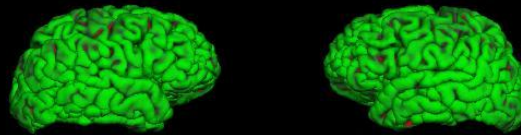
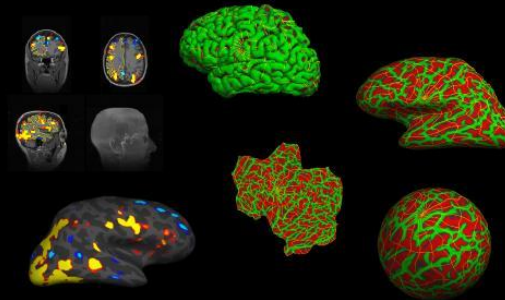


# Anatomical Analysis with FreeSurfer

[surfer.nmr.mgh.harvard.edu](http://surfer.nmr.mgh.harvard.edu)



**FreeSurfer**



# Fully Automated Reconstruction

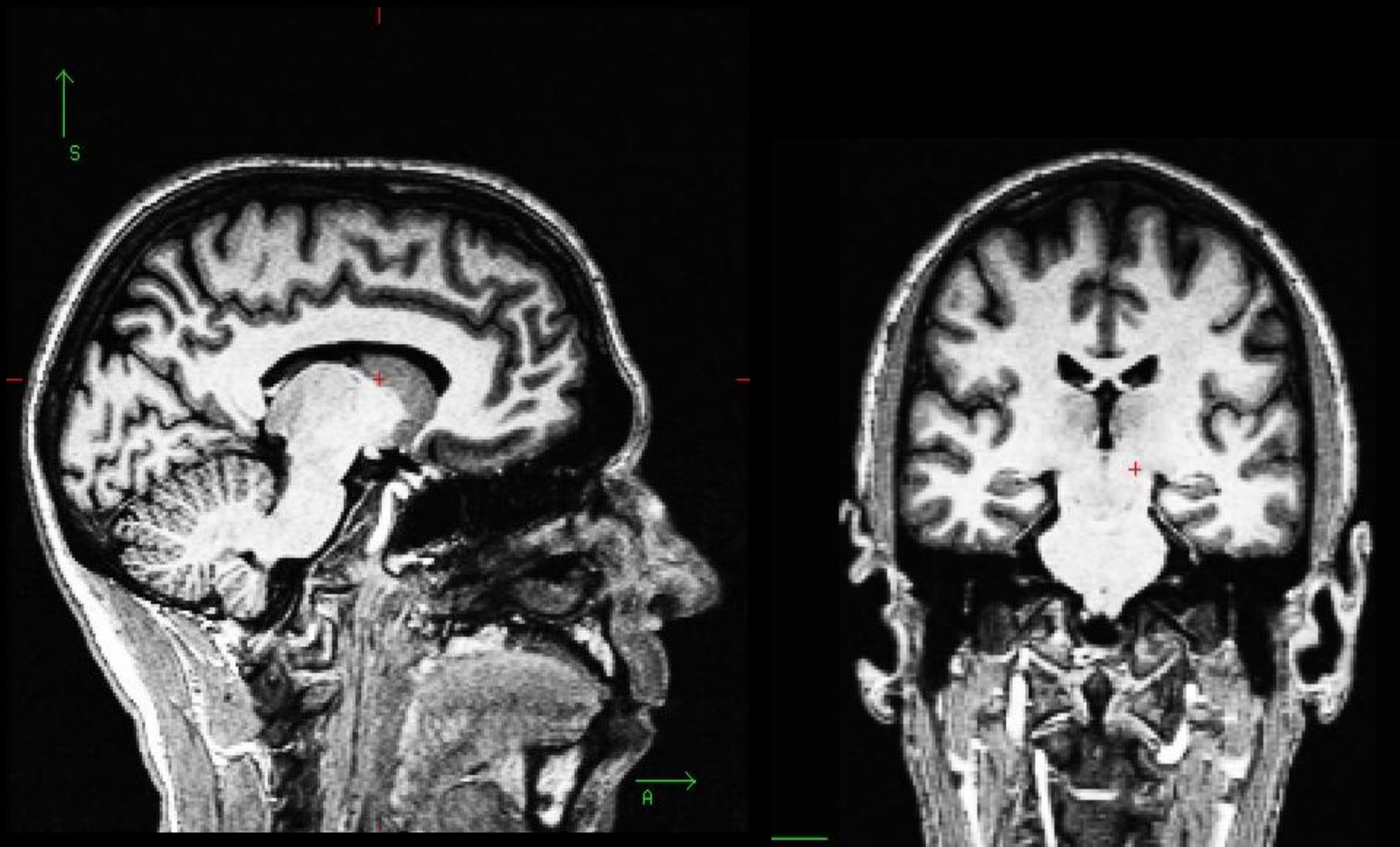
```
recon-all -i file.dcm -subject bert -all
```

Where file.dcm is one file from the correct (T1-weighted) MR series.

# Administration

- [surfer.nmr.mgh.harvard.edu](http://surfer.nmr.mgh.harvard.edu)
  - Register
  - Download
  - Mailing List
- Wiki: [surfer.nmr.mgh.harvard.edu/fswiki](http://surfer.nmr.mgh.harvard.edu/fswiki)
- Platforms: Linux and Mac
- Bug Reporting
  - Version
  - Command-line
  - Error description
  - [subjid/scripts/recon-all.log](#)
  - [freesurfer@nmr.mgh.harvard.edu](mailto:freesurfer@nmr.mgh.harvard.edu)

# T1 Weighted Image

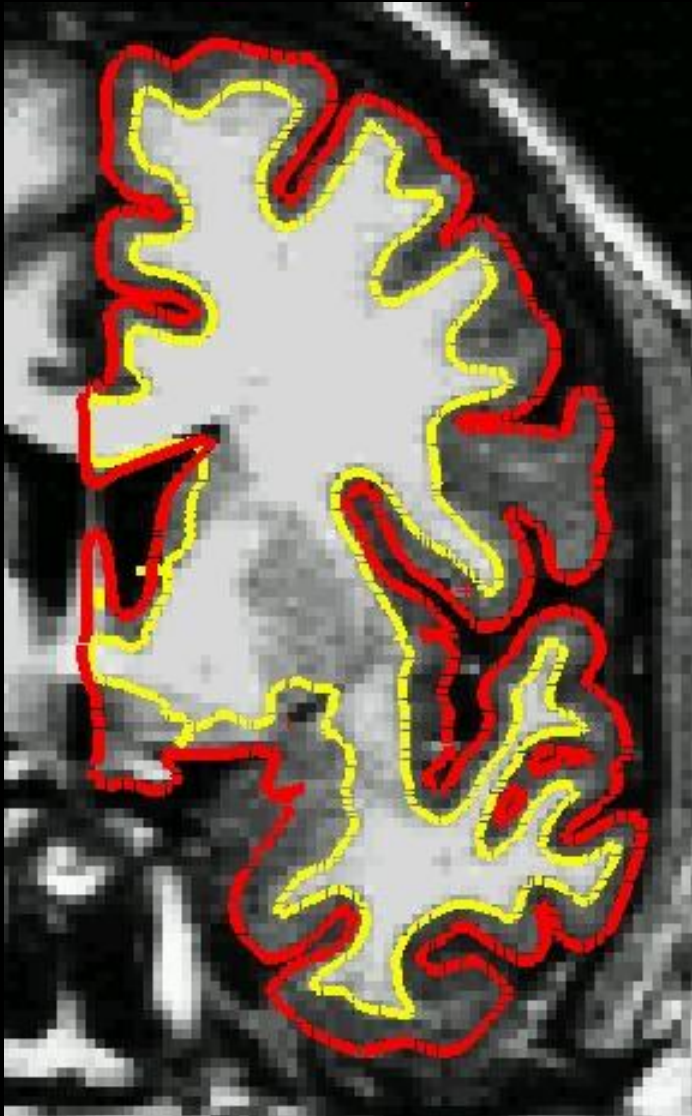


T1 Contrast: White matter brighter than gray matter

# Surface Reconstruction Overview

- Input: T1-weighted (MPRAGE,SPGR)
- Find white/gray surface
- Find pial surface
- “Find” = create mesh
  - Vertices, neighbors, triangles, coordinates
  - Accurately follows boundaries between tissue types
  - “Topologically Correct”
    - closed surface, no donut holes
    - no self-intersections
- Generate surface-based cross-subject registration
- Label cortical folding patterns
- Subcortical Segmentation along the way

# Find “Subcortical Mass”

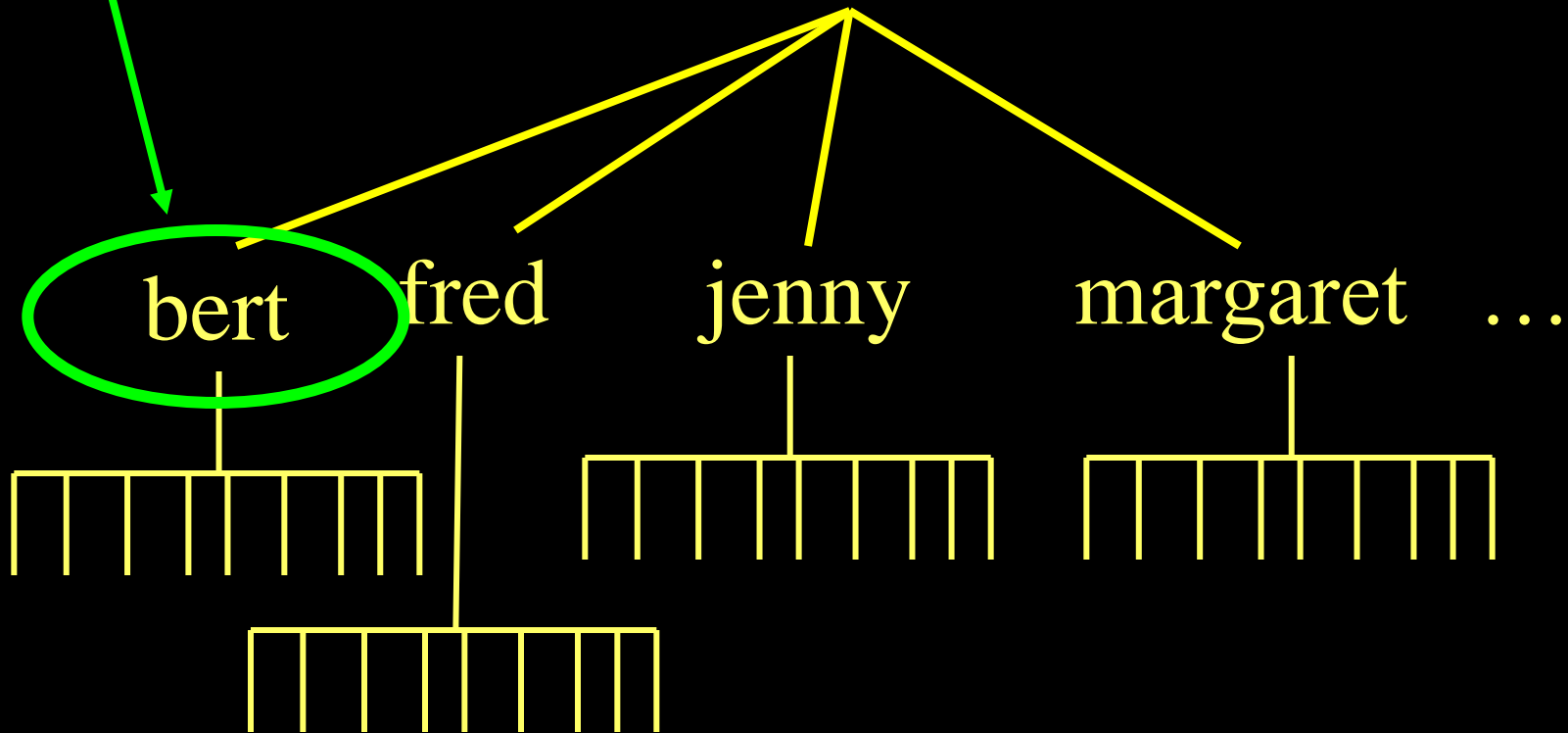


- All White Matter
- All Subcortical Structures
- Ventricles
- Excludes brain stem and cerebellum
- Hemispheres separated
- Connected (no islands)
- Many Stages ... More Later ...

# SUBJECTS\_DIR Environment Variable

Subject

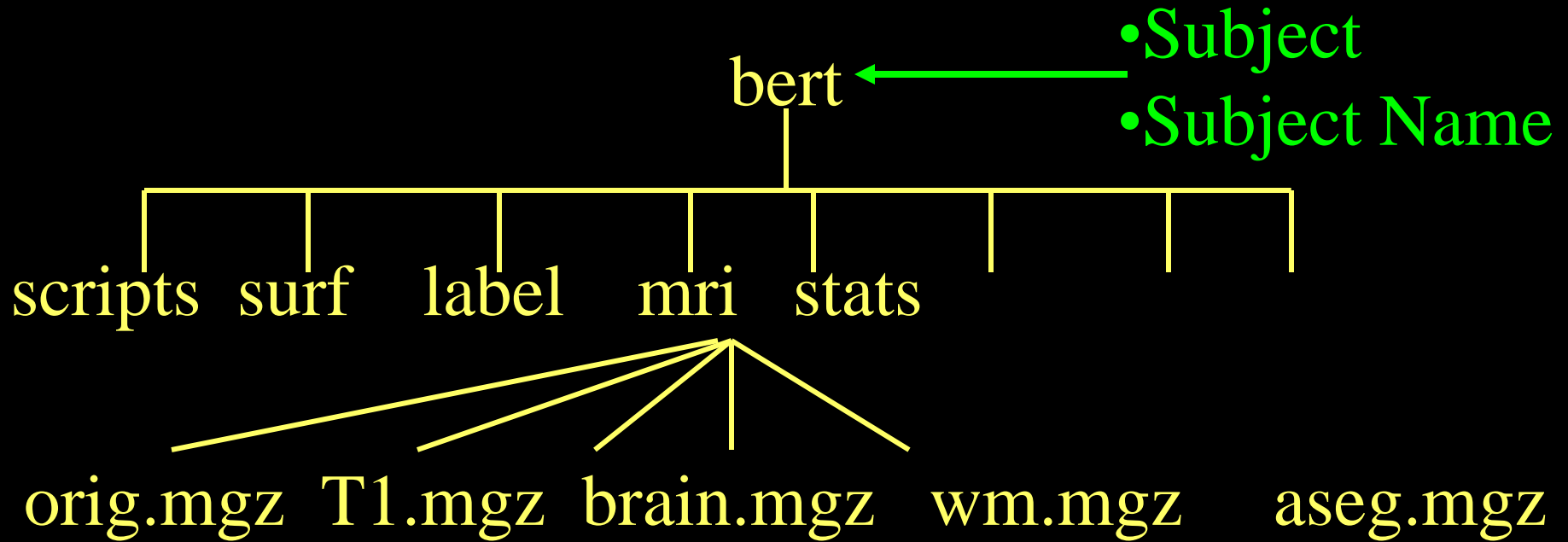
\$SUBJECTS\_DIR



recon-all -i file.dcm -subject **bert** -all

# FreeSurfer Directory Tree

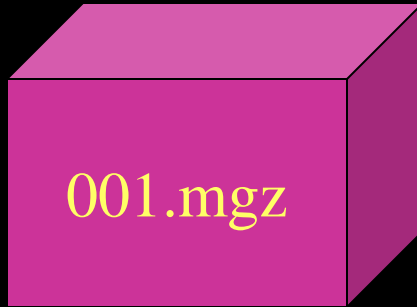
Each data set has its own unique SubjectId (eg, bert)



recon-all -i file.dcm -subject bert -all



# MGZ File Format



- mgz = compressed MGH file
- Can store 4D (like NIFTI)
- cols, rows, slices, frames
- Generic: volumes and Surfaces

