Introduction to FreeSurfer

http://surfer.nmr.mgh.harvard.edu

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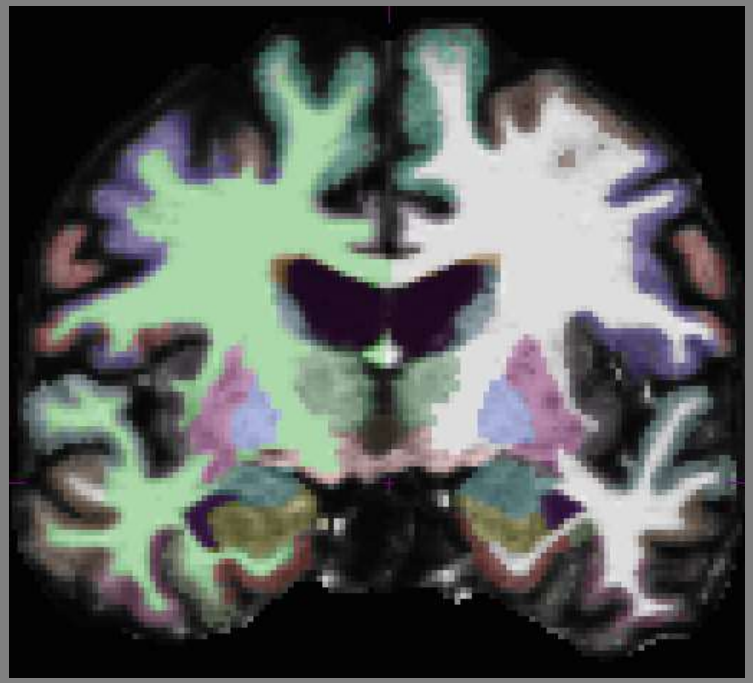


Cortical Surface Reconstruction

FreeSurfer creates computerized models of the brain from MRI data.

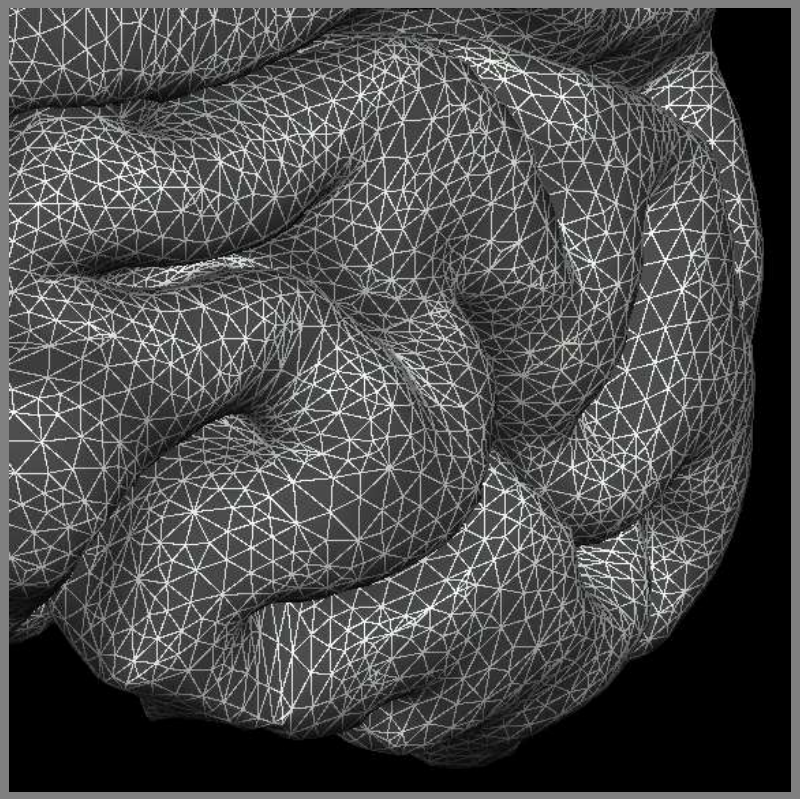
Input:

- T1-weighted (MPRAGE,SPGR)
- $1mm^3$ resolution

Cortical Surface Reconstruction

- Finds white/gray boundary – wm surface
- Finds pial/CSF boundary – pial surface
- To “Find” uses:
  - Intensity information, spatial location, geometric structure
  - Tessellation, neighbors, talairach coordinates
- Subcortical Segmentation

Surface Model



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

Cortical Reconstruction Goals

- Geometrically Accurate surfaces
  - Accurately follow the boundaries seen on the scan for each of your individual subjects
- Topologically Correct surfaces
  - Each surface is a 2-D continuous, non self-intersecting sheet and can be inflated into a perfect sphere
- Surfaces are only as good as your scan.

MR Anatomy Caveats

- Dependent on data quality
  - Contrast to noise
  - Signal to noise
  - Voxel resolution
- MR Artifacts
  - MR susceptibility
  - MR distortions
- Variations in MR tissue parameters across regions of the brain are altered in different populations

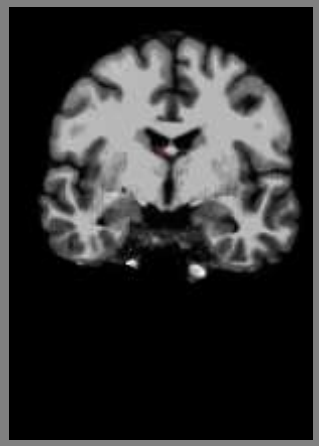
FreeSurfer Output

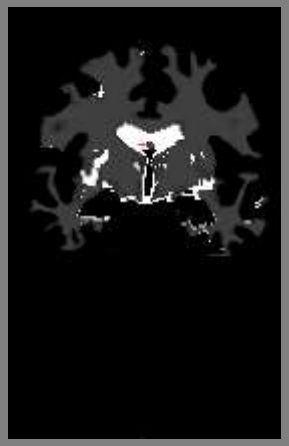
- Volumes
- Surfaces
- Surface Overlays
- ROI Summaries

Volumes


orig.mgz


T1.mgz


brainmask.mgz


wm.mgz


filled.mgz
Subcortical Mass

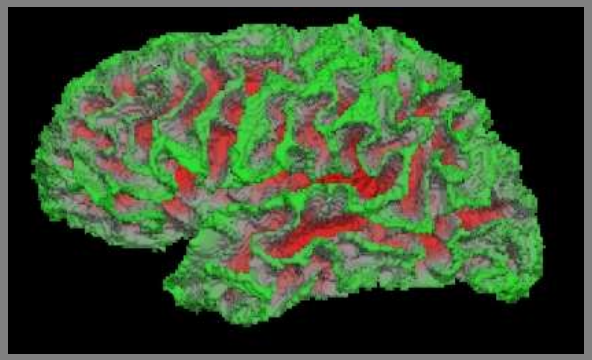

aseg.mgz


aparc+aseg.mgz

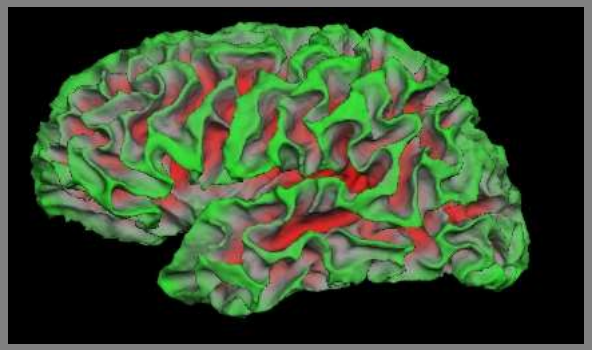
- $SUBJECTS_DIR/bert/mri
- All “Conformed” 256^3, 1mm

Volume Viewer:
tkmedit

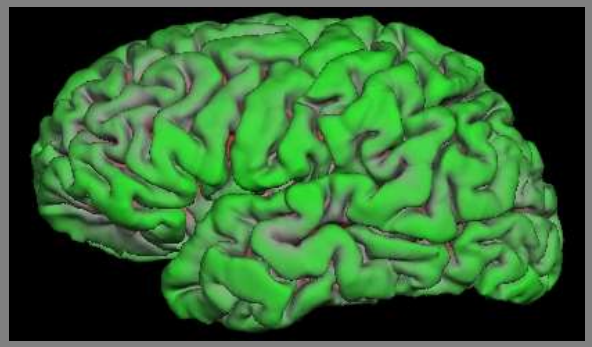
Surfaces



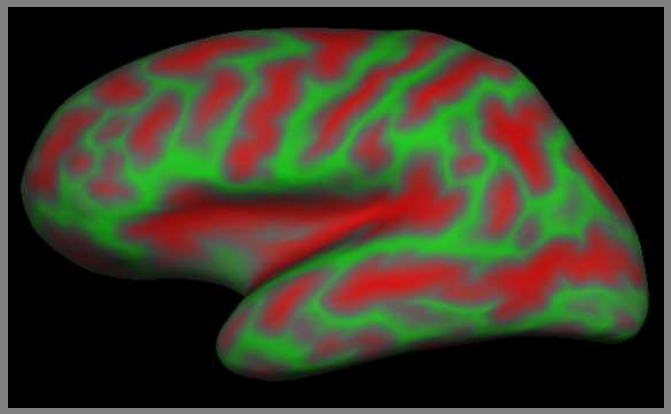
orig



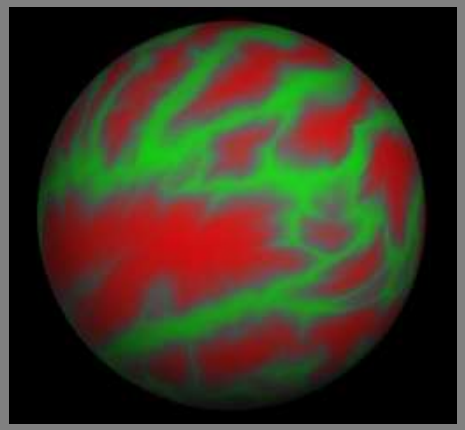
white



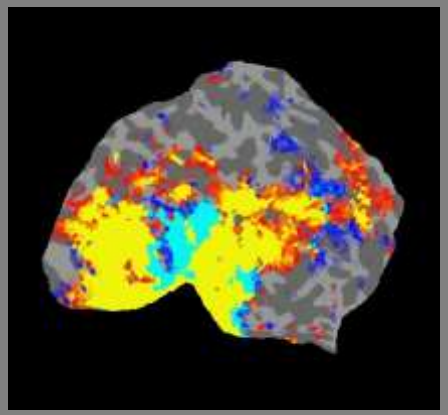
pial



inflated



sphere,sphere.reg

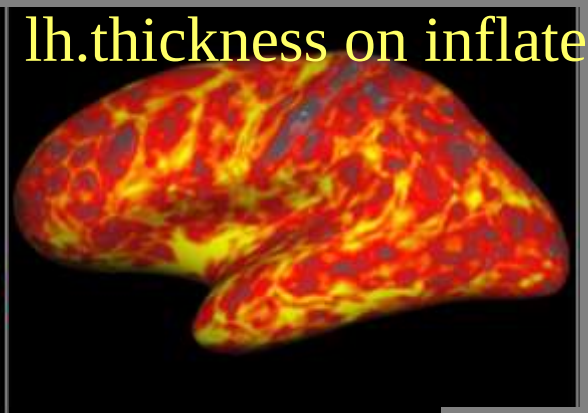


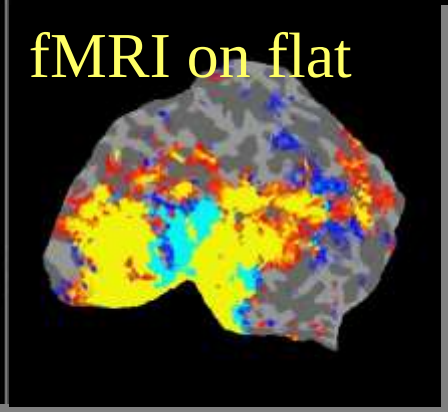
flat

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

Surface Viewer: tksurfer

Surface Overlays





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

ROI Summaries

aseg.stats

- volumes of subcortical structures (mm^3)

aparc.stats

- thickness of cortical parcellation structures (mm)
- total white matter volume (mm^3)
- number of vertices in cortex
- surface area of cortex (mm^2)

ROI Summaries: Make Your Own

yourROI.label

- Draw your own surface label
- use mris_anatomical_stats to get data

mris_volume

- Total volume within a surface you specify

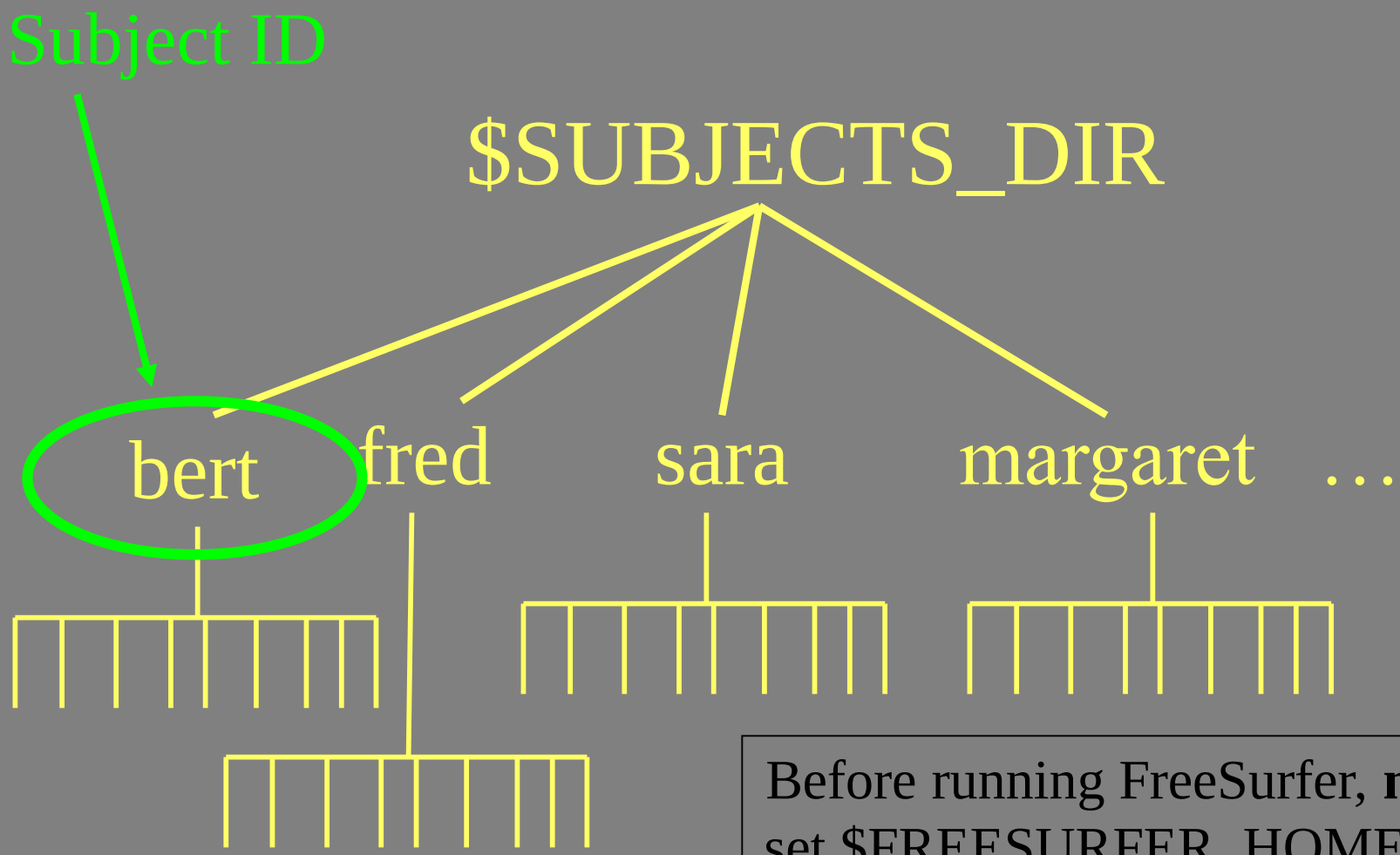
mris_wm_volume

- Total volume within white surface ignoring non-wm voxels in aseg.mgz

Reconstruction Environment

- Installation directory:
  $FREESURFER_HOME
- Set-up Environmental Variables
- Unix command-line (Linux, MacOSX)
- Directory structure, naming conventions
- File Formats

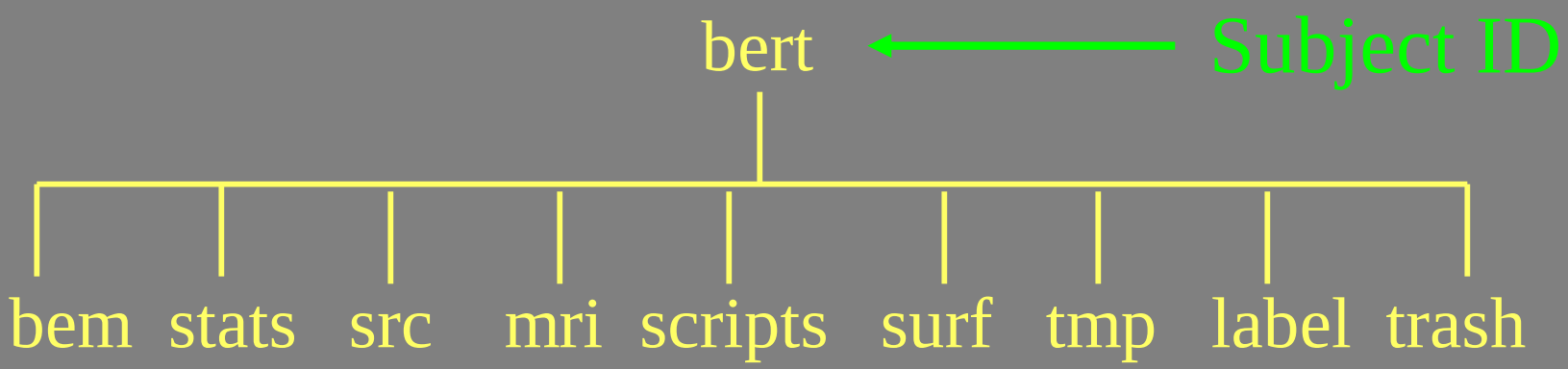
Set-up Environmental Variables



Before running FreeSurfer, **must** set $FREESURFER_HOME and $SUBJECTS_DIR

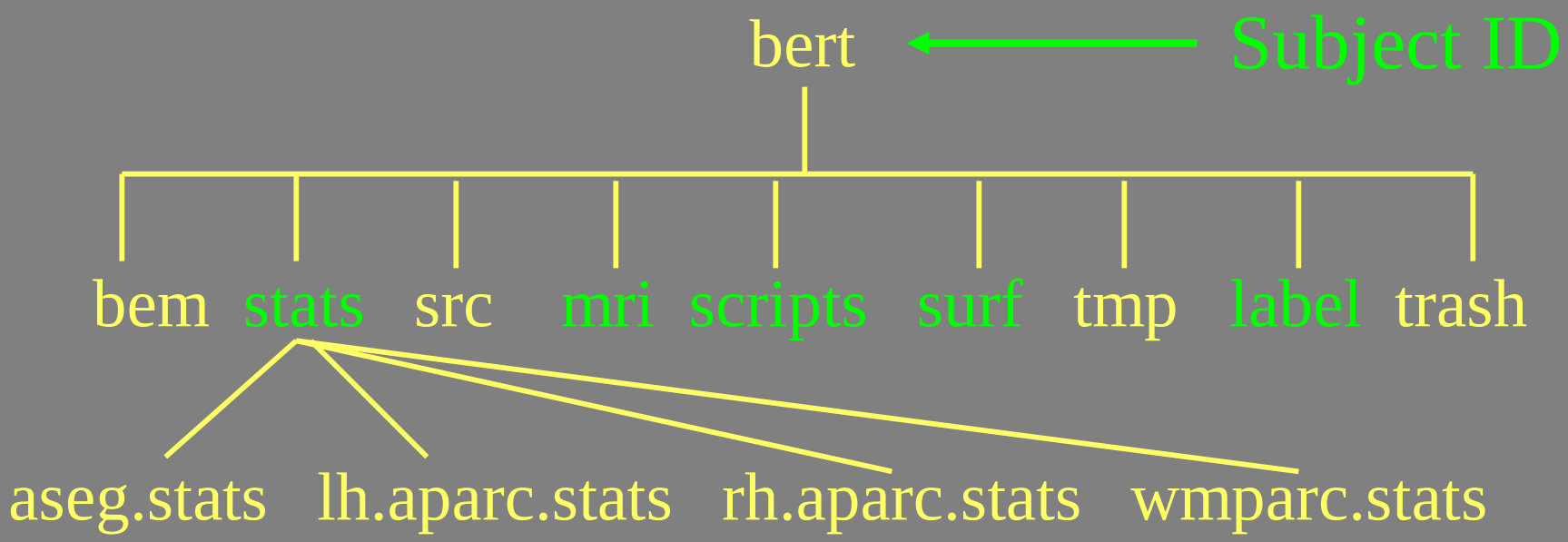
FreeSurfer Directory Tree

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

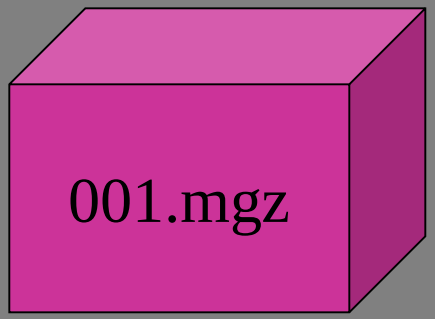


FreeSurfer Directory Tree

Directories used often are in green.



