Part 1: Structural and diffusion-weighted MRI

Cajal Course on Aging Cognition

Workshop: Approaches to functional and structural neuroimaging analysis

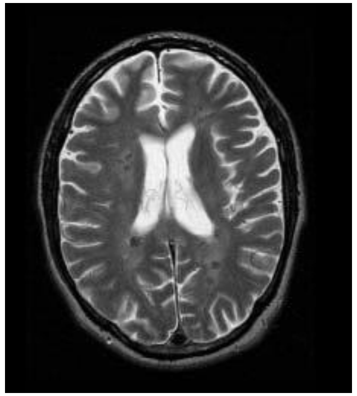
Materials: https://github.com/jennyrieck/workshops/tree/master/2021_Cajal_NeuroImaging

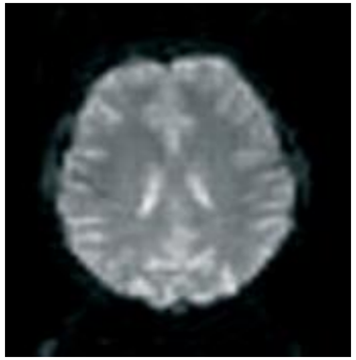
27 Sep 2021

Jenny Rieck

A very brief intro to MR

- Magnetic resonance is based on emission and absorption of energy in radio frequency range of electromagnetic spectrum
- Hydrogen atoms absorb radio frequency energy and release it at different rates depending on tissue makeup (e.g., fat, water)
- MR acquisition parameters can be manipulated to better contrast brain tissue of interest (e.g., gray matter vs. white matter) or brain (e.g., oxygenated vs. de-oxygenated hemoglobin)





MRI terminology

- Image or volume = single 3D representation of brain data, acquired in a series of slices
- Timeseries = multiple 3D brain volumes collected over time, as in functional MRI (i.e., 4D data)
- Voxel = volumetric pixel in the brain image that has XYZ coordinates
- Native-space = participant specific brain space
- Standard space = common space used to compare across participants based on a template (e.g., MNI, Talairach)
- Region of interest (ROI) = defines the borders of a specific area to examine

MRI software (structural and functional)

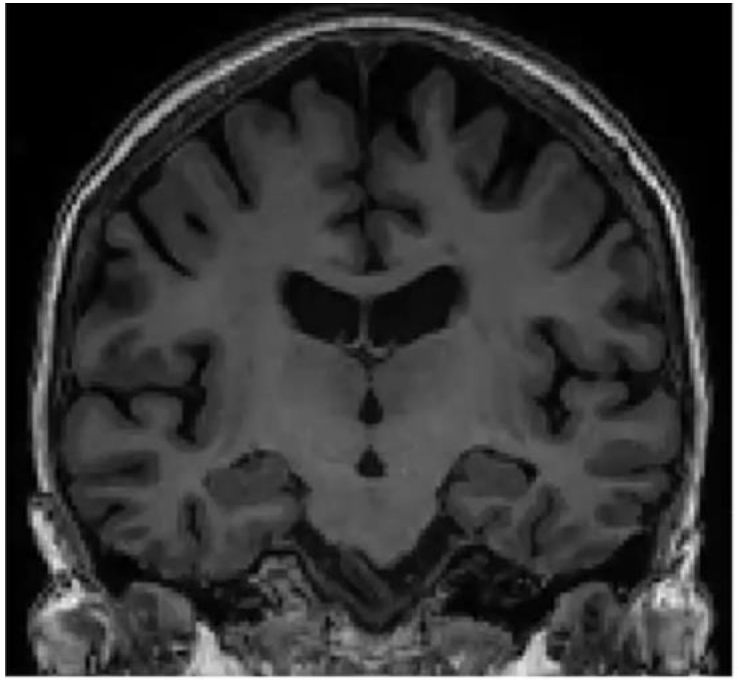
	SPM	FSL	AFNI	BrainVoyager
Operating system	Mac, Linux, Windows	Mac, Linux	Mac, Linux	Mac, Linux, Windows
Scripting language	MATLAB	Shell	Shell, Python	JavaScript, Python
GUI	Yes	Yes	Yes	Yes
Costs	Free* (MATLAB license required)	Free	Free	$$

Other fMRI software: BrainVISA, BrainSuite, MIALAB

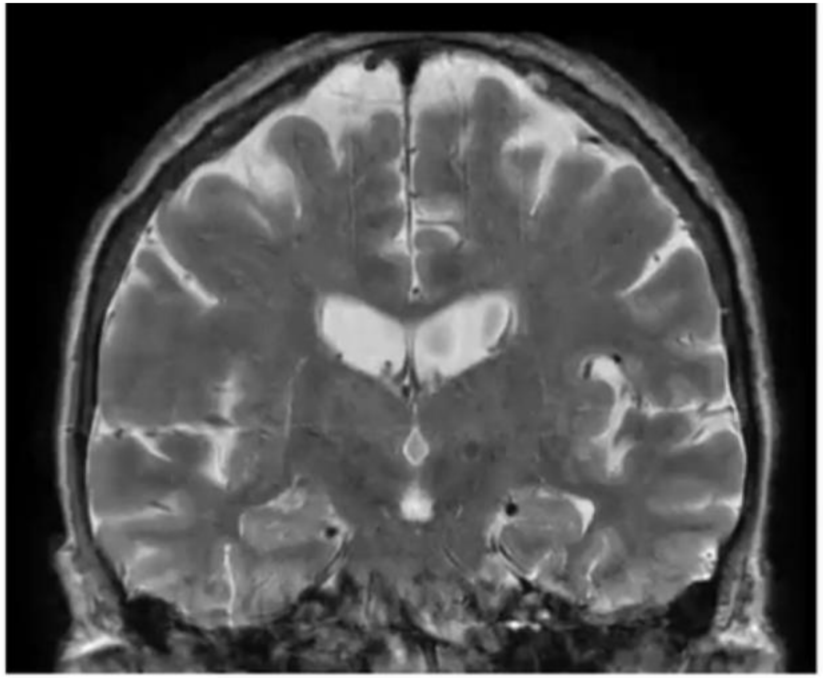
Structural imaging

What is structural neuroimaging with MRI?

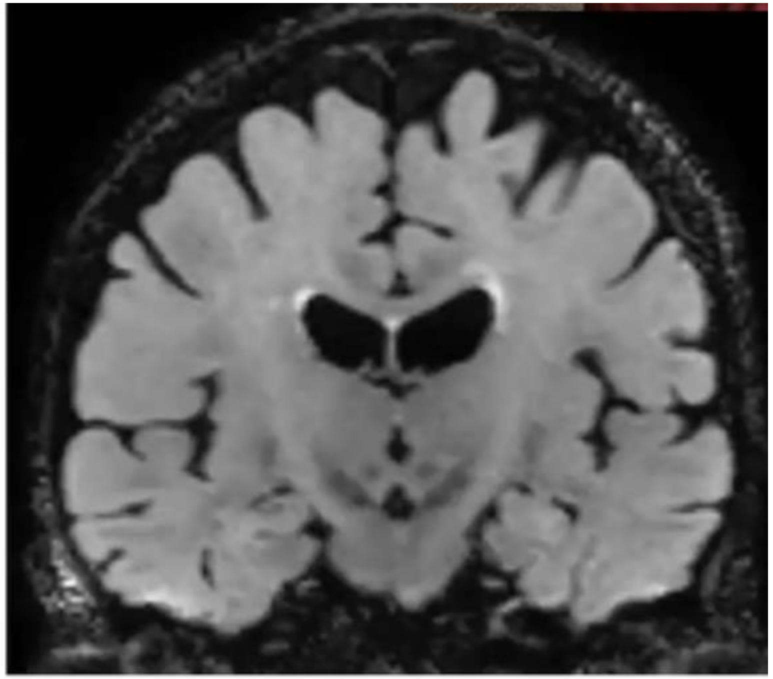
- Structural neuroimaging encompasses many types of acquisitions and modalities



T1-weighted



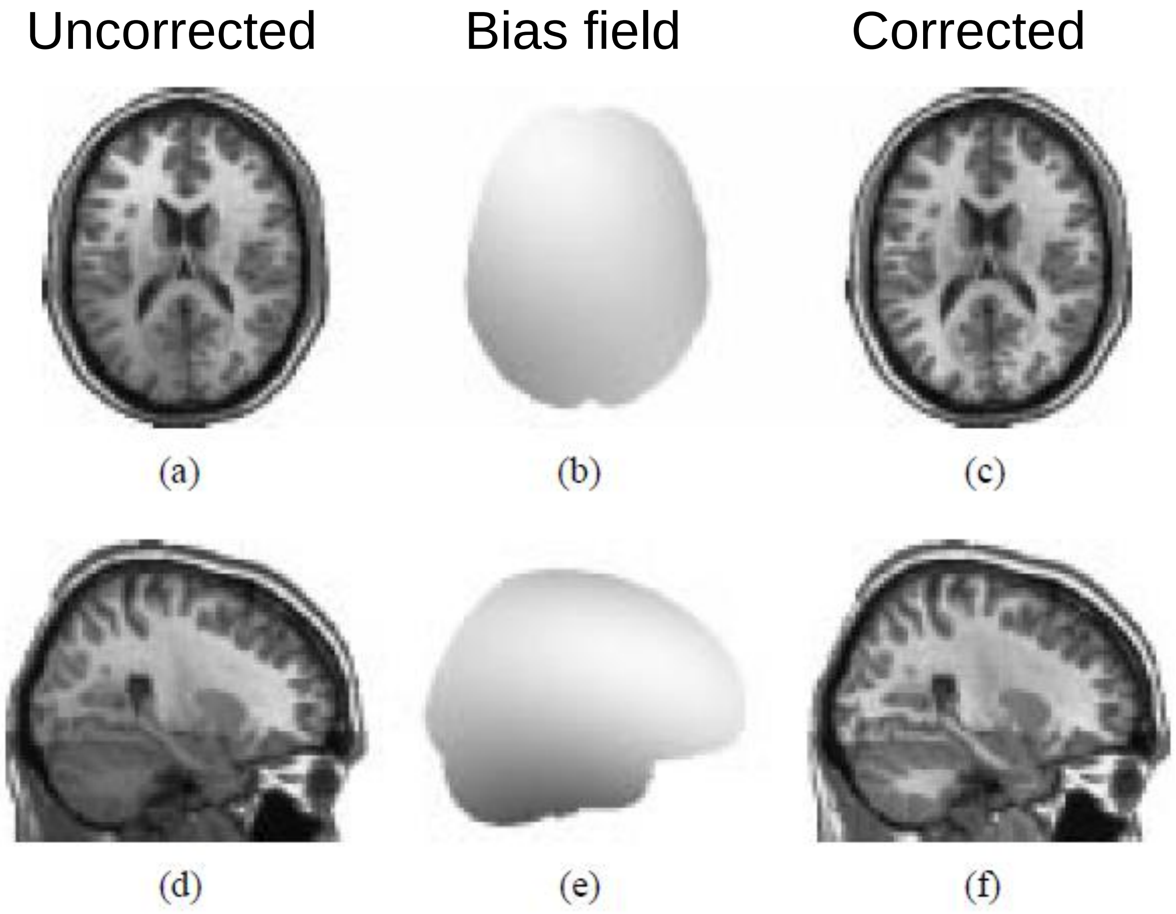
T2-weighted



FLAIR

Intensity inhomogeneity correction

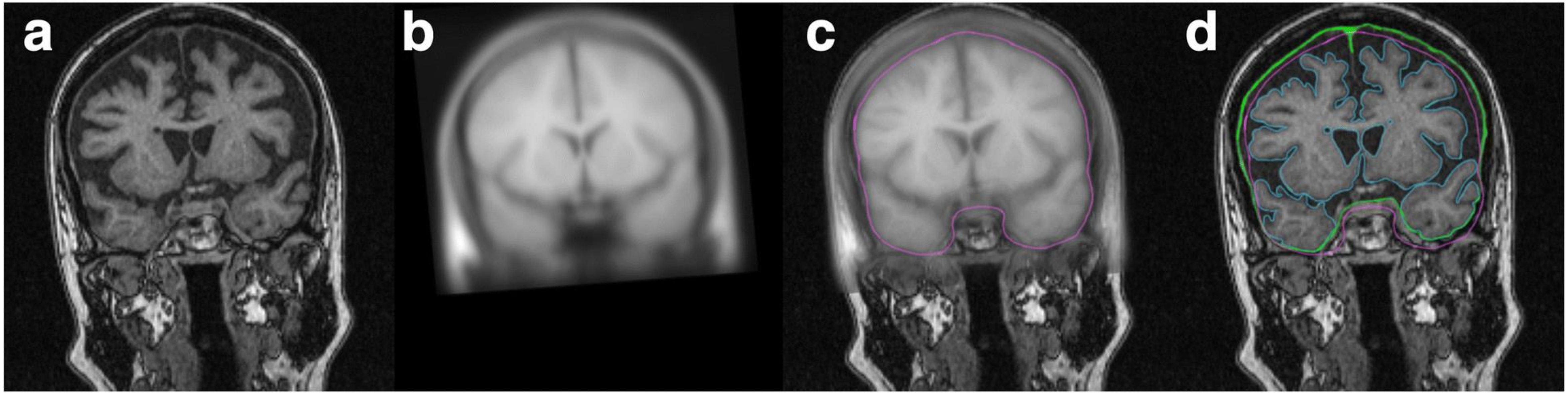
- Magnetic field is not completely uniform which can lead to darkening or brightening of the image
- Intensity inhomogeneity can be corrected to improve gray and white matter contrast