- Eg, Typical Anatomical volume: 256 x 256 x 128 x 1

## “Volume-encoded” Surface Files

A long, thin 3D blue rectangular prism representing a surface file. The text 'lh.thickness.sm10.mgz' is written in white on the top face of the prism.

lh.thickness.sm10.mgz

- nvertices, 1, 1, frames (eg, 163214 x 1 x 1 x 40)
- No geometry information

# Other File Formats

- Surface: Vertices, XYZ, neighbors (lh.white)
- Curv: lh.curv, lh.sulc, lh.thickness
- Annotation: lh.aparc.annot
- Label: lh.pericalcarine.label
- Unique to FreeSurfer
- FreeSurfer can read/write:
  - NIFTI, Analyze, MINC
- FreeSurfer can read:
  - DICOM, Siemens IMA, AFNI

# Fully Automated Reconstruction

## 1. Launch reconstruction:

```
recon-all -i file.dcm -subject bert -all
```

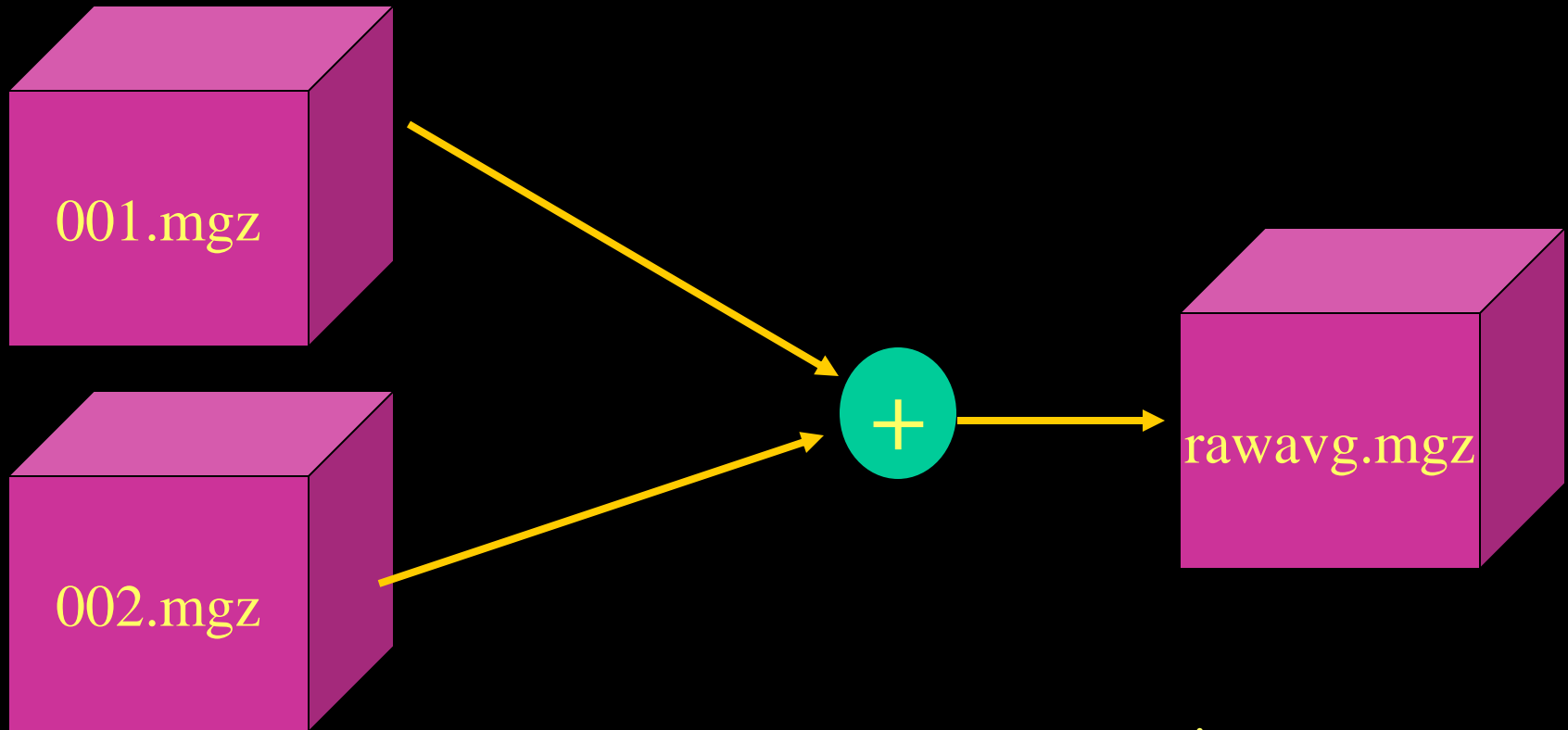
Where file.dcm is one file from the correct (T1-weighted) MR series.

Come back in 20 hours ...

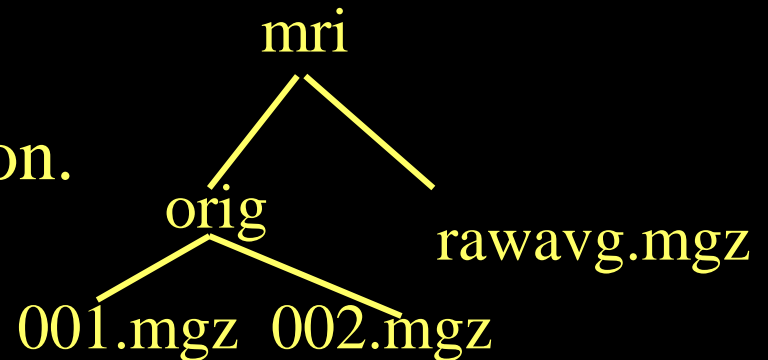
Check your results – do the white and pial surfaces follow the boundaries?

-- Can be broken up

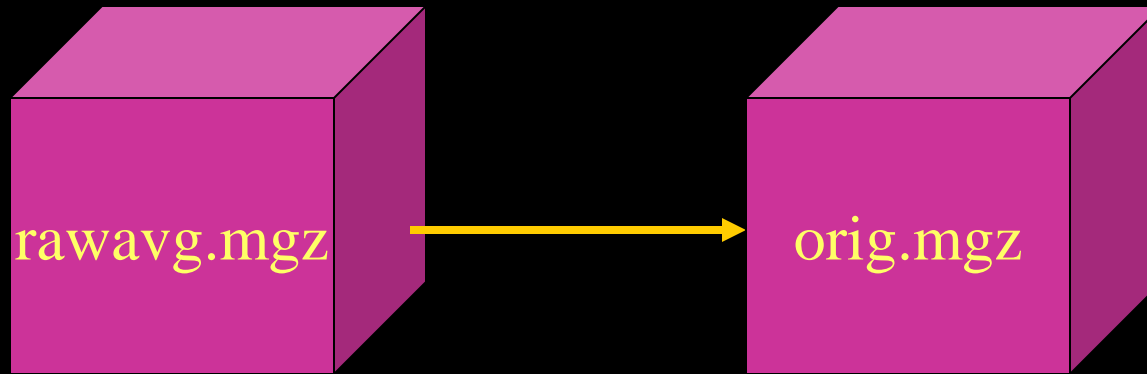
# Motion Correction and Averaging



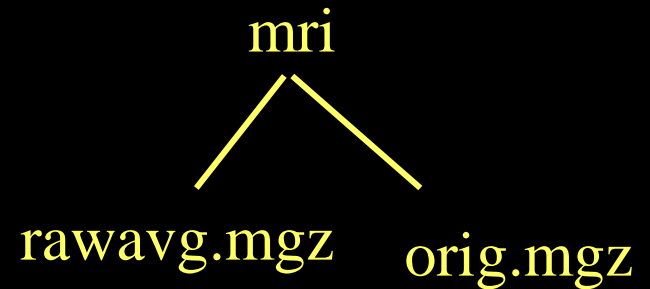
Does not change native resolution.  
Usually only need one.



# Conform

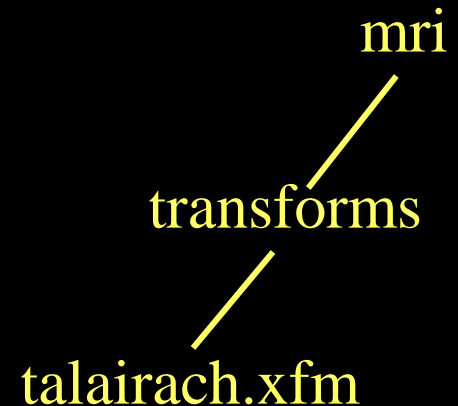


Changes to  $256^3$ ,  $1\text{mm}^3$   
All volumes will be conformed.

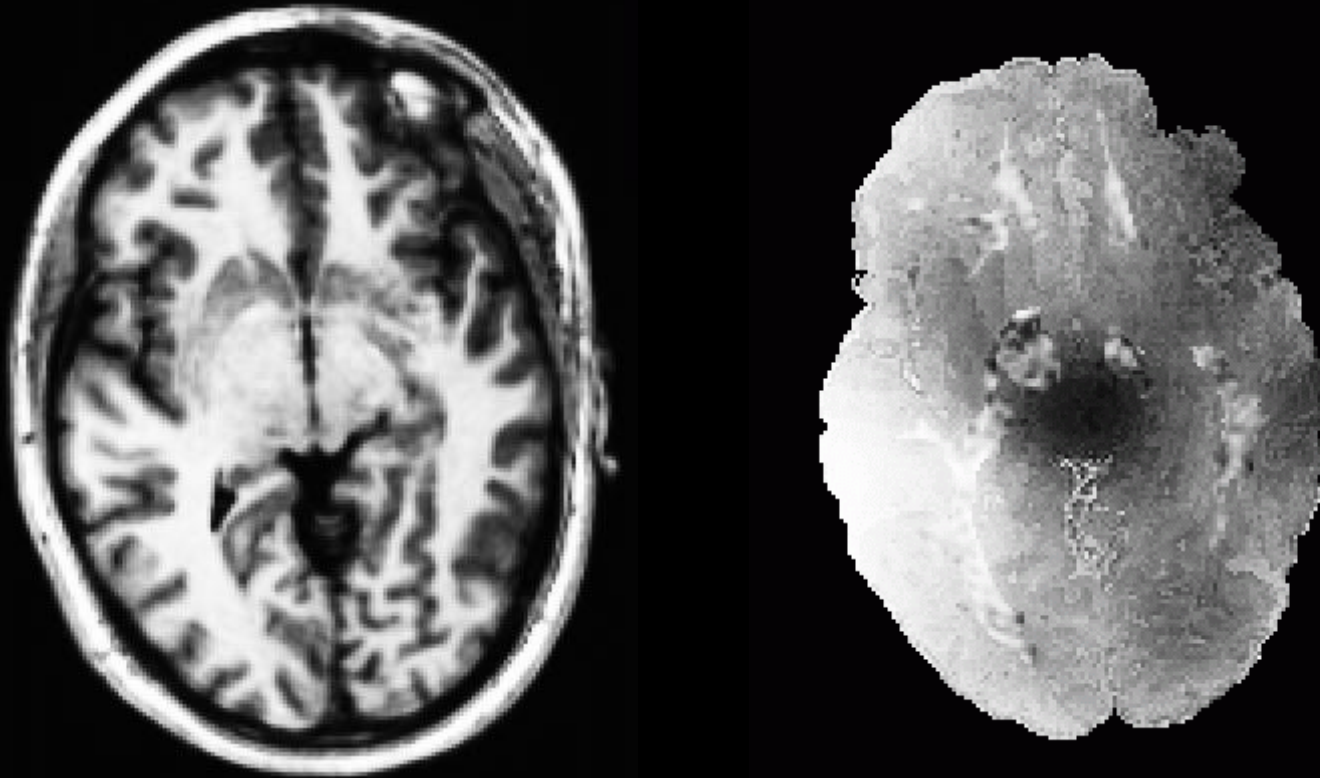


# Talairach Transform

- Computes 12 DOF transform matrix
- Does NOT resample
- MNI305 template
- Mostly used to report coordinates
- `mri/transforms/talairach.xfm`



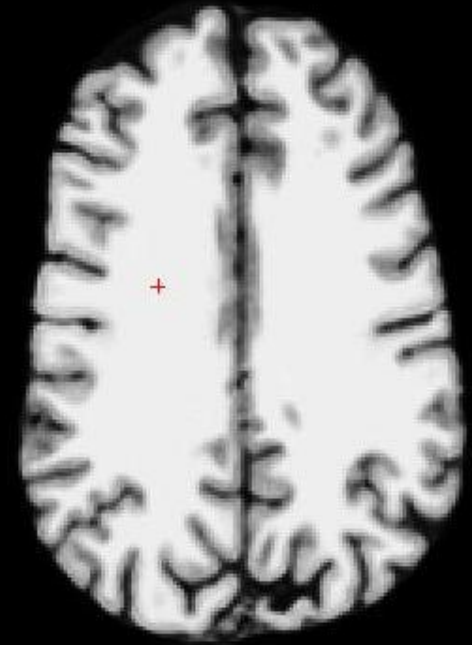
# Intensity Bias



- Left side of the image much brighter than right side
- Worse with many coils
- Makes gray/white segmentation difficult

# Intensity Normalization

- Removes B1 bias field
- NU (MNI) nu.mgz
- Presegmentation (T1.mgz)
  - Most WM = 110 intensity
  - Pre- and Post-Skull Strip

