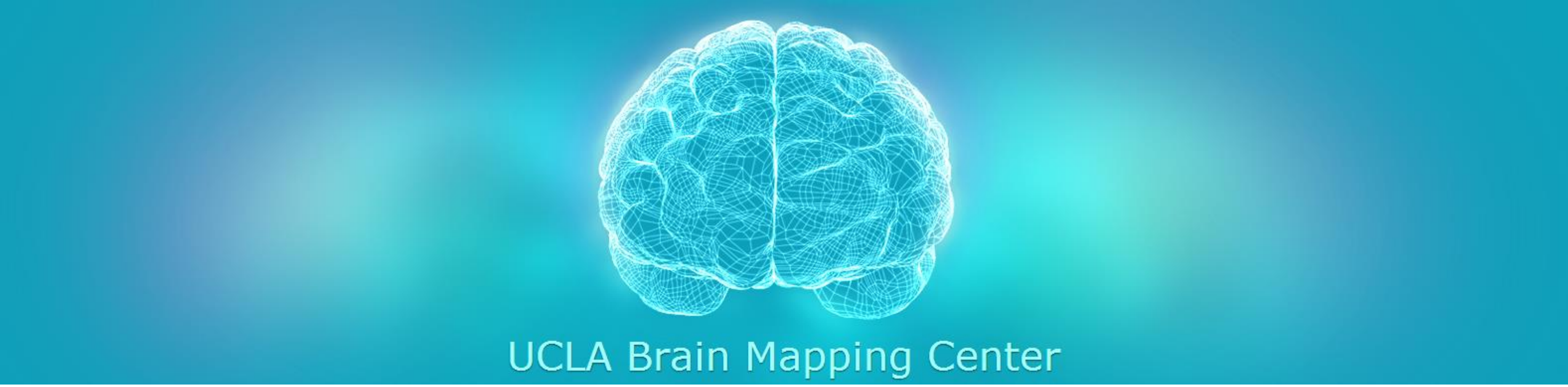

BrainSuite

presented at the UCLA/NITP Advanced Neuroimaging Summer Program
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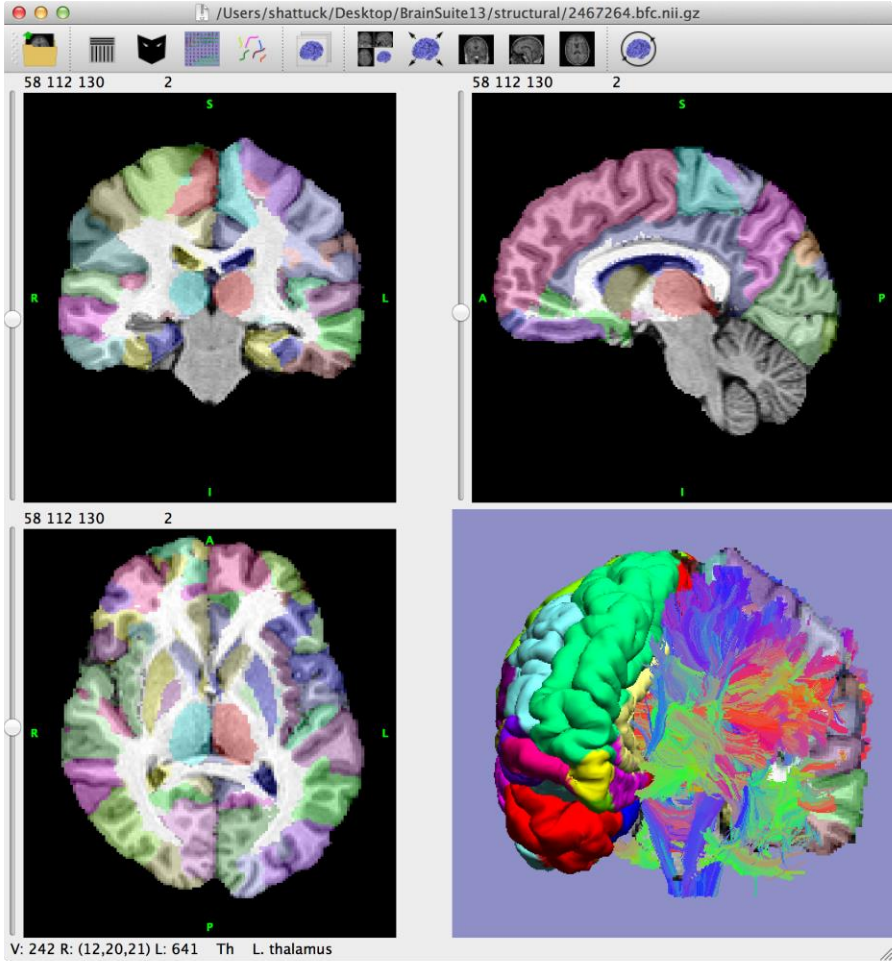
BrainSuite

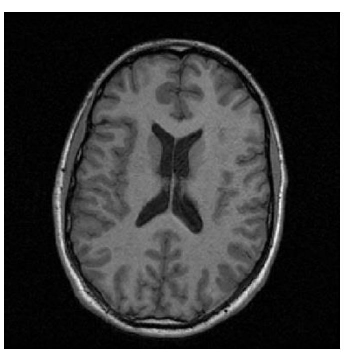
- Collection of image analysis tools designed to process structural and diffusion MRI
  - Automated sequence to extract cortical surface models from T1-MRI
  - Tools to register surface and volume data to an atlas to define anatomical ROIs
  - Tools for processing diffusion imaging data, including coregistration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

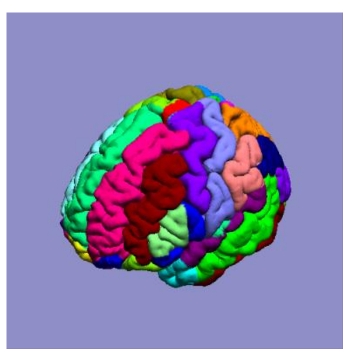


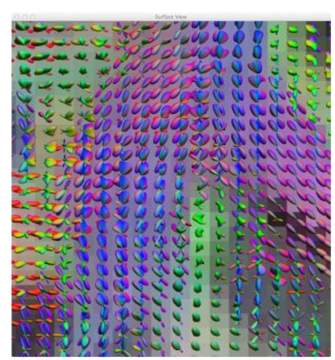
* GUI for Linux version is not yet released

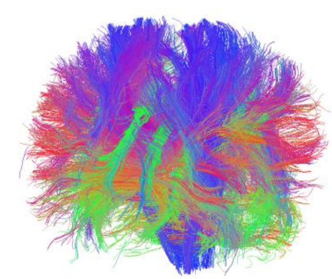
Overview

- Background
- Cortical Surface Extraction
- Atlas-Based Registration and Labeling
- Processing of Diffusion Data
- Ongoing Work





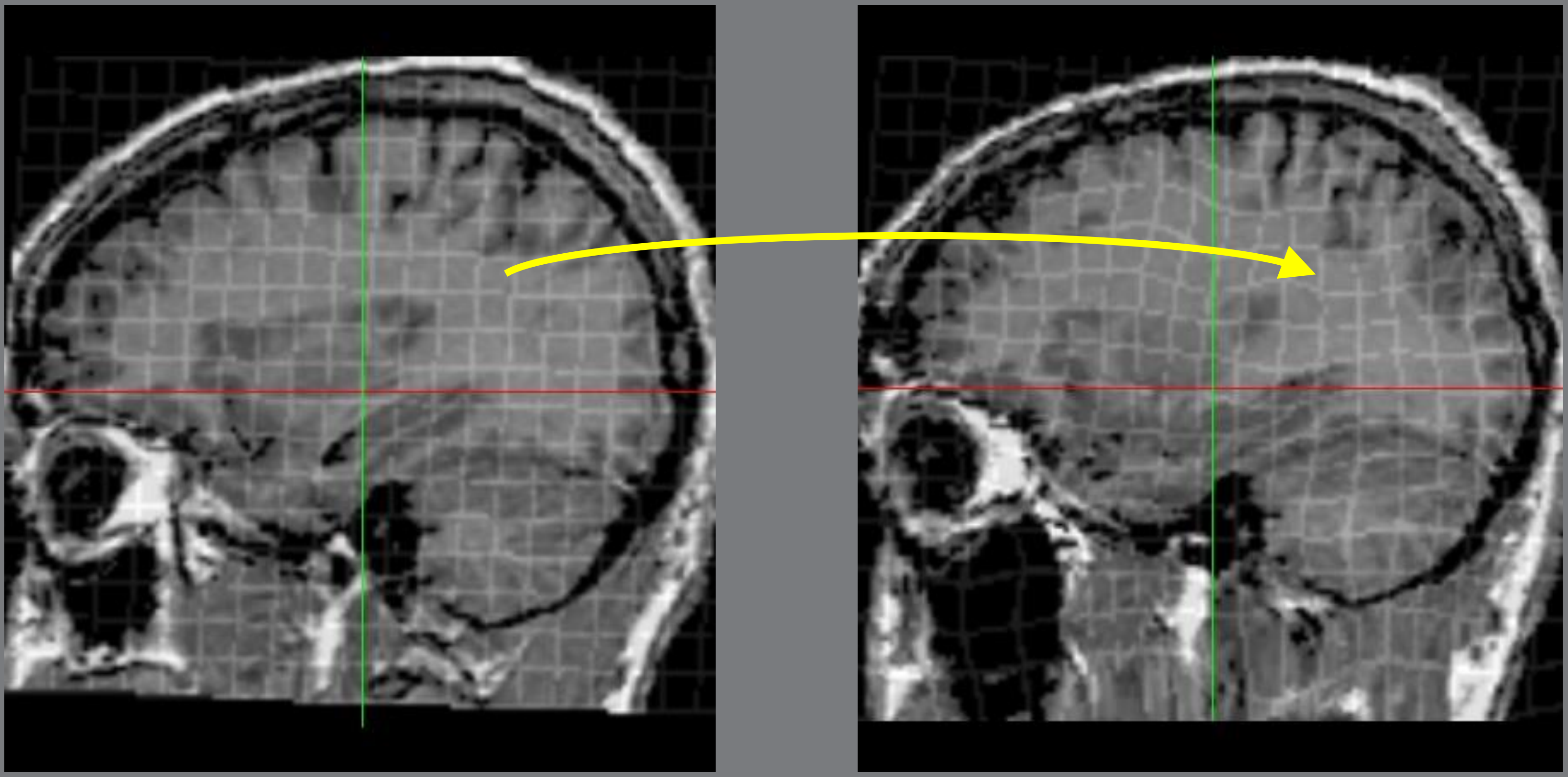




Motivation

- We are typically interested in performing 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 across the data
- Once correspondence is established, we can study 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

Image Registration

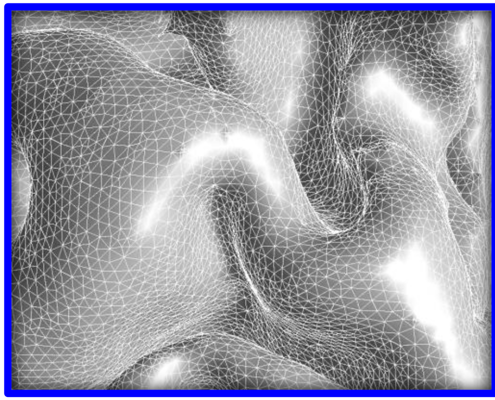


Brain image with grid overlay

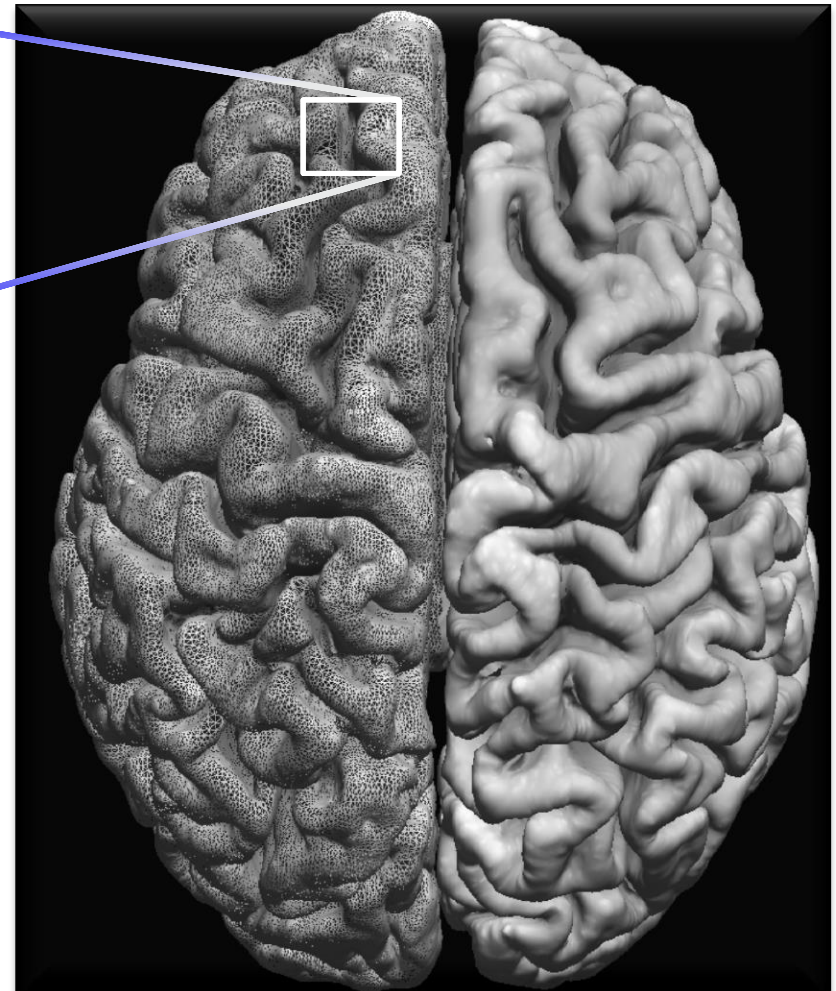
Warped brain with grid overlay

- Mapping from points in a template brain image to matching points in a target brain image.

Cortical Surface Mesh Models



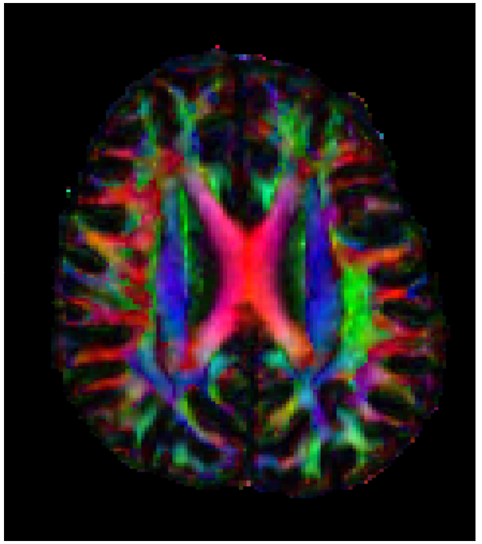
- Cortex is often represented as a high resolution triangulated mesh with ~700,000 triangles
- Many volumetric-based approaches do not align the cortical anatomy well
- We are often interested in functional areas in the cortex
- Surface-based features, e.g., cortical thickness, are of interest in the 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

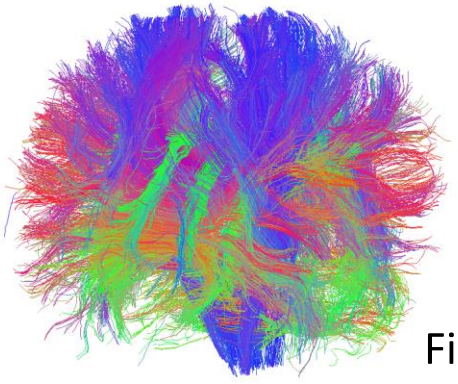


Cortical surface mesh representation

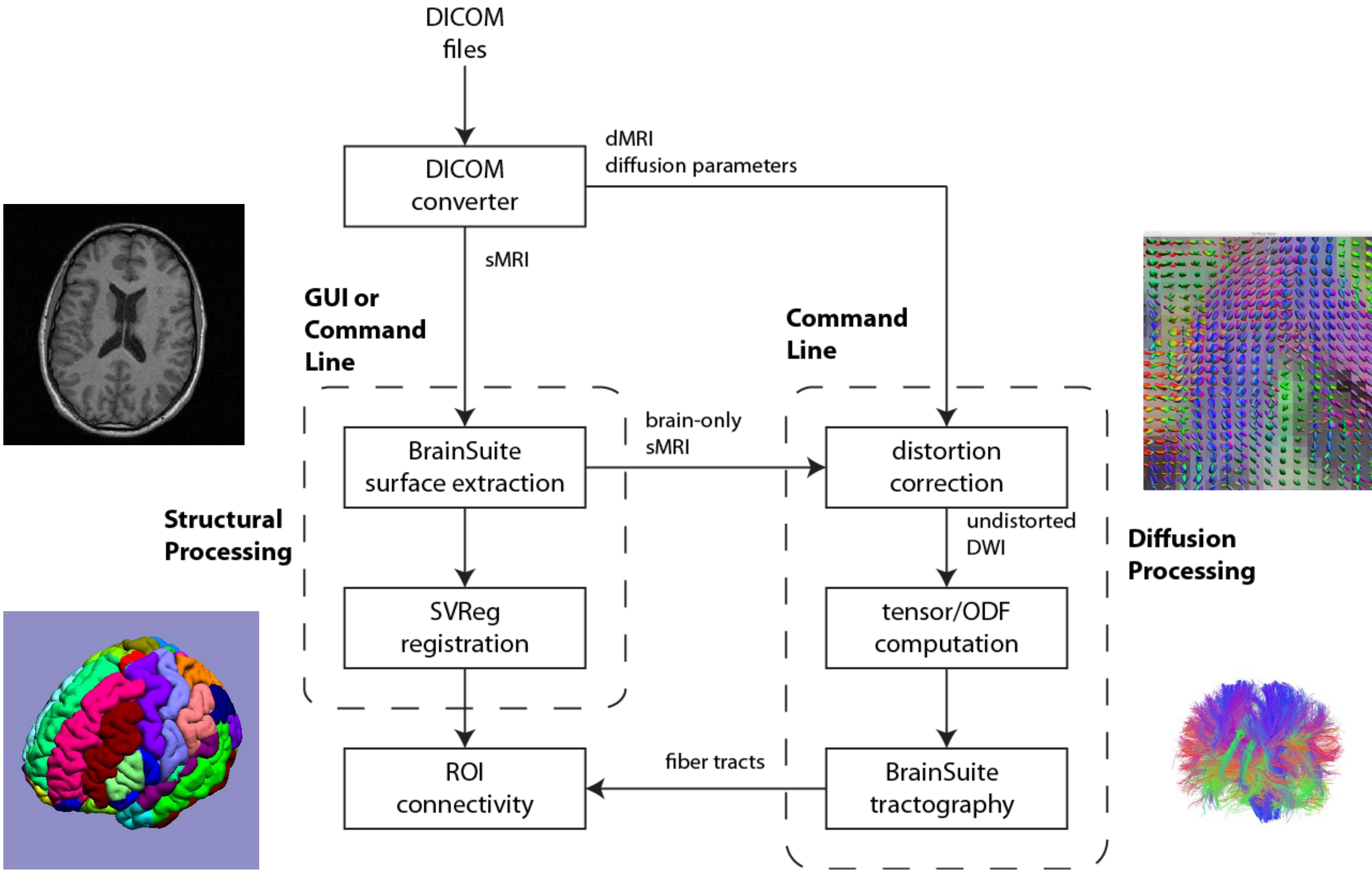
Diffusion MRI

- 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)