Sled, 1998, *IEE TMI*

Brain extraction

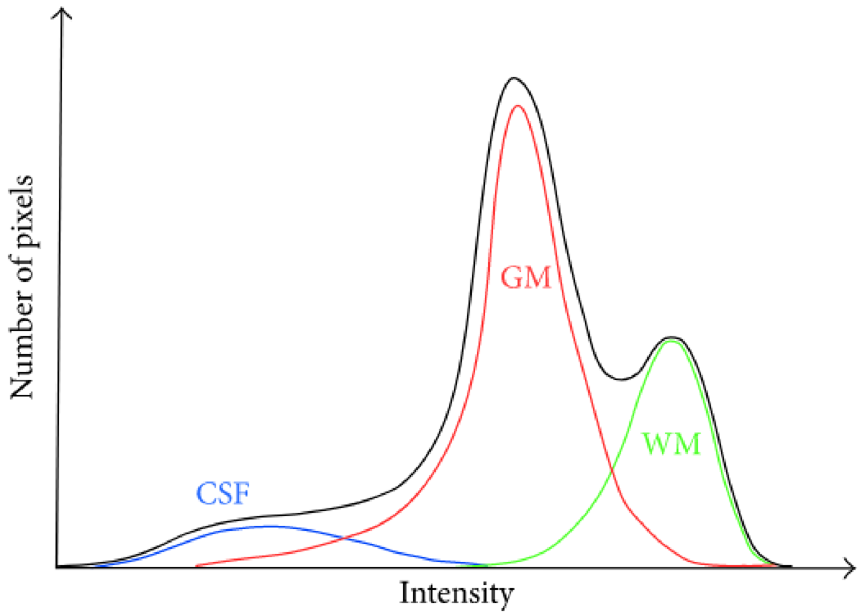
- Extract brain and remove non-brain tissue by matching image to a template space
- Brains with atrophy may require extra attention



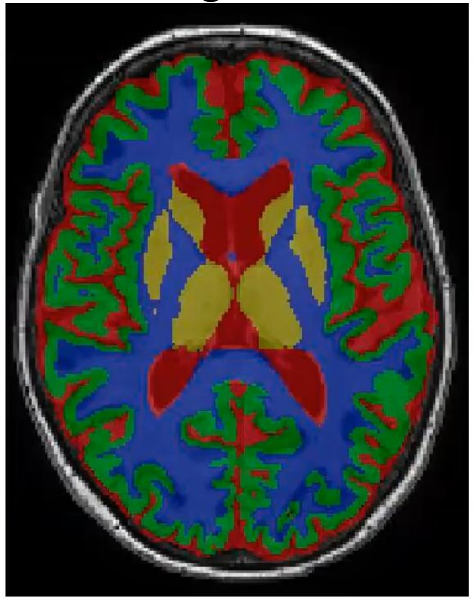
Klasson, 2018, *Euro Rad Exp*

Tissue segmentation

- Map brain to a template and segment tissue using probabilities of different tissue types based on signal intensity



Full segmentation



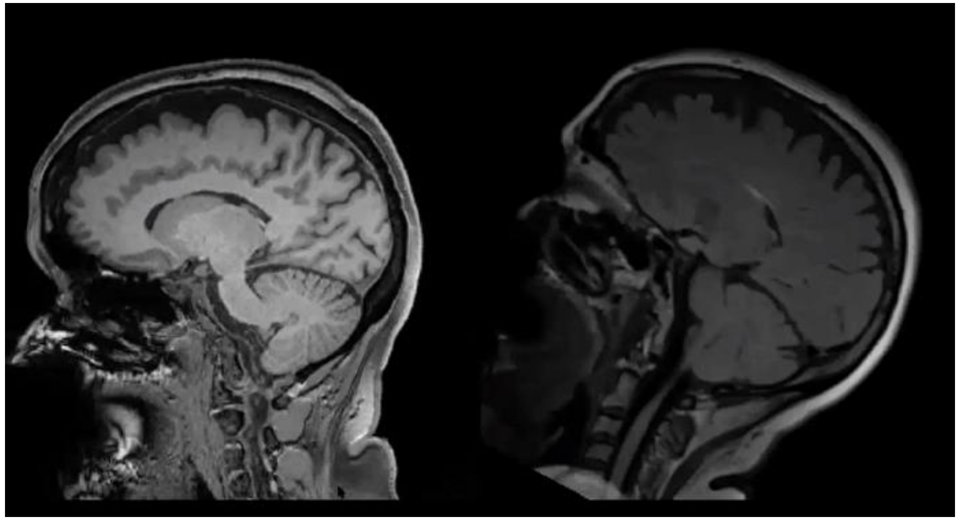
White matter

Gray matter

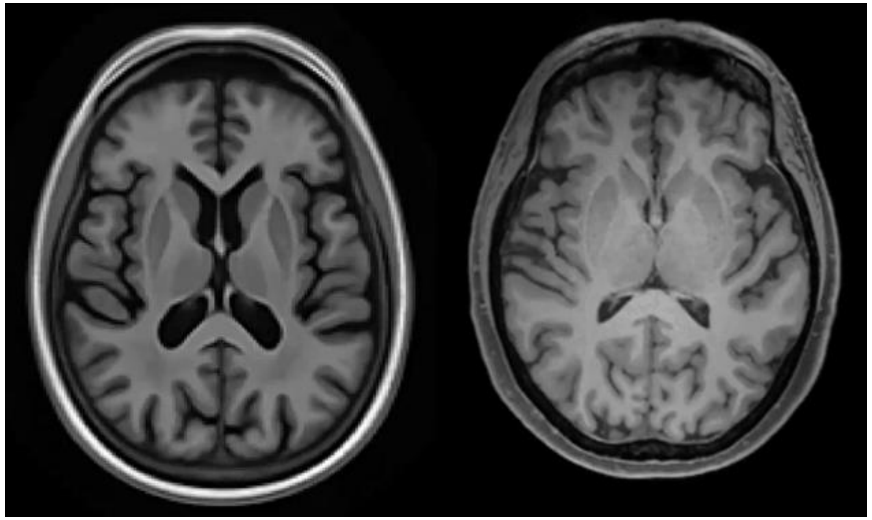
Registration

- Rigid (linear) registration
  - Within participant, between scans
  - Translates and rotates brain X, Y, Z translations and rotations
- Affine (non-linear) registration
  - Participant to a template
  - Reshapes, translates, and rotates brain to match template

Rigid registration T2w → T1w

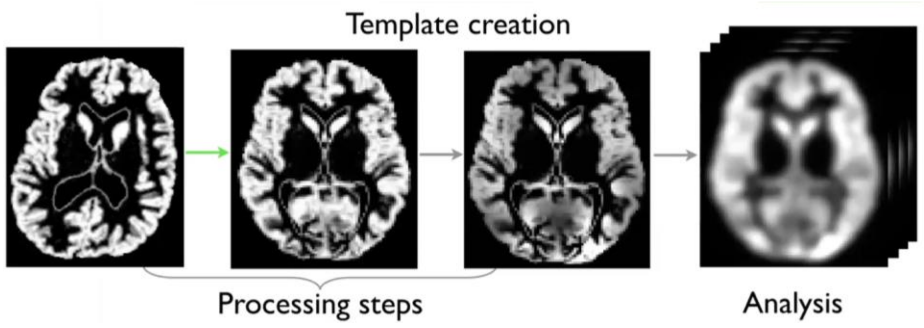


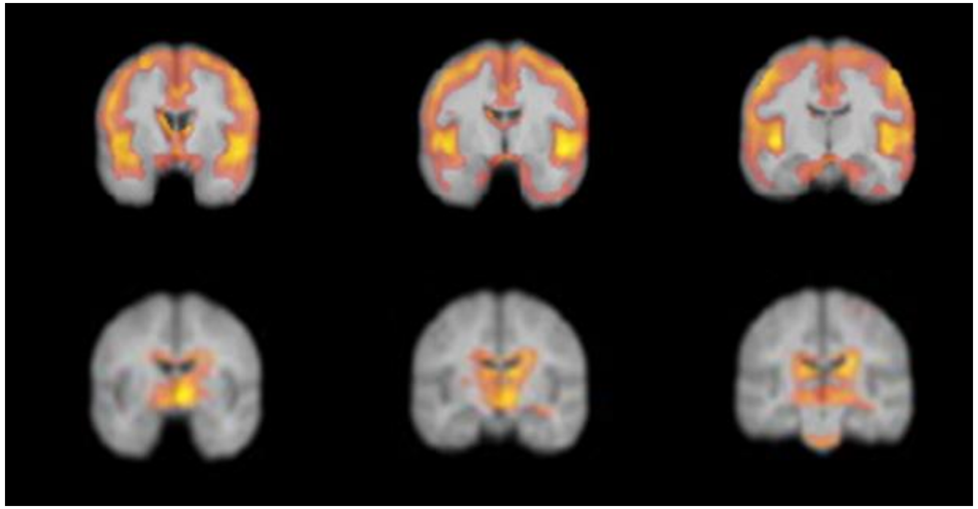
Affine registration T1w → MNI template



Voxel-based morphometry (VBM)

- Whole brain analysis of tissue density based on segmentation and registration
- Pros:
  - Easy to implement
- Cons:
  - Poor registration will affect results
  - Individual (or systematic) differences in neuroanatomy will affect results