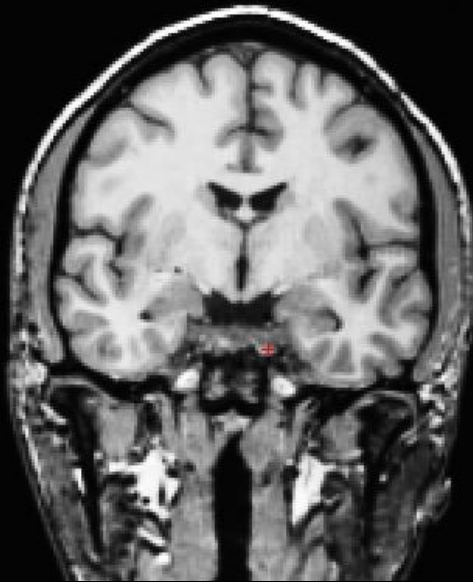


T1.mgz Volume



# Skull Strip

- Removes all non-brain
  - Skull, Eyes, Neck, Dura
- `brainmask.mgz` (cf, `brain.mgz`)

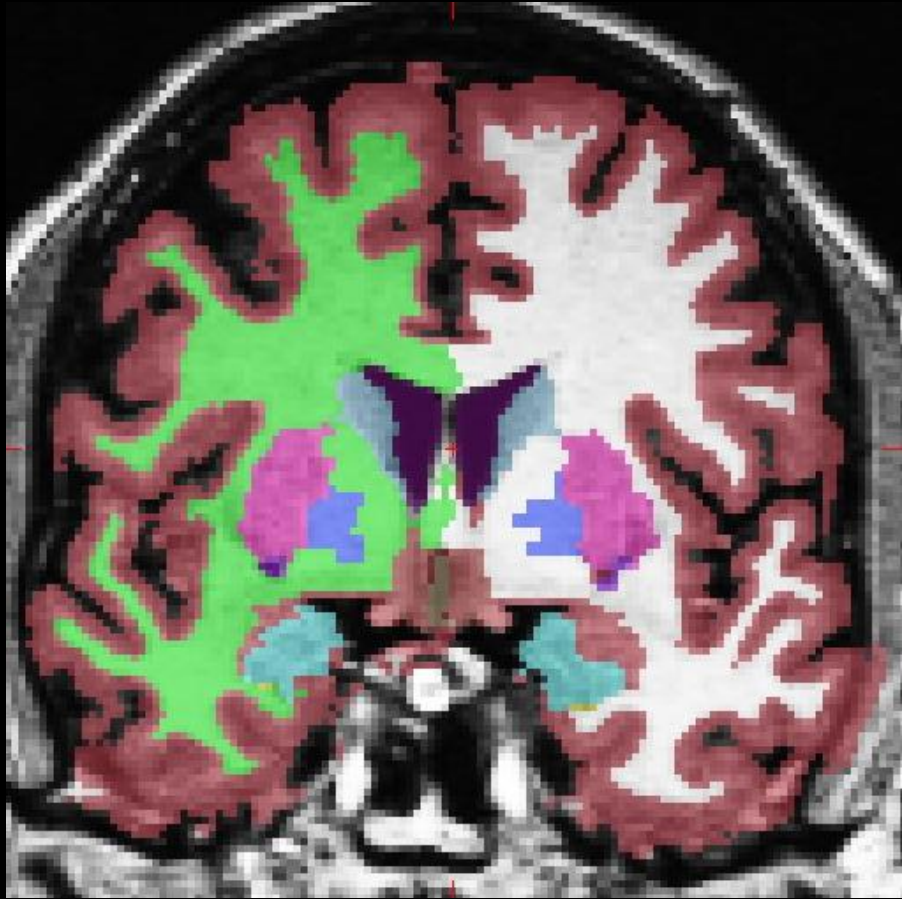


Orig Volume



Brain Volume

# Automatic Volume Labeling



ASeg Volume

- Used to fill in subcortical structures for creating subcortical mass
- Useful in its own right
- aseg.mgz
- More in ROI Talk

# White Matter Segmentation

- Separates white matter from everything else
- Uses aseg to “fill in” subcortical structures
- Cerebellum removed, brain stem still there
- Somewhat redundant with aseg
- wm.mgz
- Not otherwise useful



WM Volume

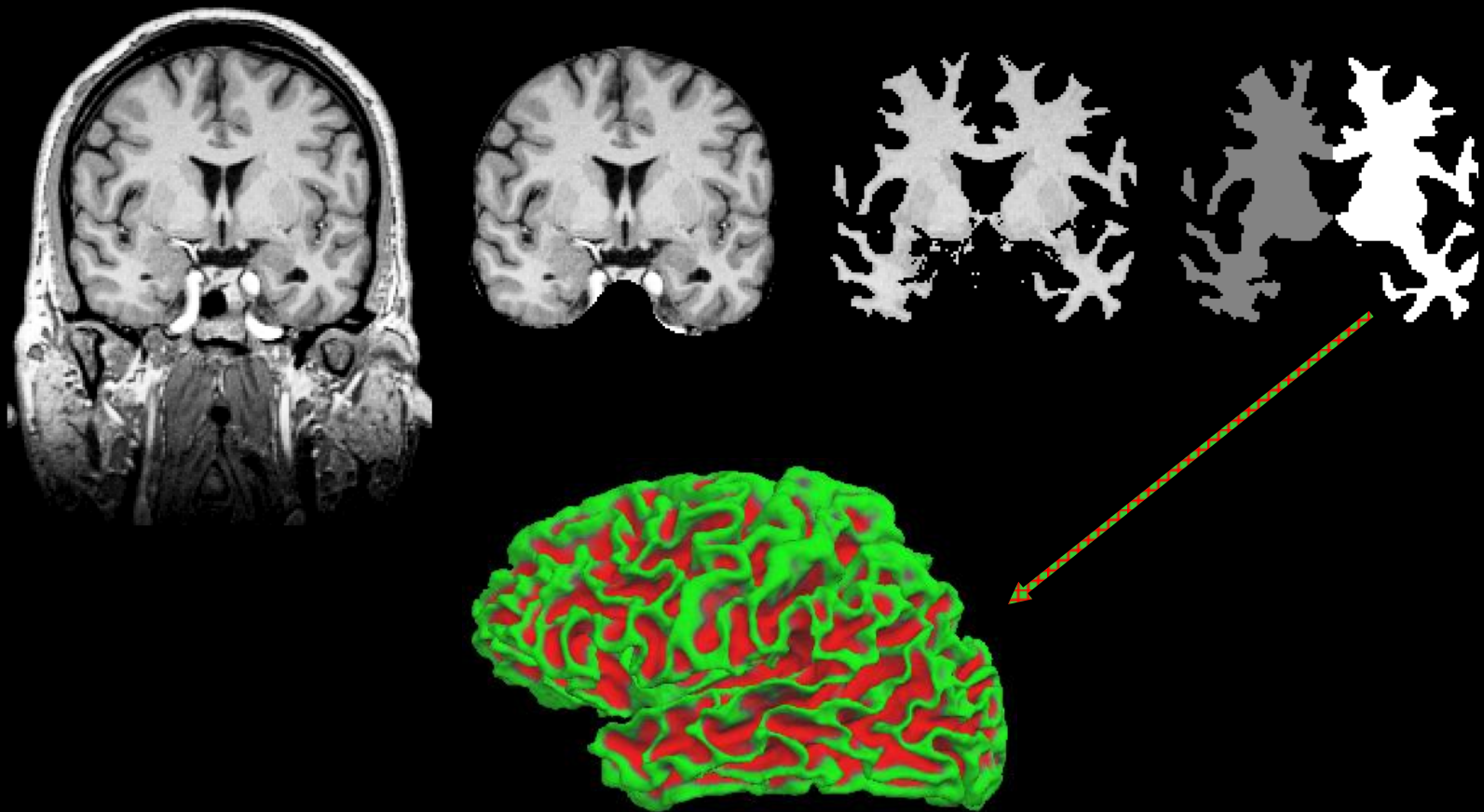
# Fill and Cut (Subcortical Mass)

- Fills in any holes.
- Removes any islands
- Removes brain stem
- Separates hemispheres (each hemi has different value)
- filled.mgz = “Subcortical Mass”



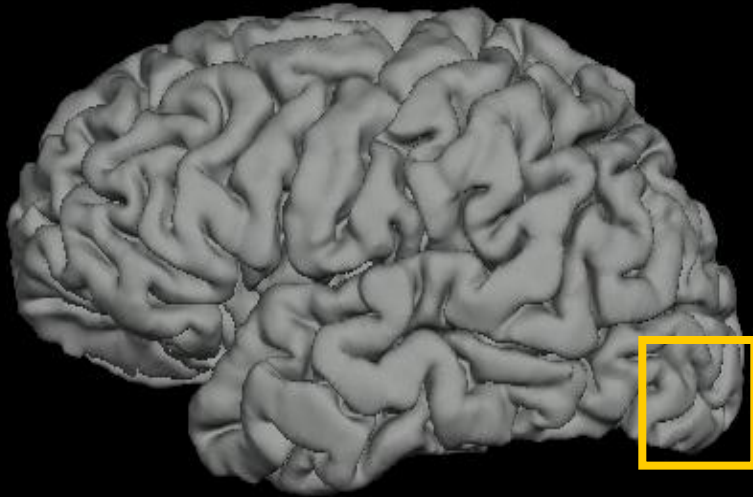
WM Volume (wm.mgz)    Filled Volume (filled.mgz)  
(Subcortical Mass)

# MRI Segmentation and Surface Reconstruction

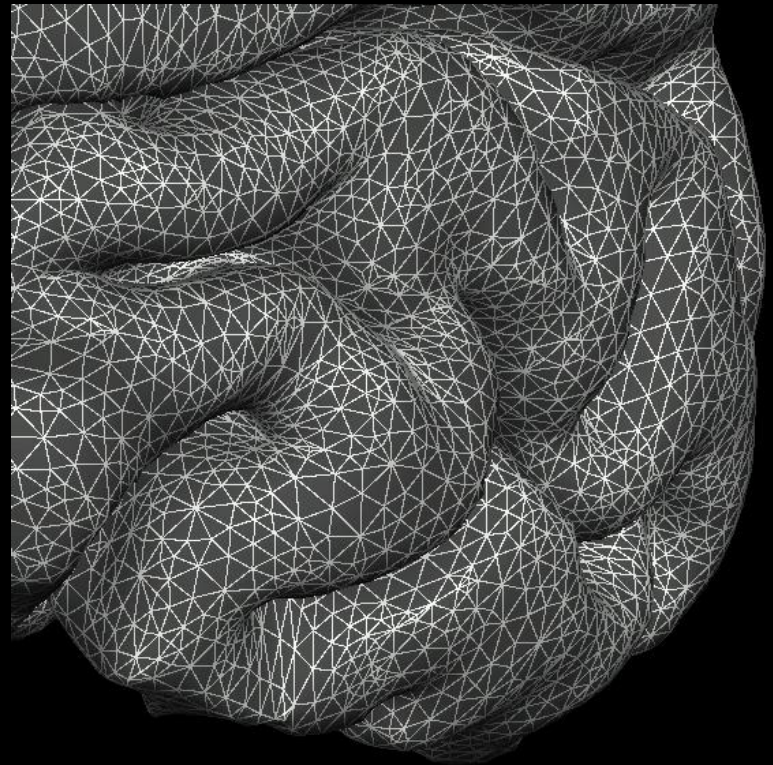




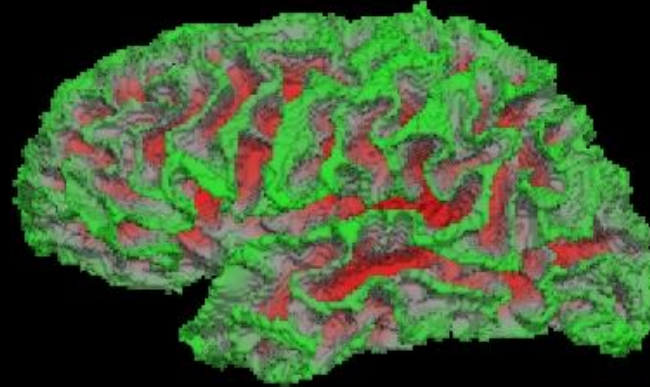
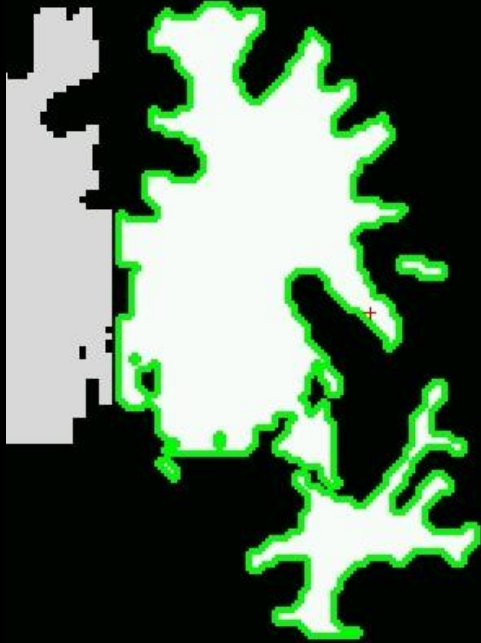
# Surface Model



- Mesh (“Finite Element”)
- Vertex = point of 6 triangles
- Neighborhood
- XYZ at each vertex
- Triangles/Faces ~ 150,000
- Area, Distance
- Curvature, Thickness
- Moveable