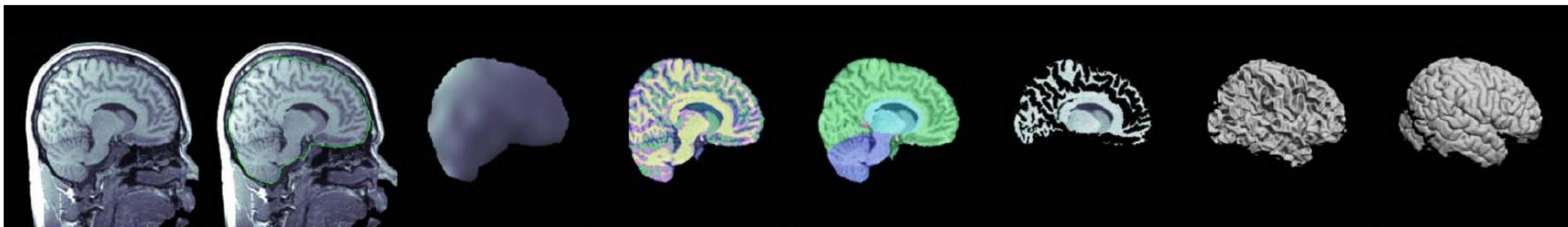

FA map


Fiber tracks

BrainSuite Workflow

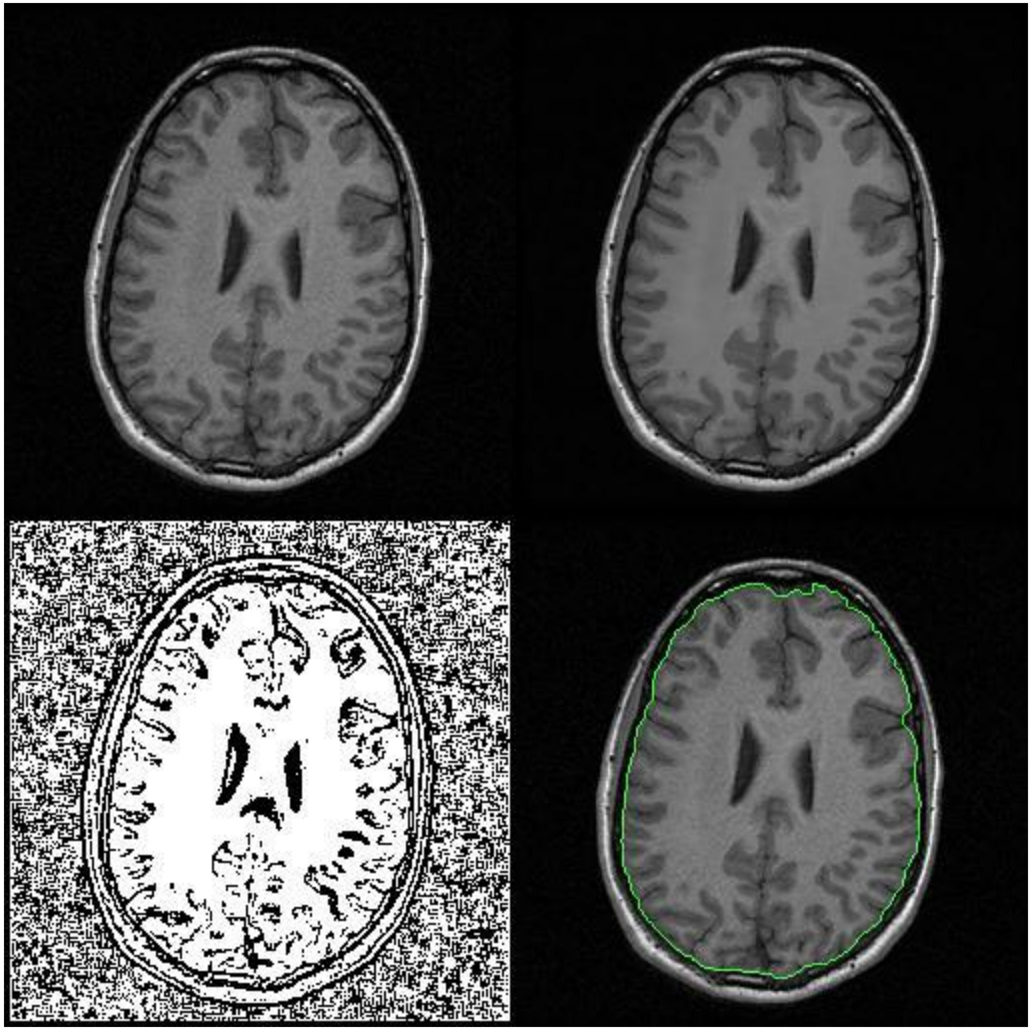


Cortical Surface Extraction



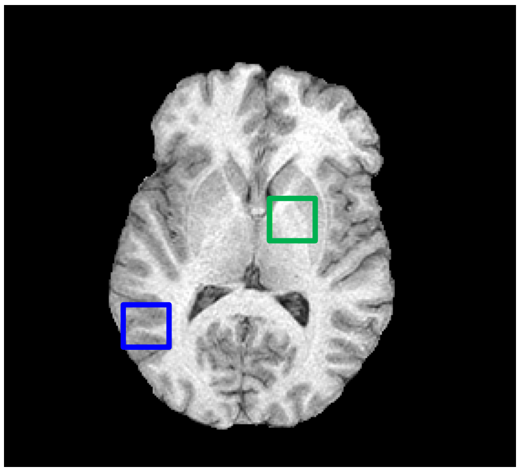
MRI	skull stripping	nonuniformity correction	tissue classification	cerebrum labeling	topology correction	inner cortical surface generation	pial surface generation
	<2 sec	40s - 4 min	<5 sec	<20 sec	<40 sec	<2 sec	<10 min

Skull Stripping

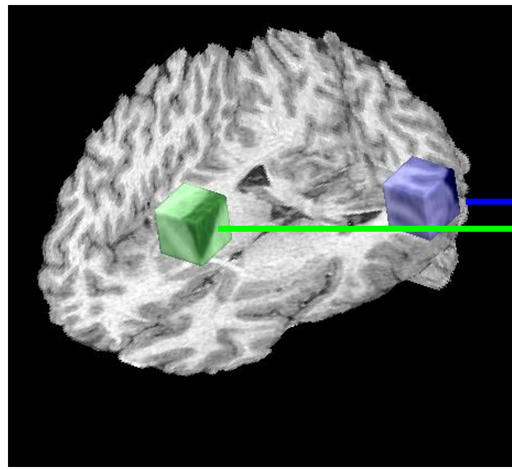


- Brain Surface Extractor (BSE) extracts the brain from non-brain tissue using a combination of:
  - anisotropic diffusion filtering
  - edge detection
  - mathematical morphological operators
- This method can rapidly identify the brain within the MRI

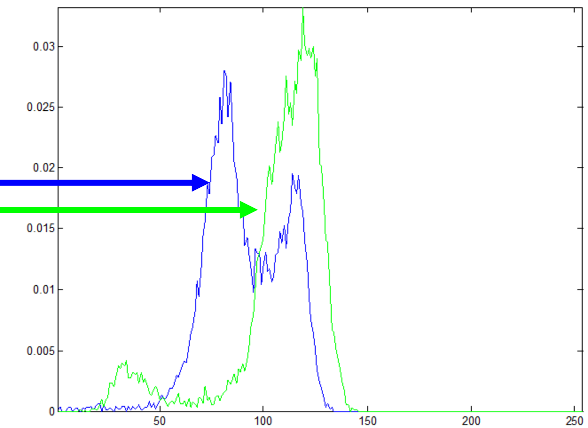
Nonuniformity Correction



Two cubic regions ROIs



3D rendering of the ROIs

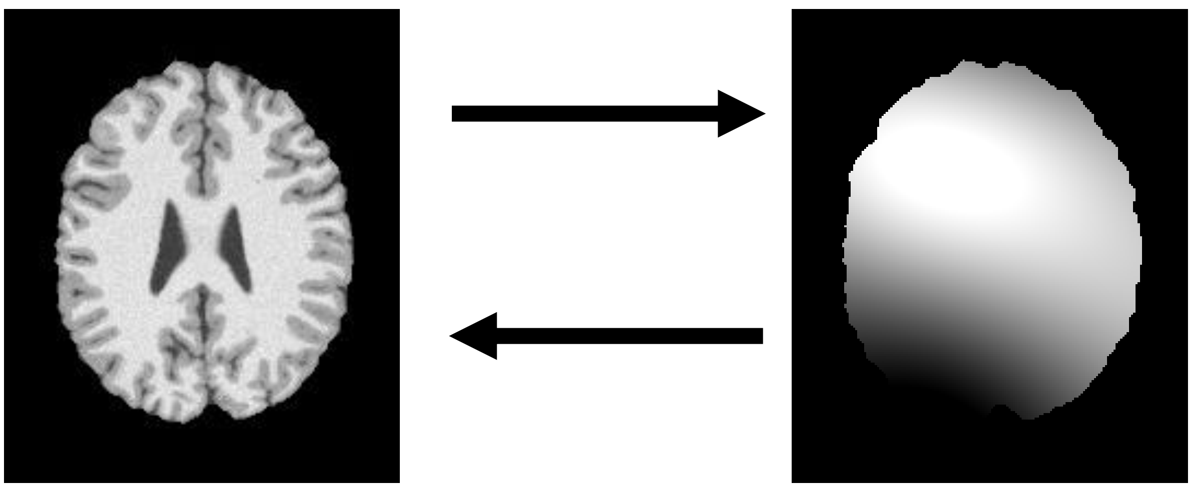


Histograms of the two ROIs

- Nonuniform signal gain can confound tissue classification techniques
- Bias Field Corrector (BFC) performs nonuniformity correction by analyzing the intensity profiles of regions of interest (ROIs)
- We can fit a histogram model to these ROIs and estimate the local gain variation

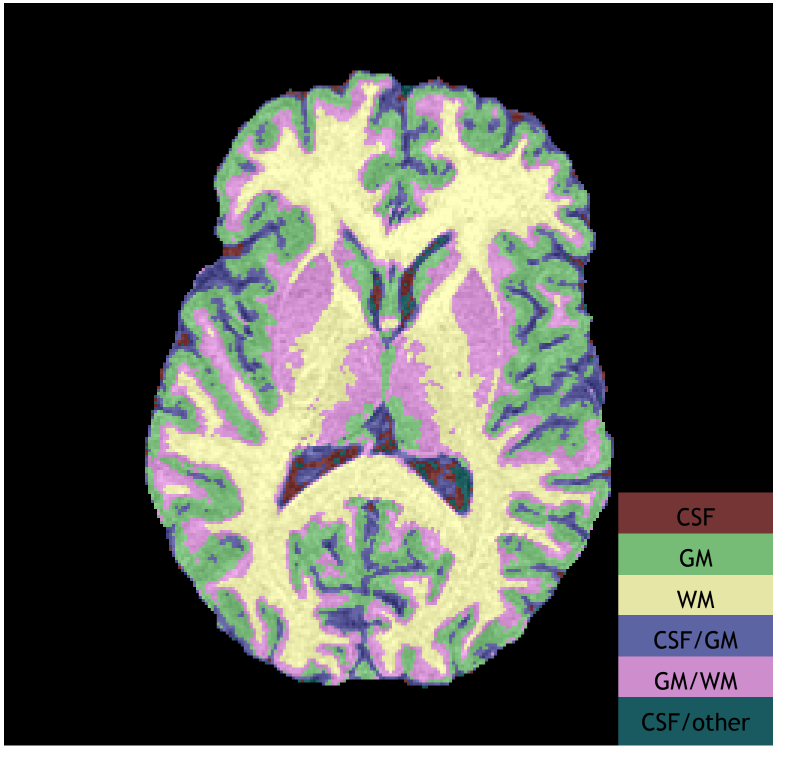
Nonuniformity Correction

- 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.



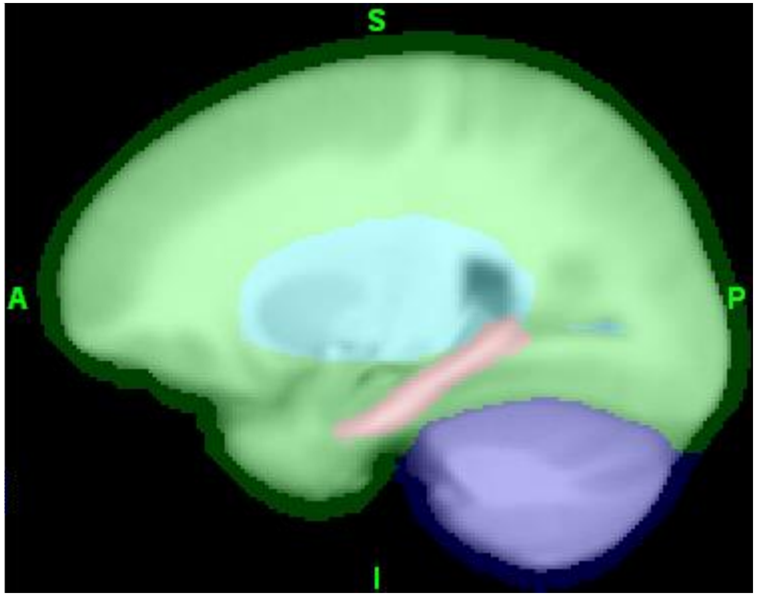
Tissue Classification

- We use a statistical tissue classifier to label each voxel according to tissue type.
  - Initialize with a maximum likelihood classification
  - Refine with a maximum a posteriori (MAP) classifier that produces more contiguous regions of tissue
- Tissue categories are
  - Pure: GM, WM, CSF
  - Mixed: GM/CSF, GM/WM, CSF/Other
- Also estimate tissue fractions at each voxel

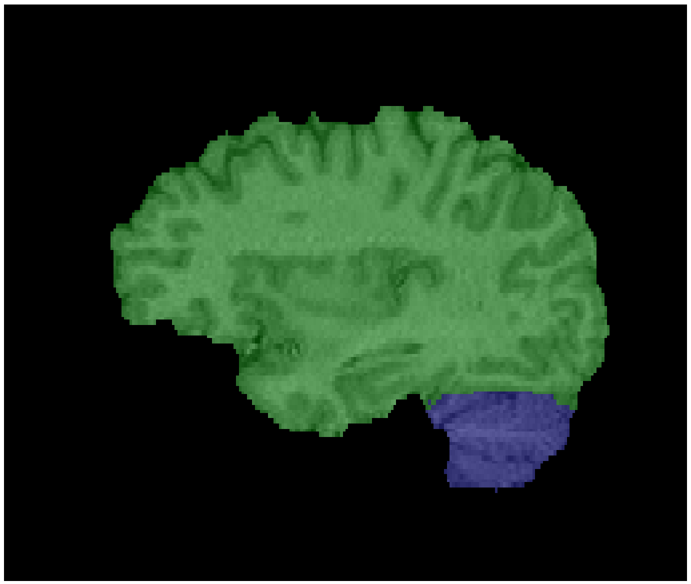


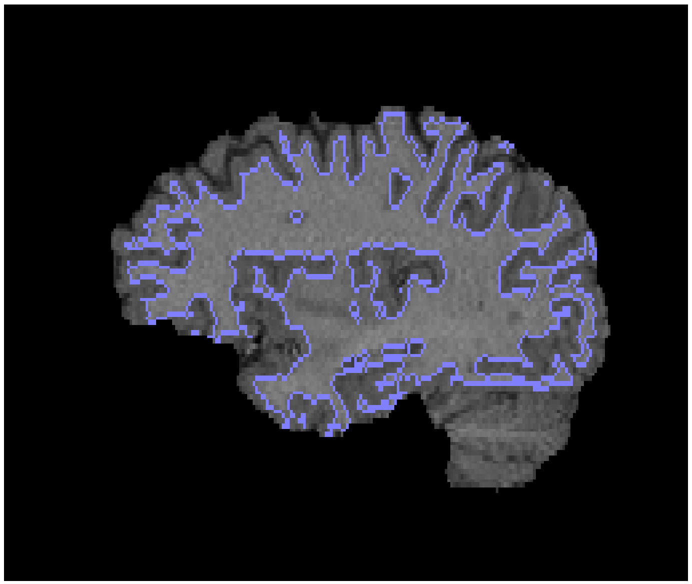
Cerebrum Labeling

- 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 hemispheres



Inner Cortical Mask

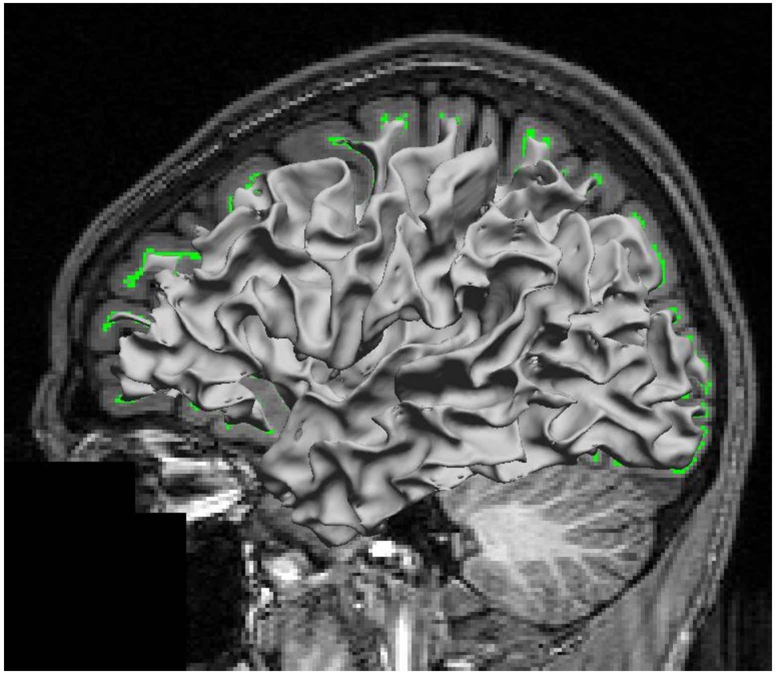




- We combine our registered brain atlas with our tissue map
  - Retain subcortical structures, including nuclei
  - Identify the inner boundary of the cerebral cortex

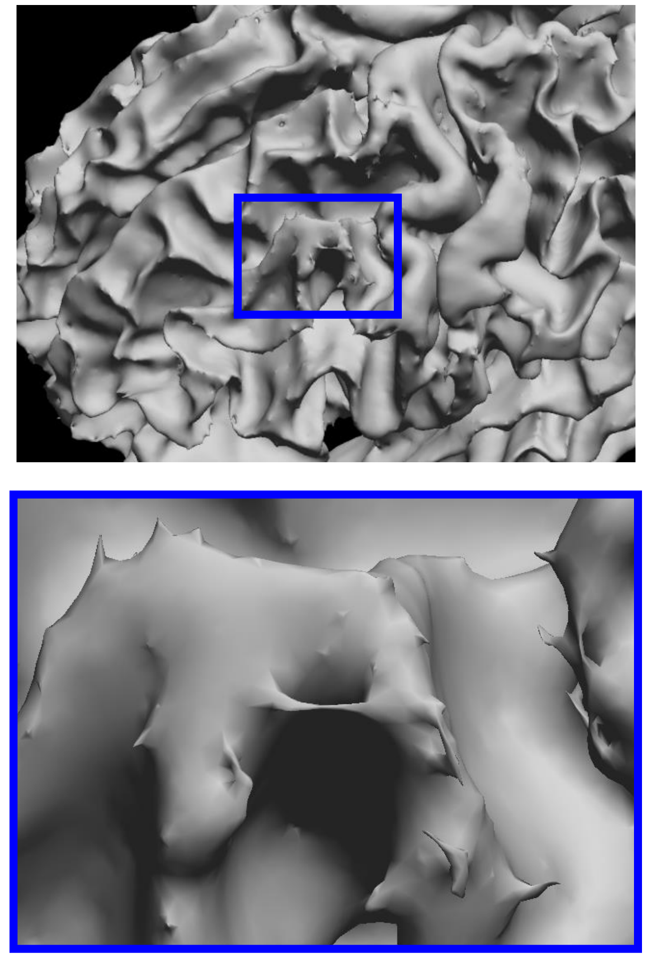
Surface Generation

- By applying a tessellation algorithm, we can generate a surface mesh from a 3D volume.