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

- FreeSurfer can read/write:
  NIFTI, Analyze, MINC
  Careful with NIFTI! (32k limit)

- FreeSurfer can read:
  DICOM, Siemens IMA, AFNI

Other FreeSurfer File Formats

Unique to FreeSurfer

- Surface: lh.white, lh.pial, lh.orig
- Curv: lh.curv, lh.sulc, lh.thickness
- Annotation: lh.aparc.annot
- Label: lh.pericalcarine.label

Starting the Reconstruction Process

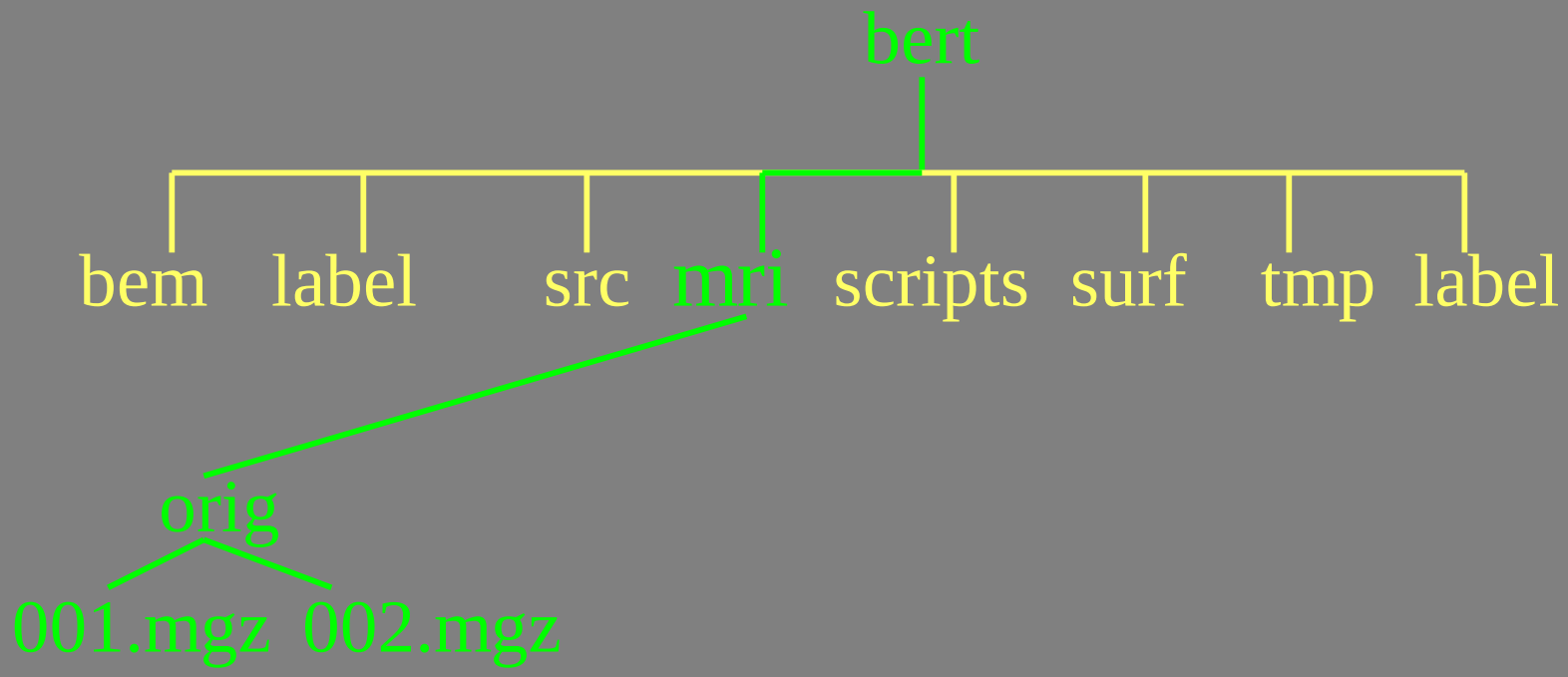
Before running FreeSurfer, **must** set $FREESURFER_HOME and $SUBJECTS_DIR

recon-all -i /path/to/your/raw/data1 **-i** /path/to/your/raw/data2 **-all -s** subject_id

- This will create the subject directory ‘subject_id’ in your $SUBJECTS_DIR and convert your 2 raw acquisitions to mgz and use them as input for the ‘-all’ command.

Alternative: Add Your Data

- cd $SUBJECTS_DIR
- mkdir –p bert/mri/orig
- mri_convert yourdicom.dcm bert/mri/orig/001.mgz
- mri_convert yourdicom.dcm bert/mri/orig/002.mgz
- recon-all –all –s bert



Individual Steps

Volumetric Processing Stages (subjid/mri):

1. Motion Cor, Avg, Conform (orig.mgz)
2. Non-uniform inorm (nu.mgz)
3. Talairach transform computation (talairach/talairach.xfm)
4. Intensity Normalization 1 (T1.mgz)
5. Skull Strip (brainmask.mgz)

6. EM Register (linear volumetric registration)
7. CA Intensity Normalization (norm.mgz)
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)

Blue = Manual Intervention

Surface Processing Stages (subjid/surf):

14. Tessellate (?h.orig.nofix)
15. Smooth1
16. Inflate1
17. QSphere (?h.qsqhere)
18. Automatic Topology Fixer (?h.orig)
19. Final Surfs (?h.white ?h.pial ?.thickness)
20. Smooth2 (?h.smoothwm)
21. Inflate2 (?h.inflated)
22. Aseg Statistics (stats/aseg.stats)
23. Cortical Ribbon Mask (?h.ribbon.mgz)

24. Spherical Morph
25. Spherical Registration (?h.sphere.reg)
26. Map average curvature to subject
27. Cortical Parcellation (Labeling)
28. Cortical Parcellation Statistics
29. Cortical Parcellation mapped to Aseg
30. White Matter Parcellation (wmparc.mgz)

recon-all -help

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

Reconstrution Stages

recon-all is broken into three stages

- autorecon1
- autorecon2
- autorecon3

-autorecon1

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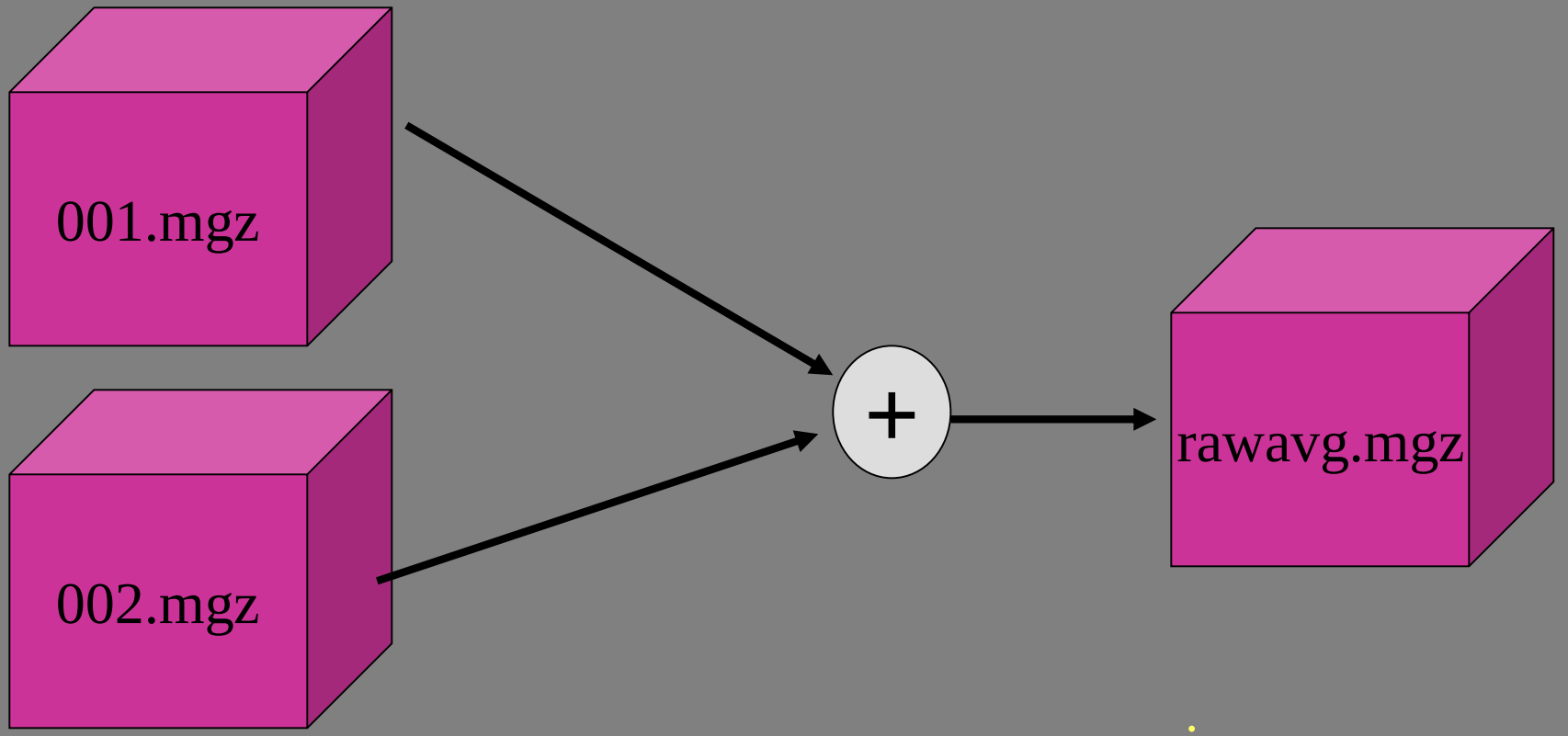
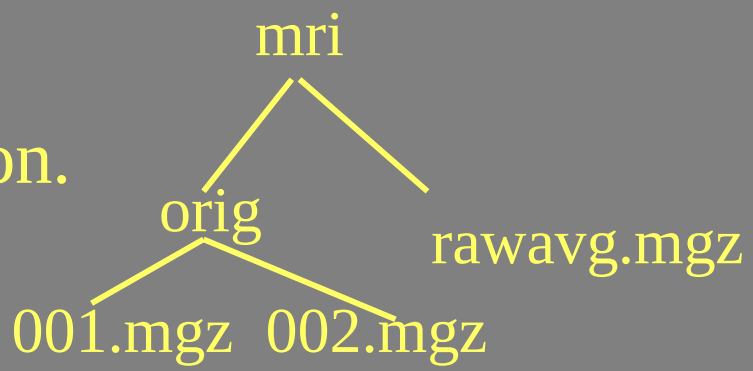
recon-all -help

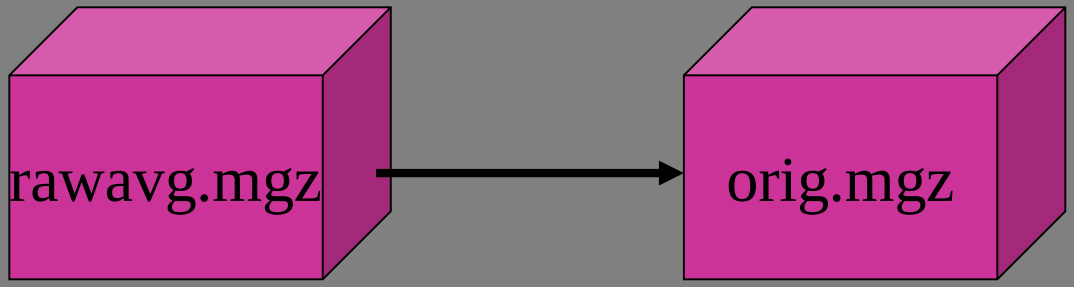
Motion Correction and Averaging

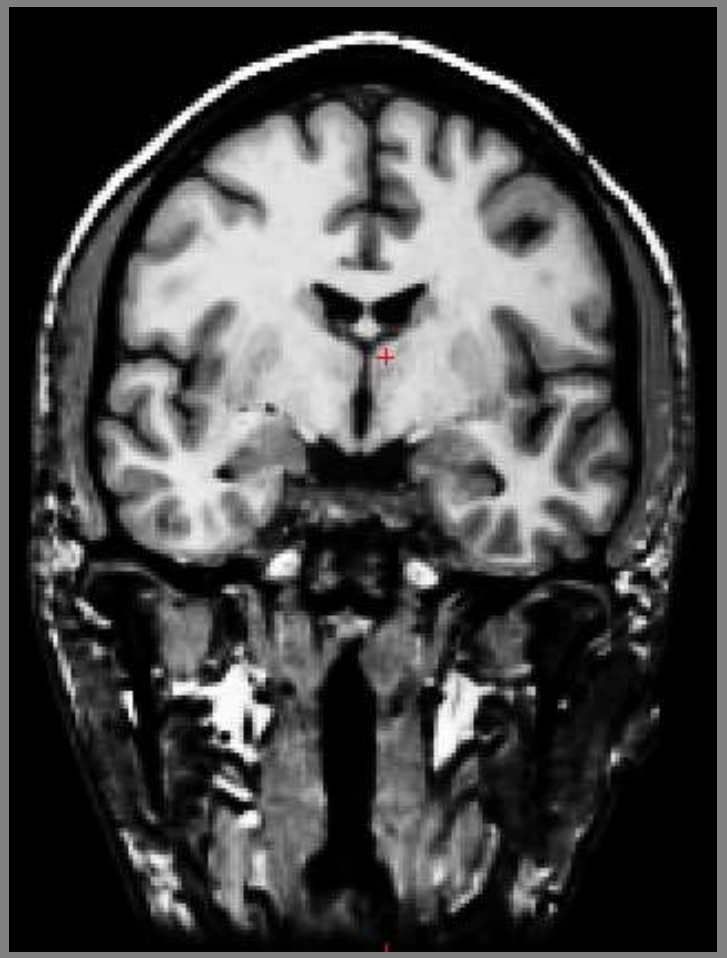


Does not change native resolution.



Conform





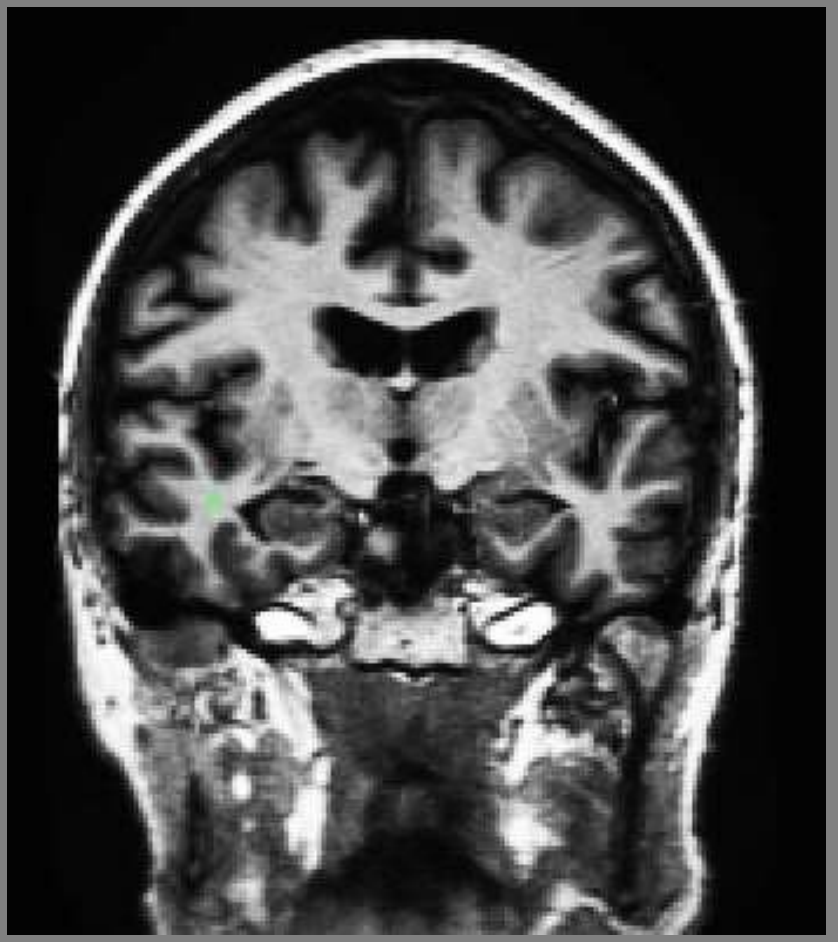
orig Volume

Changes to 256^3, 1mm^3
All volumes will be conformed.

mri_convert -conform

Non-Uniform Intensity Correction

- Uses MNI tool
- Removes B1 bias field

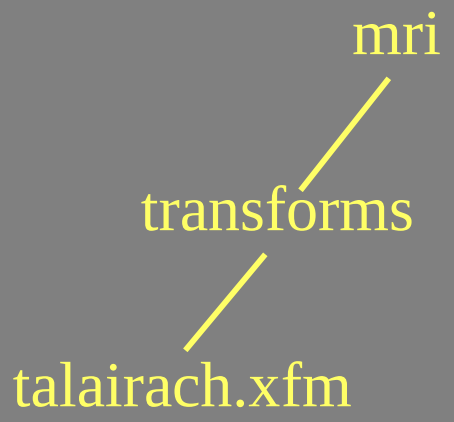


nu Volume

mri_nu_correct.mni

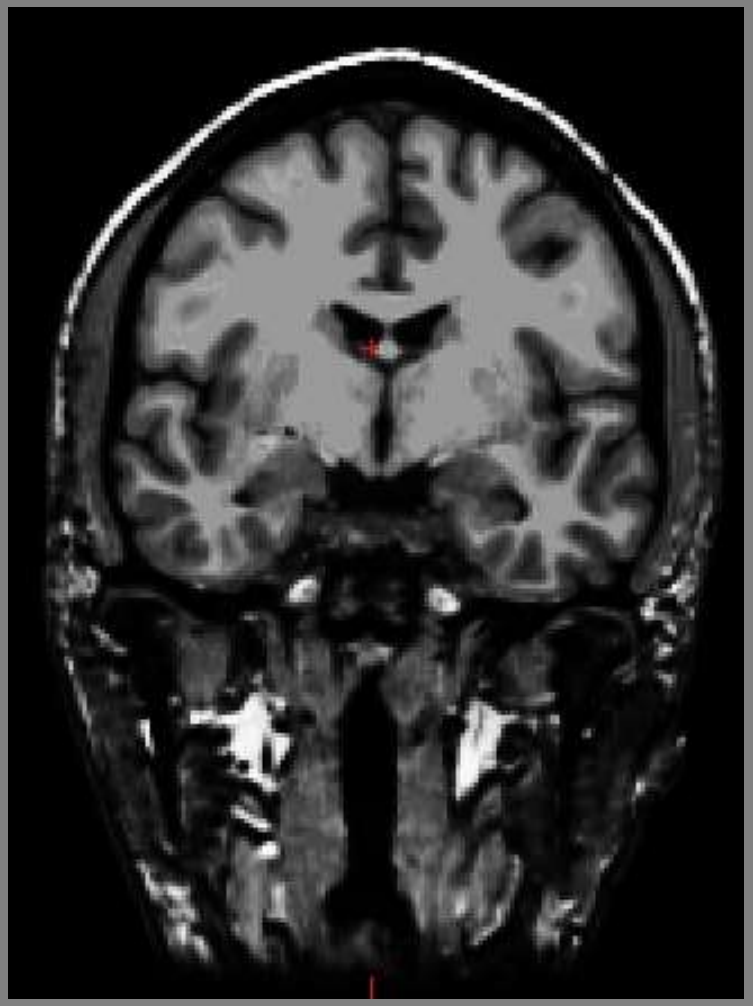
Talairach Transform

- Computes 12 DOF transform matrix
- Does NOT resample
- MNI305 template
- Used to help find structures (eg, CC)
- Can also be used to localize functional activation
- mri/transforms/talairach.xfm



Intensity Normalization

- Presegmentation (T1.mgz)
  - All WM = 110 intensity
  - Pre- and Post-Skull Strip

