Basic Operations & Processing of Neuroimages

Autumn 2023

Session 3 – 10/03/2023

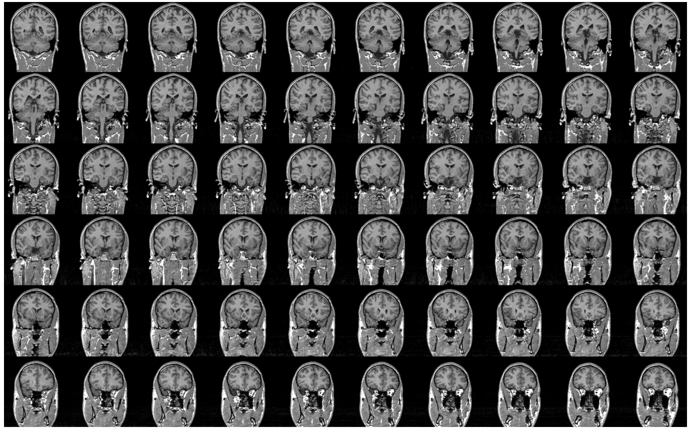
Computational Neuroscience Laboratory

Today…

- MRI Processing
- Tools for Processing

Problem

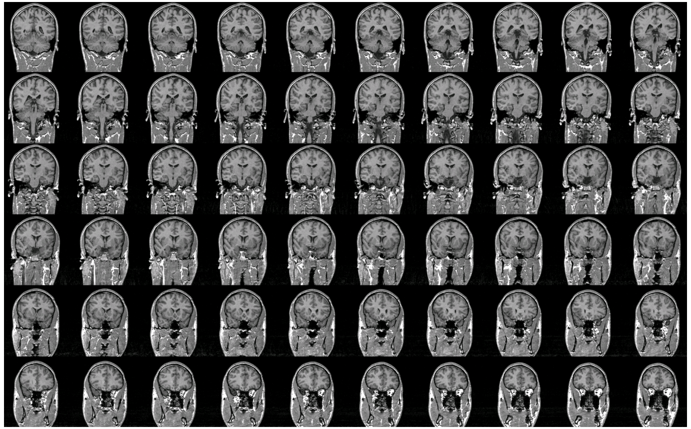
Machine learning generally requires a large number of well-curated, high-quality samples



Raw neuroimages are noisy and consist of a large number of un-labelled measurements

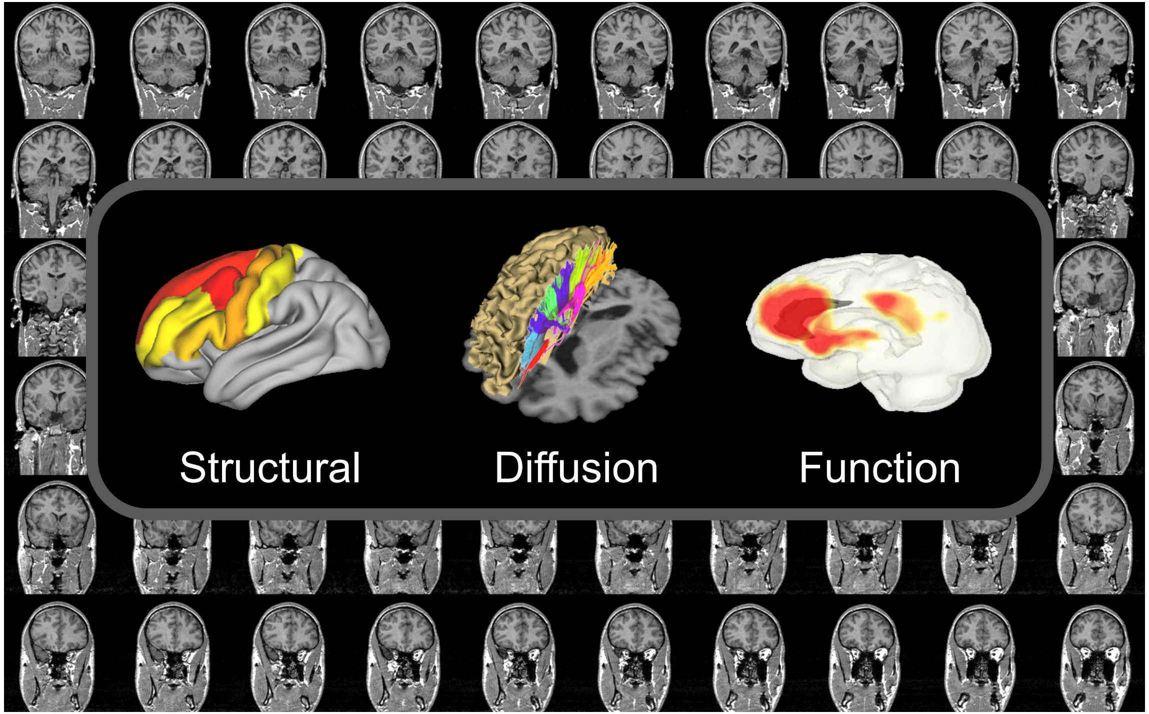
Solution

Carefully process MRI to extract meaningful measurements

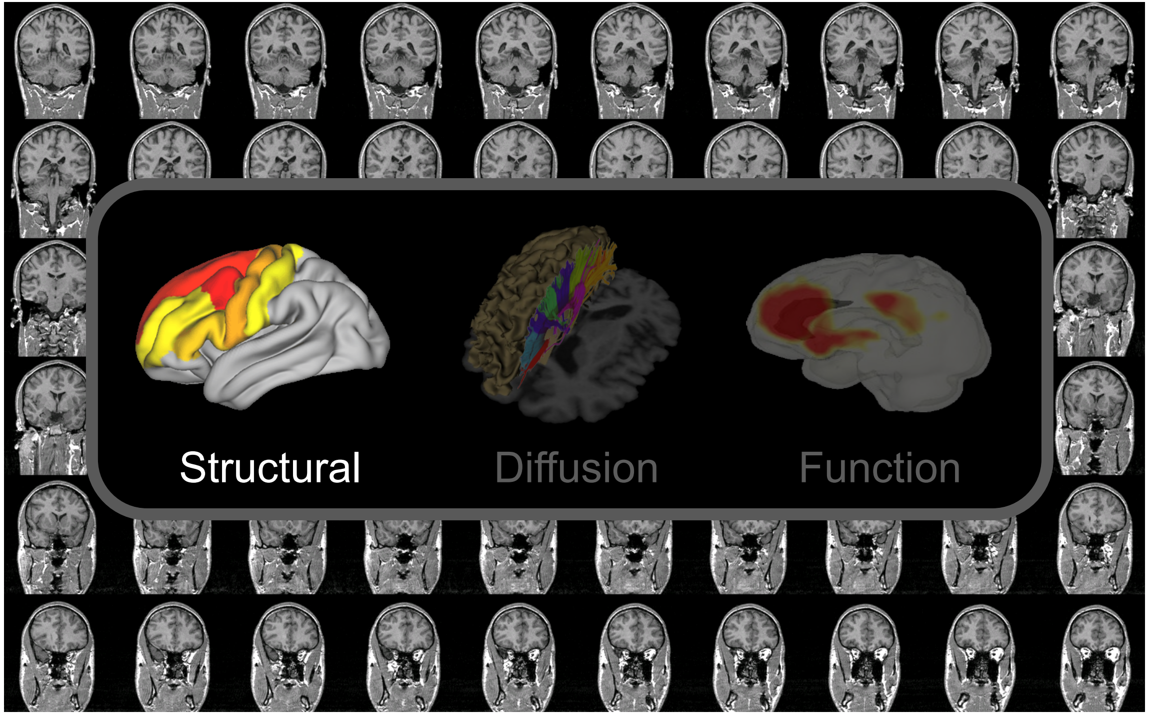


Process

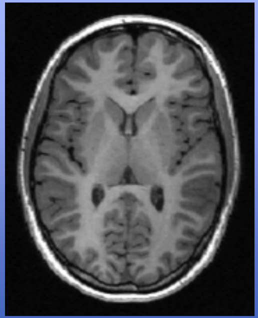
Processing by MRI Type



Processing of T1 MRI



Processing of Structural MRI



T1

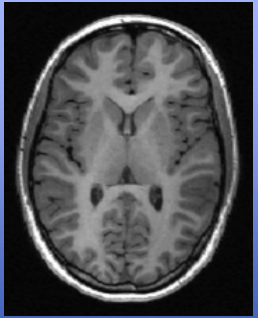
. . .

Volume of Brain Region

What to do ?

Why not perform simple thresholding ?

Why thresholding fails ?



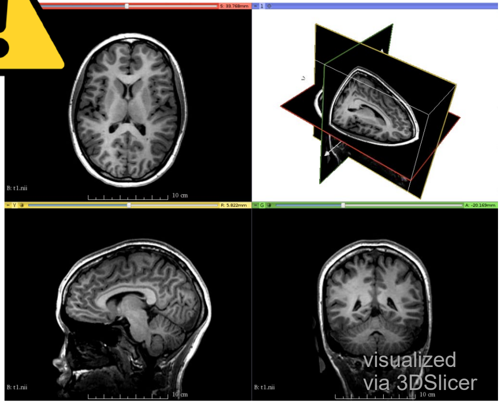
T1

. . .