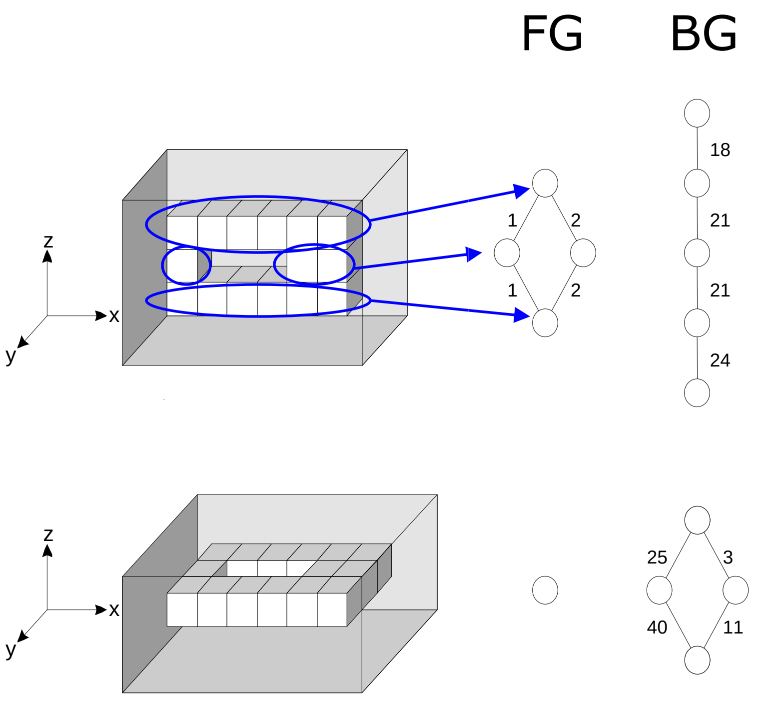
Topological Errors

- 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.



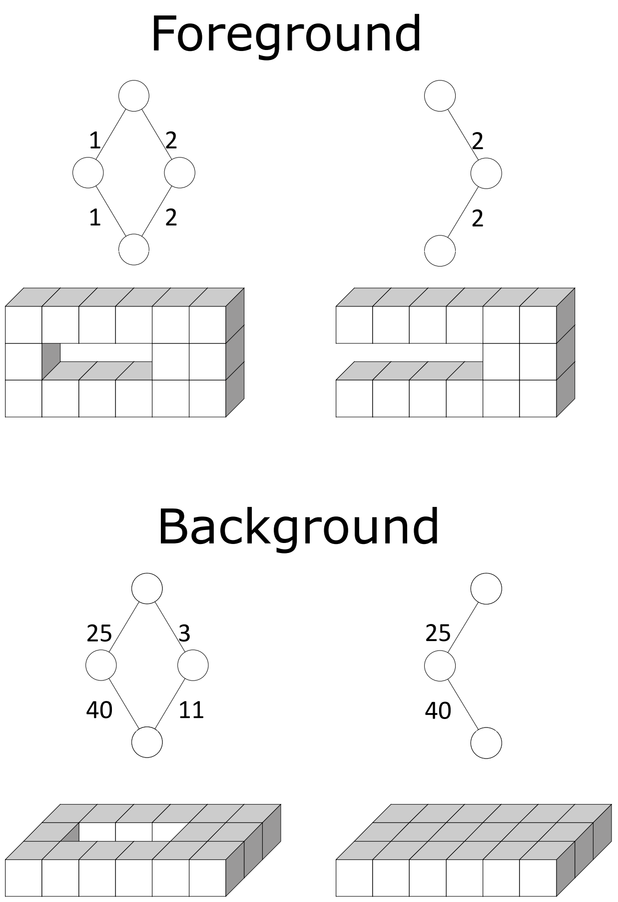
Topological Errors

- 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.

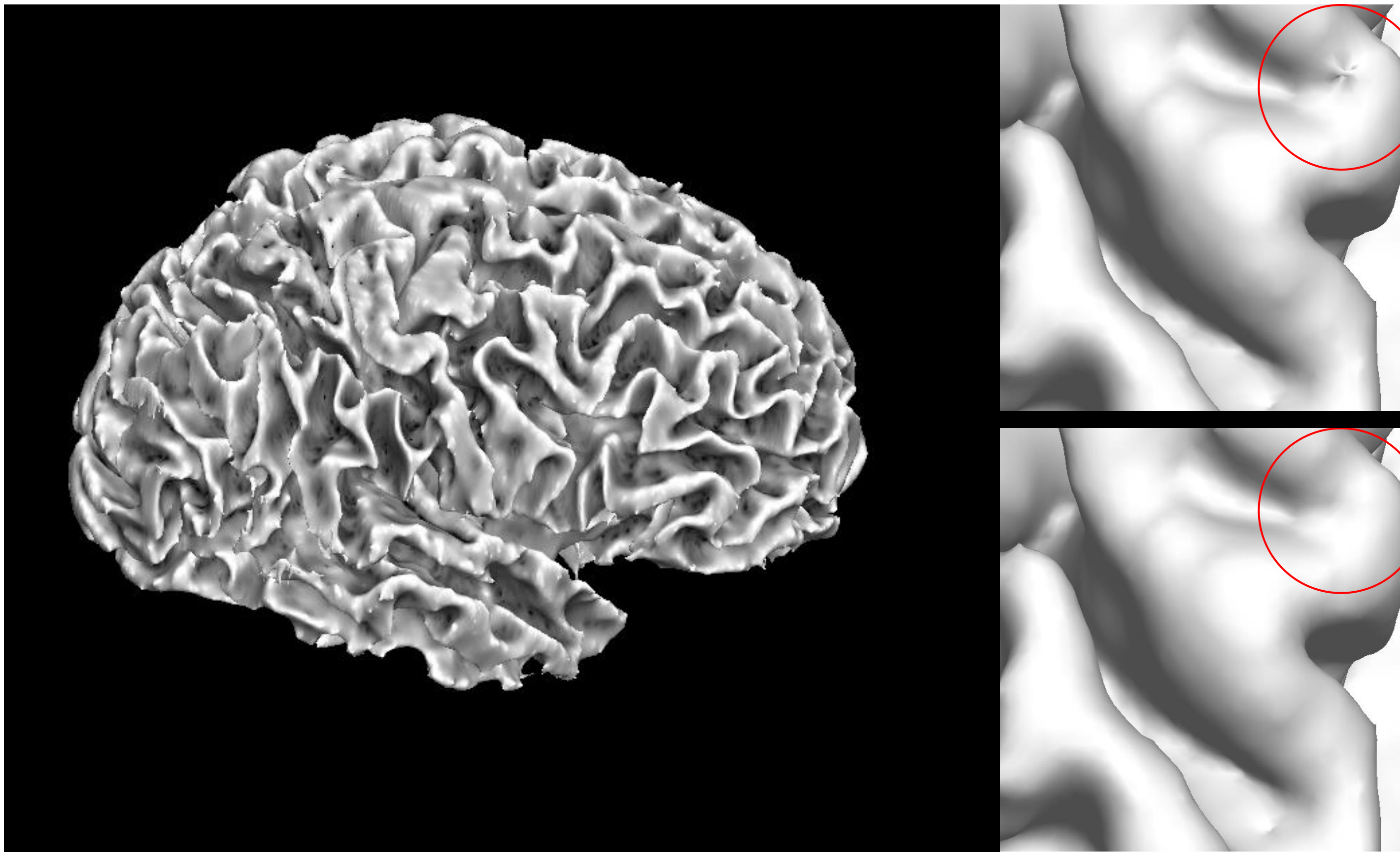


Topological Editing

- 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

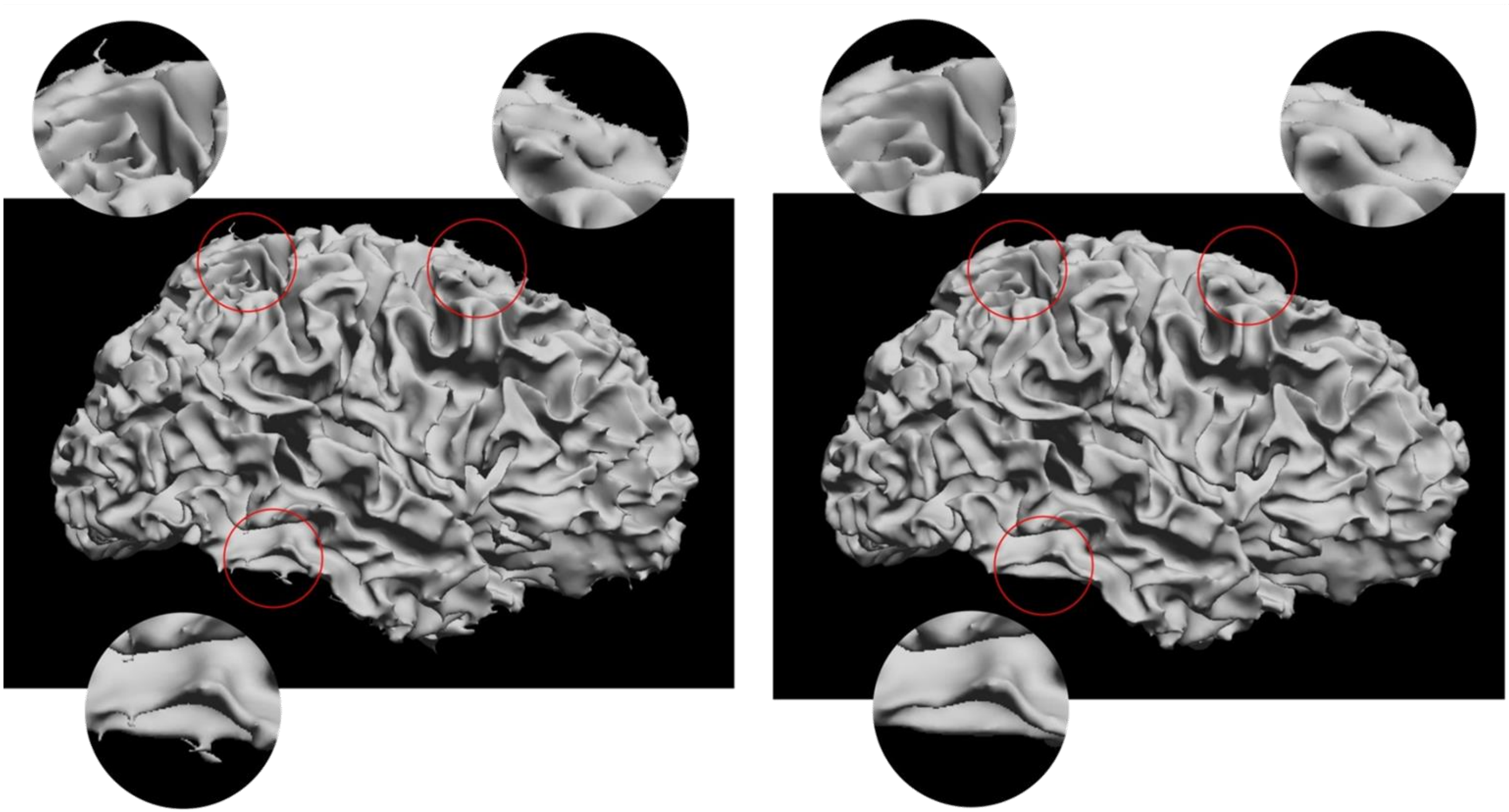


(left) cortical surface model produced from binary masks

(top right) close-up view of a handle on the surface generated from the volume before topological correction

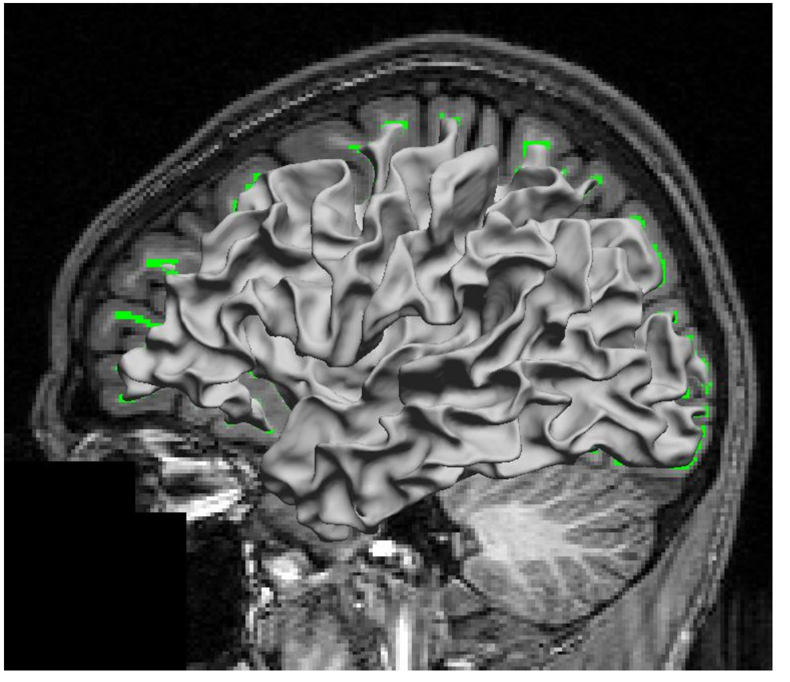
(bottom right) close-up view of the same region on the surface generated from the same volume after topology correction.

Wisp Removal



Inner Cortical Surface

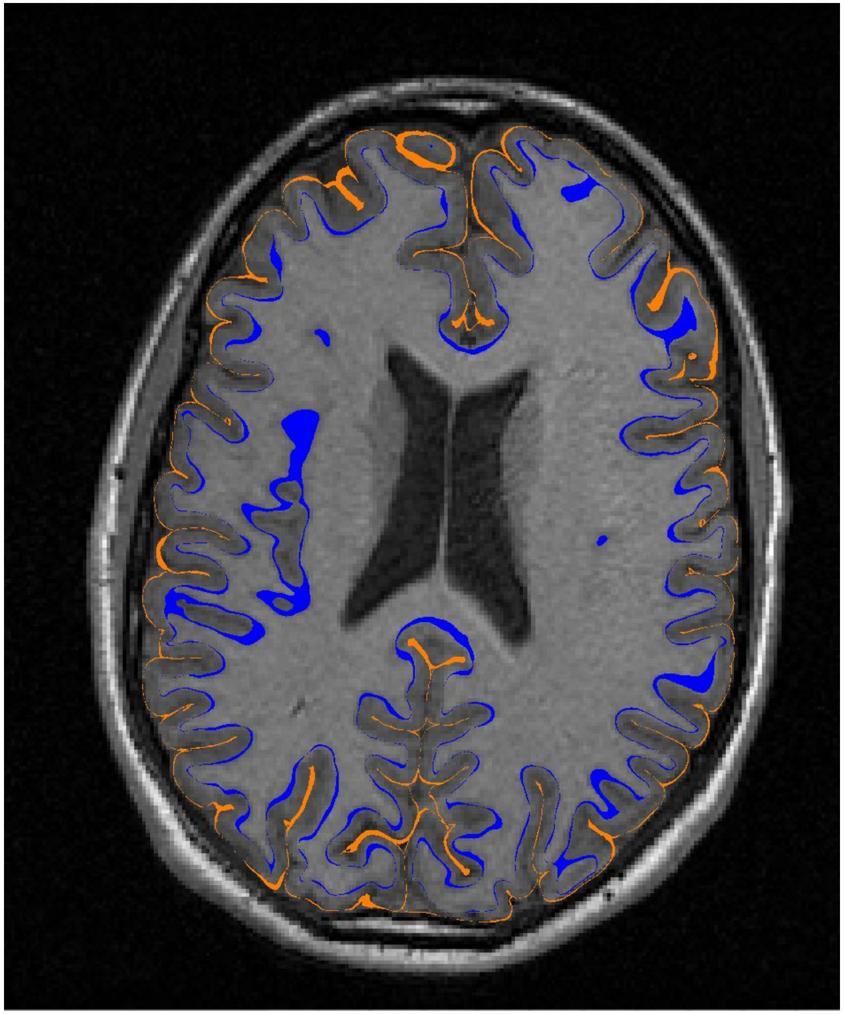
- After applying the topology correction and dewisp filters, we applying Marching Cubes to generate a representation of the inner cortical boundary.



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

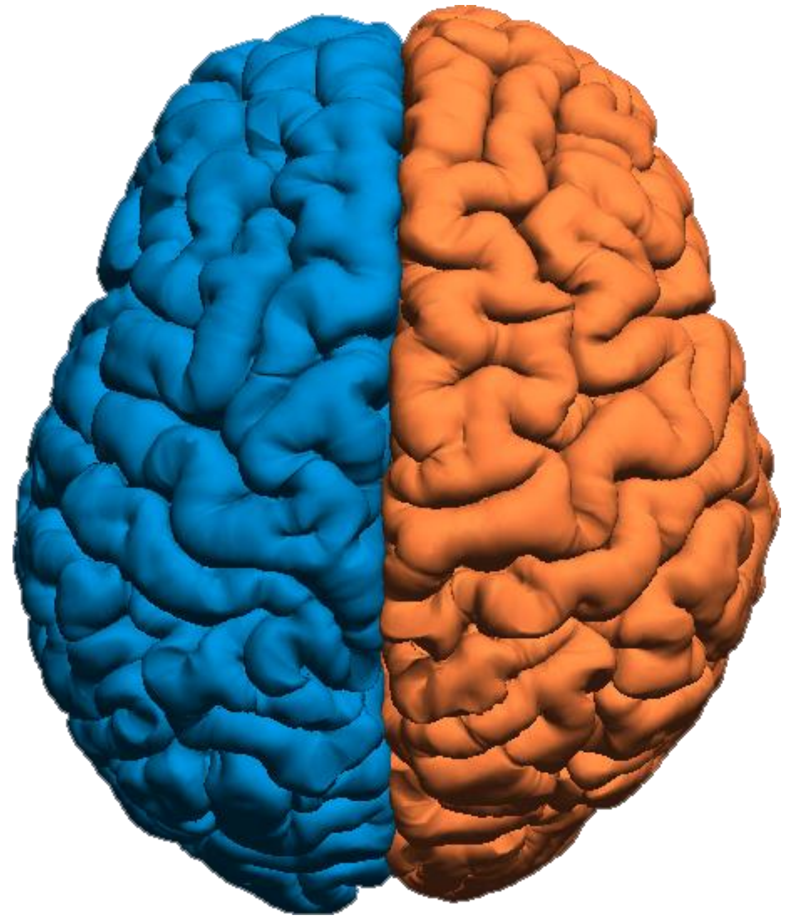
Pial Surface



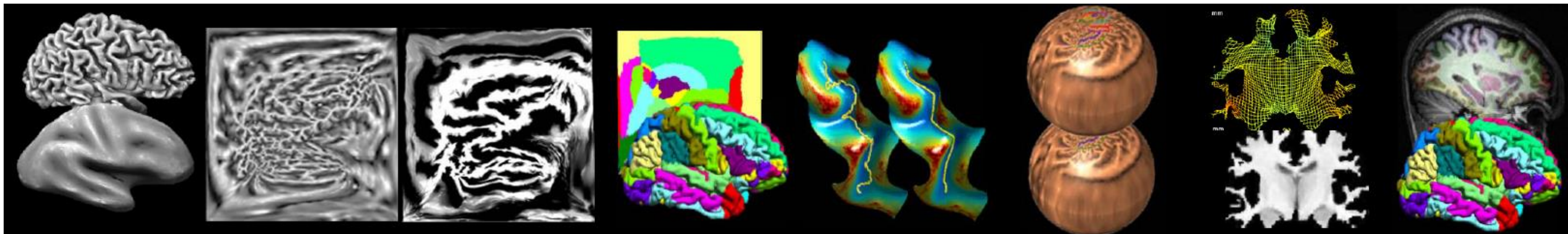
Contour view showing the inner (blue) and outer (orange) boundaries of the cortex.