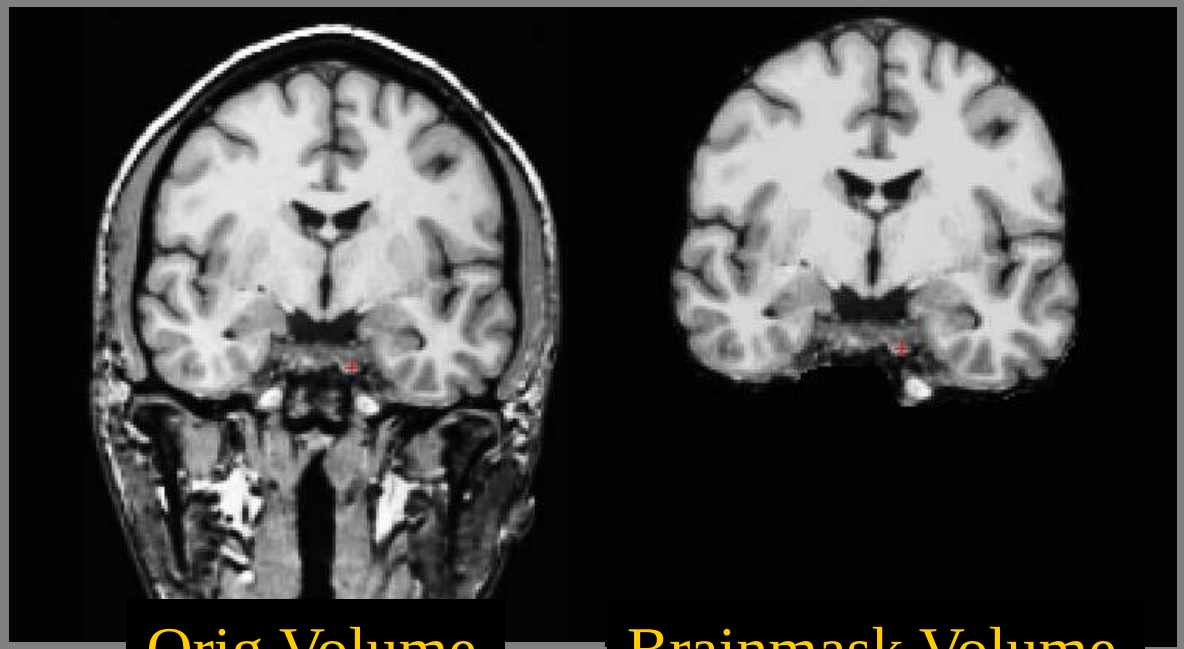


T1 Volume

mri_normalize

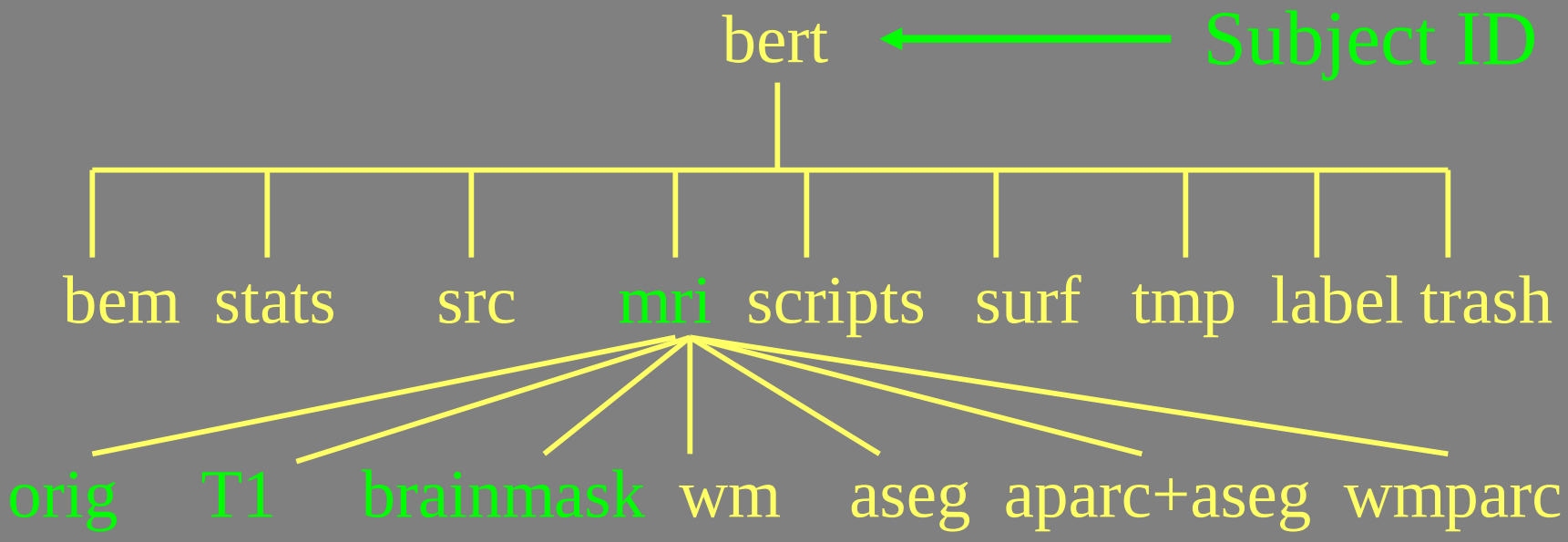
Skull Strip

- Removes all non-brain
  - Skull, Eyes, Neck, Dura
- brainmask.mgz



FreeSurfer Directory Tree

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



-autorecon2

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9. CA Label (Volumetric Labeling) (aseg.mgz)
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Surface Processing Stages (subjid/surf):

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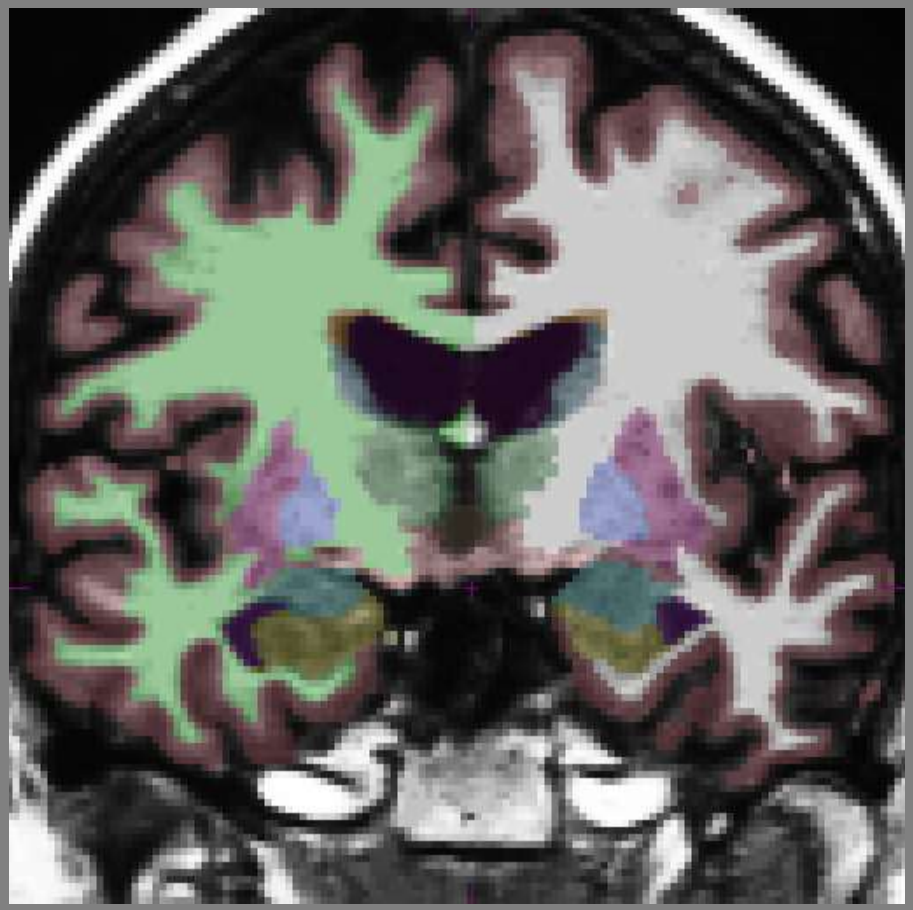
recon-all -help

Note: lh processed completely first, then rh.

-subcortseg

-autorecon2

Automatic Volume Labeling



ASeg Volume

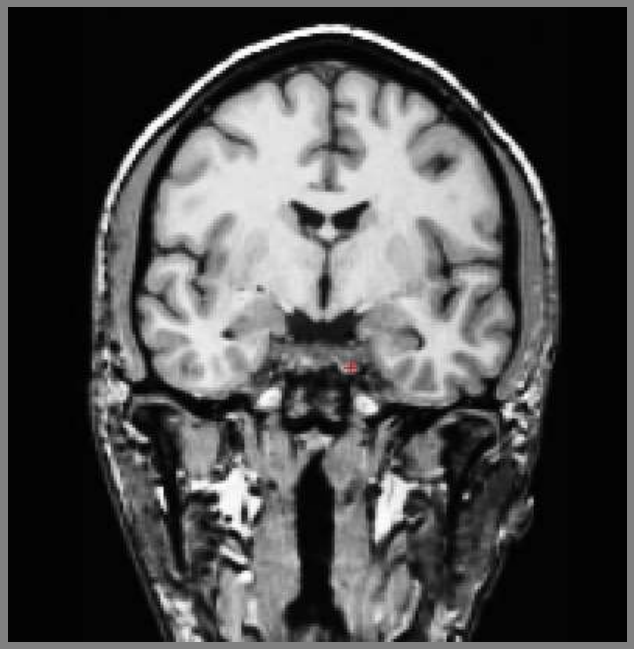
- Used to determine volumes of subcortical structures
- Used to fill in subcortical structures for creating subcortical mass
- aseg.mgz

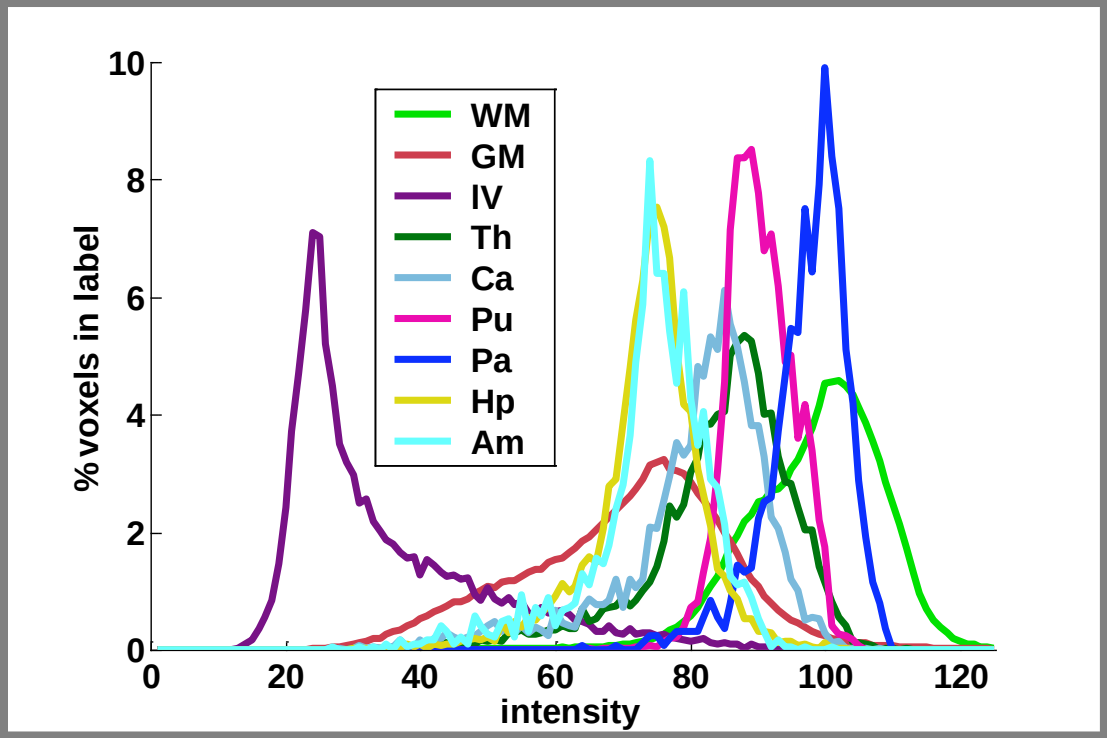
steps 6-9, 22

Atlas: RB_all_2007-08-08

-subcortseg -autorecon2

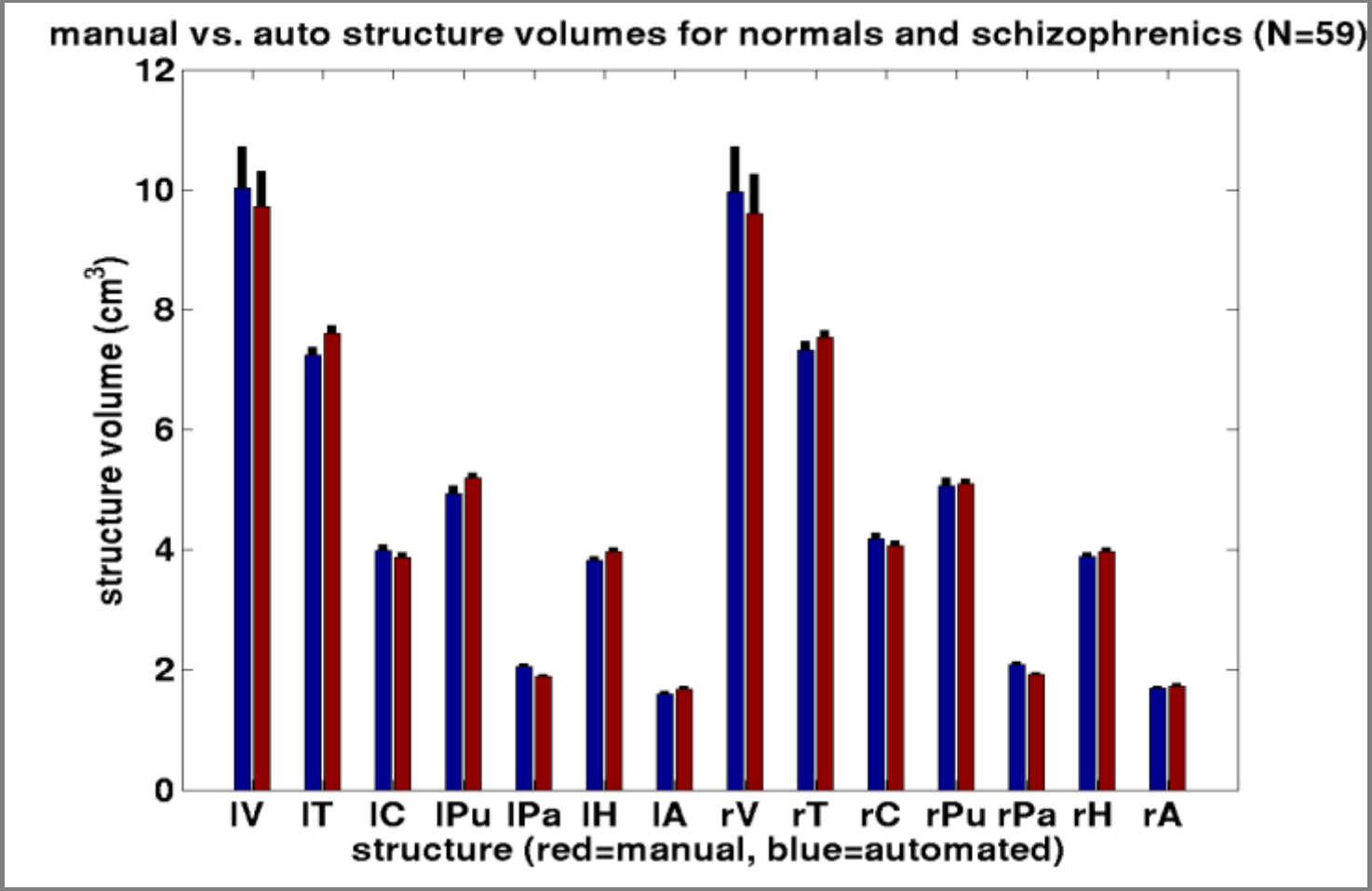
Volume-based Labeling





Labeling is determined by location and intensity.

Validation of Volume Labeling *



Manual labeling done by Center for Morphometric Analysis (CMA)

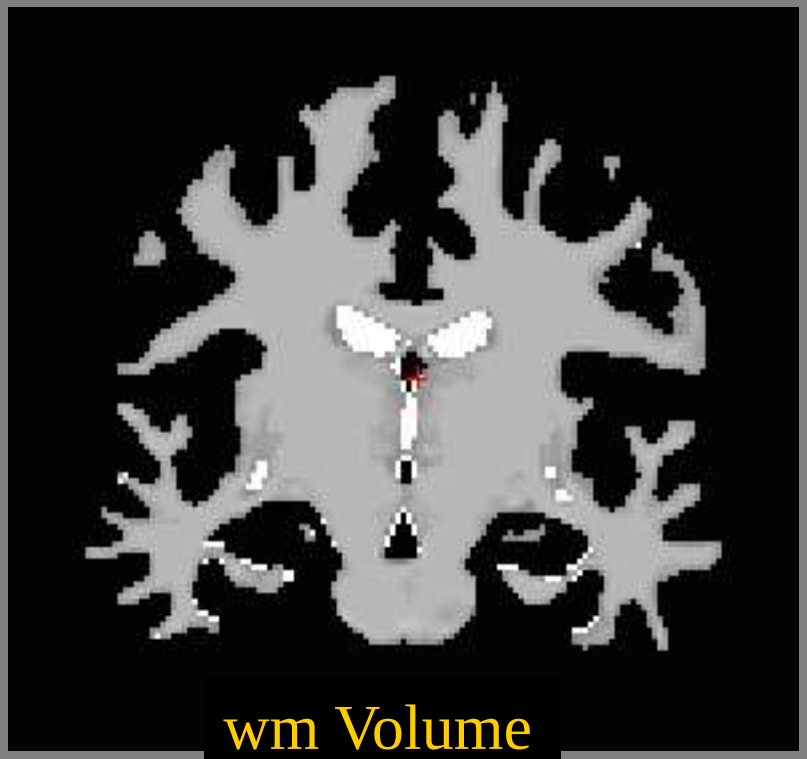
*Thanks to Drs Larry Seidman and Jill Goldstein for providing this data.

Find “Subcortical Mass”

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

White Matter Segmentation

- Separates white matter from everything else
- “Fills in” subcortical structures
- Cerebellum removed, brain stem still there



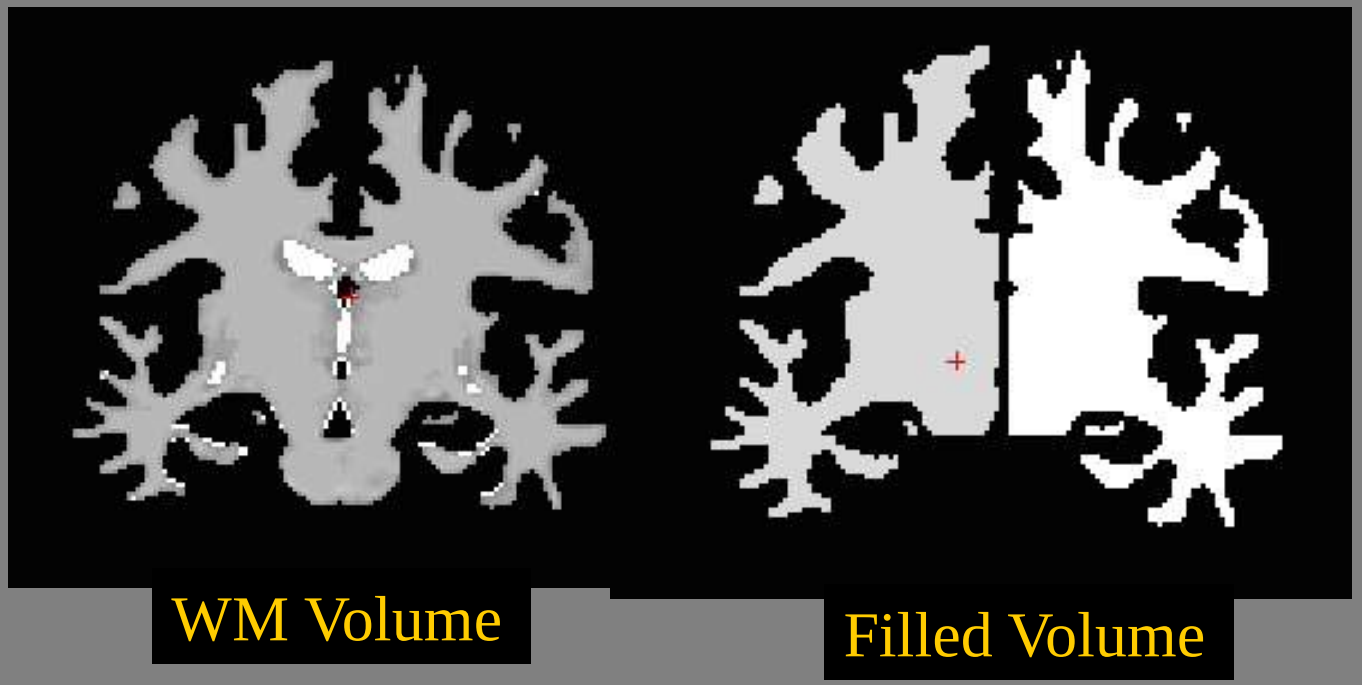
mri_segment

mri_edit_wm_with_aseg

mri_pretess

Fill and Cut (Subcortical Mass)

