BrainSuite

UCLA Advanced Neuroimaging Summer Program
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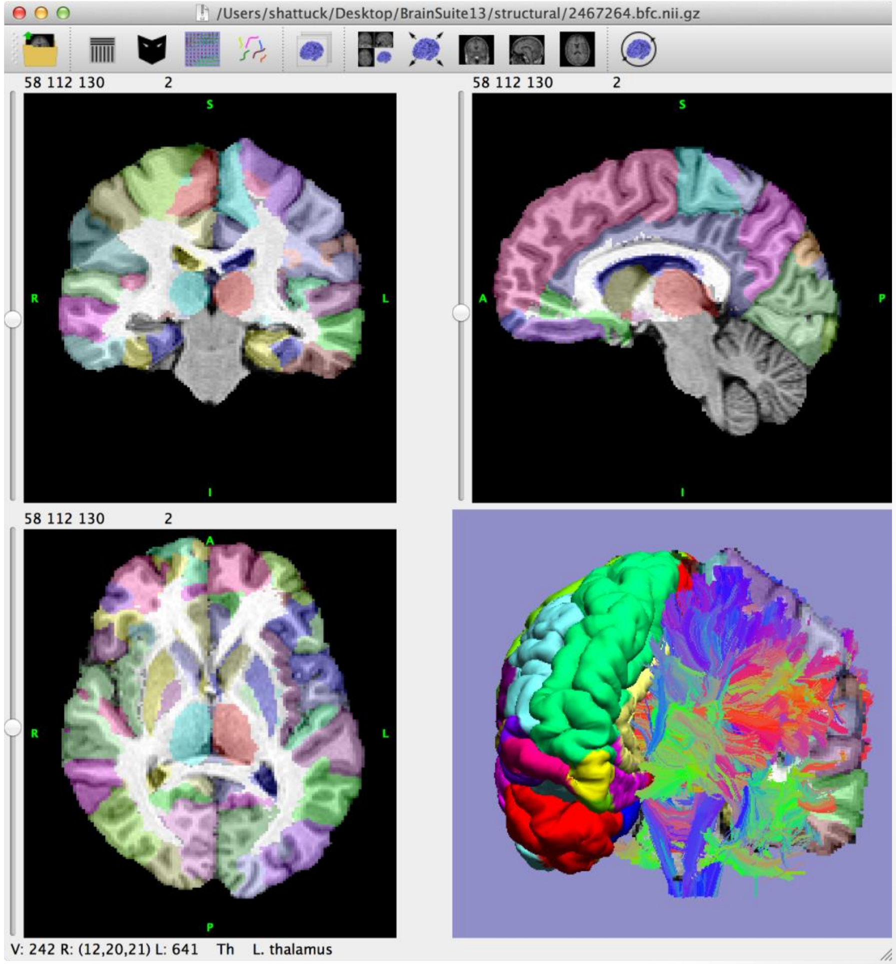
What is BrainSuite?

- Collection of image analysis tools designed to process structural and diffusion MRI
  - Automated sequence to extract cortical surface models from T1-MRI
  - Tools to register surface and volume data to an atlas to define anatomical ROIs
  - Tools for processing diffusion imaging data, including coregistration to anatomical T1 image, ODF and tensor fitting, and tractography.
  - Visualization tools for exploring these data.
- Runs on Windows, Mac, and Linux*



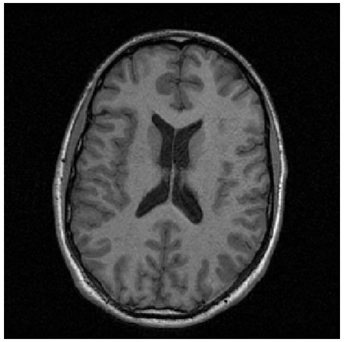
* GUI for Linux version is not yet released

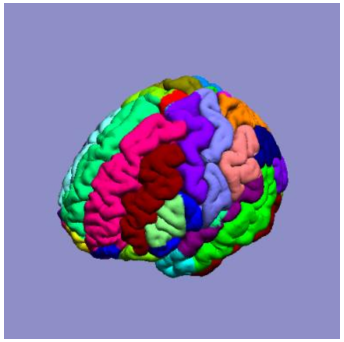
Overview

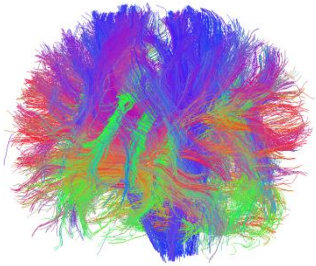
Presentation

- Background
- Cortical Surface Extraction
- Surface/Volume Registration
- BrainSuite Diffusion Pipeline
- Visualization Tools

Lab will follow with sample data and exercises





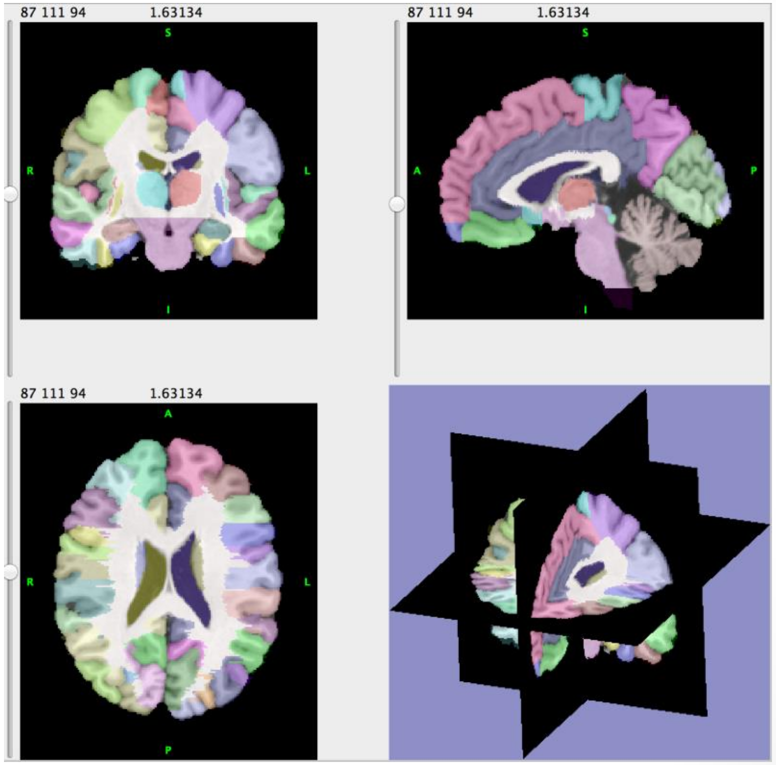


Motivation for Mapping

- It is often the goal to perform comparisons across different brains or brains at different points in time
- For these comparisons to be meaningful, we must be able to establish spatial anatomical correspondence among the data
- Once correspondence is established, we can look for significant differences in various neuroanatomical features
  - Size of structures
  - Cortical thickness
  - Cortical complexity
  - White matter architecture
  - Connectivity relationships
  - How these change over time or in the presence of disease or trauma

Automate all the things?

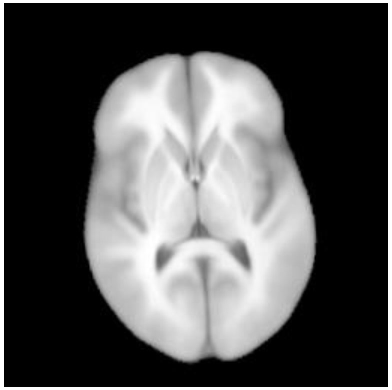
- One approach to comparative neuroimaging is to manually delineate anatomical structures.
- Drawbacks to manual methods:
  - Raters must be trained to be consistent and to follow a specified protocol
  - Learning effects may bias their processing
  - Raters don't always visualize 3D relationships when viewing slice-based data
- Human raters still constitute the 'gold standard' for many applications
- Automated methods can benefit from the expertise of the rater, which may be superior to an automated algorithm.
- Important to recognize that automated methods may need supervision or correction



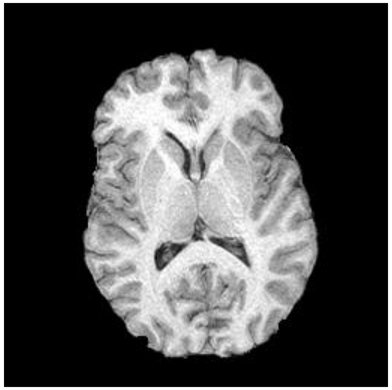
A manually delineated brain atlas (BrainSuiteAtlas1)

Image Registration

Goal: identify a transformation that maps from one image to another, such that image features or landmarks are matched.

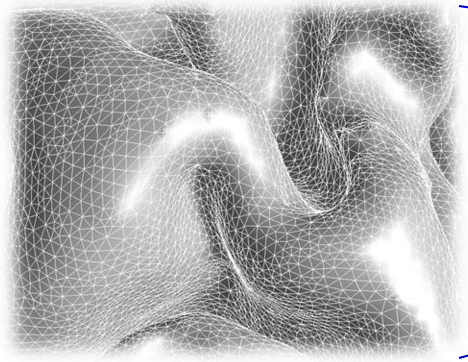


ICBM452 Atlas, aligned to subject image using AIR affine transform and 5th order warp

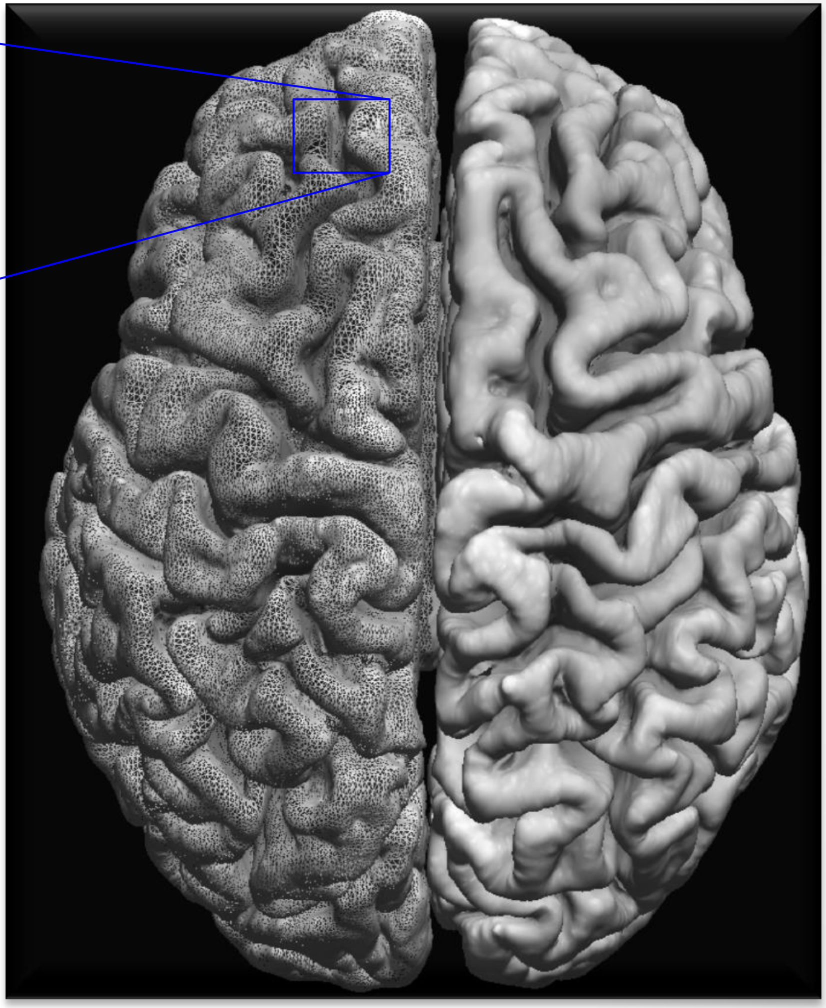


Subject Image

Why use surface models?



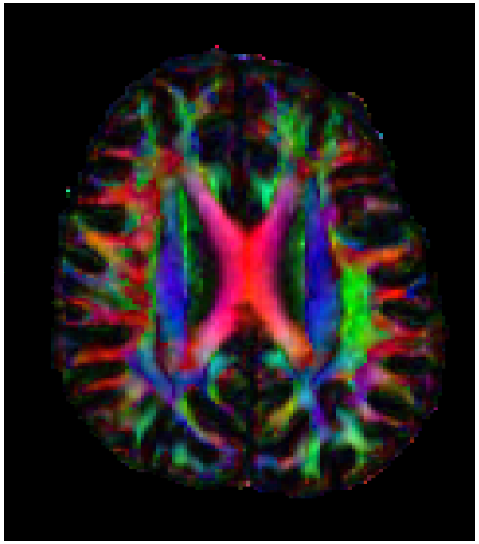
- Cortex is often represented as a high resolution triangulated mesh with ~700,000 triangles
- Many volumetric-based approaches do not align the cortical anatomy well
- We are often interested in functional areas in the cortex
- Surface-based features, e.g., cortical thickness, are of interest in the study of development or disease processes
- For applications such as EEG/MEG source localization, the location and orientation of the cortical surface can provide additional information



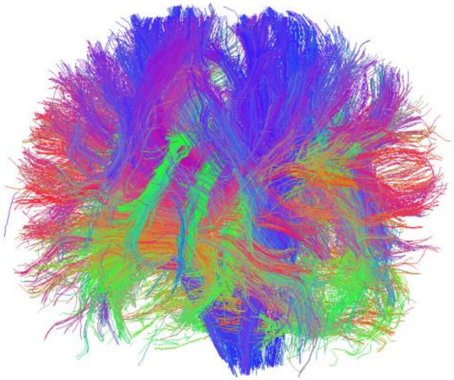
Cortical surface mesh representation

Why diffusion MRI?

- Quantify microstructural tissue characteristics
- Structural connectivity – connectomics (Sporns 2005; Wedeen 2008; Hagmann 2007)
- Clinical – investigation of abnormalities in white matter – e.g., stroke, Alzheimer's disease (Jones 2011; Johansen-Berg 2009)

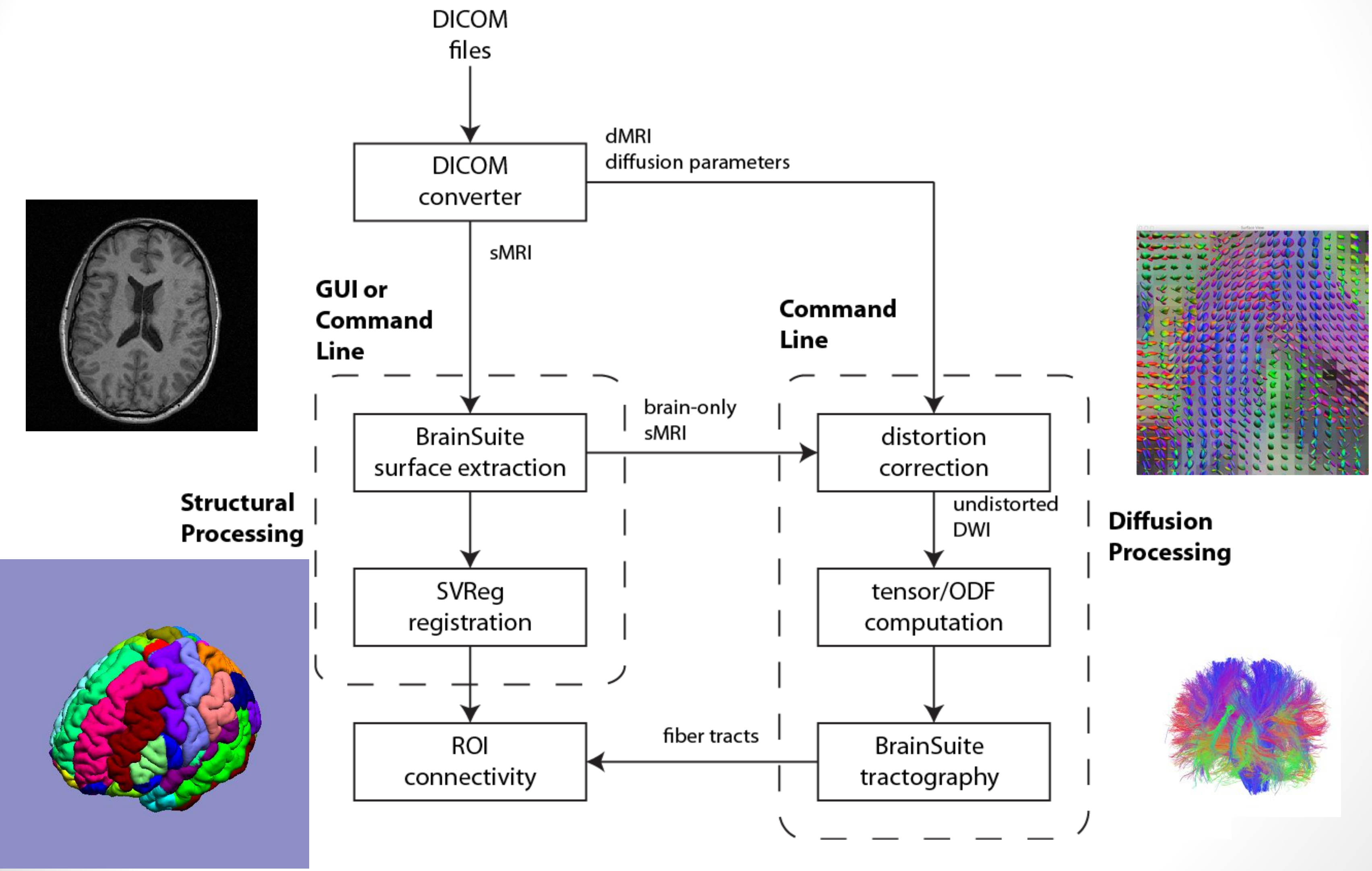


FA map



Fiber tracks

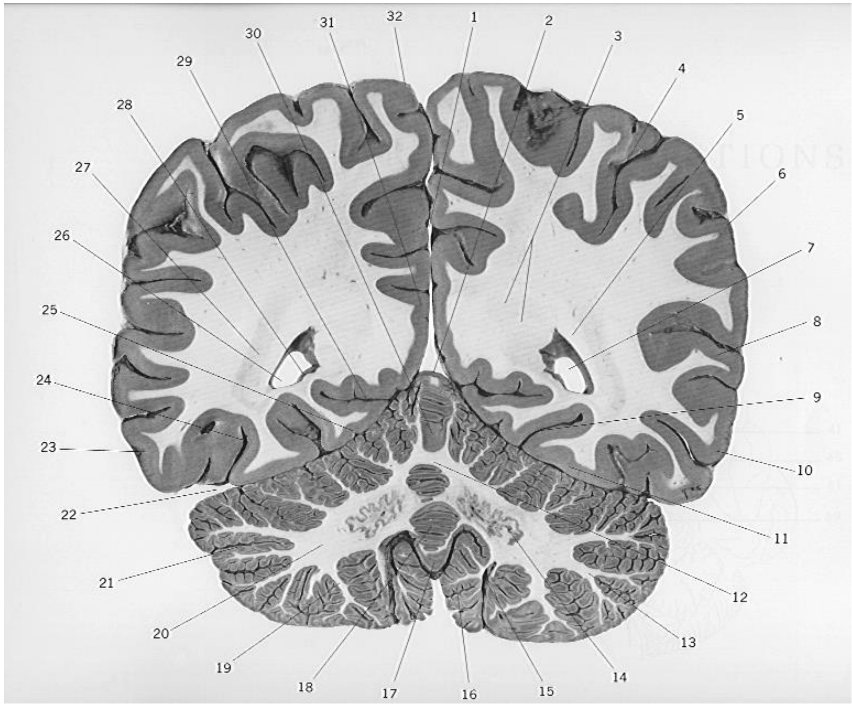
BrainSuite Workflow



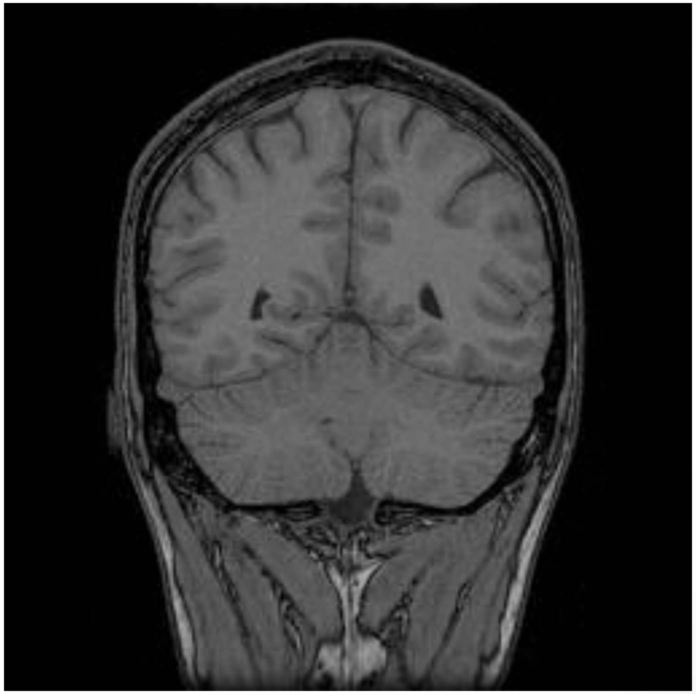
Cortical Surface Extraction

Magnetic Resonance Images

MRI provide noisy, limited resolution representations of brain anatomy

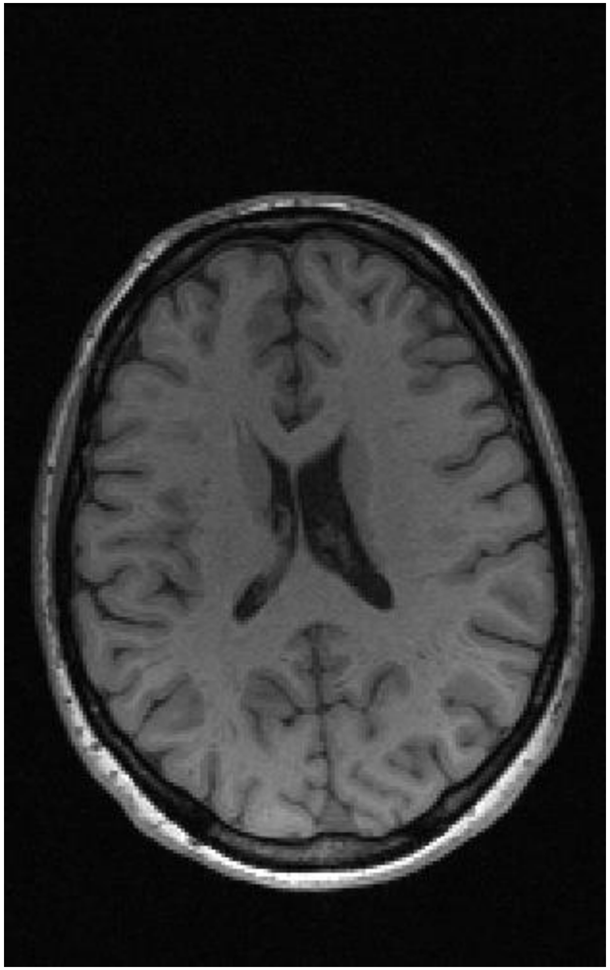


Stained section from a photographic atlas
(Roberts et al.)