Split Hemispheres

- We can separate the meshes into left and right hemispheres based on hour cerebrum labeling
- These surface models are then used by the surface/volume registration and labeling routine (SVReg)



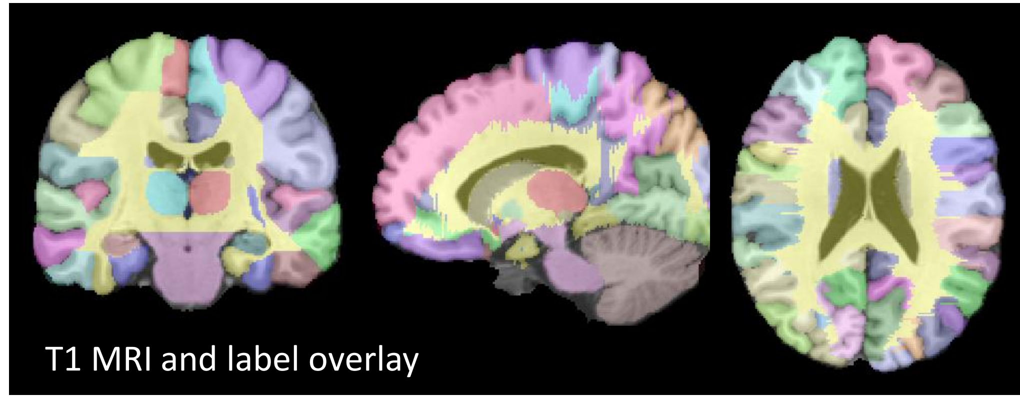
Surface-constrained Volumetric Registration

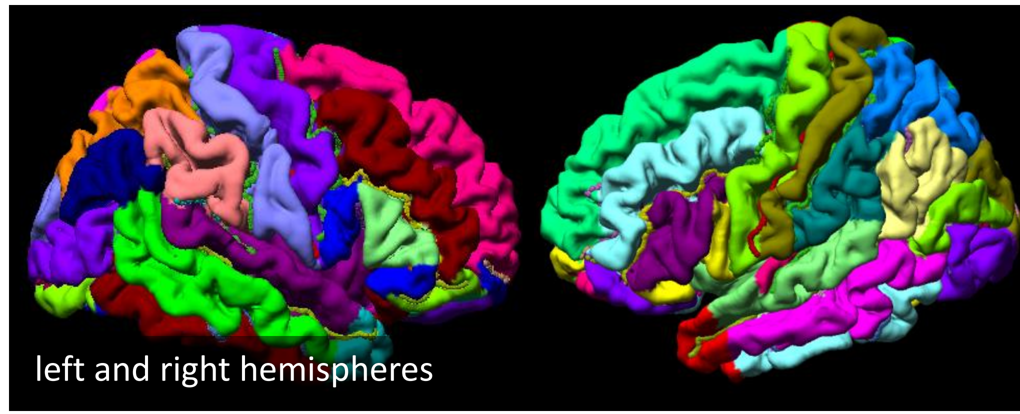


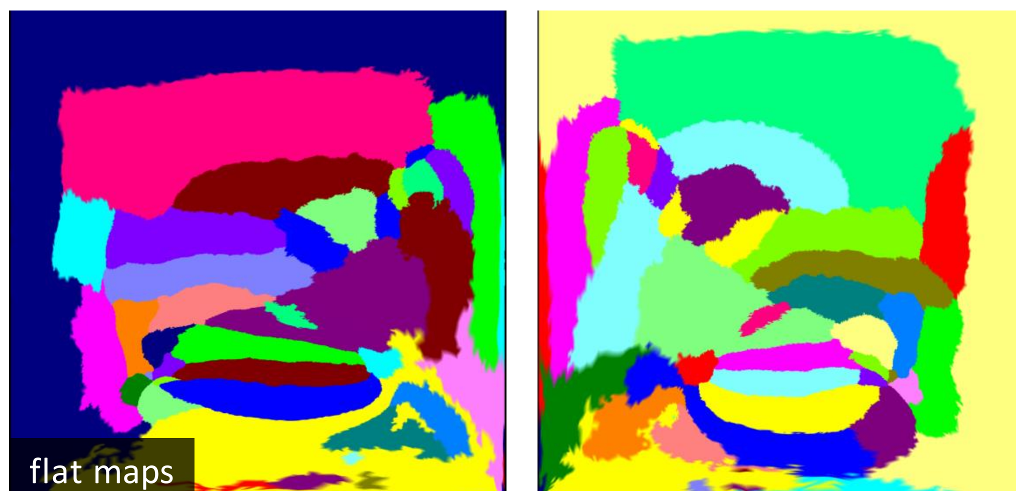
3D surface L2 alignment	flat mapping	curvature alignment	transfer of labels	boundary refinement	3D harmonic mapping	intensity registration	volumetric label transfer
~10 min	~1 min	~10 min	<1 min	~10 min	~10 min	~20 min	~2 min

BrainSuite Atlas1

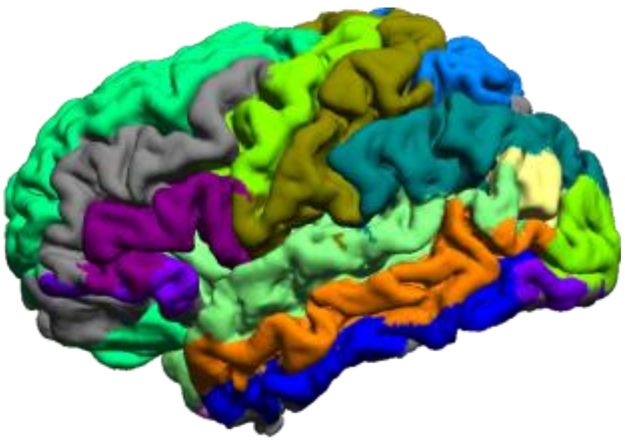
- Single subject atlas labeled at USC by an expert neuroanatomist
- 26 sulcal curves per hemisphere
- 98 volumetric ROIs, 35x2=70 cortical ROIs





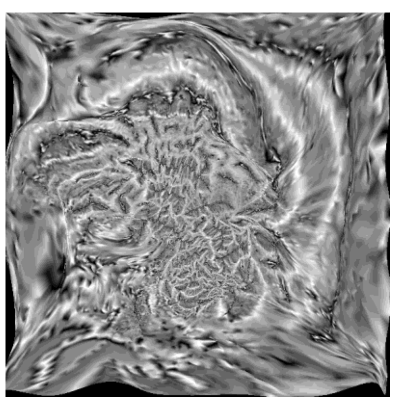


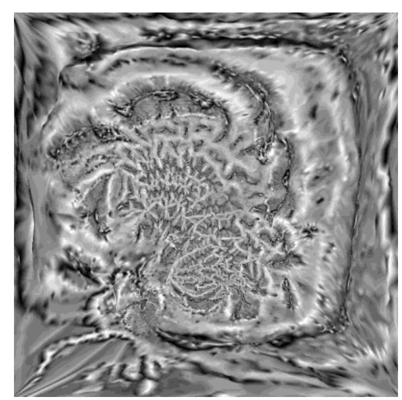
Transfer of Labels



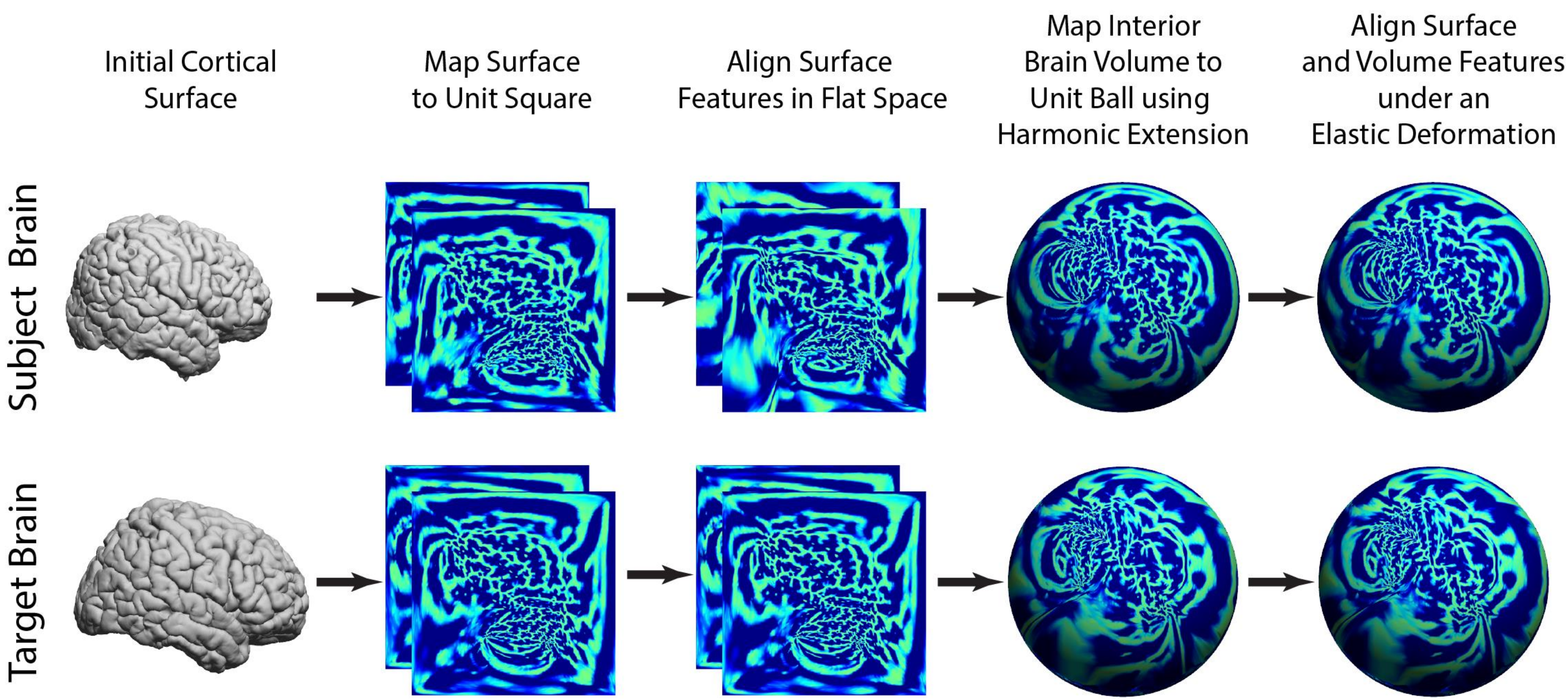
subject

atlas



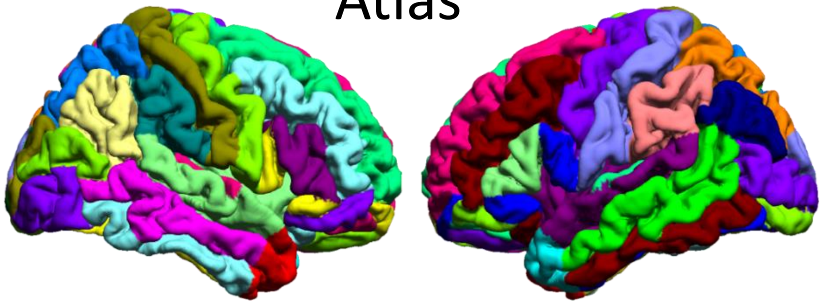


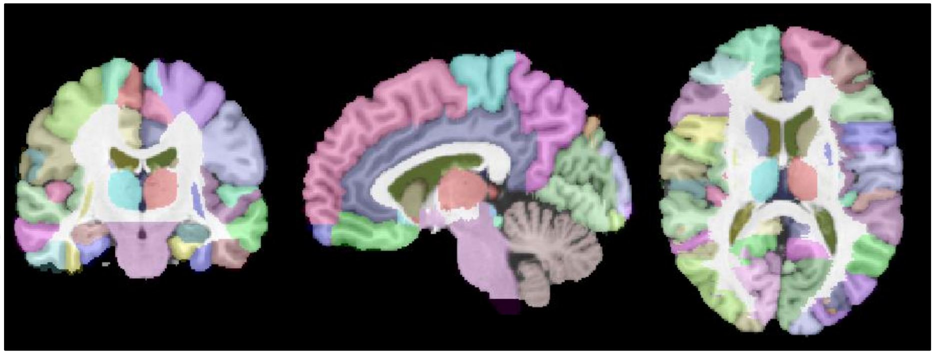
3D Harmonic Mapping & Intensity Registration



Volumetric Label Transfer

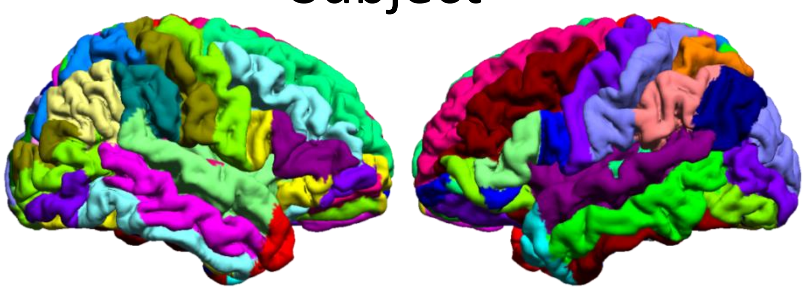
Atlas

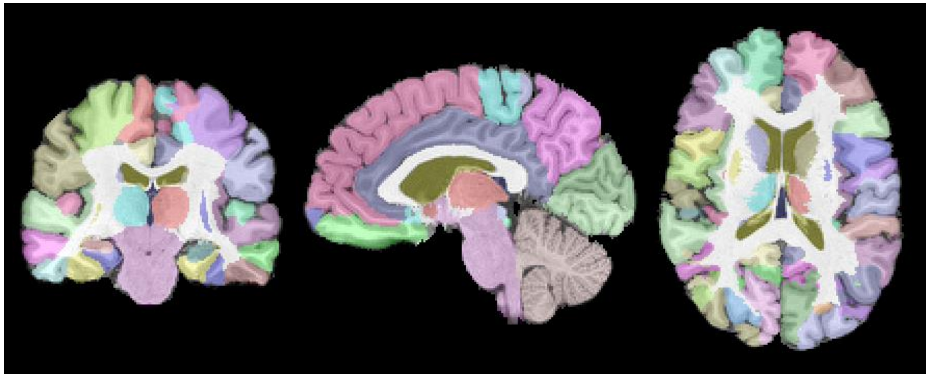




Views of the BrainSuite anatomical atlas, delineated into anatomical ROIs.

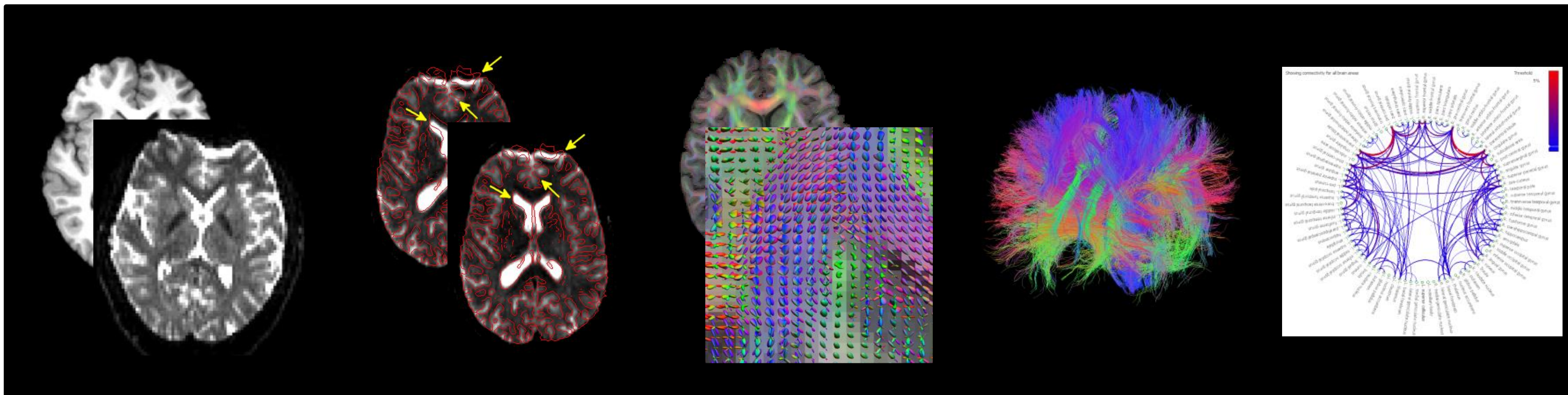
Subject





Similar views of an automatically labeled subject dataset.