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



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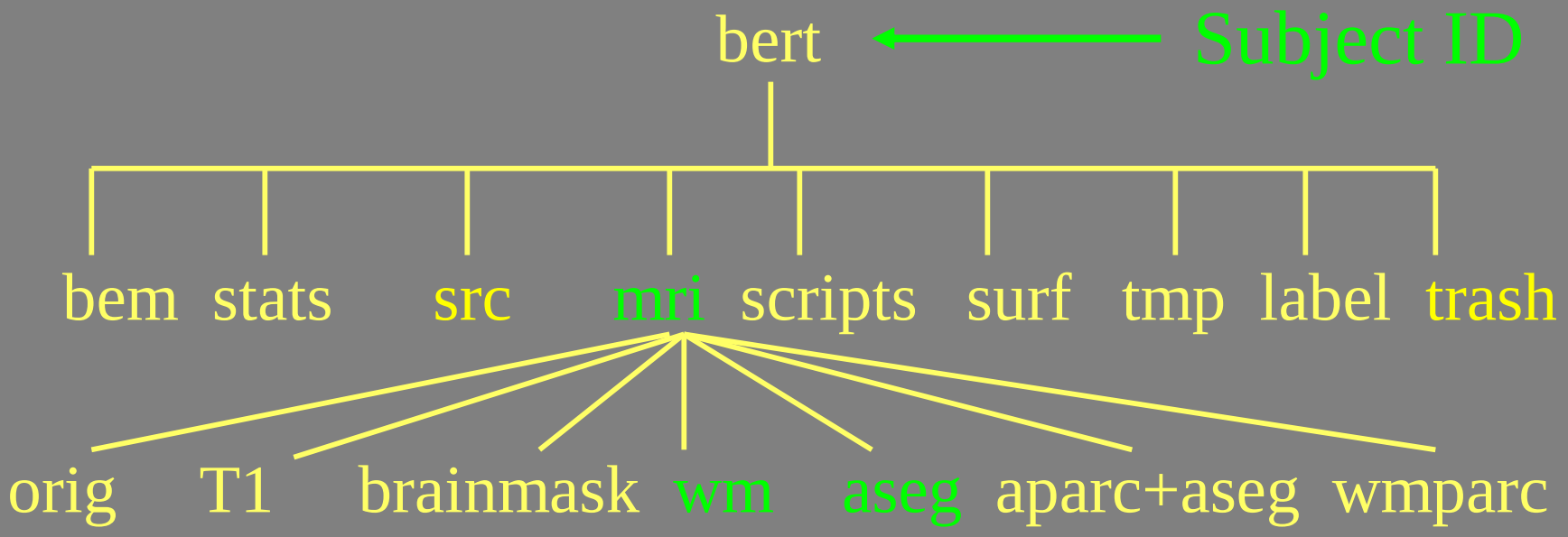
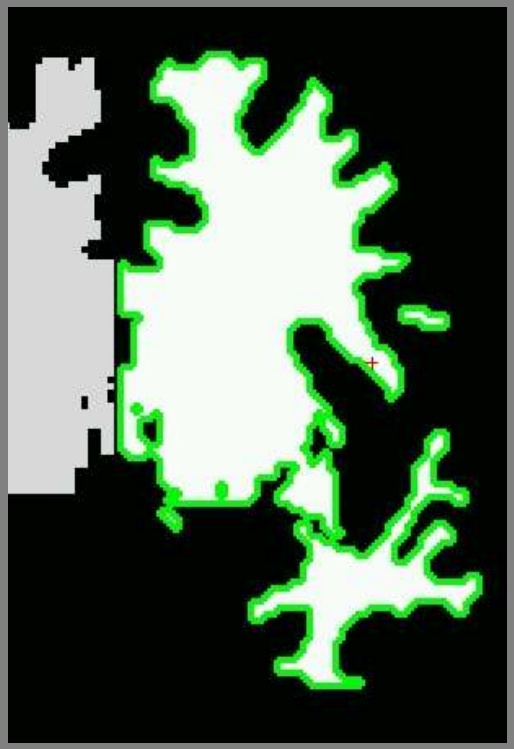
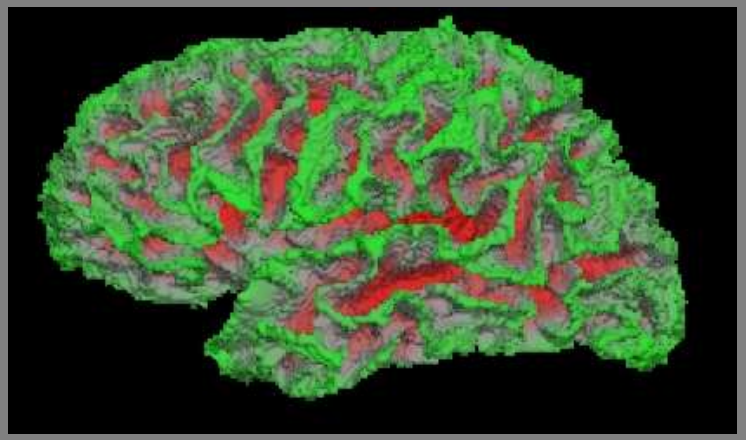
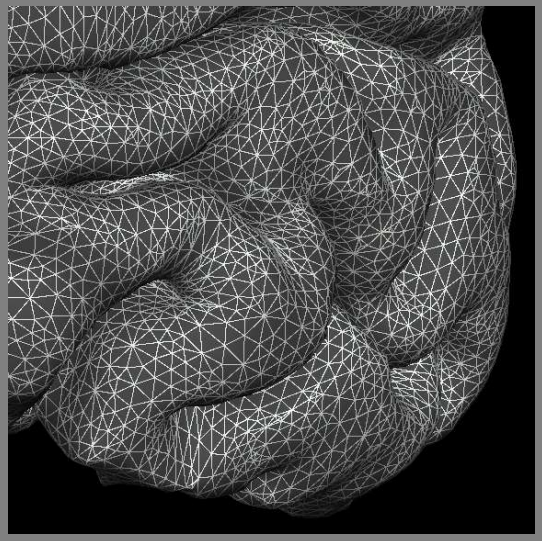


Tessellation



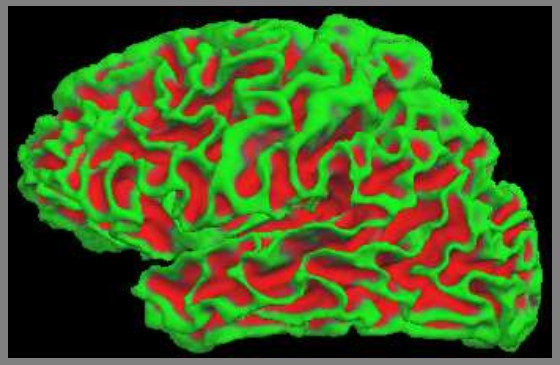


orig surface
surf/lh.orig
surf/rh.orig

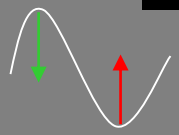


- Mosaic of triangles (“tessellation”)
- Errors: Donut holes, handles
  - Subsequently fixed by the automatic topology fixer

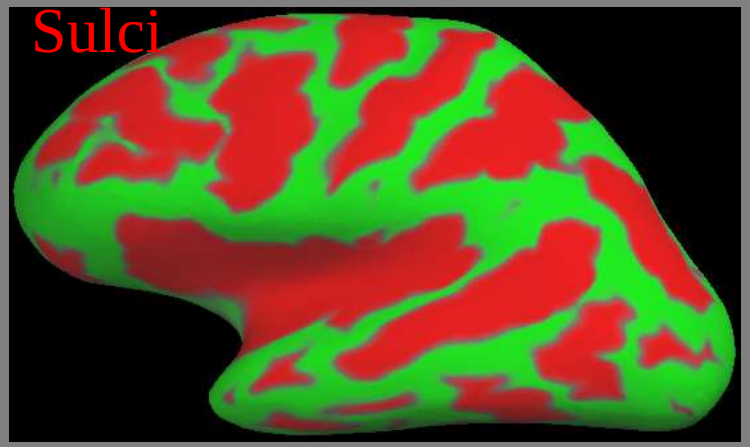
Inflation: Visualization

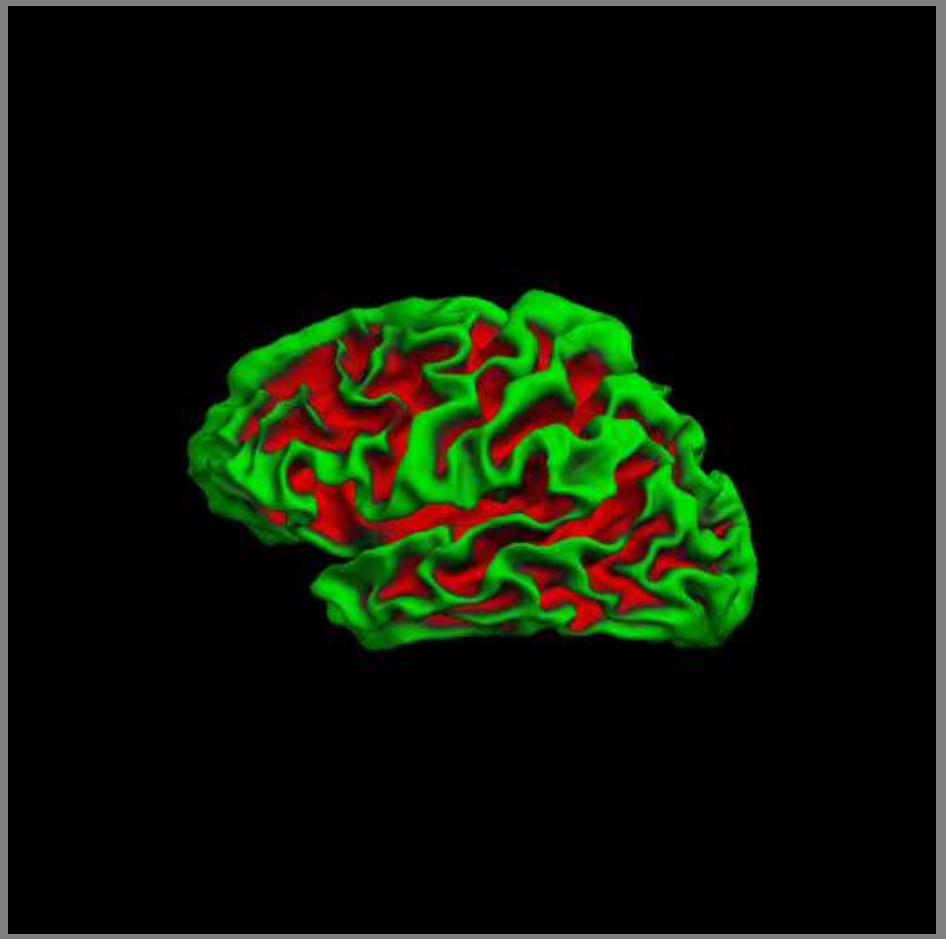


Gyri



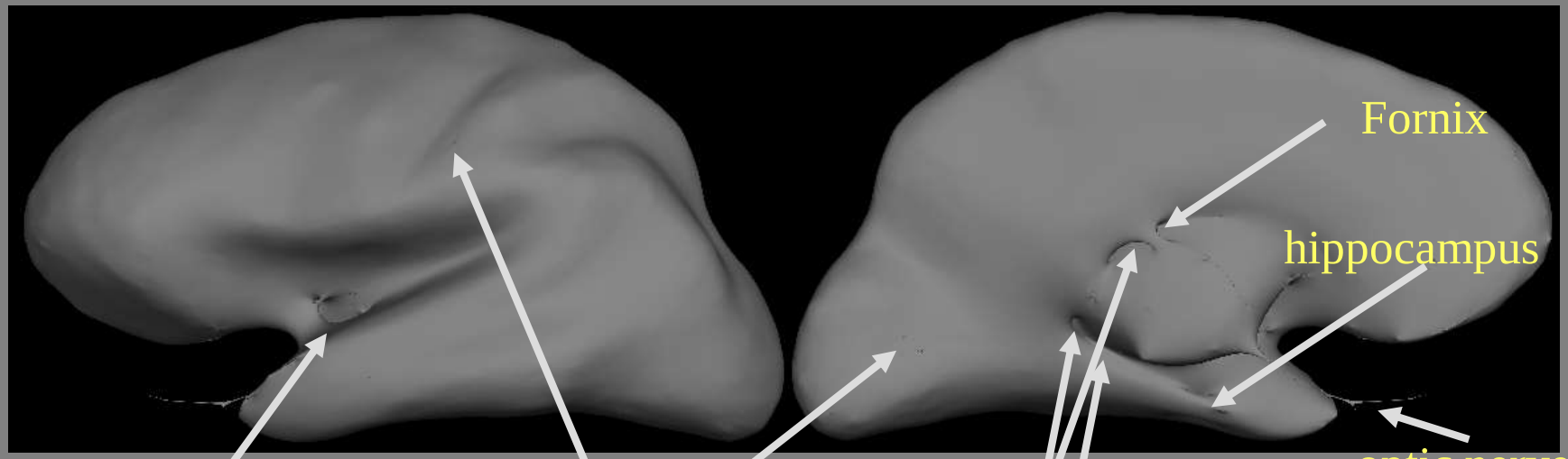
Sulci

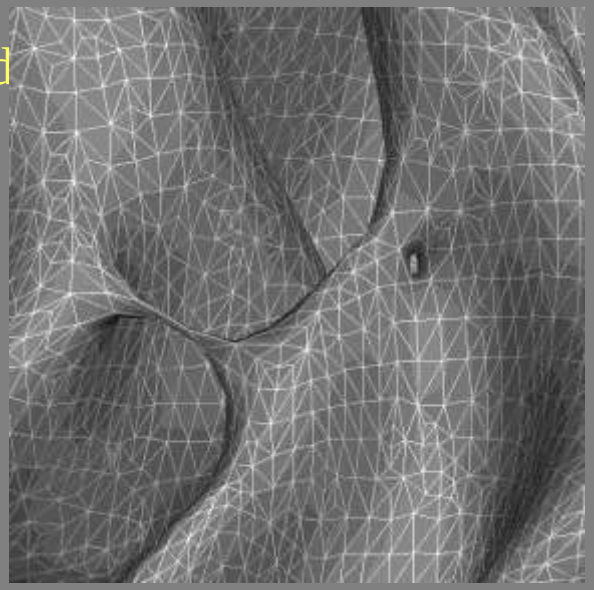




Dale and Sereno, 1993; Dale et al., Dale et al., 1999; Fischl et al., 1999; Fischl et al., 2000; Fischl et al., 2001

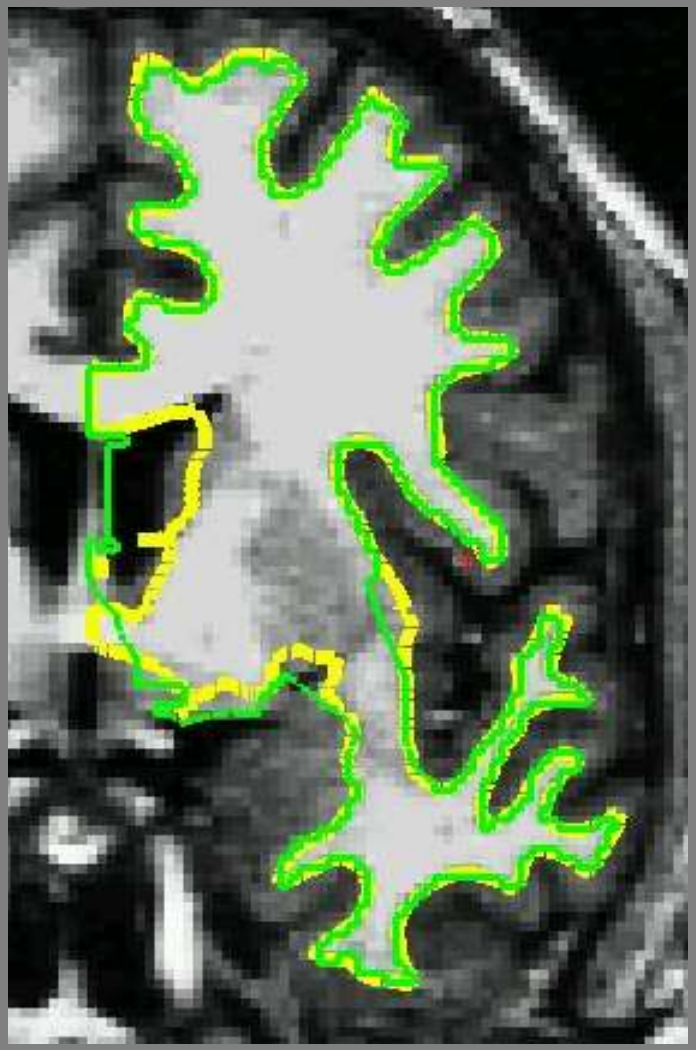
Automatic Topology Fixer



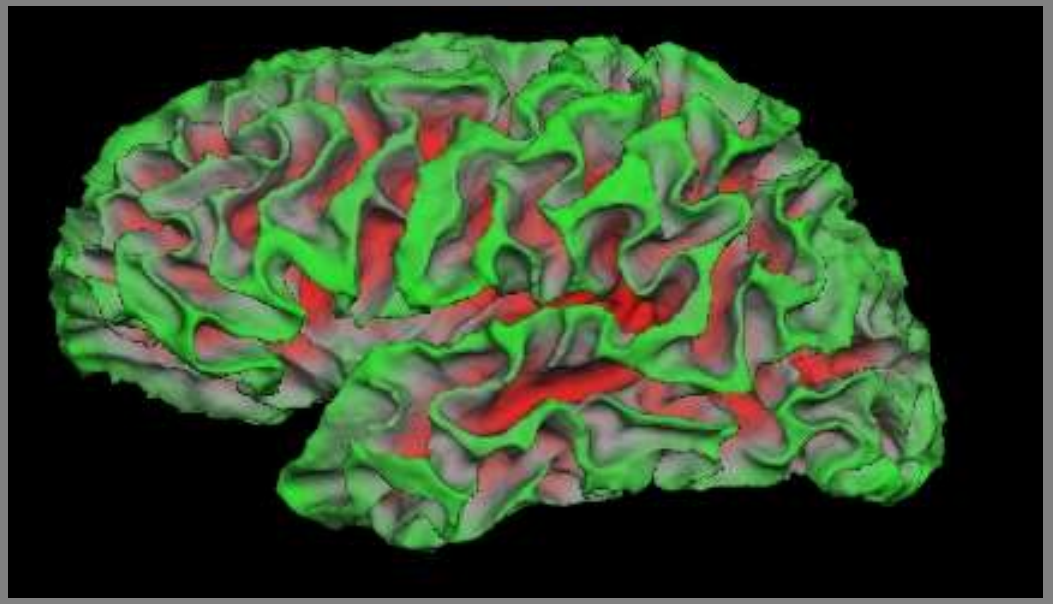


- Holes
- Handles
- Automatically Fixed

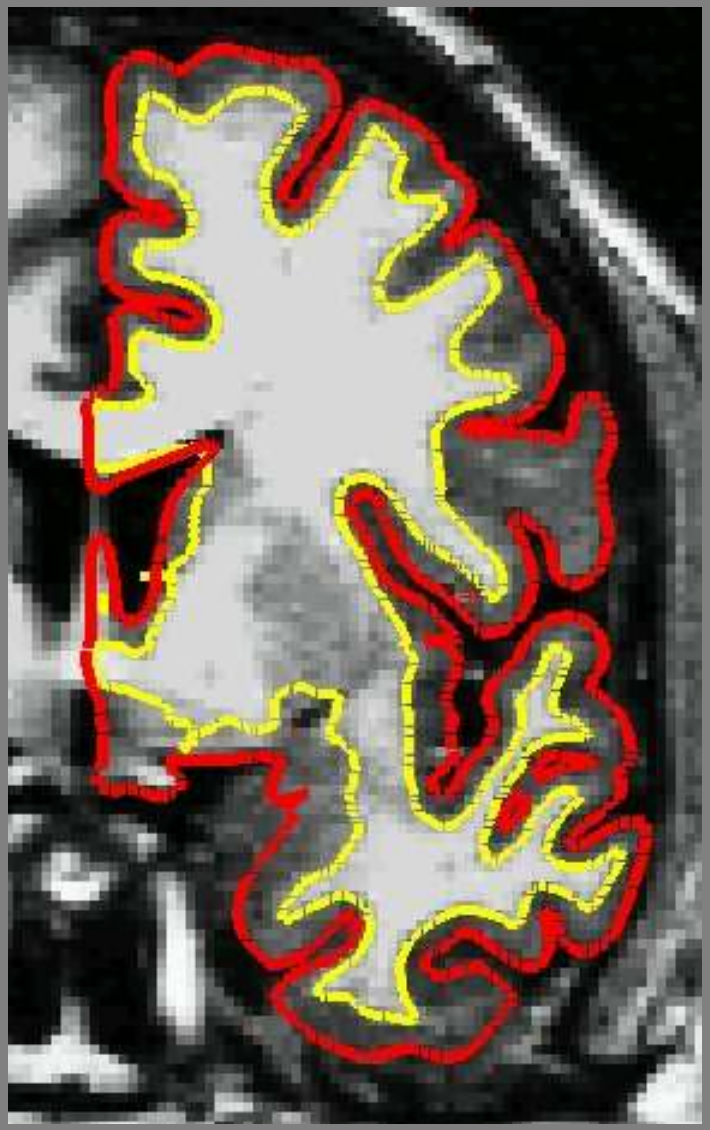
White Matter Surface



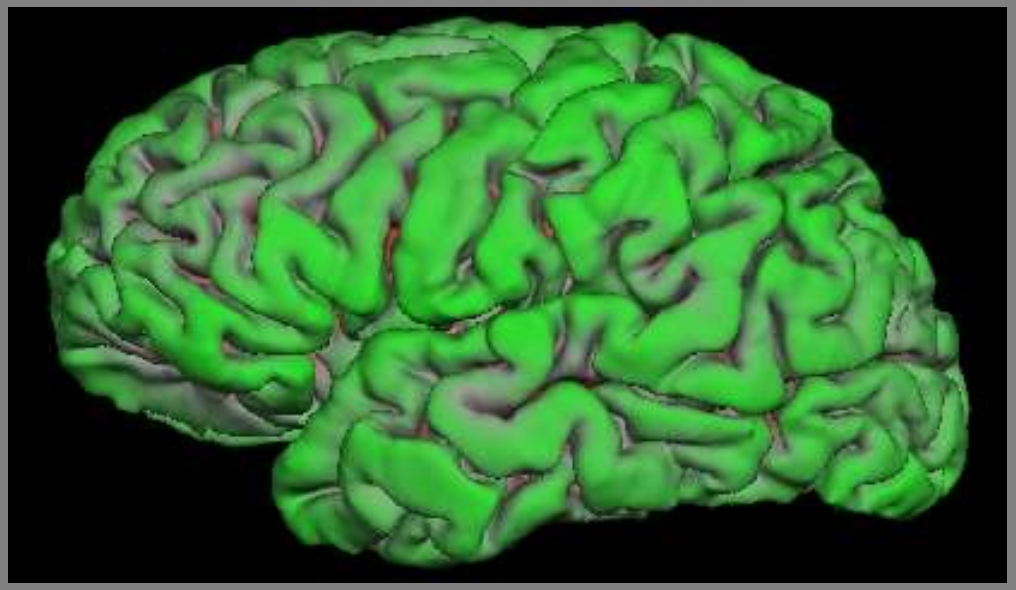
- Nudge orig surface
- Follow T1 intensity gradients
- Smoothness constraint
- Vertex Identity stays constant



