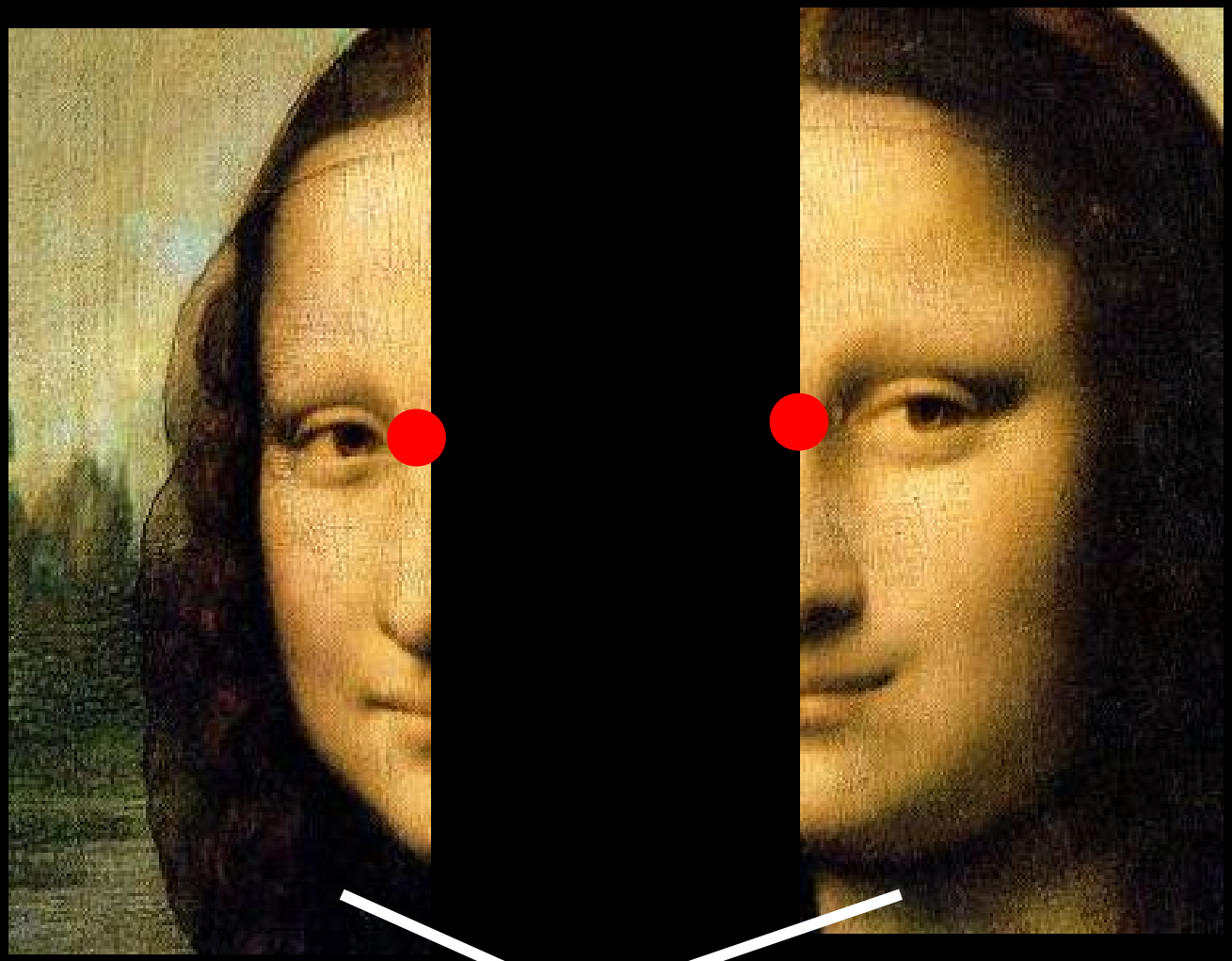


Outline

- Anatomical Analysis
  - Surface-based (Cortex)
  - Volume-based
- Thickness analysis
- Multi-modal integration
  - DTI/Tractography
  - fMRI – retinotopy

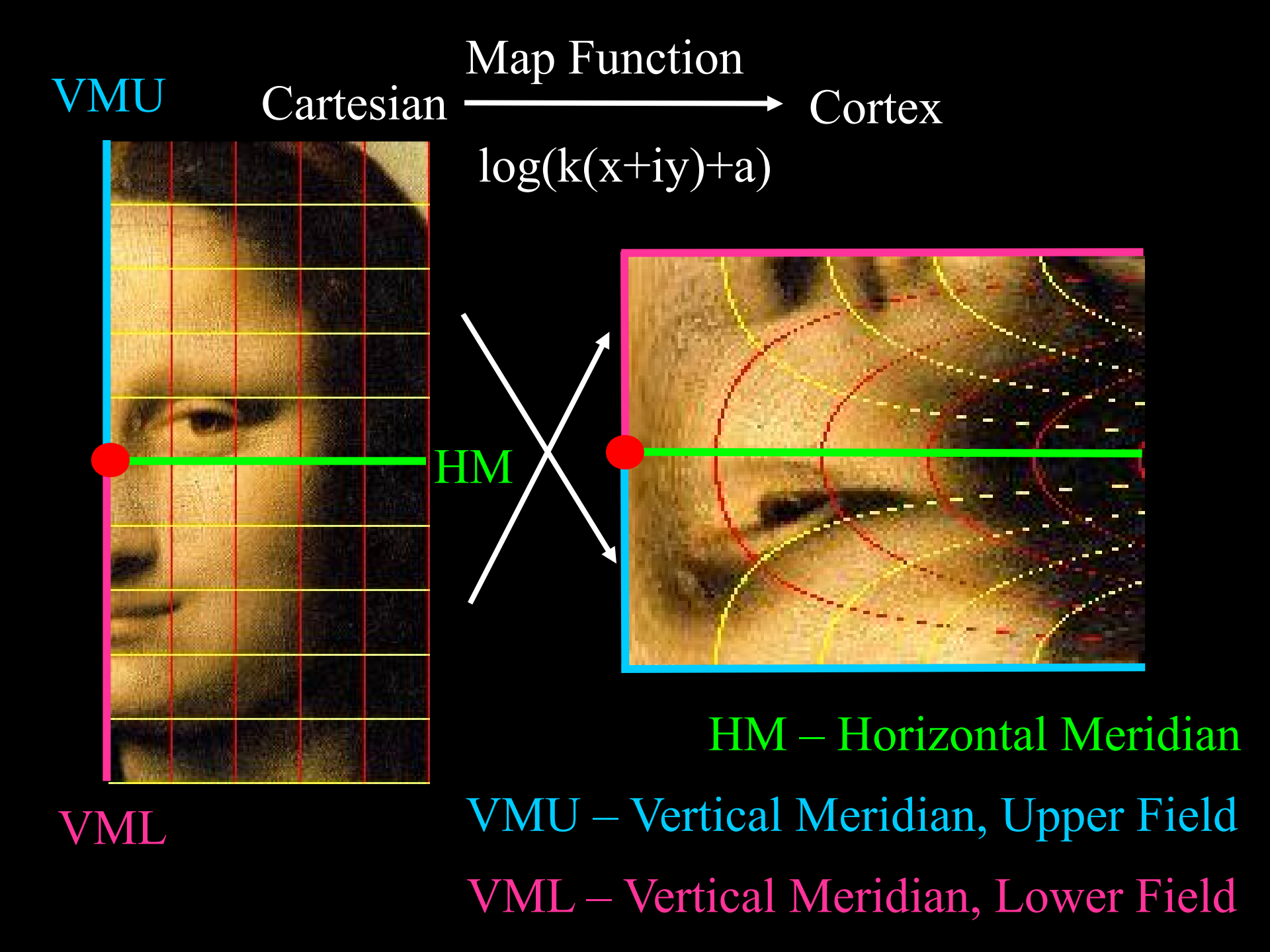
What does your brain do to Mona?



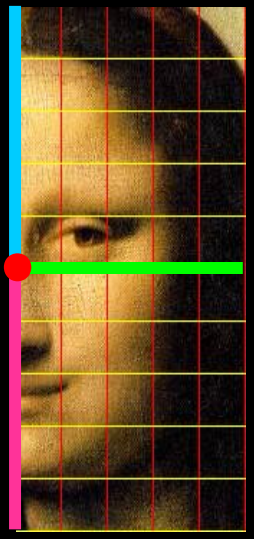


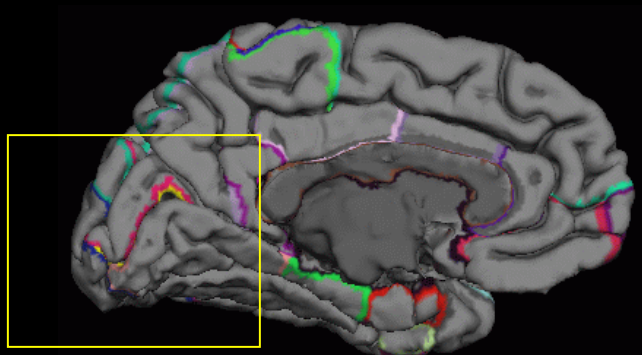
Left Cortical Hemisphere

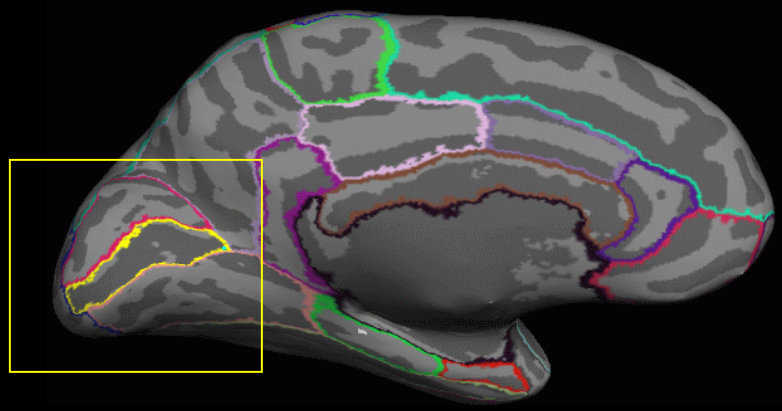
Right Cortical Hemisphere

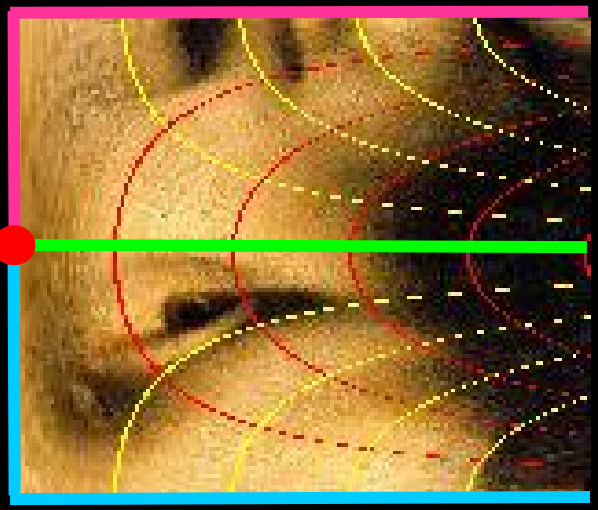

VMU
Cartesian
Map Function
Cortex
log(k(x+iy)+a)
HM
VML
HM – Horizontal Meridian
VMU – Vertical Meridian, Upper Field
VML – Vertical Meridian, Lower Field

V1 – Primary Visual Cortex





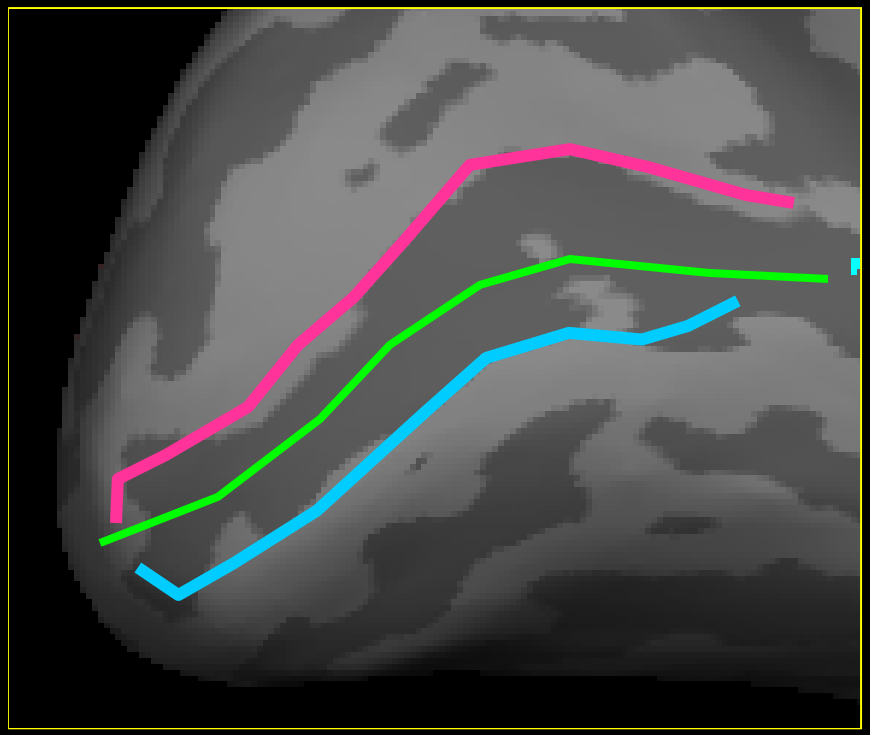




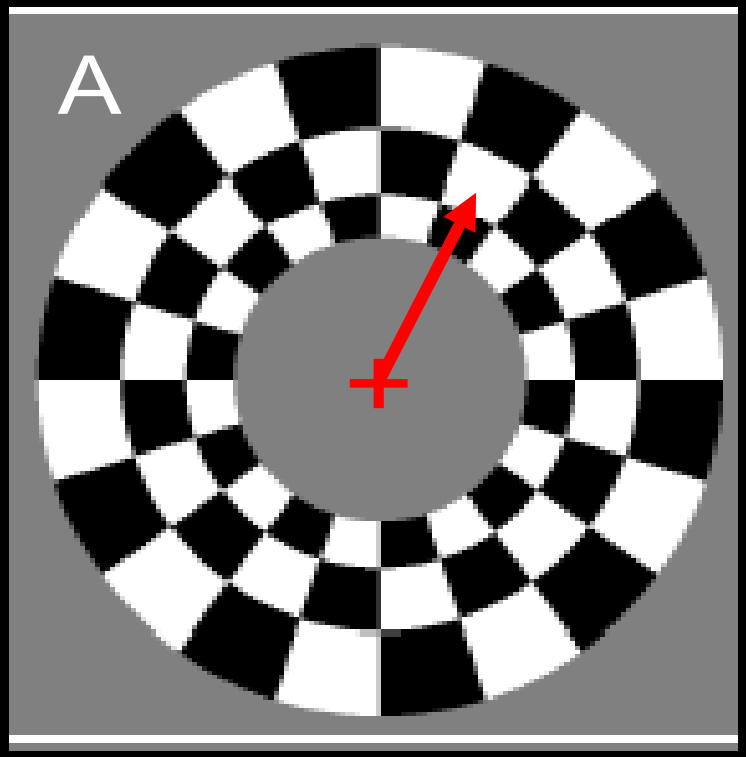
VML

HM

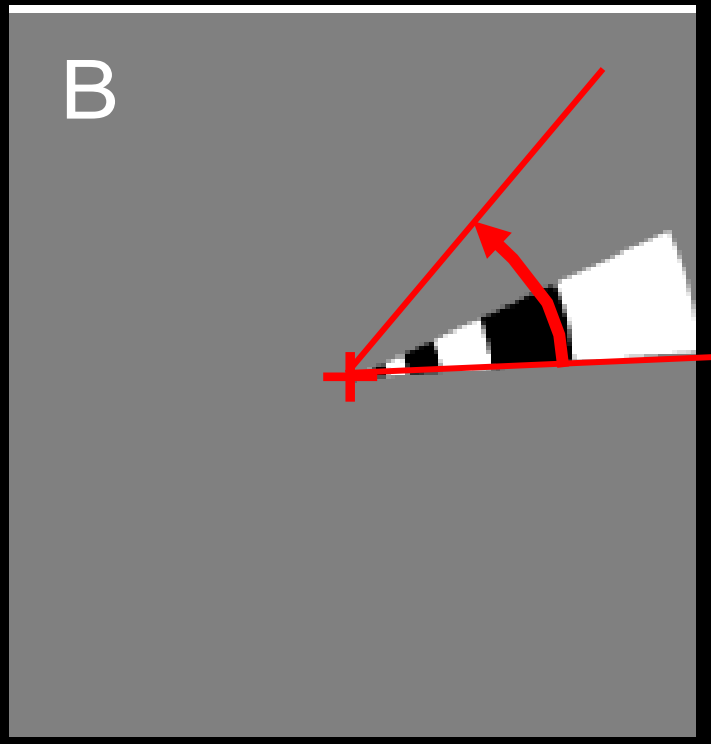
VMU



Retinotopic fMRI



Ring (Exp/Con)
(Eccentricity)