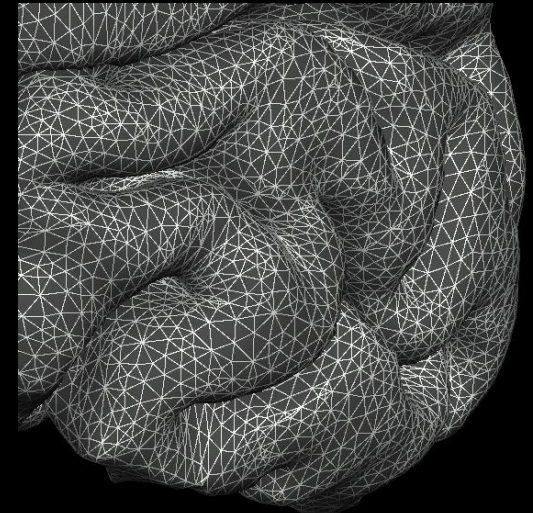


# Tessellation and Topology Fixing

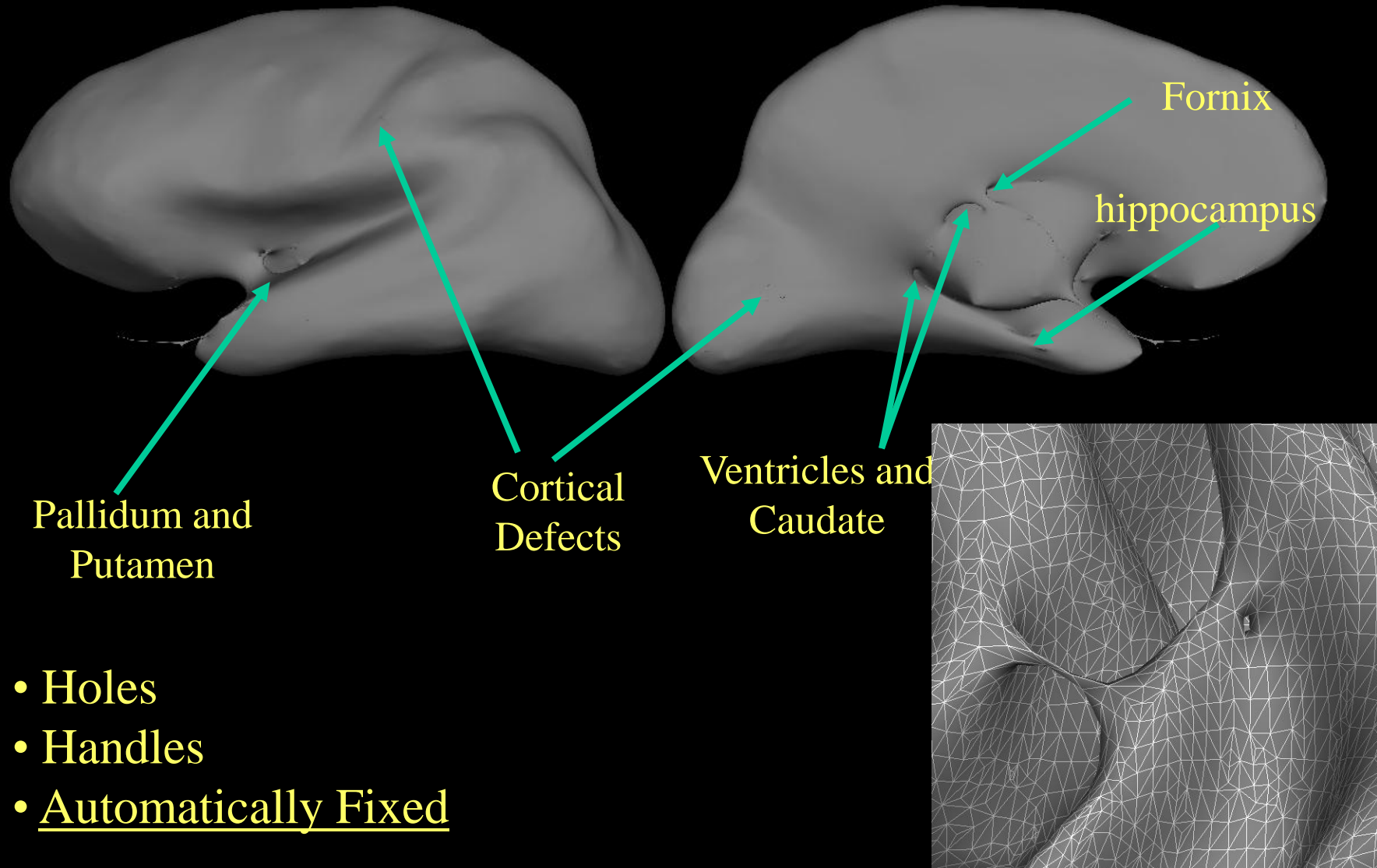


orig surface  
surf/lh.orig  
surf/rh.orig

- Mosaic of triangles (“tessellation”)
- Errors: Donut holes, handles
- Automatic topology fixer

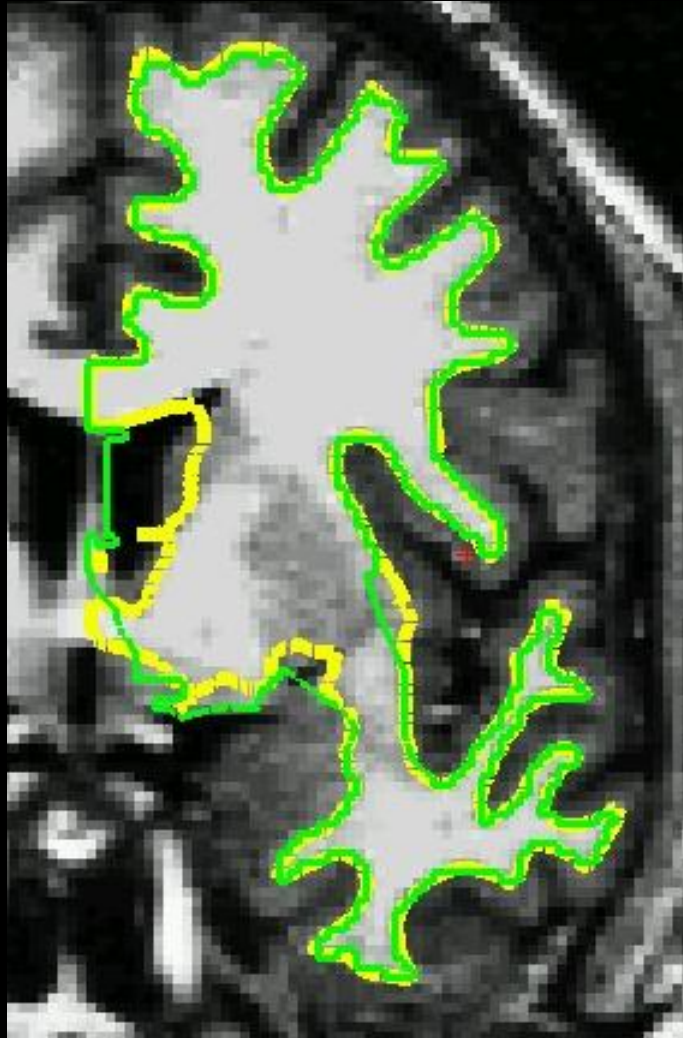


# Topological Defects

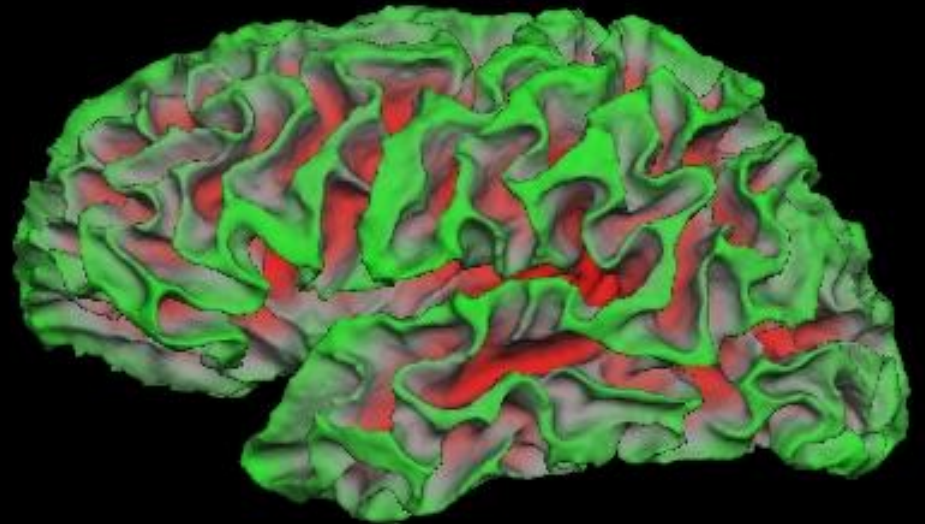




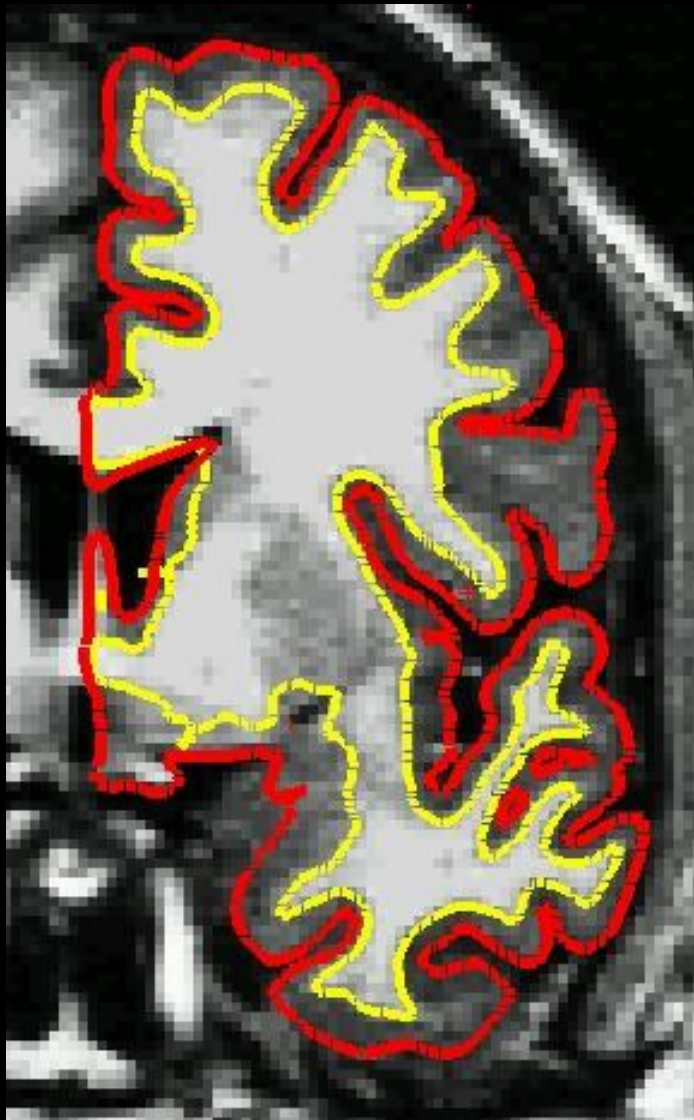
# White Matter Surface



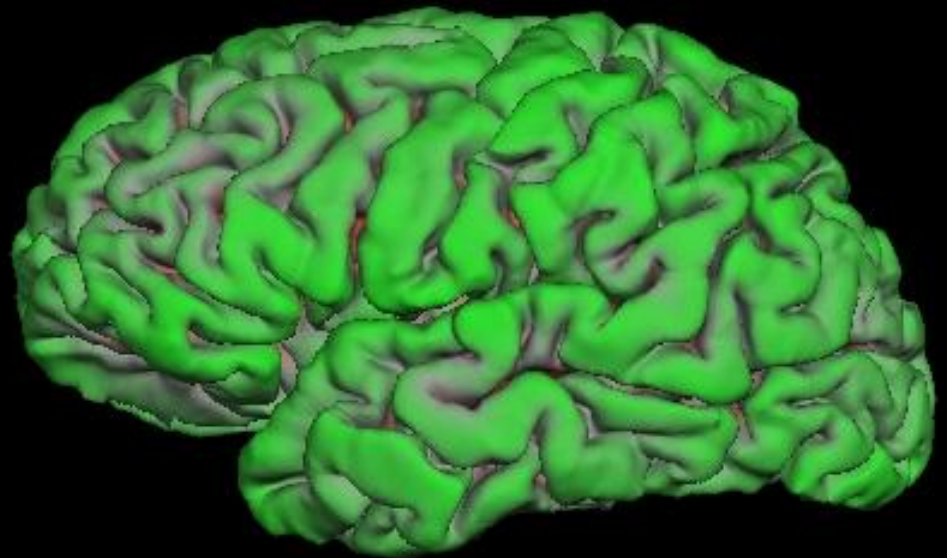
- Nudge orig surface
- Follow T1 intensity gradients
- Smoothness constraint
- Vertex identity preserved



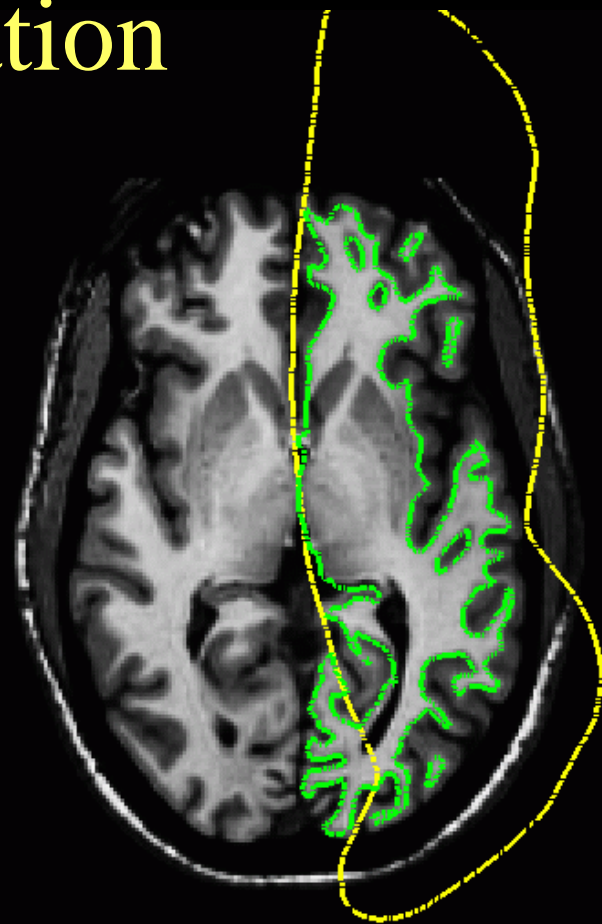
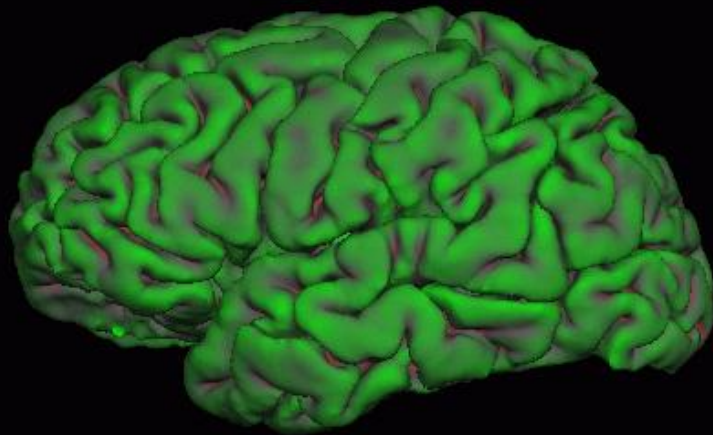
# Pial Surface