T1 weighted MRI

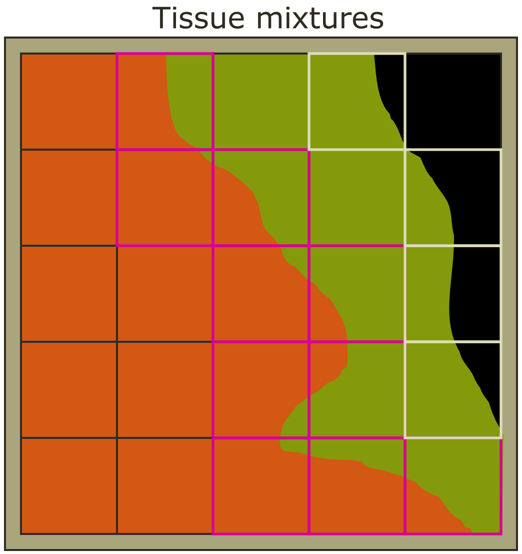
Nonuniformity and Noise

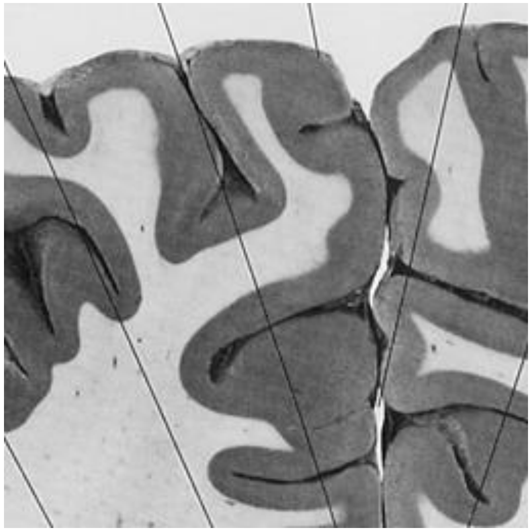


- The intensity of voxel would ideally be given only by the tissues present in that voxel.
- Imperfections in the scanner hardware, as well as susceptibility variations in the subject, introduce magnetic field artifacts that produce shading in the image.
- Other noise in the system will also confound the classification process.

Partial Volume Effects

- Finite resolution of MRI is insufficient for some neuroanatomical details.
- Each measurement is an average of the tissue signals in the voxel.





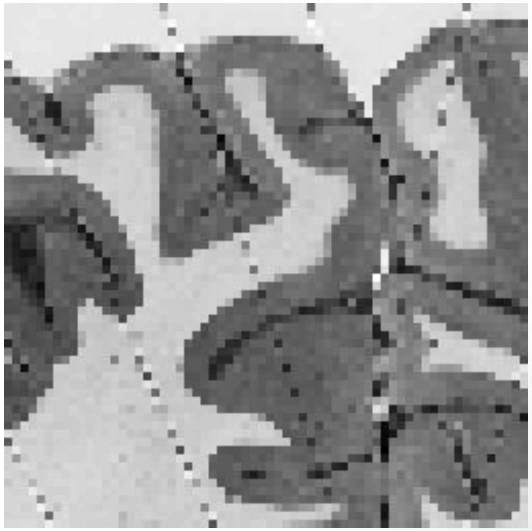
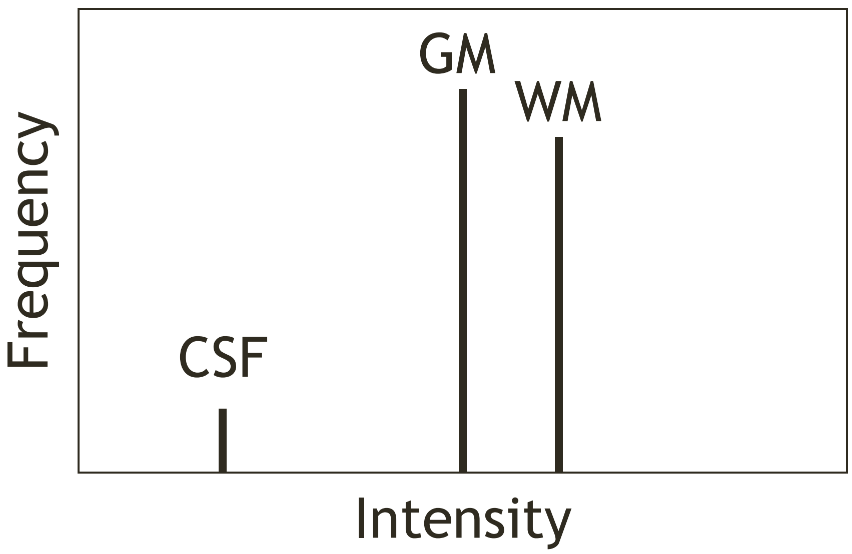
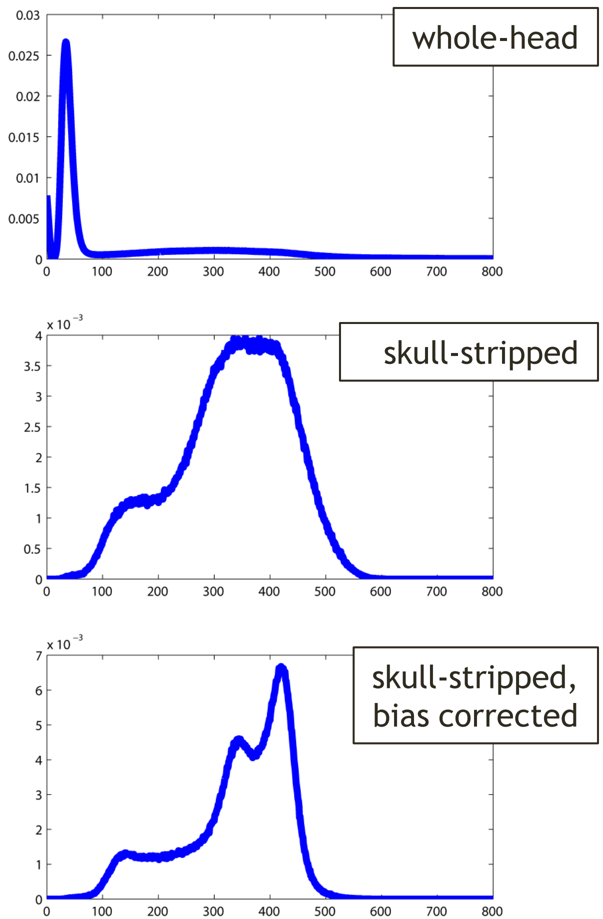


Image Formation: Ideal Case



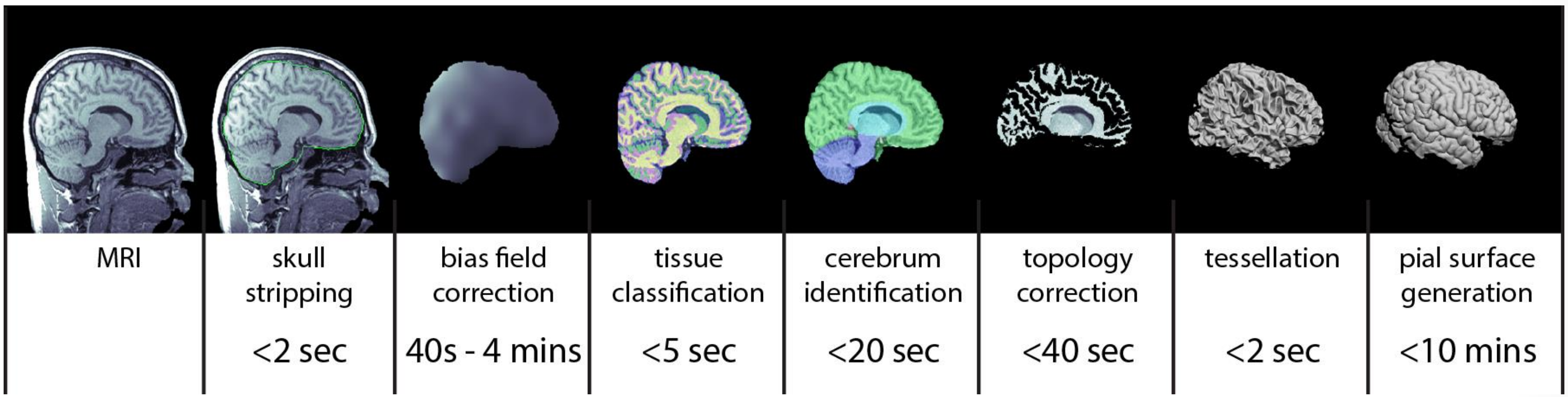
- In the ideal case:
  - An extracted brain would contain only GM, WM, and CSF
  - We would measure a single intensity value for each type of tissue present in the image.
  - The resolution would be sufficient that each voxel would be composed of a single tissue type
- If this were true, then classification would be simple

Image Formation: Reality



Histograms of: (top) a whole-head MRI (middle) a skull-stripped MRI (bottom) non-uniformity corrected skull-stripped MRI

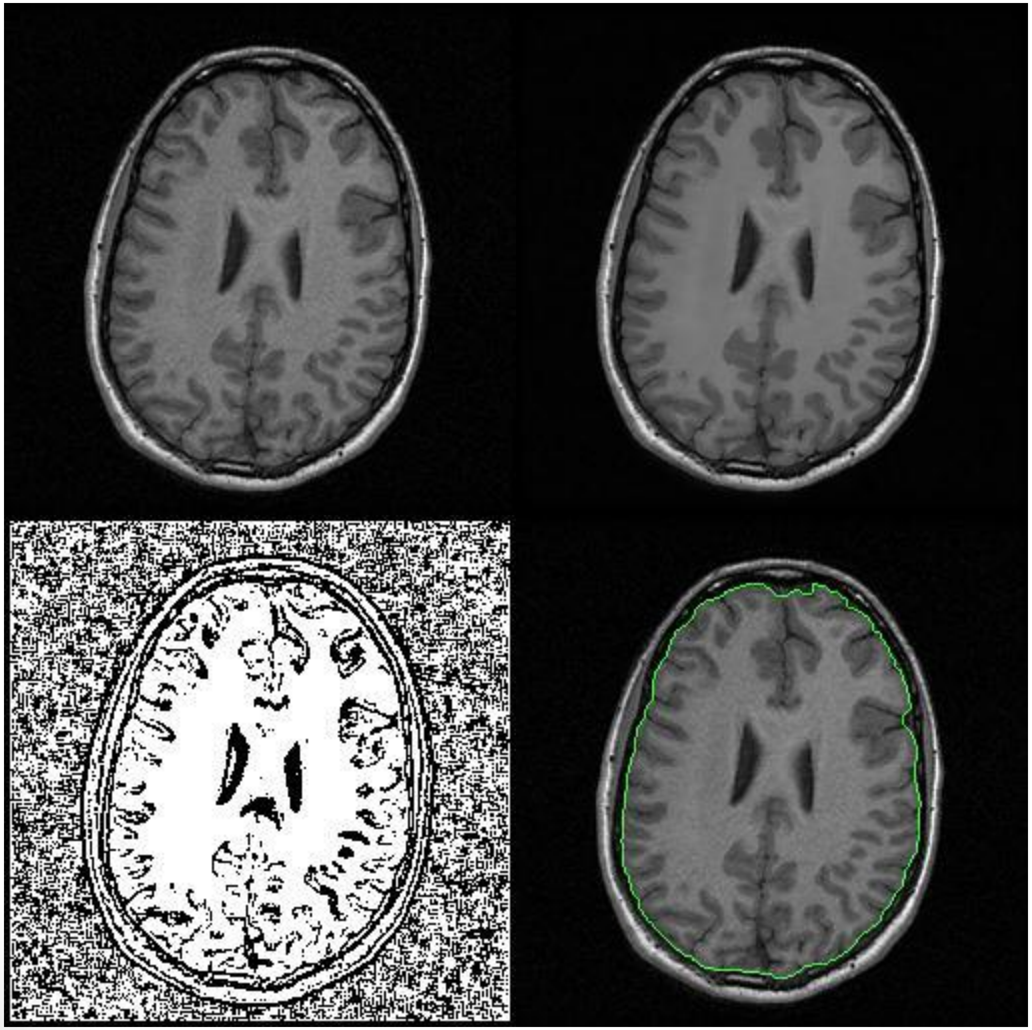
- Some other types of tissue are likely to be present (vessels, sinuses, etc.)
- Image artifacts produce variations in the measured intensity for the tissues
  - Slow spatial gain variation
  - Spatially independent noise
- Neuroanatomical detail is much too fine for the mm^3 voxel size typical in MRI



Cortical Surface Extraction

Brain Surface Extractor (BSE)

MRI Filtered MRI

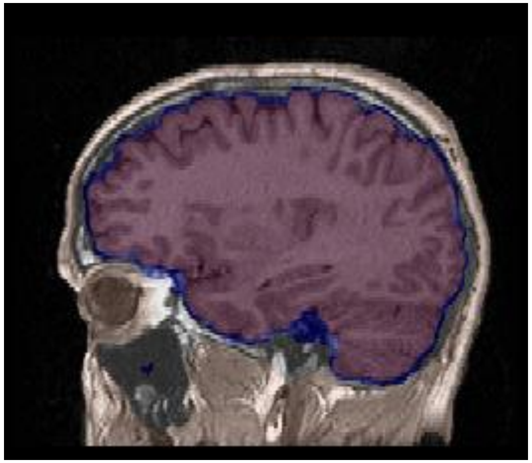


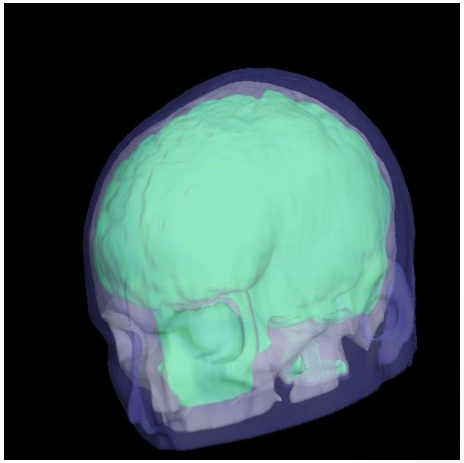
Edge Mask Brain Boundary (green)

- Extracts the brain from non-brain tissue (skull-stripping)
- We apply a combination of:
  - anisotropic diffusion filtering
  - edge detection
  - mathematical morphological operators
- This method can rapidly identify the brain within the MRI

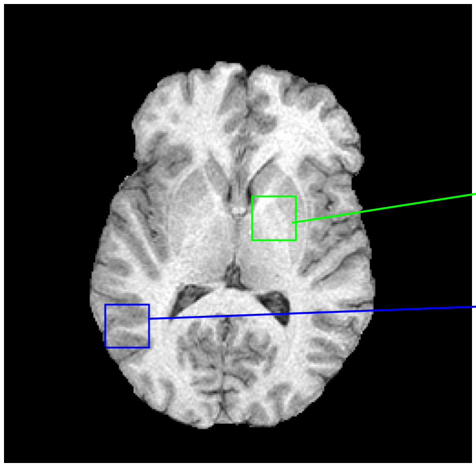
Skull and Scalp Modeling

- We can apply thresholding, mathematical morphology, and connected component labeling to MRI to identify skull and scalp regions.
  - The method builds upon the BSE skull stripping result.
  - The volumes produced by this algorithm will not intersect.
  - We can produce surface meshes from the label volume.
- The results are suitable for use in MEG/EEG source localization.

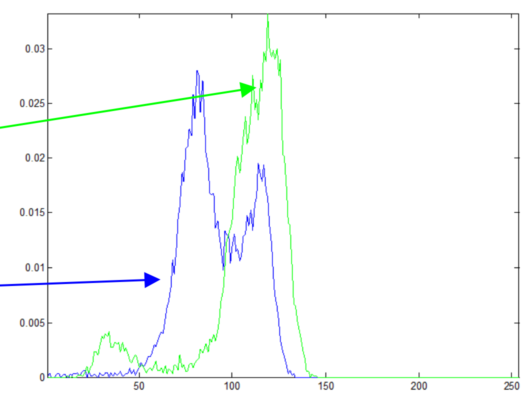




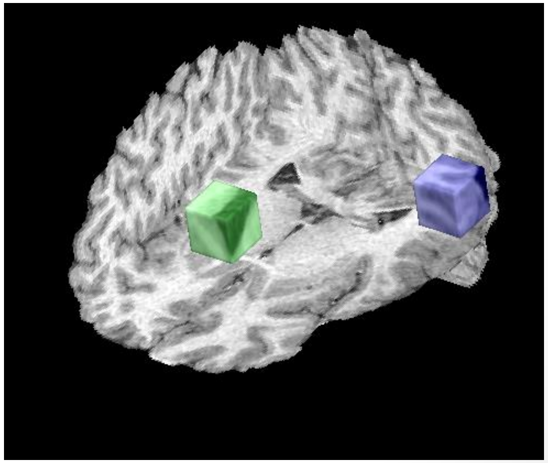
Bias Field Corrector



Two cubic regions of interest (ROIs)



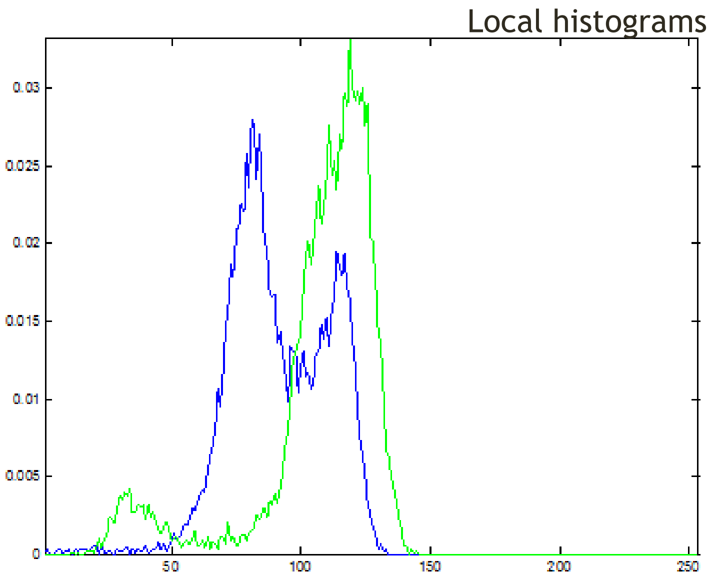
Histograms of the two ROIs

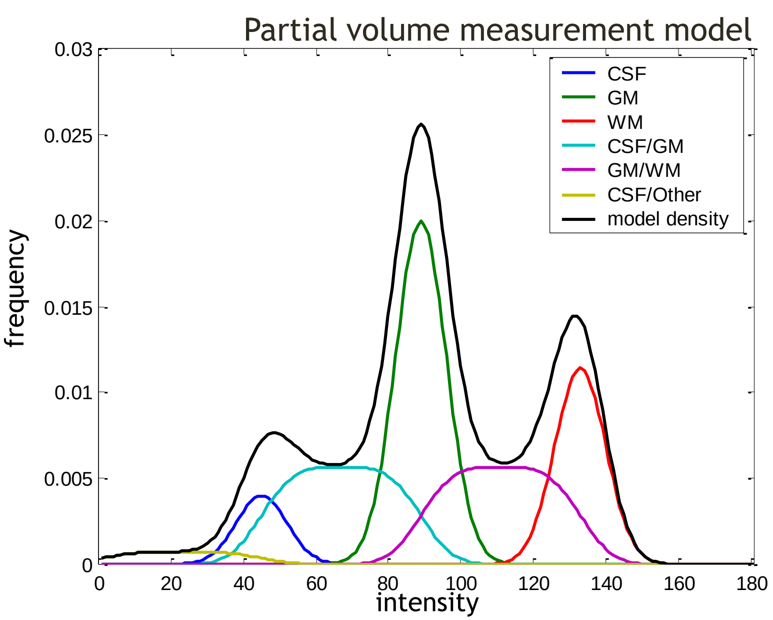


3D rendering of the ROIs

- Performs non-uniformity correction by analyzing regional histograms
- Sub-volumes have dramatically different profiles.
- Regional histograms reflect this.