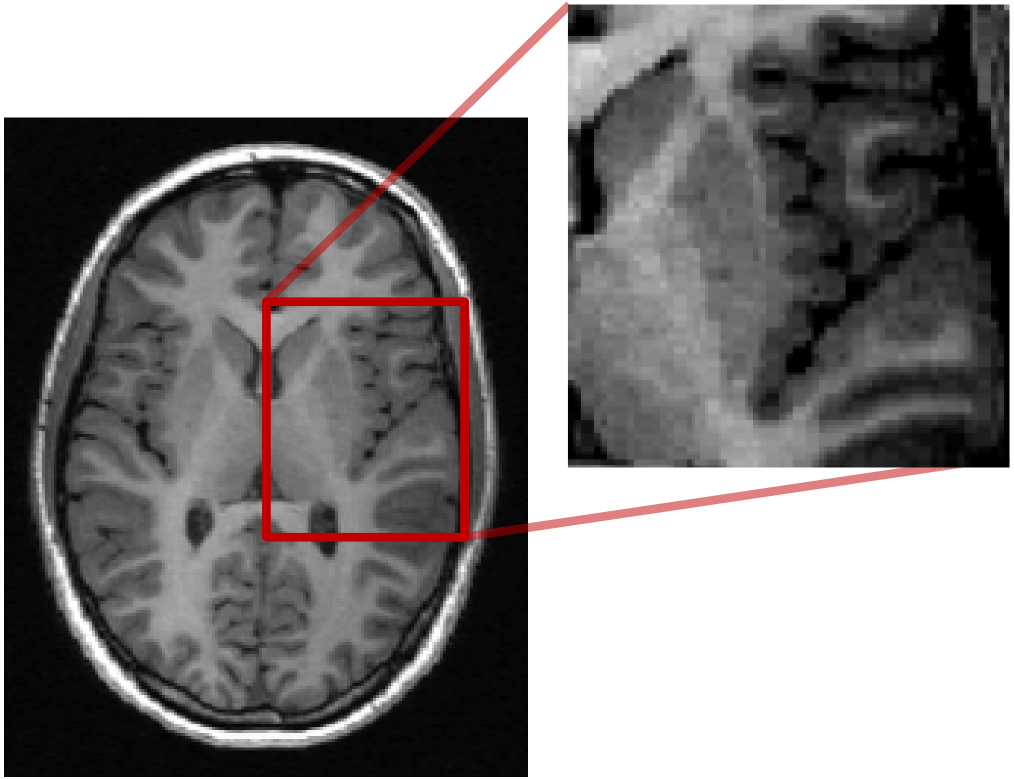
Volume
of
Brain
Region

- Noise
- Image inhomogeneity
- Intensities of structures overlap
- Intensities are relative measurements
- No clear boundaries between regions

Processing is done in 3D !

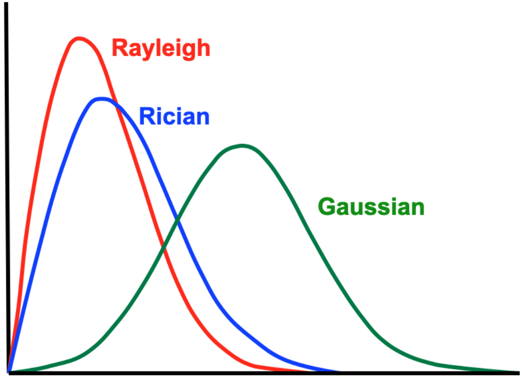


1. Problem: Noise



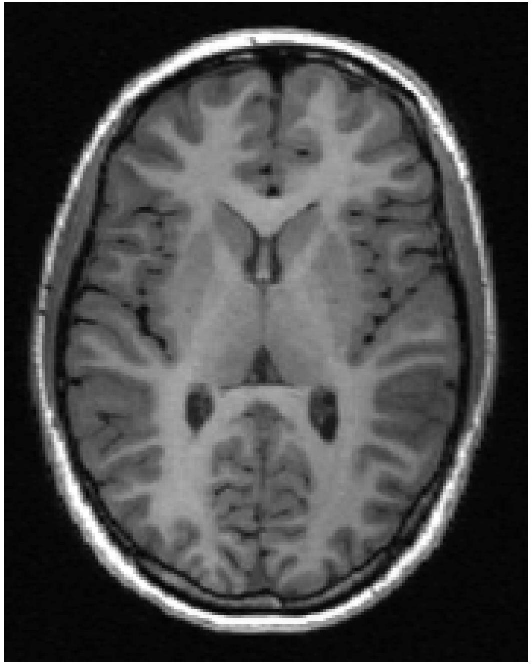
(magnitude) T1 MRI

By converting the "raw" MRI (defined in complex space with Gaussian noise) into a magnitude image, the noise becomes ***Rician*** distributed.

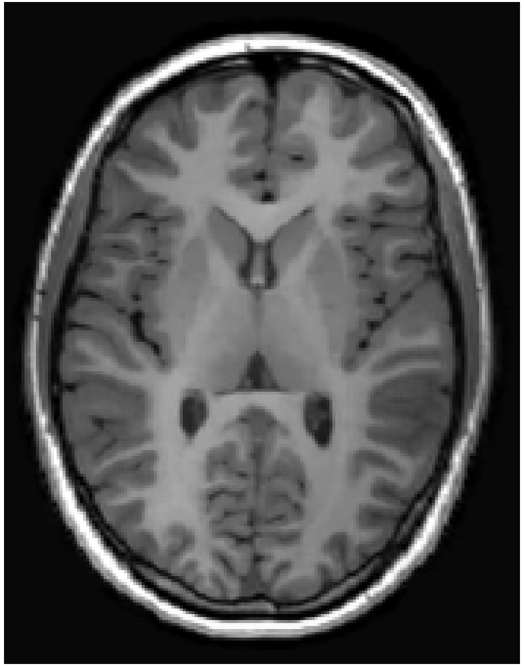


https://mriquestions.com/signal-to-noise.html

1. Problem: Noise

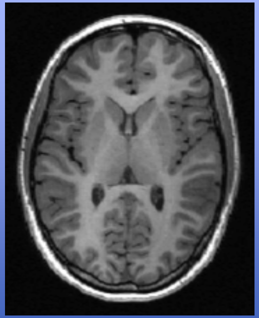


Filter*

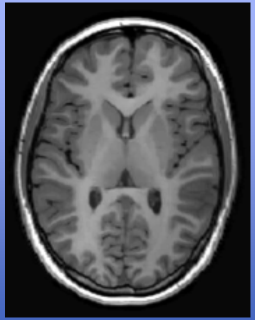


* Manjon et al., JMRI, 2010 - https://github.com/djkwon/naonlm3d

Why thresholding fails ?



T1

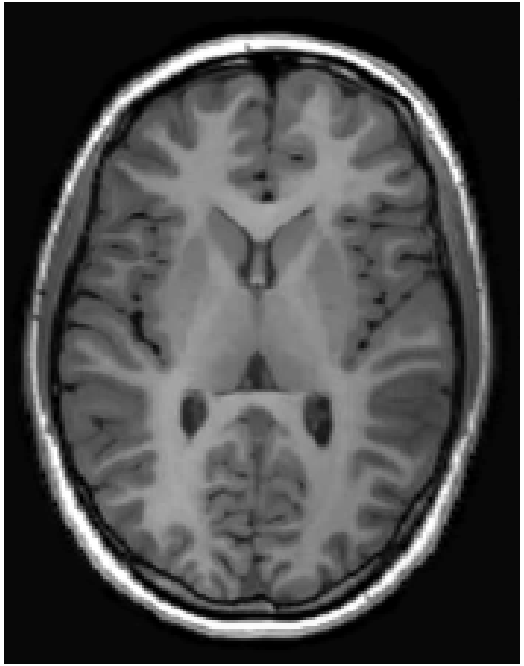


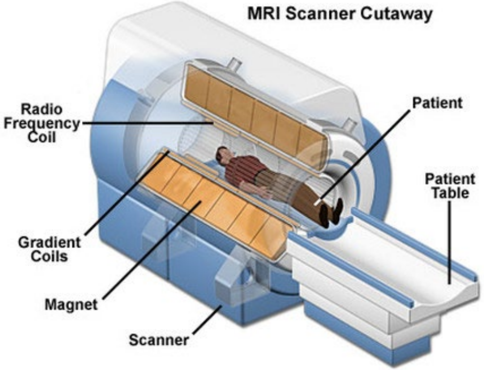
Noise Removal

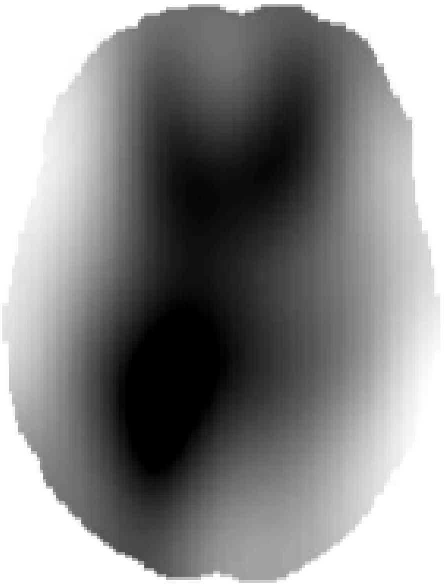
Volume of Brain Region

- Image inhomogeneity
- Overlapping intensities
- Intensities are relative
- No clear boundaries