- Nudge white surface
- Follow T1 intensity gradients
- Vertex identity preserved



# Surface Inflation

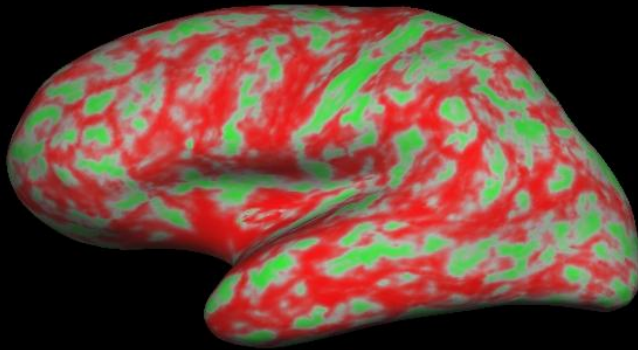


- Nudge vertices
- No intensity constraint
- Distances do not change
- See inside sulci
- Used for sphere



# Cortical Thickness

- Distance between white and pial surfaces
- One value per vertex
- Surface-based more accurate than volume-based

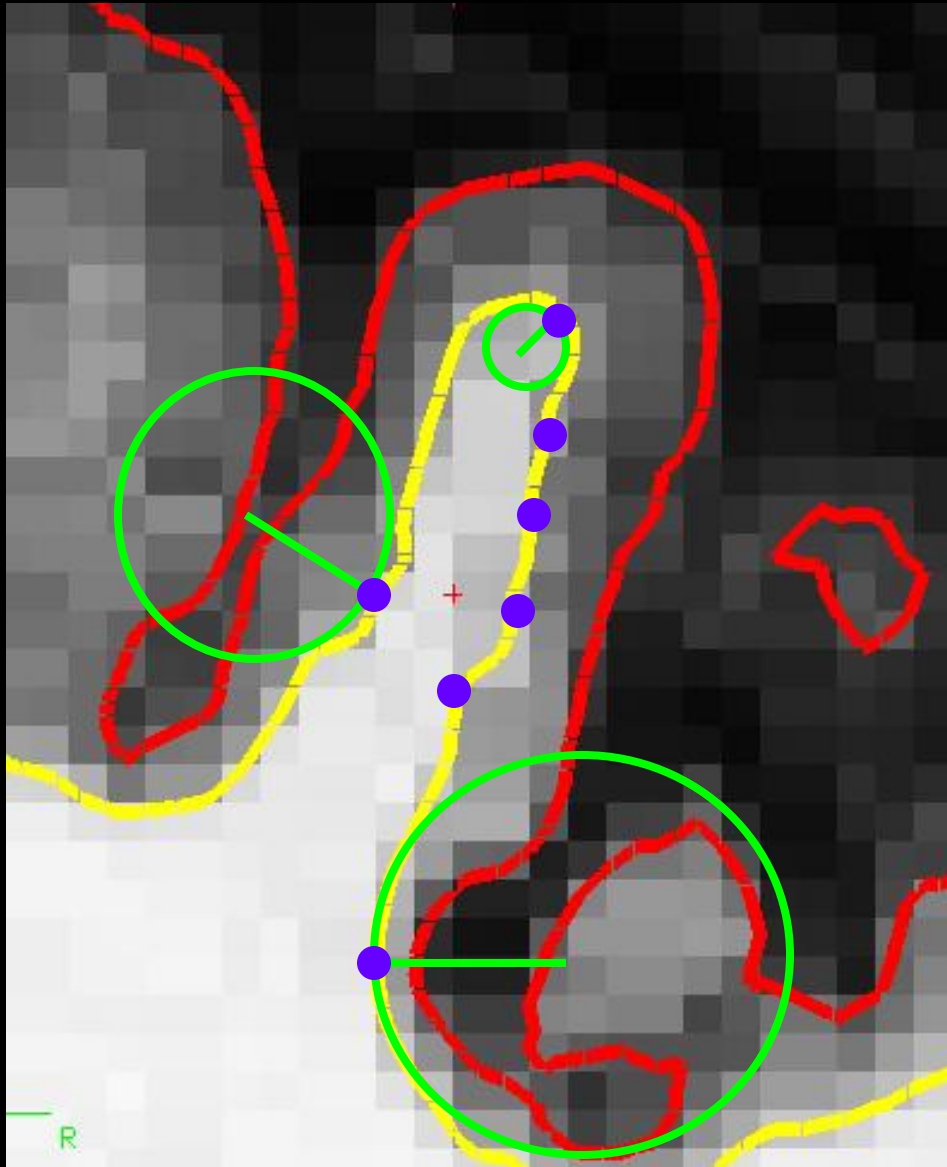


white/gray surface

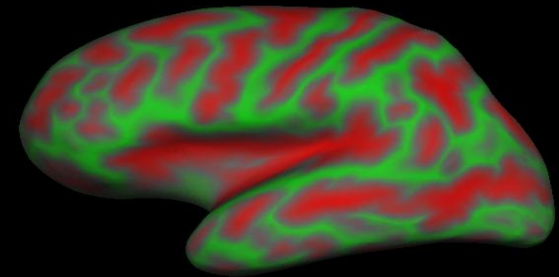
lh.thickness, rh.thickness



# Curvature (Radial)

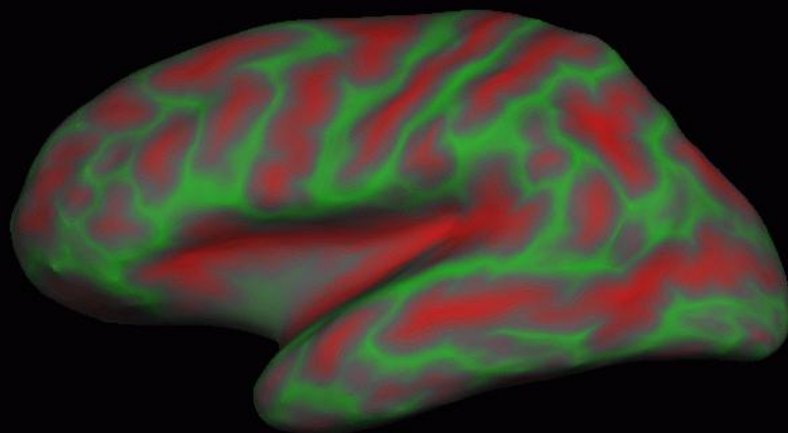
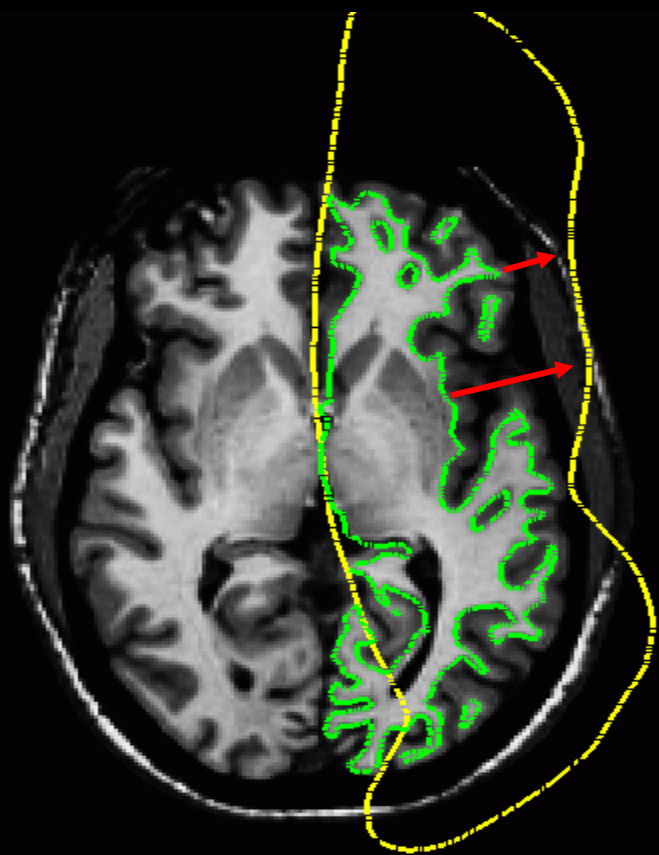


- Circle tangent to surface at each vertex
- Curvature measure is  $1/\text{radius of circle}$
- One value per vertex
- Signed (sulcus/gyrus)
- Actually use gaussian curvature

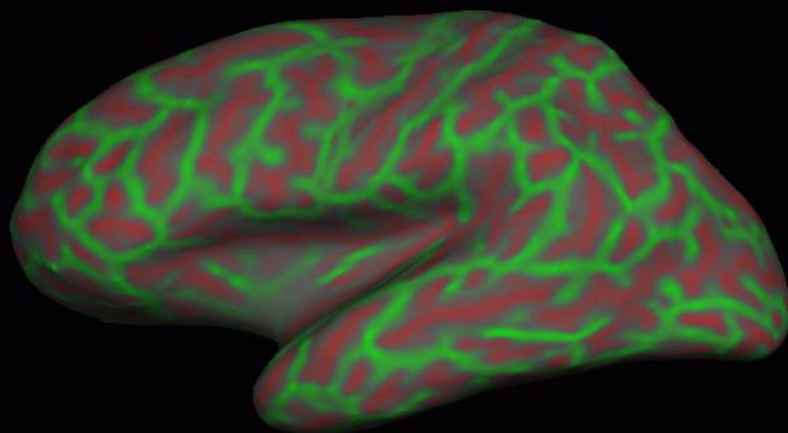


lh.curv, rh.curv

# Sulcal Depth

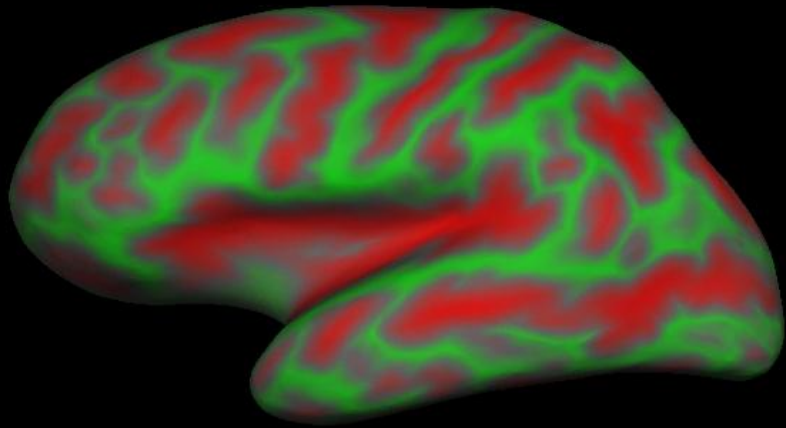


lh.sulc, rh.sulc



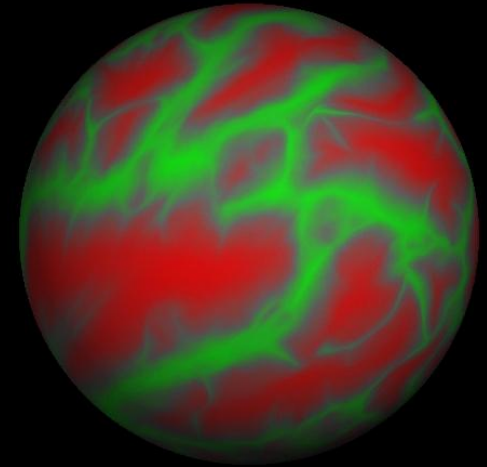
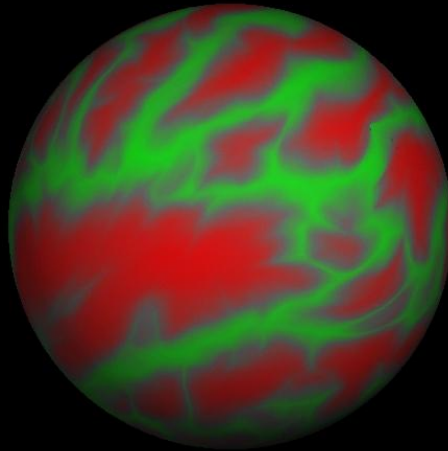
lh.curv, rh.curv

# Spherical Registration



Sulcal Map

Spherical Inflation



High-Dimensional  
Registration to  
Spherical Template

Uses population means *and* variances (more on this in the group analysis talk)

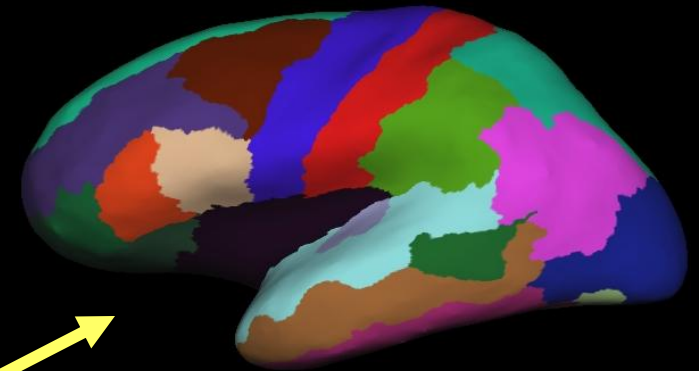
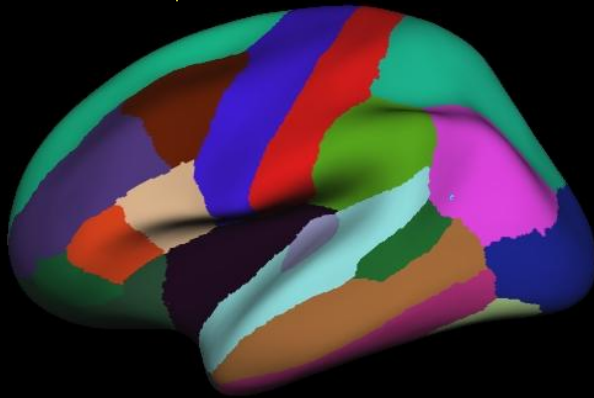


# Automatic Cortical Parcellation

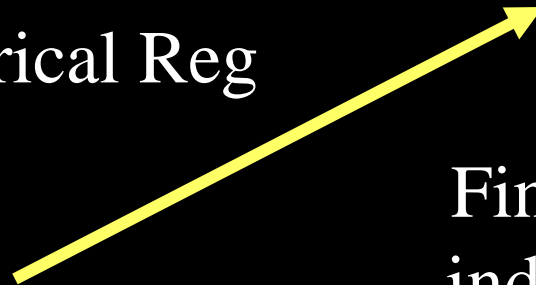
Spherical Atlas based on Manual  
Parcellations (40 of them)