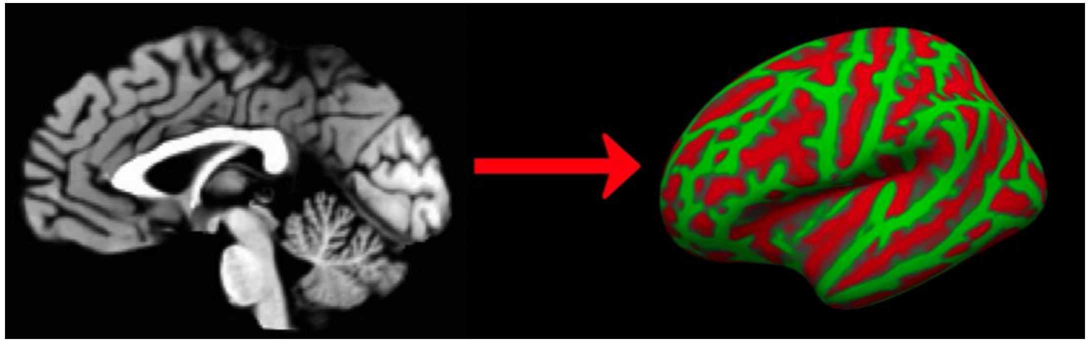


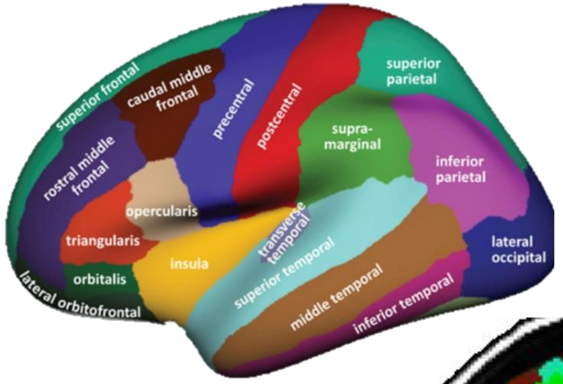


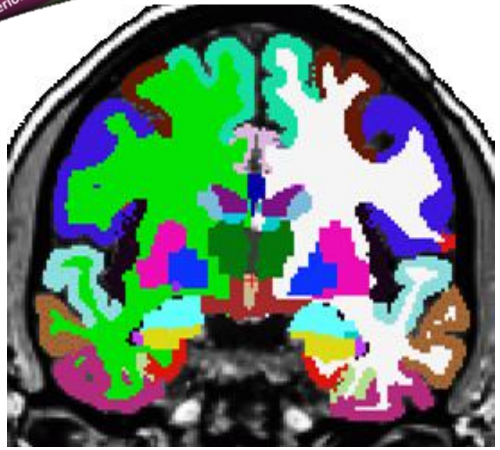
Kennedy, 2009, *Neurobio Aging*

FreeSurfer for volumetric and thickness measures

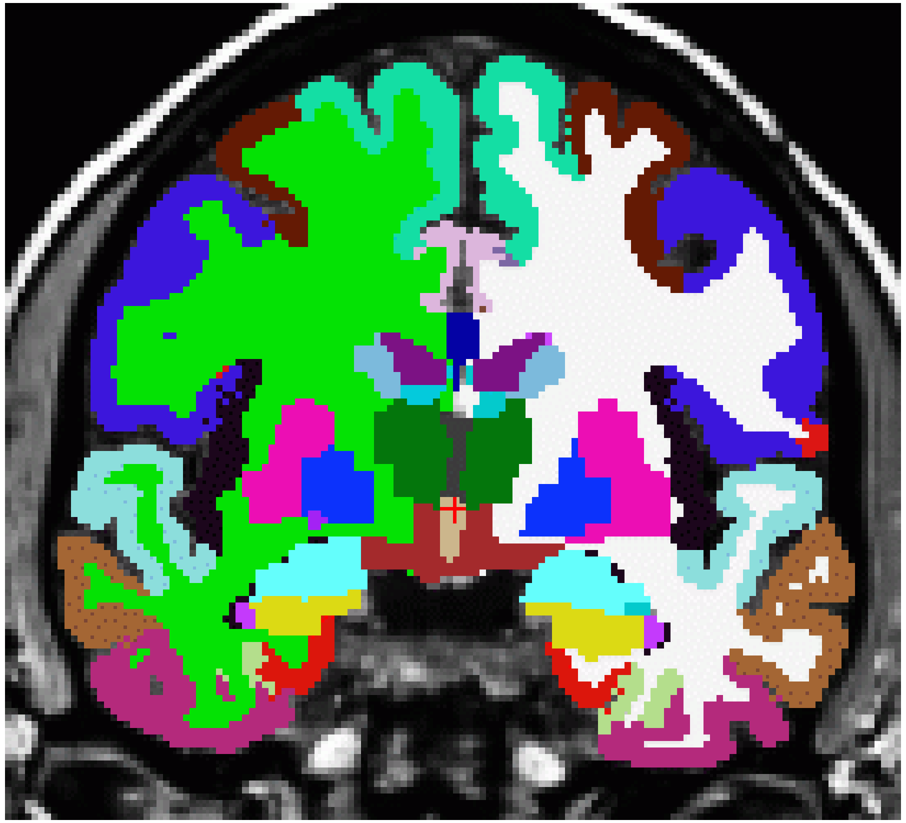
- Automated pipeline to reconstruct and label the cortical surface and subcortical volumes
- FreeSurfer can provide:
  - Participant-specific anatomical labeling
  - Regional and whole-brain estimates of thickness and folding patterns
  - Subcortical estimates of structure volumes
  - Hippocampal subfield segmentation
  - Multimodal (diffusion and functional MRI) processing and integration



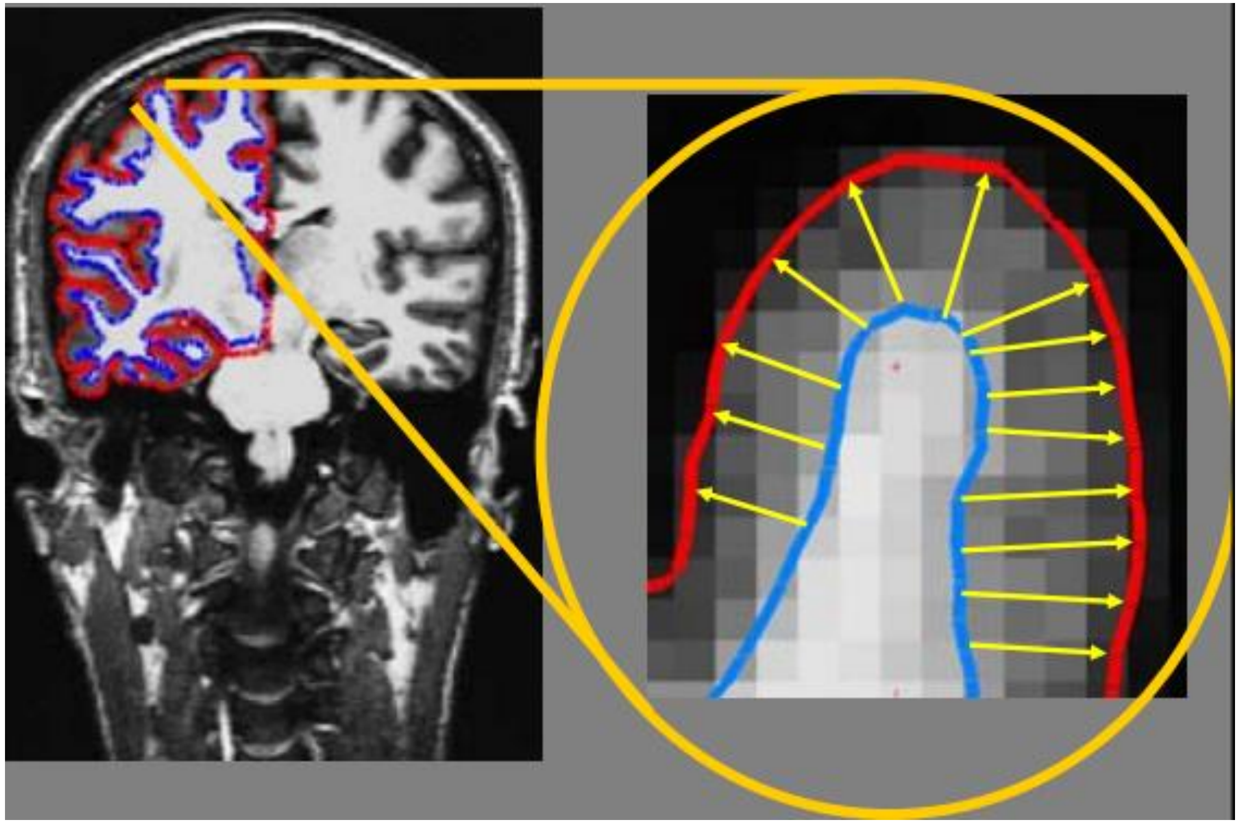




FreeSurfer outputs

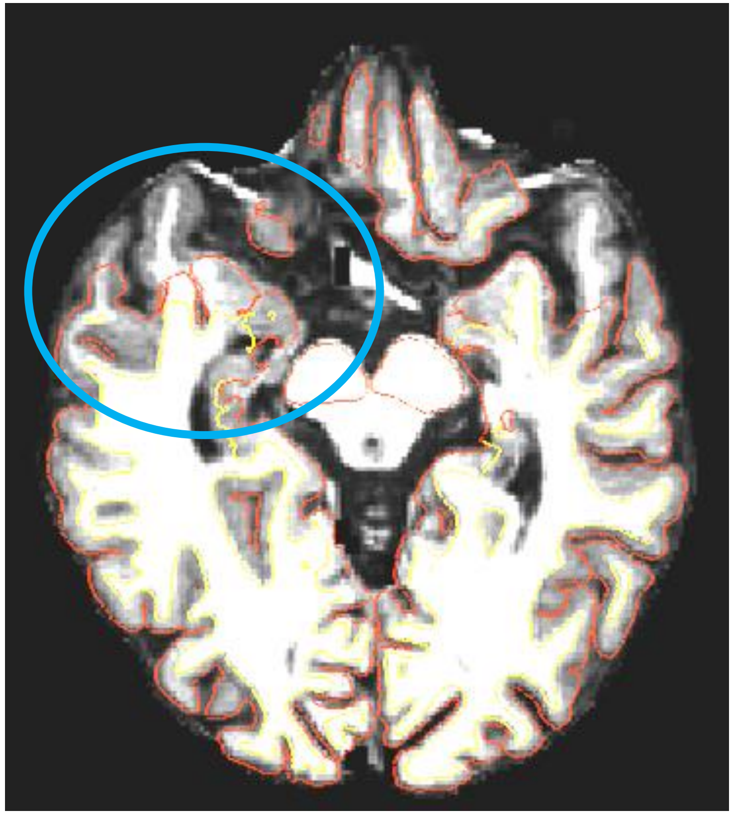


Estimates of subcortical volumes and cortical thickness, surface area, and volume (based on atlas)

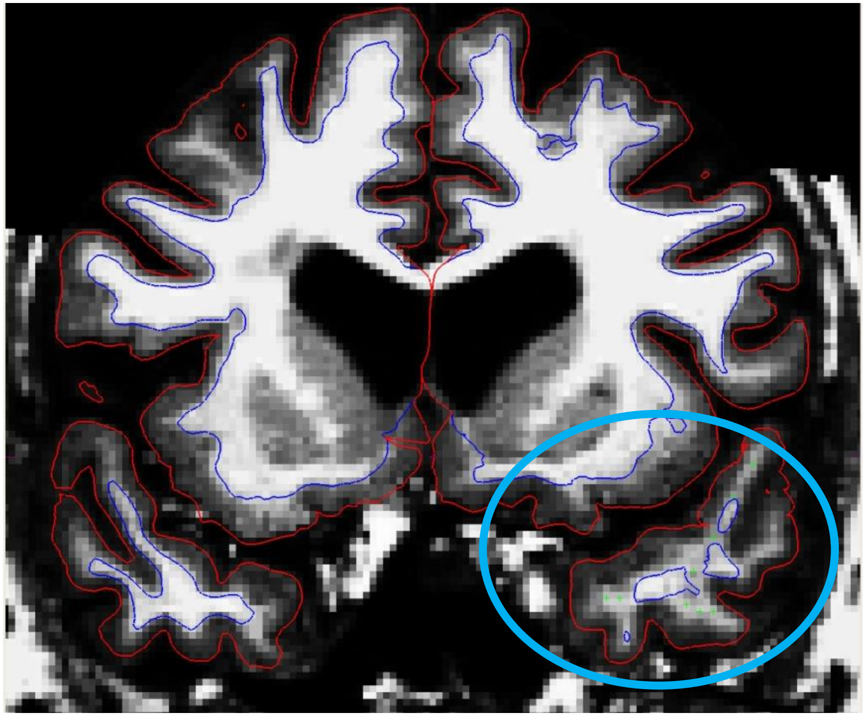


Whole brain cortical thickness, surface area, and volume (at the vertex level)

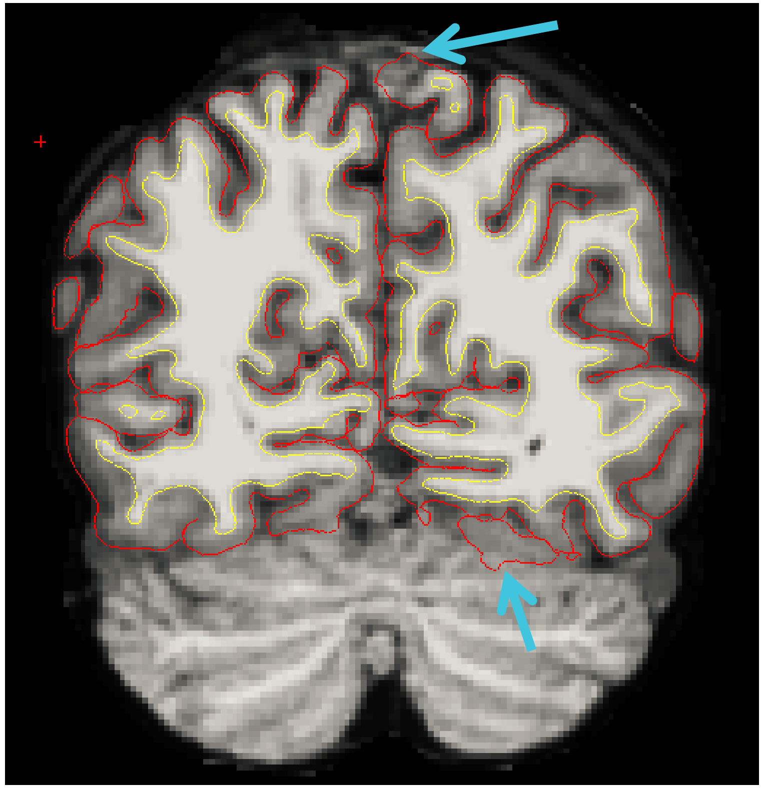
FreeSurfer may still require manual intervention