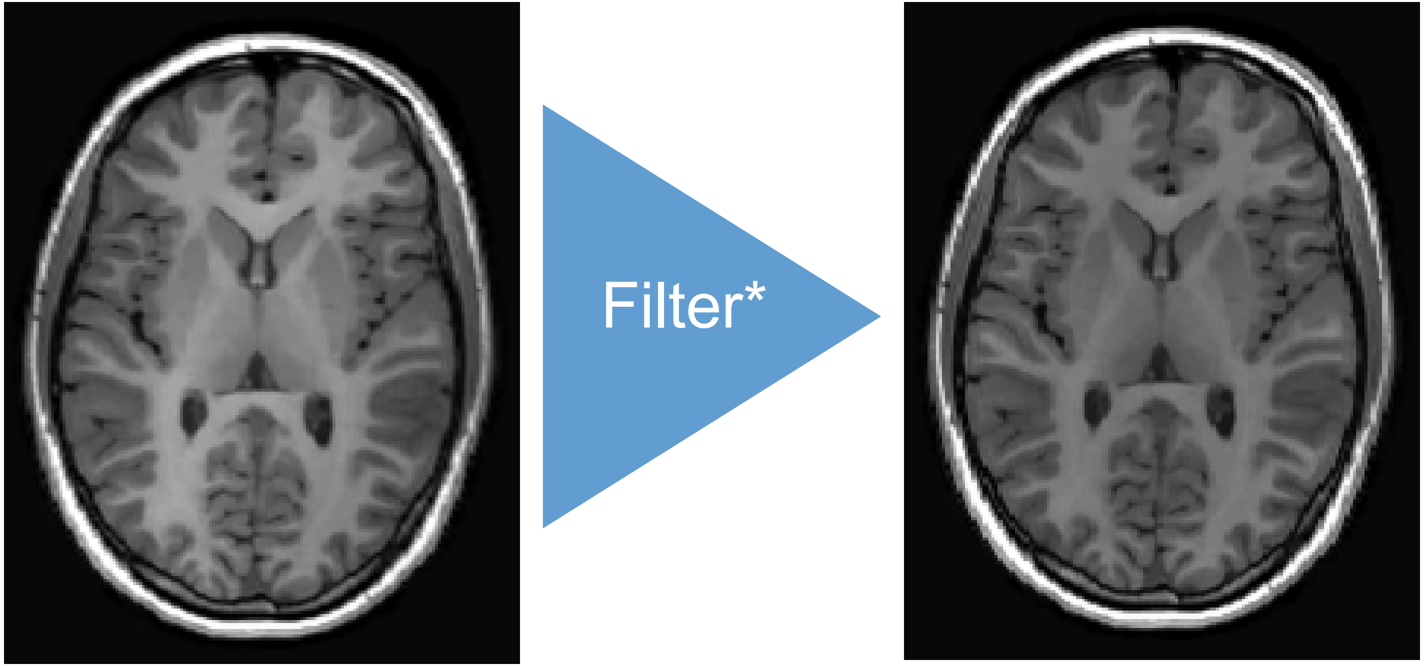
2. Problem: Image Inhomogeneity





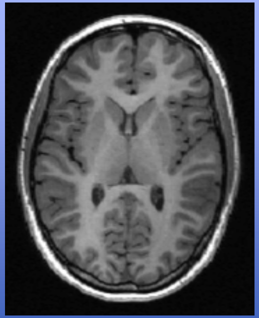


2. Problem: Image Inhomogeneity

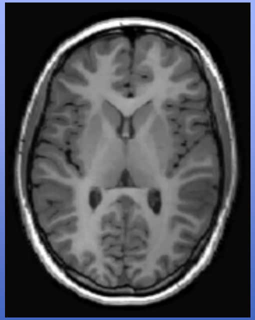


* N. Tustison al. , IEEE Transactions on Medical Imaging, 2010 - https://github.com/ANTsX/ANTs/wiki/N4BiasFieldCorrection

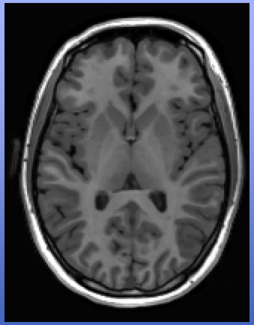
Why thresholding fails ?



T1



Noise Removal

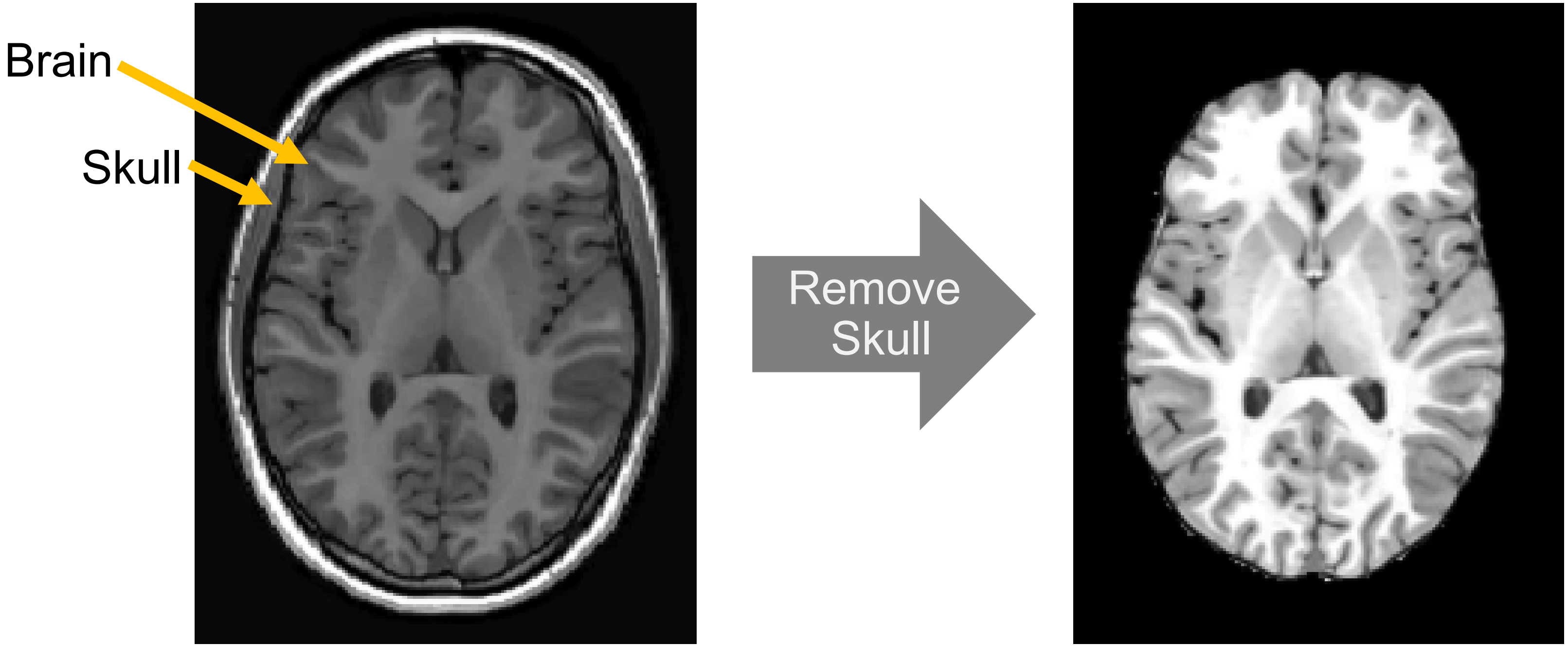


Inhomogeneity

Volume of Brain Region

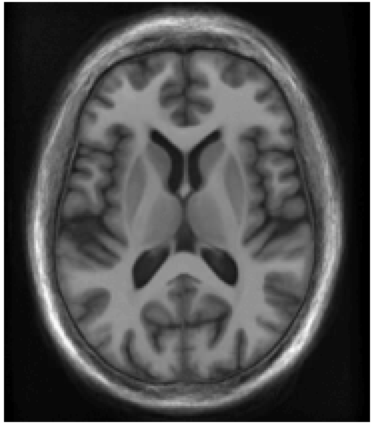
- Overlapping intensities
- Intensities are relative
- No clear boundaries