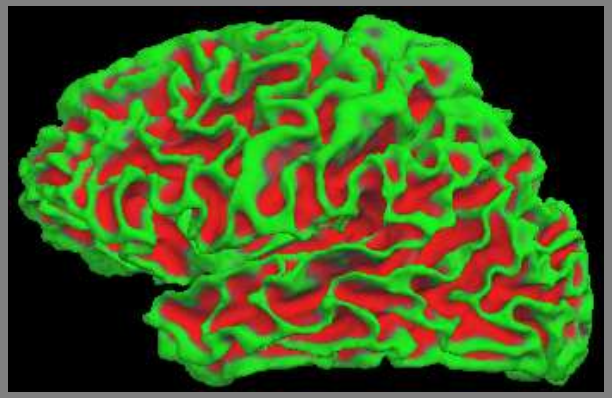
Pial Surface



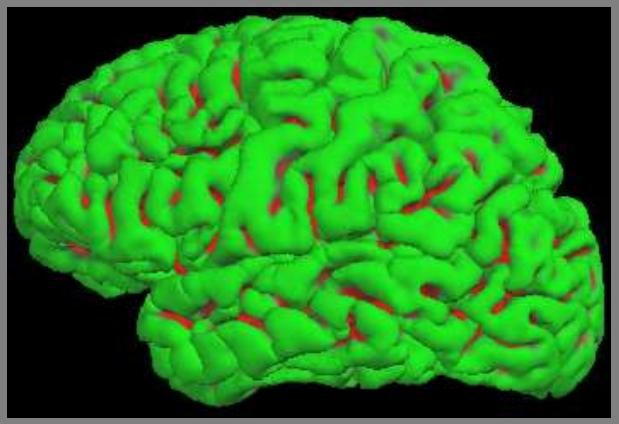
- Nudge white surface
- Follow T1 intensity gradients
- Vertex Identity Stays



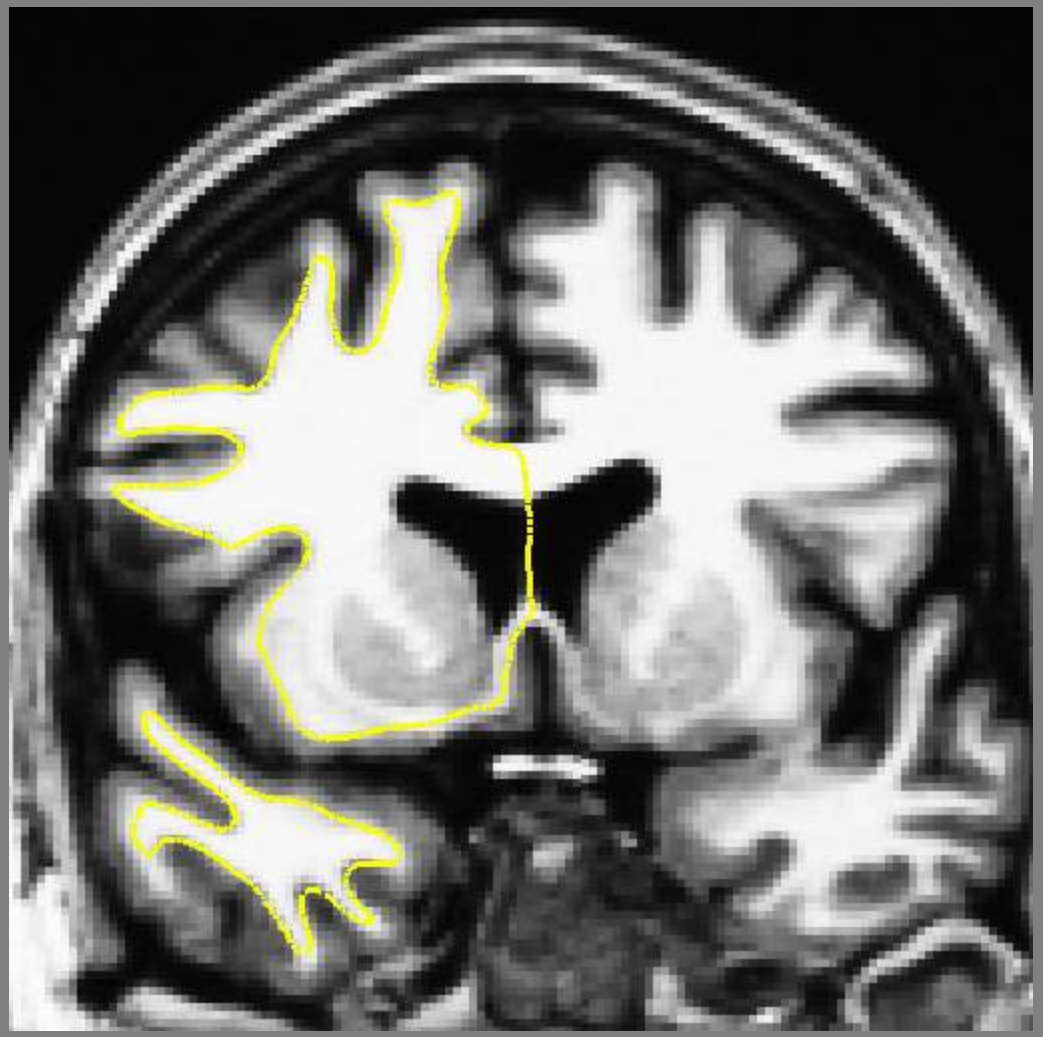
Optimal Surface Placement



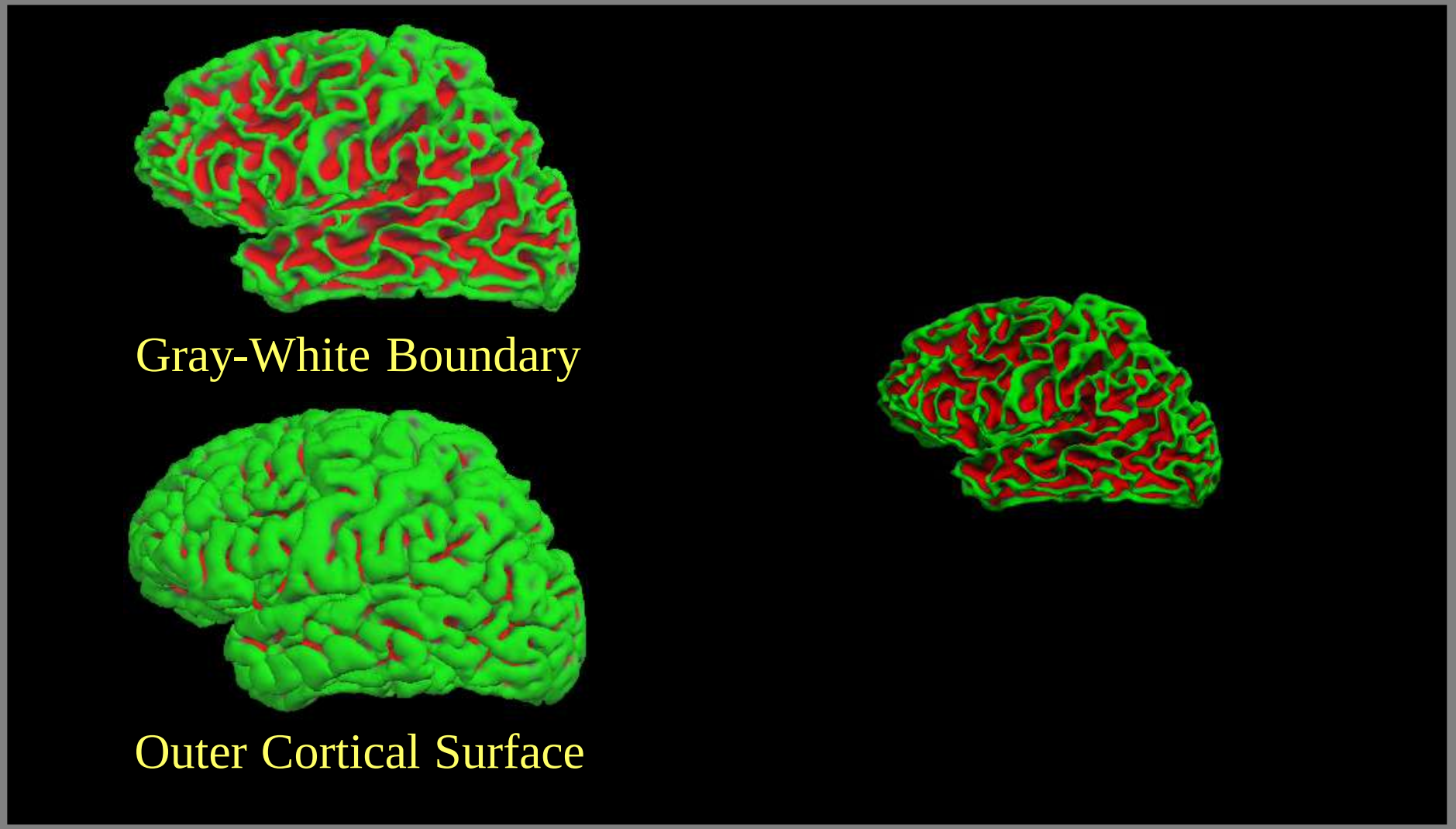
Gray-White Boundary



Outer Cortical Surface



Gray/CSF Deformation

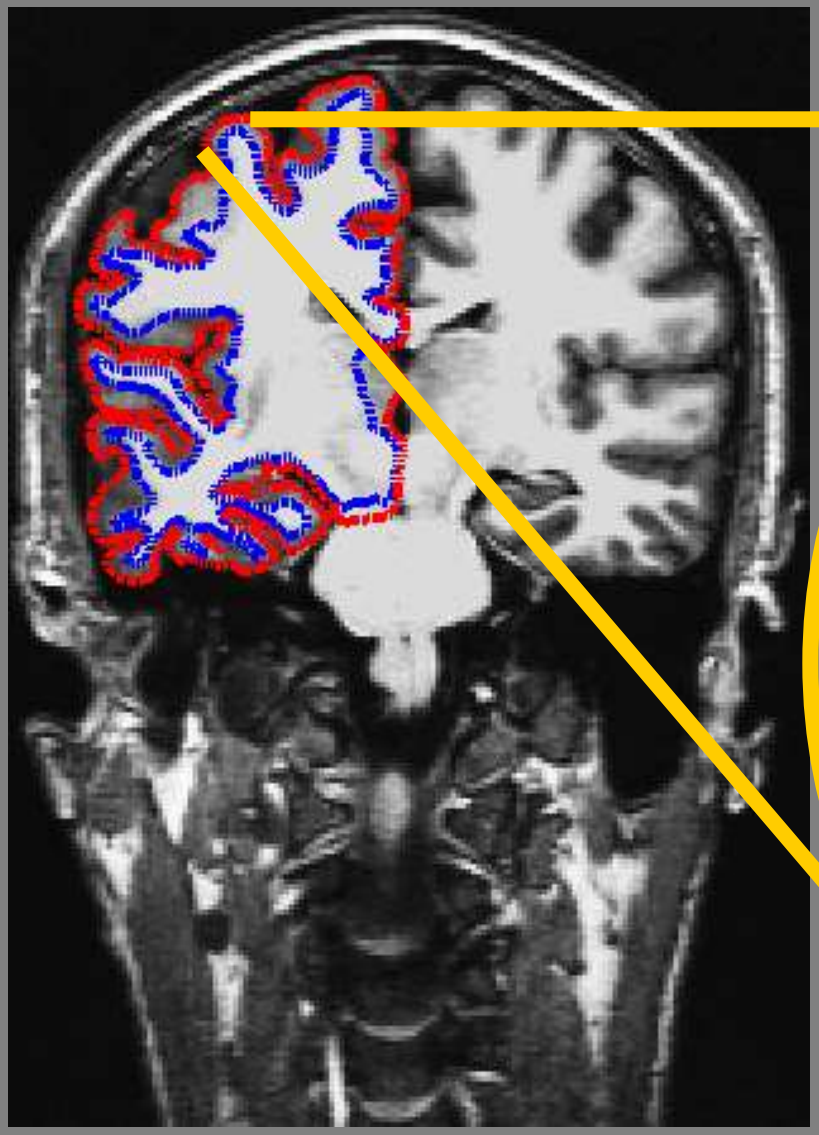


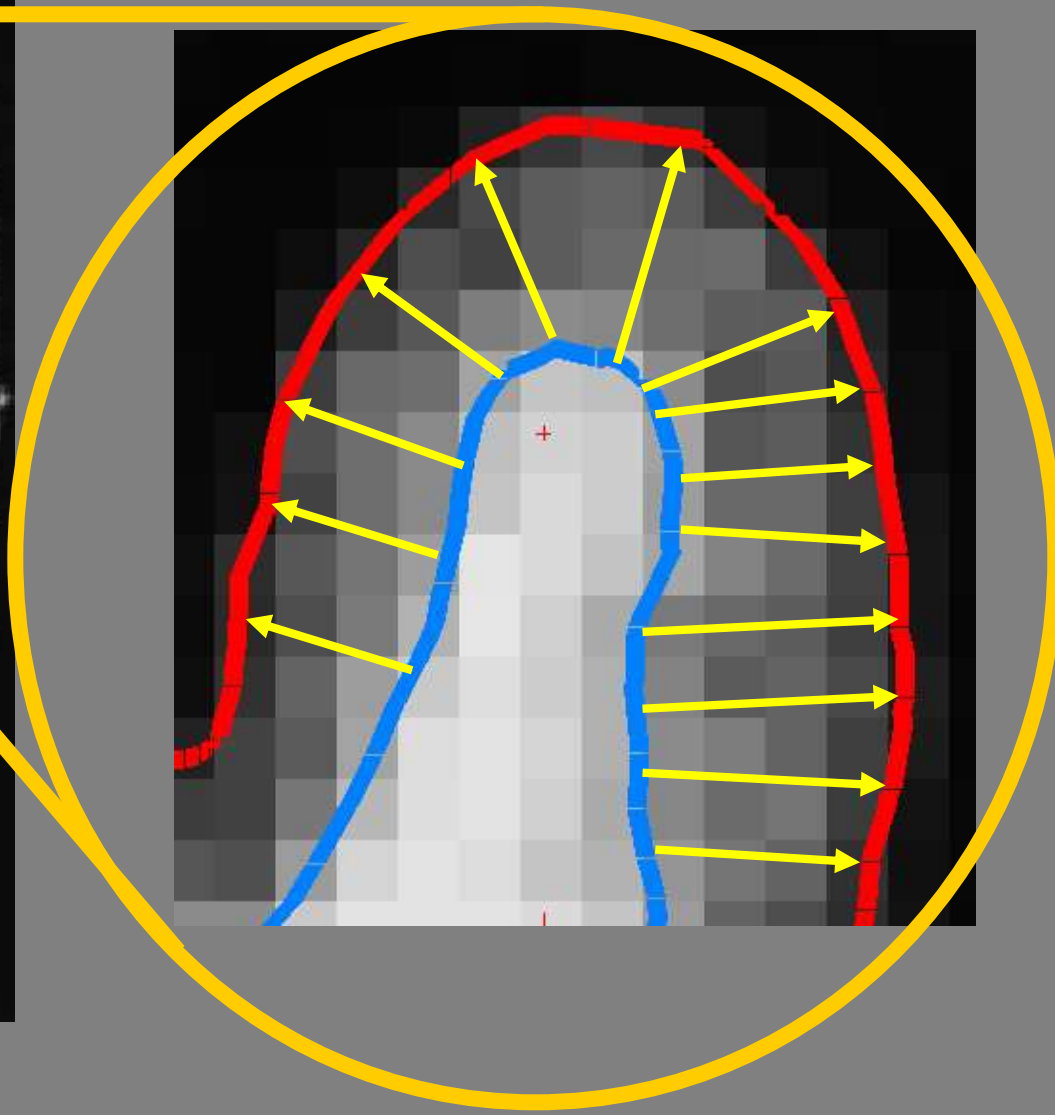
Dale and Sereno, 1993; Dale et al., Dale et al., 1999; Fischl et al., 1999; Fischl et al., 2000; Fischl et al., 2001