Gray and white matter excluded in temporal pole



White matter boundary does not extend far enough

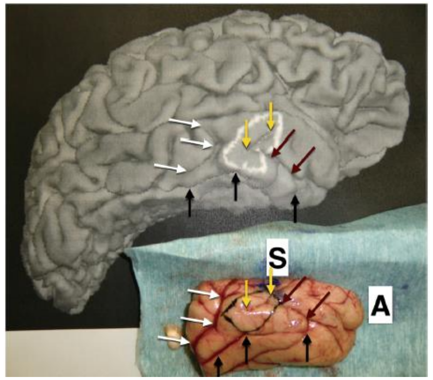


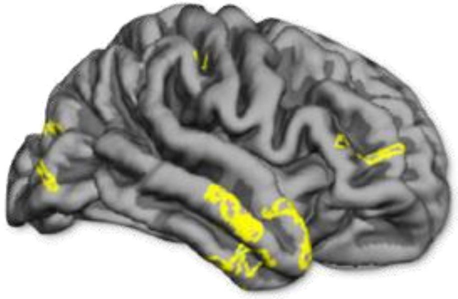
Non-brain tissue (pia) included in gray matter boundary

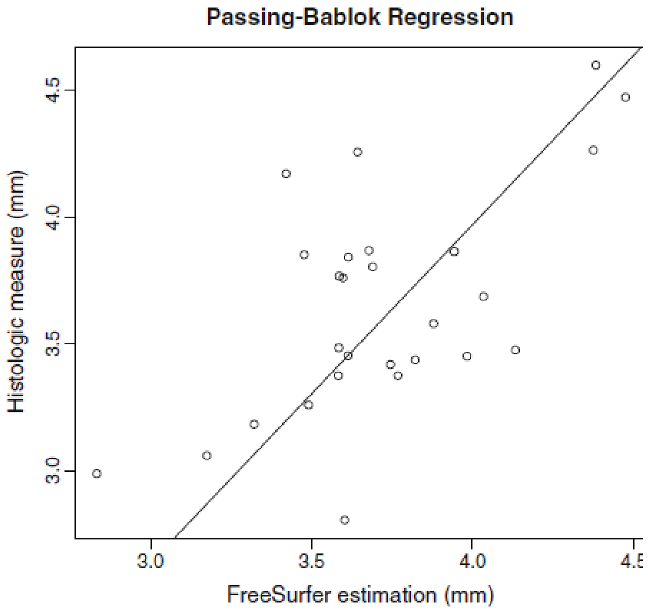
Control point, white matter, and pial surface edits can fix these issues!

Applications of FreeSurfer

FreeSurfer estimates map on to histological measurements

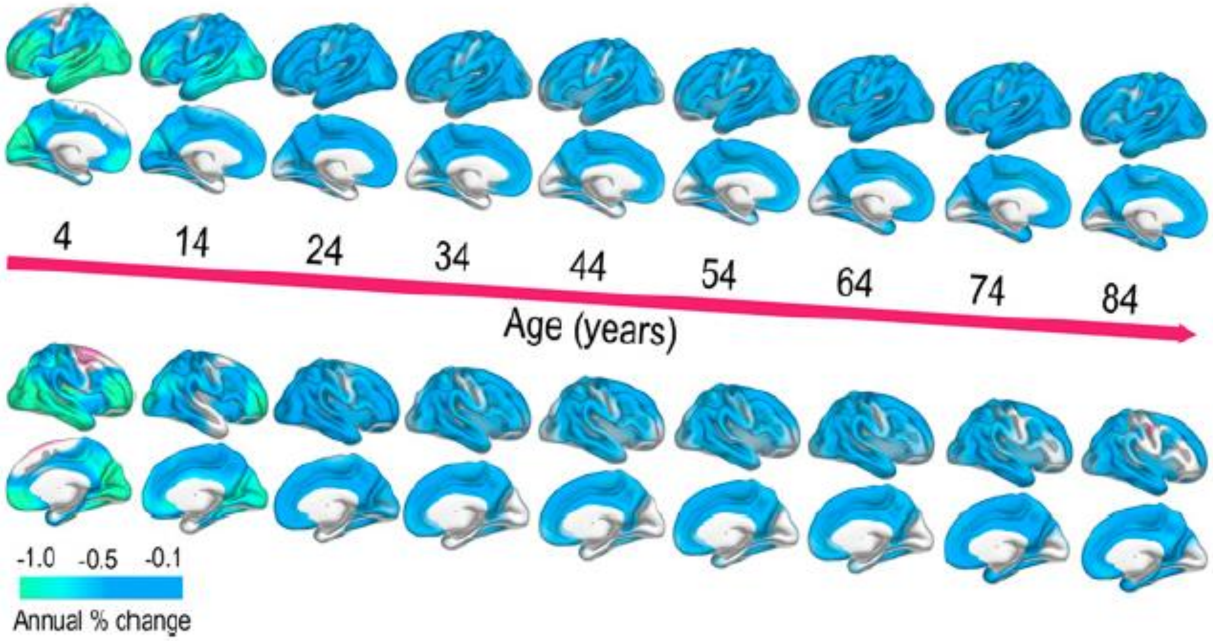






Cardinale, 2014, *NeuroInform*

Tracking longitudinal changes in cortical thickness across the lifespan

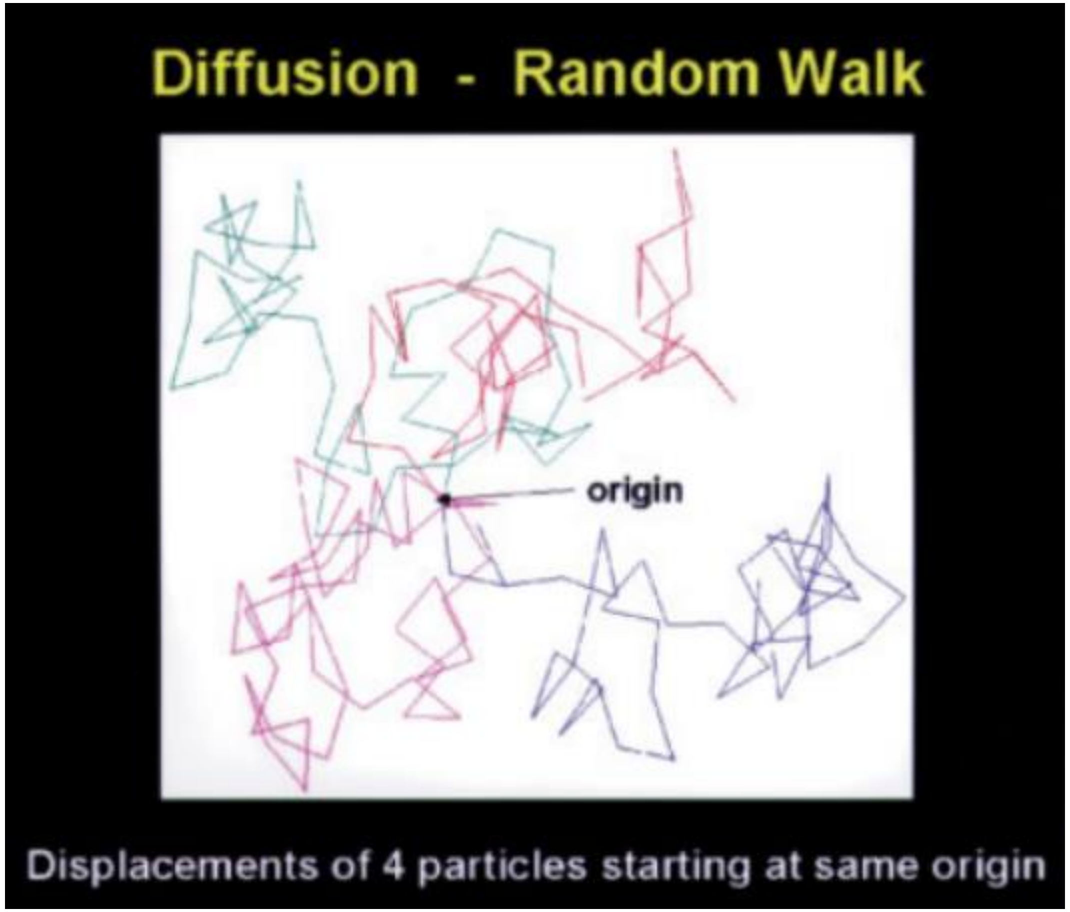


Fjell, 2015, *PNAS*

Diffusion-weighted imaging

What is diffusion?

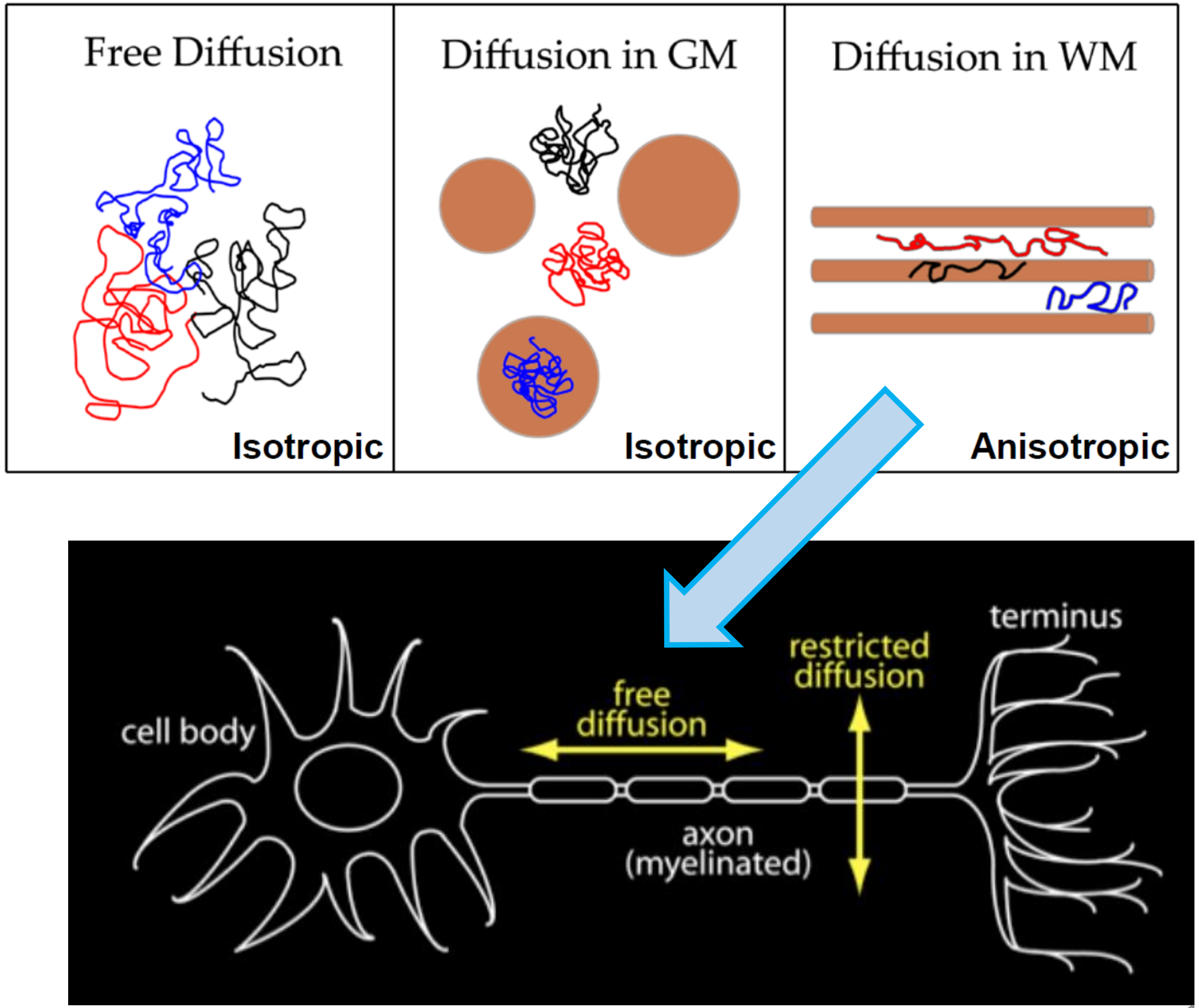
- Thermally-driven random motion of water molecules in the brain
- Greater displacement of water molecules over time indicates higher diffusion
- In the brain, water diffusion tells us about local microstructure of underlying tissue