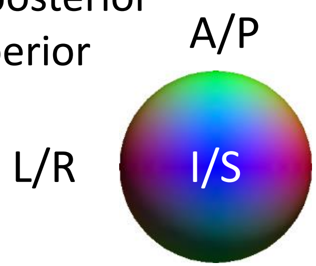
BrainSuite Diffusion Pipeline

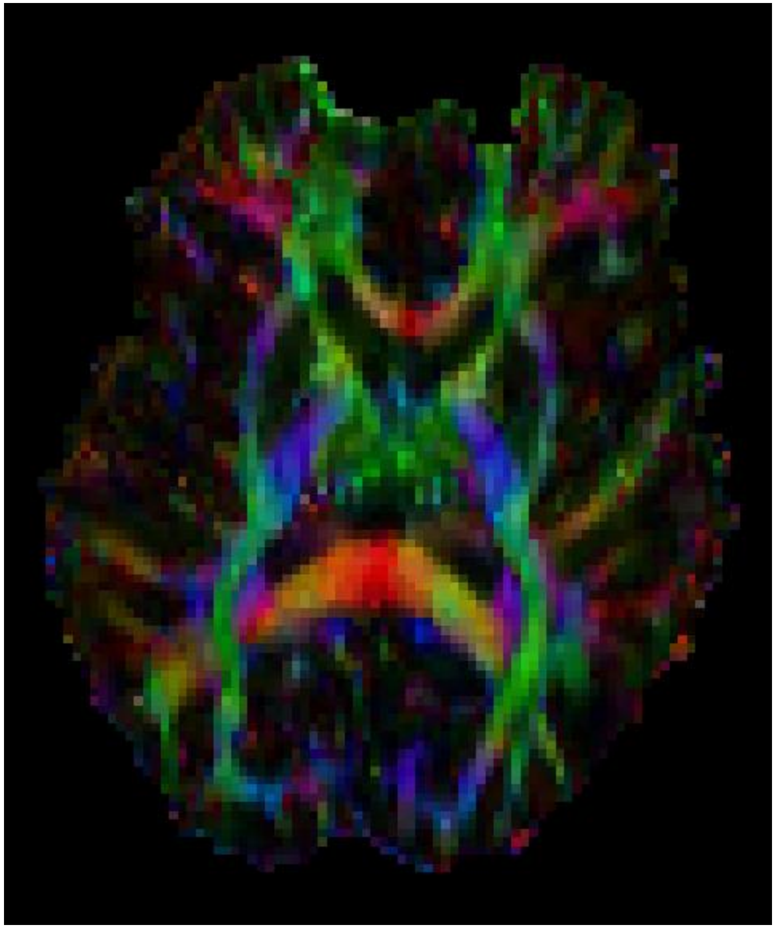


T1/DWI coregistration	distortion correction	diffusion modeling	whole-brain tractography	connectivity analysis

Diffusion Tensor Imaging

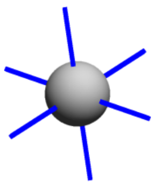
- With at least six directions and a baseline image, a tensor model can be estimated.
- Different types of tissue will have different diffusion properties
  - Oriented along nerve fibers
  - Free diffusion in CSF
- Visualization of scalar properties (e.g., fractional anisotropy)
- Visualization of major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



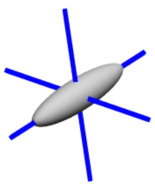


DTI Visualization

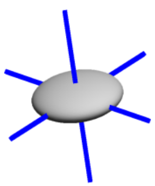
Often visualized using ellipsoids



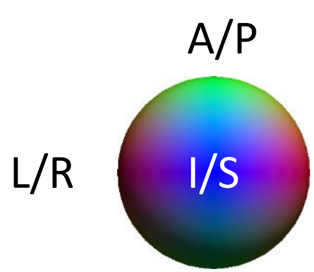
Spherical shapes indicate isotropic diffusion

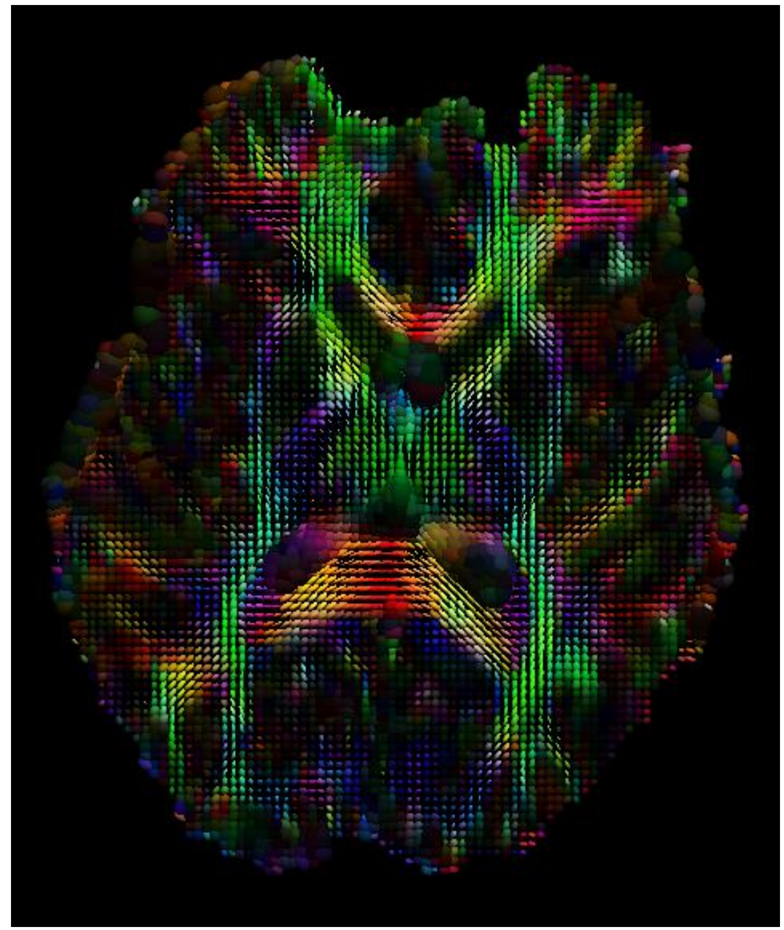


Elongated shapes indicate directionality



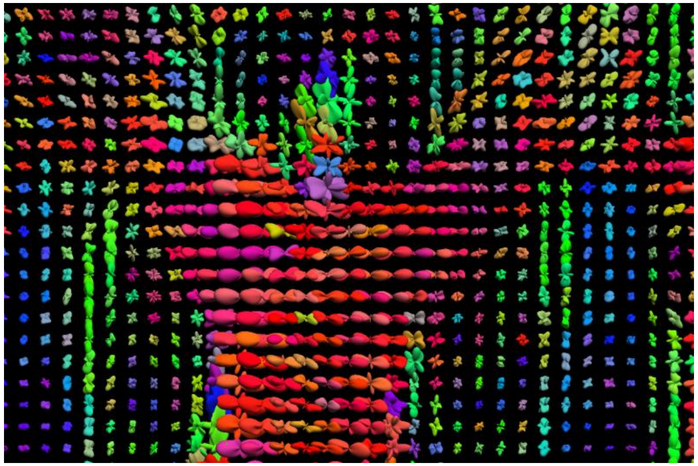
Flat discs are suggestive of the crossing or junction of nerve fibers





ODF Models

- The tensor model is limited in what it can resolve
- Nerve fibers 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



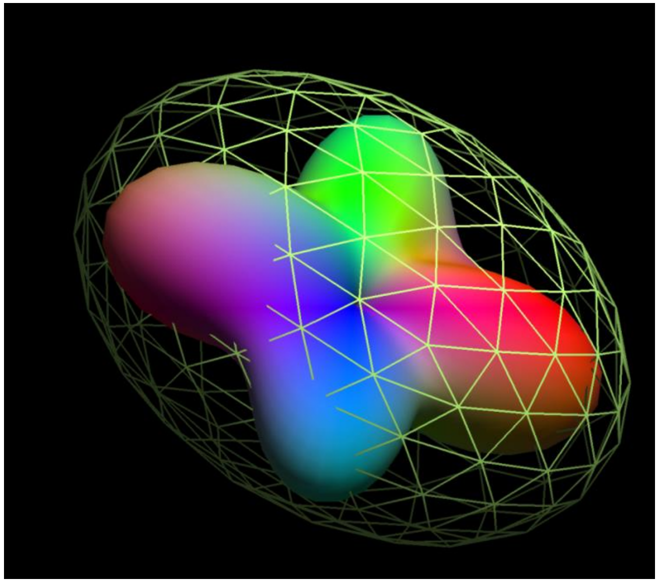
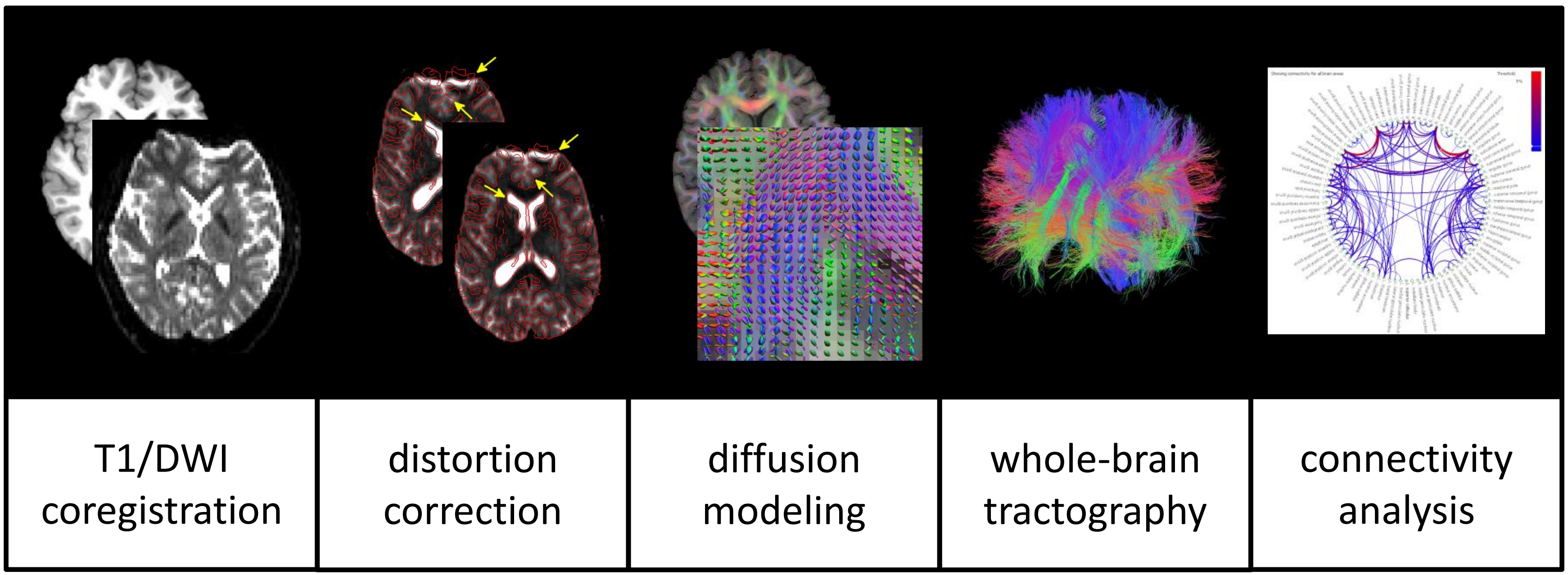


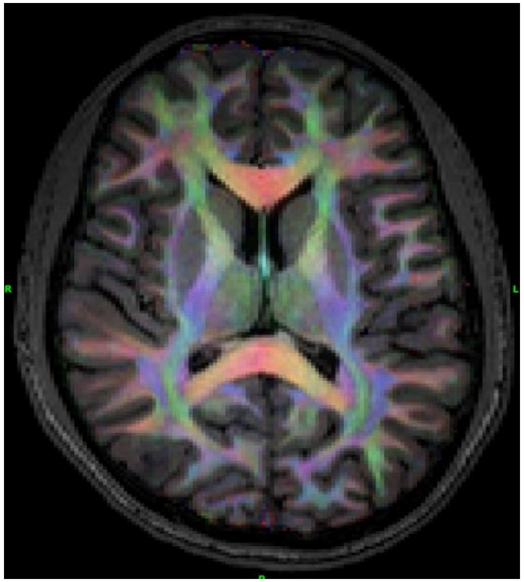
Image from Shattuck et al. (2008). Visualization Tools for High Angular Resolution Diffusion Imaging, *Medical Image Computing and Computer Assisted Intervention (MICCAI) 2008*

BrainSuite Diffusion Pipeline

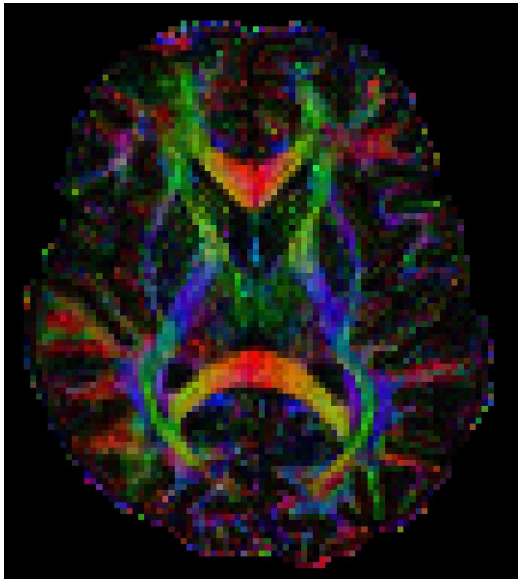


T1 / Diffusion Registration

T1 Coordinates
(Surfaces, Labels)



T1/Color-FA
Overlay

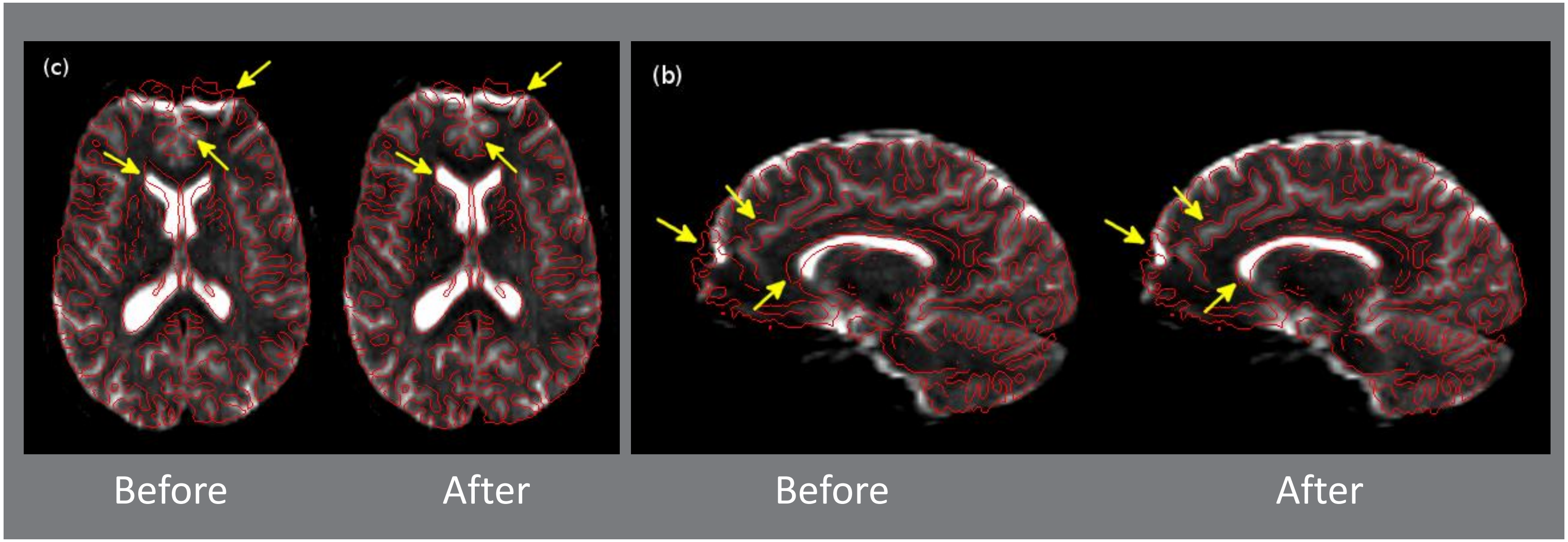


Diffusion Coordinates

- If we want to fuse information from diffusion and structural MRI, we need to co-register them.
- However, rigid registration is not enough.

Registration-based Correction

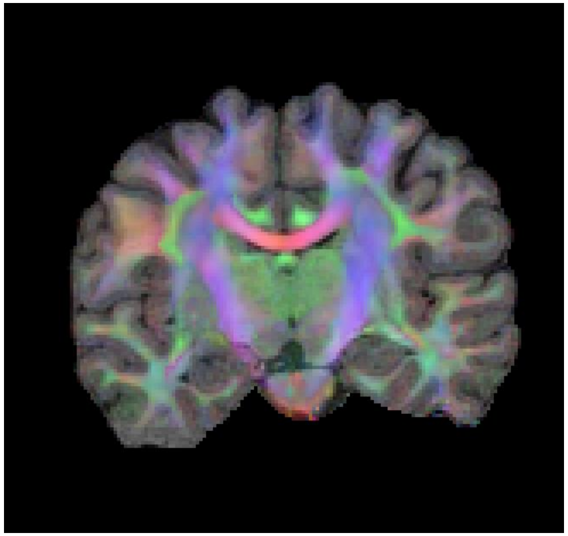
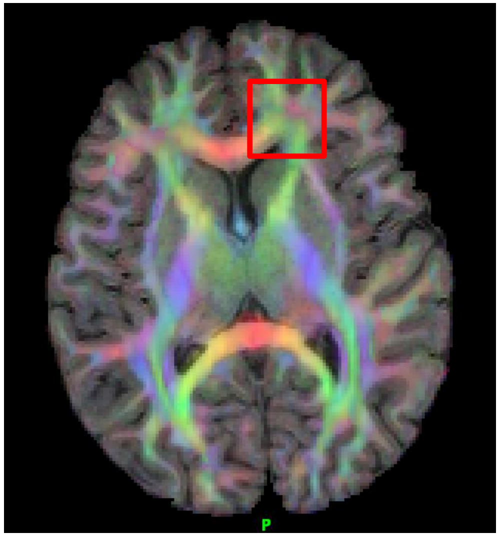
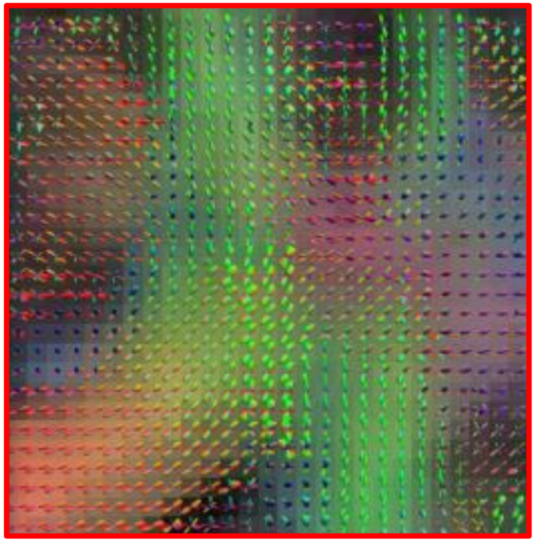
- Corrects the distortion in diffusion (EPI) images using non-rigid registration
- No fieldmap is required
- Similar performance to fieldmap method