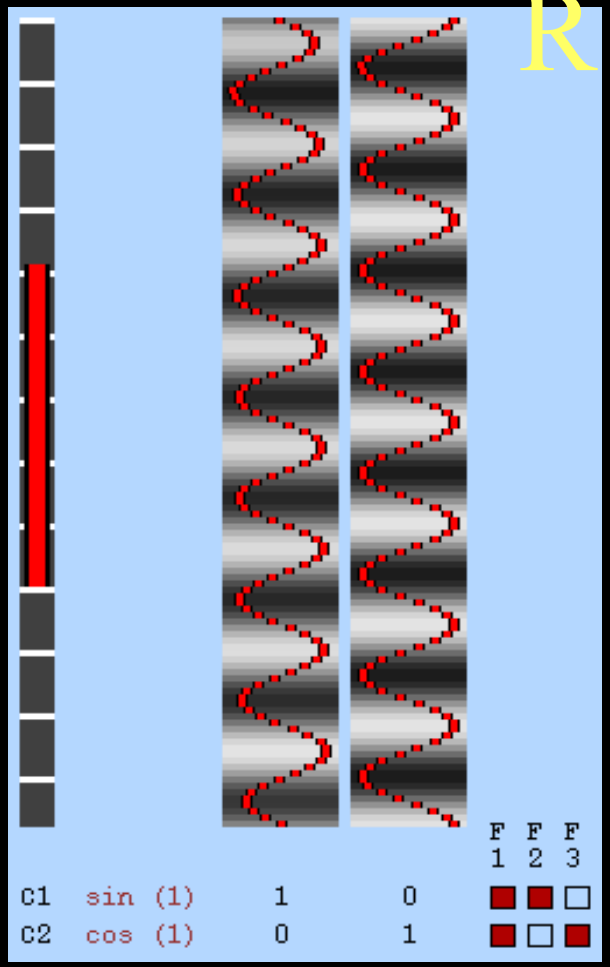


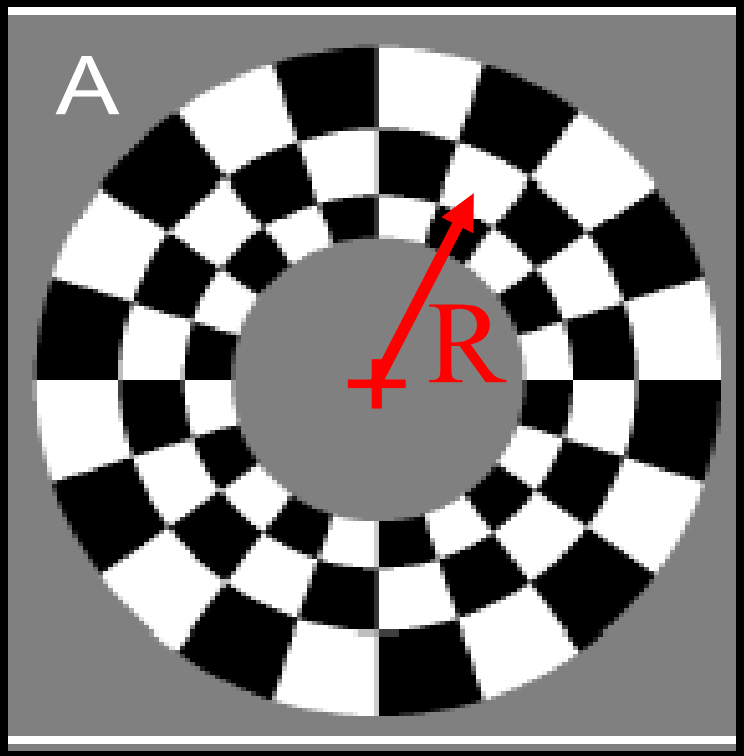
Wedge (Rot)
(Azimuth)

Retinotopic fMRI Analysis

β 1=Asin(β) 2=Acos(R) R= Eccentricity Radius

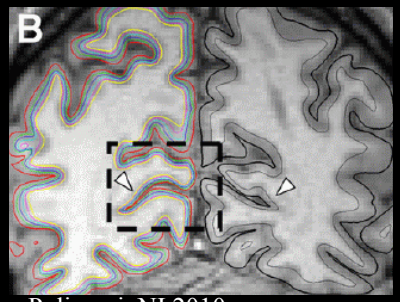
$$R = \tan^{-1}(\beta \quad 1/\beta$$



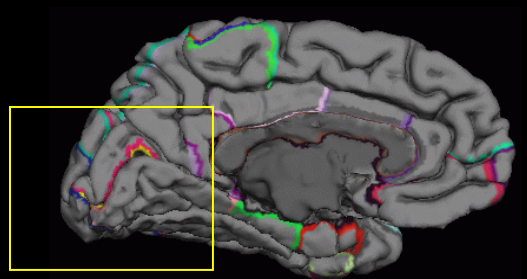


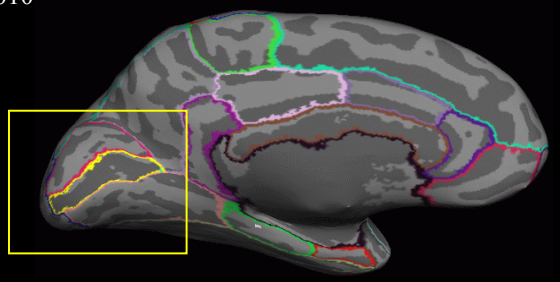
Eccentricity

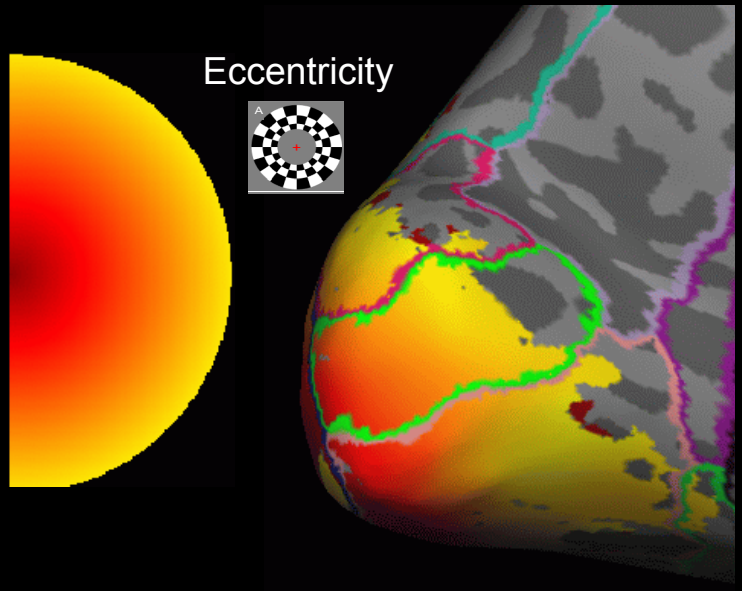
Retinotopy Results

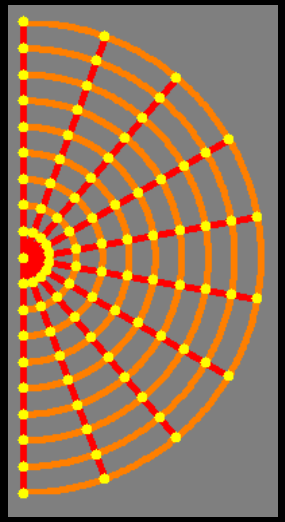


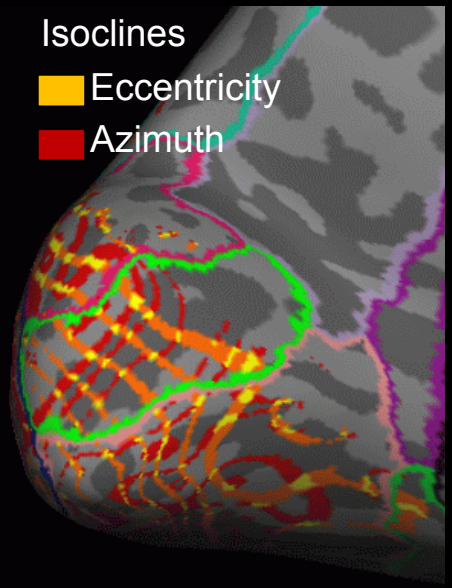
Polimeni, NI 2010

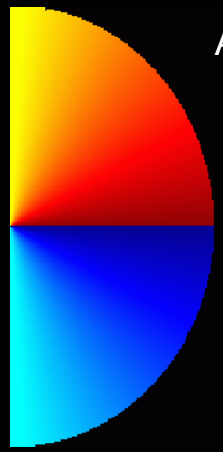


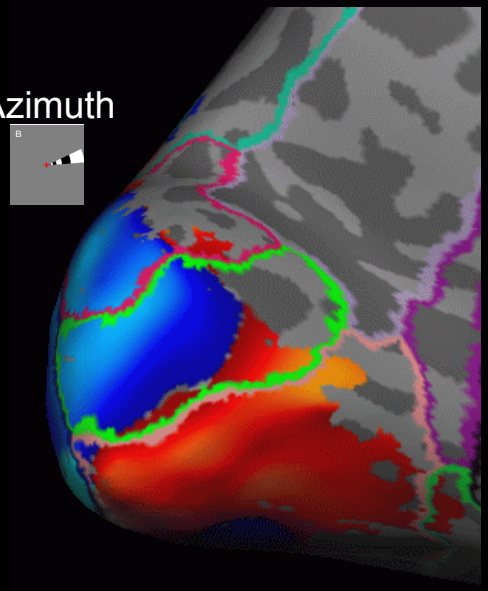










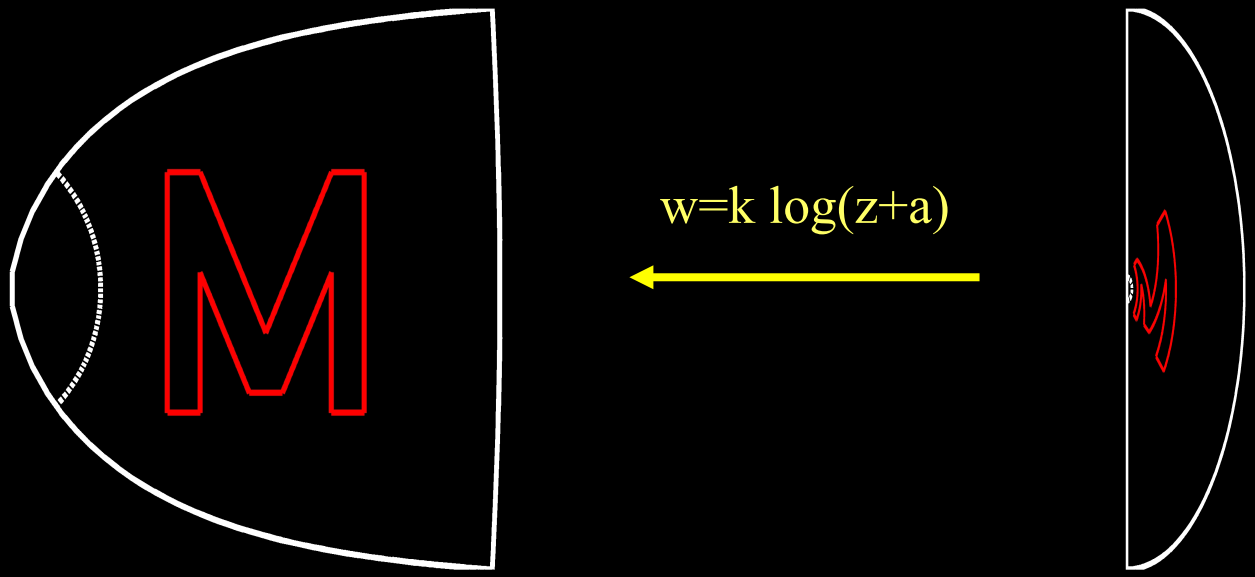


What Can One Do With A Surface Model?