-finalsurfs

-autorecon2

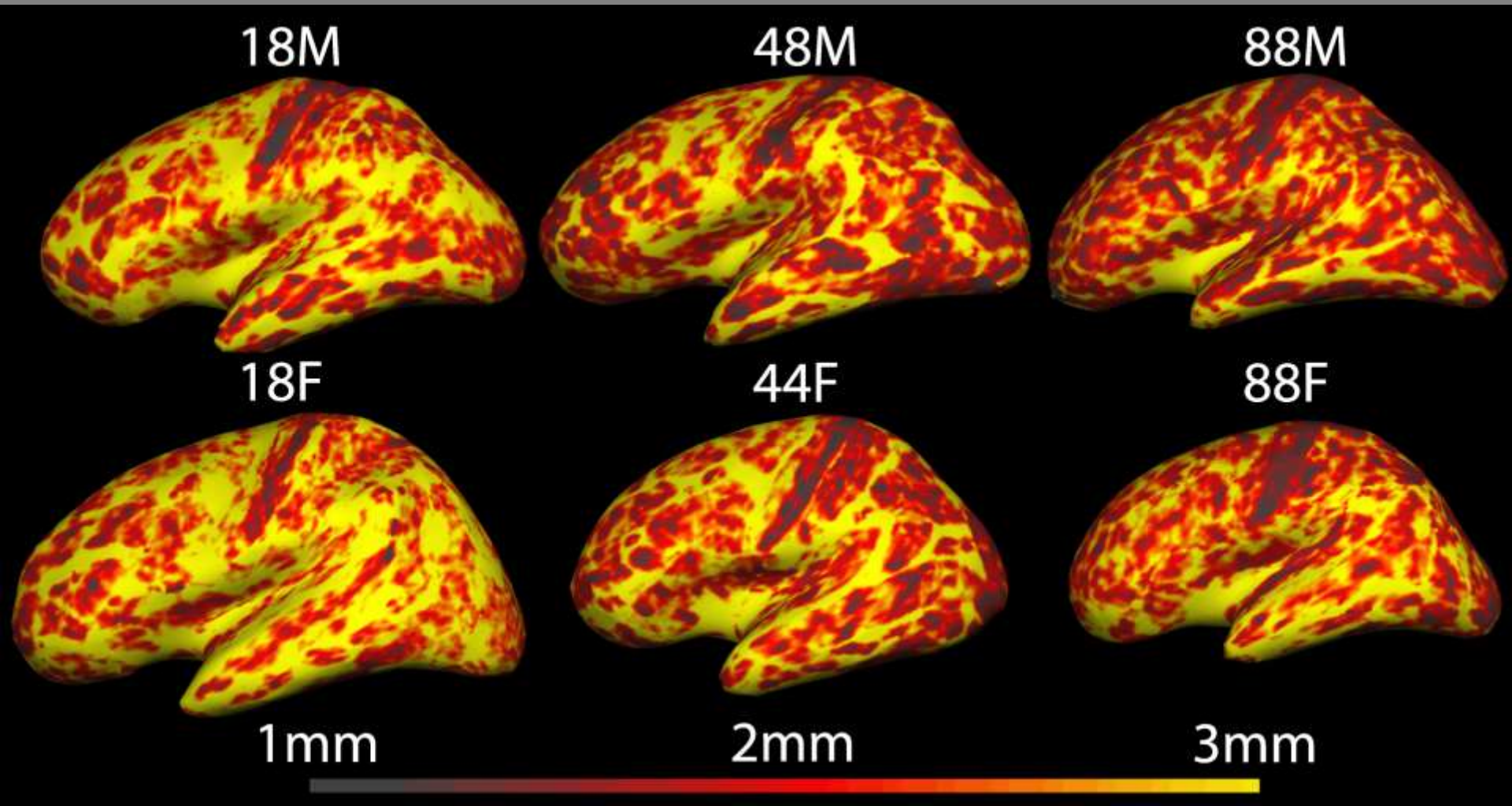
Cortical Thickness



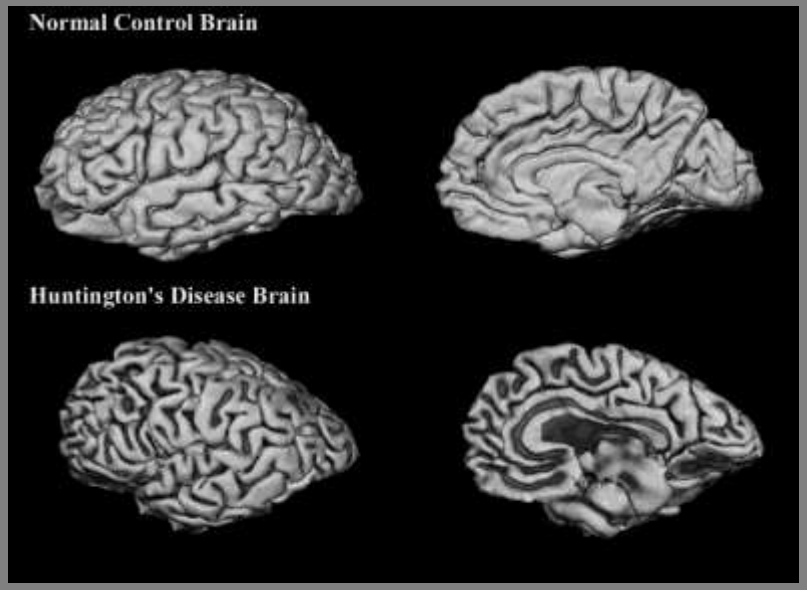


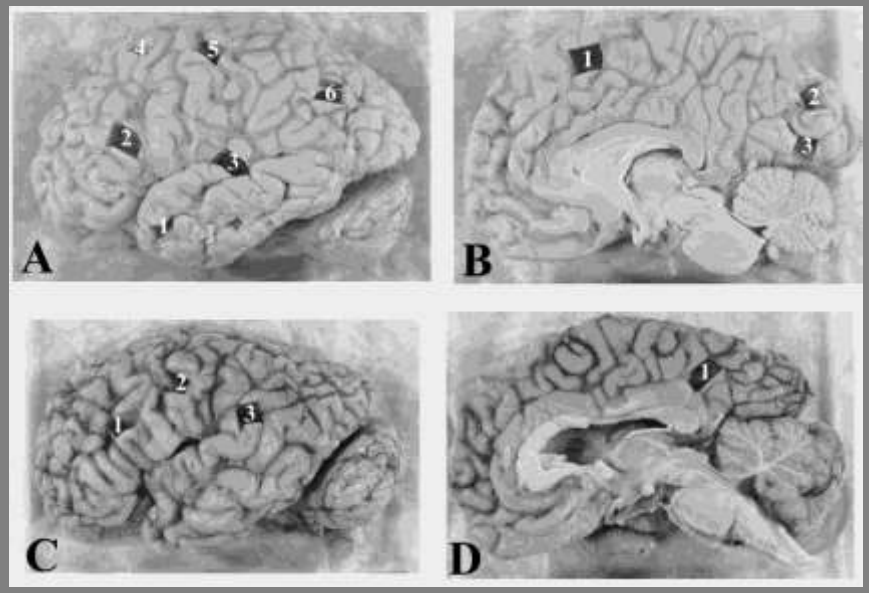
Thickness Maps

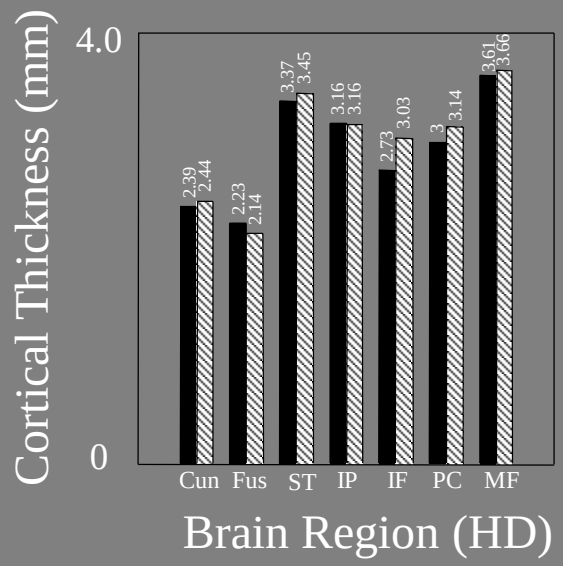
- Red regions are thinner
- Yellow regions are thicker

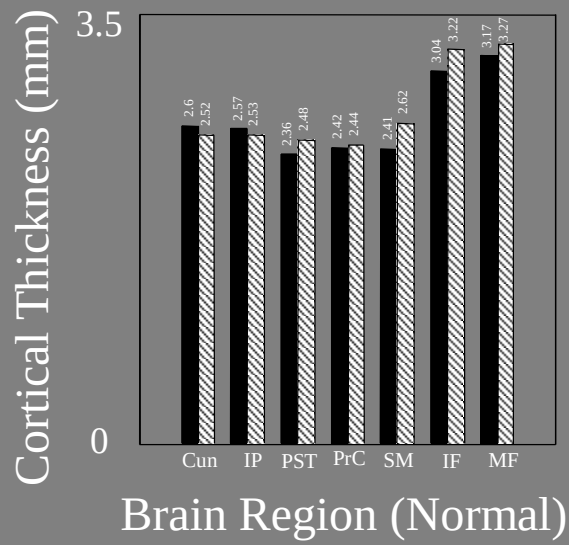


Histological Validation





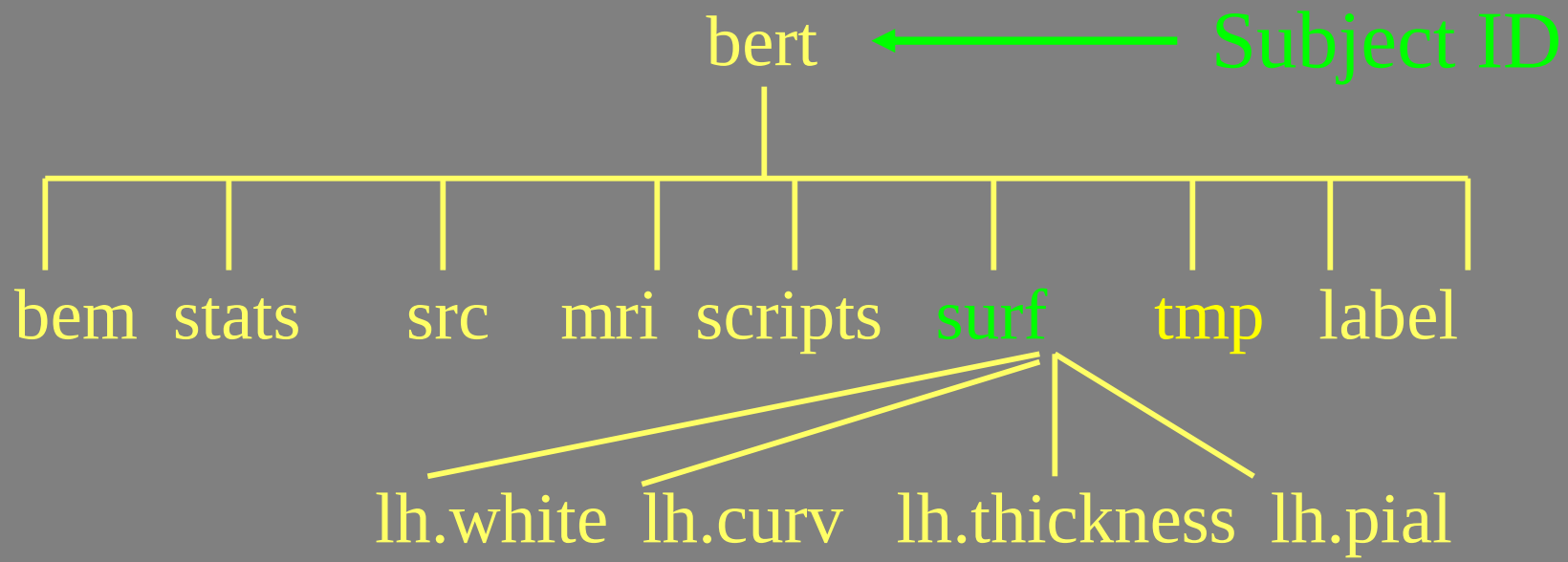




Courtesy of Diana Rosas, MGH (Rosas, et al., 2002, Neurology)

FreeSurfer Directory Tree

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



-autorecon3

Volumetric Processing Stages (subjid/mri):

1. Motion Cor, Avg, Conform (orig.mgz)
2. Non-uniform inorm (nu.mgz)
3. Talairach transform computation (talairach/talairach.xfm)
4. Intensity Normalization 1 (T1.mgz)
5. Skull Strip (brainmask.mgz)

6. EM Register (linear volumetric registration)
7. CA Intensity Normalization (norm.mgz)
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)

Surface Processing Stages (subjid/surf):

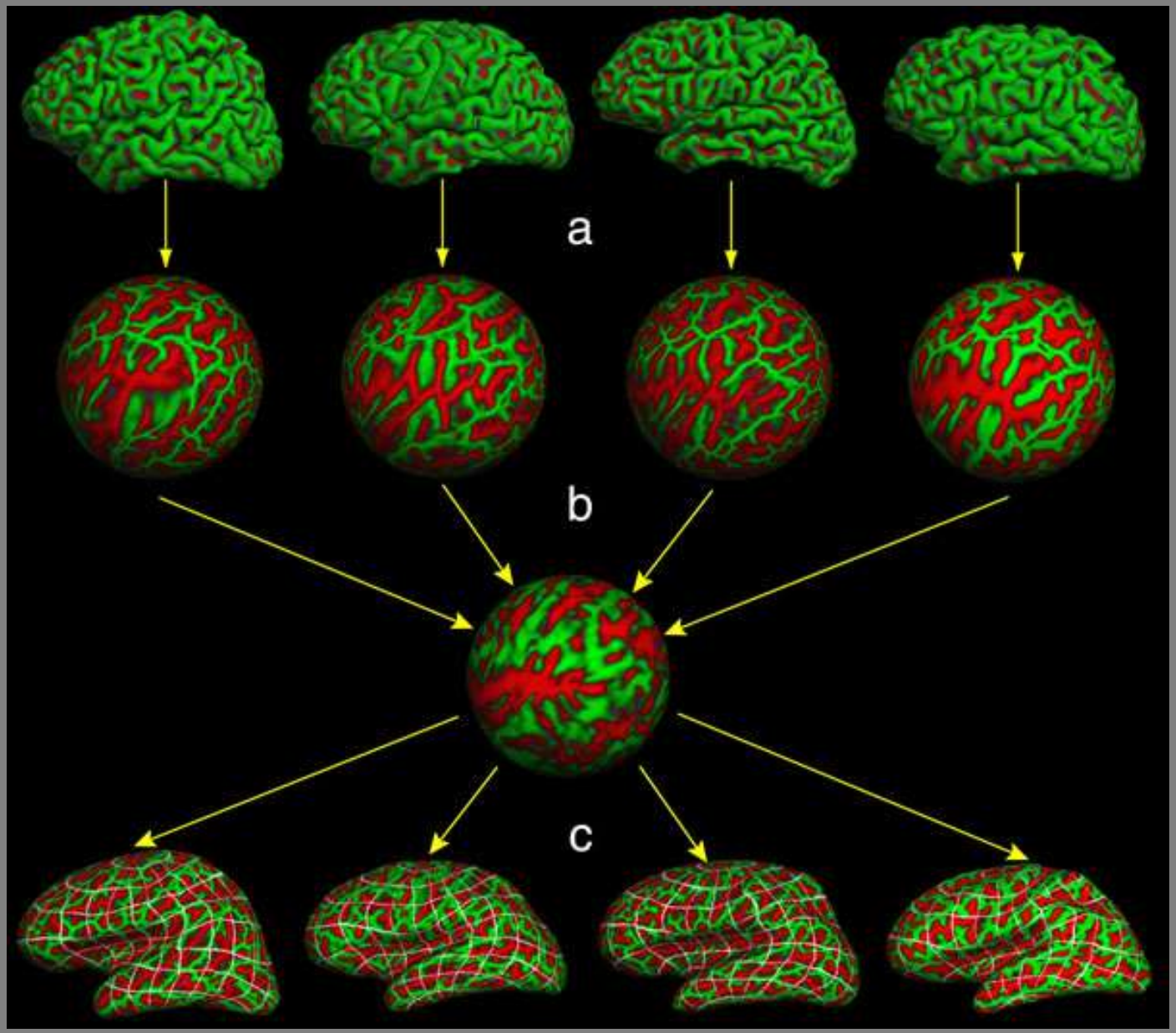
14. Tessellate (?h.orig.nofix)
15. Smooth1
16. Inflate1
17. QSphere (?h.qsqhere)
18. Automatic Topology Fixer (?h.orig)
19. Final Surfs (?h.white ?h.pial ?.thickness)
20. Smooth2 (?h.smoothwm)
21. Inflate2 (?h.inflated)
22. Aseg Statistics (stats/aseg.stats)
23. Cortical Ribbon Mask (?h.ribbon.mgz)

24. Spherical Morph
25. Spherical Registration (?h.sphere.reg)
26. Map average curvature to subject
27. Cortical Parcellation (Labeling)
28. Cortical Parcellation Statistics
29. Cortical Parcellation mapped to Aseg
30. White Matter Parcellation (wmparc.mgz)

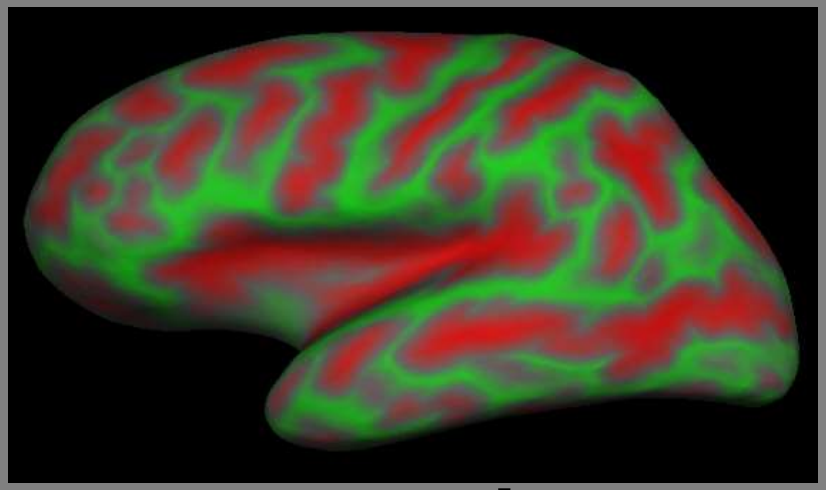
recon-all -help

Note: lh processed completely first, then rh.