Bhushan et al. 2012

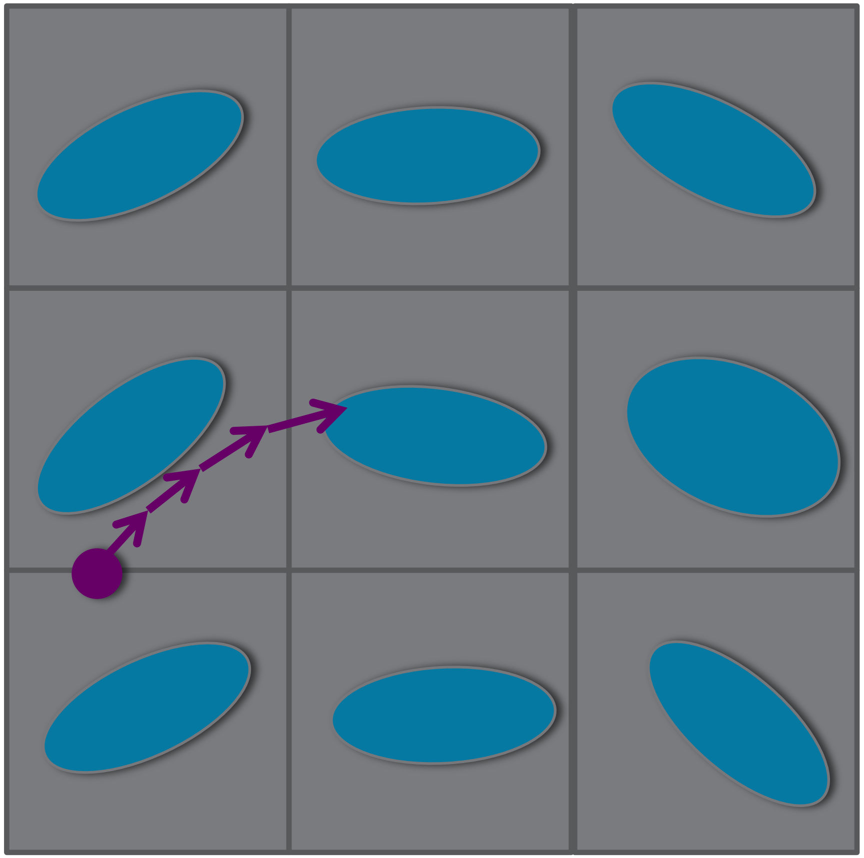
Tensor and ODF Estimation

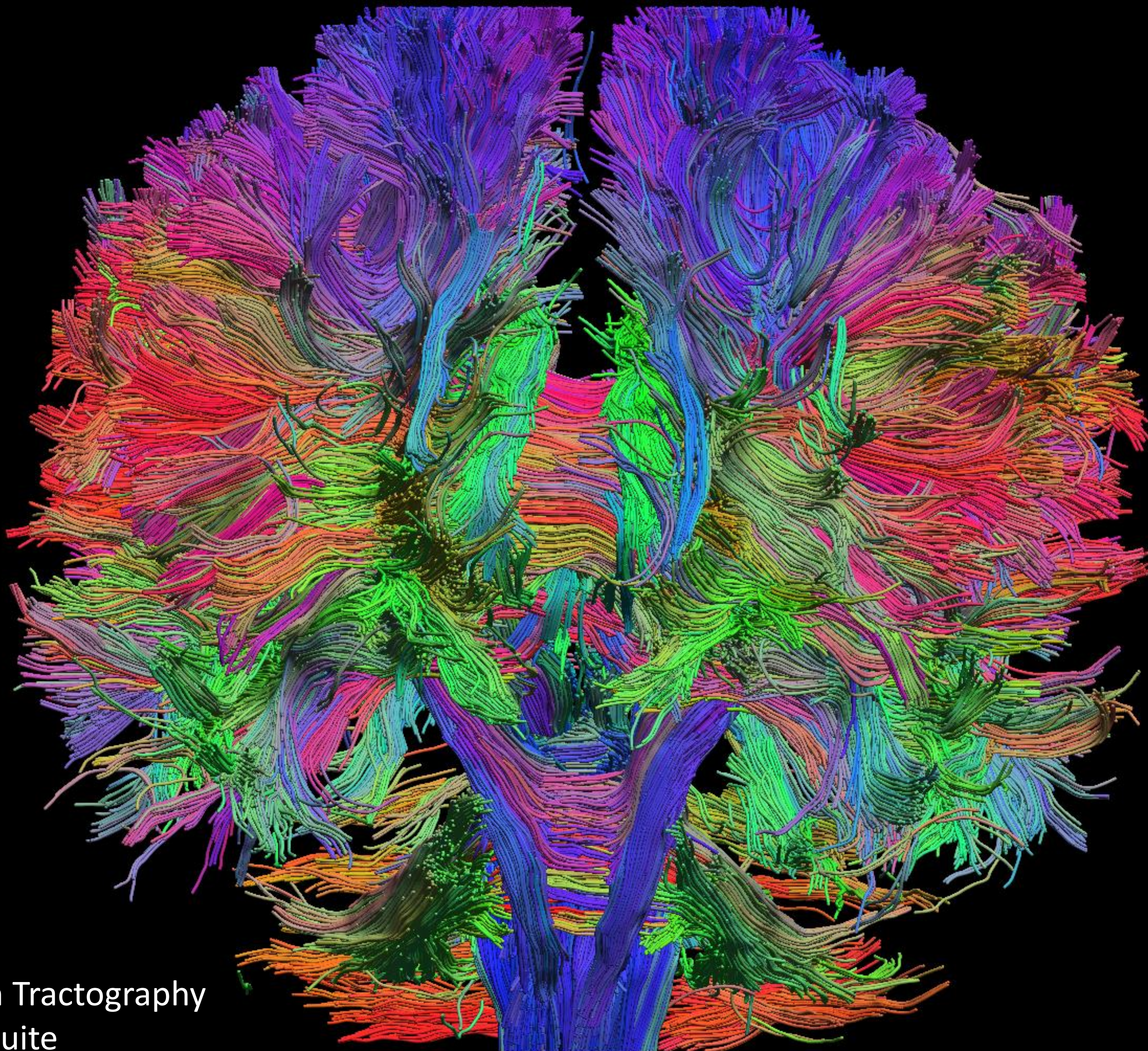
- Estimate diffusion tensors
  - FA, MD, color-FA
- Axial, Radial diffusivity
- ODFs using FRT (Tuch, 2004)
- ODFs using FRACT (Haldar and Leahy, 2013)
  - improved accuracy
  - higher angular resolution

Fiber Tracking

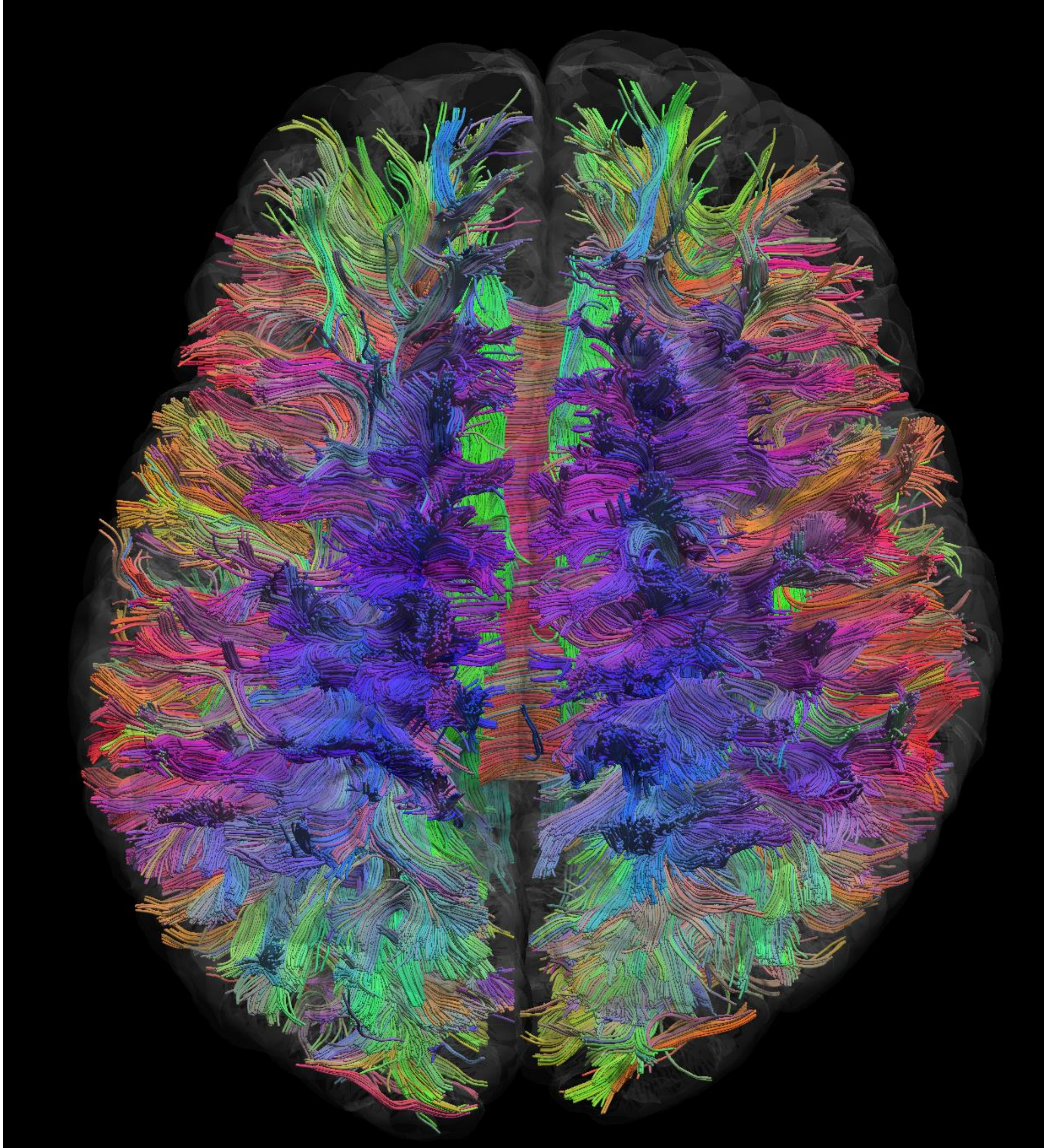
- White matter fiber tracts can be traced using direction vectors from diffusion tensors or ODFs.
- **Seed** at a point in the volume.
- **Step** forward in a direction determined by the local diffusion pattern.
- **Repeat** until a stopping criterion, such as reaching a tissue boundary or an area of low fractional anisotropy.





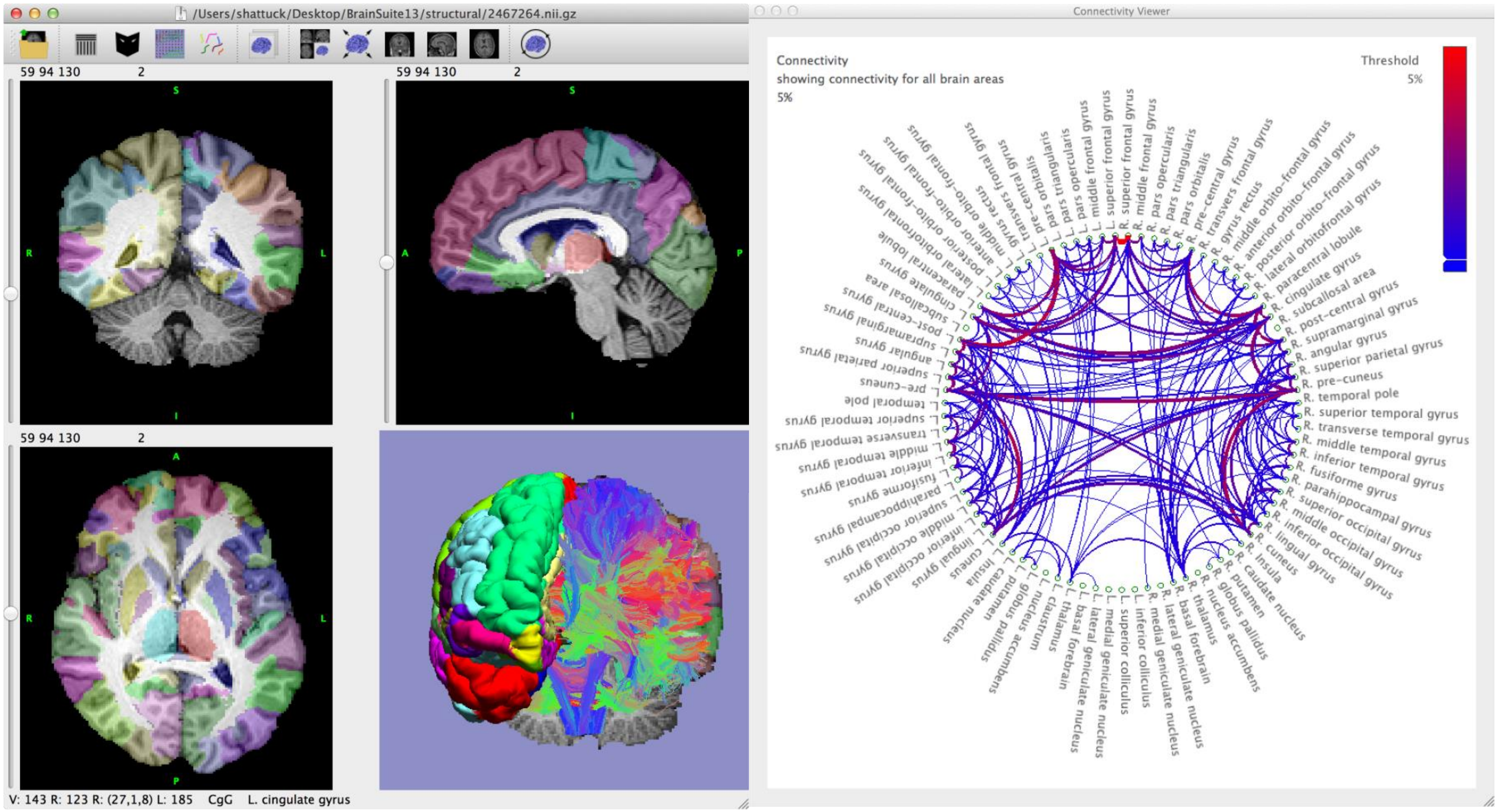
Diffusion Tractography
in BrainSuite

Axial View of Fiber Tracking



Diffusion Tractography in BrainSuite

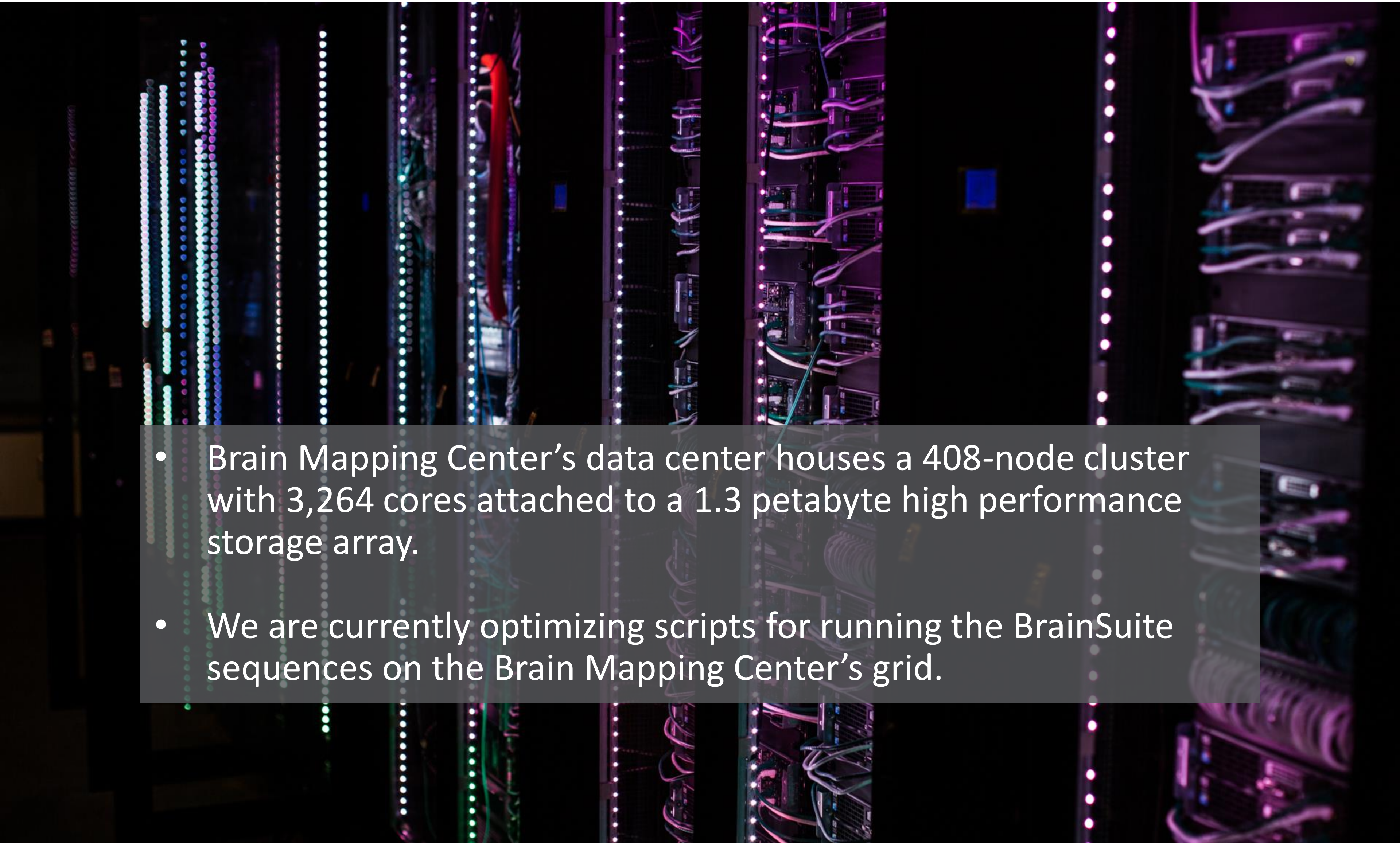
BrainSuite Connectivity



- Fiber tracking in the same space as the labeled MRI
- ROI connectivity analysis