Bias Field Corrector

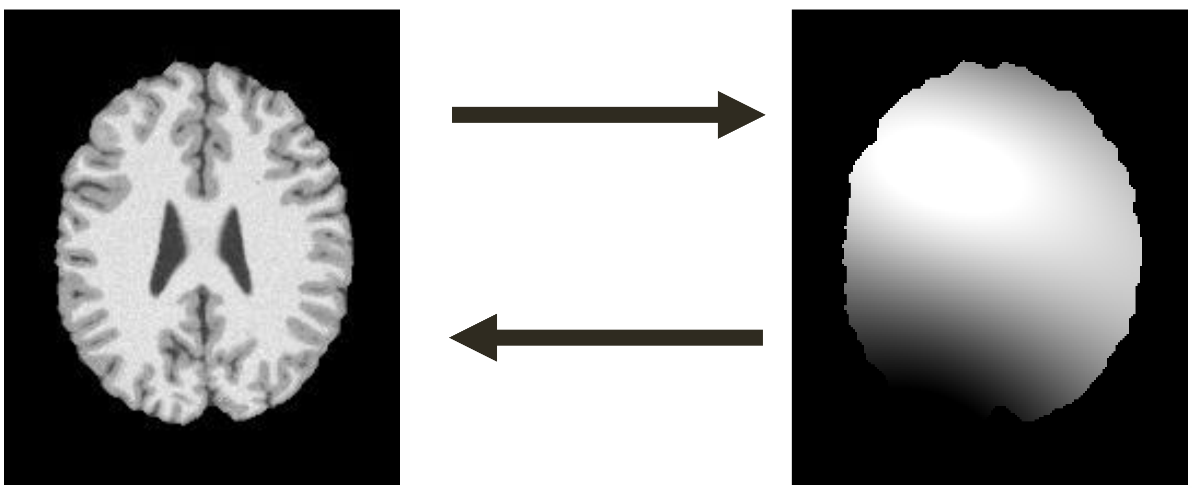




- We can fit a tunable model of the tissue profiles to many ROIs spaced throughout the brain.
- This allows us to estimate the local gain variation.

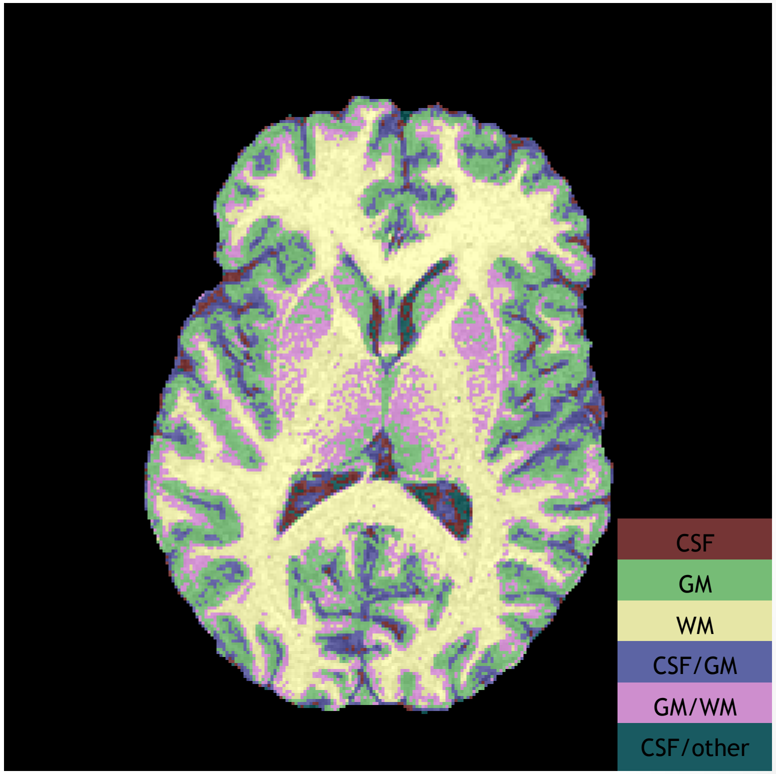
Bias Field Corrector

- Estimate bias parameter at several points throughout the image.
- Remove outliers from our collection of estimates.
- Fit a tri-cubic B-spline to the estimate points.
- Divide the image by the B-spline to make the correction.



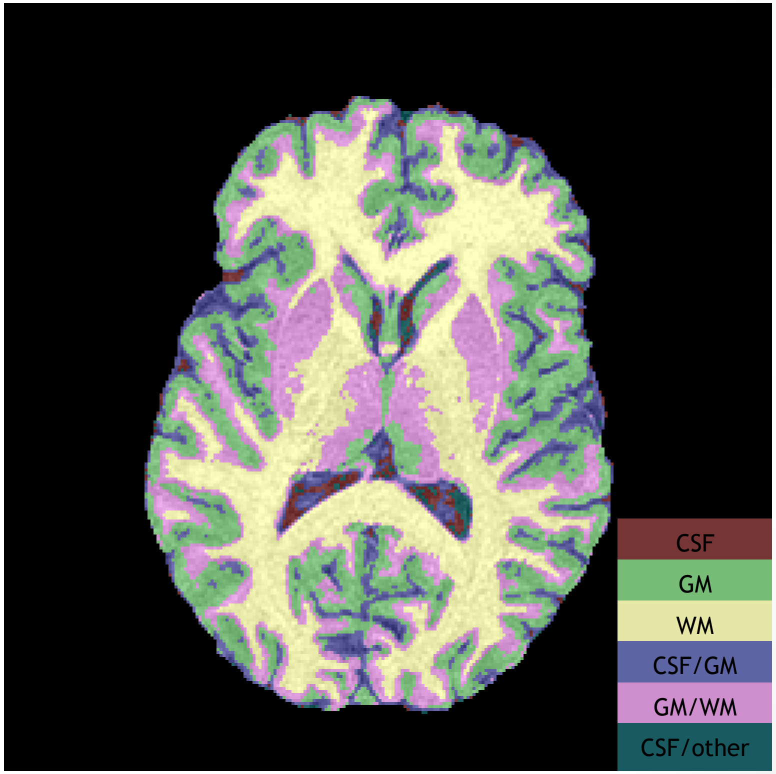
Maximum Likelihood Classifier

- We can compute a maximum likelihood classification from our measurement model.
- At each voxel, we simply compute the probability of the intensity value belonging to a particular tissue, and then select the label that has the highest likelihood.
- This maps each intensity value to a specific label, and it thus very fast.
- Does not take into account any of the surrounding labels.



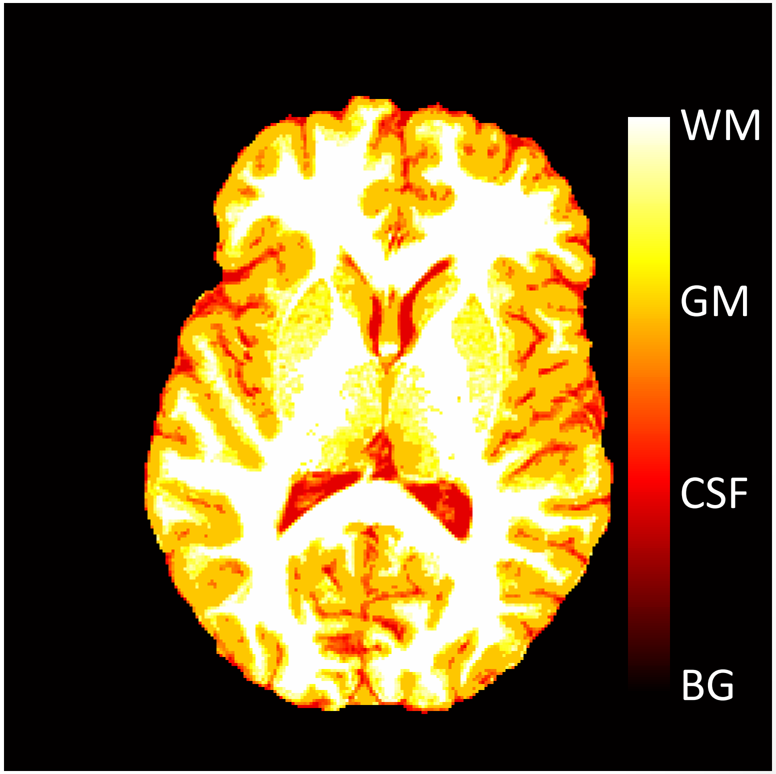
Partial Volume Classifier (PVC)

- We can construct a model that computes a score for local neighborhoods
  - Higher scores for pixel configurations that are similar
  - Lower scores for unlikely combinations (e.g., WM next to CSF)
- We use this model to produce a maximum *a posteriori* (MAP) classifier
- We maximize this function using the Iterated Conditional Modes (ICM) algorithm
  - Initialize ICM with a maximum likelihood labeling.
  - Iteratively update each individual label to maximize



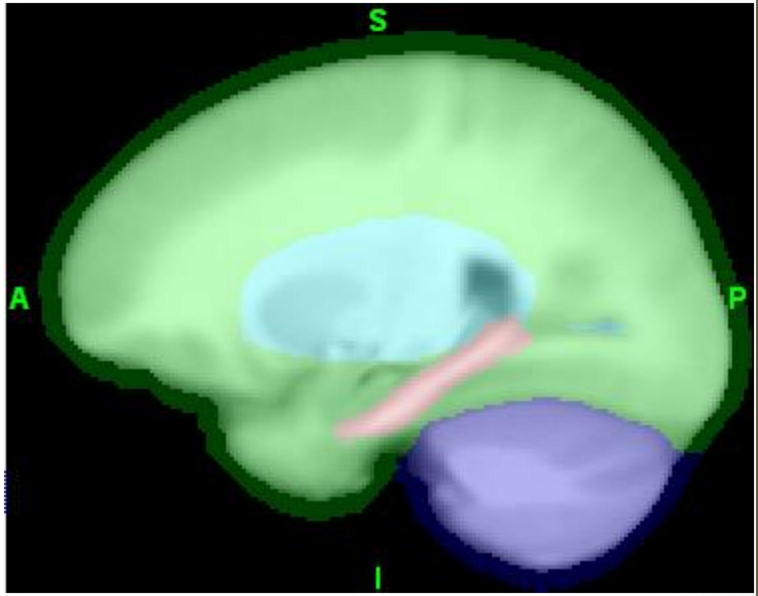
PVC Tissue Fraction Estimation

- For each brain voxel, we estimate the tissue fraction as follows:
  - Pure voxels are 100%.
  - Each mixed tissue voxel is assigned a fractional value based on where its signal intensity falls between the class means.

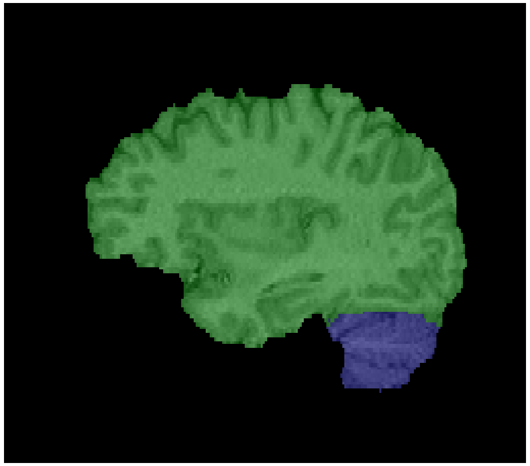


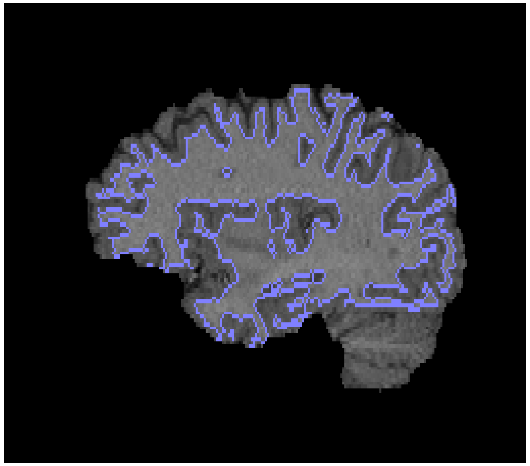
Cerebrum Identification

- For the cortical surface, we are interested in the cerebrum, which we separate from the rest of the brain.
- We achieve this by registering a multi-subject average brain (ICBM452) to the individual brain using AIR (R. Woods)
- We have labeled this atlas:
  - cerebrum / cerebellum
  - subcortical regions
  - left / right



Cortex Extraction

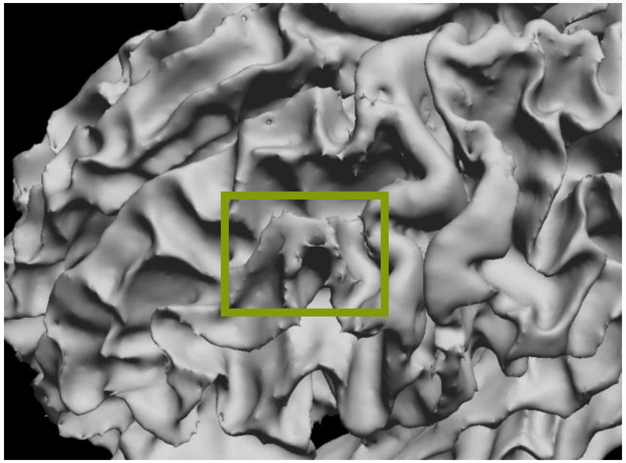


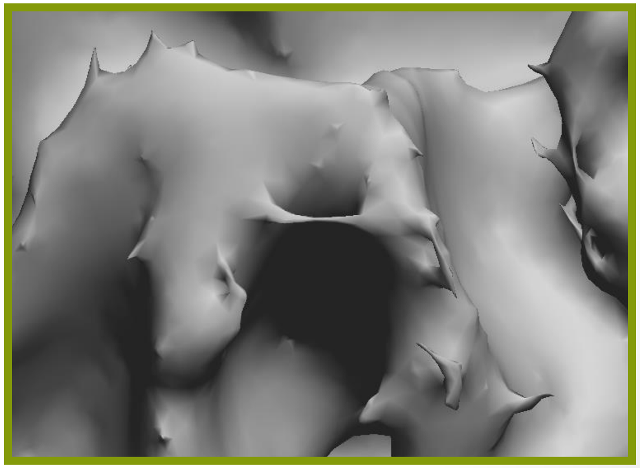


- We combine our registered brain atlas with our tissue map
  - retain subcortical structures, including nuclei
  - identify the inner boundary of the cerebral cortex

Topological Errors

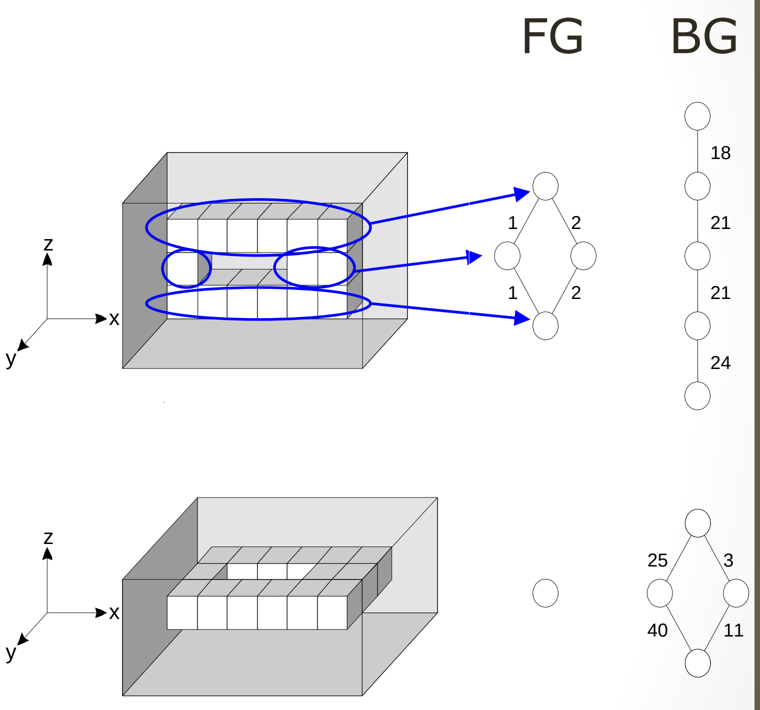
- In normal human brains, the cortical surface can be considered as a single sheet of grey matter.
- Closing this sheet at the brainstem, we can assume that the topology of the cortical surface is equivalent to a sphere, i.e., it should have no holes or handles.
- This allows us to represent the cortical surface using a 2D coordinate system.
- Unfortunately, our segmentation result will produce a surface with many topological defects.





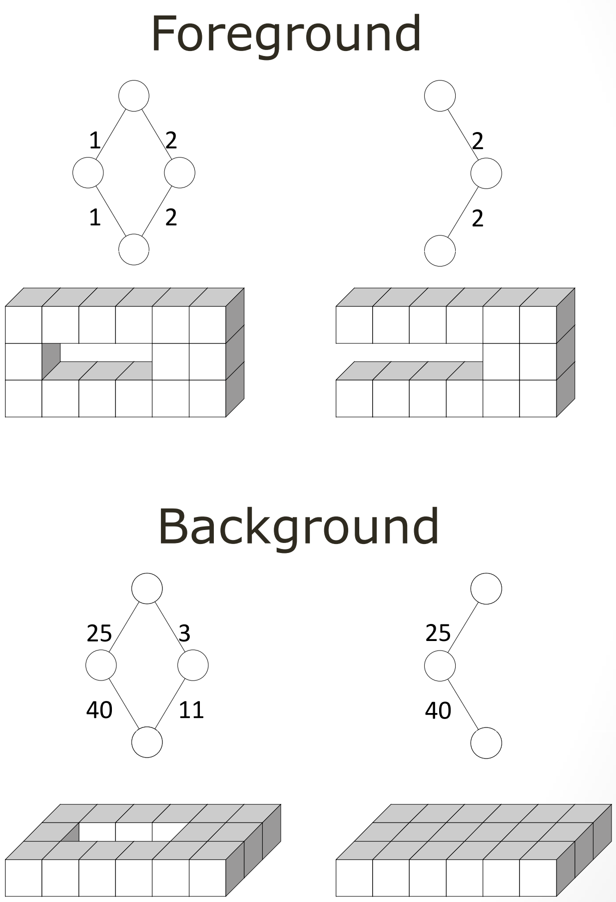
Topological Errors

- We can identify topological loops in the volume segmentation by representing it with two graphs.
- If these graphs have cycles, then topological handles exist in the object.

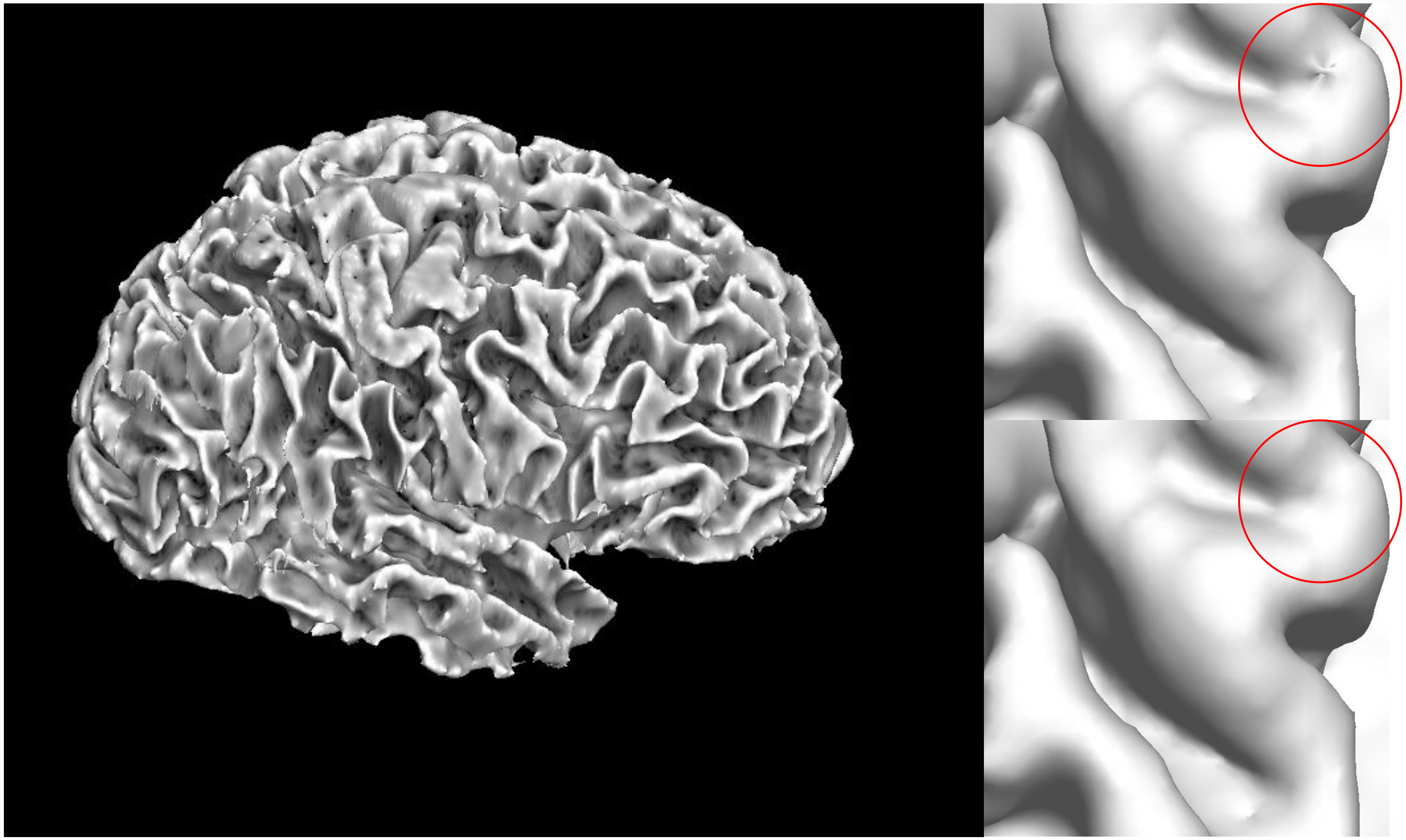


Topological Editing

- By analyzing the graphs, we can identify locations in the object where we can either remove or add voxels in order to break a cycle in the graph.
- We can make our decisions of where to edit based on making small changes to the object.
- This method allows us to rapidly remove all topological defects and produce a volumetric segmentation that will yield a genus zero surface mesh.