Beauilieu, 2002, *NMR Biomed*

Diffusion in the brain

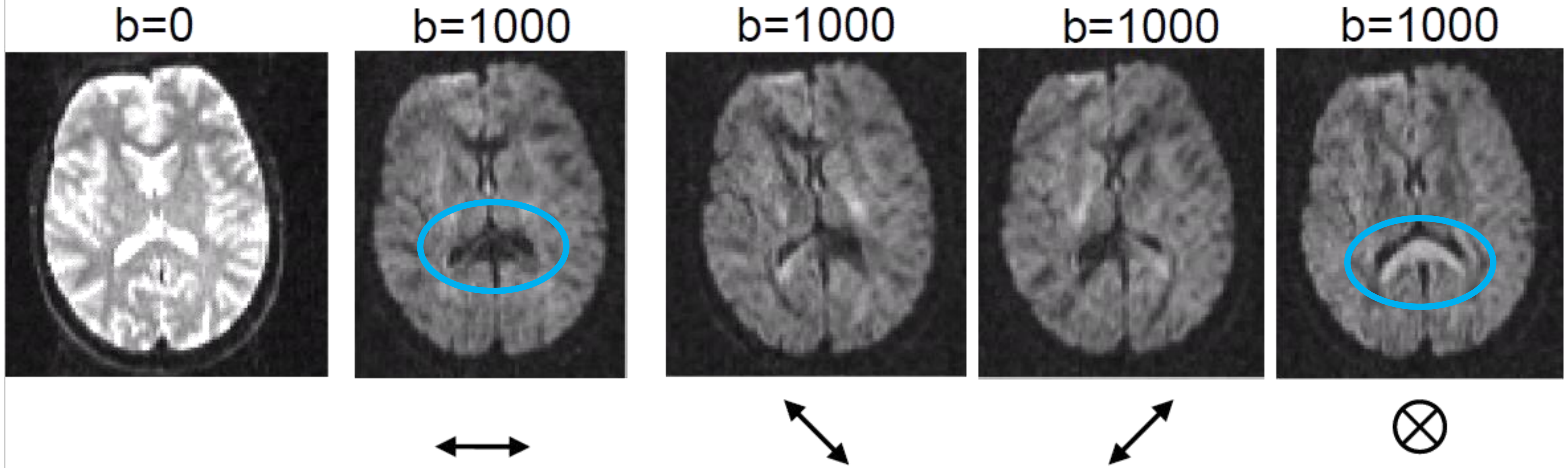
- Isotropic diffusion describes free movement in any direction
- Anisotropic diffusion occurs when there is a preferred direction (e.g., white matter)
- Diffusion is restricted by tissue boundaries and membranes



FSL course, *DTI*

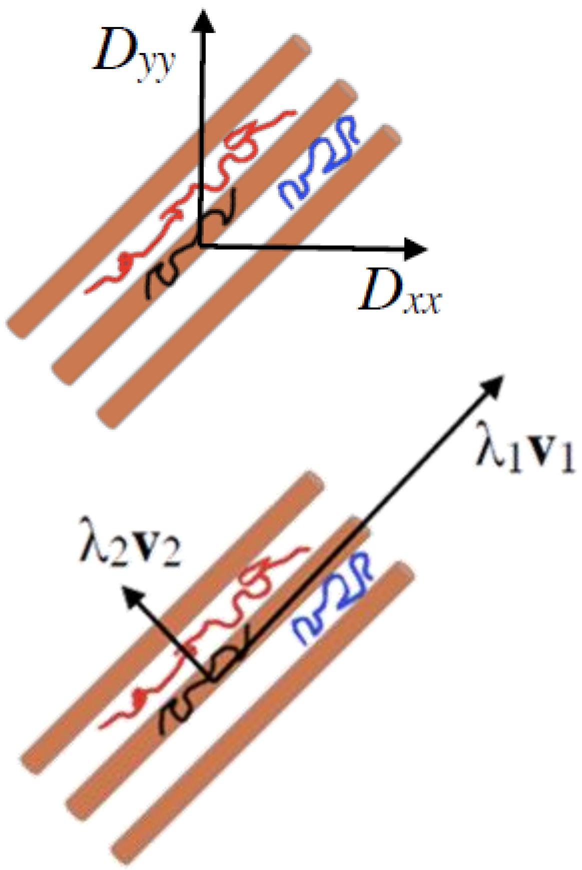
Diffusion-weighted imaging

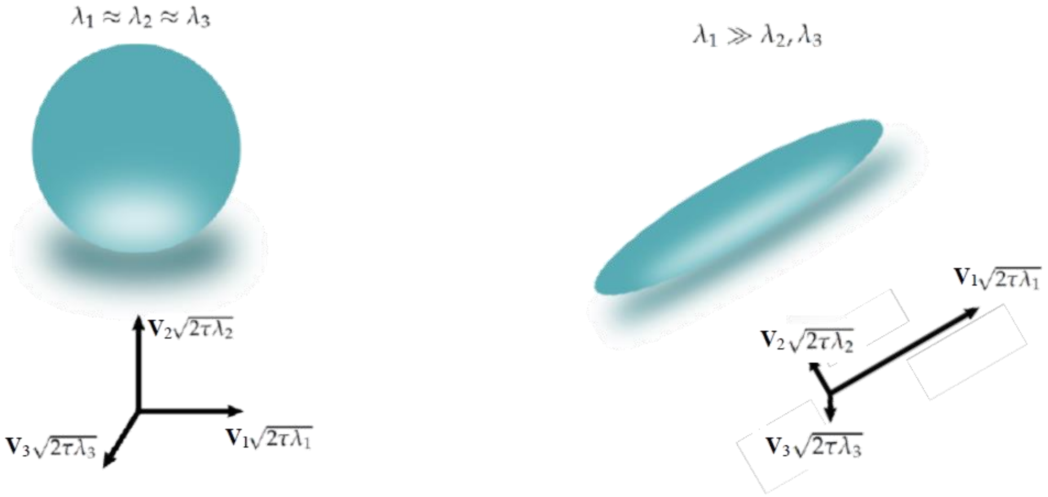
- Strong magnetic field applied along one direction (gradient) to tag stationary water molecules
- If molecules diffuse along that direction, signal attenuation will occur relative to baseline (b0)
- Minimum of 6 directions, 30-60 typical



Diffusion-tensor imaging

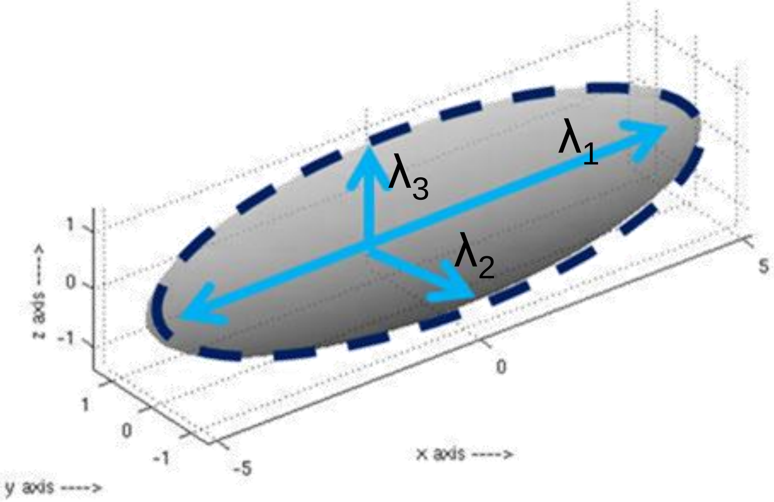
- Tensor modeling takes into account diffusion in all directions to determine amount of diffusion a 3D space (X Y Z)
- Eigen decomposition of the tensor provides the principal diffusion direction
- Assumption: principal direction of diffusion is fiber orientation



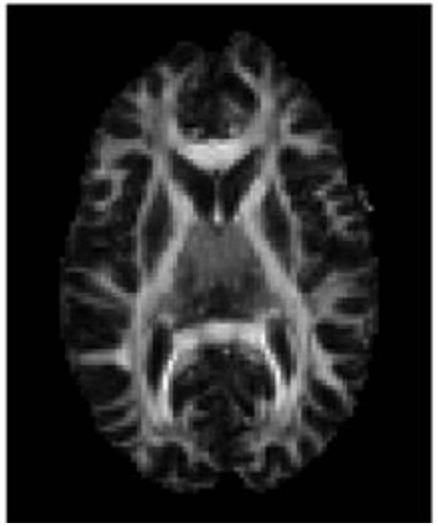


Quantifying diffusion

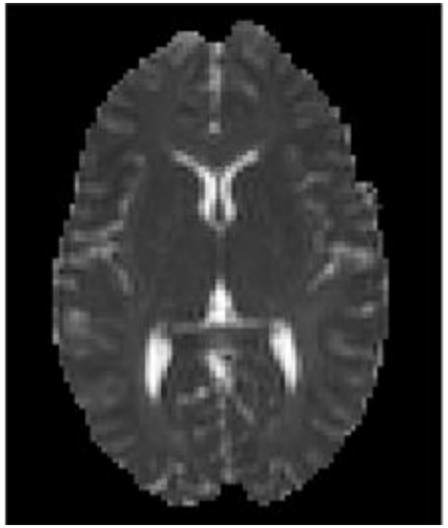
- Fractional anisotropy (FA)
  - Normalized eigenvalue variance (shape of diffusivity)
- Mean diffusivity (MD)
  - Mean of eigenvalues
- Axial diffusivity (AD)
  - First eigen value (diffusion in primary direction)
- Radial diffusivity (RD)
  - Mean of 2nd and 3rd eigenvalue (diffusion in perpendicular direction