goal: use model to imposed desired activity pattern on V1

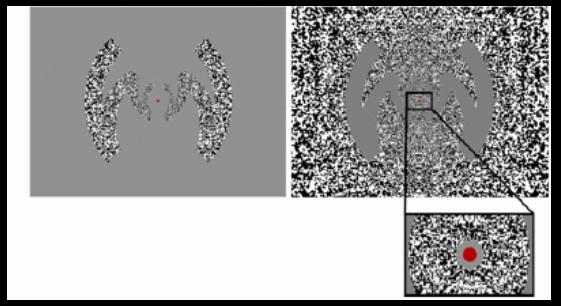
desired shape of activity pattern

required shape of stimulus



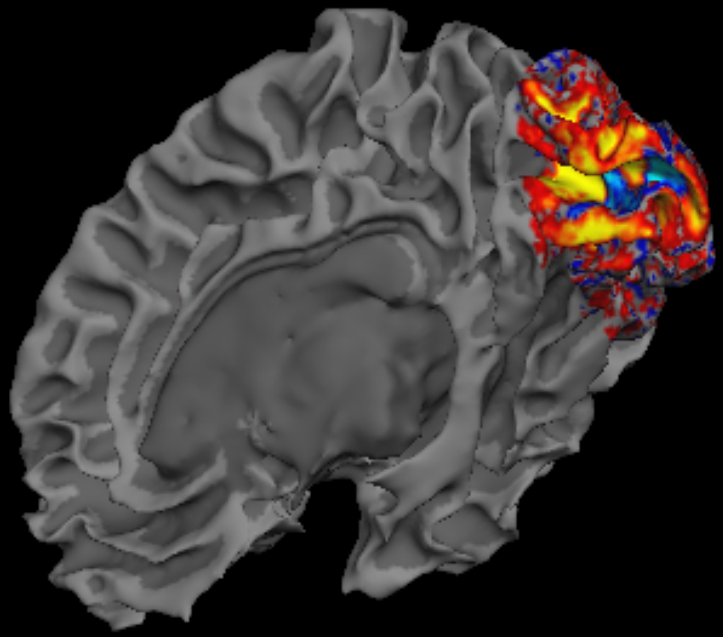
left primary visual cortex

right visual hemifield



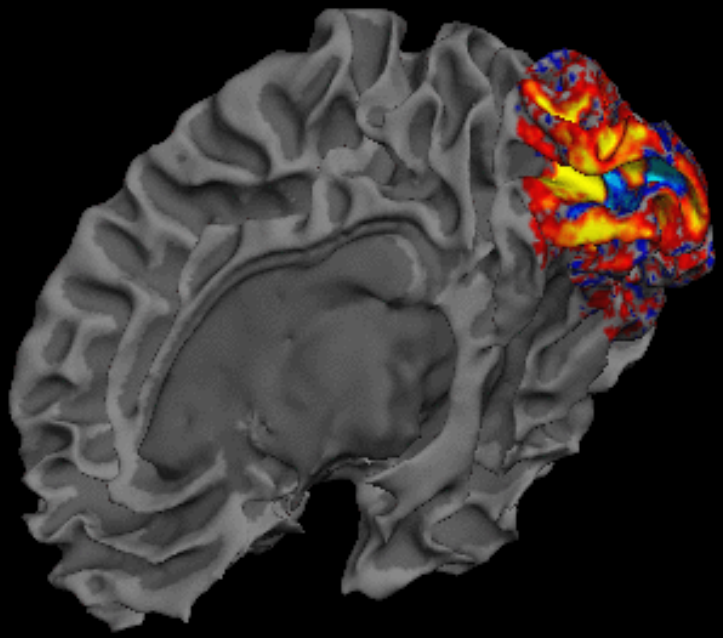
Collaboration with **Jon Polimeni** and Larry Wald.

Tangential Resolution Measured with Surface-based Analysis



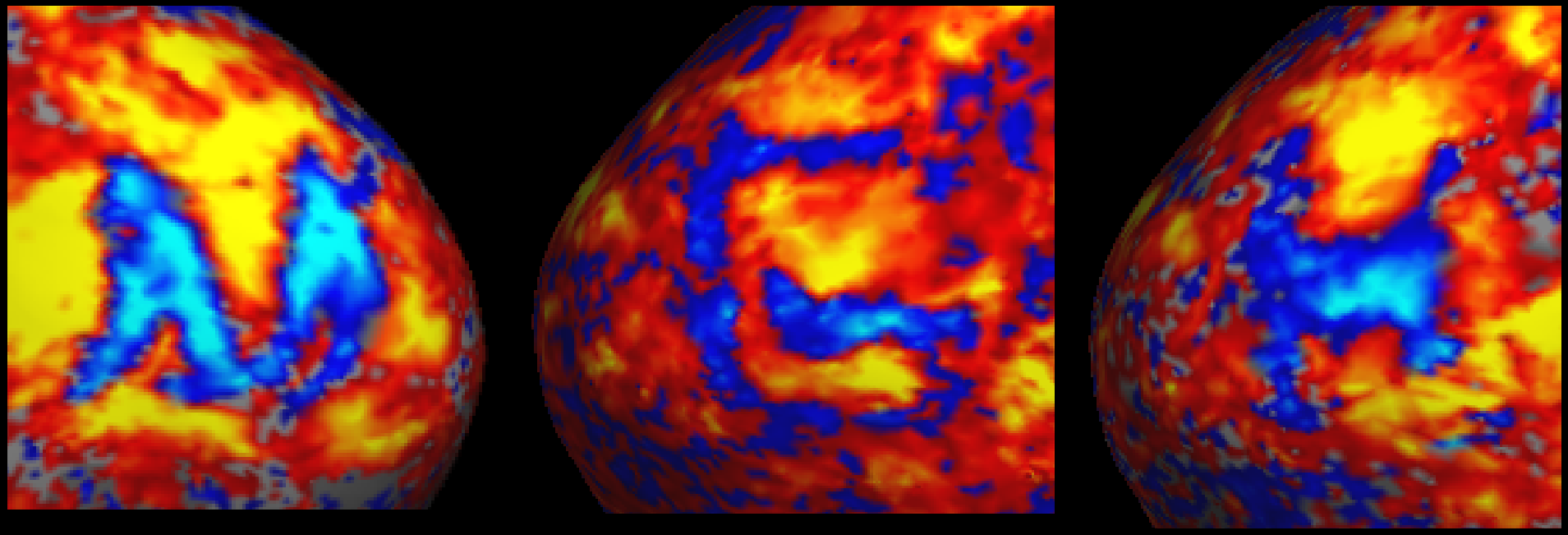
Collaboration with Jon Polimeni and Larry Wald. Polimeni, et al, 2010, NI.

Tangential Resolution Measured with Surface-based Analysis



Collaboration with Jon Polimeni and Larry Wald. Polimeni, et al, 2010, NI.

NeuroMarketing!



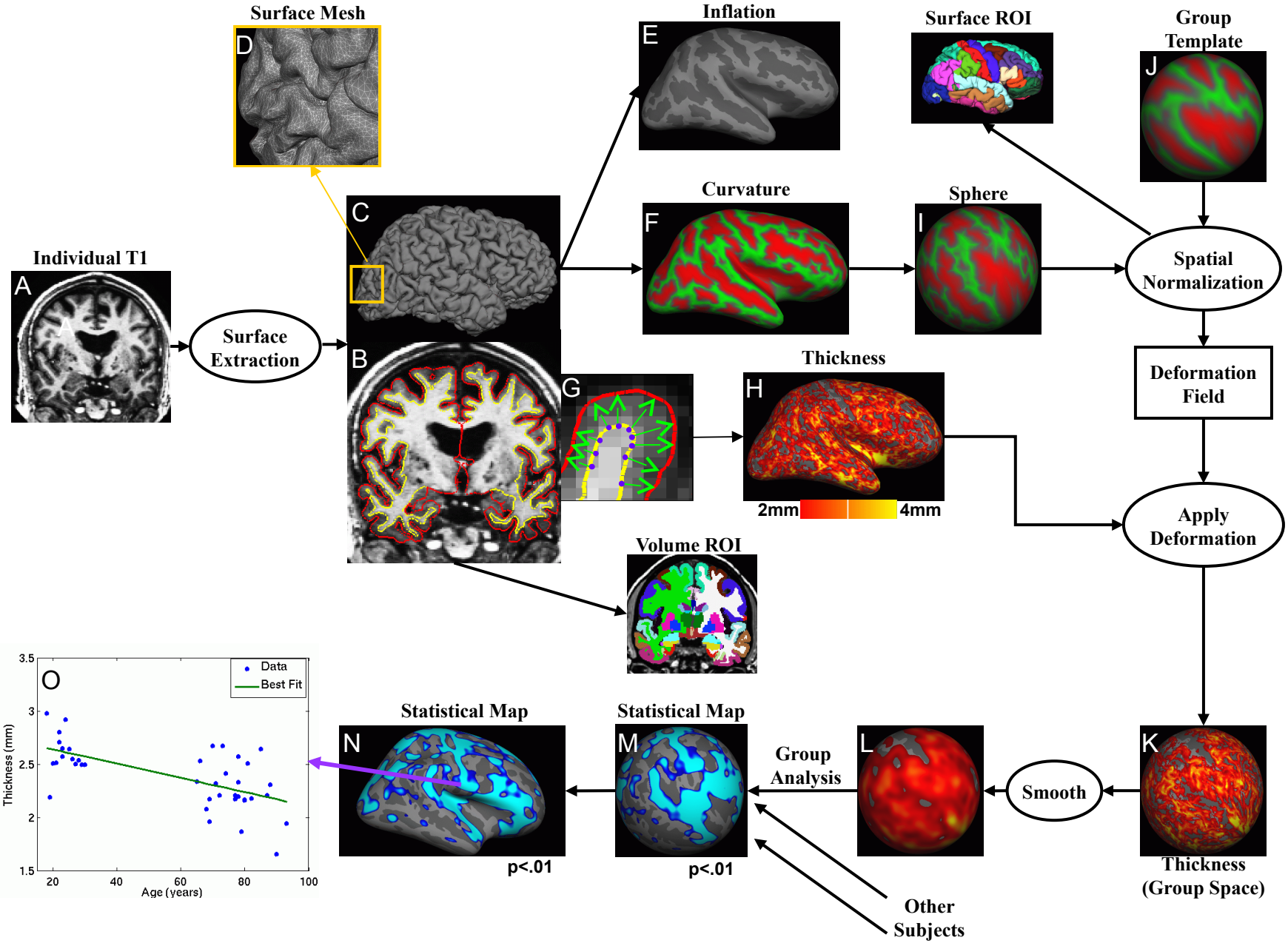
Aim 1 of our NCRR Center Grant, spelling:

"MGH Center for Functional Neuroimaging Technologies; and NCRR Center for Research Resources."

(just kidding)

Thanks to Larry Wald for this slide.

FreeSurfer Analysis Pipeline Overview



FreeSurfer Course May 2012

- Applications
- Individual Analysis
- Failure Modes
- Group Analysis
- FreeSurfer-FSL/FEAT Integration

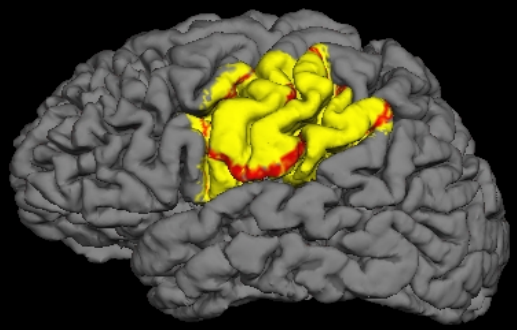
Not Covered:

- Longitudinal
- TRACULA
- Hippocampal Subfields
- Brodmann Area Labeling

What is FreeSurfer?

- Cortical extraction and labeling
- Subcortical segmentation
- Surface-based Inter-subject Registration
- (Nearly) Fully-automated
- Multi-modal integration

Use FreeSurfer



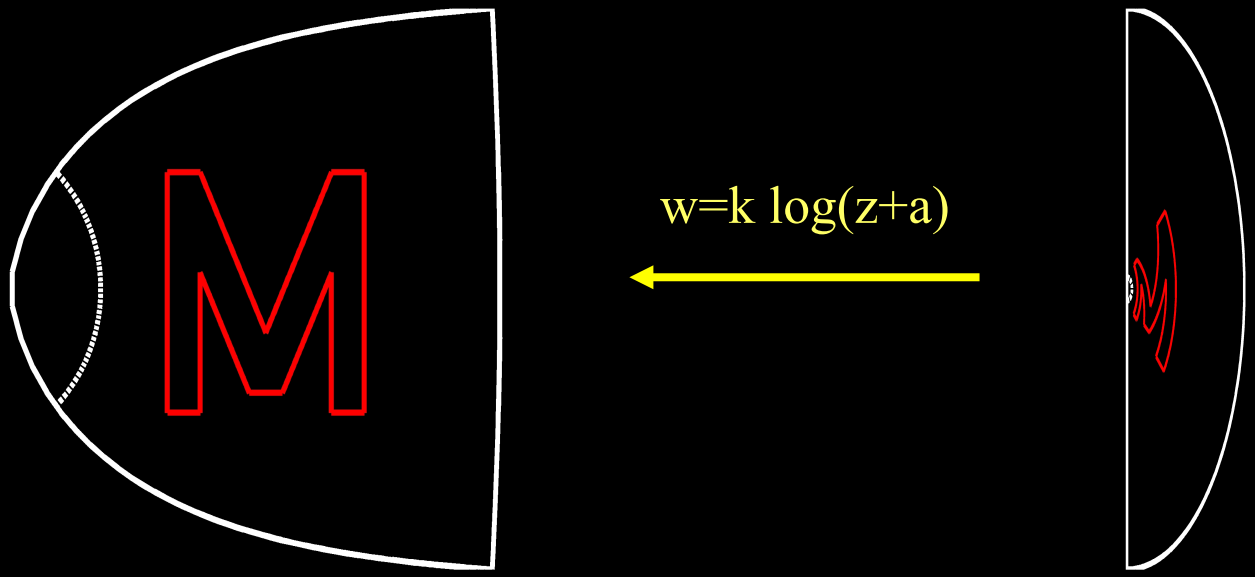
Be Happy

What Can One Do With A Surface Model?

goal: use model to imposed desired activity pattern on V1

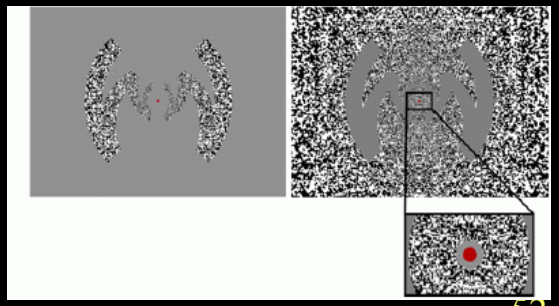
desired shape of activity pattern

required shape of stimulus



left primary visual cortex

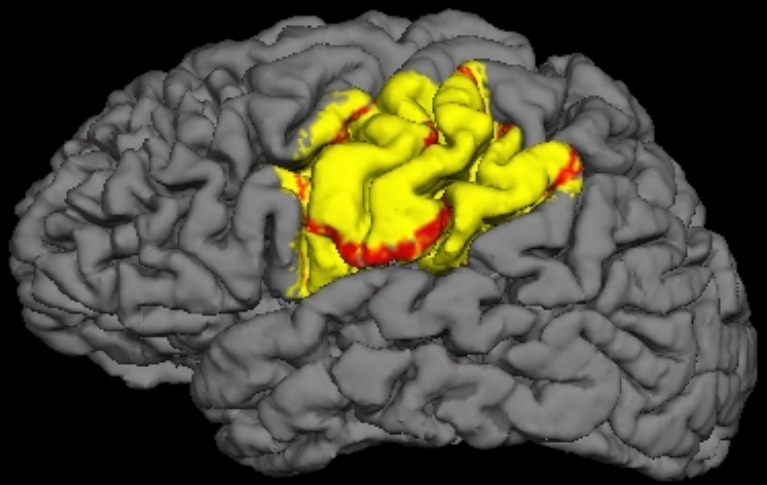
right visual hemifield



Collaboration with **Jon Polimeni** and Larry Wald.