Map to Individual  
Thru Spherical Reg



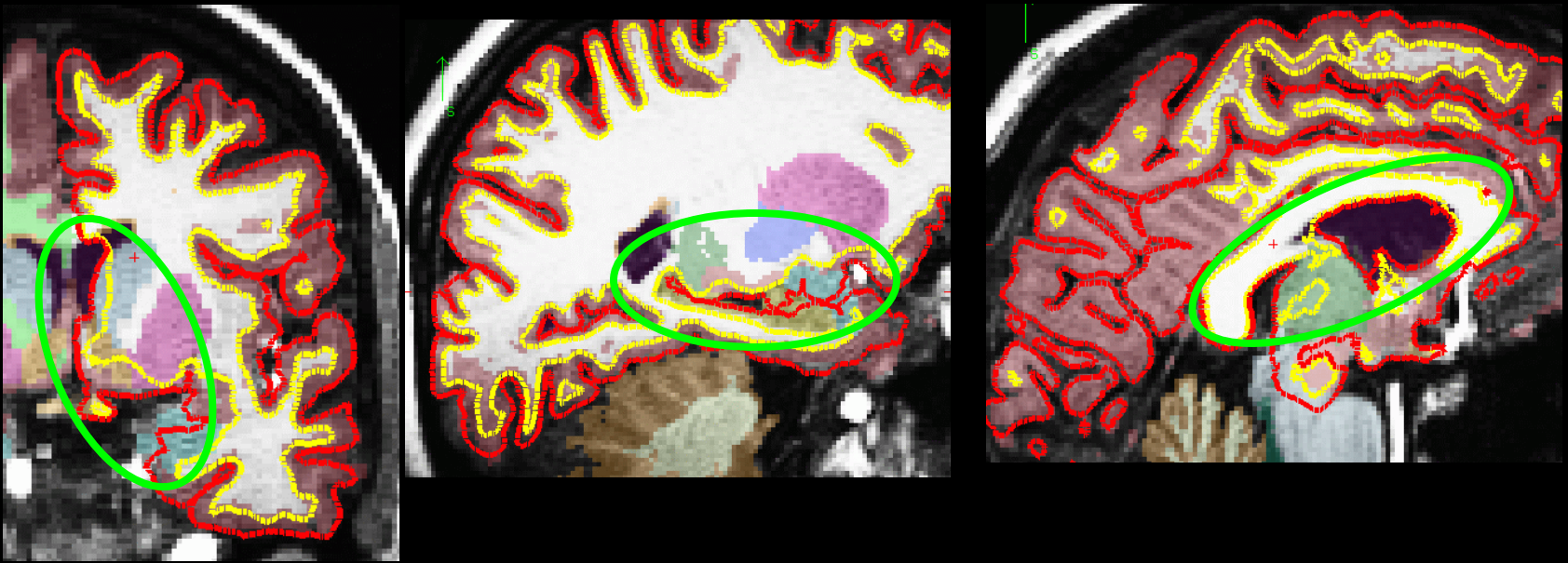
Fine-tune based on  
individual anatomy



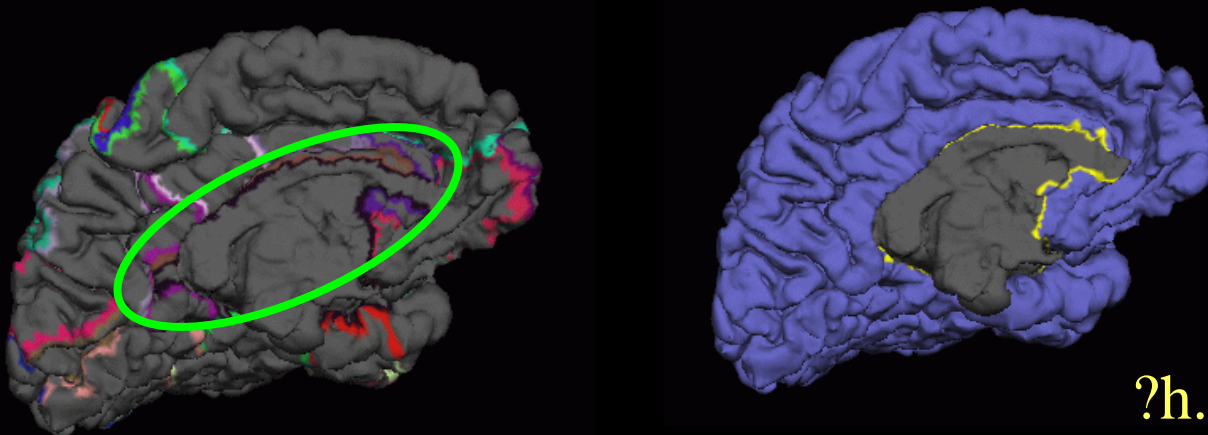
Note: Similar methodology  
to volume labeling



# Non-Cortical Areas of Surface



Amygdala, Putamen, Hippocampus, Caudate, Ventricles, CC



?h.cortex.label

# Workflow in Stages

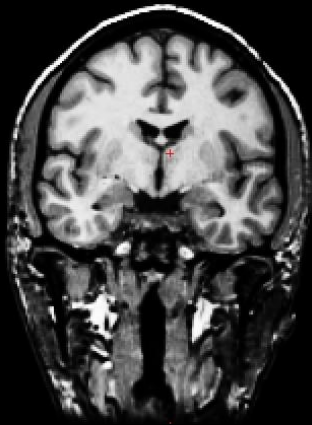
1. `recon-all --autorecon1` (Stages 1-5)
2. Check talairach transform, skull strip, normalization (?)
3. `recon-all --autorecon2` (Stages 6-23)
4. Check surfaces
  1. Add control points: `recon-all --autorecon2-cp` (Stages 10-23)
  2. Edit wm.mgz: `recon-all --autorecon2-wm` (Stages 13-23)
  3. Edit brain.mgz: `recon-all --autorecon2-pial` (Stage 23)
5. `recon-all --autorecon3` (Stages 24-30)

Note: all stages can be run individually

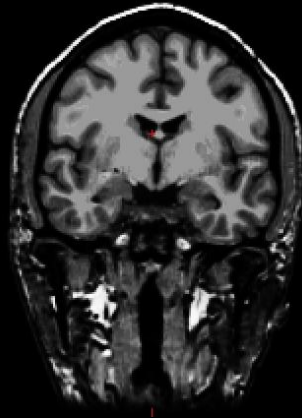
# Results

- Volumes
- Surfaces
- Surface Overlays
- ROI Summaries

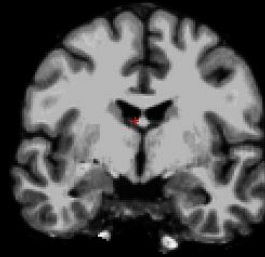
# Volumes



orig.mgz



T1.mgz



brainmask.mgz

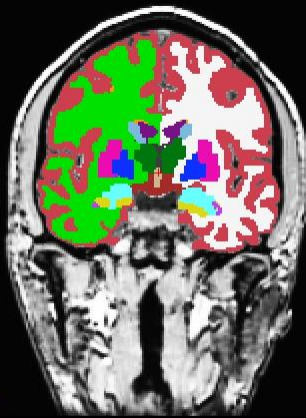


wm.mgz

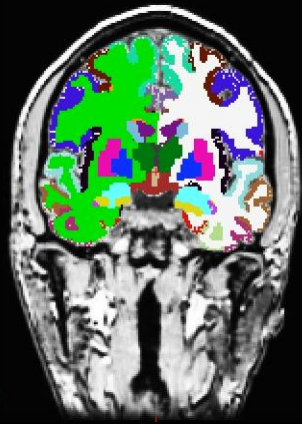


filled.mgz

Subcortical Mass



aseg.mgz

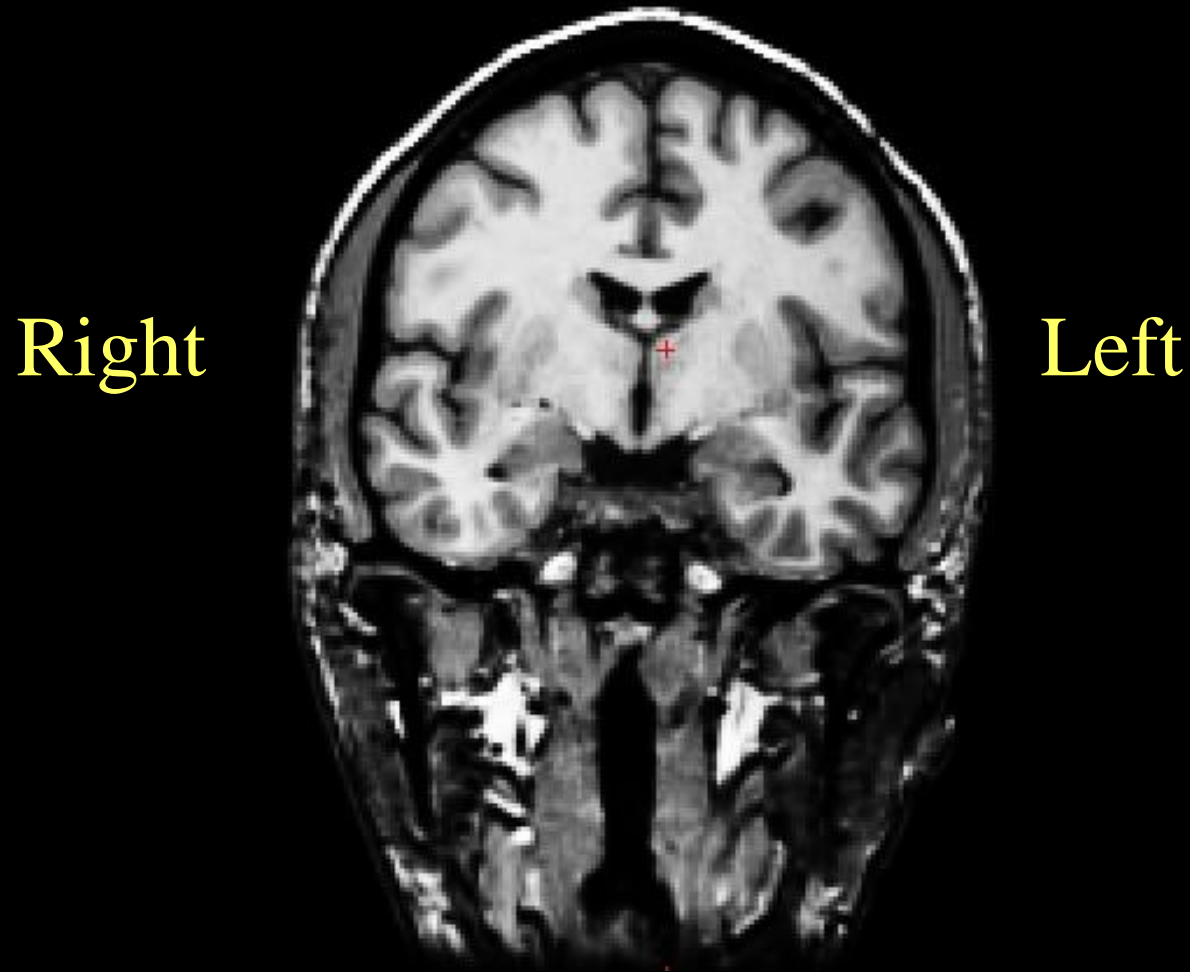


aparc+aseg.mgz

- `$SUBJECTS_DIR/bert/mri`
- All “Conformed”  $256^3$ ,  $1\text{mm}^3$
- Many more ...

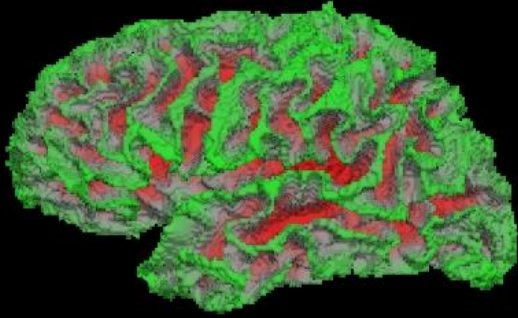
Volume Viewer:  
tkmedit

# Volume Viewer (tkmedit)

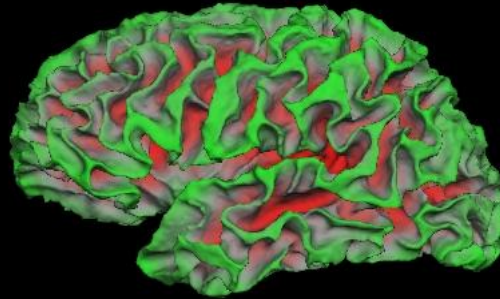




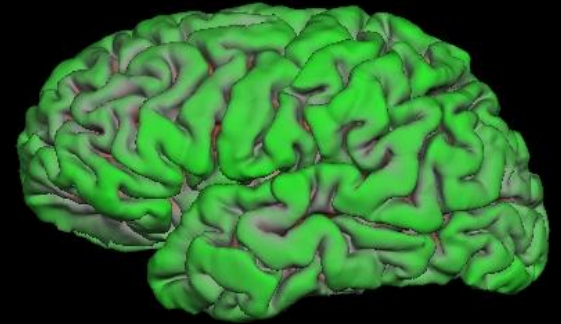
# Surfaces



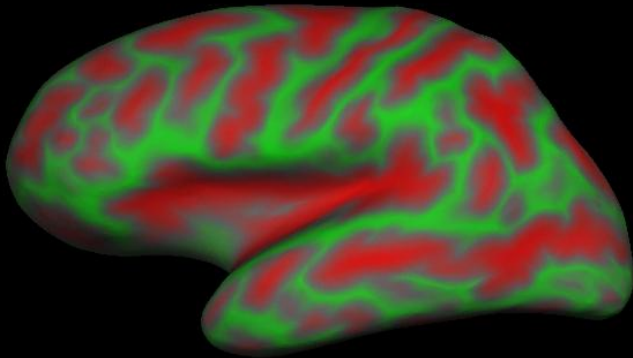
orig



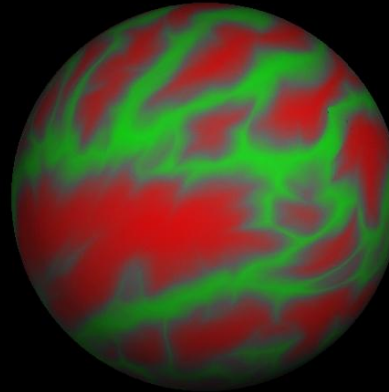
white



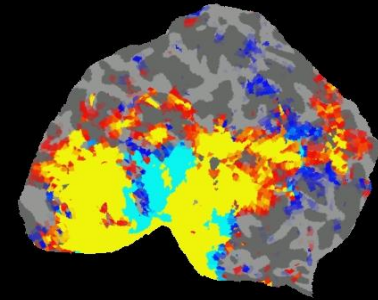
pial



inflated



sphere,sphere.reg



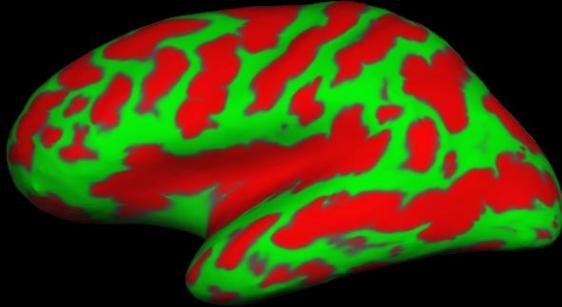
patch (flattened)