FA map

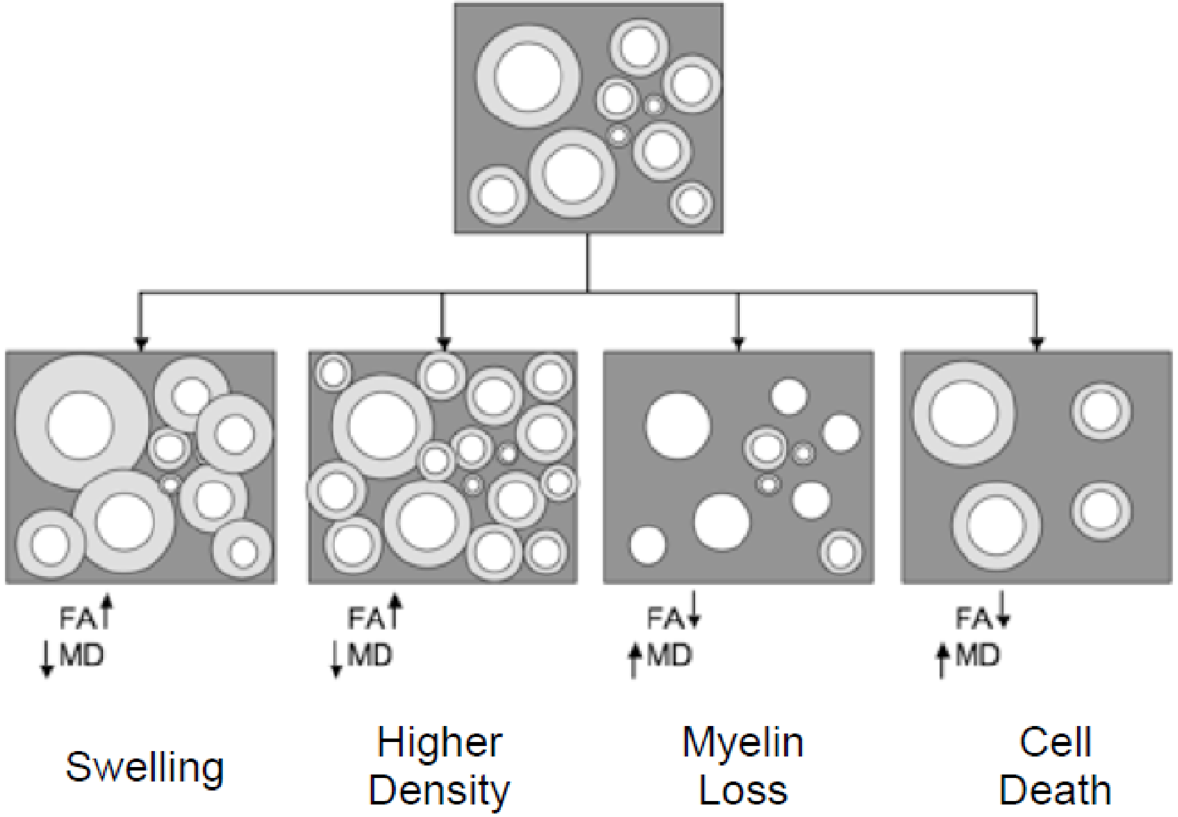


MD map



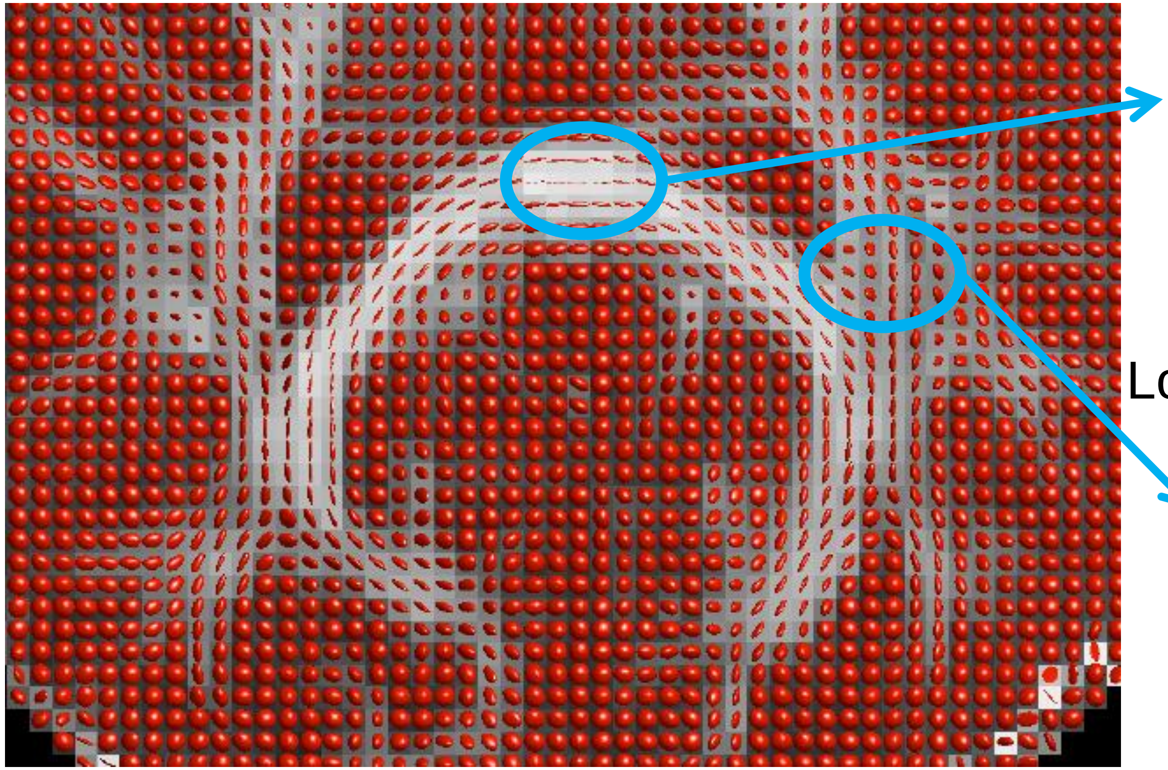
But be careful not to overinterpret

- Diffusivity measures are indirect
- Increases or decreases in FA and MD could have multiple causes
- In aging, decreased FA and increased MD in white matter generally interpreted as de-myelination



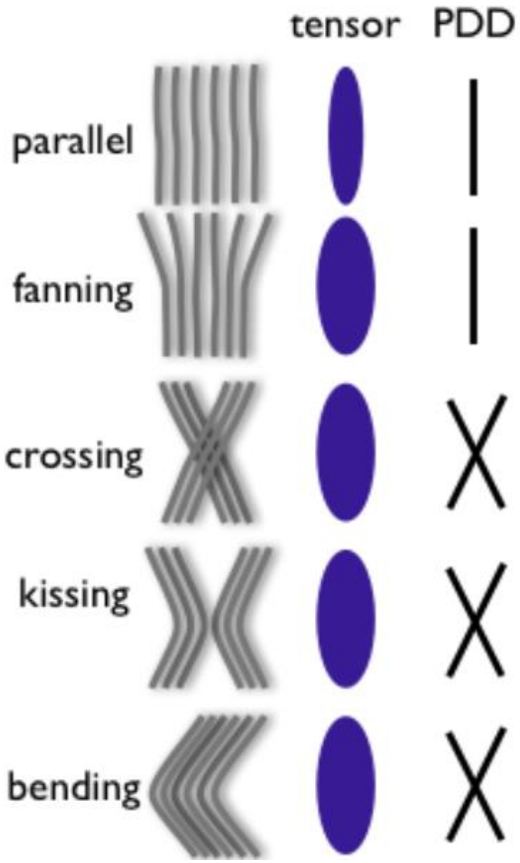
FSL course, *DTI*

Limitation: resolving crossing fibers



High anisotropy in corpus callosum fibers

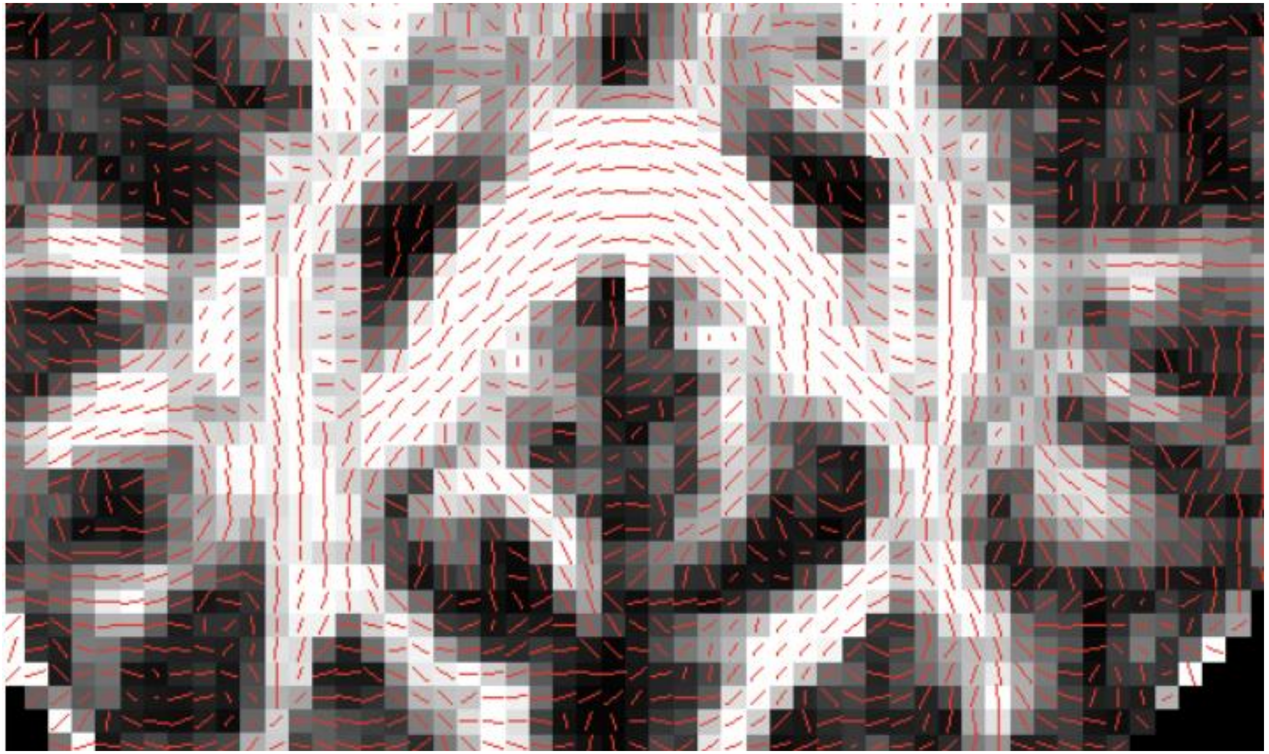
Low anisotropy in regions with crossing fibers



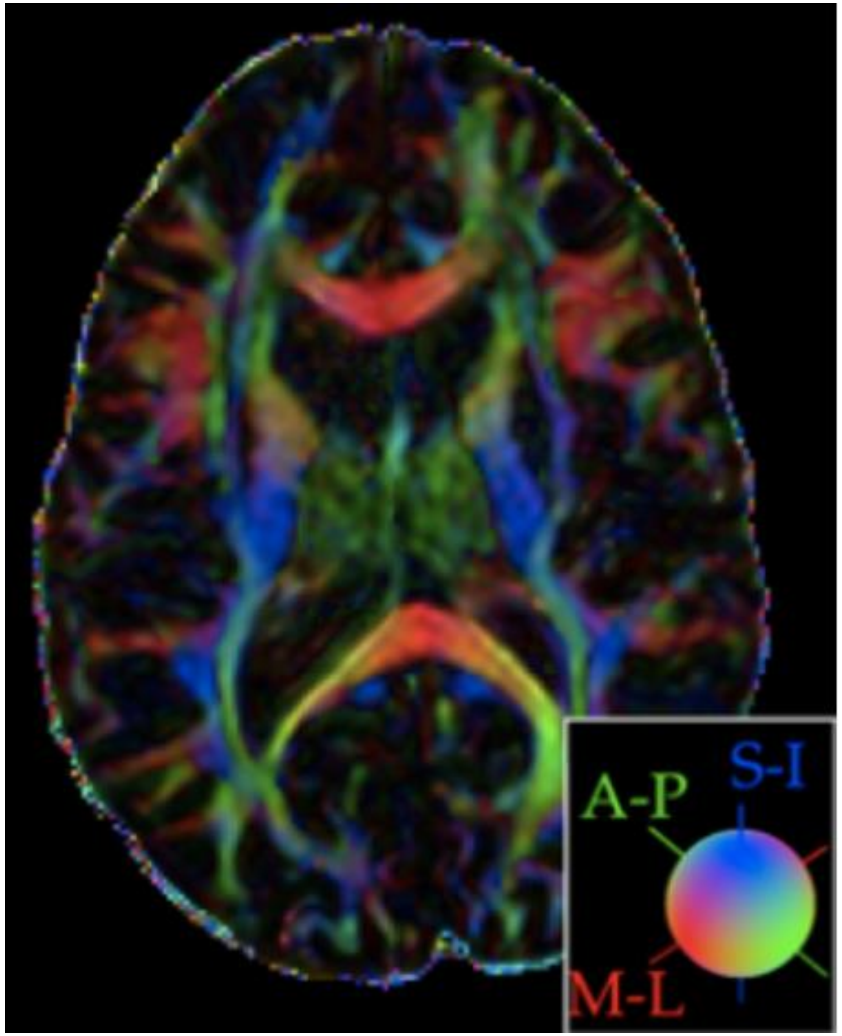
When differently oriented fibers cross, there are multiple directions of diffusion which results in lower anisotropic diffusion

Visualizing diffusion

Primary diffusion vectors (axial diffusivity, λ_1)