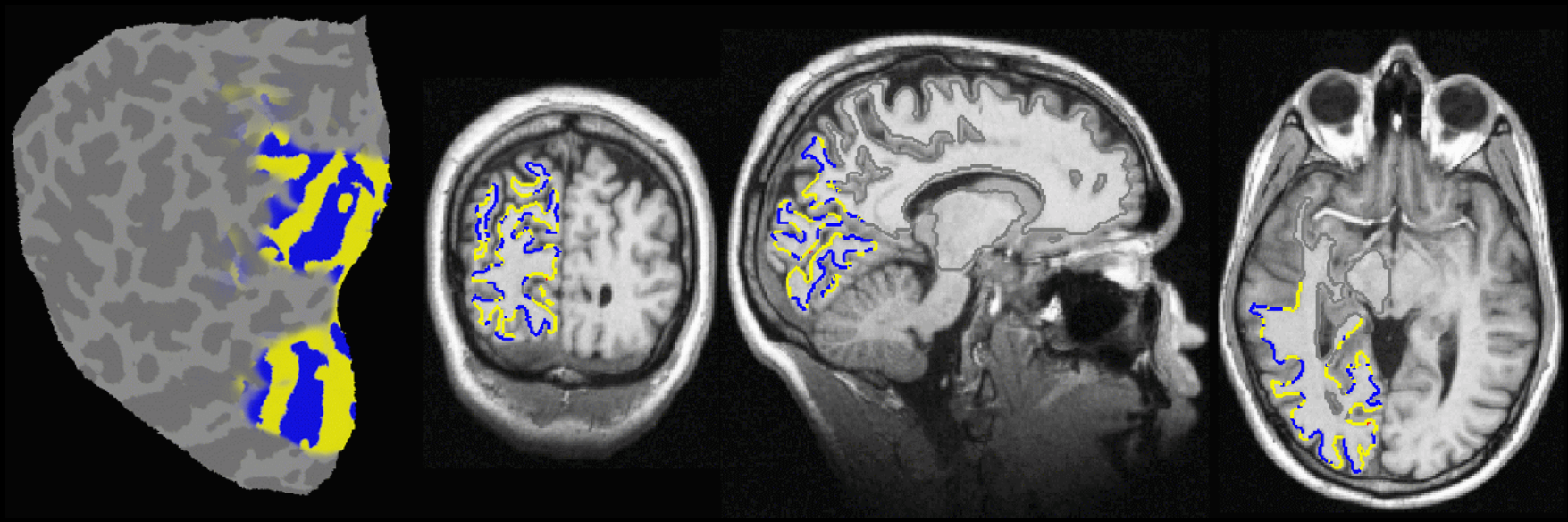
Thanks!

Use FreeSurfer



Be Happy

Retinotopy Field Sign Maps



- Changes in orientation between V1, V2, etc

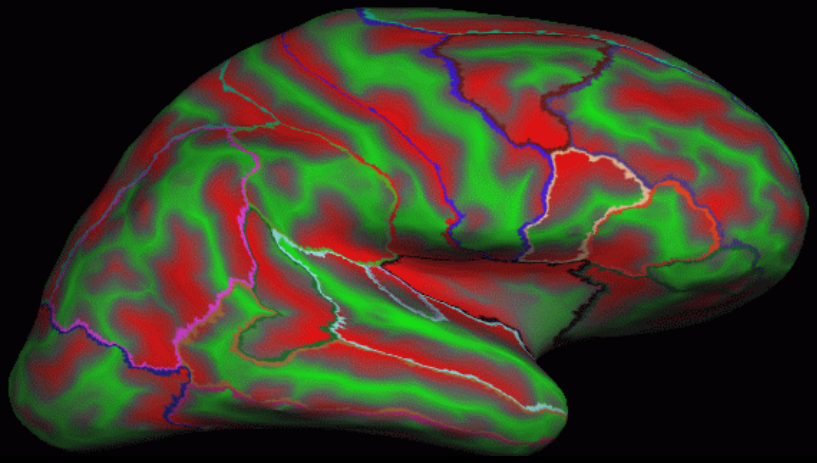
From (Sereno et al, 1995, Science).

Surface Review

- Cortex is a 2D sheet folded into 3D
- Function is organized along the sheet
- Visualization
- Better to smooth in 2D instead of 3D
- Register across subjects by aligning anatomy (folding patterns) in 2D
- Common surface space (like Talairach) for group studies

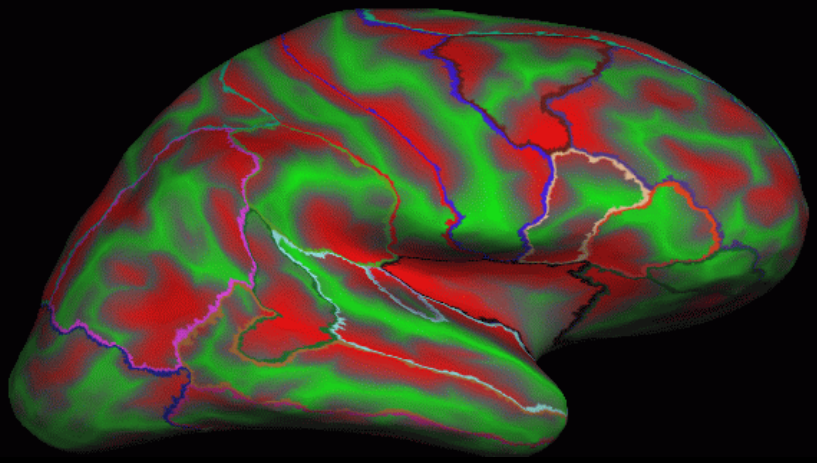
Surface Registration

Subject 1

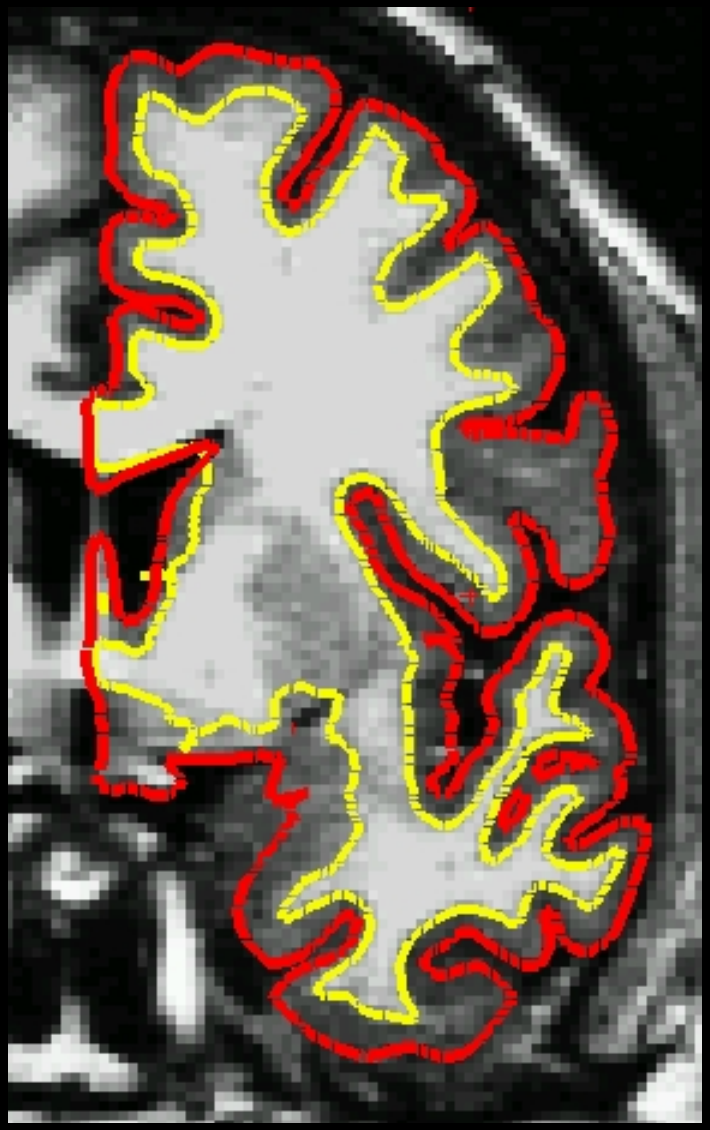


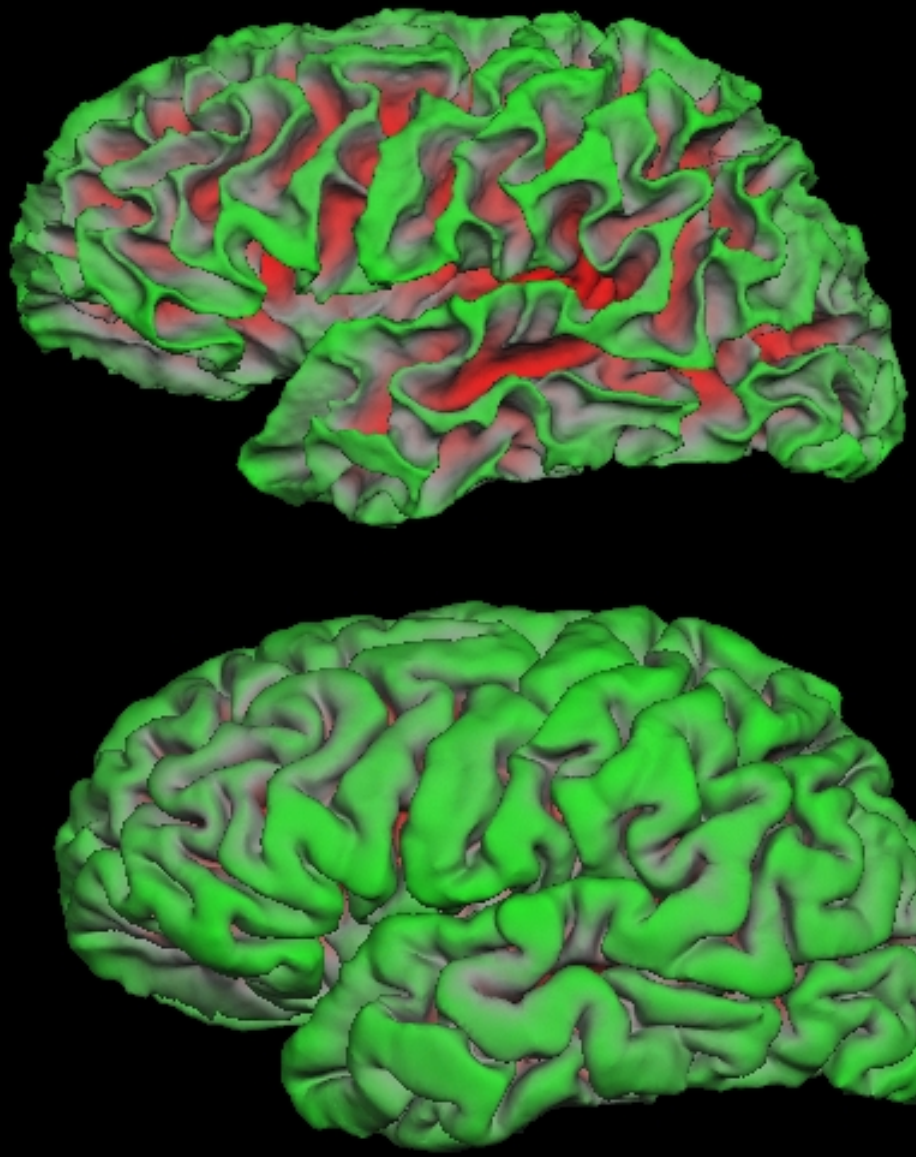
Subject 2 (Before)

Subject 2 (After)

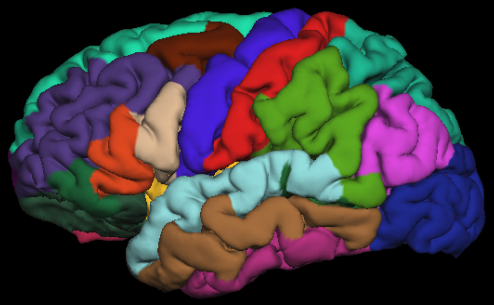


Surfaces: White and Pial

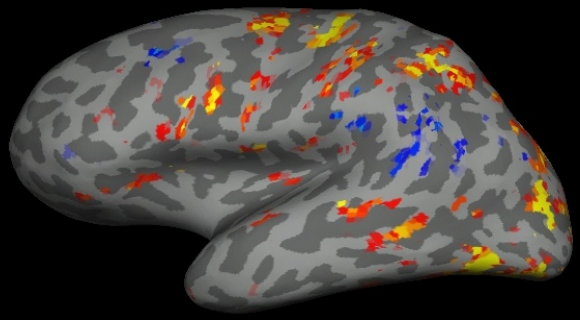




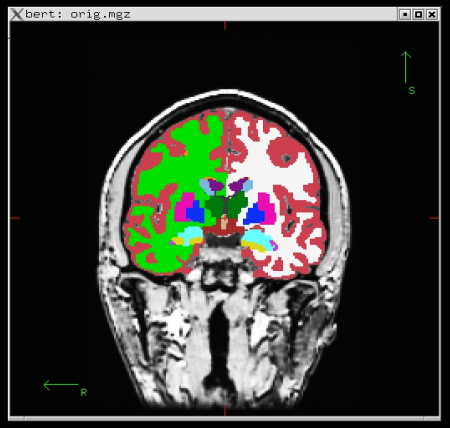
Surface and Volume Analysis



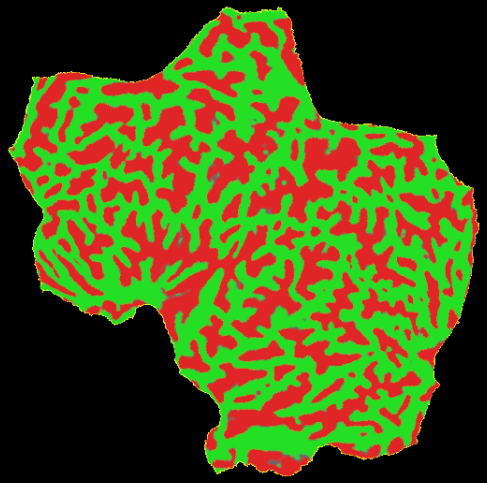
Cortical Reconstruction and Automatic Labeling



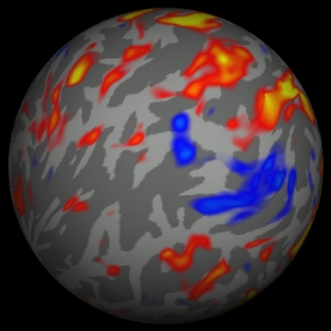
Inflation and Functional Mapping



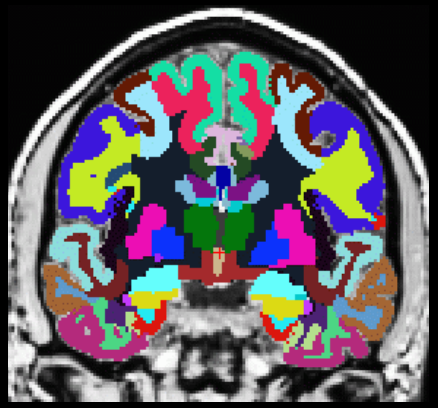
Automatic Subcortical Gray Matter Labeling