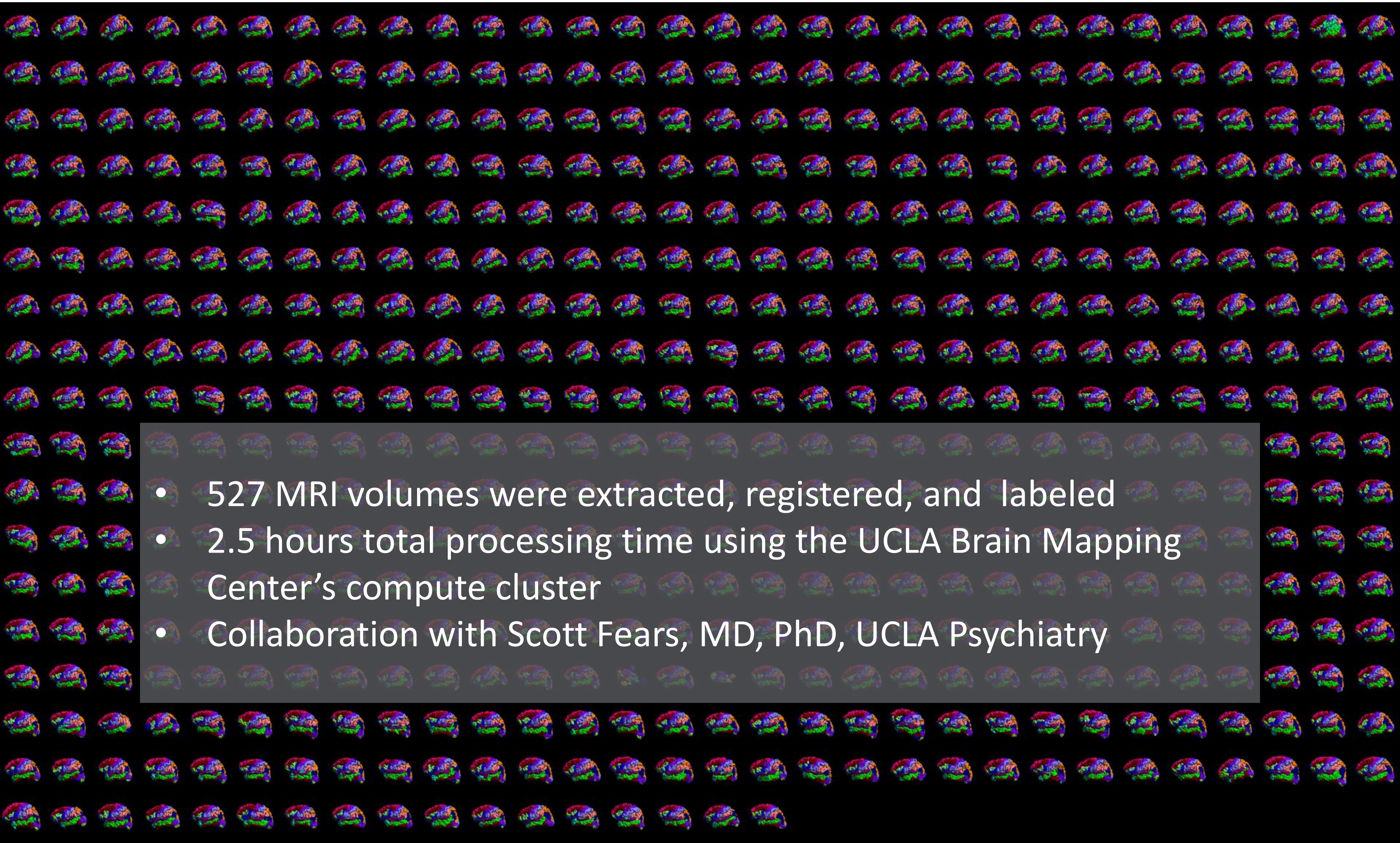
Applications and Ongoing Work

Large Scale Brain Mapping



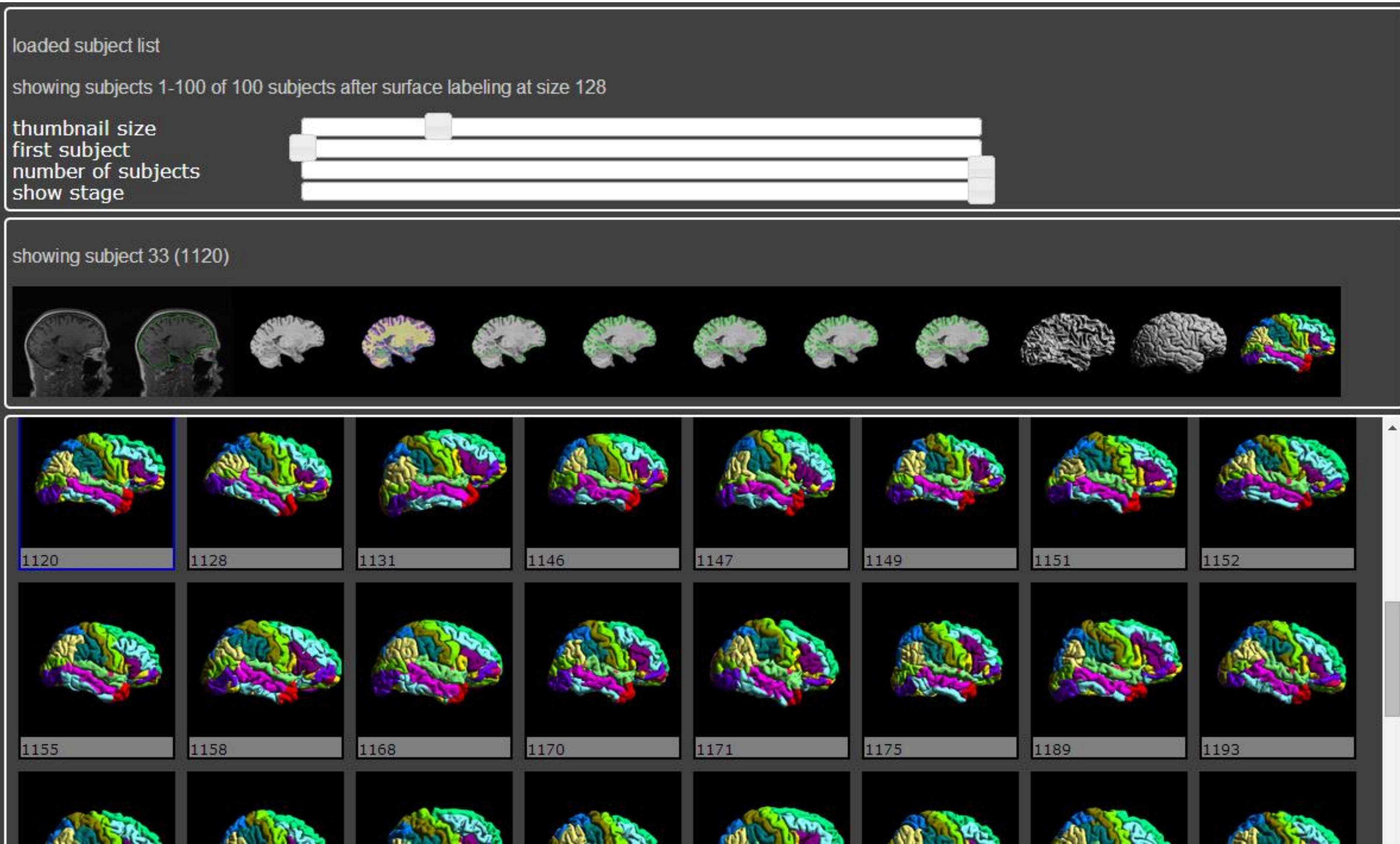
- Brain Mapping Center’s data center houses a 408-node cluster with 3,264 cores attached to a 1.3 petabyte high performance storage array.
- We are currently optimizing scripts for running the BrainSuite sequences on the Brain Mapping Center’s grid.

Large Scale Brain Mapping



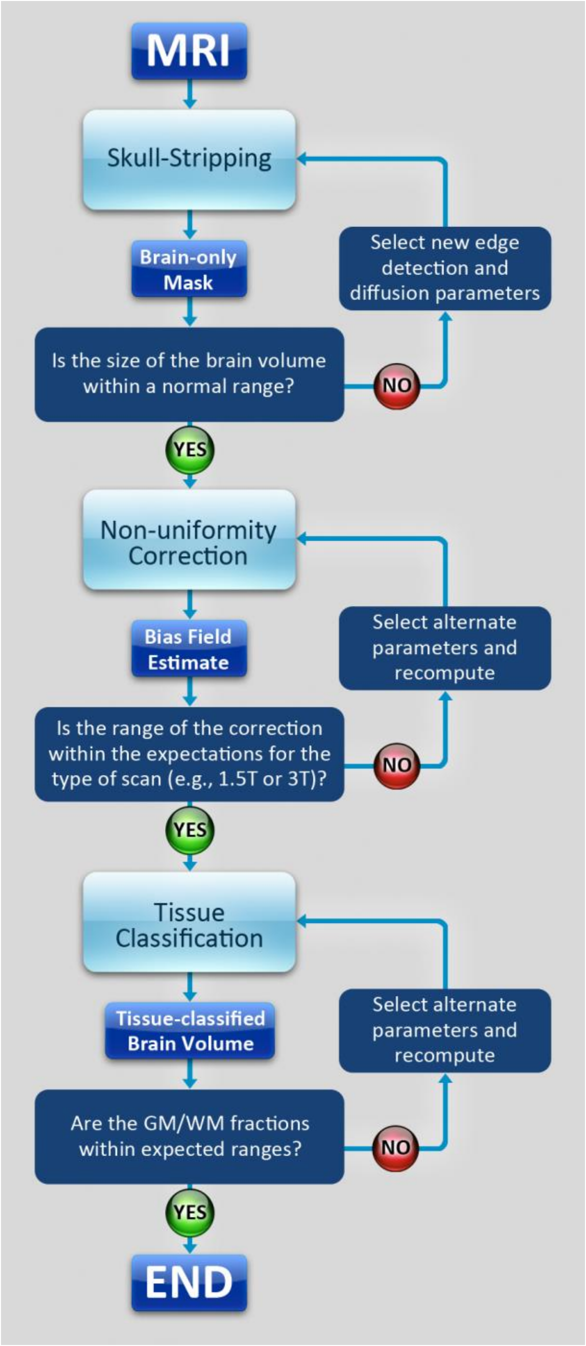
- 527 MRI volumes were extracted, registered, and labeled
- 2.5 hours total processing time using the UCLA Brain Mapping Center’s compute cluster
- Collaboration with Scott Fears, MD, PhD, UCLA Psychiatry

Quality Control



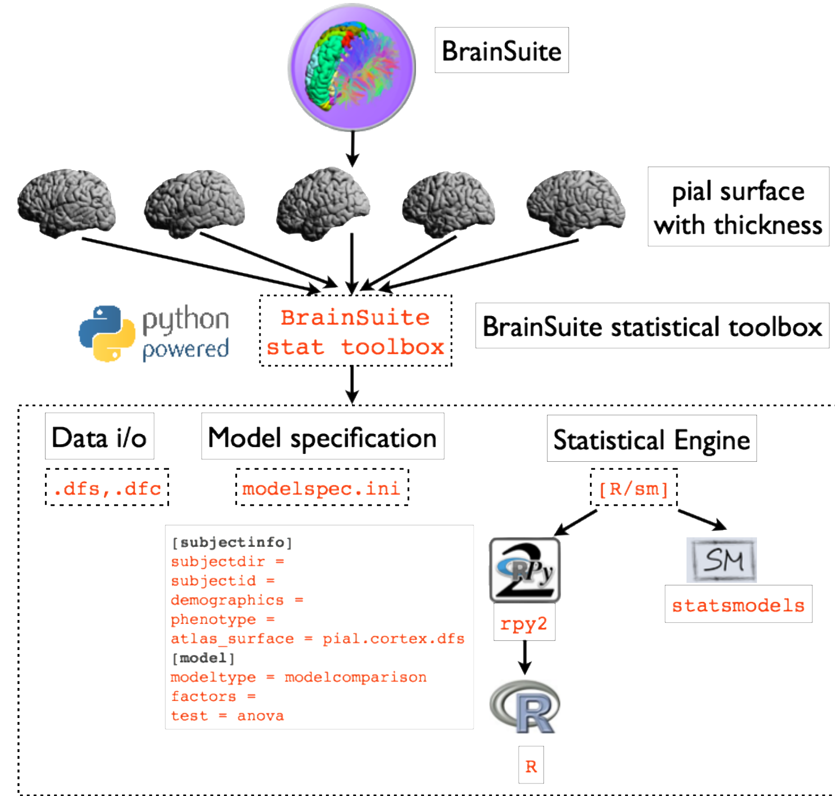
Error Detection

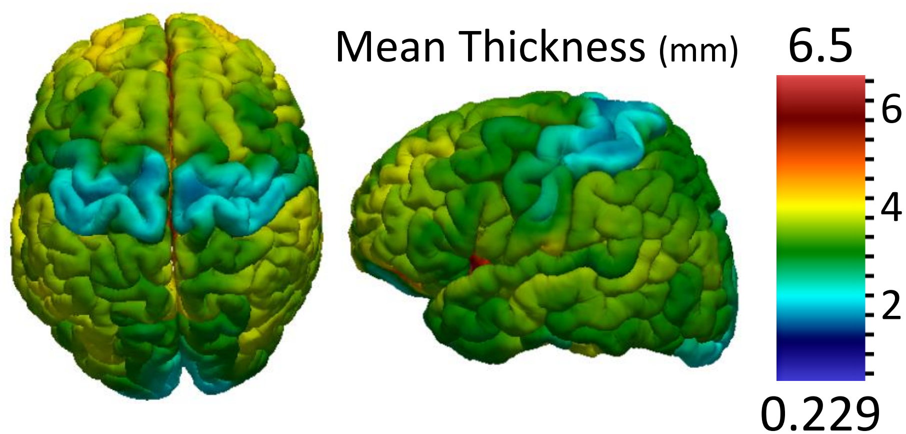
- We plan to develop interfaces that facilitate identification of errors in the processing chain.
  - Web-based reports
  - Software interfaces that allow errors to be corrected and the processing continued
- Quality assurance
  - Automatically identify potential failures based on measures.
  - For example, is the total brain volume within a normal range?



BrainSuite Statistical Toolbox

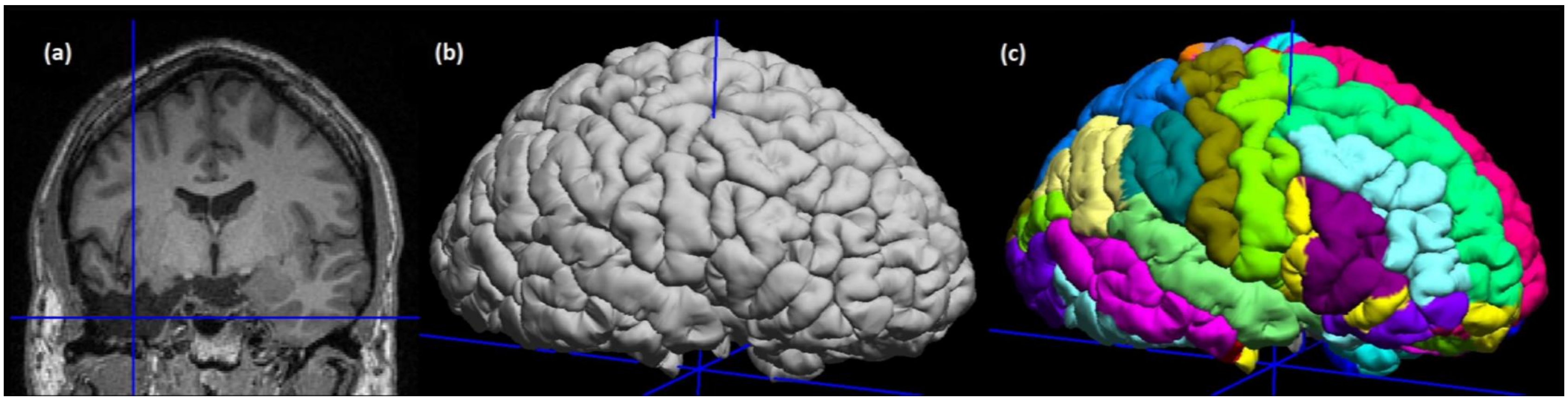
- Performs structural group analysis for cortical surfaces
- Encapsulates data representation, the model specification, and the statistical computation process.
- Implemented in Python with rpy2.
- Cross-platform - Win, Mac, Linux
- Offers statistical methods:
  - ANOVA, GLM, correlation
  - Provision for Multiple testing - FDR
  - Uses R data.table to efficiently vectorize operations
- Available at brainsuite.org/bss





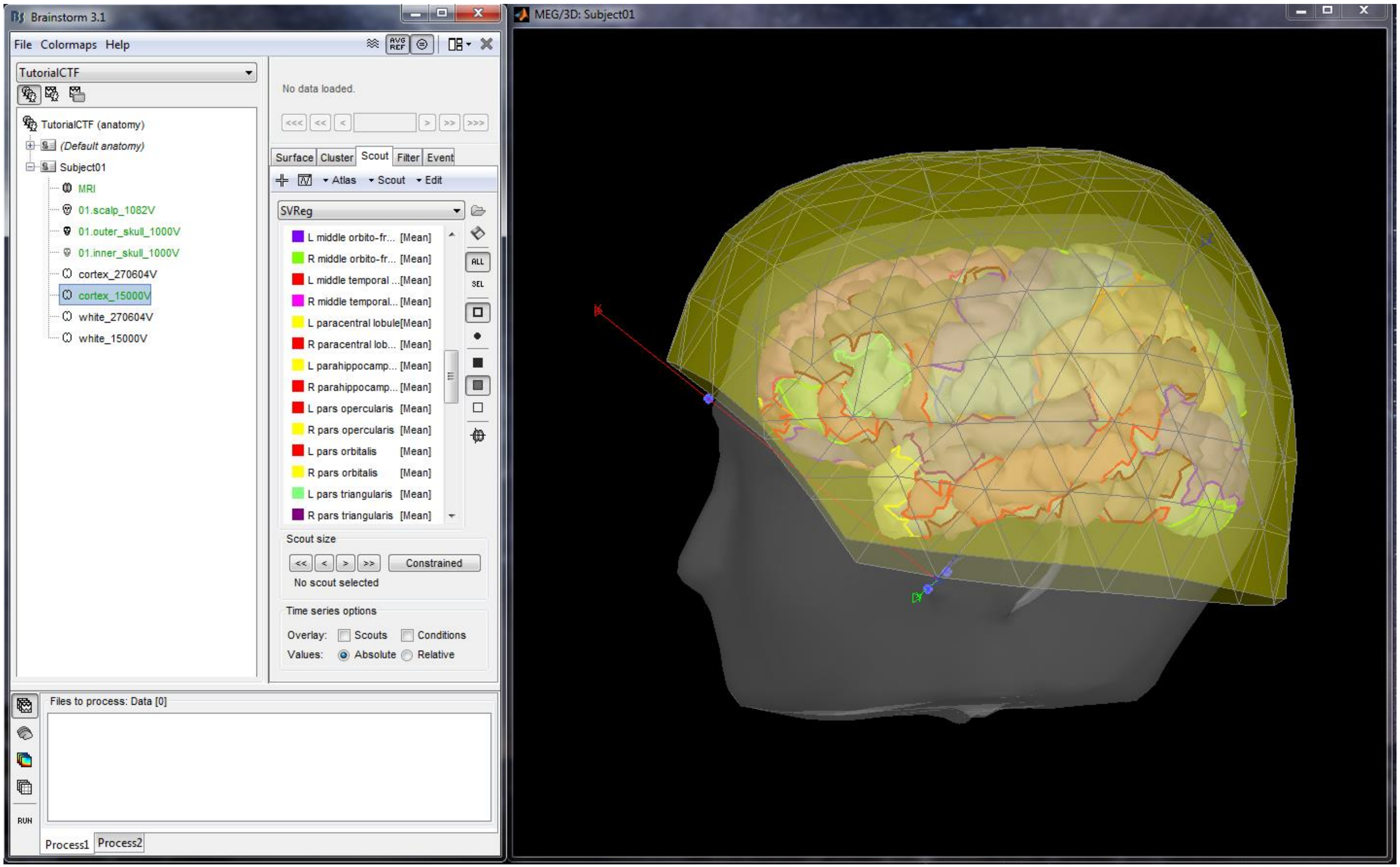
S. Joshi et al., OHBM2014

Segmentation & Labeling of Abnormal Data



- Develop methodologies to handle lesions, resections, and other pathology
- Manual identification tools
- Segmentation, registration, and labeling tools
- Lesion detection software

Integration with BrainStorm



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

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

CLARITY Technique for Neuroimaging: Hippocampus

Thy1-GFP endogenous expression

Imaged with confocal microscopy

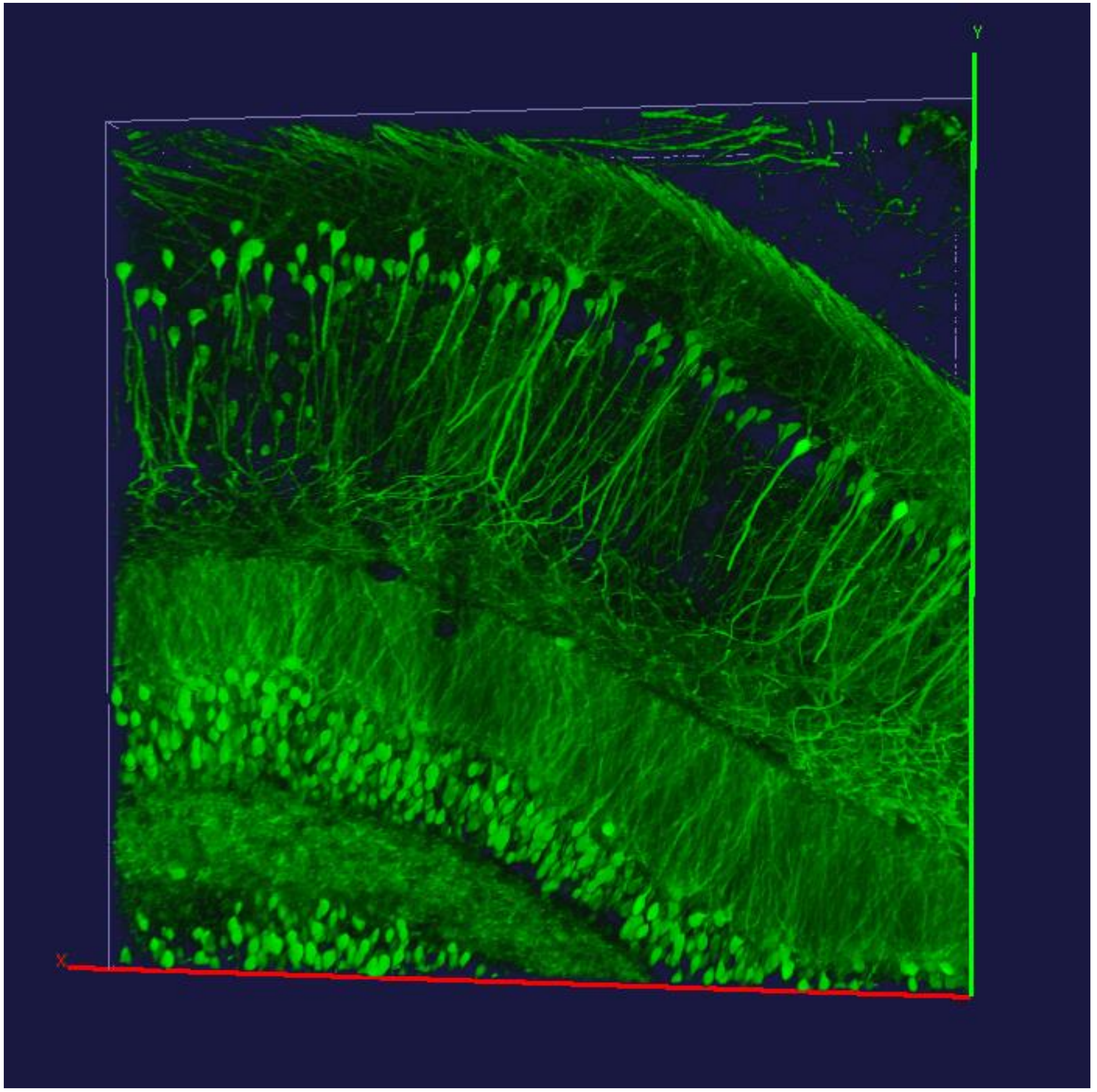


Image provided by Luis de la Torre-Ubieta, PhD, Jason Stein, PhD, and Daniel Geschwind, MD, PhD (UCLA).