- `$SUBJECTS_DIR/bert/surf`
- Number/Identity of vertices stays the same (except patches)
- XYZ Location Changes
- Flattening not done as part of standard reconstruction

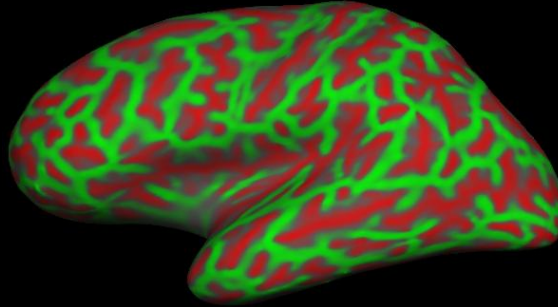
Surface Viewer:  
tksurfer

# Surface Overlays

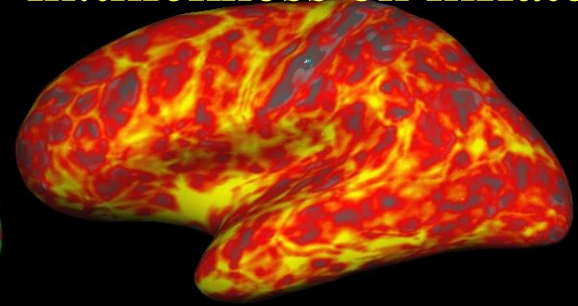
lh.sulc on inflated



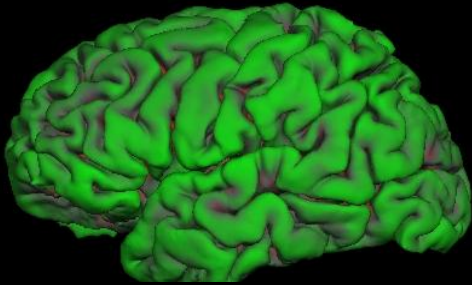
lh.curv on inflated



lh.thickness on inflated



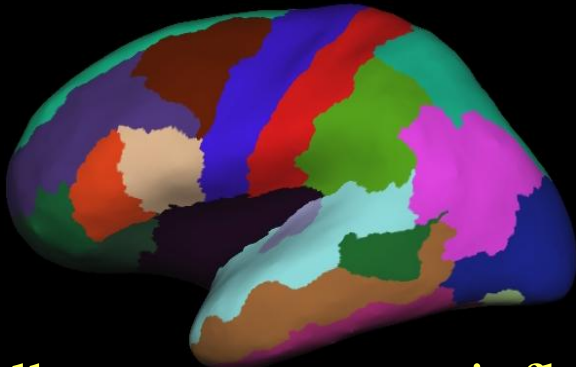
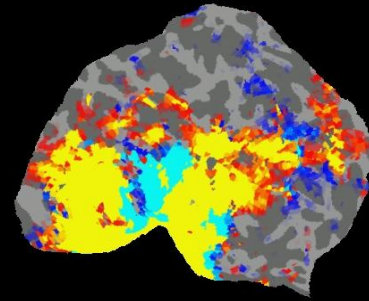
lh.sulc on pial



lh.curv on inflated



fMRI on flat



lh.aparc.annot on inflated

- Value for each vertex
- Color indicates value
- Color: gray, red/green, heat, color table
- Rendered on any surface
- fMRI/Stat Maps too

# ROI Summaries:

`$SUBJECTS_DIR/bert/stats`

`aseg.stats` – volume summaries

`?h.aparc.stats` – desikan/killiany surface summaries

`?h.aparc.a2009s.stats` – destrieux surface summaries

`wmparc.stats` – white matter parcellation

Index	SegId	NVoxels	Volume_mm3	StructName	normMean	normStdDev	normMin	normMax	normRange
1	1	0	0.0	Left-Cerebral-Exterior	0.0000	0.0000	0.0000	0.0000	0.0000
2	2	265295	265295.0	Left-Cerebral-White-Matter	106.6763	8.3842	35.0000	169.0000	134.0000
3	3	251540	251540.0	Left-Cerebral-Cortex	81.8395	10.2448	29.0000	170.0000	141.0000
4	4	7347	7347.0	Left-Lateral-Ventricle	42.5800	12.7435	21.0000	90.0000	69.0000
5	5	431	431.0	Left-Inf-Lat-Vent	66.2805	11.4191	30.0000	95.0000	65.0000
6	6	0	0.0	Left-Cerebellum-Exterior	0.0000	0.0000	0.0000	0.0000	0.0000

....

Routines to generate spread sheets of group data

- `asegstats2table --help`
- `aparcstats2table --help`

More info in Anatomical ROI talk.



# Overview

```
recon-all -i file.dcm -subject bert -all
```

- Command-line (not GUI)
- \$SUBJECTS\_DIR
- Subject Directory Tree
- MGZ File (orig.mgz)
- Subcortical Mass
- Intensity Bias
- Skull Stripping
- Surface Model
- white, pial, and inflated surfaces
- curvature vs. sulcal depth
- Automatic Segmentation

# Tutorial Tips

- Don't open tkmedit and tksurfer from the same terminal window. Open a new terminal window and open tksurfer from there. Don't put either in the background.
- Once you open tkmedit or tksurfer, you may not be able to type in the terminal window. You can open a new terminal window if you need use the command line.



# Background Slides

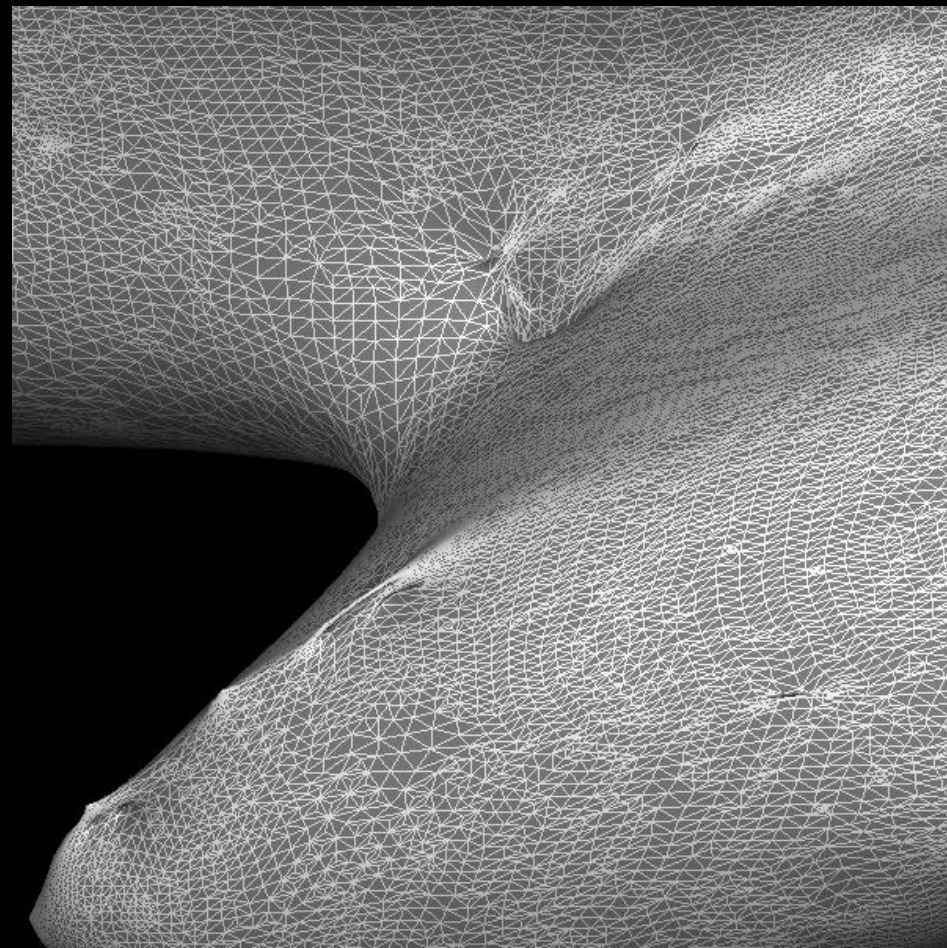
# Concepts, Ideas, Terms

Bug Report  
Reconstruction  
Surface Mesh  
Subcortical Mass  
\$SUBJECTS\_DIR  
Subject Id  
\$FREESURFER\_HOME  
MGZ File  
Conformed  
Control Point  
Topological Defect  
Intensity Normalization  
Volume-encoded Surface

Sulc  
Curv  
Thickness  
Atlas  
Sphere  
tkmedit  
tksurfer  
aseg  
aparc  
aparc+aseg  
aparc.a2005s  
White surface  
Pial surface

Manual Edit  
Segmentation  
Parcellation  
tkregister2  
register.dat  
--help  
Vertex  
FSGD  
Painting  
Skull Strip  
wmparc

# Manifold Surgery



BEFORE



AFTER



# Reconstruction Details

- Installation directory:  
\$FREESURFER\_HOME
- Unix command-line (Linux, MacOSX)
- File Formats
- Directory structure, naming conventions

# Individual Stages

## Volumetric Processing Stages (subjid/mri):

1. Motion Cor, Avg, Conform (orig.mgz)
2. Talairach transform computation
3. Non-uniform inorm (nu.mgz)
4. Intensity Normalization 1 (T1.mgz)
5. Skull Strip (brain.mgz)
6. EM Register (linear volumetric registration)
7. CA Intensity Normalization
8. CA Non-linear Volumetric Registration
9. CA Label (Volumetric Labeling) (aseg.mgz)
10. Intensity Normalization 2 (T1.mgz)
11. White matter segmentation (wm.mgz)
12. Edit WM With ASeg
13. Fill and cut (filled.mgz)

Green = Manual Intervention?

recon-all -help

## Surface Processing Stages (subjid/surf):

14. Tessellate (?h.orig)
15. Smooth1 (?h.smoothwm)
16. Inflate1 (?h.inflated)
17. QSphere (?h.qsphere)
18. Automatic Topology Fixer (?h.orig)
19. Euler Number
20. Smooth2
21. Inflate2
22. Final Surfs (?h.white,?h.pial)
23. Cortical Ribbon Mask
24. Spherical Morph
25. Spherical Registration
26. Spherical Registration
27. Map average curvature to subject
28. Cortical Parcellation (Labeling)
29. Cortical Parcellation Statistics
30. Cortical Parcellation mapped to ASeg

Note: ?h.orig means lh.orig or rh.orig

# Individual Stages

## Volumetric Processing Stages (subjid/mri):

1. Motion Cor, Avg, Conform (orig.mgz)
2. Talairach transform computation
3. Non-uniform inorm (nu.mgz)
4. Intensity Normalization 1 (T1.mgz)
5. Skull Strip (brain.mgz)
6. EM Register (linear volumetric registration)
7. CA Intensity Normalization
8. CA Non-linear Volumetric Registration
9. CA Label (Volumetric Labeling) (aseg.mgz)
10. Intensity Normalization 2 (T1.mgz)
11. White matter segmentation (wm.mgz)
12. Edit WM With ASeg
13. Fill and cut (filled.mgz)

Green = Manual Intervention?

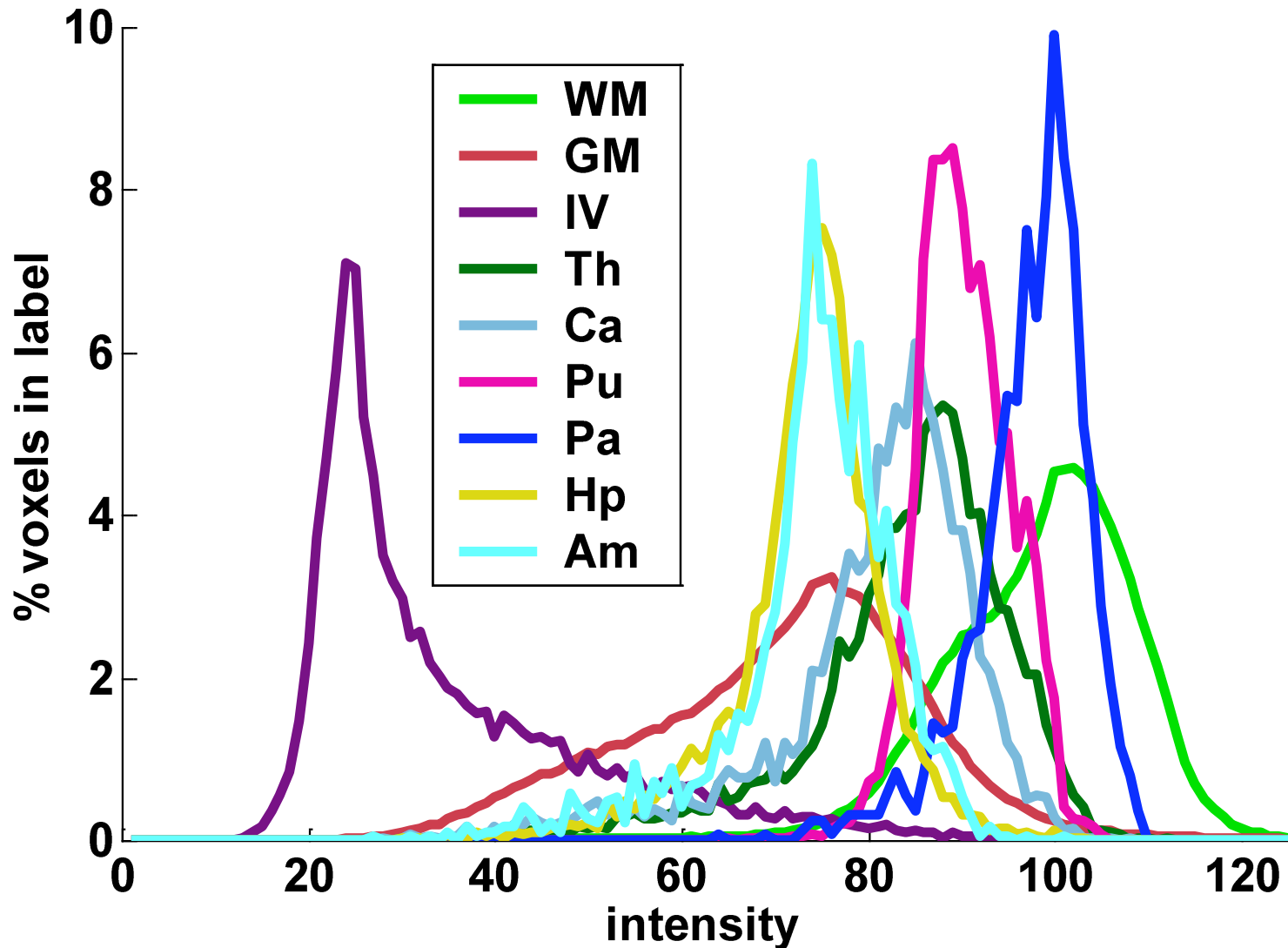
recon-all -help

## Surface Processing Stages (subjid/surf):

14. Tessellate (?h.orig)
15. Smooth1 (?h.smoothwm)
16. Inflate1 (?h.inflated)
17. QSphere (?h.qsphere)
18. Automatic Topology Fixer (?h.orig)
19. Euler Number
20. Smooth2
21. Inflate2
22. Final Surfs (?h.white,?h.pial)
23. Cortical Ribbon Mask
24. Spherical Morph
25. Spherical Registration
26. Spherical Registration
27. Map average curvature to subject
28. Cortical Parcellation (Labeling)
29. Cortical Parcellation Statistics
30. Cortical Parcellation mapped to ASeg