Surface Flattening

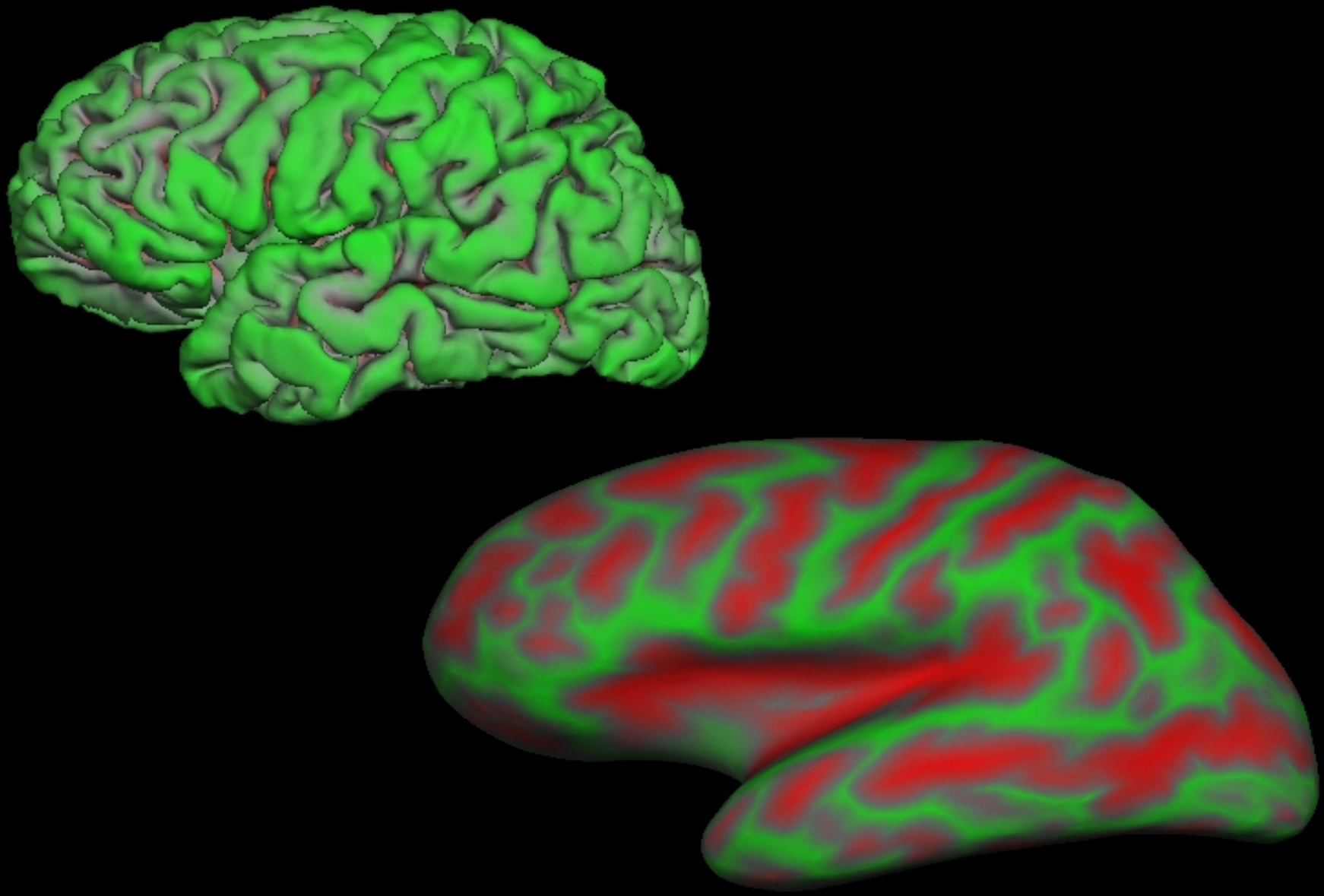


Surface-based Intersubject Alignment and Statistics

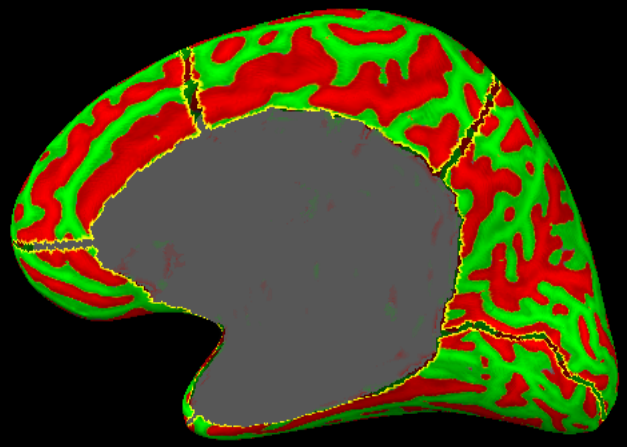


Automatic Gyral White Matter Labeling

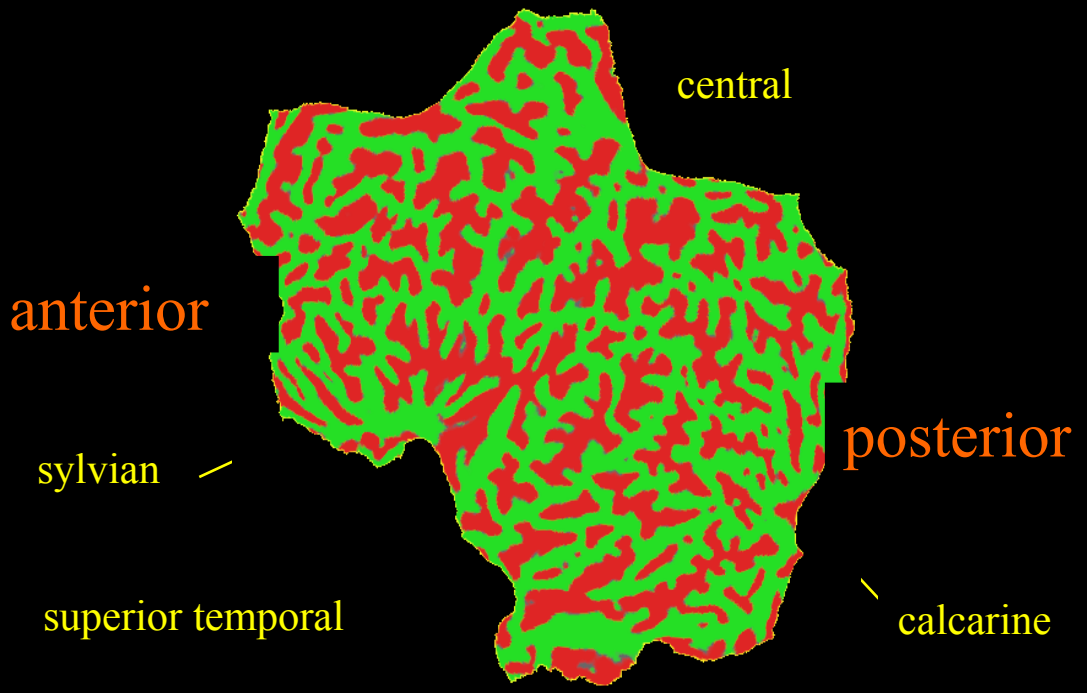
Inflation



Surface Flattening – Whole Hemisphere

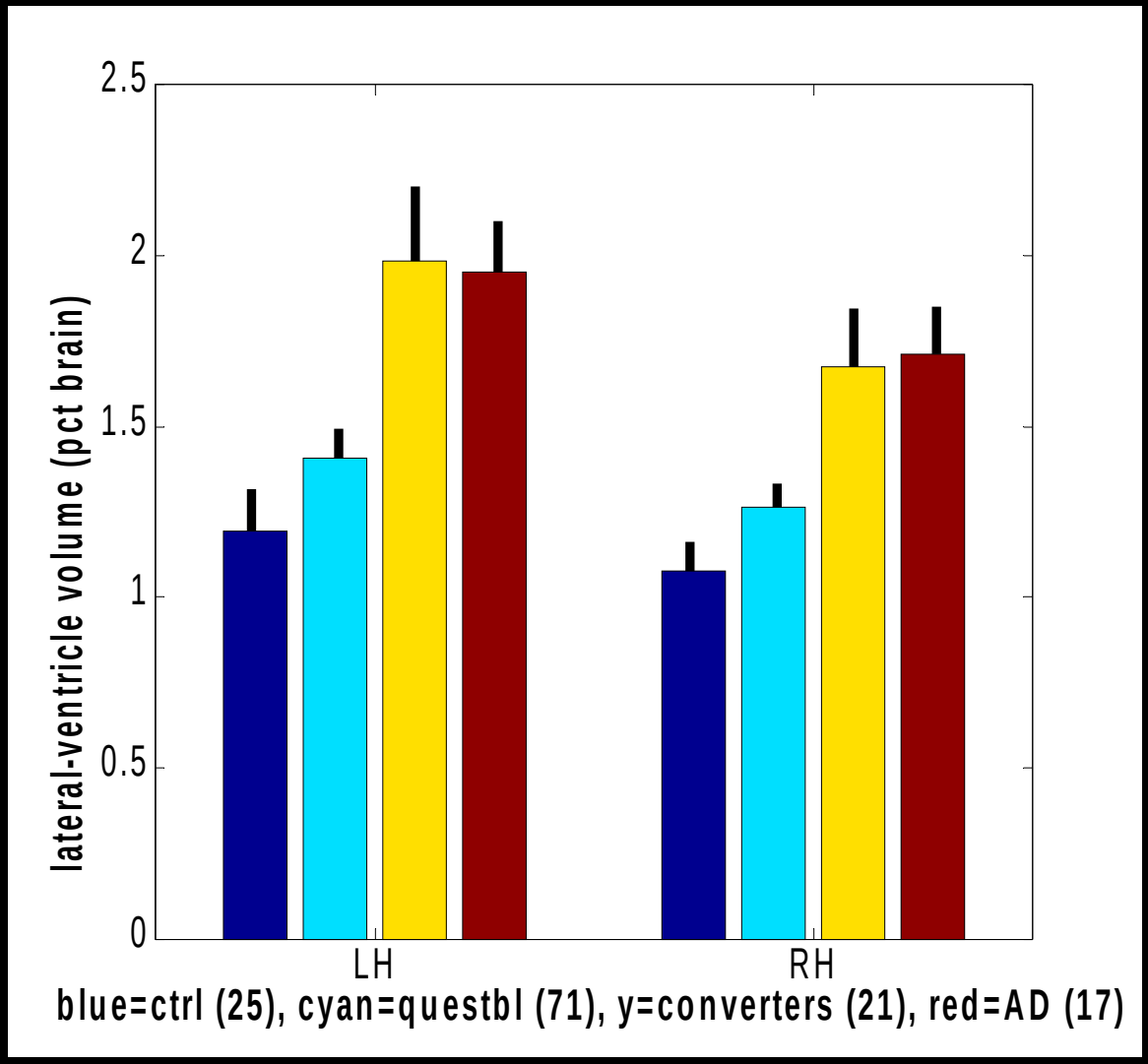


Inflated surface with cuts



Metrically optimal flat map

Volume Differences Predictive of AD



Data courtesy of Drs Marilyn Albert and Ron Killiany

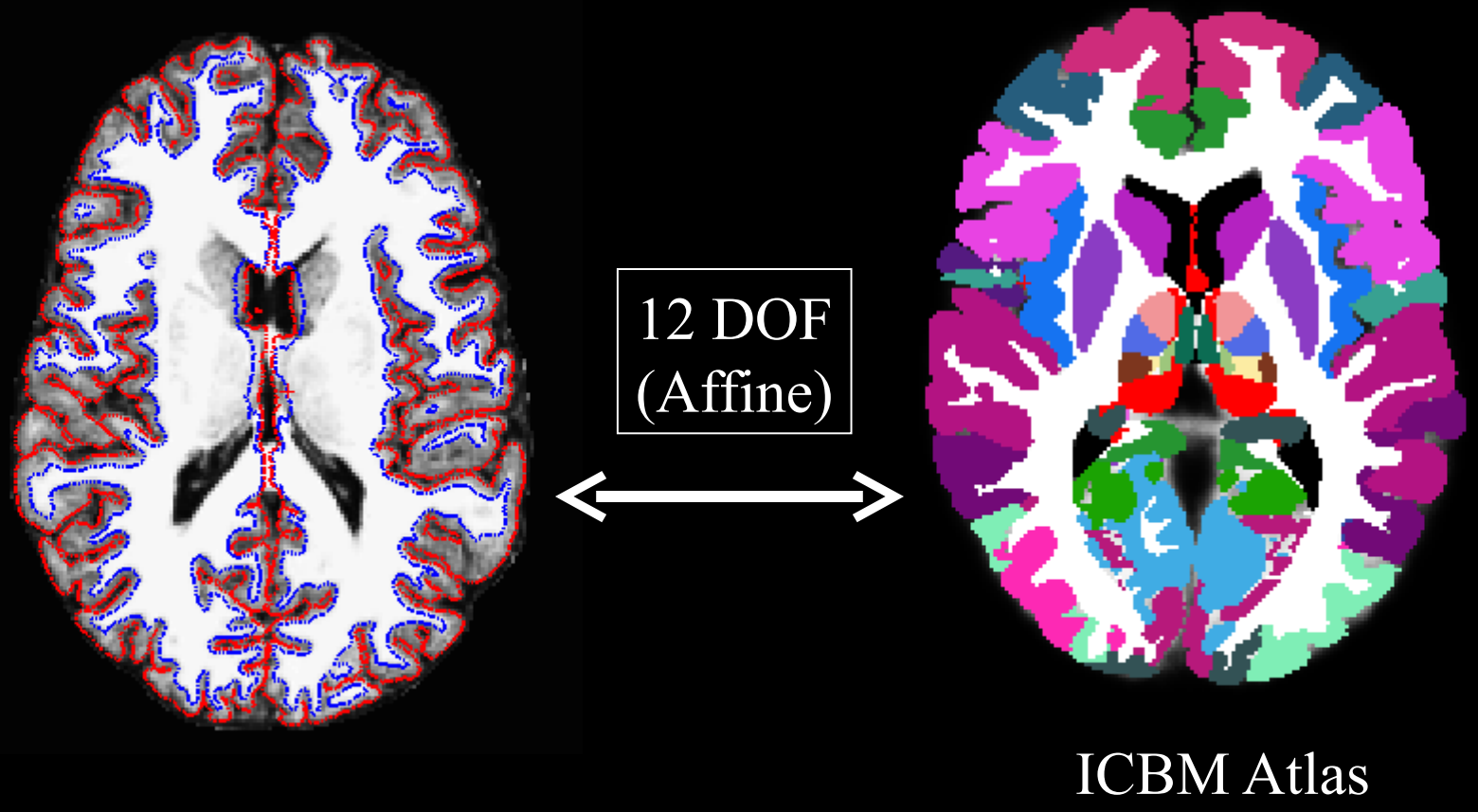
Why FreeSurfer?