3. Problem: Intensities of Skull Match Brain

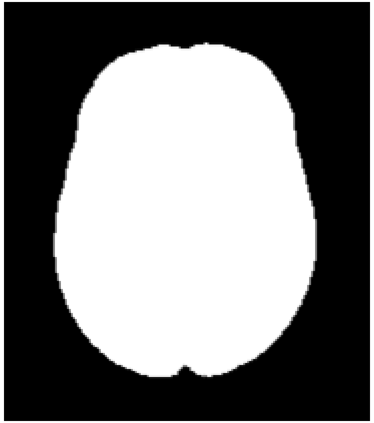


Use Mask of an Atlas

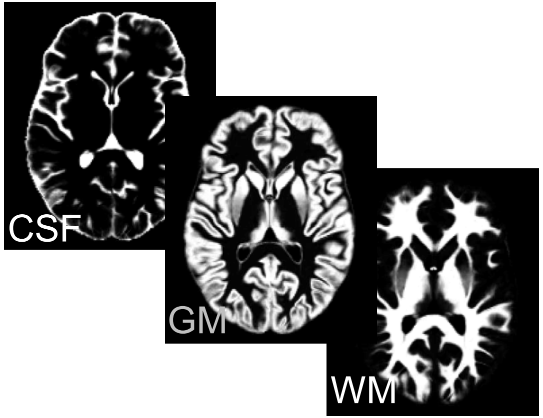
Atlas contains a mask of the brain and parcellation



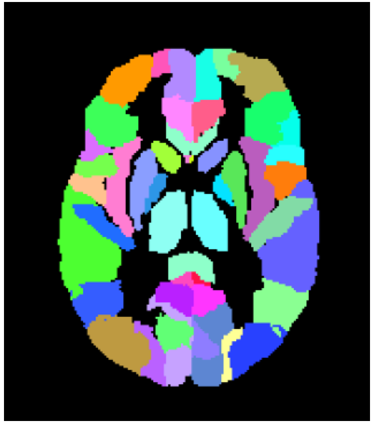
T1 Avg



Mask



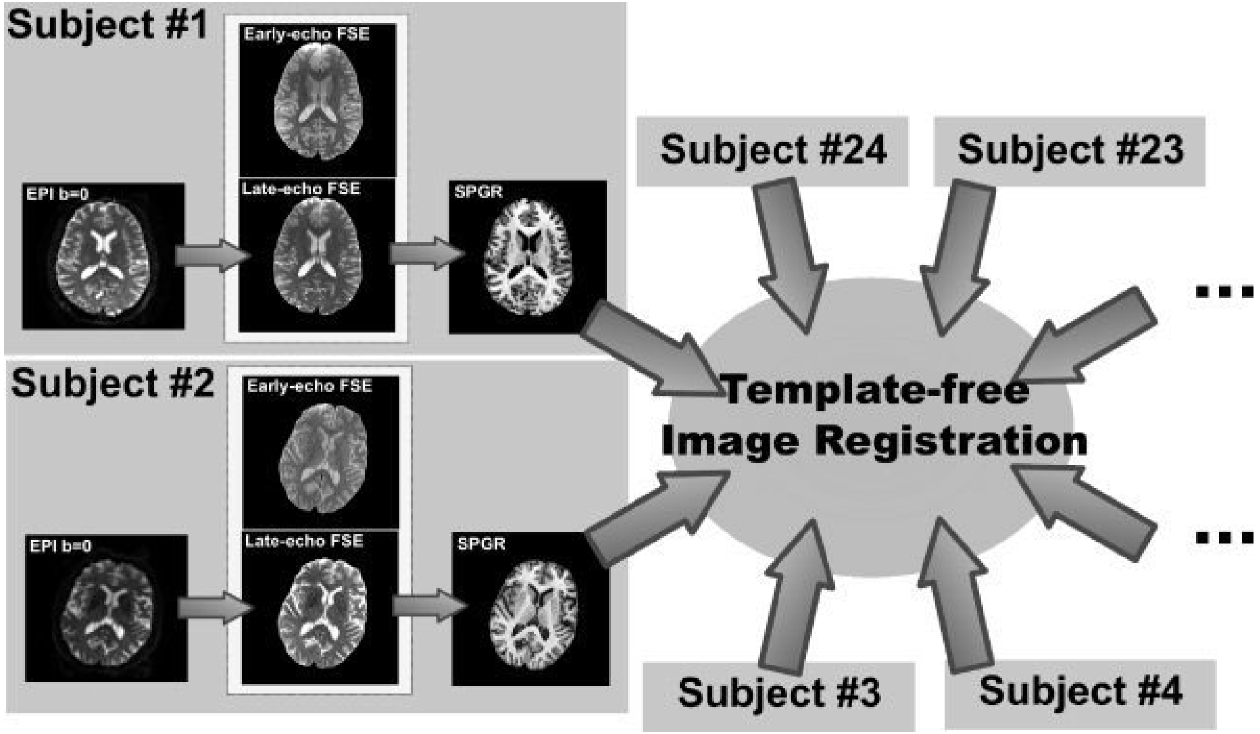
Spatial Atlas



Parcellation

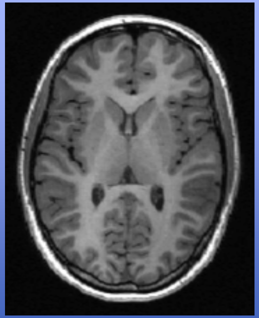
T. Rohlfing et al, Human Brain Mapping, 2010
https://www.nitrc.org/projects/sri24

Atlas

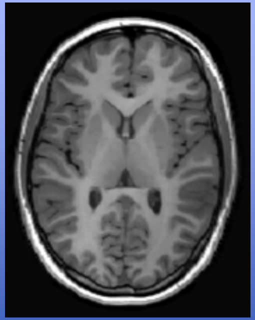


T. Rohlfing et al, Human Brain Mapping, 2010

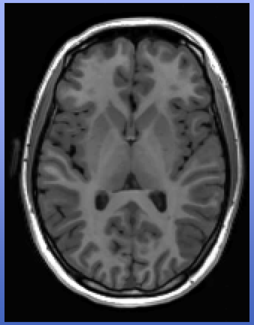
Why thresholding fails ?