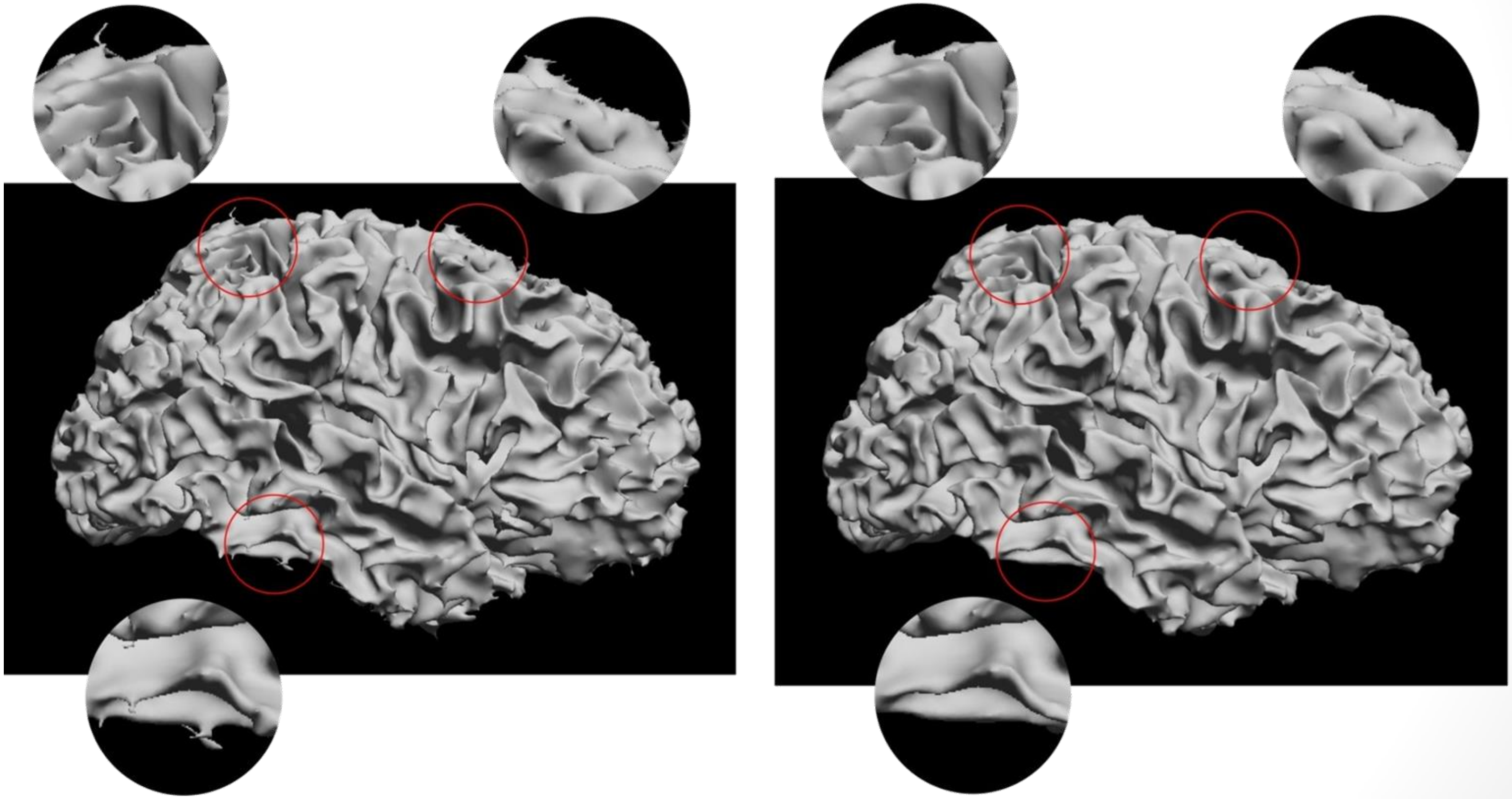
Topology Correction



Cortical surface model produced from binary masks

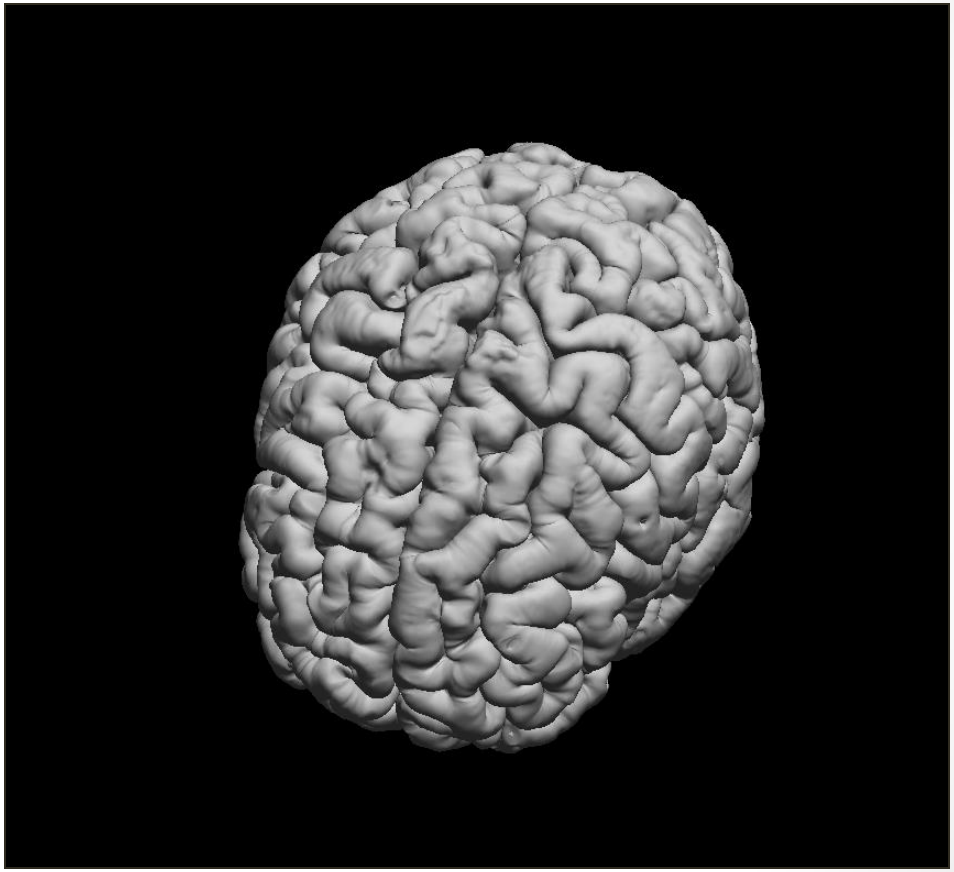
- (top right) close-up view of a handle on the surface generated from the volume before topological correction
- (bottom right) close-up view of the same region on the surface generated from the same volume after topology correction.

Digital Object Filtering

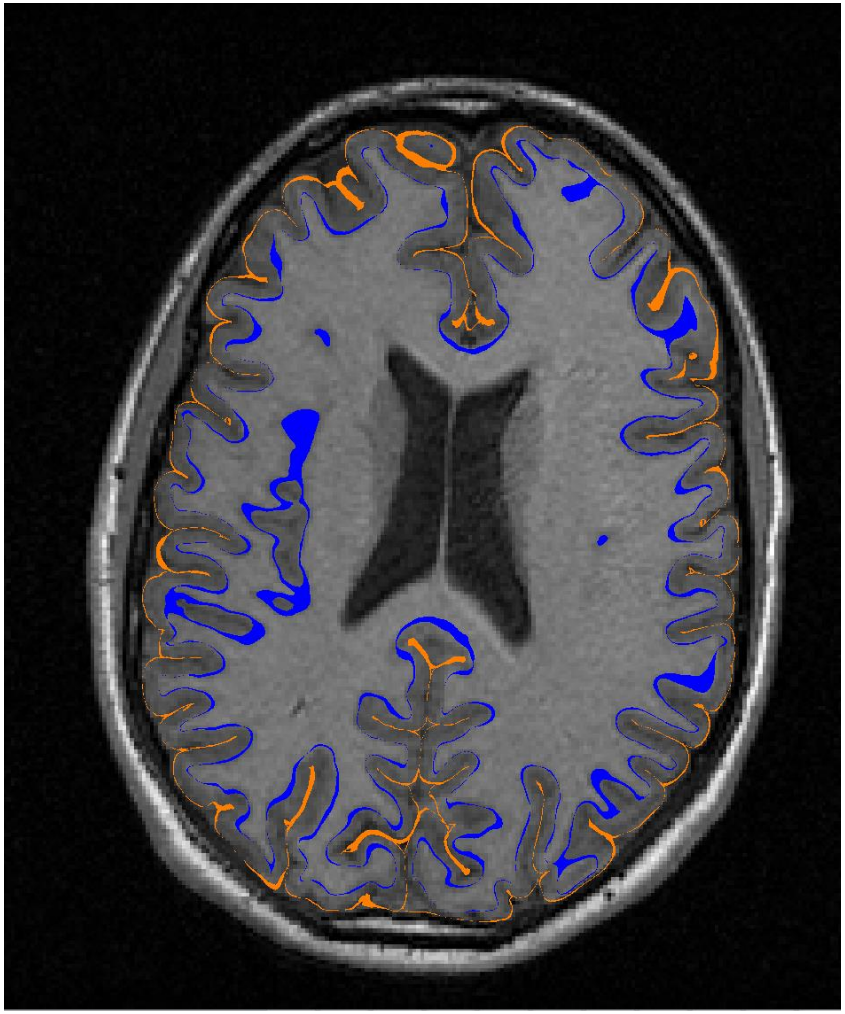


Pial Surface

- Expand inner cortex to outer boundary
- Produces a surface with 1-1 vertex correspondence from GM/WM to GM/CSF
  - Preserves the surface topology
  - Provides direct thickness computation
  - Data from each surface maps directly to the other



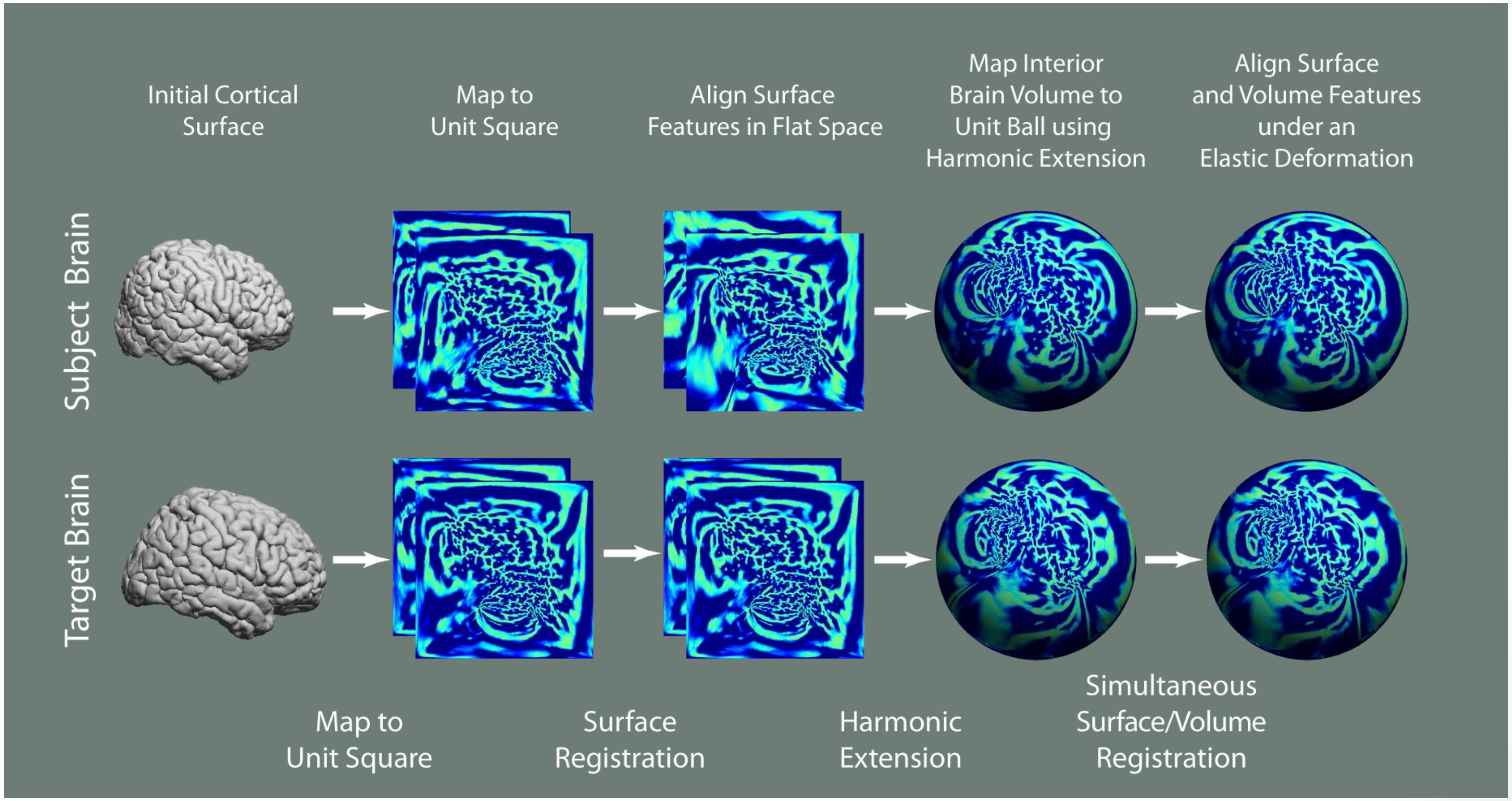
Pial Surface



Contour view showing the inner (blue) and outer (orange) boundaries of the cortex.

SVReg: Surface-constrained Volumetric Registration

Surface-constrained Volumetric Registration



BrainSuite Atlas

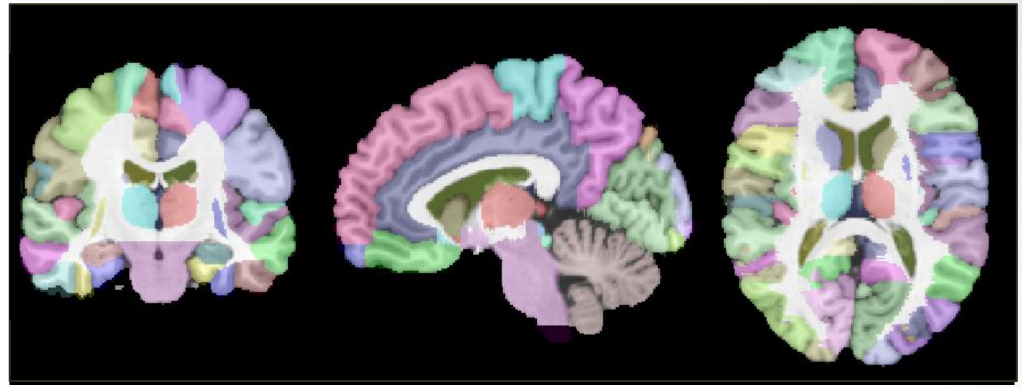
Single subject atlas labeled at USC by expert neuroanatomist

26 sulcal curves per hemisphere

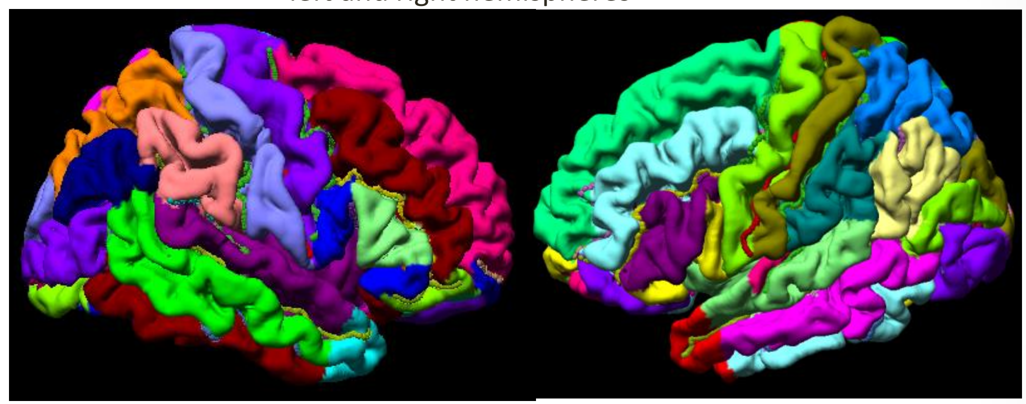
98 volumetric regions of interest (ROIs), 35*2=70 cortical ROIs

Included with BrainSuite13 as 'BrainSuiteAtlas1'