Surface-Based Spherical Coord System

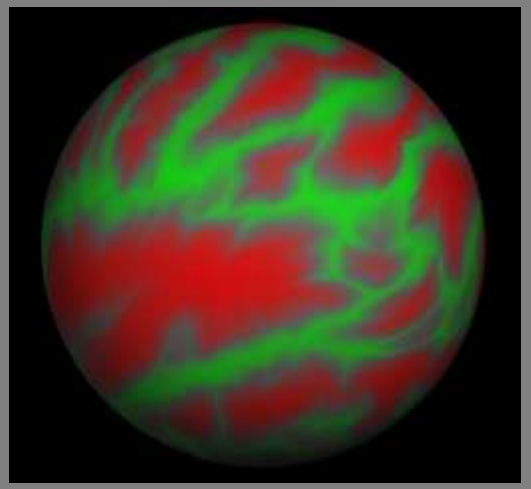


“Spherical” Registration

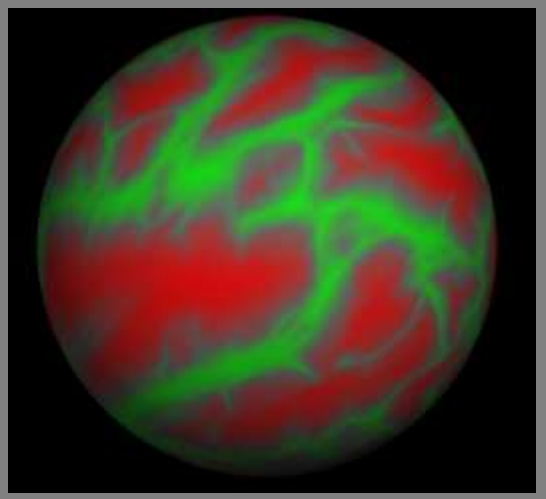


Sulcal Map

Spherical Inflation

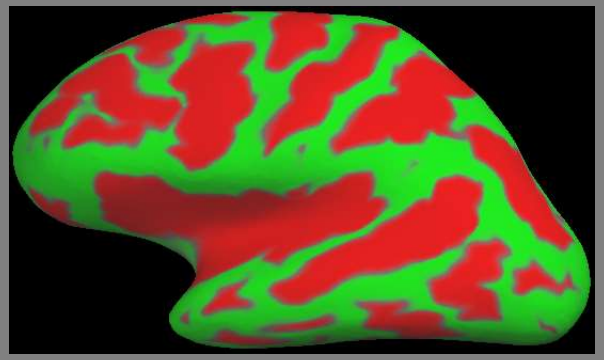


High-Dimensional
Registration to
Spherical Template

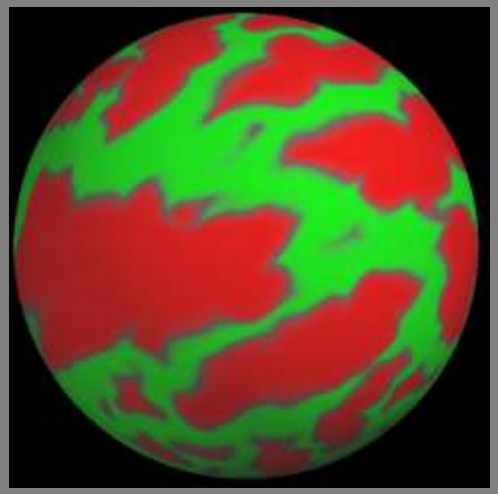


Template: average.curvature.filled.buckner.40.tiff

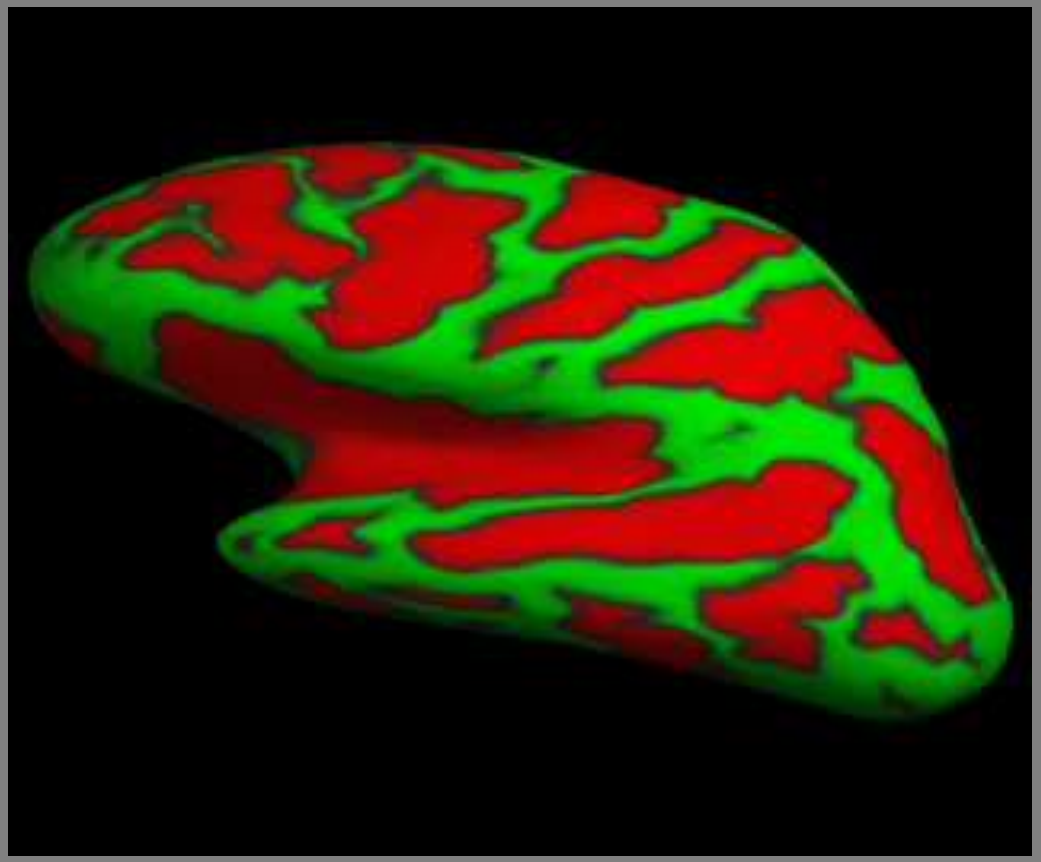
Spherical Inflation



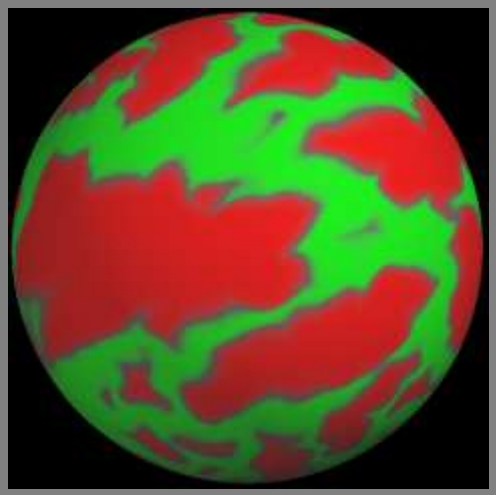
Inflated Surface



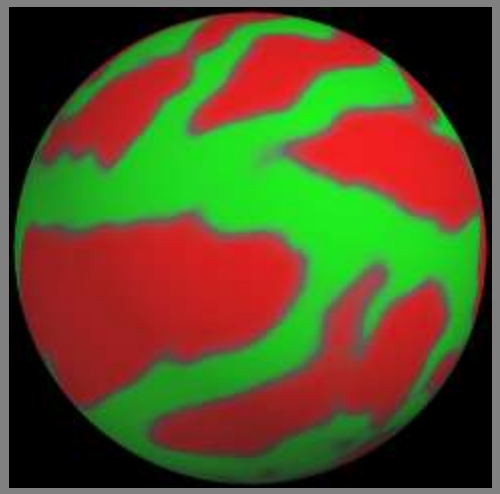
Transformed Surface



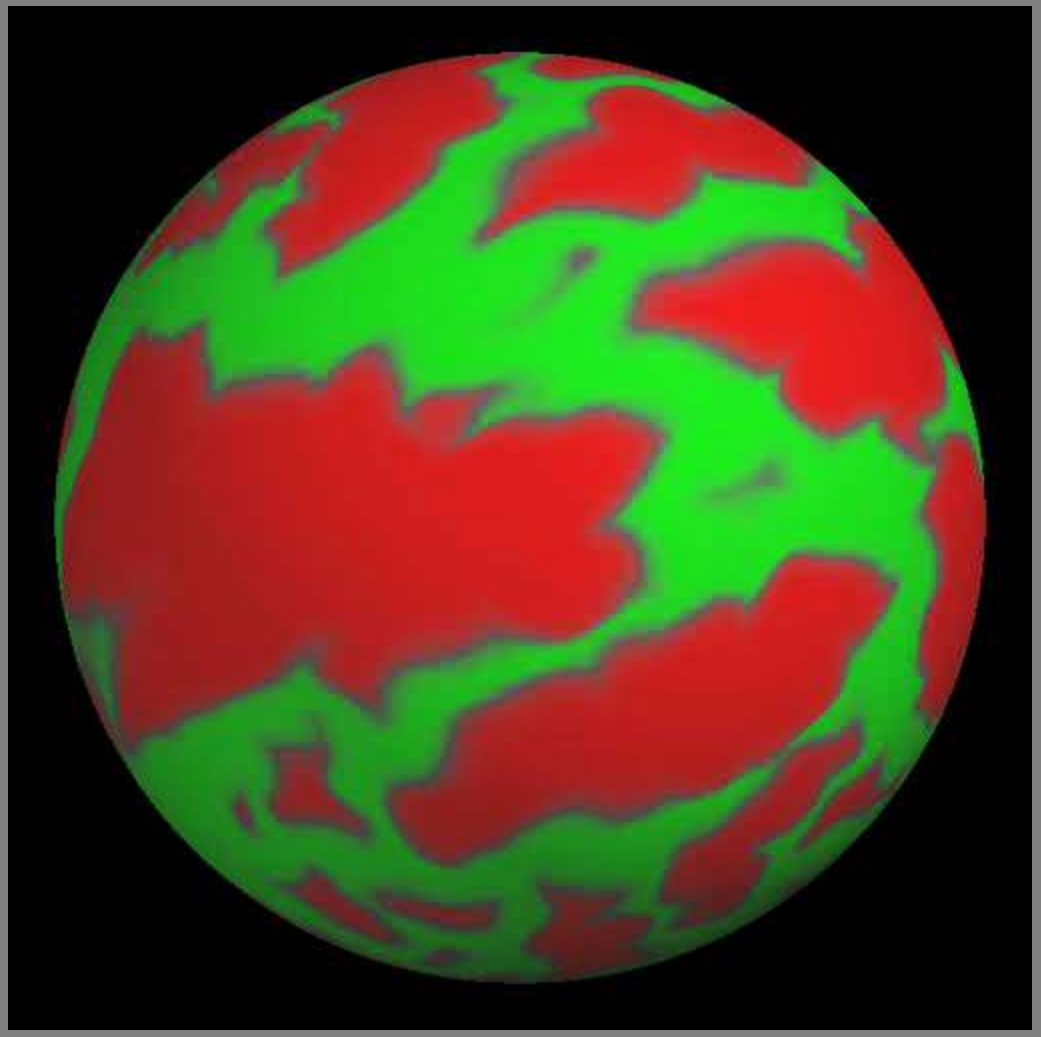
Spherical Registration to Atlas



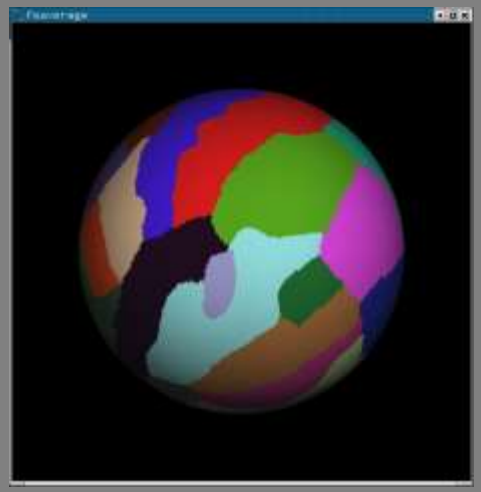
Individual Subject



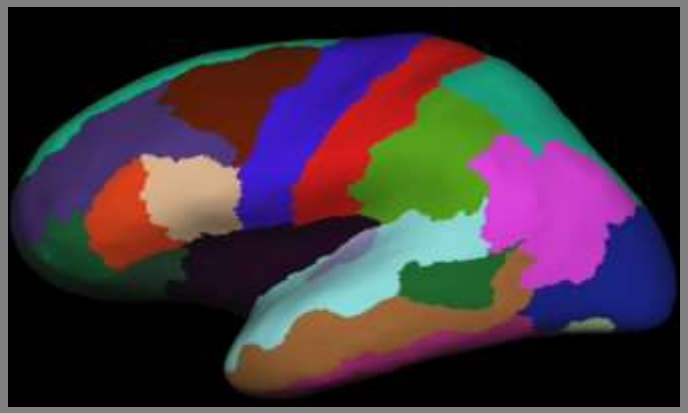
Atlas (Target)



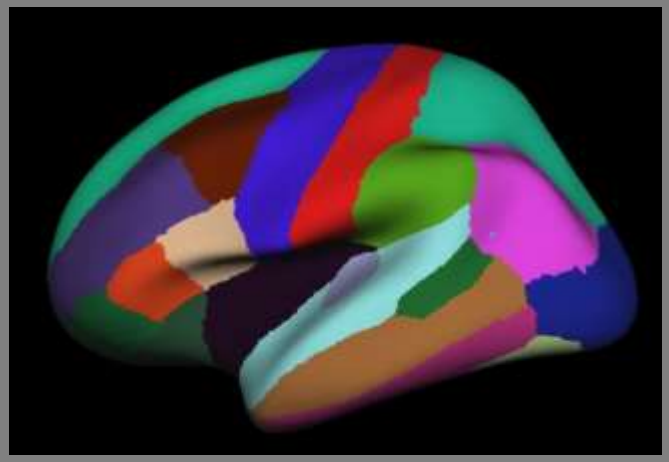
Cortical Parcellation



Spherical Template based on Manual Parcellation



Map to Individual Thru Spherical Reg

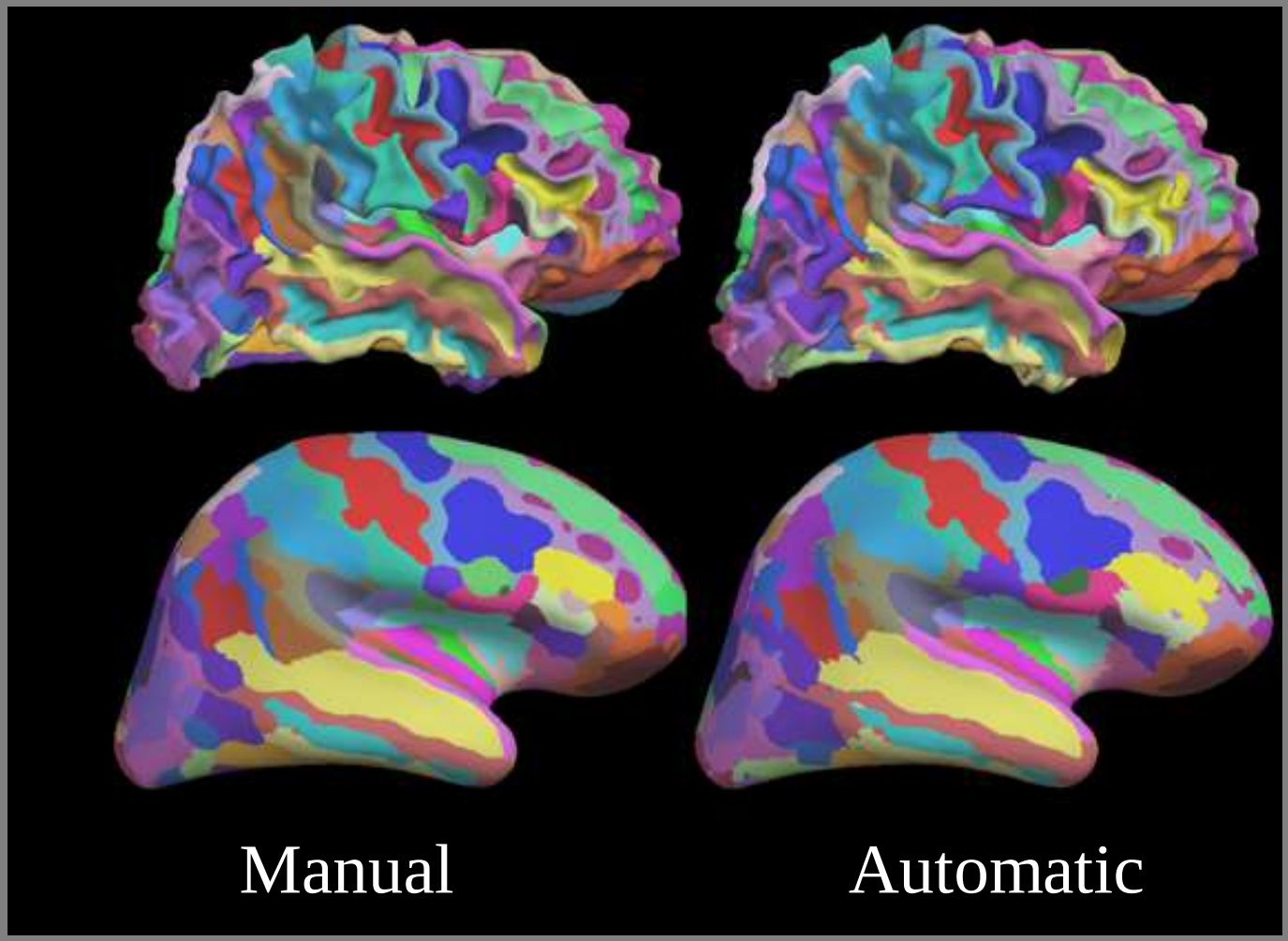


Fine-tune based on individual anatomy

Atlases: curvature.buckner40filled.desikan_killiany, atlas_2005_simple

-cortparc2 -autorecon3

Cortical Parcellation: 2

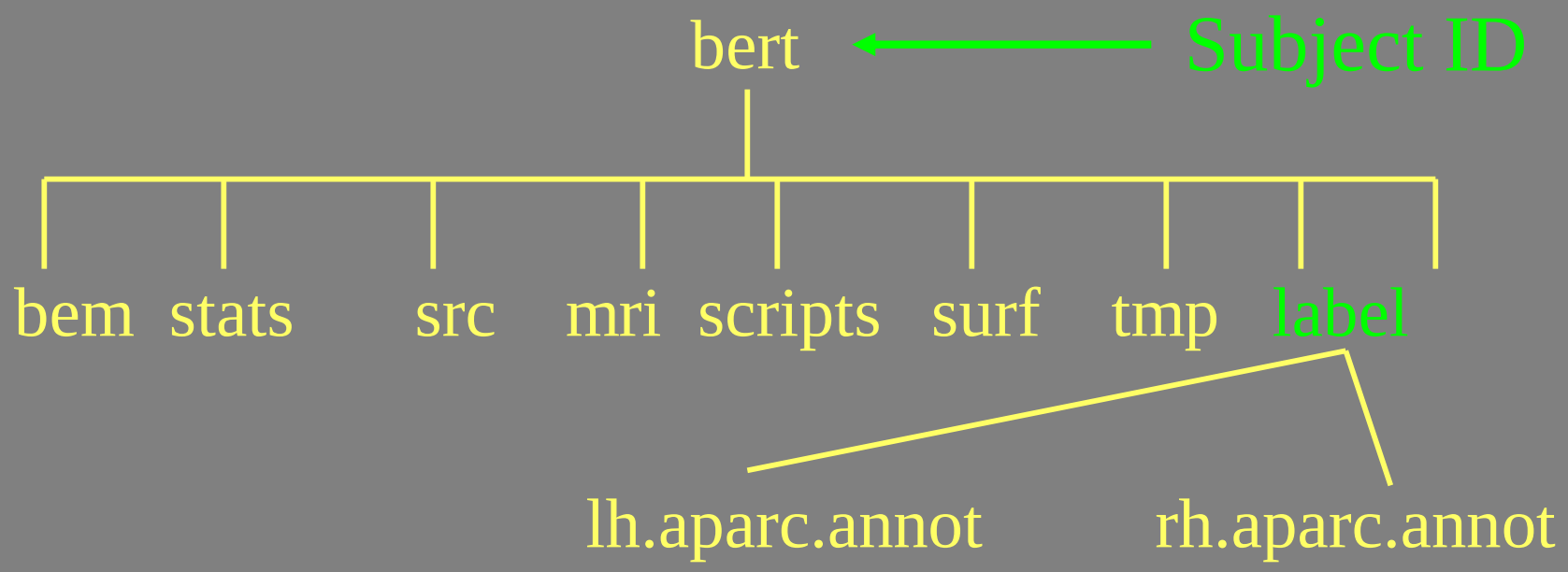


Atlases: curvature.buckner40filled.desikan_killiany, atlas_2005_simple

Thanks to Christophe Destrieux for this slide.

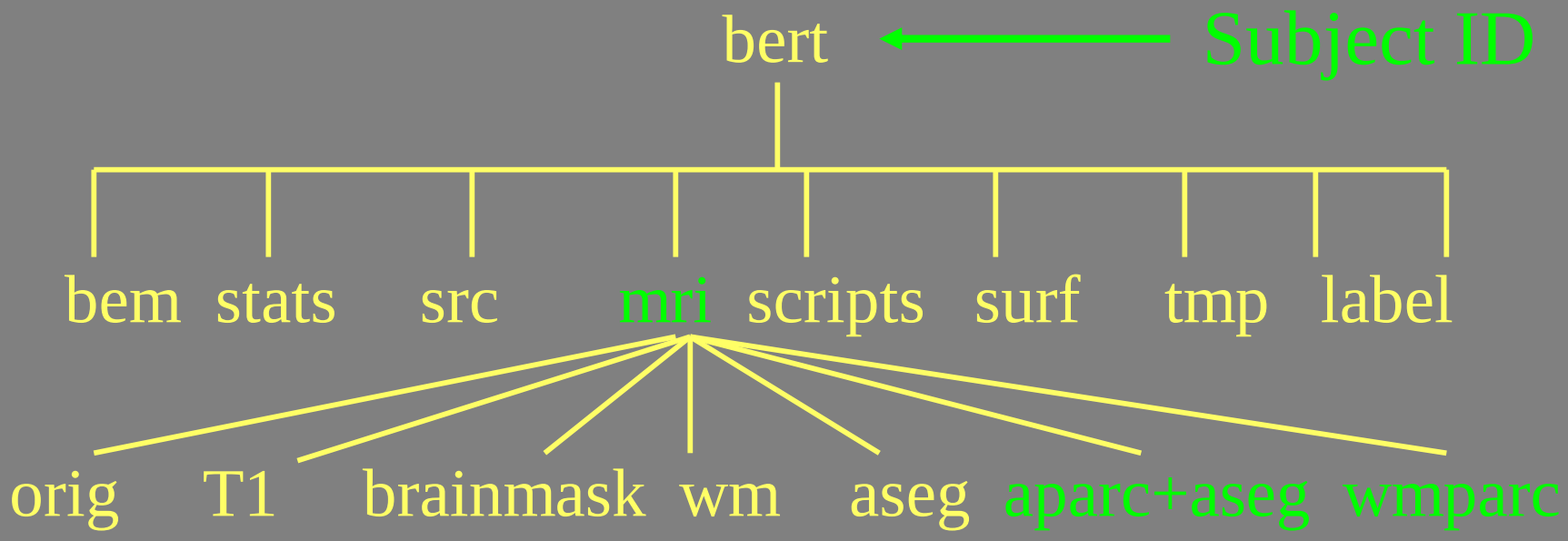
FreeSurfer Directory Tree

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



FreeSurfer Directory Tree

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



Actual Workflow: version 1

1. recon-all –all (Stages 1-20) ~30 hours
2. Check talairach transform, skull strip, normalization
3. Check surfaces
    1. Add control points: recon-all –autorecon2-cp –autorecon3 (Stages 10-29)
    2. Edit wm.mgz: recon-all –autorecon2-wm –autorecon3 (Stages 13-29)
    3. Edit brain.mgz: recon-all –autorecon2-pial (Stage 19-22)

Note: all stages can be run individually

Actual Workflow: version 2

1. recon-all –autorecon1 (Stages 1-5) ~45 min
2. Check talairach transform, skull strip, normalization
3. recon-all –autorecon2 (Stages 6-22) ~20 hours
4. Check surfaces
    1. Add control points: recon-all –autorecon2-cp (Stages 10-22)
    2. Edit wm.mgz: recon-all –autorecon2-wm (Stages 13-22)
    3. Edit brain.mgz: recon-all –autorecon2-pial (Stage 19-22)
5. recon-all –autorecon3 (Stages 23-29) ~6 hours

Note: all stages can be run individually

Tutorials

https://surfer.nmr.mgh.harvard.edu/fswiki/FsTutorial

On Linux Machines:

- setenv FREESURFER_HOME /usr/pubsw/freesurfer
- source $FREESURFER_HOME/SetUpFreeSurfer.csh
- setenv SUBJECTS_DIR /ircuser/FSWorkshop/buckner_data/tutorial_subjs

On Macs:

- setenv FREESURFER_HOME /Applications/freesurfer
- source $FREESURFER_HOME/SetUpFreeSurfer.csh
- setenv SUBJECTS_DIR /FSWorkshop/buckner_data/tutorial_subjs

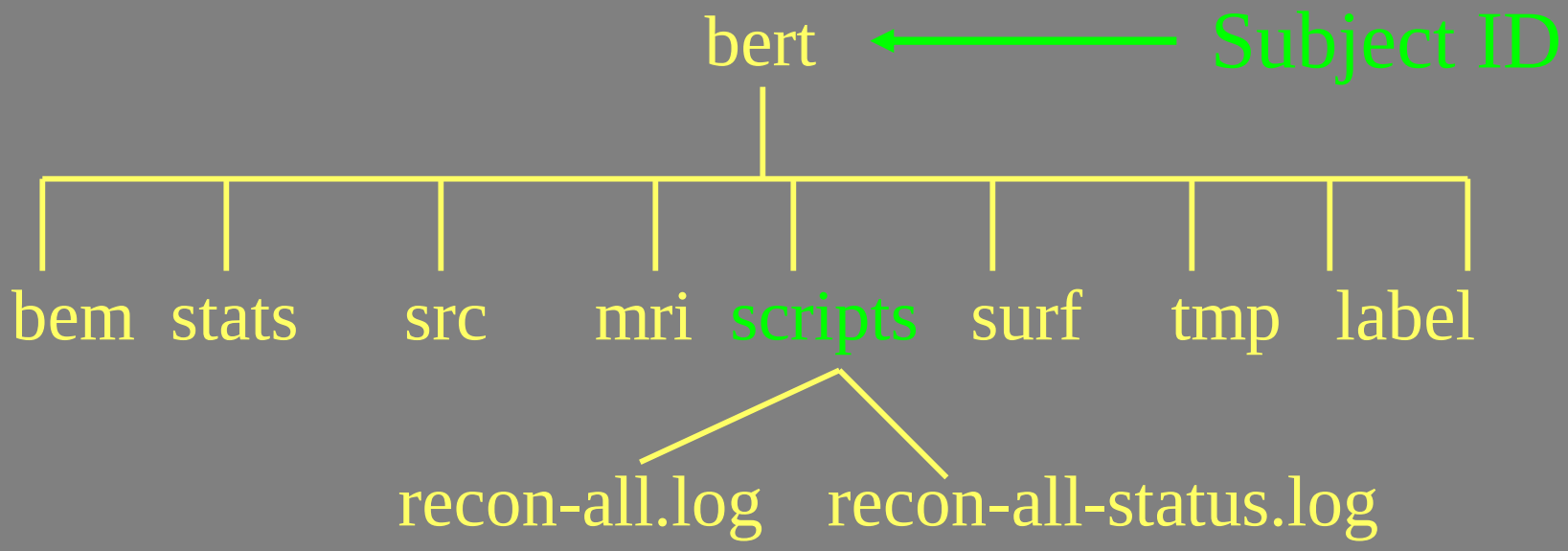
- Use the volume and surface viewing tools to look at correct output from all steps.