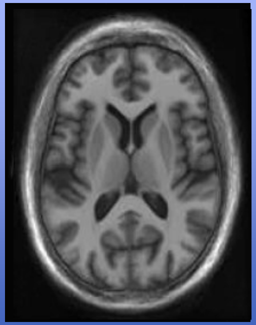
T1



Noise Removal



Inhomogeneity

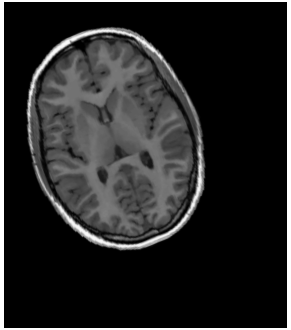


Atlas

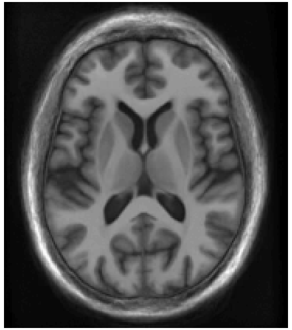
Volume of Brain Region

- Overlapping intensities
- Intensities are relative
- No clear boundaries

4. Problem: Align Atlas to Subject (or vice versa)

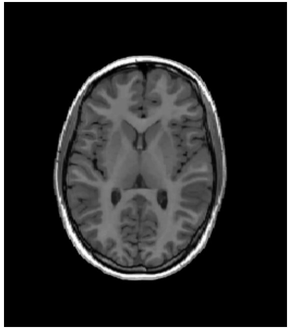


Subject



Atlas

Rigid

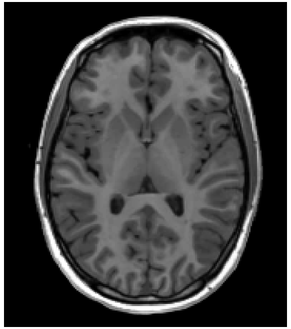


Rotation & Translation

Affine

Rigid + Scale & Shear

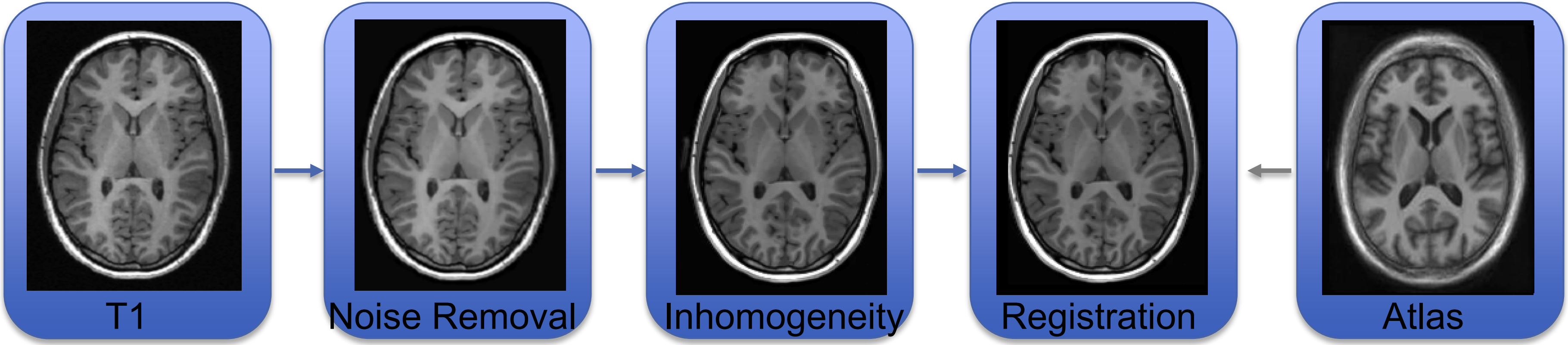
Non-Rigid



Affine + Local Transformations

http://stnava.github.io/ANTs

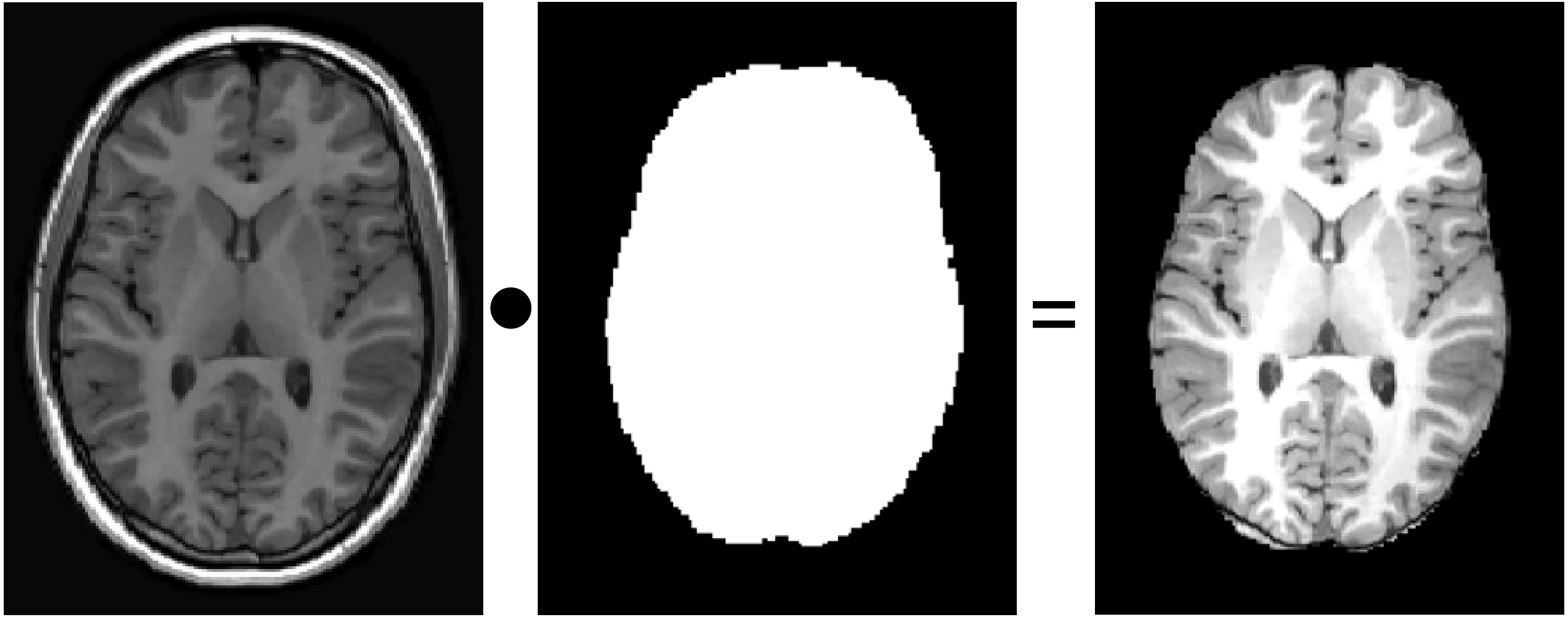
Why thresholding fails ?



Volume of Brain Region

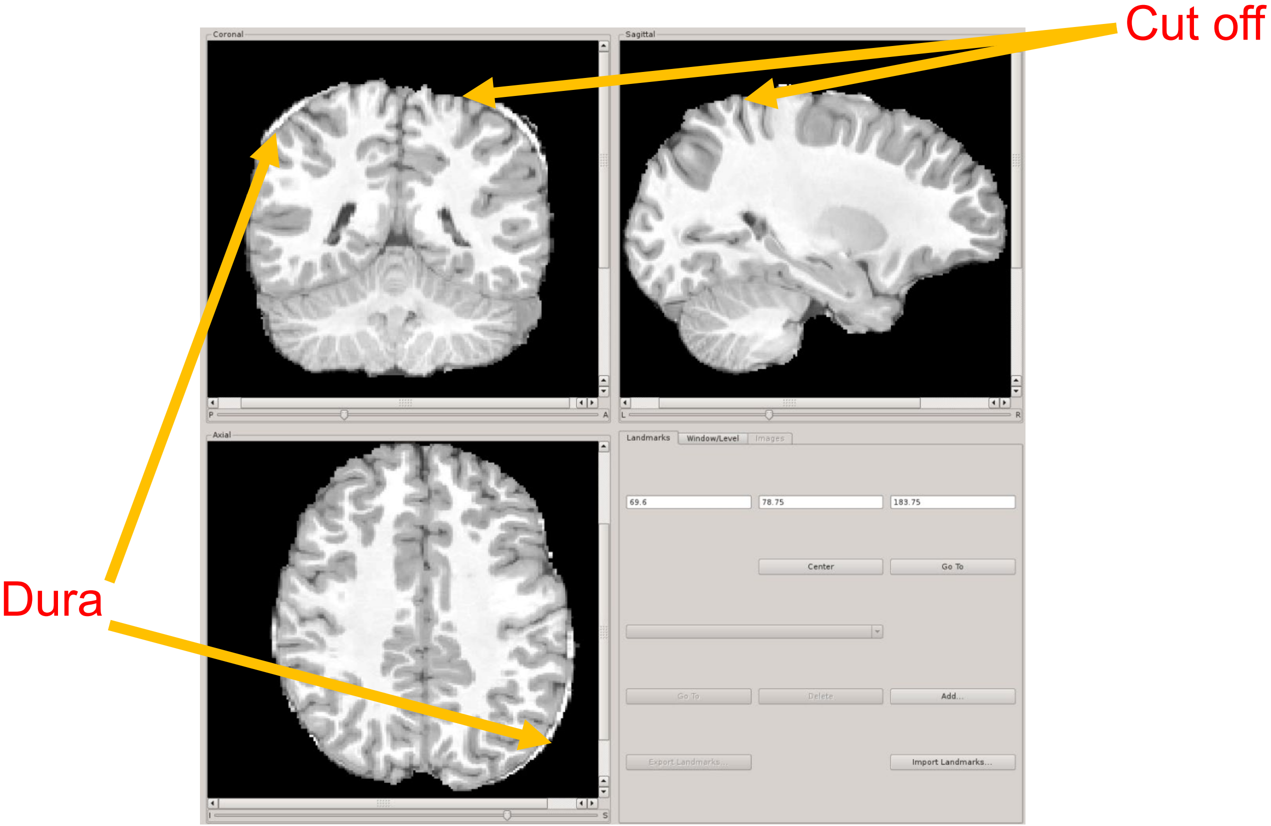
- Overlapping intensities
- Intensities are relative
- No clear boundaries

Skull Stripping



Subject Aligned Mask Brain

5. Problem: Generate Accurate Mask

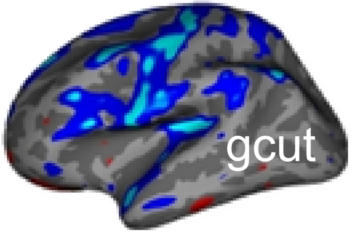


Possible Solution: Skull Stripping Tools

AFNI!