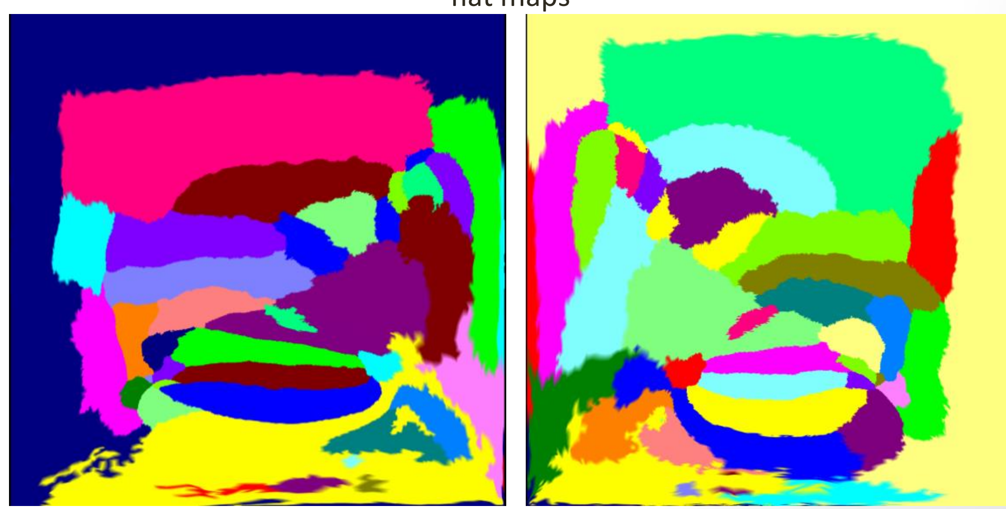
T1 MRI and label overlay



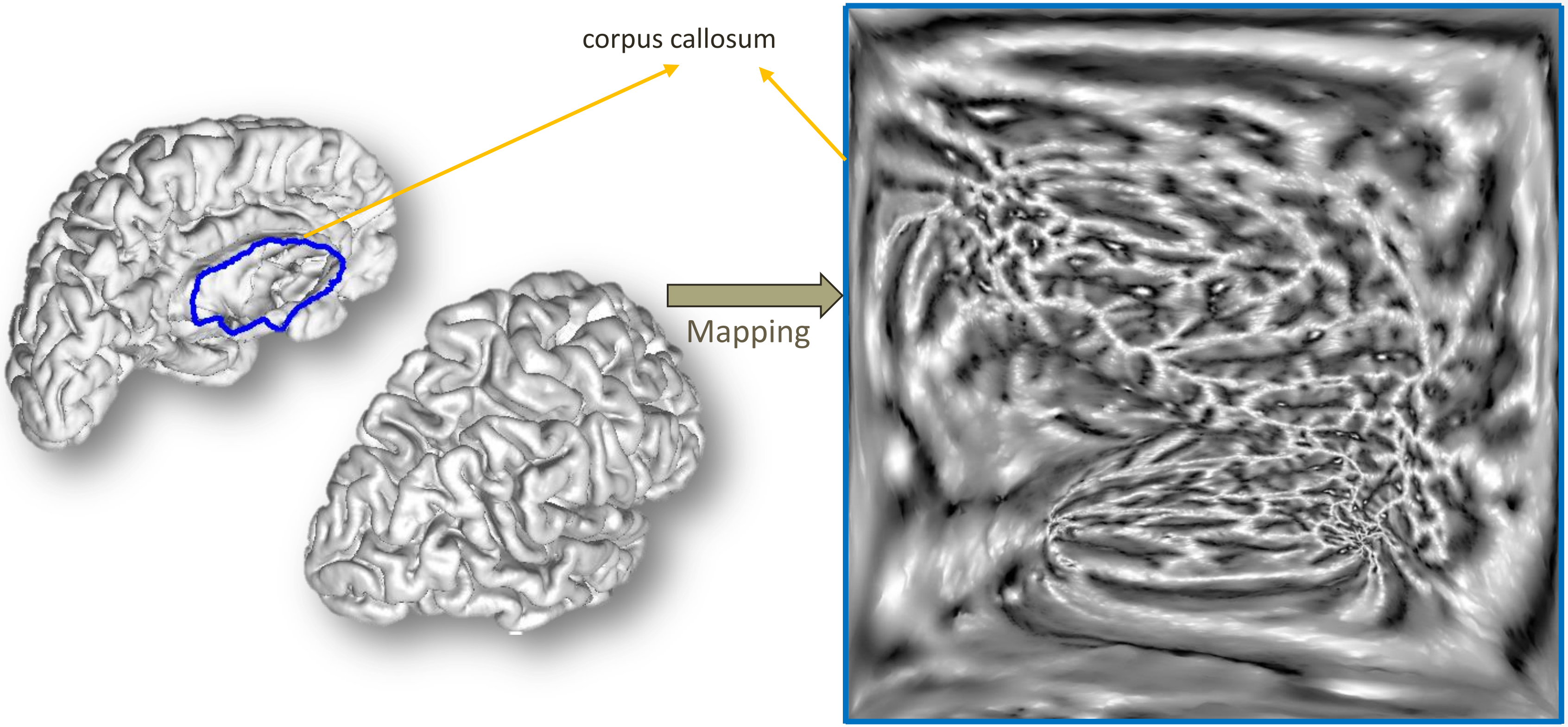
left and right hemispheres



flat maps



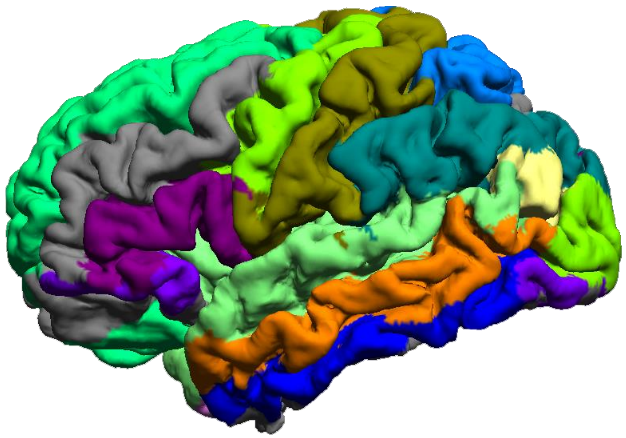
Cortical Surface Parameterization

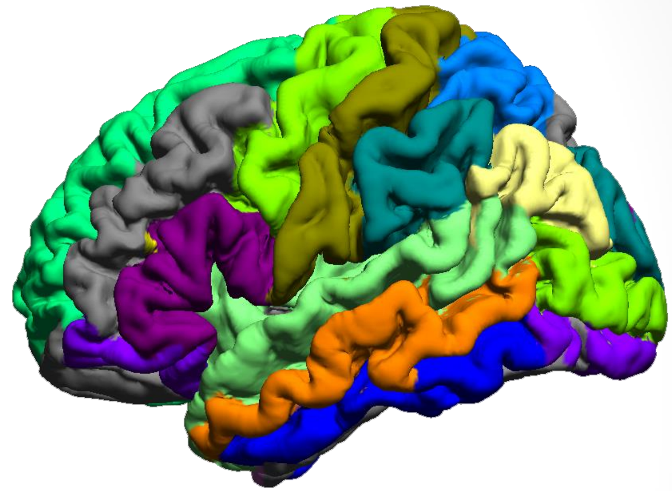


Flat-map color coded by curvature

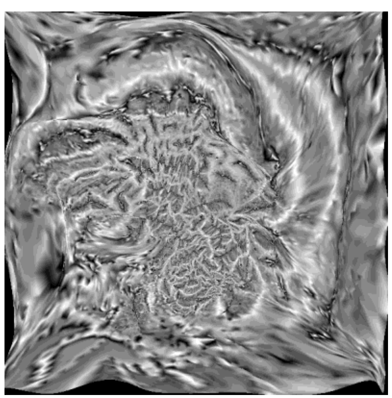
Each hemisphere is mapped to the unit square using an energy-minimization technique.

Curvature-based Registration

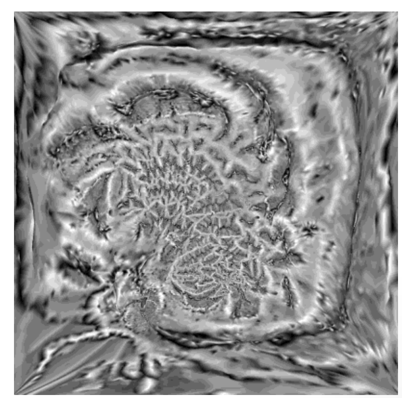




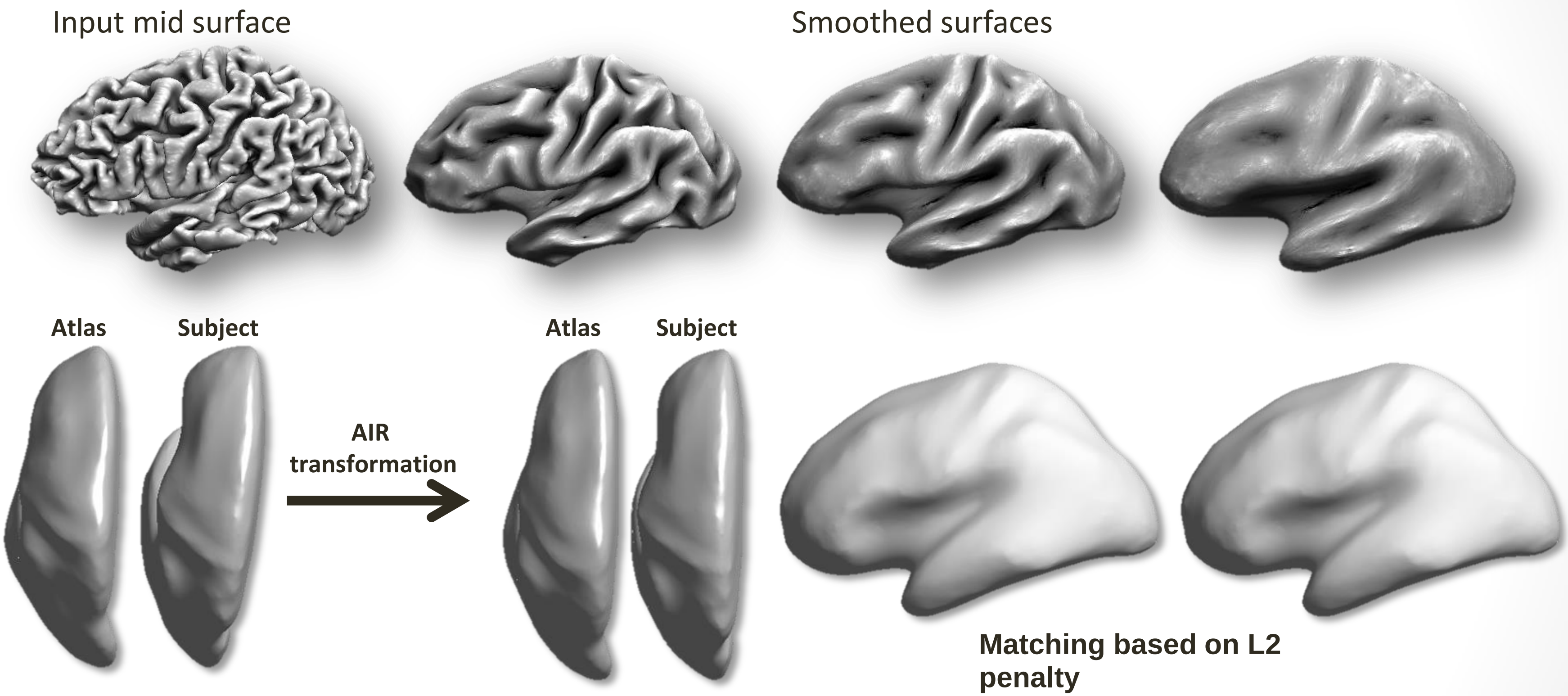
subject



atlas



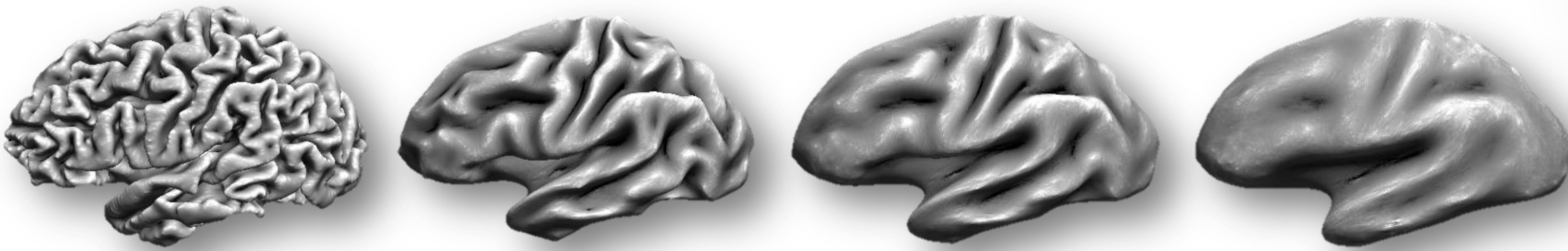
3D Alignment



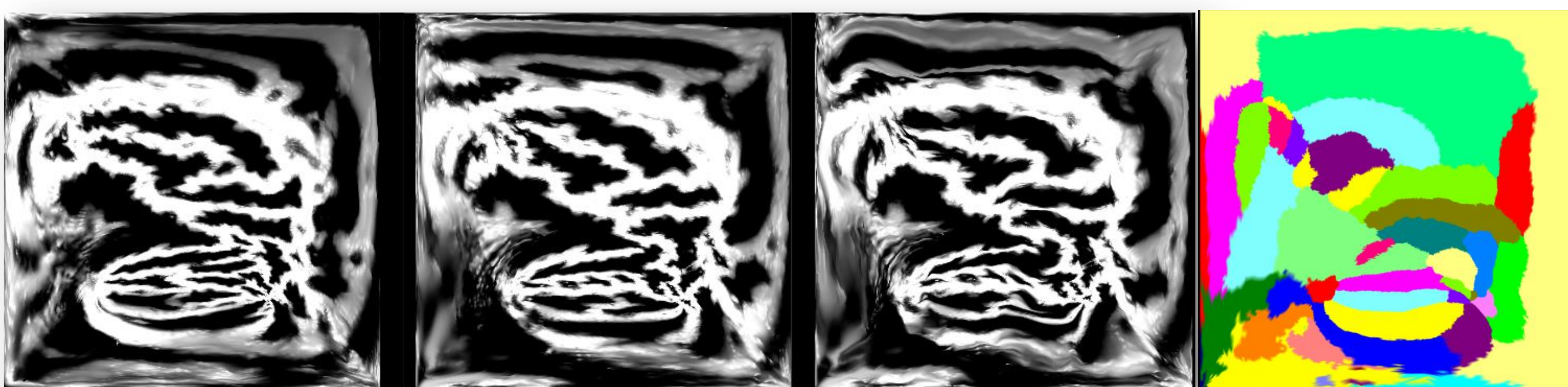
Multi-resolution Surface Matching

Input mid surface

Smoothed surfaces

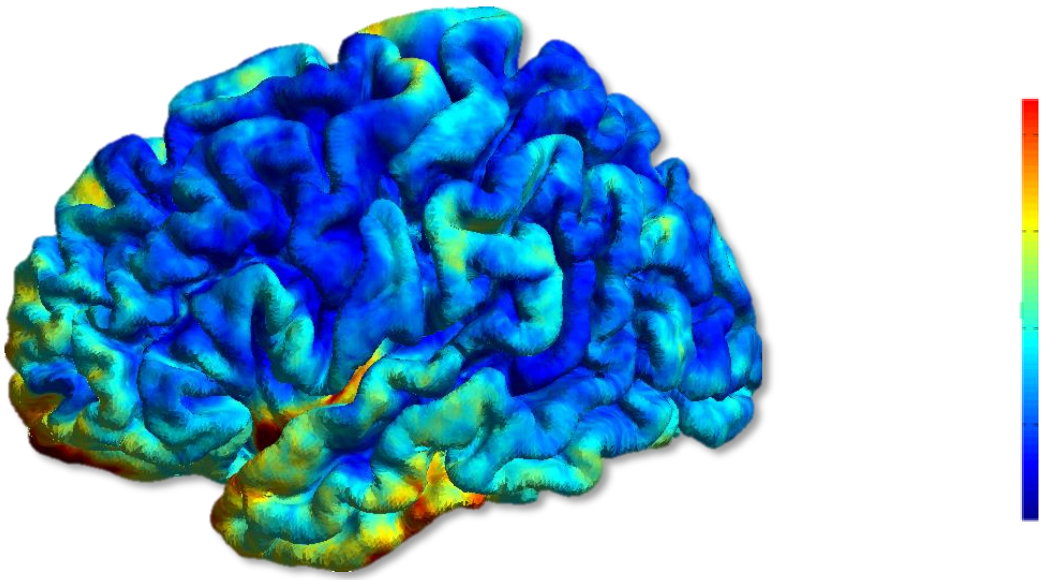


Cumulative curvature computation for multi-resolution representation



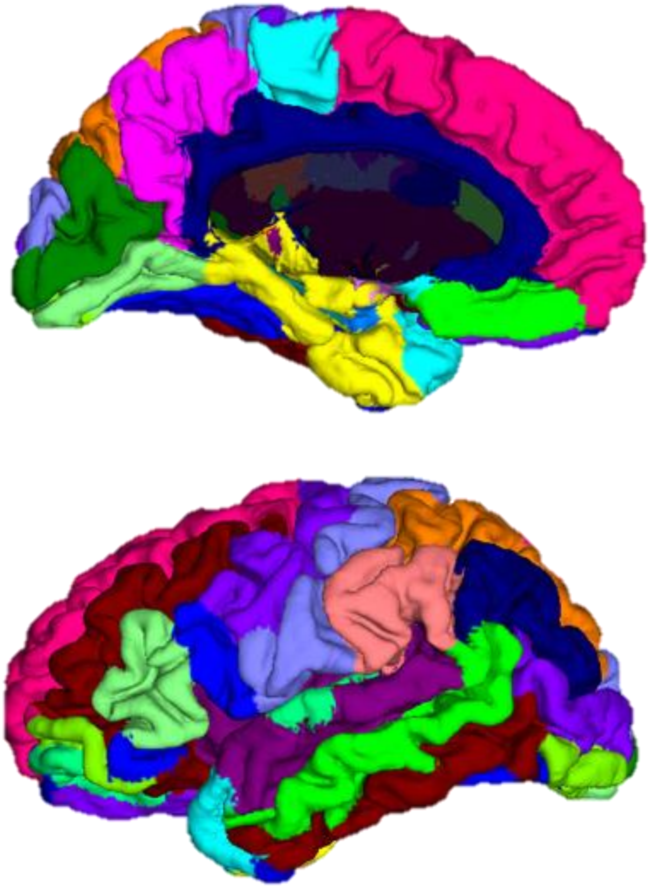
Elastic matching for atlas and subject flat maps

Curvature Weighting

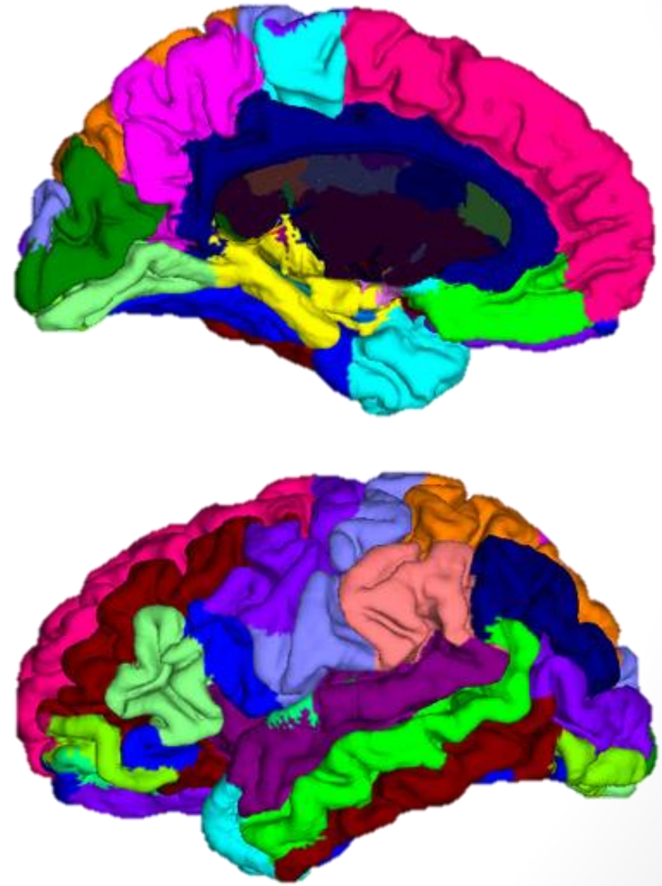


- Shown is the color-coded curvature variance, as computed by aligning 100 normal adult brains.
- Inverse of curvature variance is used as a weighting on the curvature cost function to reduce the influence of highly variable areas.