1. Anatomical analysis is not like functional analysis – it is completely stereotyped.

2. Registration to a template (e.g. MNI/Talairach) doesn't account for individual anatomy.

3. Even if you don't care about the anatomy, anatomical models allow functional analysis not otherwise possible.

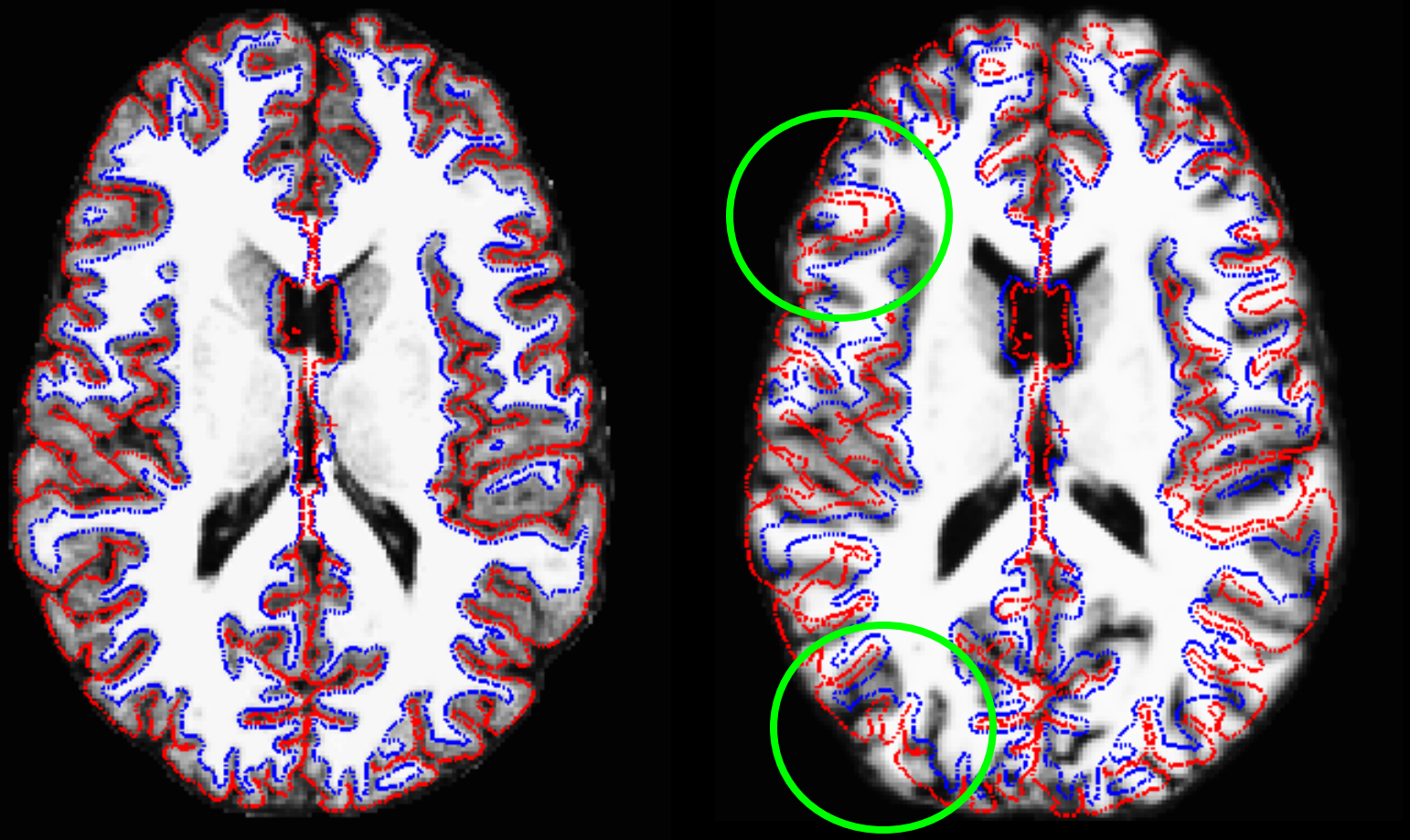
Why not just register to an ROI Atlas?



Problems with Affine (12 DOF) Registration

Subject 1

Subject 2 aligned with Subject 1
(Subject 1's Surface)



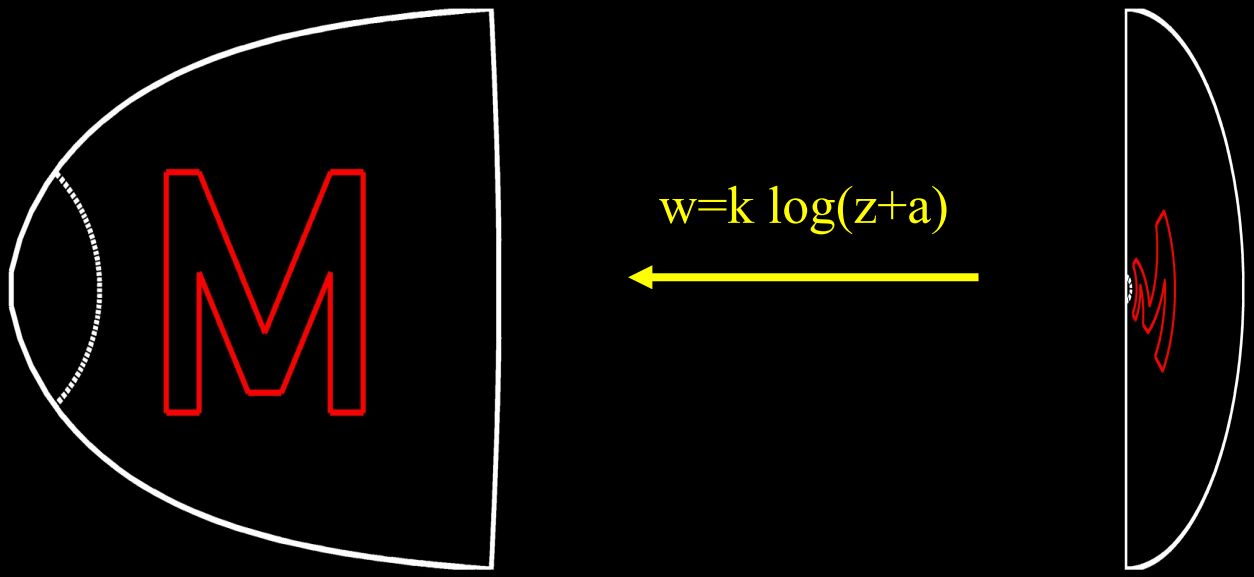
Talk Outline

1. Cortical (surface-based) Analysis.
2. Volume Analysis.
3. New Features in 5.1.

What Can One Do With A Surface Model?

goal: use model to imposed desired activity pattern on V1

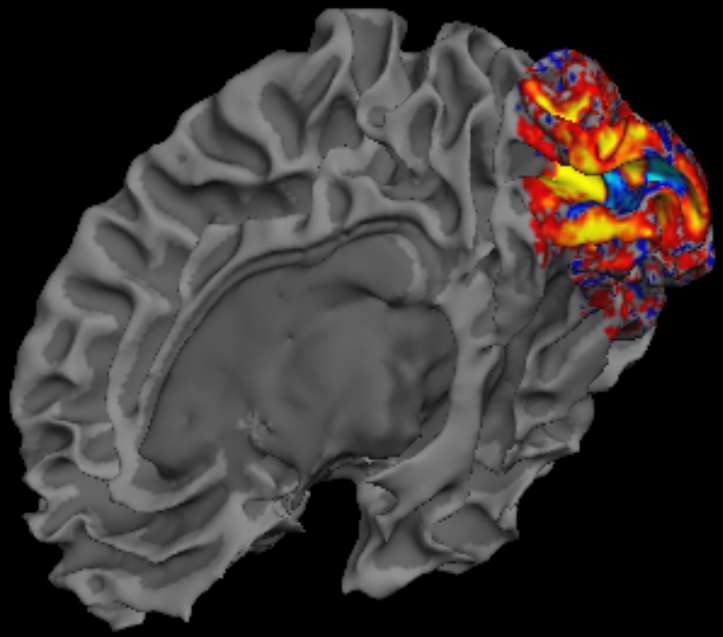
desired shape of activity pattern *required* shape of stimulus



left primary visual cortex right visual hemifield

Collaboration with **Jon Polimeni** and Larry Wald.

Tangential Resolution Measured with Surface-based Analysis



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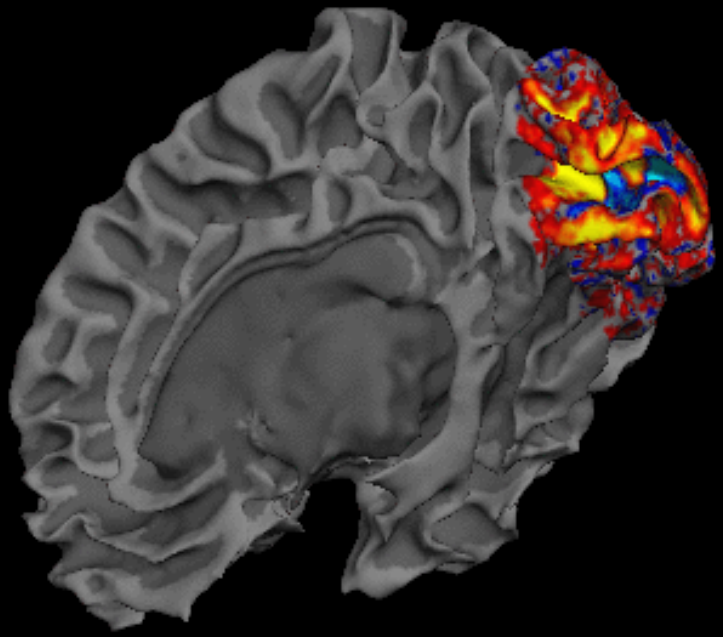
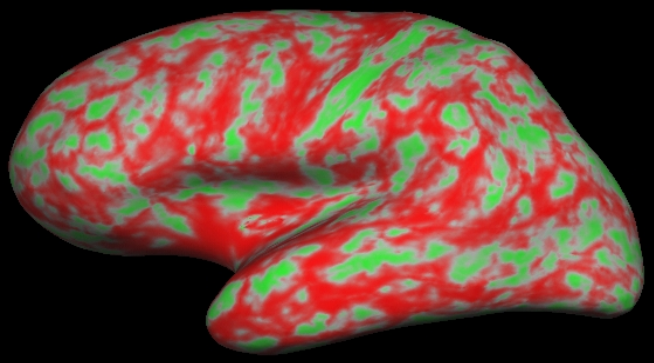
Tangential Resolution Measured with Surface-based Analysis



Collaboration with Jon Polimeni and Larry Wald.