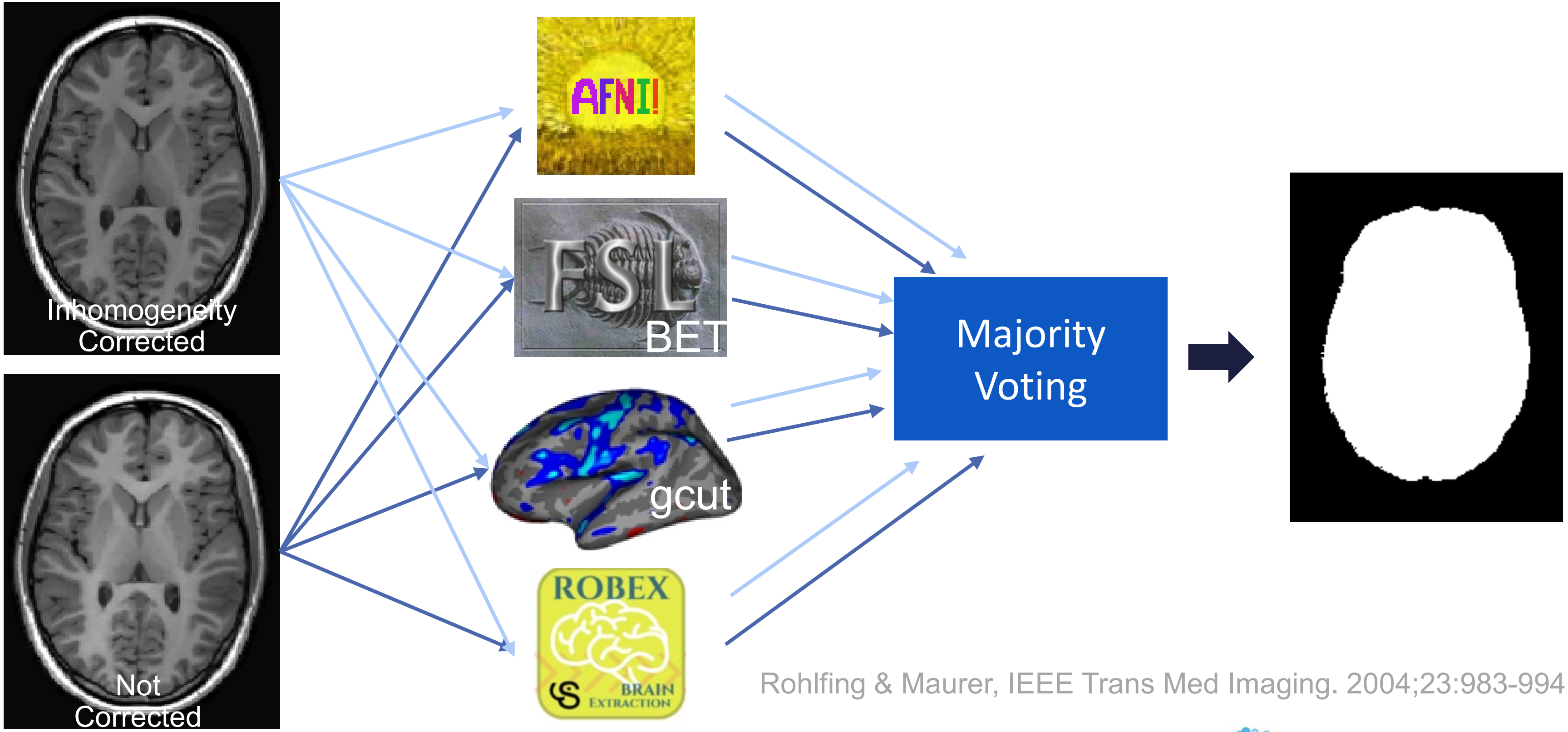
ROBEX
BRAIN EXTRACTION

FSL
BET



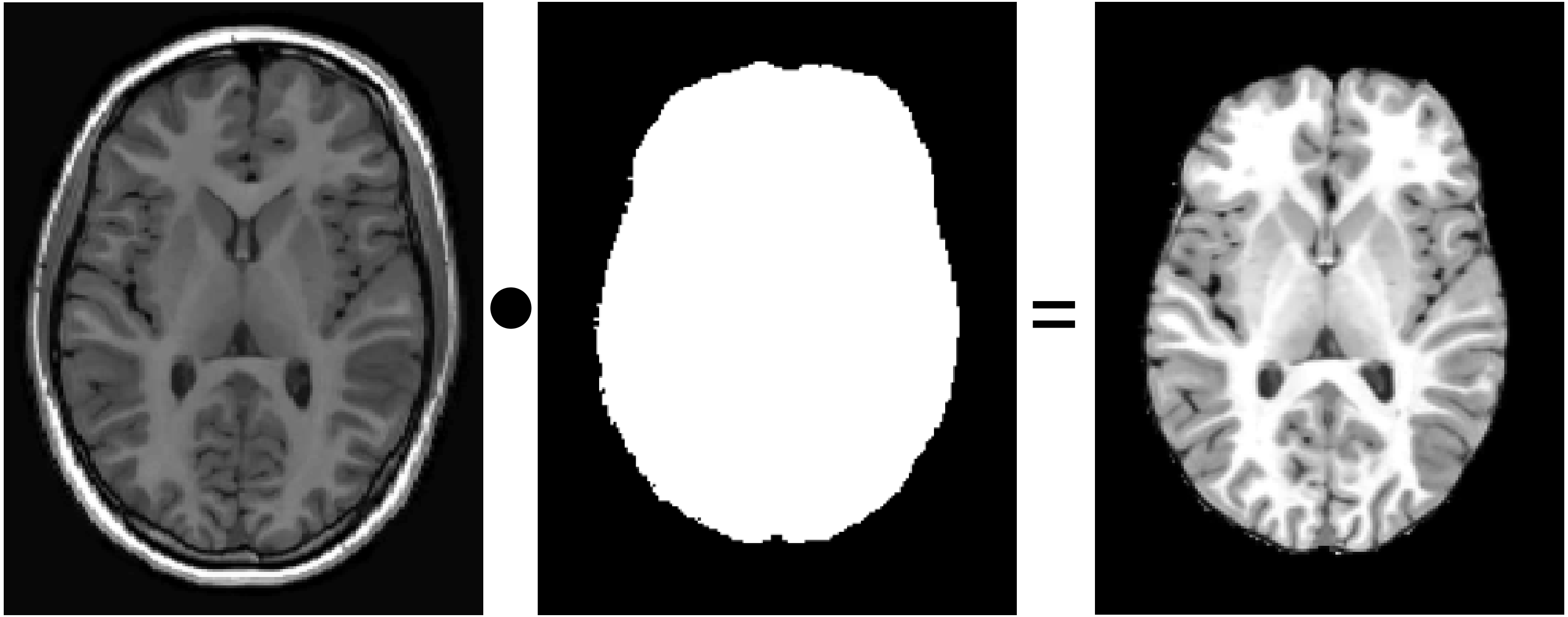
Does not solve problem !

Best Solution: Majority Voting



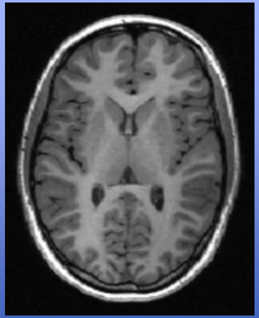
Rohlfing & Maurer, IEEE Trans Med Imaging. 2004;23:983-994.

Skull Stripping

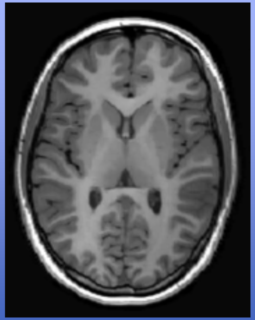


Subject | Mask of Majority Voting | Brain

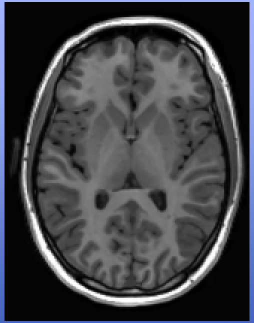
Why thresholding fails ?



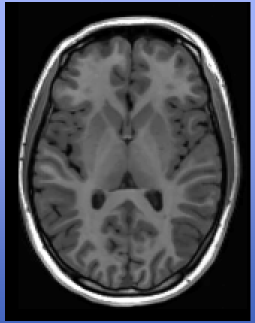
T1



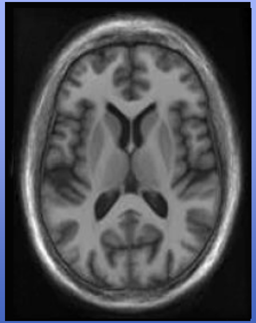
Noise Removal



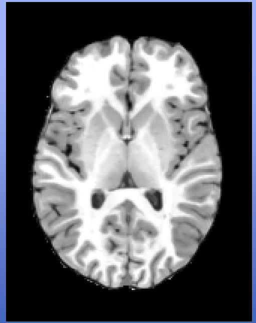
Inhomogeneity



Registration



Atlas

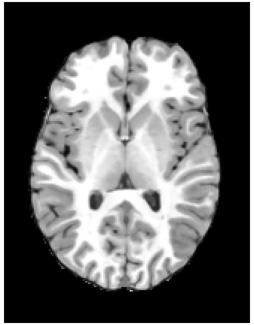


Skull Stripping

Volume of Brain Region

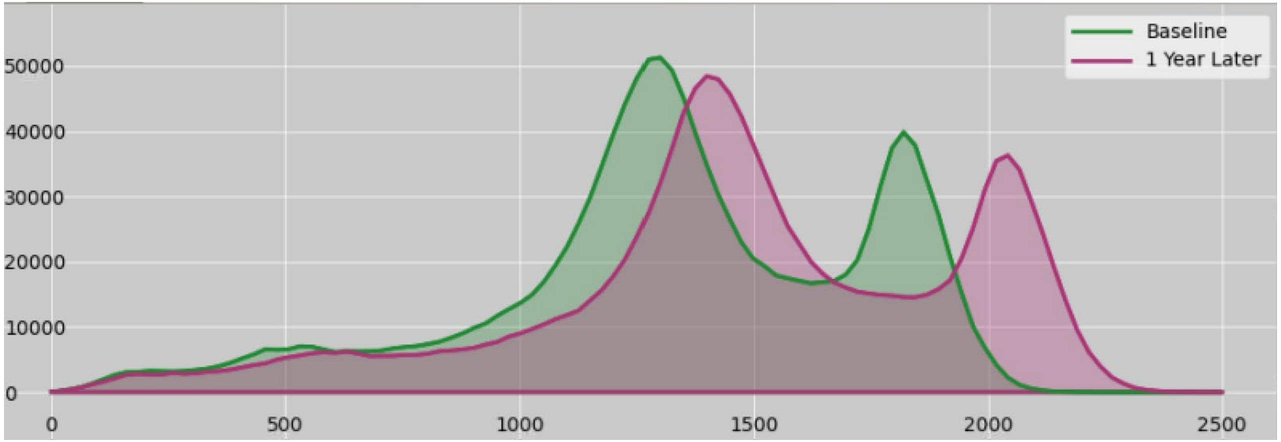
- Overlapping intensities
- Intensities are relative
- No clear boundaries