Curvature Weighting Results

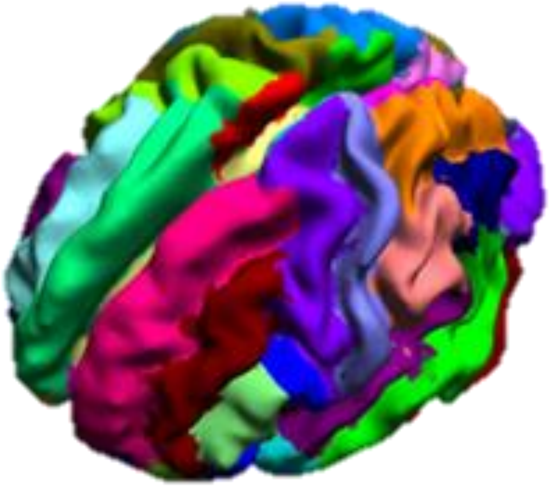


No curvature variance weighting

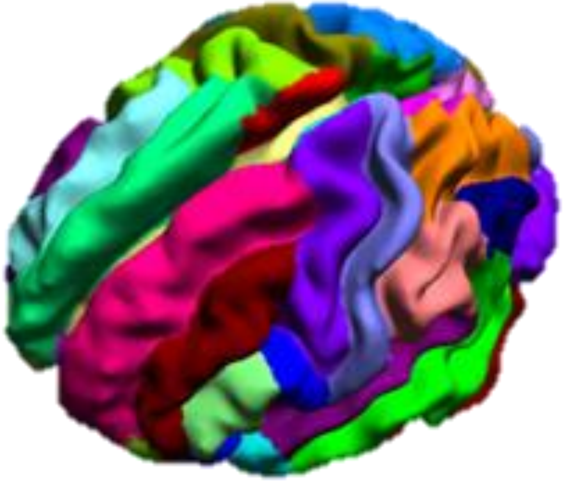


With curvature-variance weighting

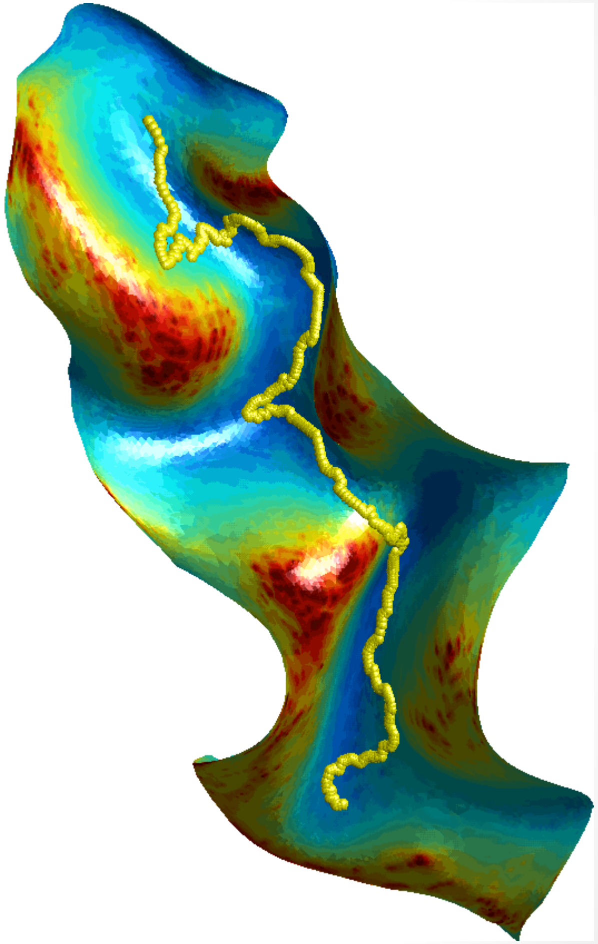
Refinement of labels and sulci



Original labels plotted on a smoothened representation of a cortical surface

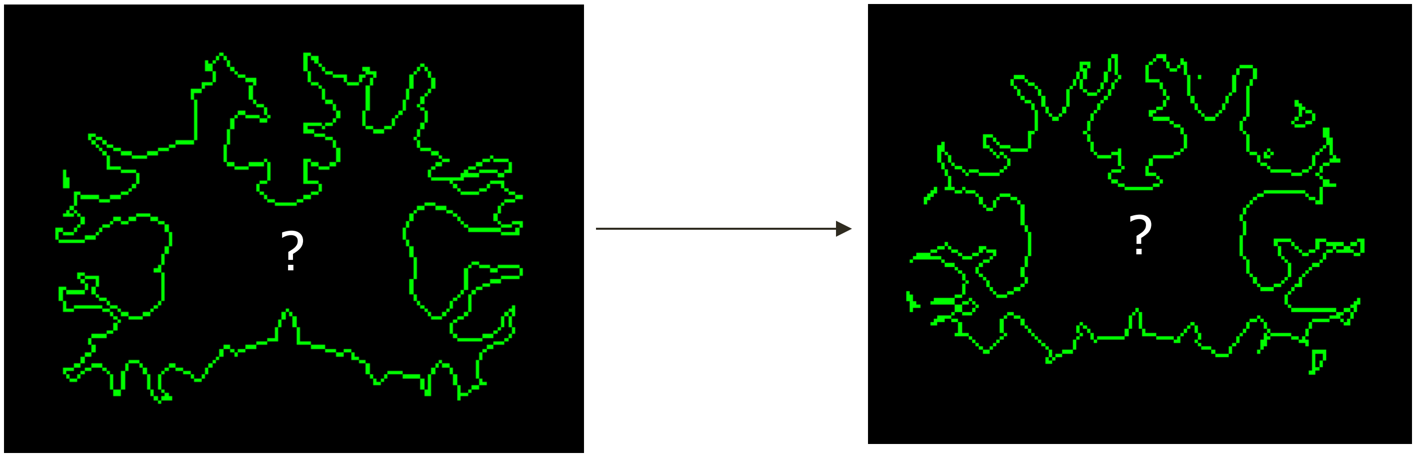


Labels after geodesic curvature Flow plotted on a smoothened representation of a cortical surface



Animation of the geodesic curvature flow for sulcal refinement

Surface Registration Methods

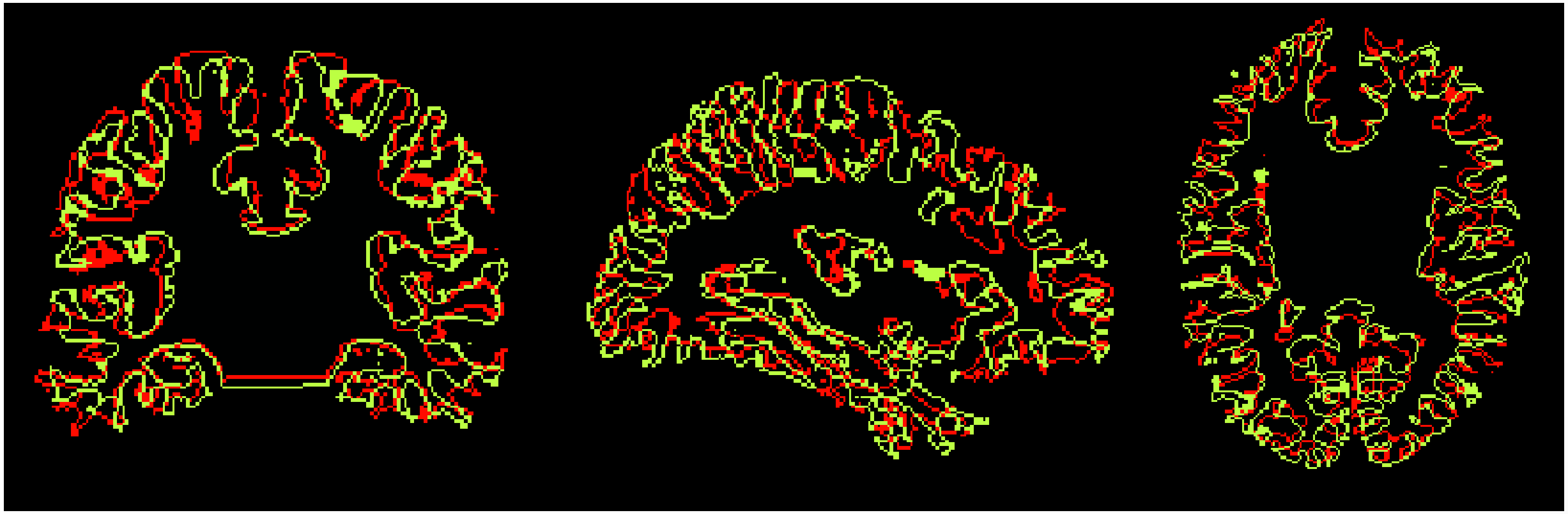


+ Accurate sulcal alignment

- Doesn't define volumetric correspondence

Motivation for Surface-constrained Volumetric Registration

Alignment of 2 brains by AIR (5^{th} order)



+ Good alignment of subcortical structures

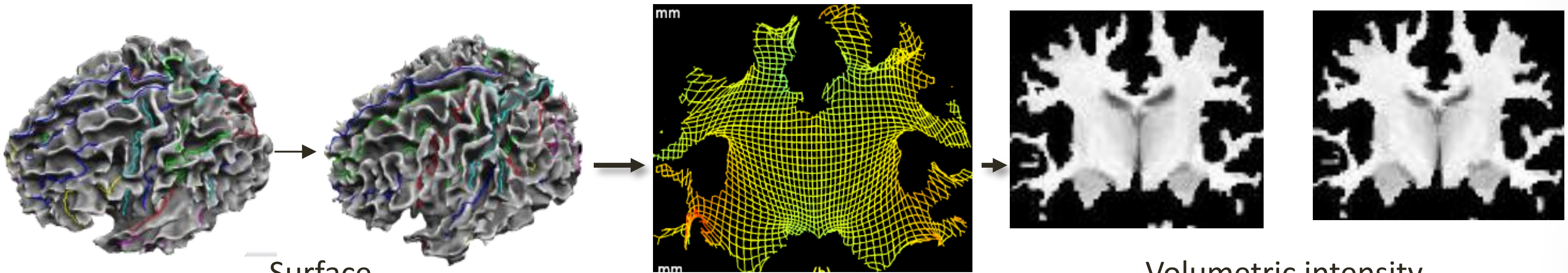
- Sulcal alignment inaccurate

Extension to Volumetric Registration

Accurate Sulcal Alignment

Accurate Subcortical Feature Alignment

Intensity-based Alignment



Surface registration

Extrapolation to volume

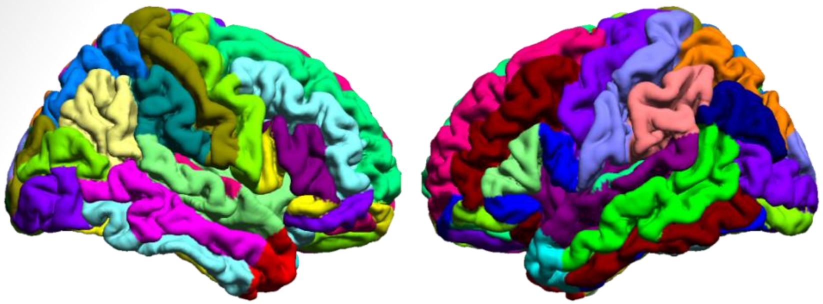
Volumetric intensity registration

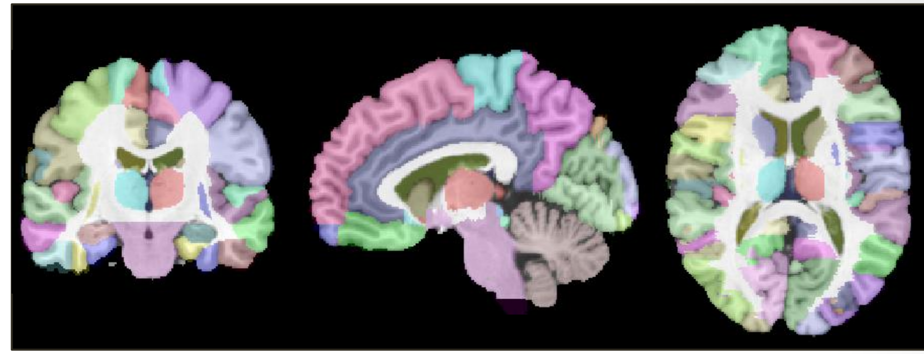
Solves the difficult problem of surface/sulcal registration in 3D volume

Surface and Volume Registration (SVReg) method performs accurate alignment of both cortical surfaces as well as subcortical volumes.

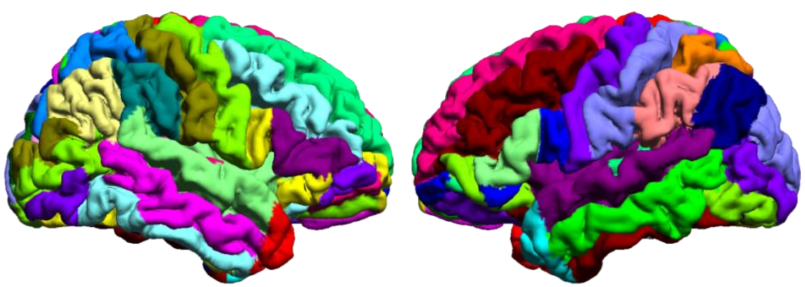
Joshi et al. (2007) IEEE Trans. Med. Imag.

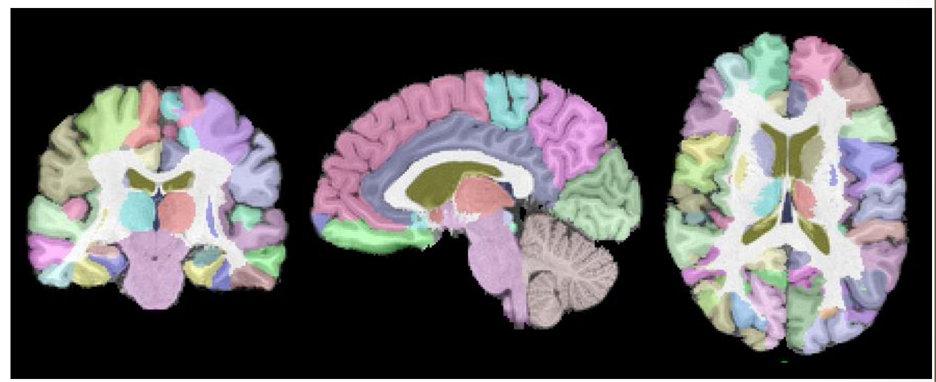
Atlas





Subject



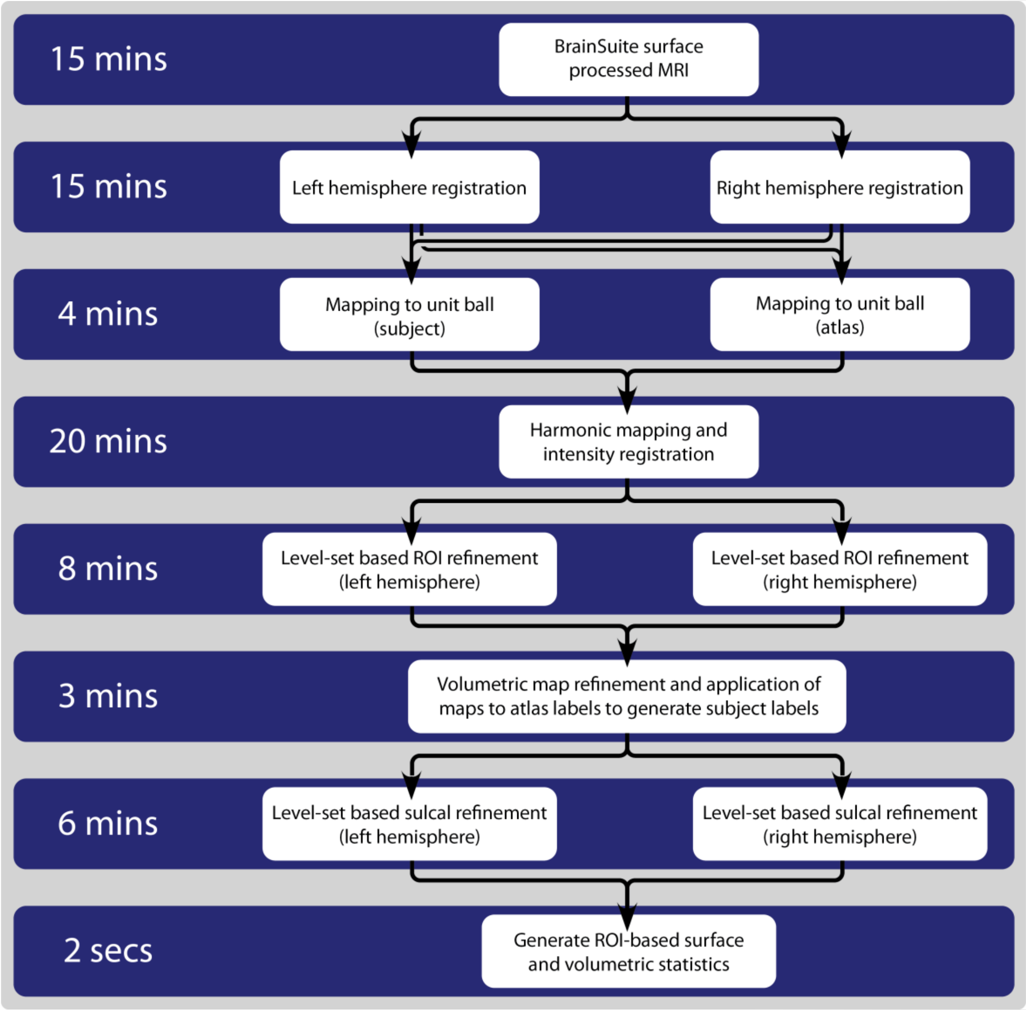


BrainSuite ROI Labeling (top) Surface and volume views of the BrainSuite13 anatomical atlas, delineated into anatomical regions of interest. (bottom) Similar views of an automatically labeled subject dataset.

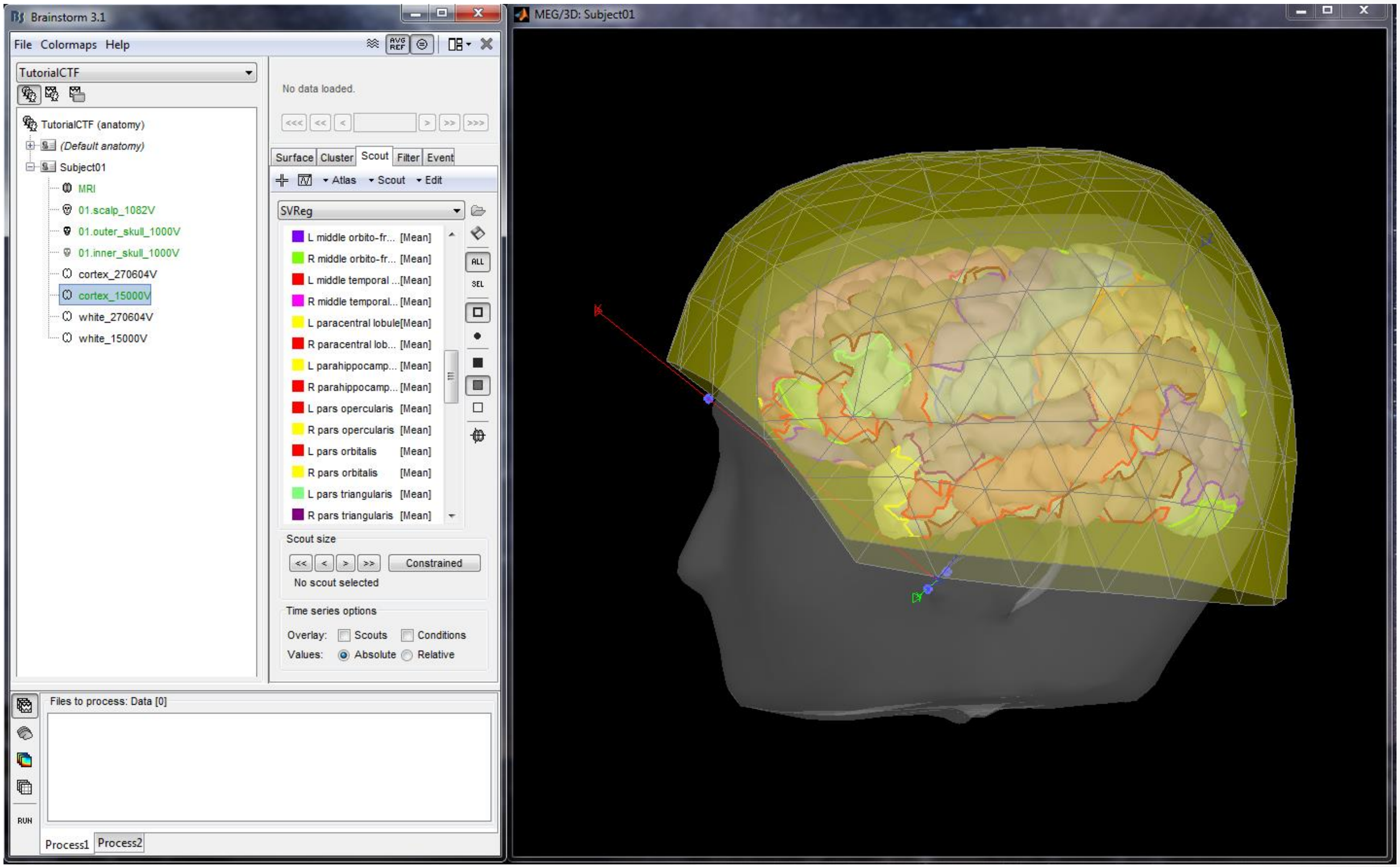
SVReg Software Workflow

SVReg Outputs

- Labeled cortical surfaces
- Labeled brain volume
- Measurements for each ROI (area, volume)
- Mappings to atlas space
- Mapped sulcal curves



Integration with BrainStorm



BrainSuite Cortical Surface Model with ROIs Labeling imported into BrainStorm. The BrainSuite parcellation can be directly imported into BrainSuite, where the ROIs are useful for interpreting current sources.

see also: http://neuroimage.usc.edu/brainstorm/Tutorials/SegBrainSuite

BDP:
BrainSuite Diffusion Pipeline

Diffusion Image Acquisition

- A set of diffusion-weighted images is acquired with diffusion-sensitizing magnetic field gradients
- Gradients are oriented in different directions
- A 3D volume image is acquired for each direction
- Reconstruction methods are used to estimate the local diffusion properties