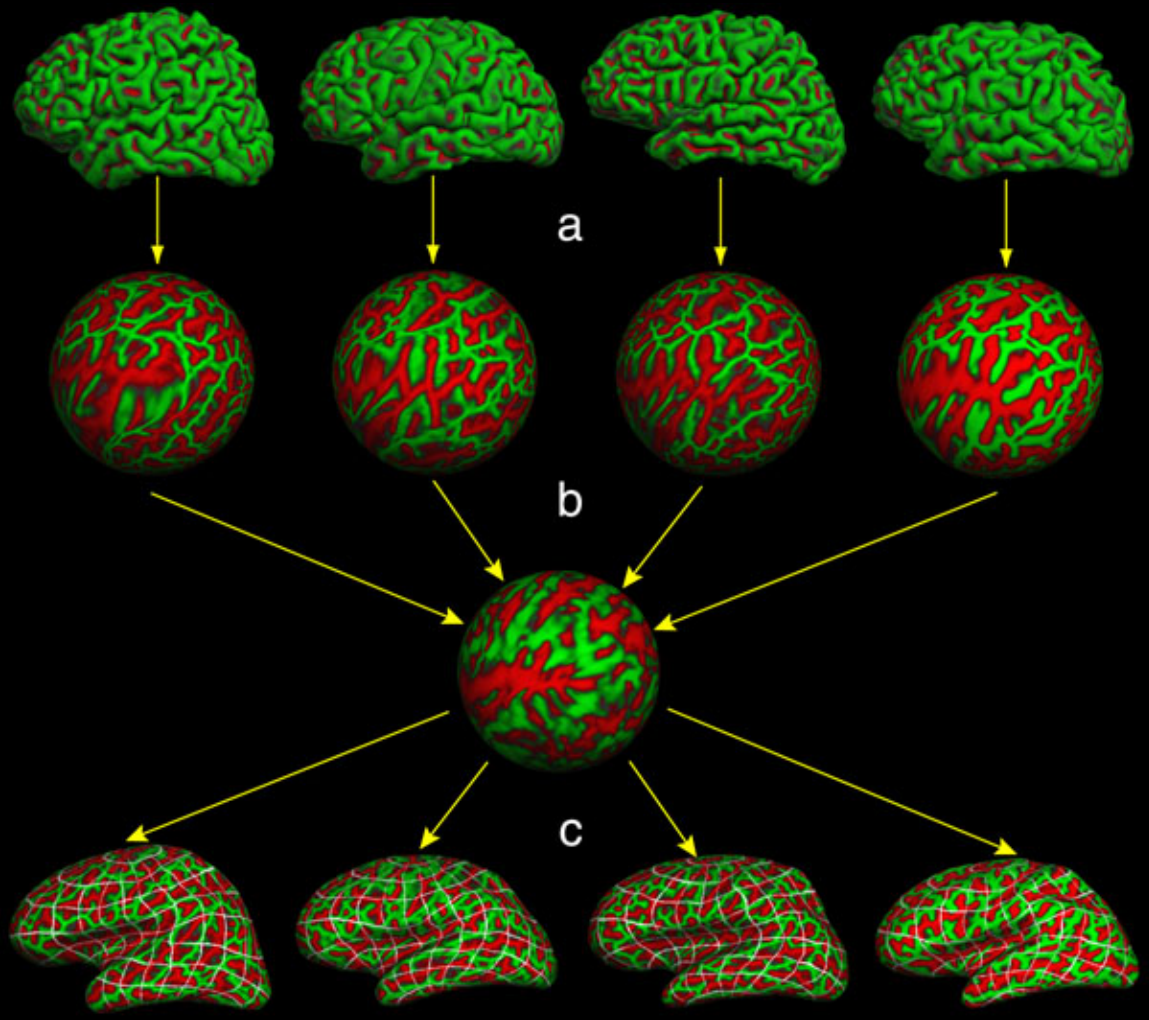
Cortical Thickness

- Distance between white and pial surfaces
- One value per vertex

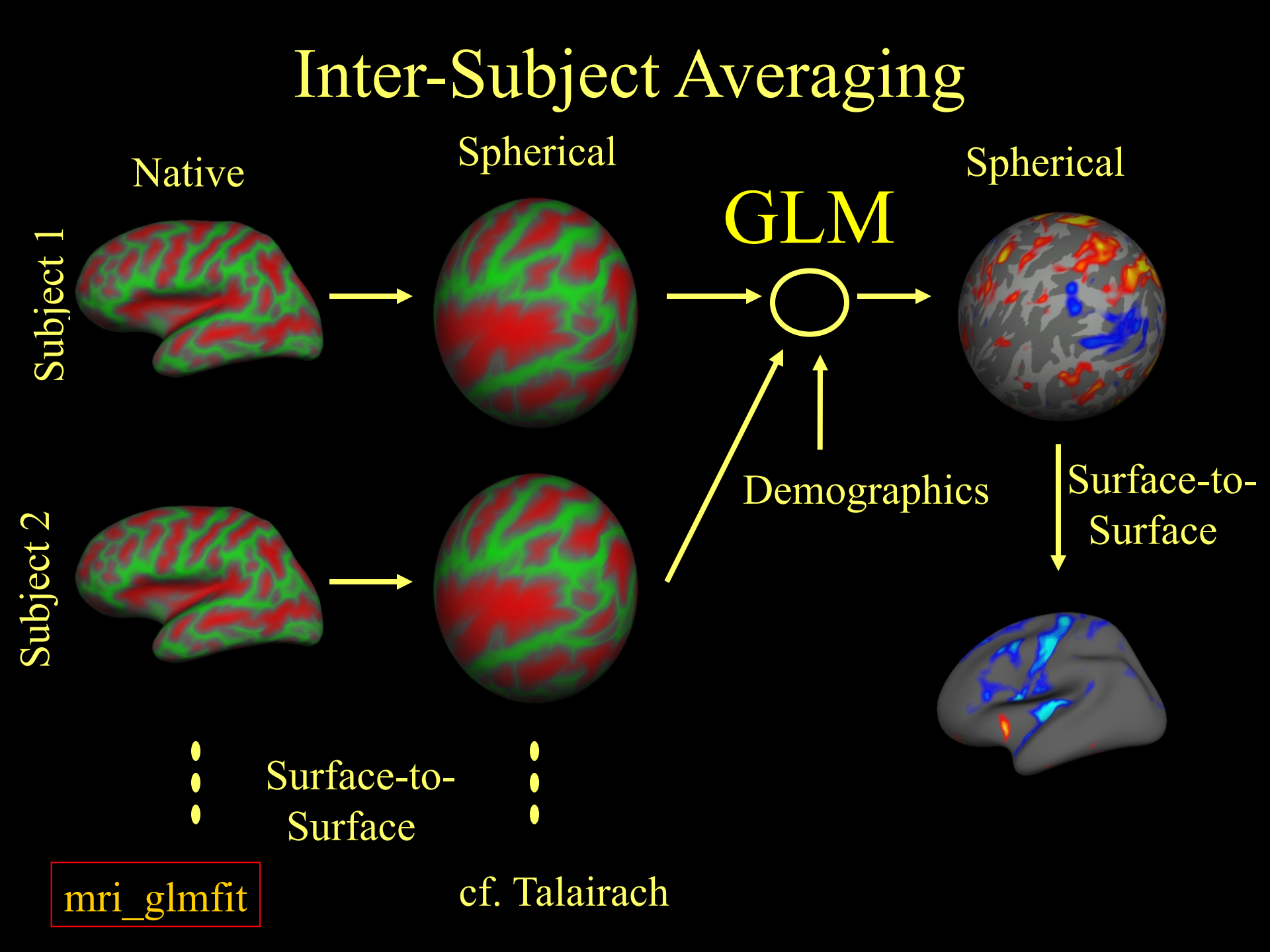


lh.thickness, rh.thickness

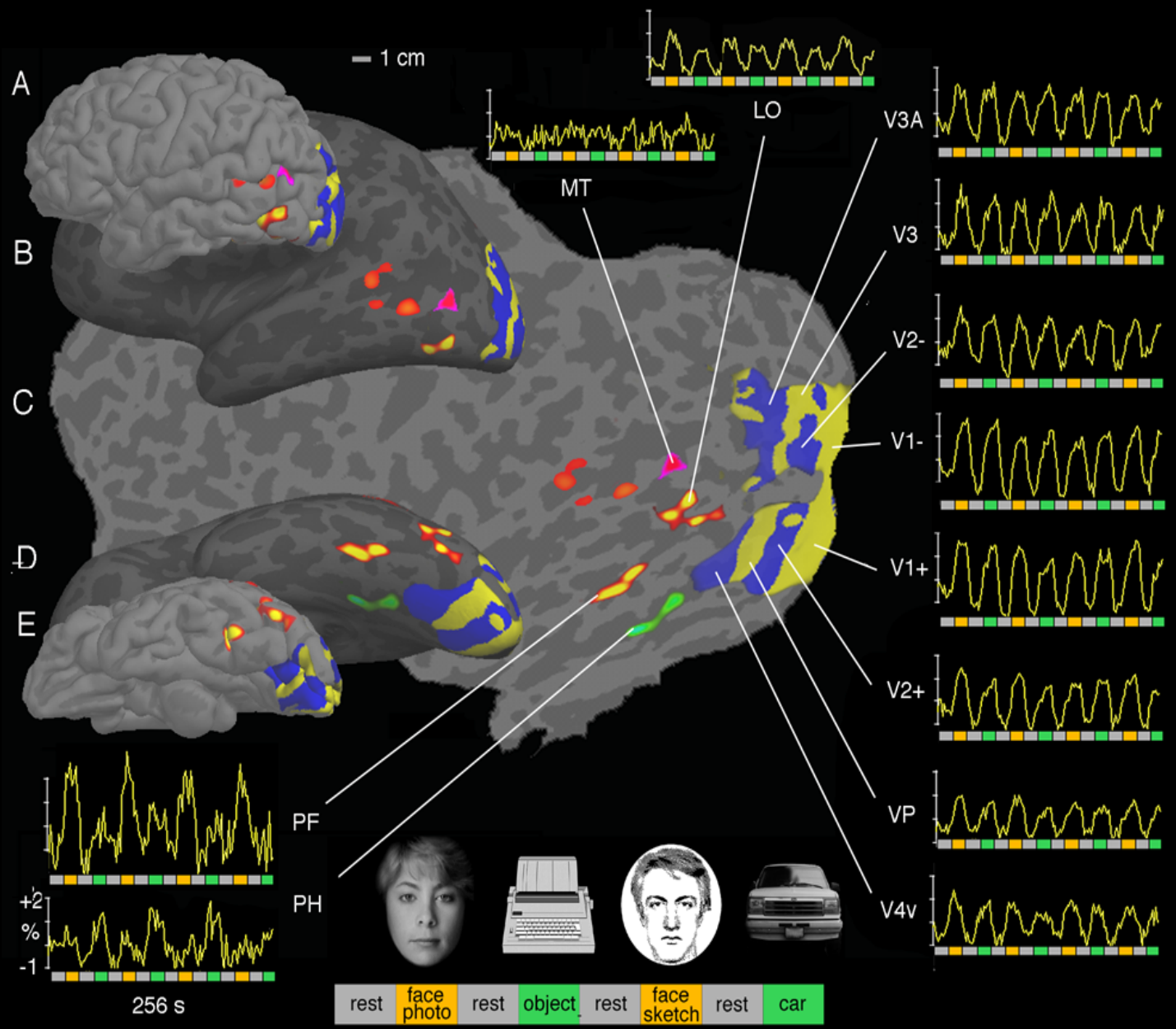
A Surface-Based Coordinate System



Inter-Subject Averaging

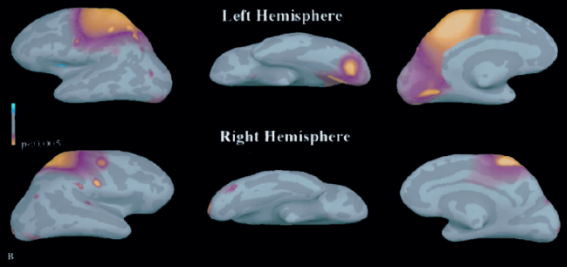


Visualization



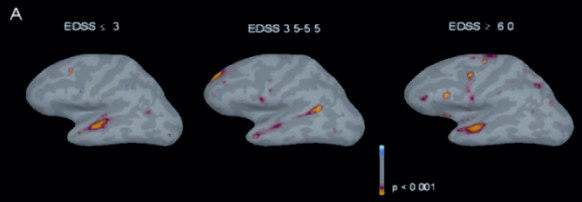
Borrowed from (Halgren et al., 1999)

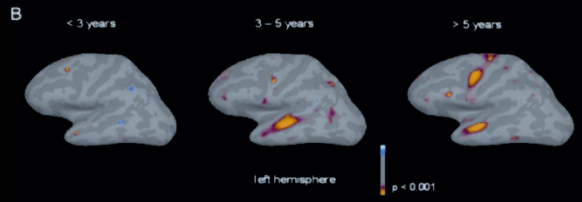
Huntington's Disease



Rosas et al., 2002

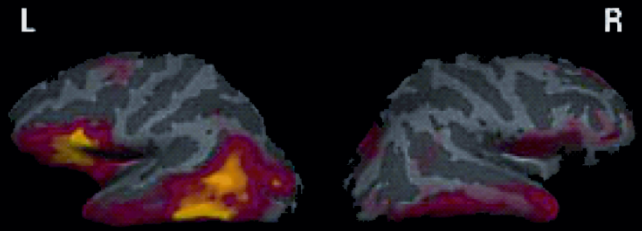
Multiple Sclerosis



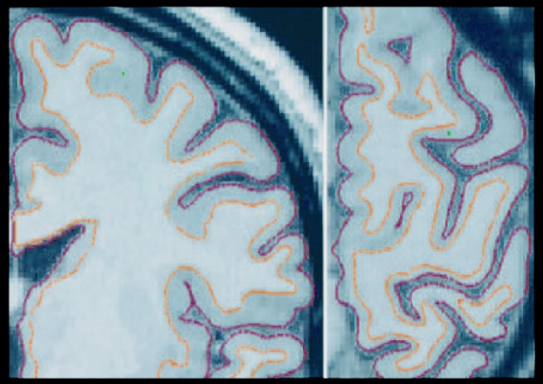


Sailer et al., 2003

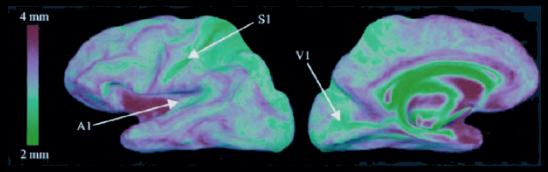
Schizophrenia



Kuperberg et al., 2003

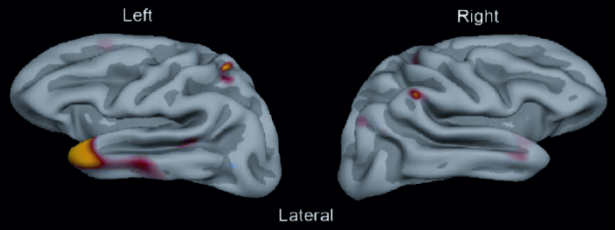


Normal Variation



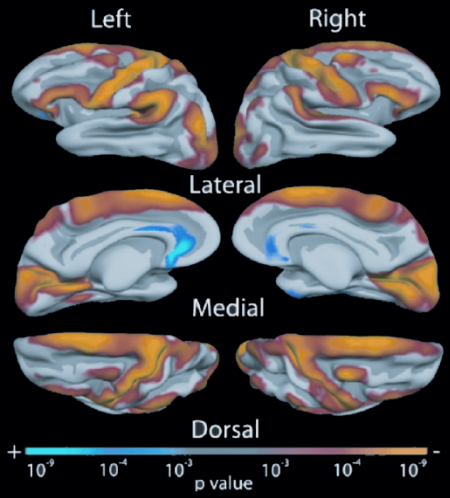
Fischl et al., 2000

Semantic Dementia



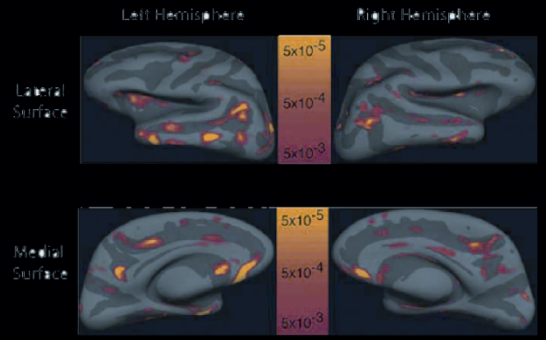
Gold et al., 2005

Aging



Salat et al., 2004

Animal Phobia



Rauch et al., 2004

Talk Outline

1. Cortical (surface-based) Analysis.
2. Volume Analysis.
3. New Features in 5.1.

Volume Analysis: Automatic Individualized Segmentation

Surface-based coordinate system/registration appropriate for cortex but not for thalamus, ventricular system, basal ganglia, etc…

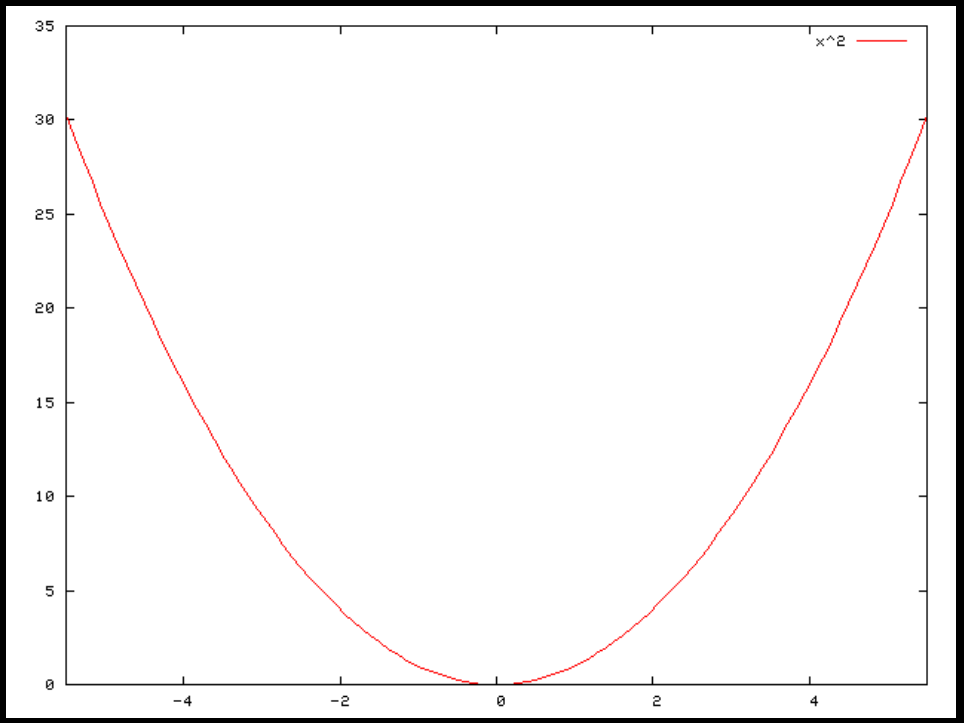
Anatomy is extremely variable – measuring the variance and accounting for it is critical (more in the individual subject talk)!