6. Problem: Intensities Vary across Visits



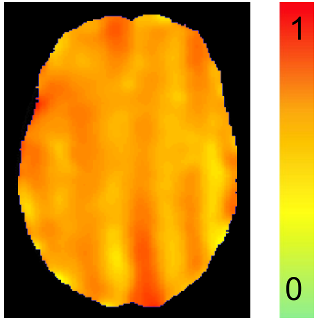
Baseline

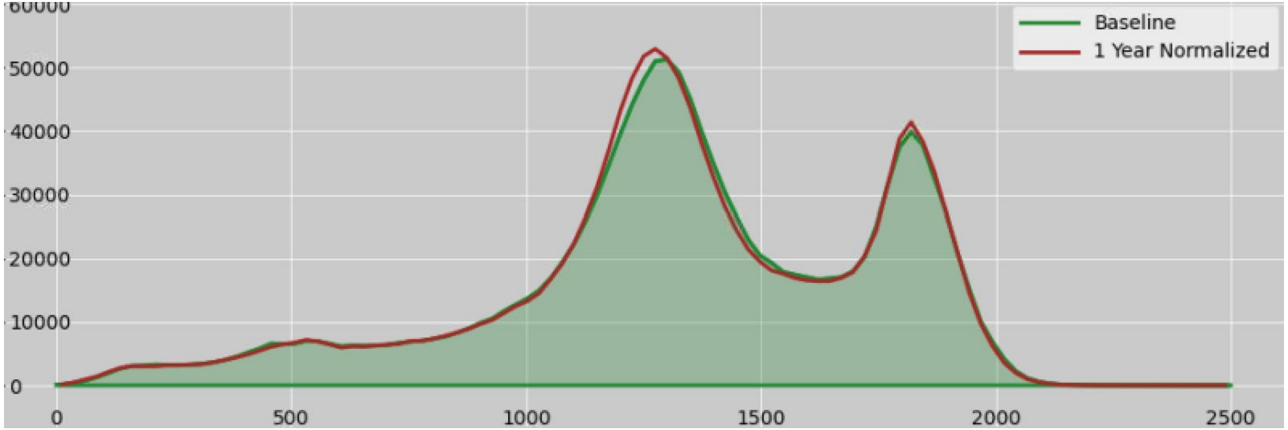
1 Year Later



Normalize across Visits

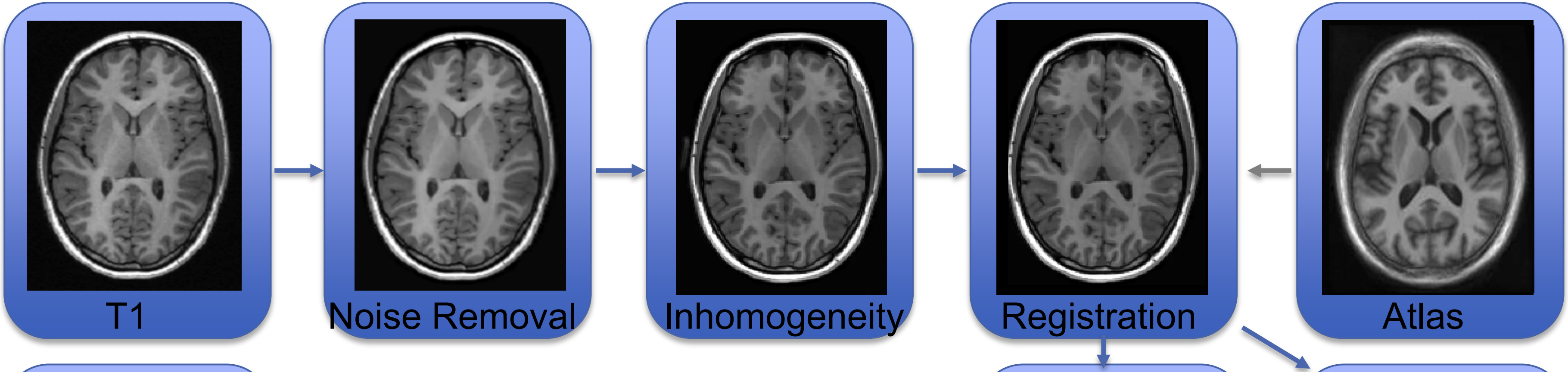
- Register Baseline to 1 Year Follow up
- Smooth both 1 Year Follow up and Baseline
- Divide smooth 1 Year Follow up by Baseline
- Multiply output with 1 Year Follow Up

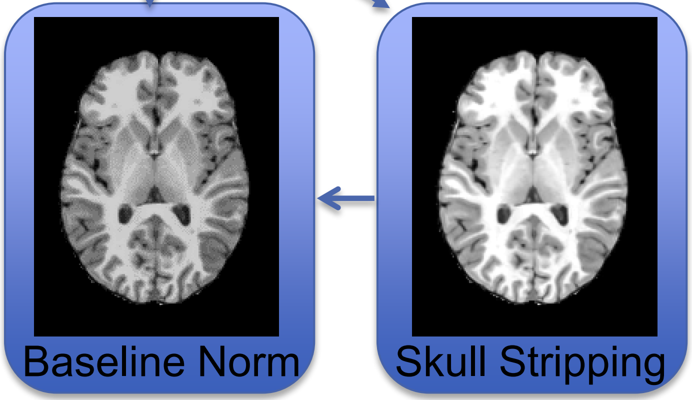




Pfefferbaum et al. American Journal of Psychiatry, 175(4), pp. 370-380, 201

Why thresholding fails ?



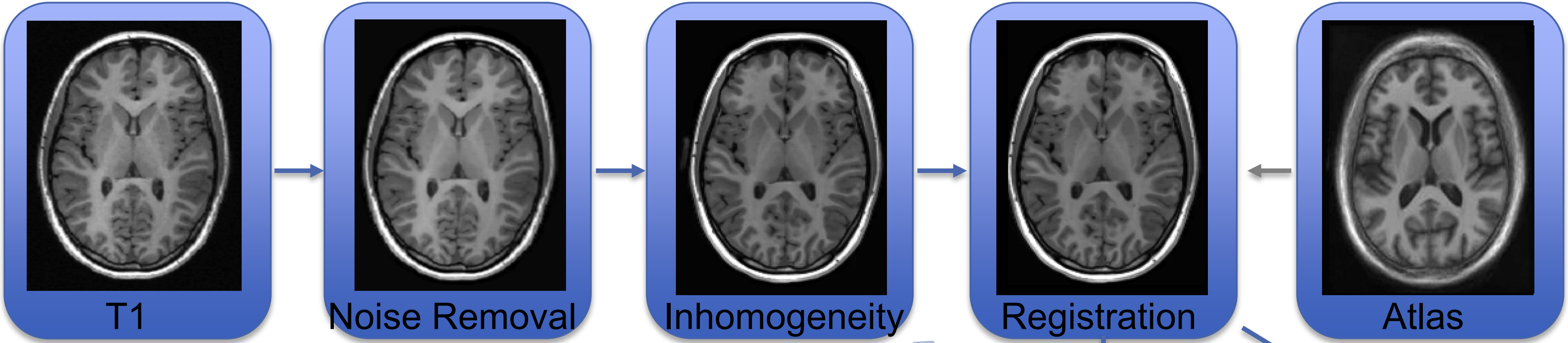


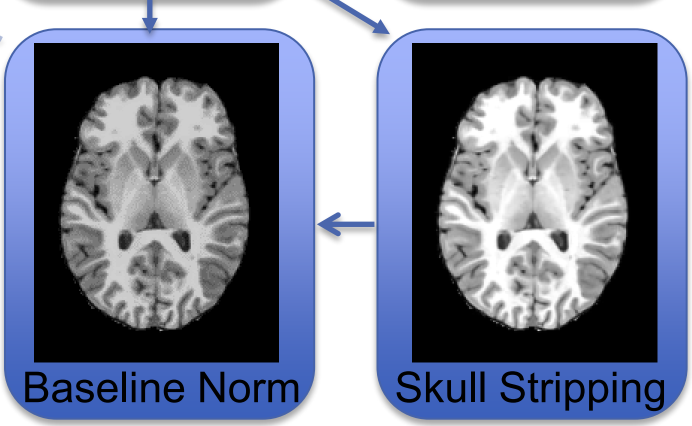
Volume
of
Brain
Region

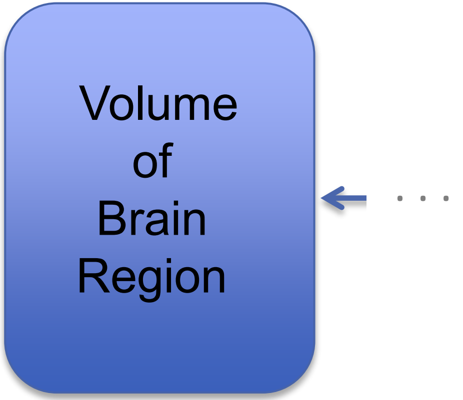
. . .