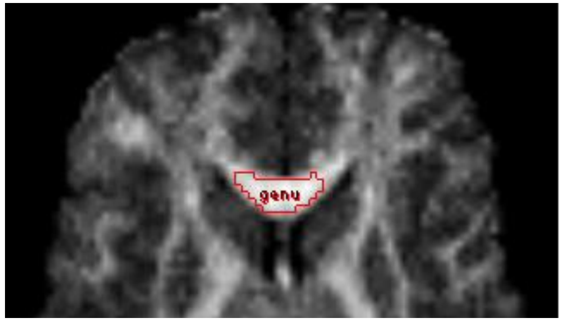


Color based on primary diffusion direction

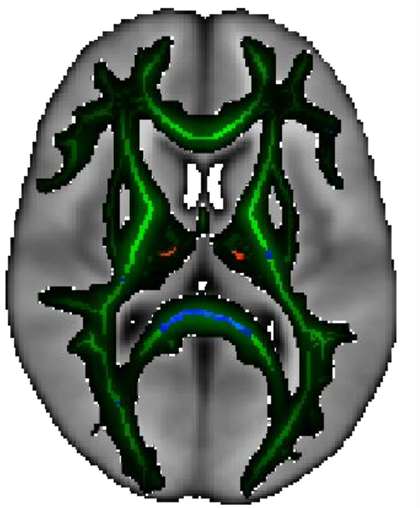


Approaches to analyzing diffusion data

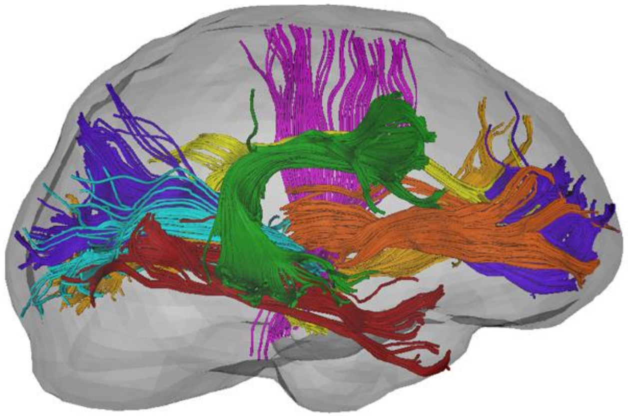
- Region of interest analysis
  - Examine diffusivity in specific regions



- Tract-based spatial statistics
  - Examine diffusivity across all white matter voxels in the brain

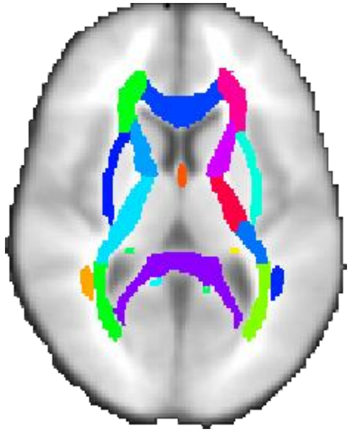


- Tractography
  - Use fiber orientation to reconstruct fiber bundles connecting regions of interest



Region of interest analysis

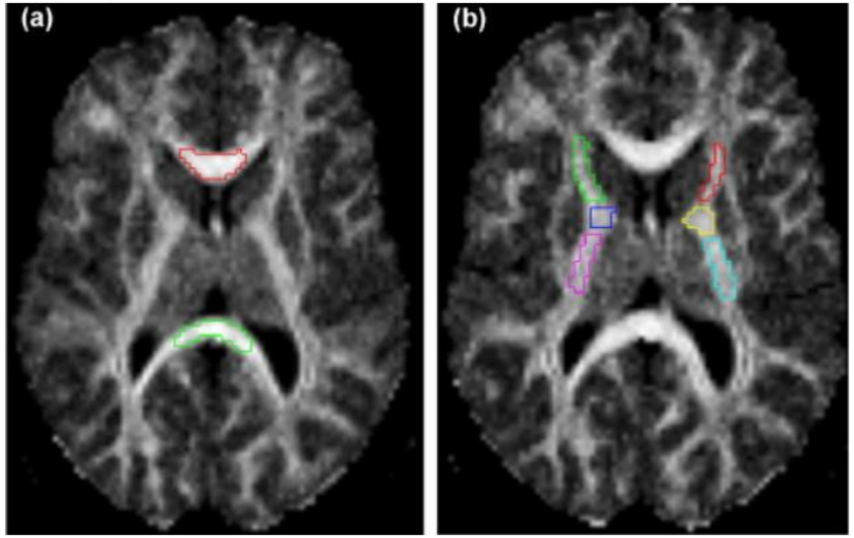
- Manual (or atlas-based) approach to define specific regions of interest on diffusivity maps
- Pros:
  - Precisely isolate anatomical region ("gold standard")
- Cons
  - Manual methods are time and labor intensive
  - User bias depending on which brain map used for hand-drawn
  - Poor registration to standard space for atlas-based ROIs



JHU white matter atlas

Hand-drawn ROIs

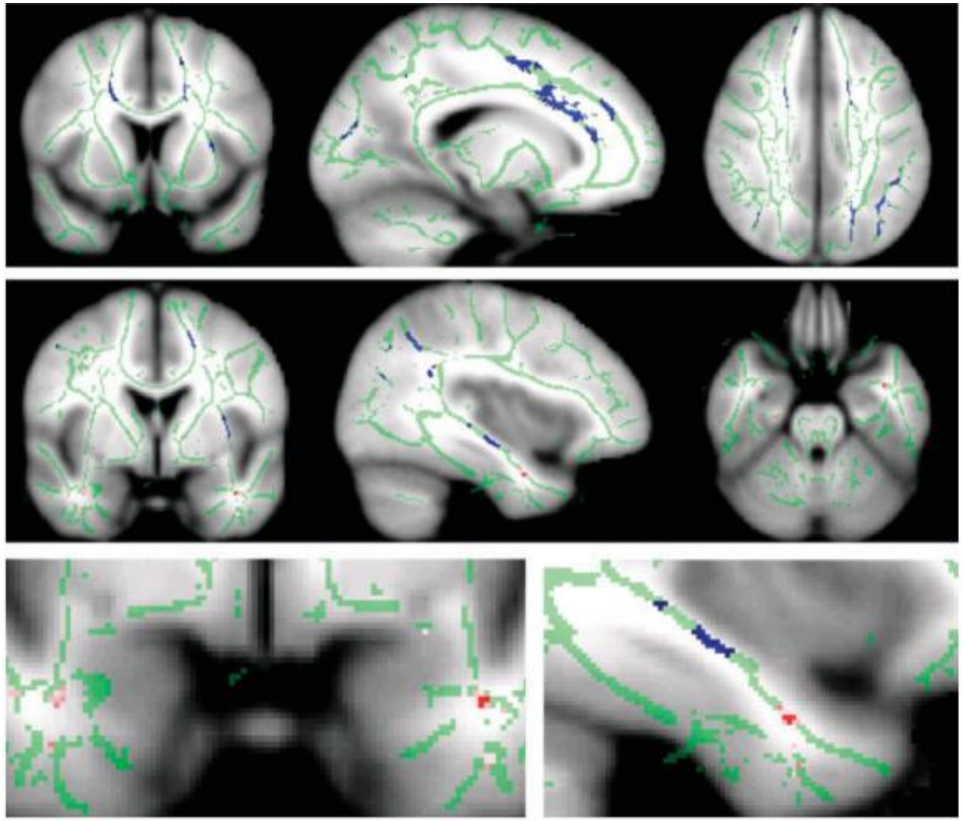
Corpus callosum Internal capsule



Kennedy & Raz, 2009, *Neuropsychologia*

Tract-based spatial statistics (TBSS)

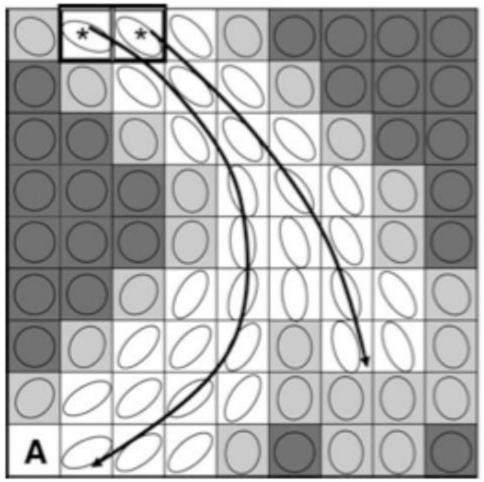
- Register diffusion to a common space and derive a whole brain “skeleton”
- Pros:
  - Fully automated and quick
  - No *a priori* region of interest needed
- Cons:
  - Alignment of diffusion maps across participants is difficult
  - Limited to white matter “skeleton”

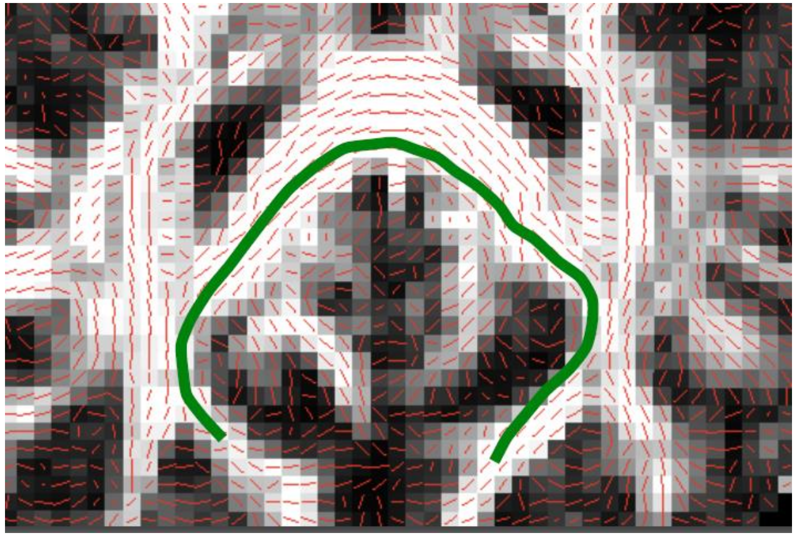


Damoiseaux, 2009, *Human Brain Mapp*

Tractography

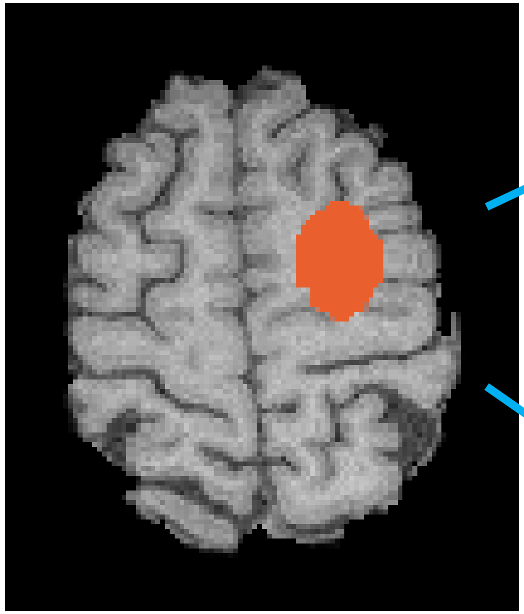
- Estimates trajectory of fiber tracts based on direction of diffusion to reconstruct white matter bundles
- Pros:
  - Examine specific regional connections
  - Can be computed in native diffusion space
  - Can apply “connectomics” approaches
- Cons:
  - Requires *a priori* region definition
  - Limited to major bundles
  - Computationally intense