FreeSurfer Version 5.1: New Features

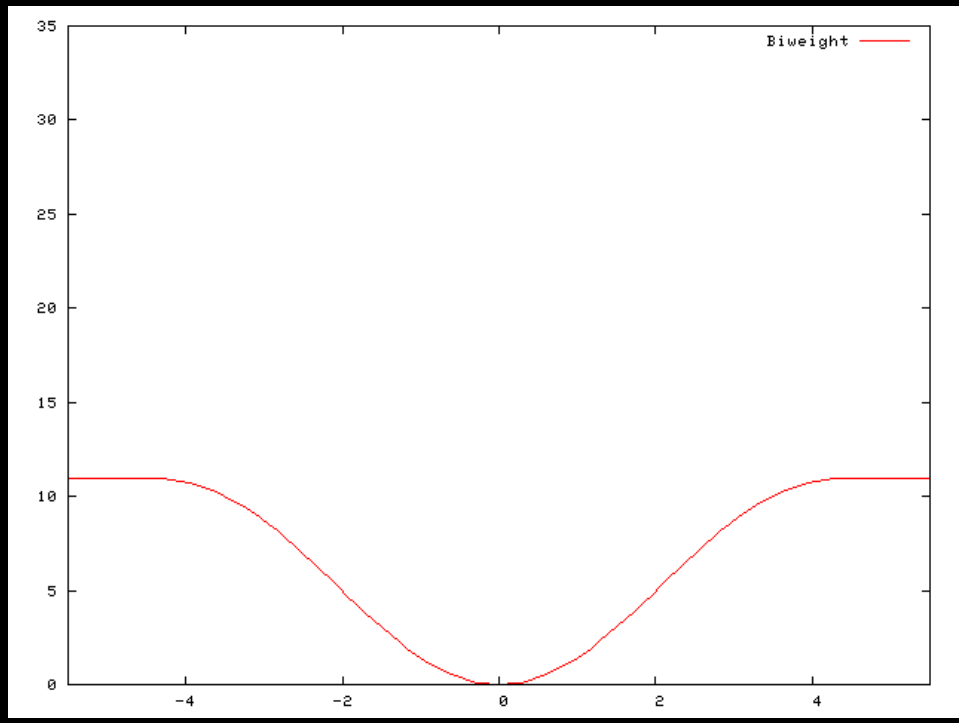
1. Longitudinal Analysis (Martin Reuter).
2. Automated tractography with Tracula (Anastasia Yendiki).
3. Automated Hippocampal Subfield segmentation (Koen van Leemput).
4. New Architectonic Areas (entorhinal cortex, Jean Augustinack).
5. Open Source! (modified BSD/MIT license)

Unbiased Robust Registration*

- The contribution of error is limited for outliers:



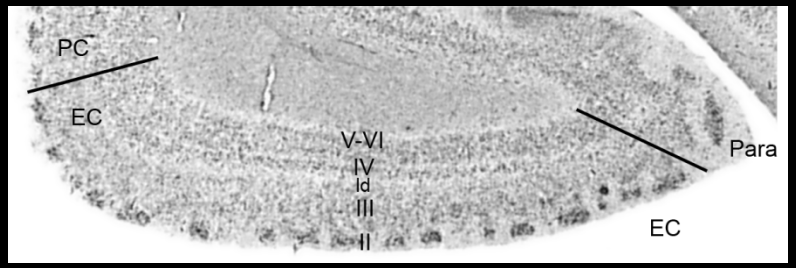
Squared Error

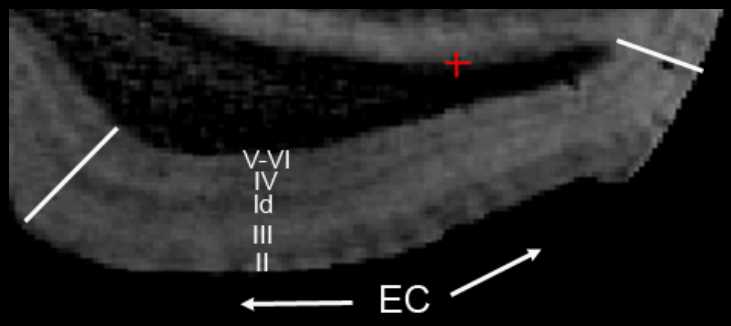


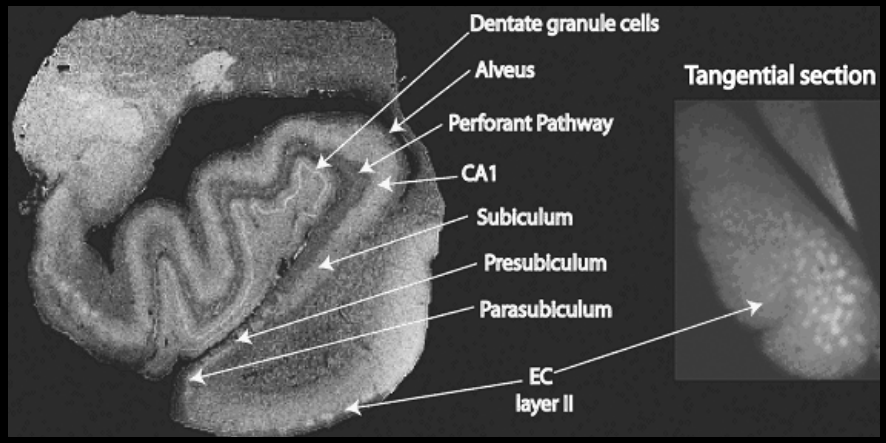
Tukey's Biweight

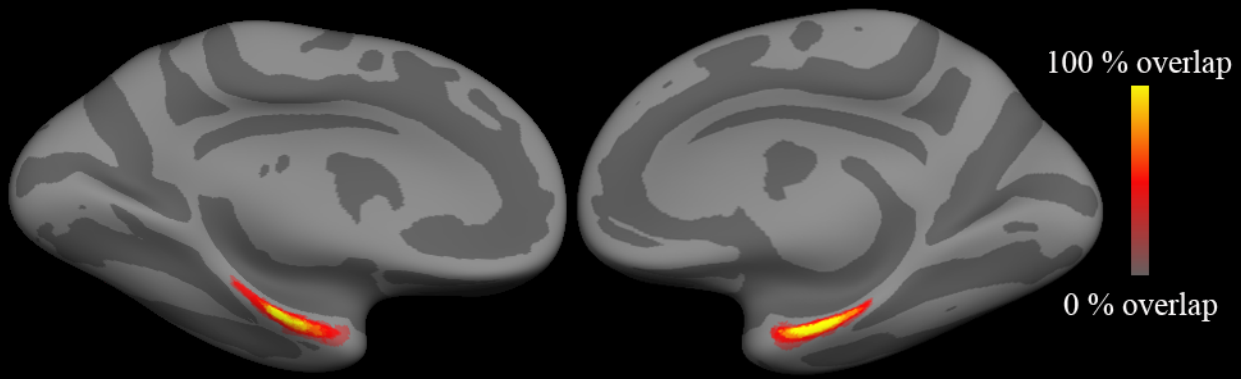
*Reuter, Rosas and Fischl, 2010, NeuroImage

New Areas: Entorhinal Cortex



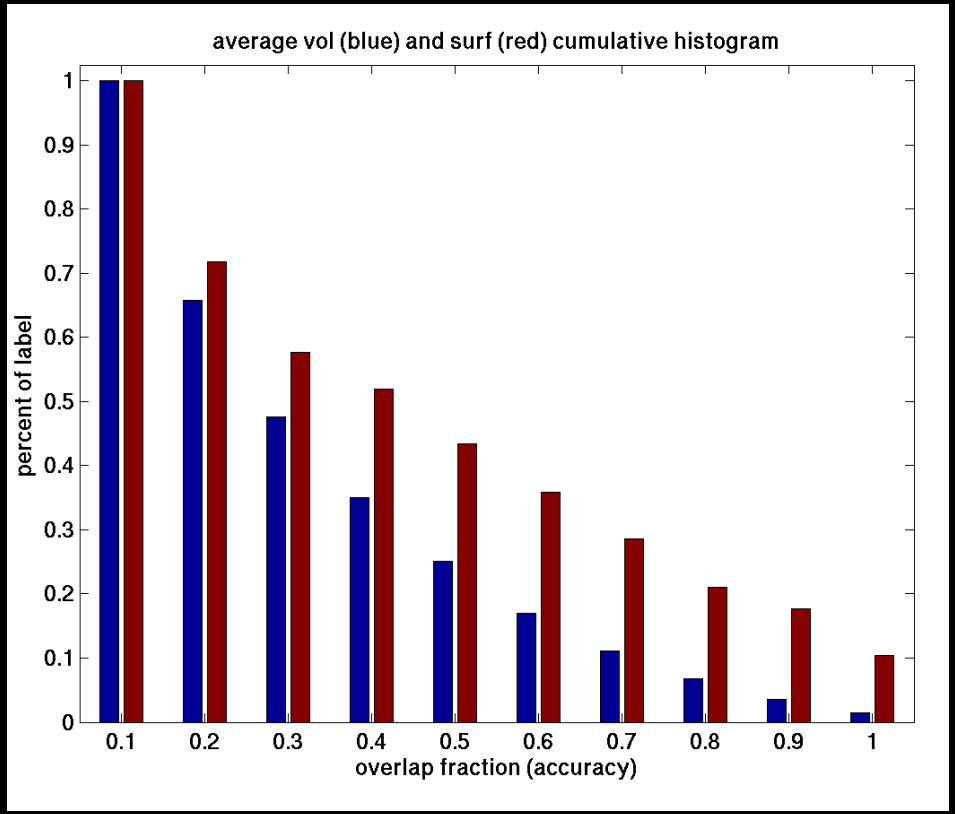




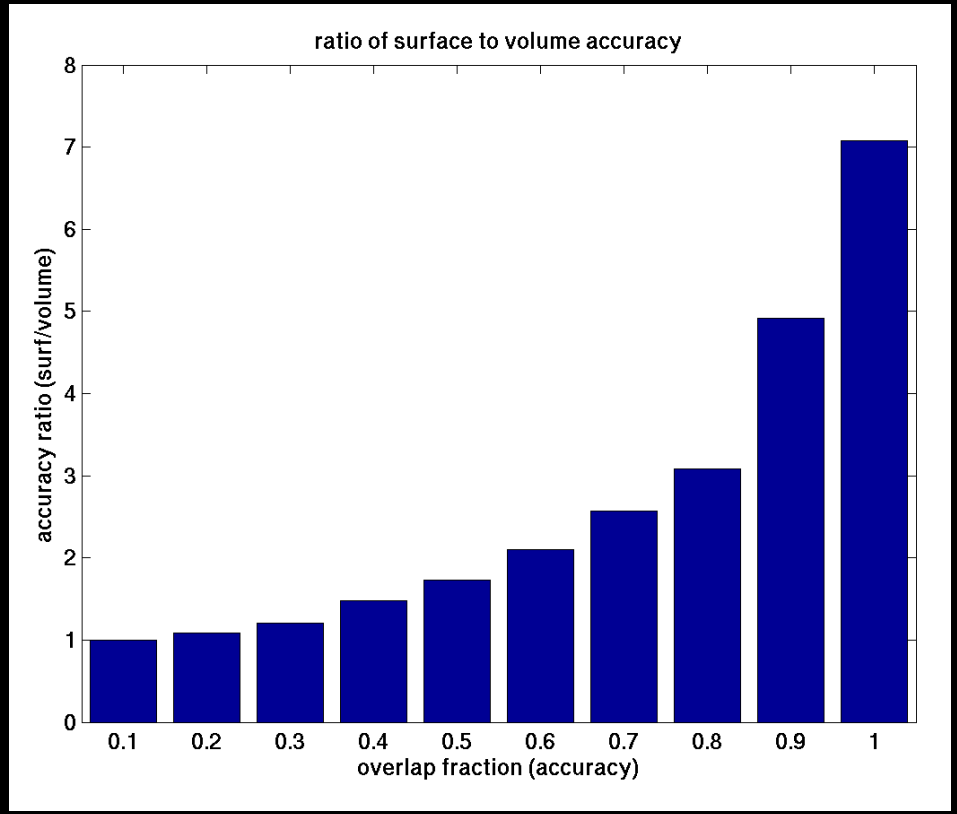


Fischl et al., 2009, NeuroImage

Comparing Coordinate Systems and Brodmann Areas

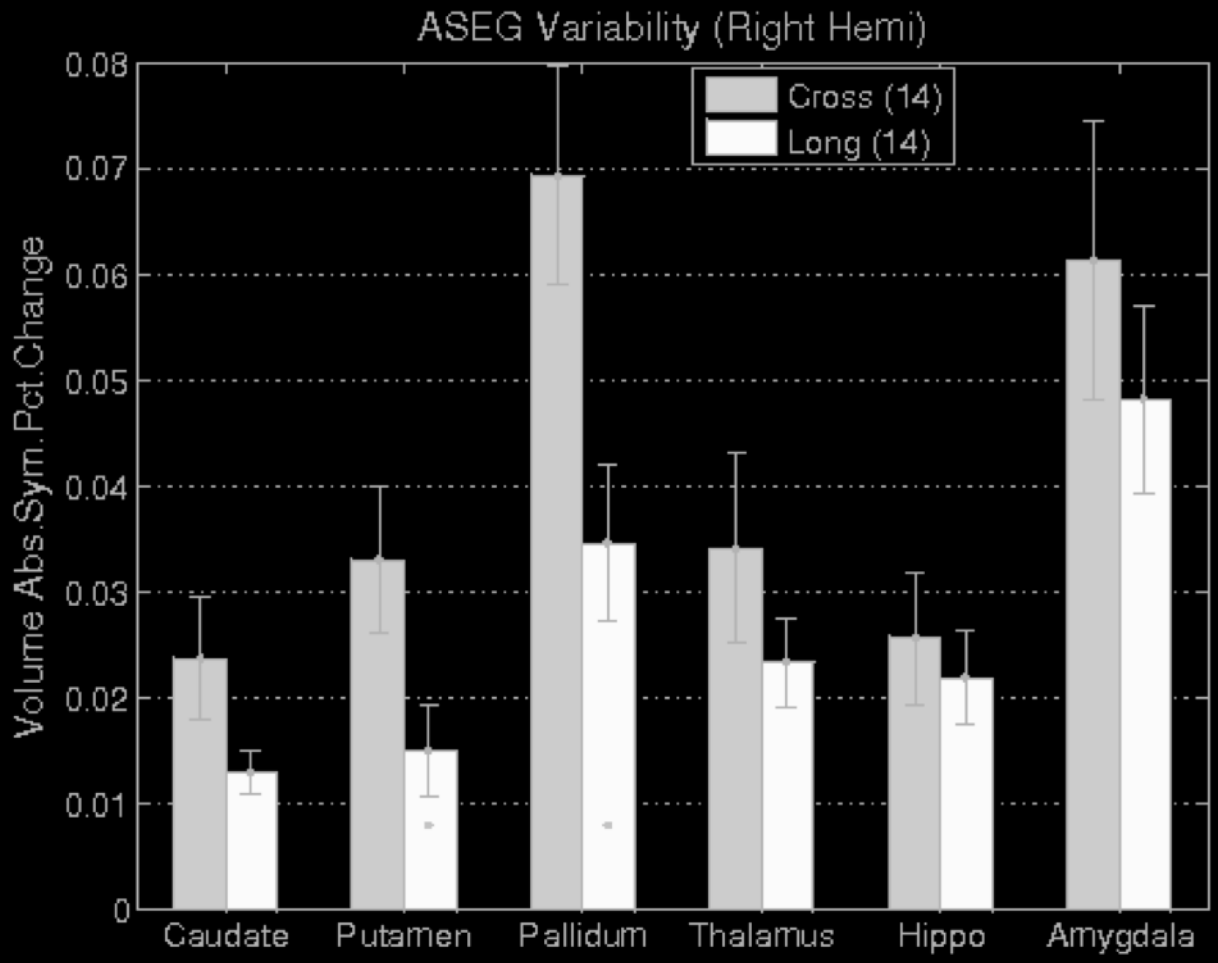


Cumulative histogram (red=surface, blue=nonlinear Talairach)



Ratio of surface accuracy to volume accuracy

Longitudinal Analysis: Increased Reliability



14 subjects scanned twice, two weeks apart.

Collaboration with Martin Reuter