Note: ?h.orig means lh.orig or rh.orig

# 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

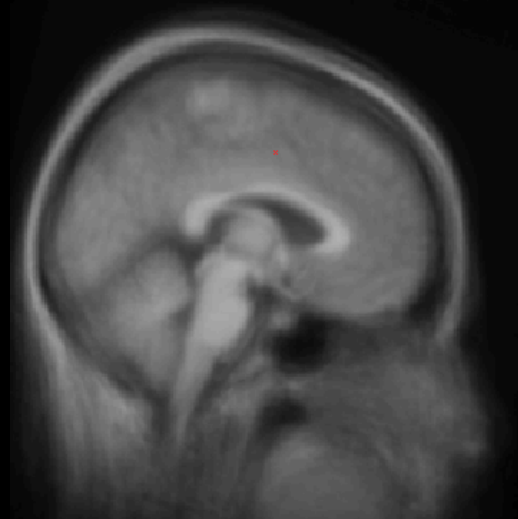
**Typical solution:** align image intensities and hope this results in alignment of function/structure as well.

# Mean-squared Error Registration: Low Quality Data

$I(r)$



$T(r)$



$I(Lr)$

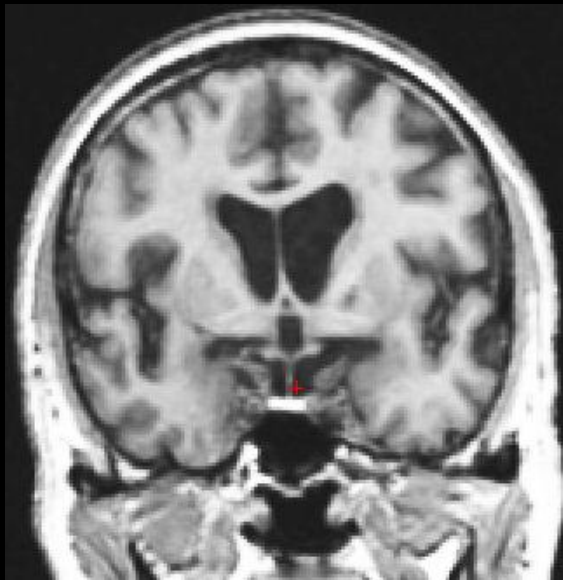




# Mean-squared Error Registration

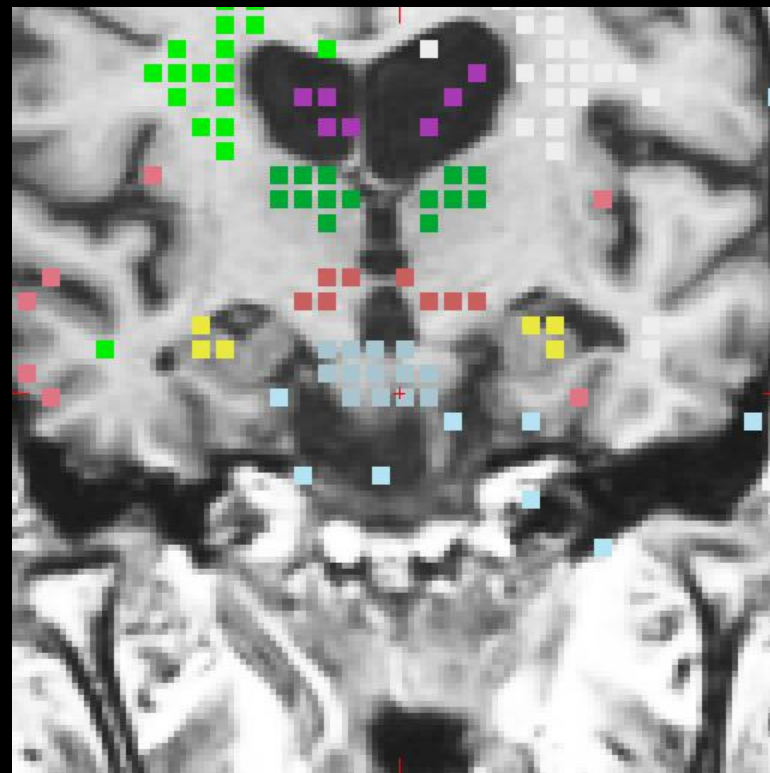
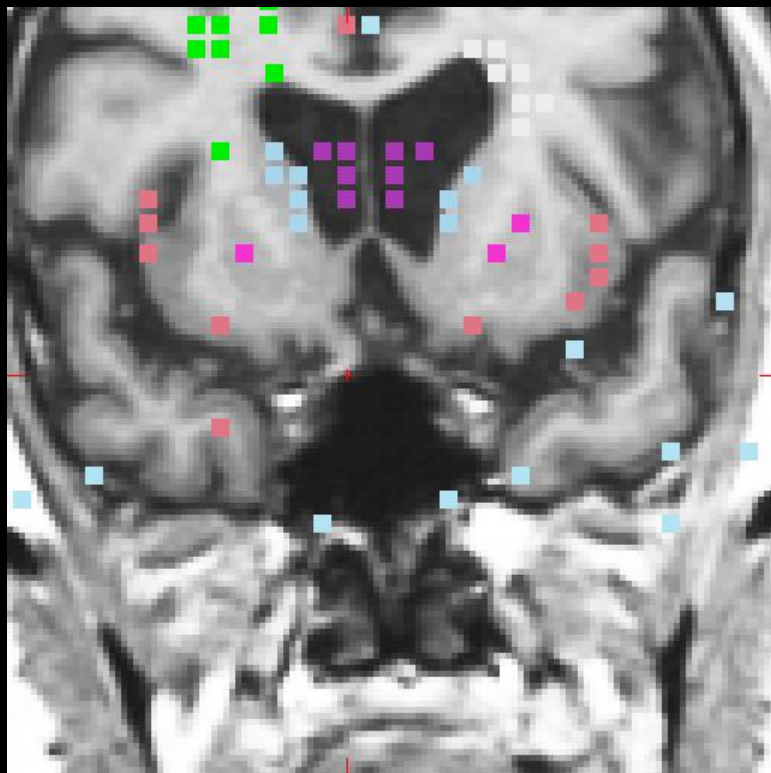
Anatomy is variable, particularly in cases of pathology\*

→ *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.

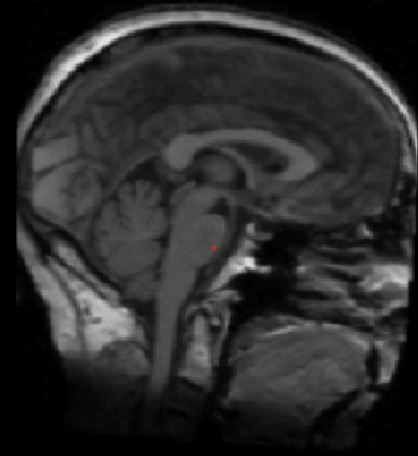
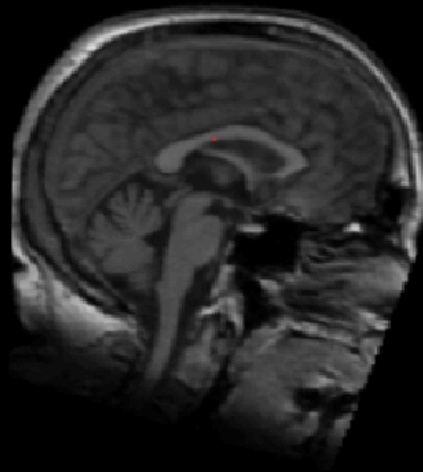
# Atlas Points After Registration



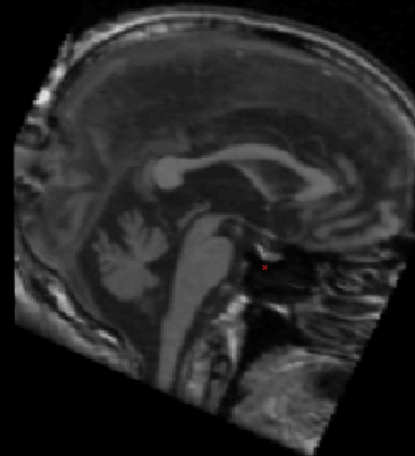
- |                     |                  |                     |
|---------------------|------------------|---------------------|
| ● Cerebellar cortex | ● LH cerebral WM | ● Cerebral cortex   |
| ● Cerebellar WM     | ● Hippocampus    | ● Misc.             |
| ● 4th ventricle     | ● LH pallidum 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

# Segmentation-based Registration: Results

Normal

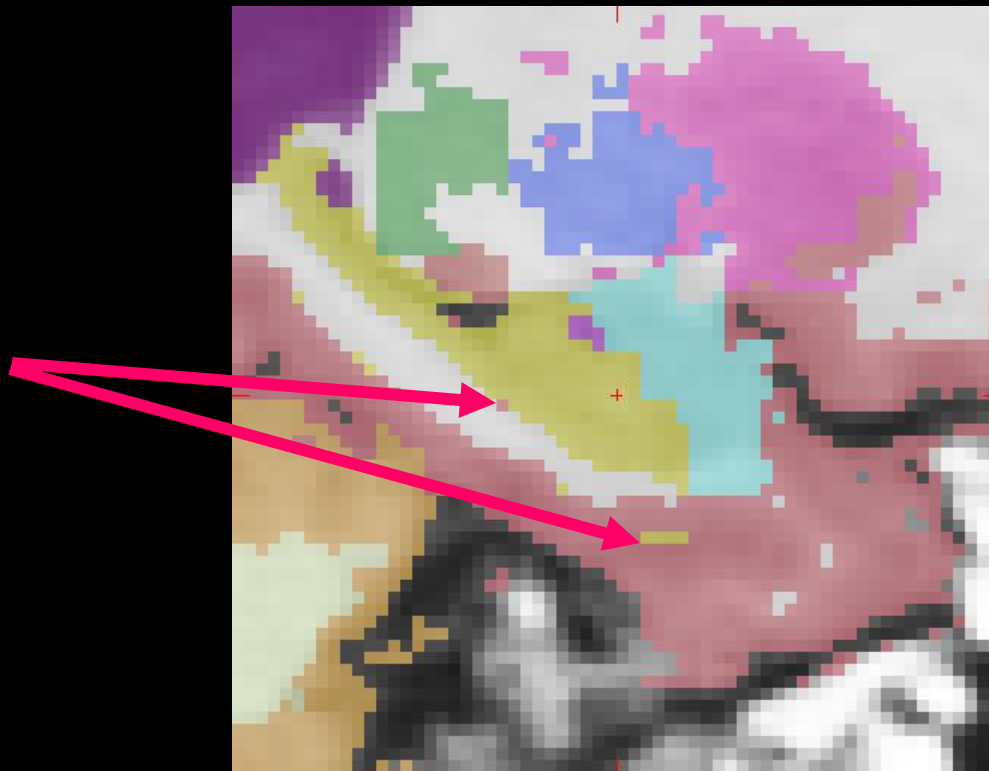


AD



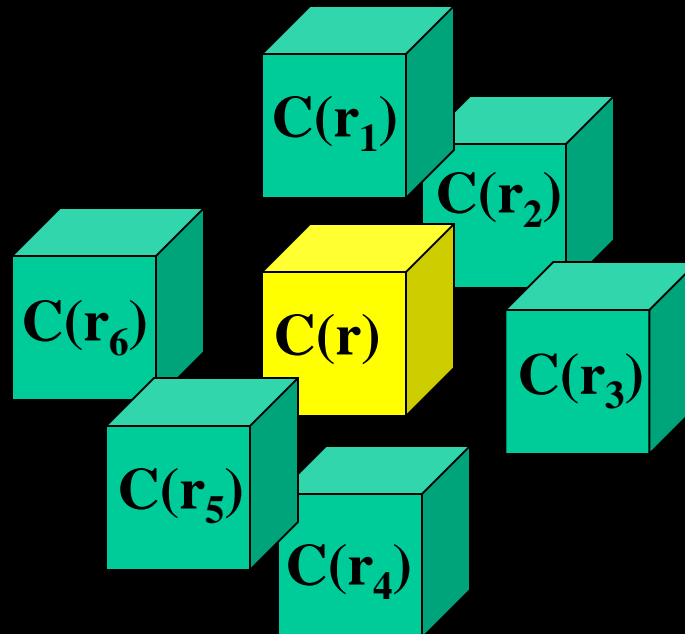
# Markov Random Field: Motivation

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



# Segmentation: MRF

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



# Segmentation: MRF



Preliminary Segmentation