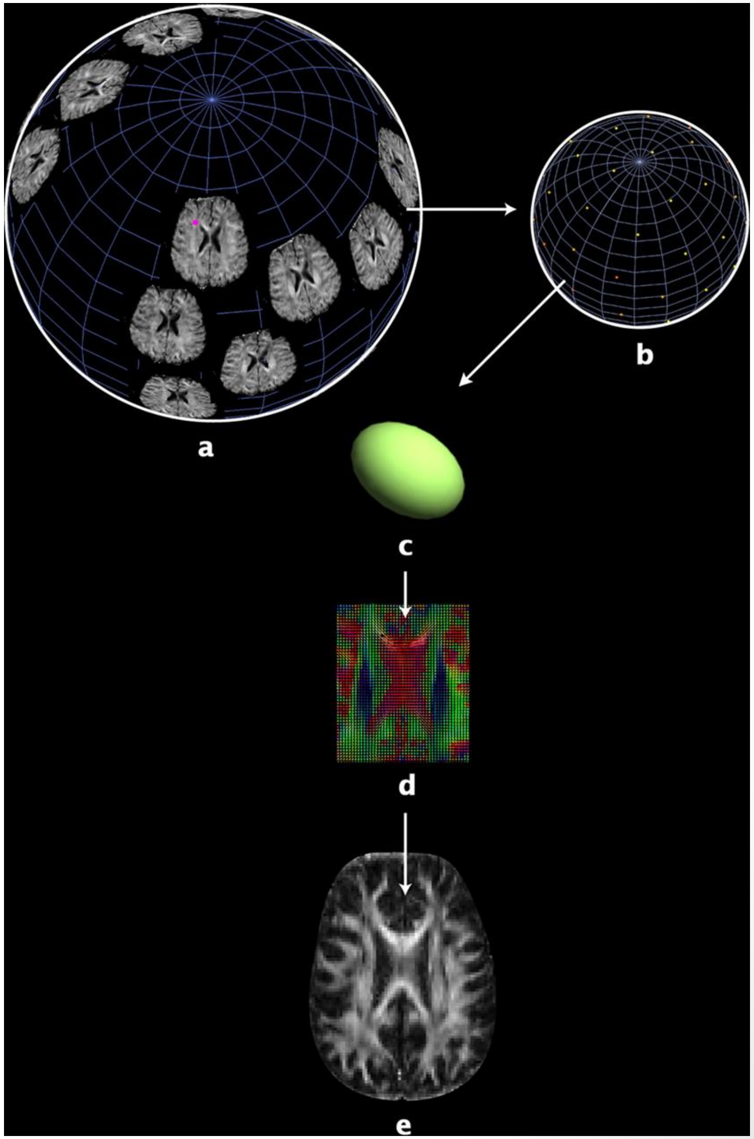
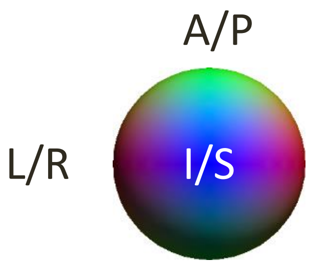
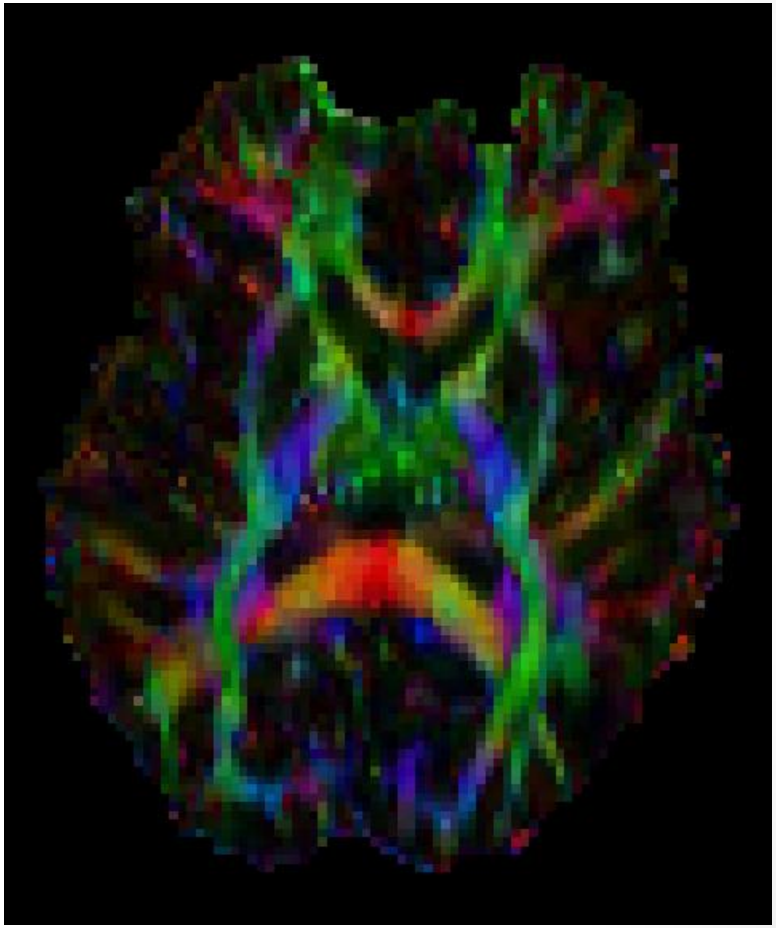


Image from: Chiang M et al. (2009) Genetics of Brain Fiber Architecture and Intellectual Performance J. Neurosci. 29:2212-2224

Diffusion Tensor Imaging (DTI)

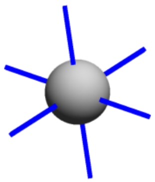
- With at least six directions and a baseline image, a tensor model can be estimated.
- Different types of tissue will have different diffusion properties
  - Oriented along nerve fibers
  - Free diffusion in CSF and grey matter
- Visualization of scalar properties (e.g., fractional anisotropy)
- Visualization of major eigenvector using direction encoded color (DEC) maps
  - Red: x, left/right
  - Green: y, anterior/posterior
  - Blue: z, inferior/superior

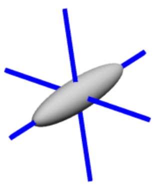


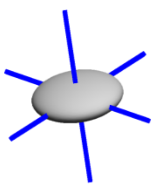


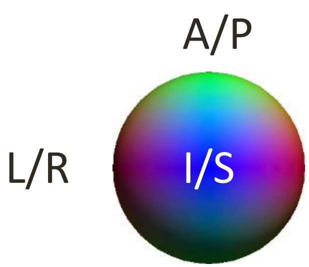
DTI Visualization

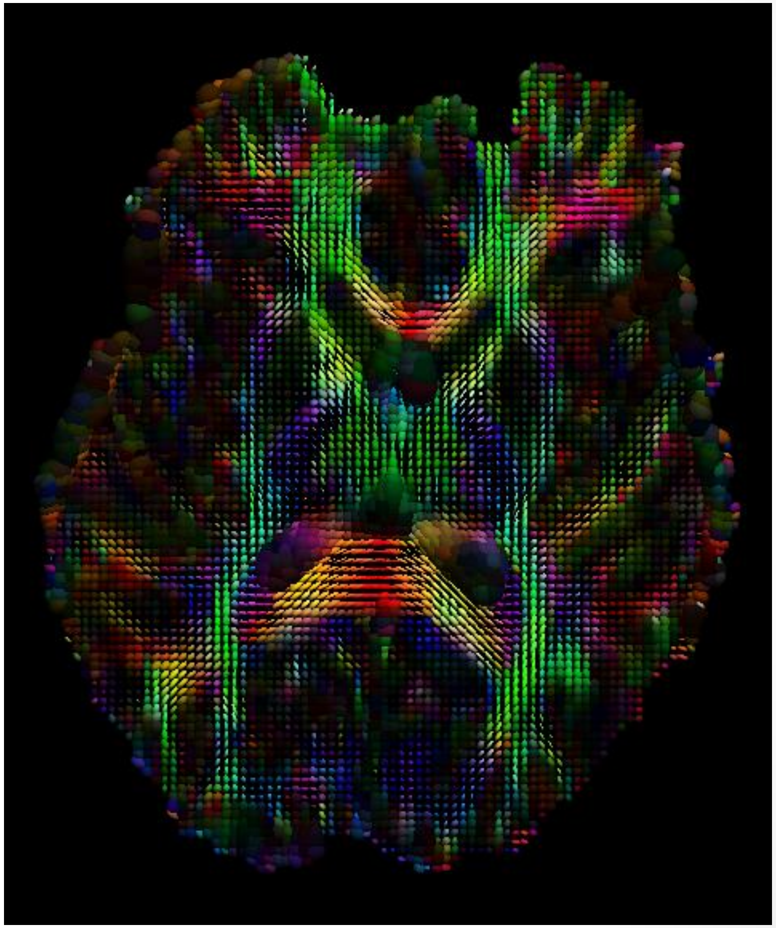
Often visualized using ellipsoids


Spherical shapes indicate isotropic diffusion


Elongated shapes indicate directionality

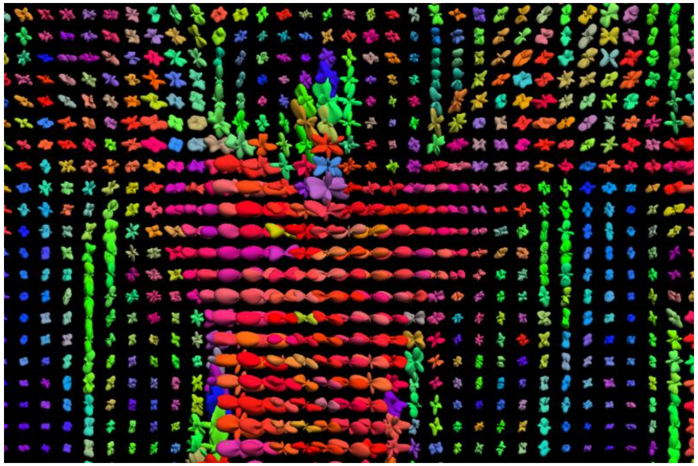

Flat discs are suggestive of the crossing or junction of nerve fibers





High Angular Resolution Diffusion Imaging (HARDI)

- The tensor model is limited in what it can resolve
- Fiber tracts may cross in a voxel, presenting ambiguities in determining the meaning of the diffusion pattern
- By sampling in many more directions, we can get a more complete picture of the diffusion pattern
- Examples include Q-Ball imaging (Tuch, 2004)
- Can be processed and visualized using spherical harmonics



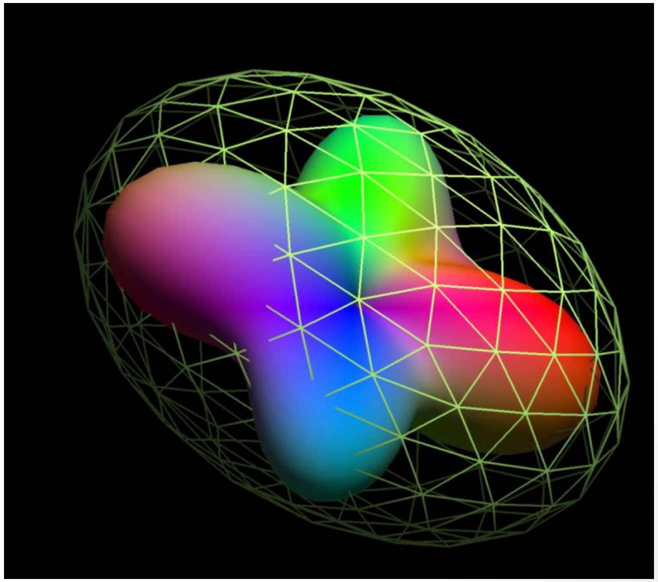
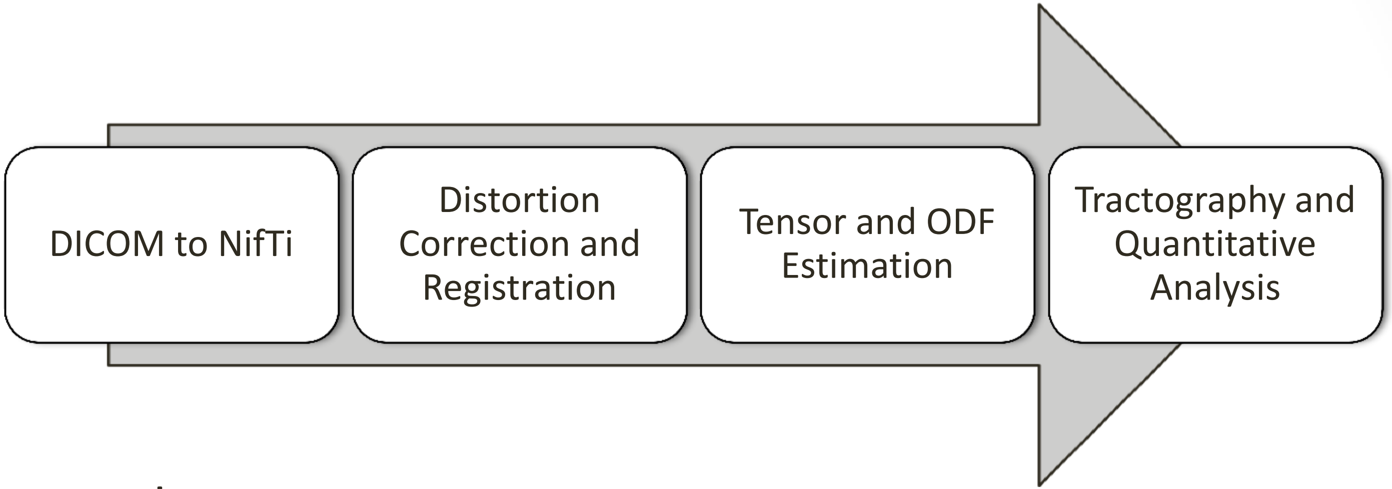


Image from Shattuck et al. (2008) Visualization Tools for High Angular Resolution Diffusion Imaging, *Medical Image Computing and Computer Assisted Intervention (MICCAI) 2008*

BrainSuite Diffusion Pipeline

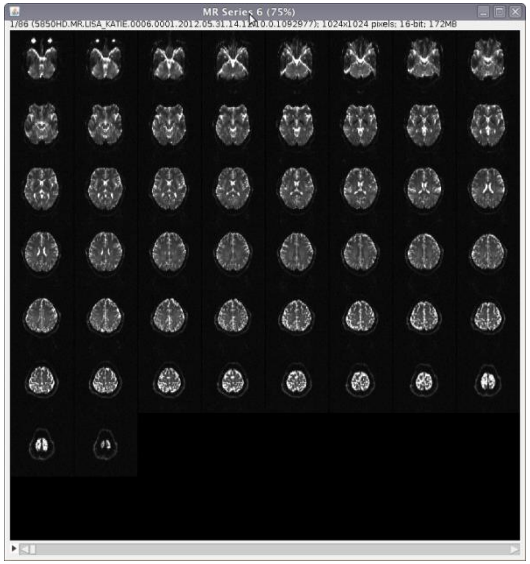


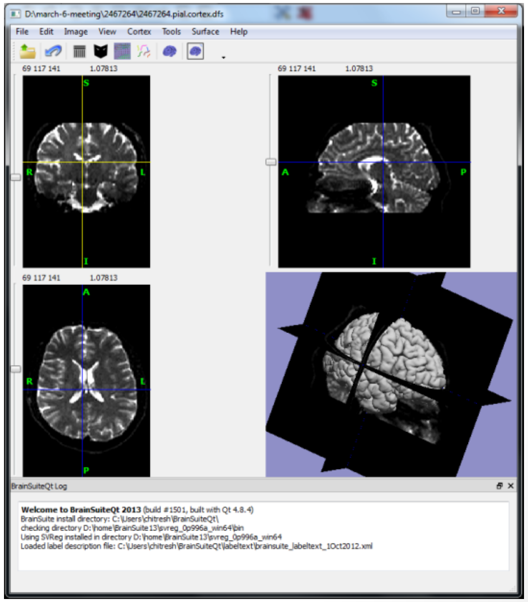
A framework to:

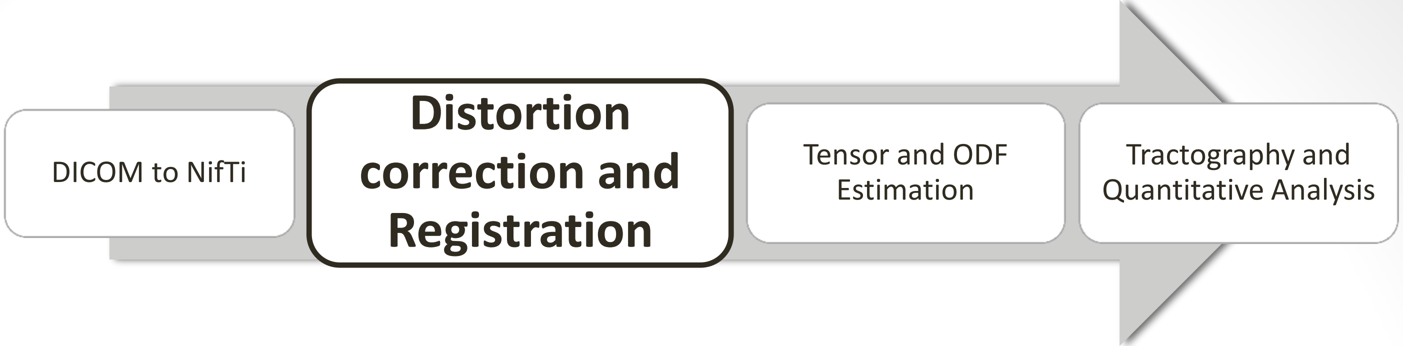
- Read diffusion data from DICOM images
- Align diffusion and MPRAGE image
- Correct diffusion data for distortions
- Fit different diffusion models – tensor and ODFs
- Compute different quantitative diffusion parameters
- Compute diffusion tracks and connectivity matrix

DICOM to NifTi → Distortion Correction and Registration → Tensor and ODF Estimation → Tractography and Quantitative Analysis

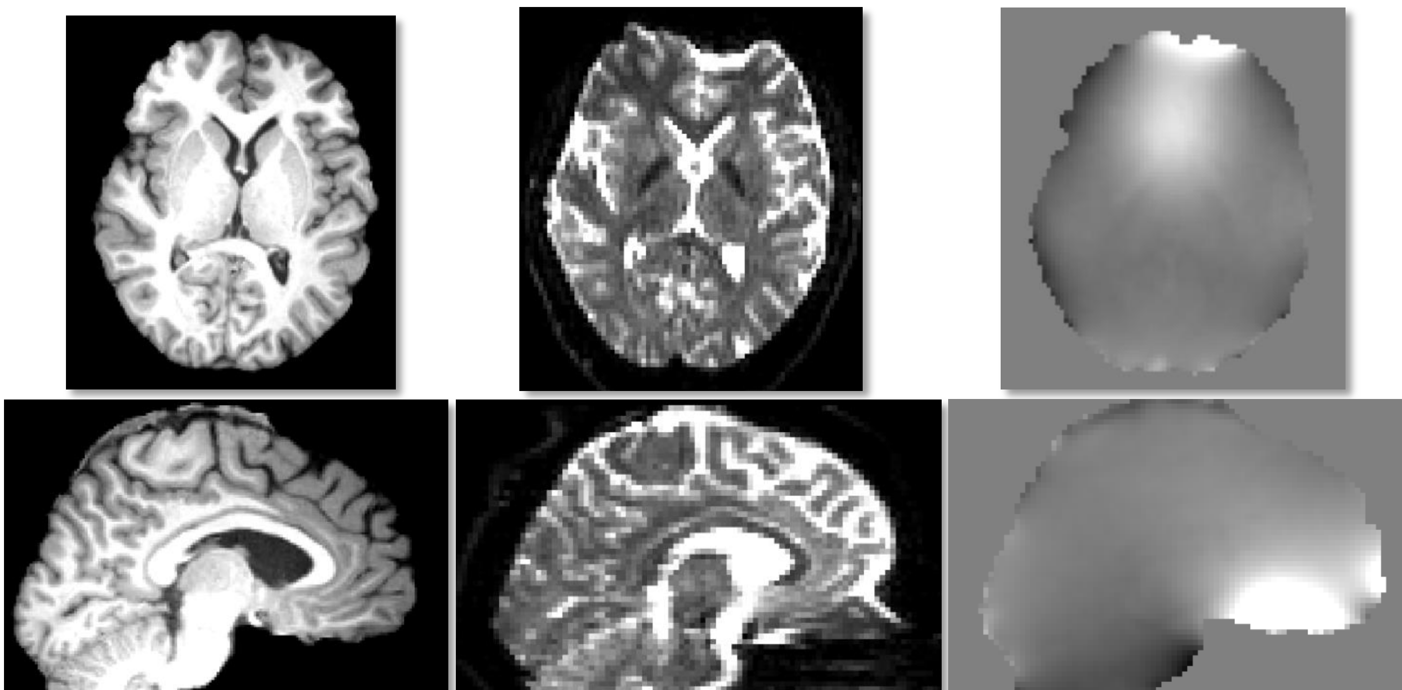
- Scanner saved DICOM images, as input
- De-mosaic the diffusion images
- Extracts diffusion parameters
  - bmat, bval, bvec
- Re-orients diffusion gradients to voxel coordinates
- Writes standard 4D nifti files



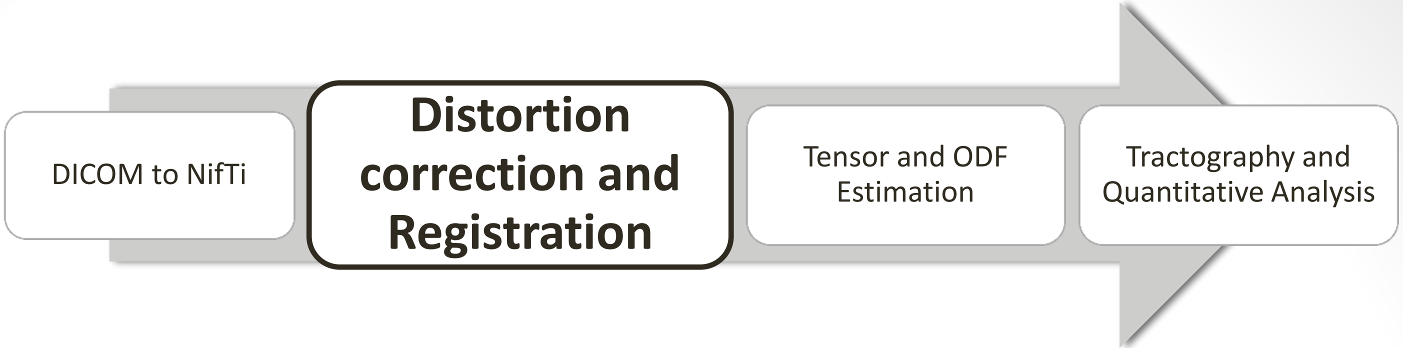




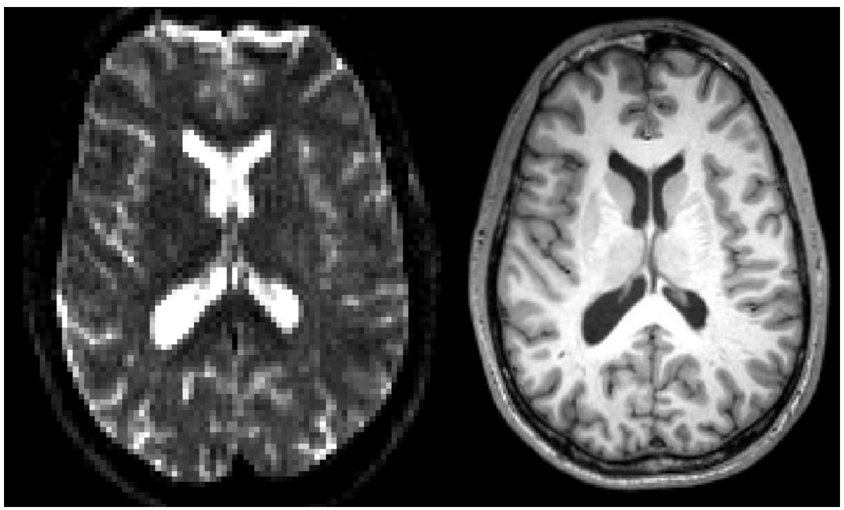
- Diffusion MRI uses fast acquisition – Echo planar Imaging (EPI)
- EPI is sensitive to magnetic field (B_0) inhomogeneity ➔ Localized geometric distortion