Troubleshooting

- Skull Strip Errors
- Intensity Normalization
- Segmentation Errors
- Pial Surface
- Talairach Errors

FreeSurfer Directory Tree

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

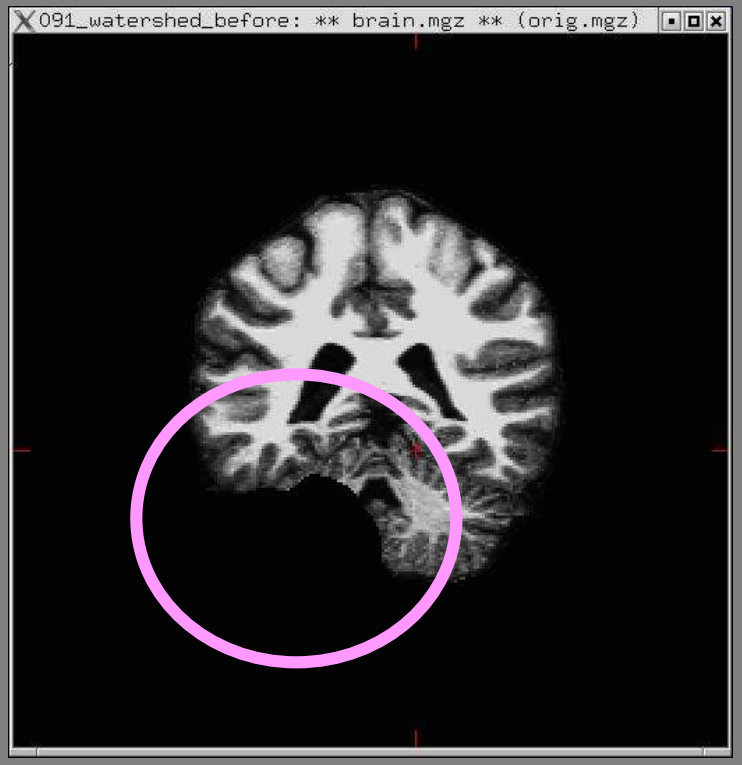


Actual Workflow

1. recon-all –autorecon1 (Stages 1-5)
2. Check talairach transform, skull strip, normalization
3. recon-all –autorecon2 (Stages 6-22)
4. Check surfaces
    1. Add control points: recon-all –autorecon2-cp (Stages 10-22)
    2. Edit wm.mgz: recon-all –autorecon2-wm (Stages 13-22)
    3. Edit brain.mgz: recon-all –autorecon2-pial (Stage 19-22)
5. recon-all –autorecon3 (Stages 23-29)

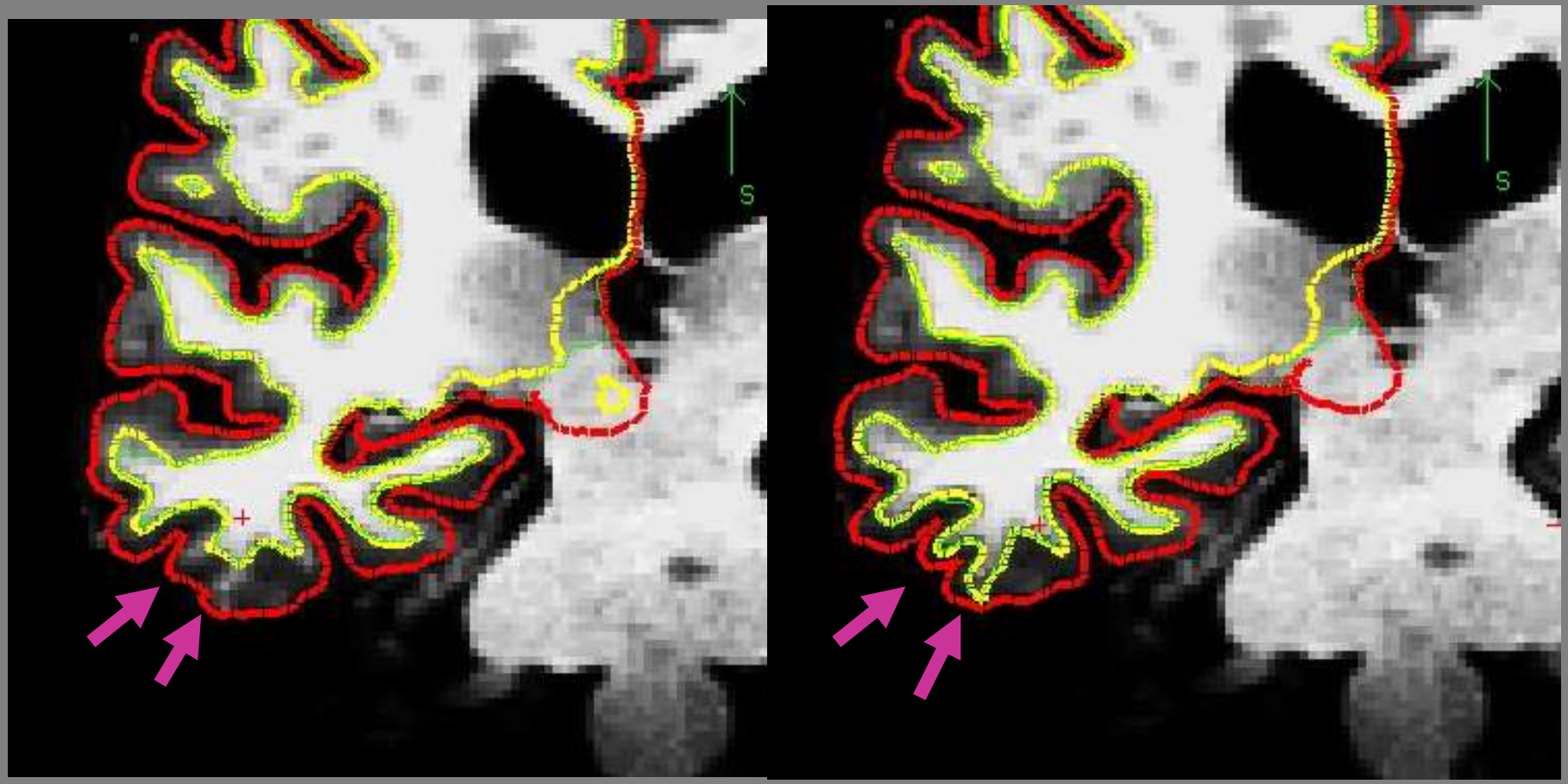
Note: all stages can be run individually

Troubleshooting: Skull Strip



brainmask.mgz

Troubleshooting: Intensity Normalization



Intensity Normalization Failure.
All WM in T1 volume (T1.mgz) should be 110.
Can fix by adding “Control Points”. Beware partial voluming!

Actual Workflow

1. recon-all –autorecon1 (Stages 1-5)
2. Check talairach transform, skull strip, normalization
3. recon-all –autorecon2 (Stages 6-22)
4. Check surfaces
    1. Add control points: recon-all –autorecon2-cp (Stages 10-22)
    2. Edit wm.mgz: recon-all –autorecon2-wm (Stages 13-22)
    3. Edit brain.mgz: recon-all –autorecon2-pial (Stage 19-22)
5. recon-all –autorecon3 (Stages 23-29)

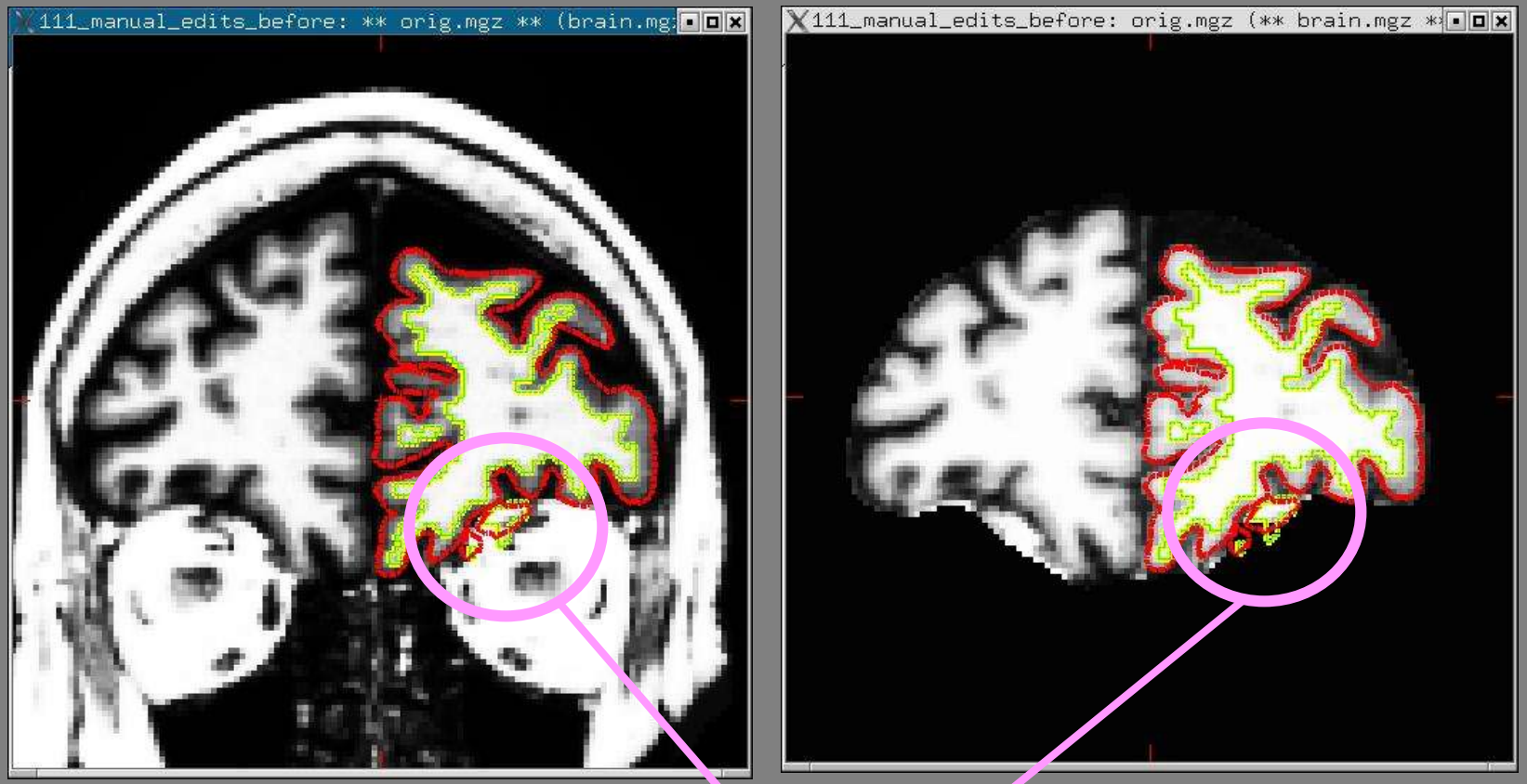
Note: all stages can be run individually

Actual Workflow

1. recon-all –autorecon1 (Stages 1-5)
2. Check talairach transform, skull strip, normalization
3. recon-all –autorecon2 (Stages 6-22)
4. Check surfaces
    1. Add control points: recon-all –autorecon2-cp (Stages 10-22)
    2. Edit wm.mgz: recon-all –autorecon2-wm (Stages 13-22)
    3. Edit brain.mgz: recon-all –autorecon2-pial (Stage 19-22)
5. recon-all –autorecon3 (Stages 23-29)

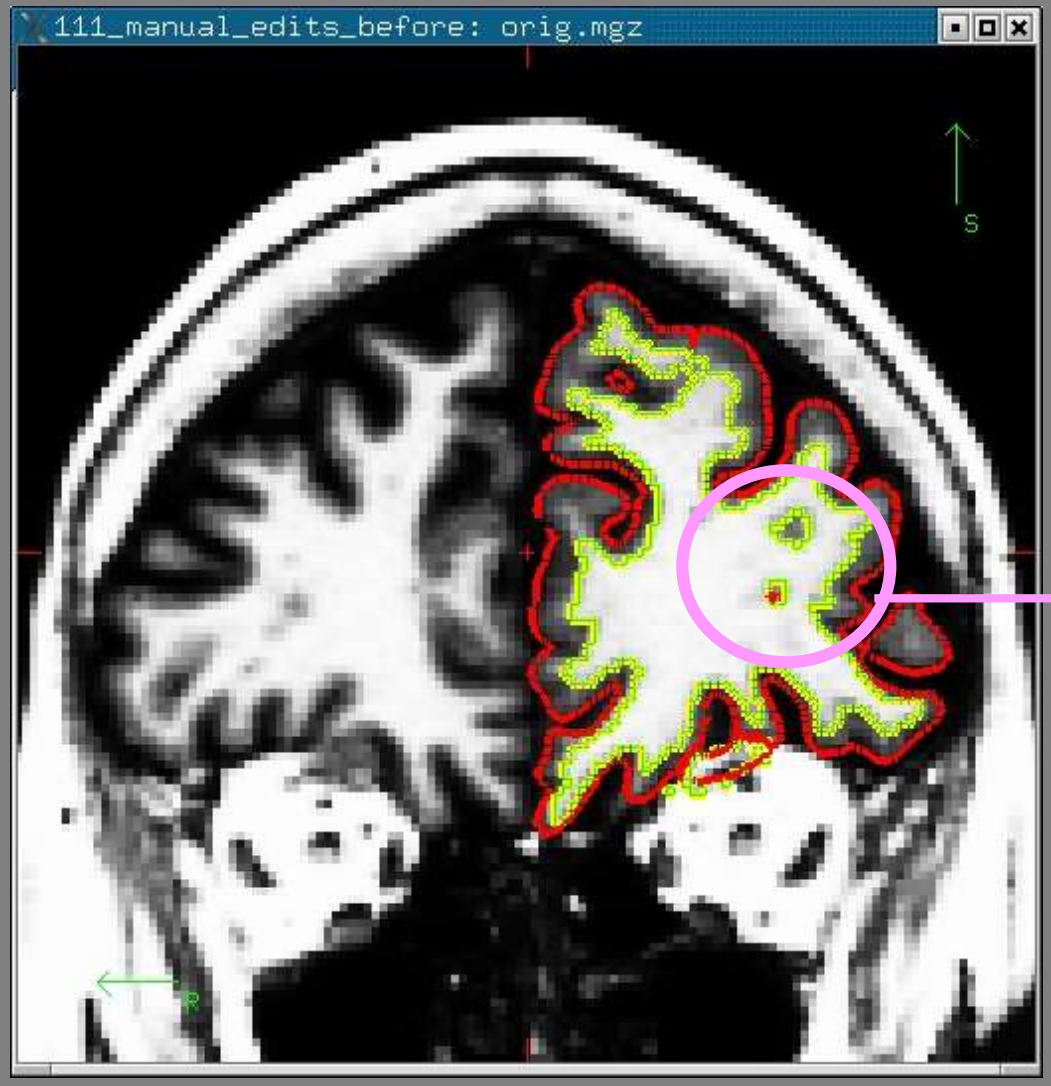
Note: all stages can be run individually

Troubleshooting: Segmentation Error



Eye Socket classified as WM.
Skull Strip Failure.

Troubleshooting: Segmentation Error



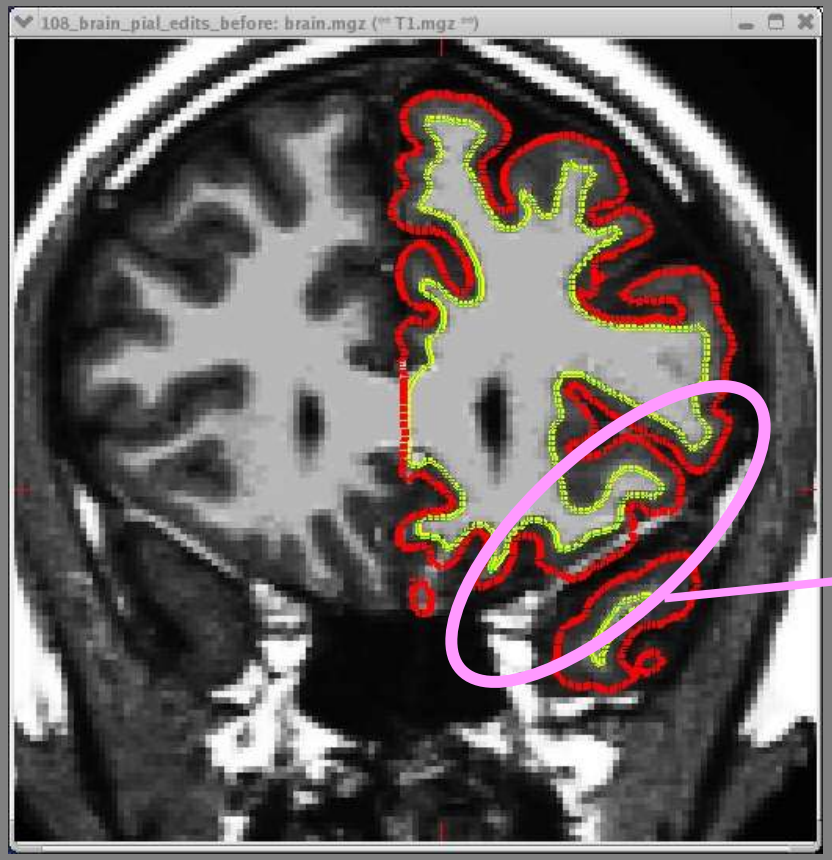
"Hypo-Intensities"
White Matter Lesions

Actual Workflow

1. recon-all –autorecon1 (Stages 1-5)
2. Check talairach transform, skull strip, normalization
3. recon-all –autorecon2 (Stages 6-22)
4. Check surfaces
    1. Add control points: recon-all –autorecon2-cp (Stages 10-22)
    2. Edit wm.mgz: recon-all –autorecon2-wm (Stages 13-22)
    3. Edit brain.mgz: recon-all –autorecon2-pial (Stage 19-22)
5. recon-all –autorecon3 (Stages 23-29)

Note: all stages can be run individually

Troubleshooting: Pial Surface Error



White/Gray OK, but
Pial Inaccurate

Actual Workflow

1. recon-all –autorecon1 (Stages 1-5)
2. Check talairach transform, skull strip, normalization
3. recon-all –autorecon2 (Stages 6-22)
4. Check surfaces
    1. Add control points: recon-all –autorecon2-cp (Stages 10-22)
    2. Edit wm.mgz: recon-all –autorecon2-wm (Stages 13-22)
    3. Edit brain.mgz: recon-all –autorecon2-pial (Stage 19-22)
5. recon-all –autorecon3 (Stages 23-29)

Note: all stages can be run individually

The End!

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