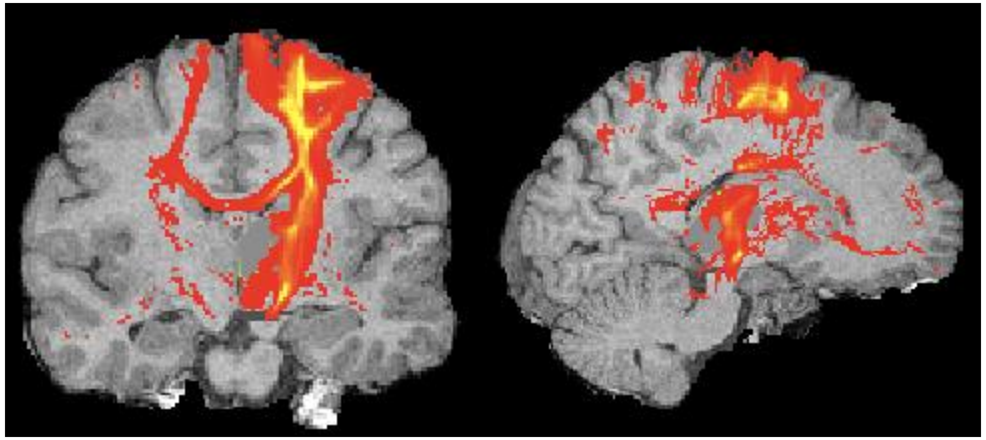




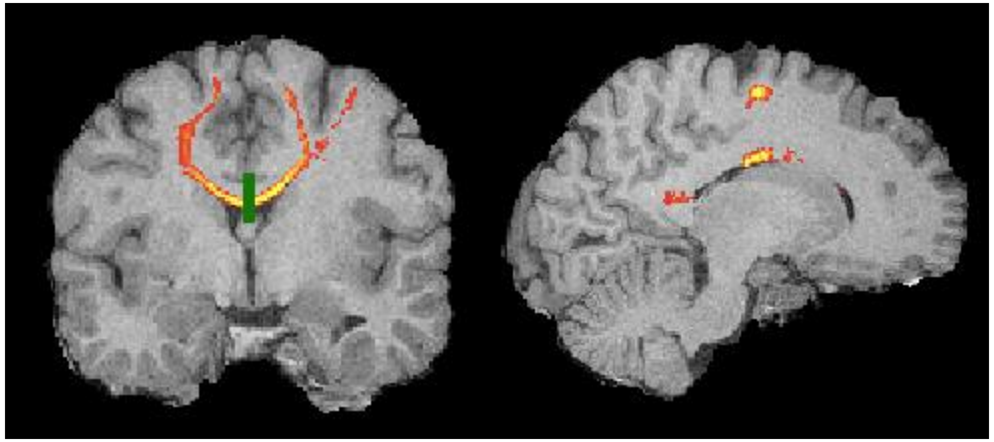
Tracking white matter bundles

Seed: dorsal primary motor cortex (dPMC)





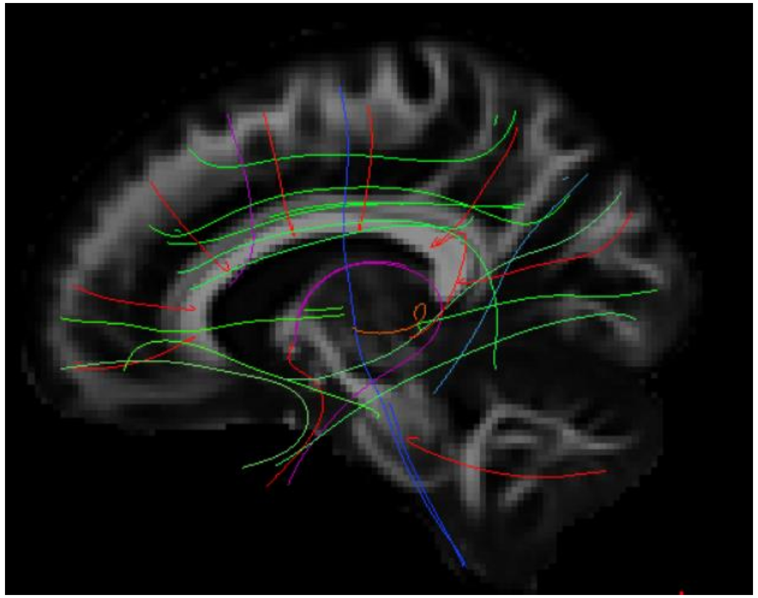
All white matter fibers connected to seed



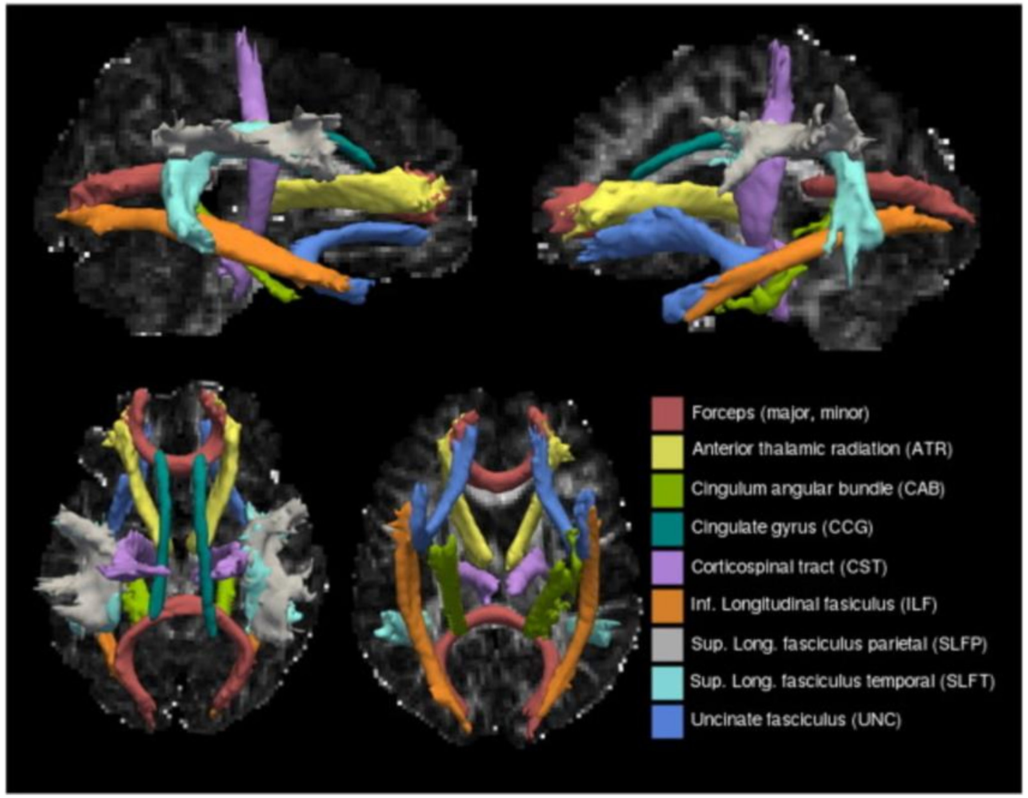
White matter fibers originating in dPMC and passing through corpus callosum waypoint

TRACULA (FreeSurfer)

- Automated tract reconstruction of major bundles using cortical regions defined via FreeSurfer
- Isolates 18 (now 42!) major white matter bundles



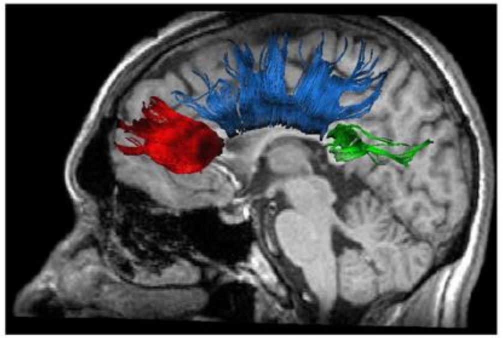
TBSS-like skeleton for regional diffusivity estimates

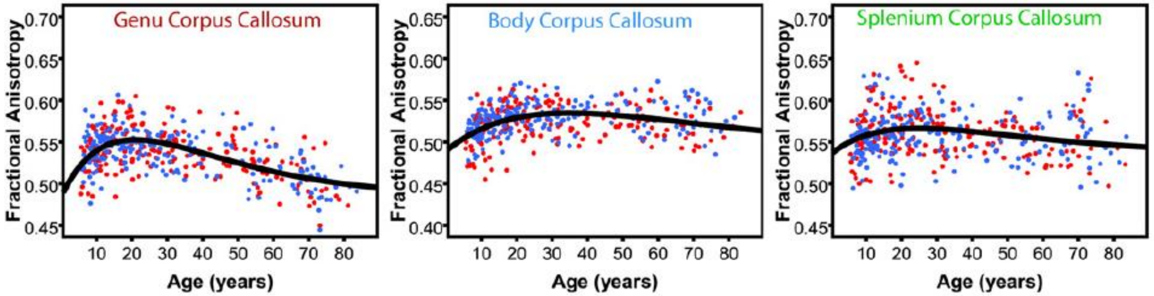


Extract diffusivity metrics (FA, MD) from whole pathway

Tractography in aging

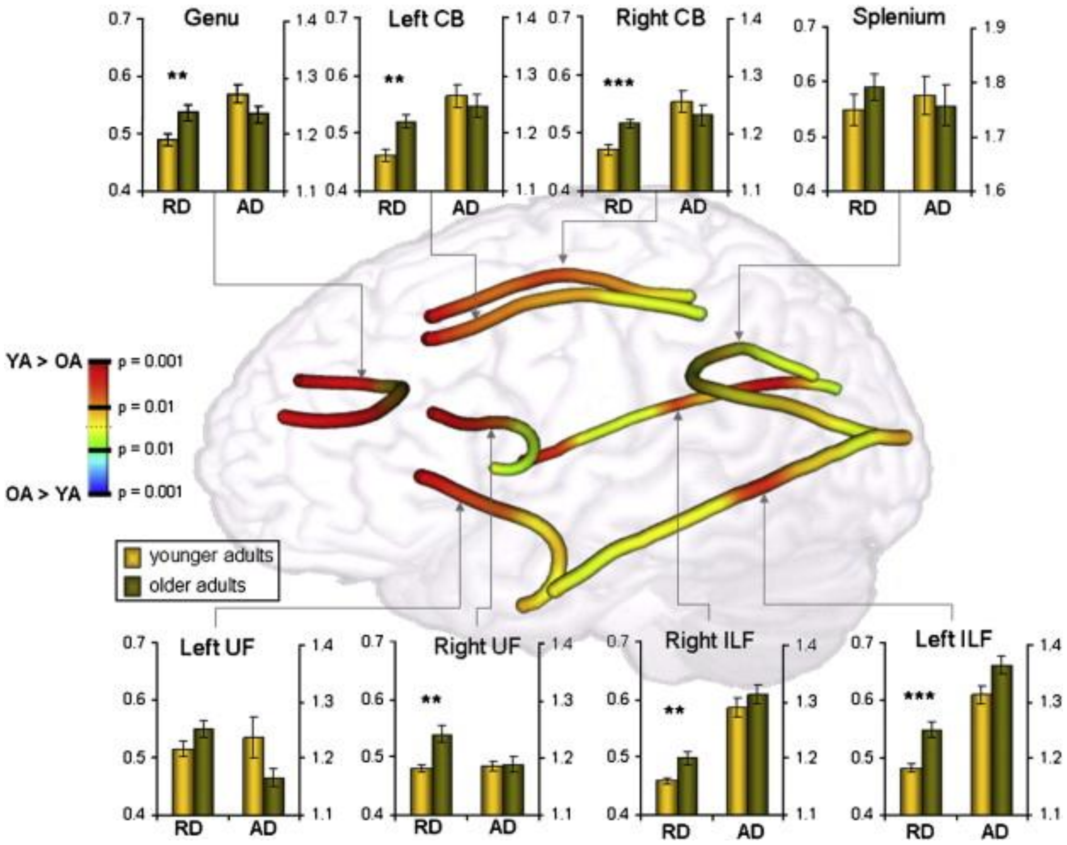
Fractional anisotropy (FA) in the corpus callosum decreases after age 20





Lebel, 2012, *NeuroImage*

Anterior portions of white matter pathways show greater age-related decreases in FA



Davis, 2009, *NeuroImage*

Open datasets with structural and diffusion MRI

- Parkinson's Progression Markers Initiative (PPMI): https://www.ppmi-info.org/
- Harvard Aging Brain study (HABS): https://habs.mgh.harvard.edu/
- Alzheimer's Disease Neuroimaging Initiative (ADNI): http://adni.loni.usc.edu/
- Human Connectome Project (HCP) – Aging: https://www.humanconnectome.org/study/hcp-lifespan-aging
- Open Access Series of Imaging Studies (OASIS)-3: https://www.oasis-brains.org
- Nathan Kline/Rockland: http://fcon_1000.projects.nitrc.org/indi/enhanced/
- Cambridge-Center for Aging and Neuroscience (Cam-CAN): https://camcan-archive.mrc-cbu.cam.ac.uk/
- UK Biobank: https://www.ukbiobank.ac.uk/
- www.openneuro.org

Resources

- FSL courses: https://open.win.ox.ac.uk/pages/fslcourse/website/
- FreeSurfer tutorials: https://surfer.nmr.mgh.harvard.edu/fswiki/Tutorials
- Alzheimer’s Association webinars for dementia and Alzheimer’s researchers: https://www.alz.org/research/for_researchers/grants/medsci-webinars/on-demand-research-webinars