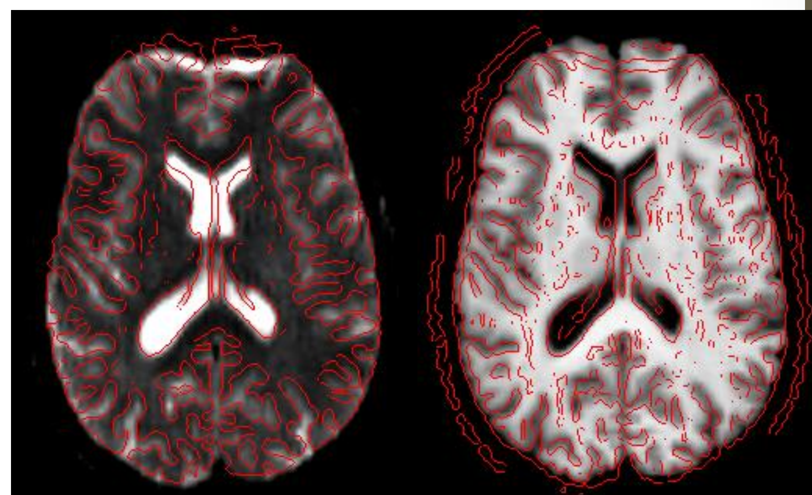
MPRAGE image | b=0 image | Field inhomogeneity map



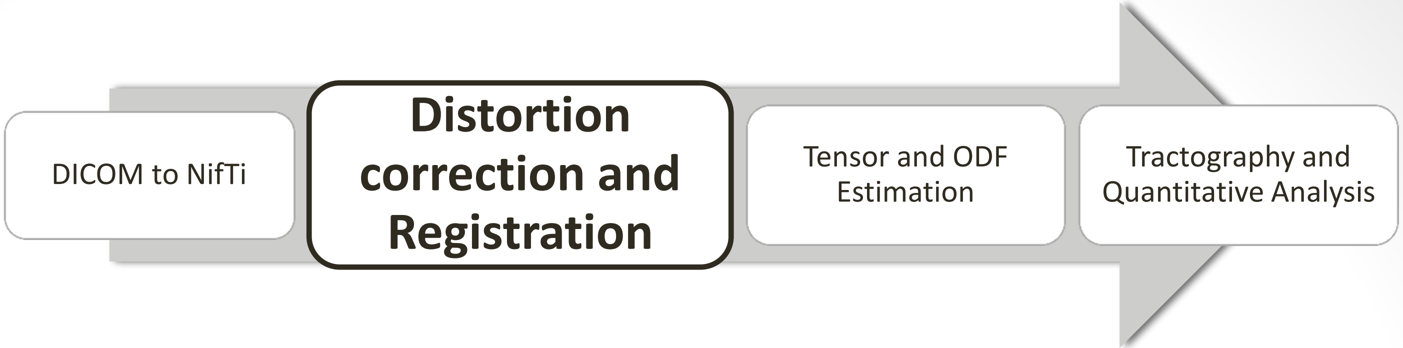
- Distortions results in misalignment with structural scans by several millimeters
- Limits the accuracy of multi-modal analysis



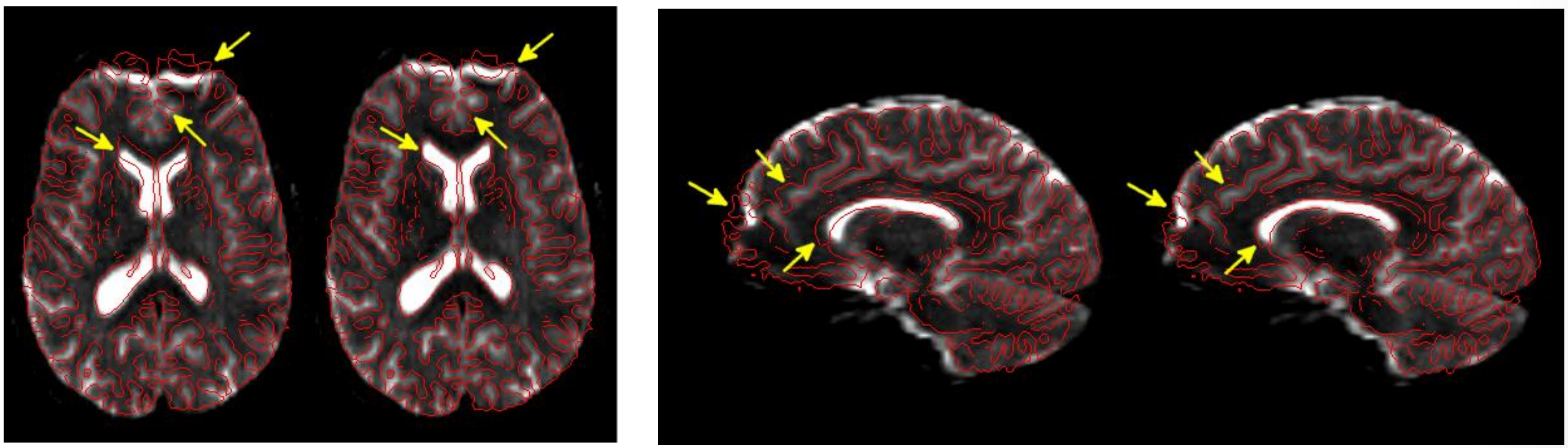
b=0 image MPRAGE image



Overlay with edges



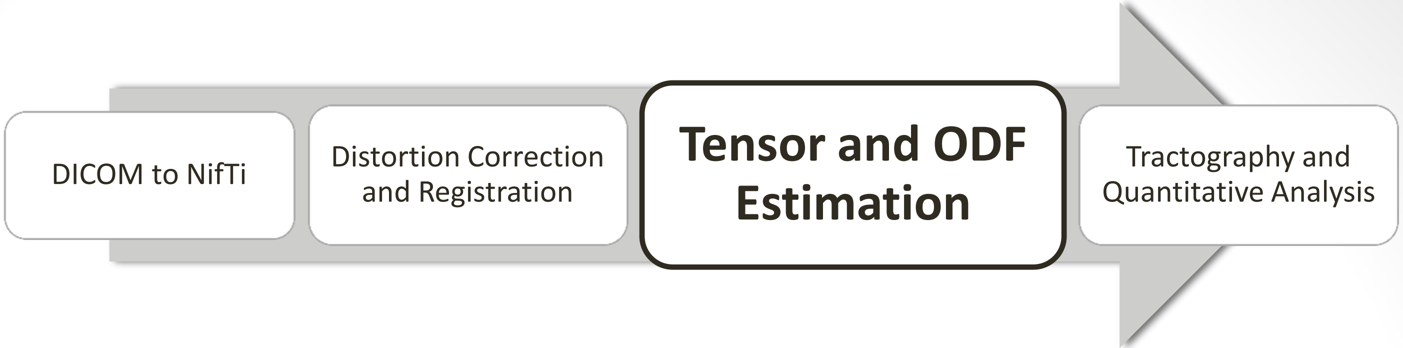
- Corrects the distortion in diffusion (EPI) images using non-rigid registration
- No fieldmap is required for correction



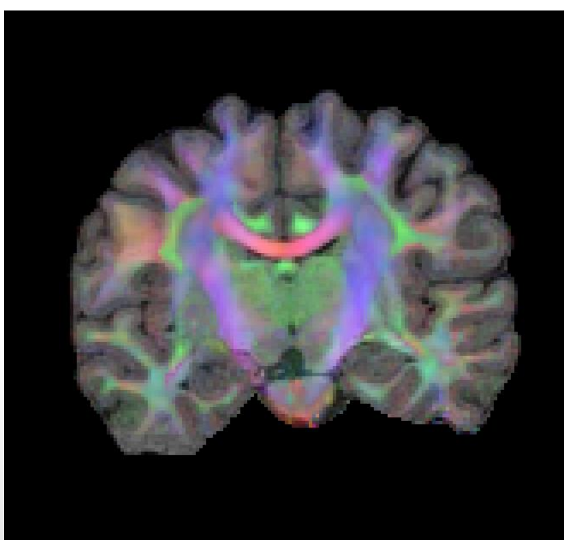
Before After Before After

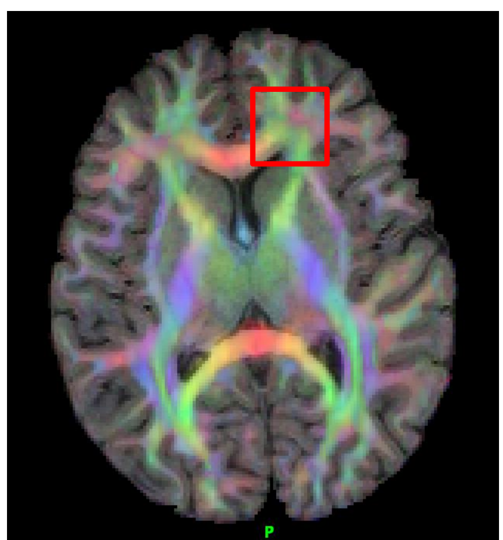
Each figure shows (left) distorted and (right) corrected b=0 image, overlaid with the edge-map (red outline) generated from the T1-weighted image. Arrows indicate areas of significant correction.

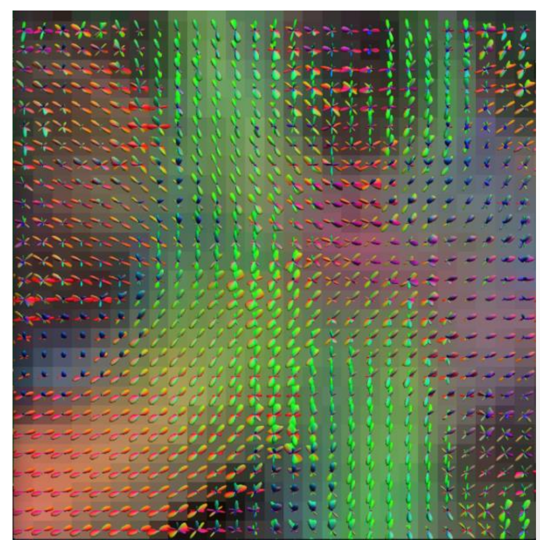
Bhushan et al. 2012 Correcting Susceptibility-Induced Distortion in Diffusion-Weighted MRI using Constrained Nonrigid Registration, APSIPA 2012.



- Estimates diffusion tensors
  - FA, MD, color-FA
- Axial, Radial Diffusivity
- ODFs using FRT and FRACT
- FRACT (Haldar and Leahy, 2013)
  - improved accuracy
  - higher angular resolution

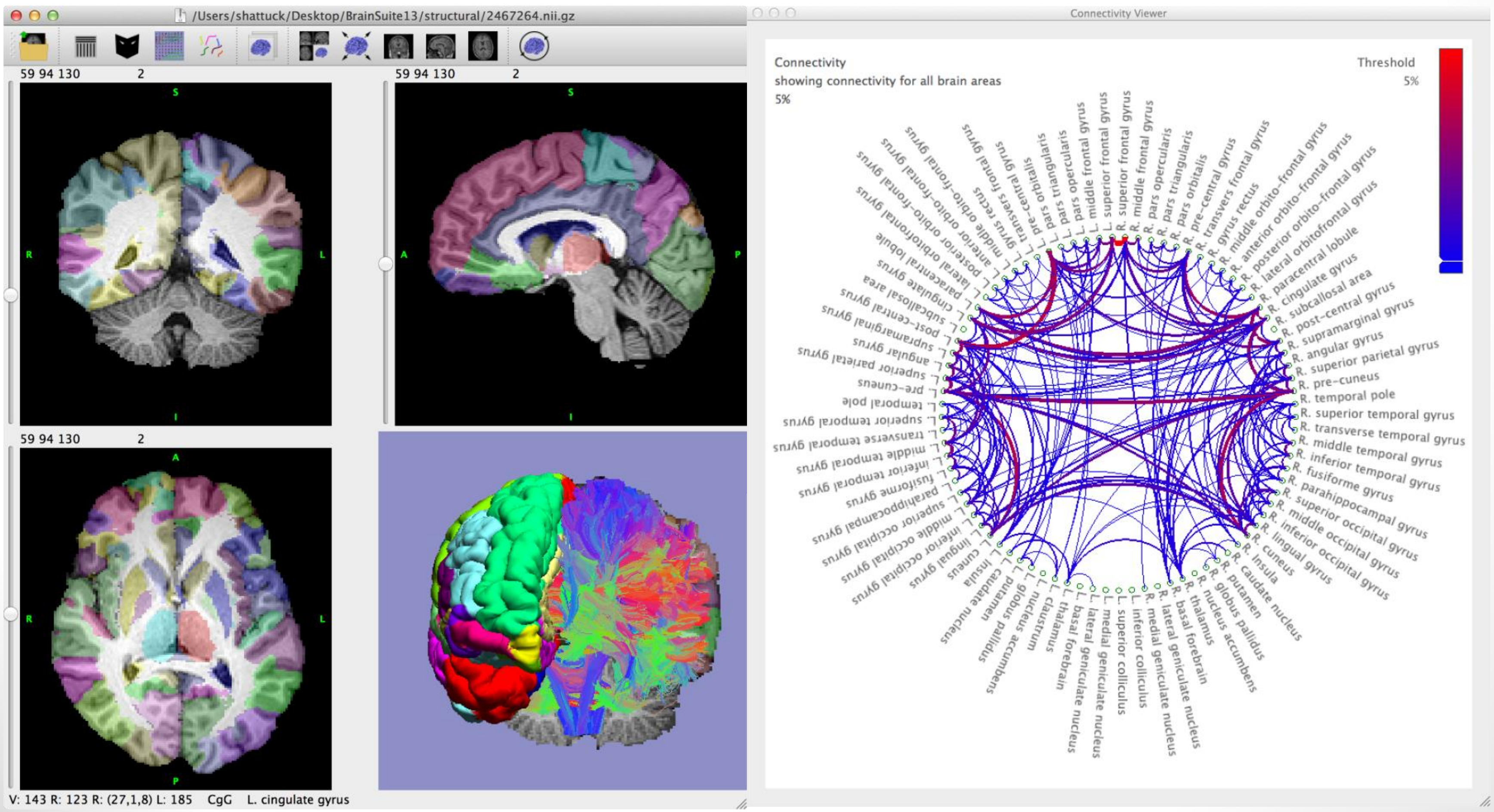






DICOM to NifTi → Distortion Correction and Registration → Tensor and ODF Estimation → **Tractography and Quantitative Analysis**

- Fiber tracking in T1-structural space
- ROI-based connectivity analysis



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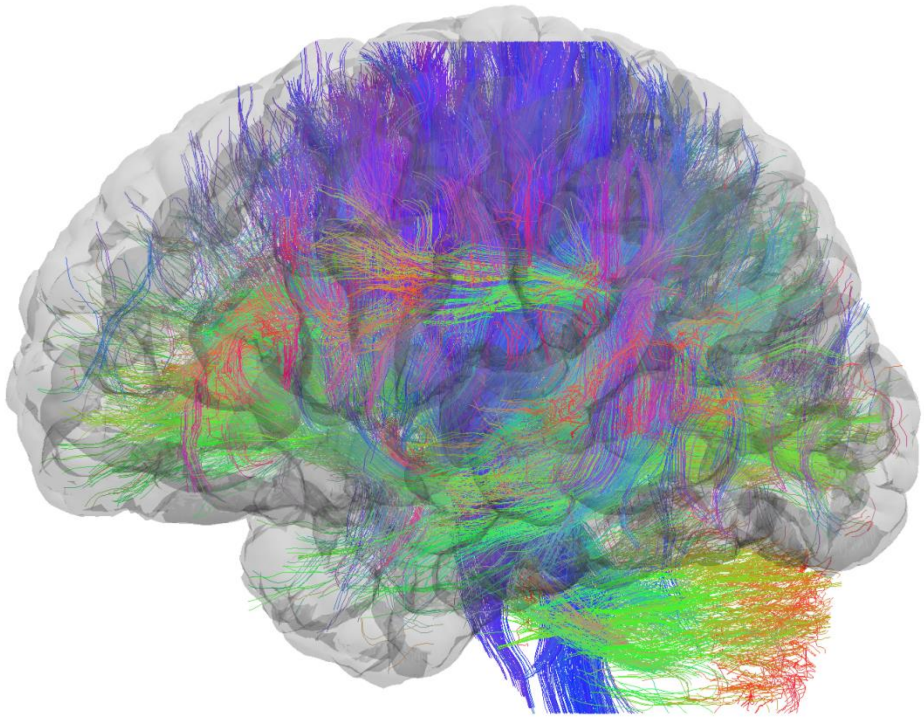
- Andrew Krause
- Jessica Wisnowski, PhD
- Hanna Damasio, MD



This work was supported in part by NIH grants R01-NS074980, R01-EB009048, P41-EB015922, and U01-MH93765.

Questions

References

The software is available online at: http://brainsuite.loni.ucla.edu/

Additional documentation at: http://www.loni.ucla.edu/~shattuck/brainsuite/

User forum: http://forum.loni.ucla.edu/brainsuite

More details for the methods described in this talk can be found in the following papers:

Segmentation

- Shattuck DW, Sandor-Leahy SR, Schaper KA, Rottenberg DA and Leahy RM (2001) Magnetic Resonance Image Tissue Classification Using a Partial Volume Model *NeuroImage*, 13(5):856-876
- Shattuck DW and Leahy RM (2001) Graph Based Analysis and Correction of Cortical Volume Topology, *IEEE Transactions on Medical Imaging*, 20(11)1167-1177
- Shattuck DW and Leahy RM (2002) BrainSuite: An Automated Cortical Surface Identification Tool *Medical Image Analysis*, 8(2):129-142
- Dogdas B, Shattuck DW, and Leahy RM (2005) Segmentation of Skull and Scalp in 3D Human MRI Using Mathematical Morphology *Human Brain Mapping*26(4):273-85

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- Joshi AA, Leahy RM, Thompson PM, Shattuck DW (2004) Cortical Surface Parameterization by P-Harmonic Energy Minimization. ISBI 2004: 428-431
- Joshi AA, Shattuck DW, Thompson PM, and Richard M. Leahy (2007) Surface-Constrained Volumetric Brain Registration Using Harmonic Mappings *IEEE Trans. on Medical Imaging* 26(12):1657-1669
- Joshi AA, Shattuck DW, Thompson PM, and Leahy RM (2009) A Parameterization-based Numerical Method for Isotropic and Anisotropic Diffusion Smoothing on Non-Flat Surfaces, *IEEE Trans. on Image Processing*18(6):1358-1365
- Shattuck DW, Joshi AA, Pantazis D, Kan E, Dutton RA, Sowell ER, Thompson PM, Toga AW, Leahy RM (2009) Semi-automated Method for Delineation of Landmarks on Models of the Cerebral Cortex, *Journal of Neuroscience Methods* 178(2):385-392
- Joshi AA, Pantazis D, Li Q, Damasio H, Shattuck D, Toga A, Leahy RM (2010) Sulcal set optimization for cortical surface registration *NeuroImage* 50(3):950-9
- Pantazis D, Joshi AA, Jintao J, Shattuck DW, Bernstein LE, Damasio H, and Leahy RM (2010) Comparison of landmark-based and automatic methods for cortical surface registration, *NeuroImage* 49(3):2479-93
- Joshi AA, Shattuck DW and Leahy RM, A Fast and Accurate Method for Automated Cortical Surface Registration and Labeling, Proc. WBIR LNCS Springer 2012, 180-189

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Diffusion MRI

- Haldar JP and Leahy RM (2013) Linear transforms for Fourier data on the sphere: Application to high angular resolution diffusion MRI of the brain *NeuroImage 71:233-247*
- Bhushan C, Haldar JP, Joshi AA, and Leahy RM (2012) Correcting susceptibility-induced distortion in diffusion-weighted MRI using constrained nonrigid registration, *Asia-Pacific Signal & Information Processing Association Annual Summit and Conference (APSIPA ASC), 1-9, Los Angeles, California, 3-6 Dec 2012*