CLARITY Technique for Neuroimaging: Cortex

Thy1-GFP mouse cortex

Endogenous GFP (red) and GFP immunostaining (green)

Prepared from 1mm thick coronal slices

Imaged with confocal microscopy

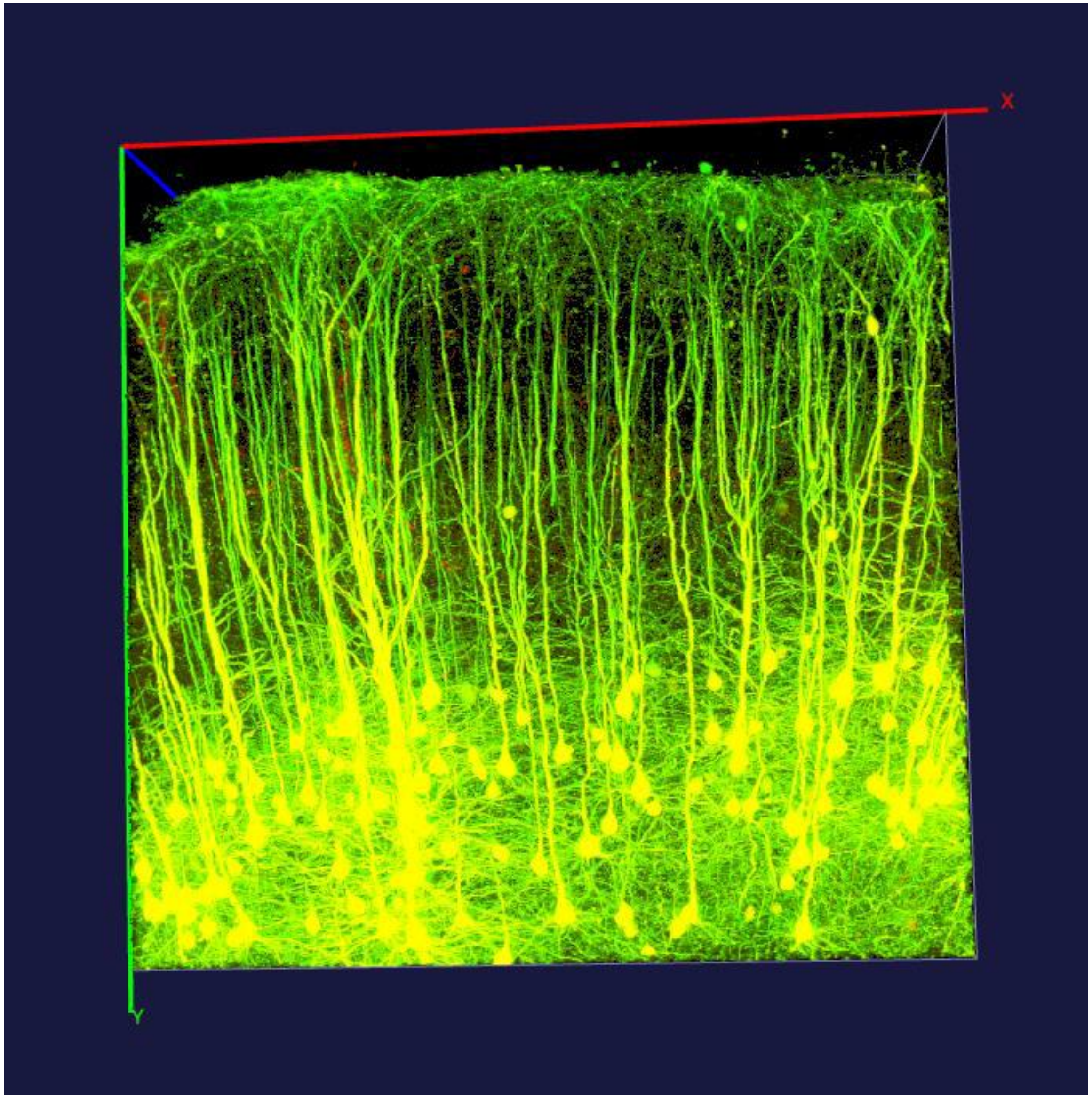
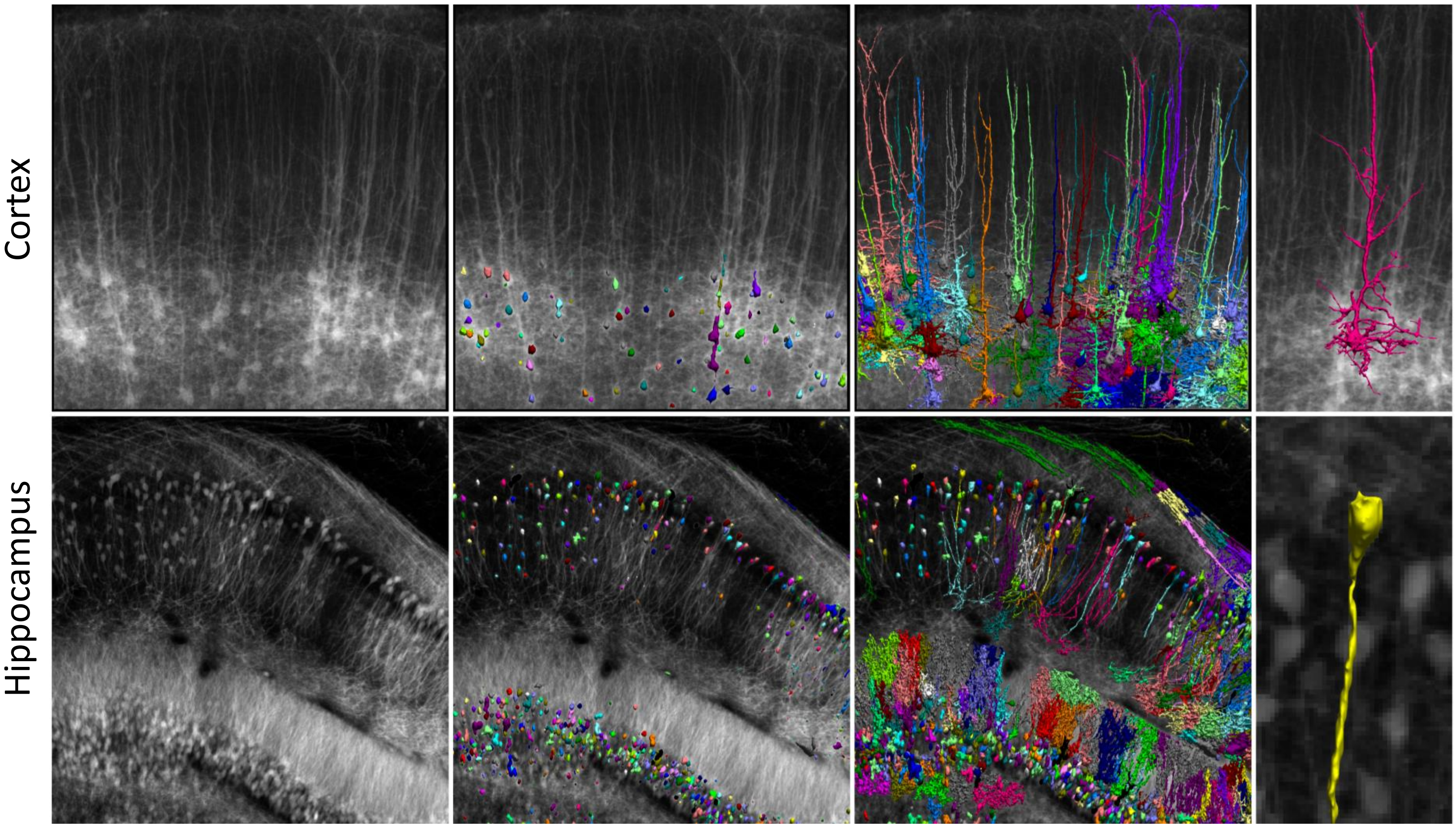


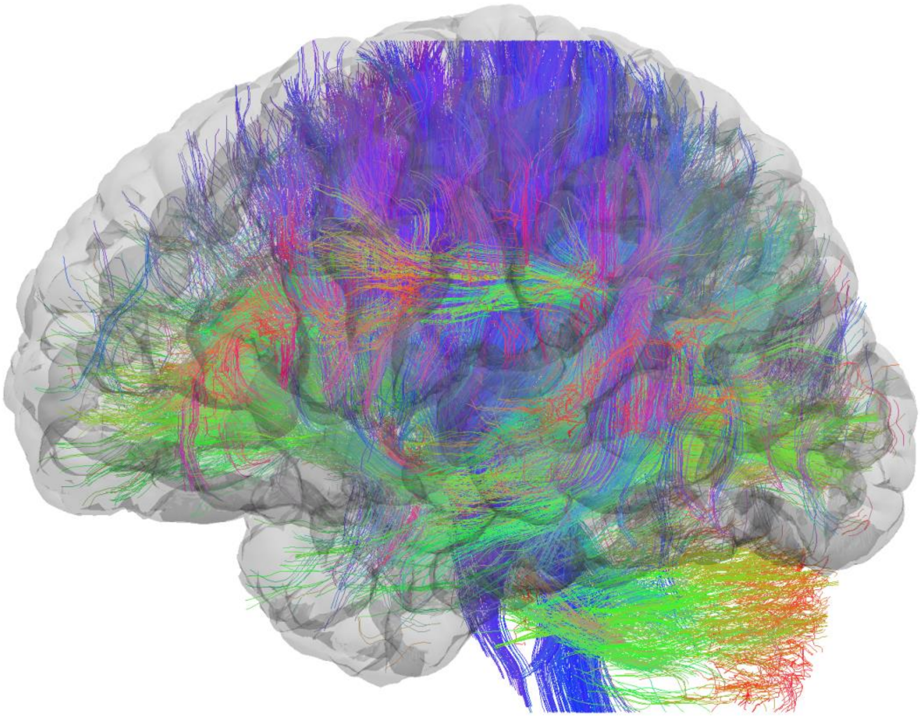
Image provided by Luis de la Torre-Ubieta, PhD, Jason Stein, PhD, and Daniel Geschwind, MD, PhD (UCLA).

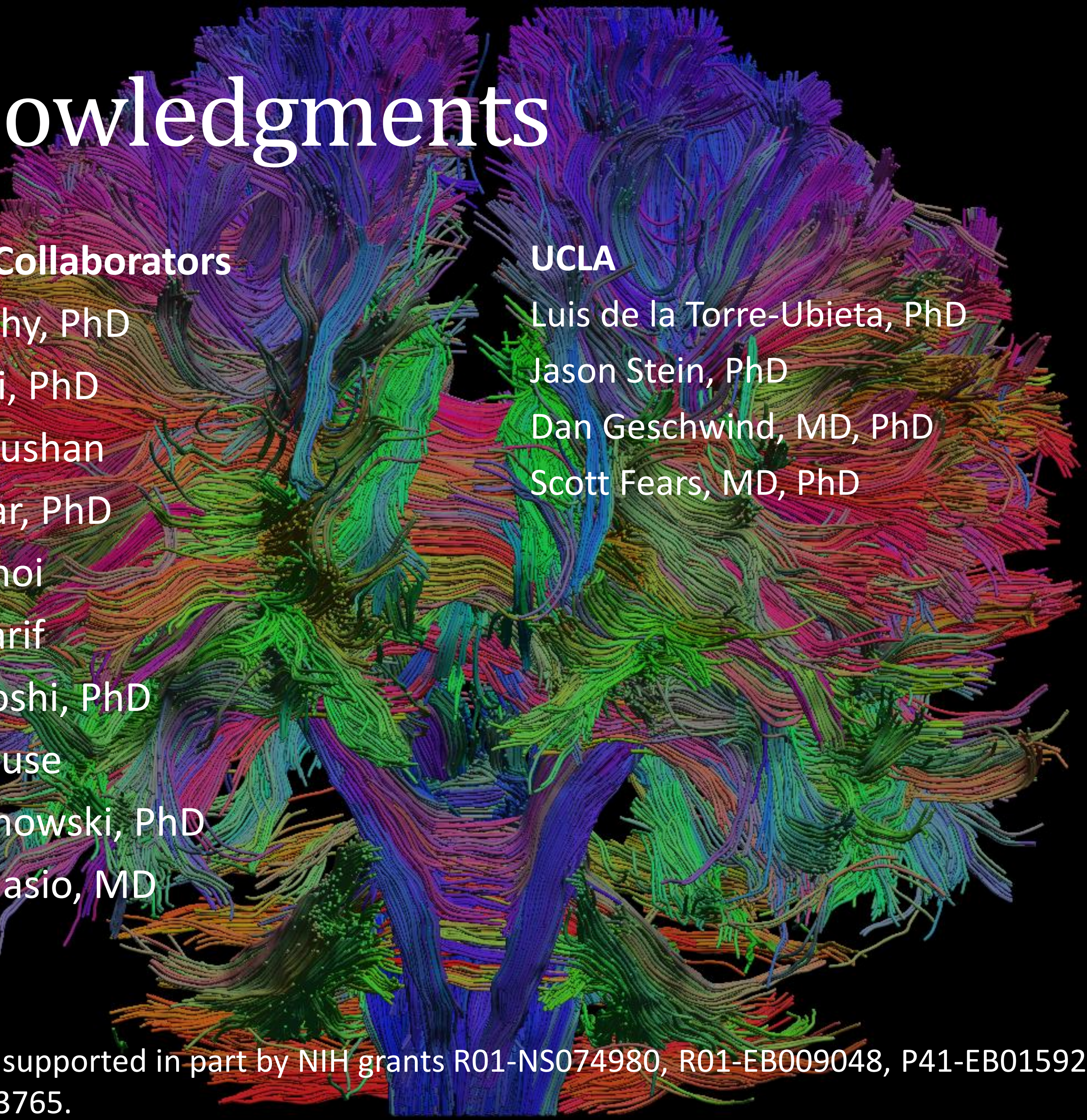
CLARITY Image Analysis



BrainSuite Highlights

- Interactive processing
- Visualization capabilities
- Joint surface/volume registration
- New BCI-DNI brain atlas
- Customizable atlases
- Unique diffusion modeling (FRACT)
- Multiple methods for B0-distortion correction
- Atlas-based connectivity analysis





Acknowledgments

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UCLA

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Scott Fears, MD, PhD

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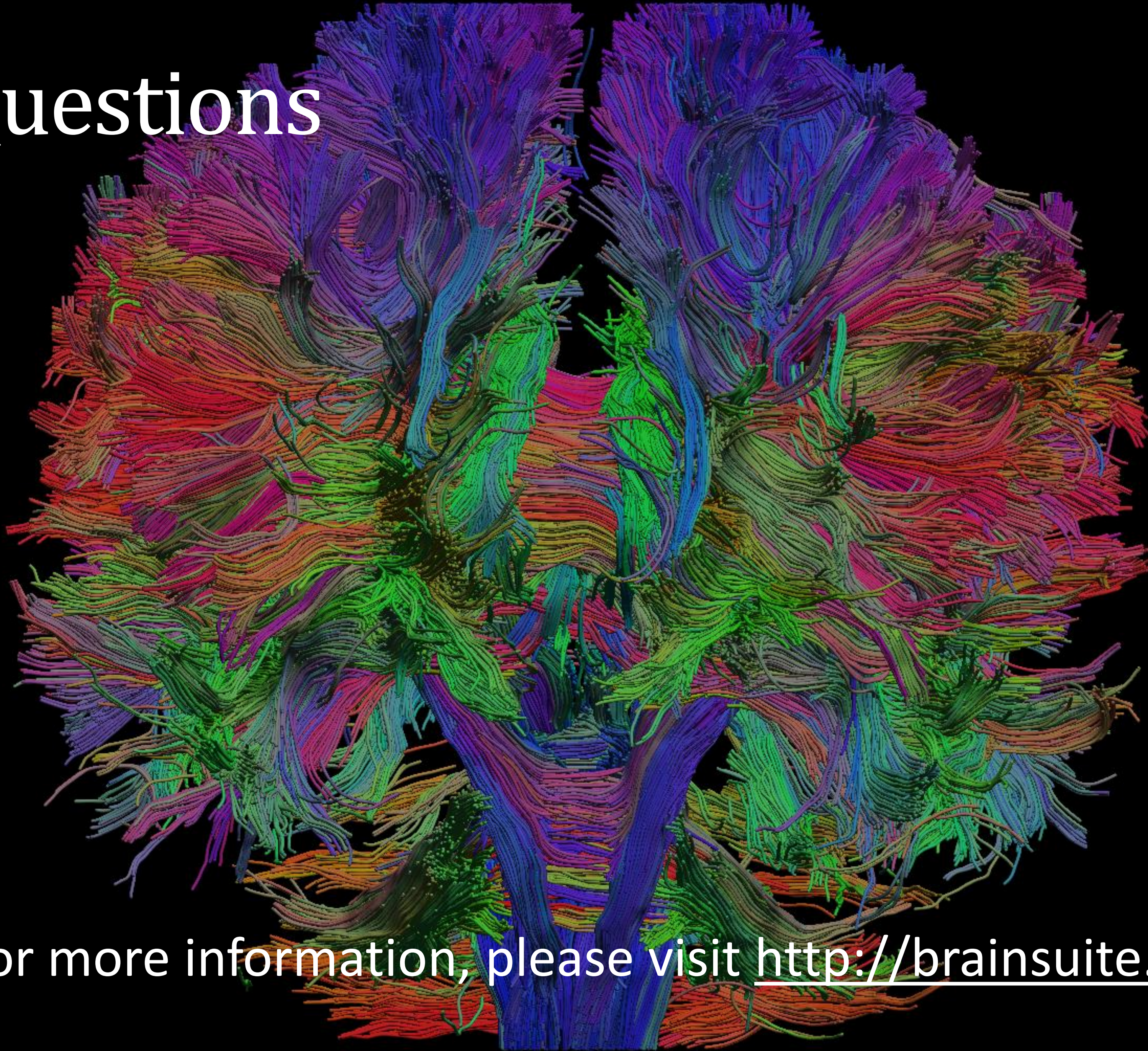
Questions



For more information, please visit http://brainsuite.org