- Overlapping intensities
- No clear boundaries

Why thresholding fails ?

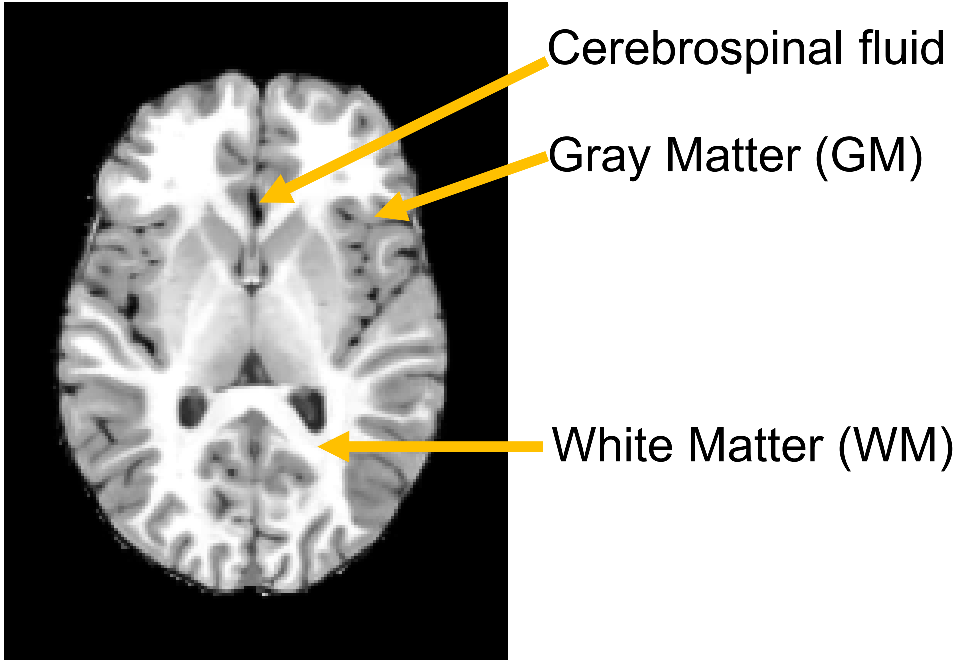


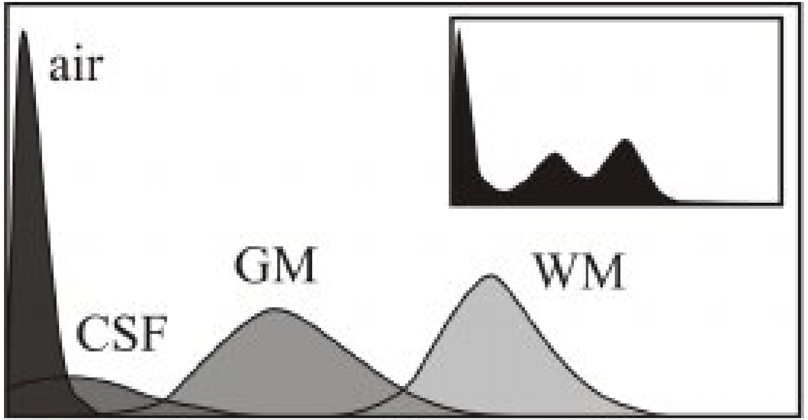




- Overlapping intensities
- No clear boundaries

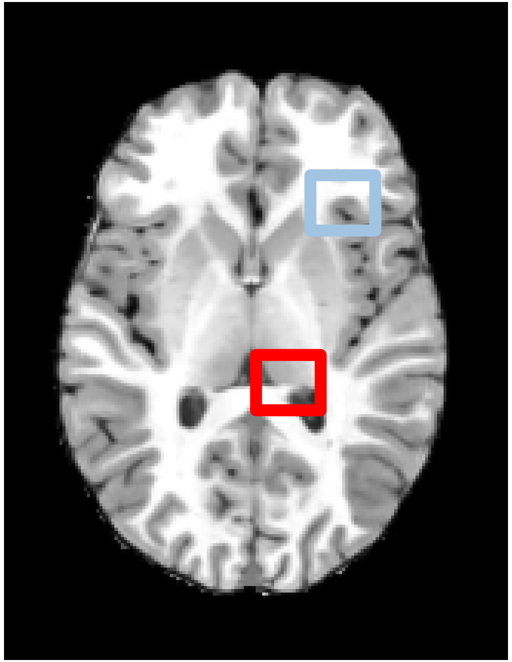
5. Problem: Intensities of Structures Overlap



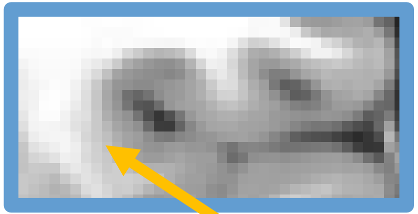


Not only due intensity distributions of structures overlap ….

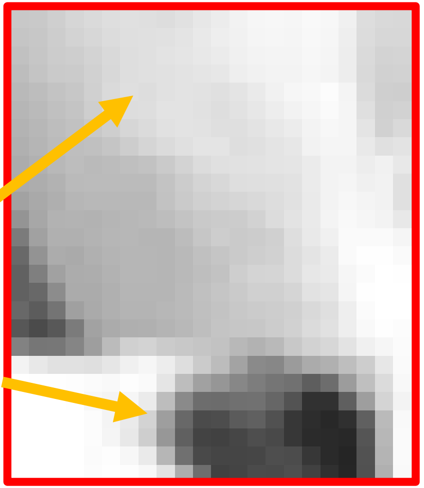
5. Problem: Intensities of Tissues Overlap



Partial Volume Effects



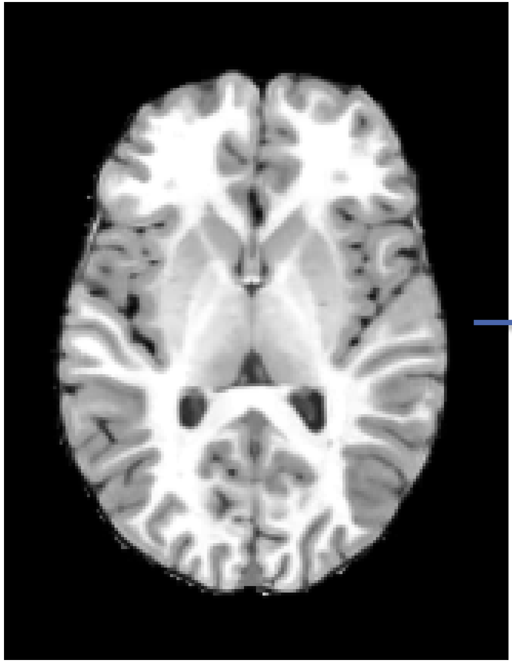
Gray & White Matter



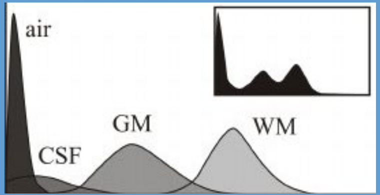
Gray Matter & CSF

How to deal with overlapping intensity distributions ?

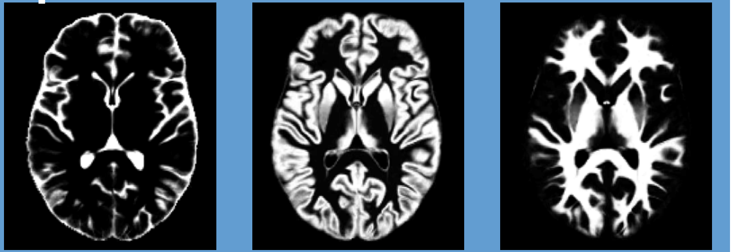
Segment Brain Tissue

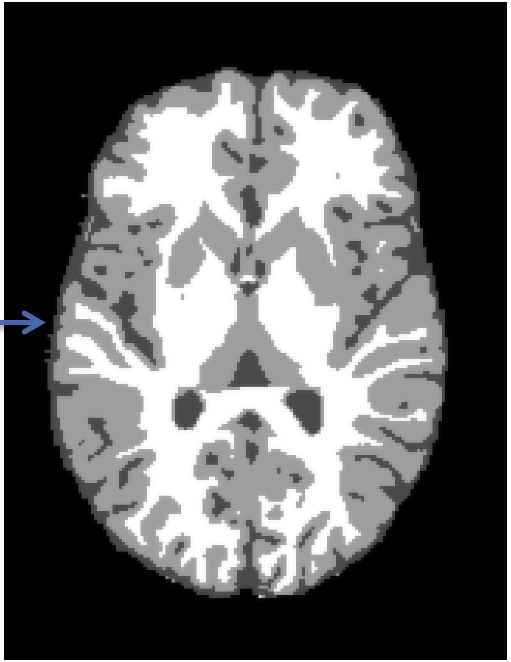


Automatic Segmentation



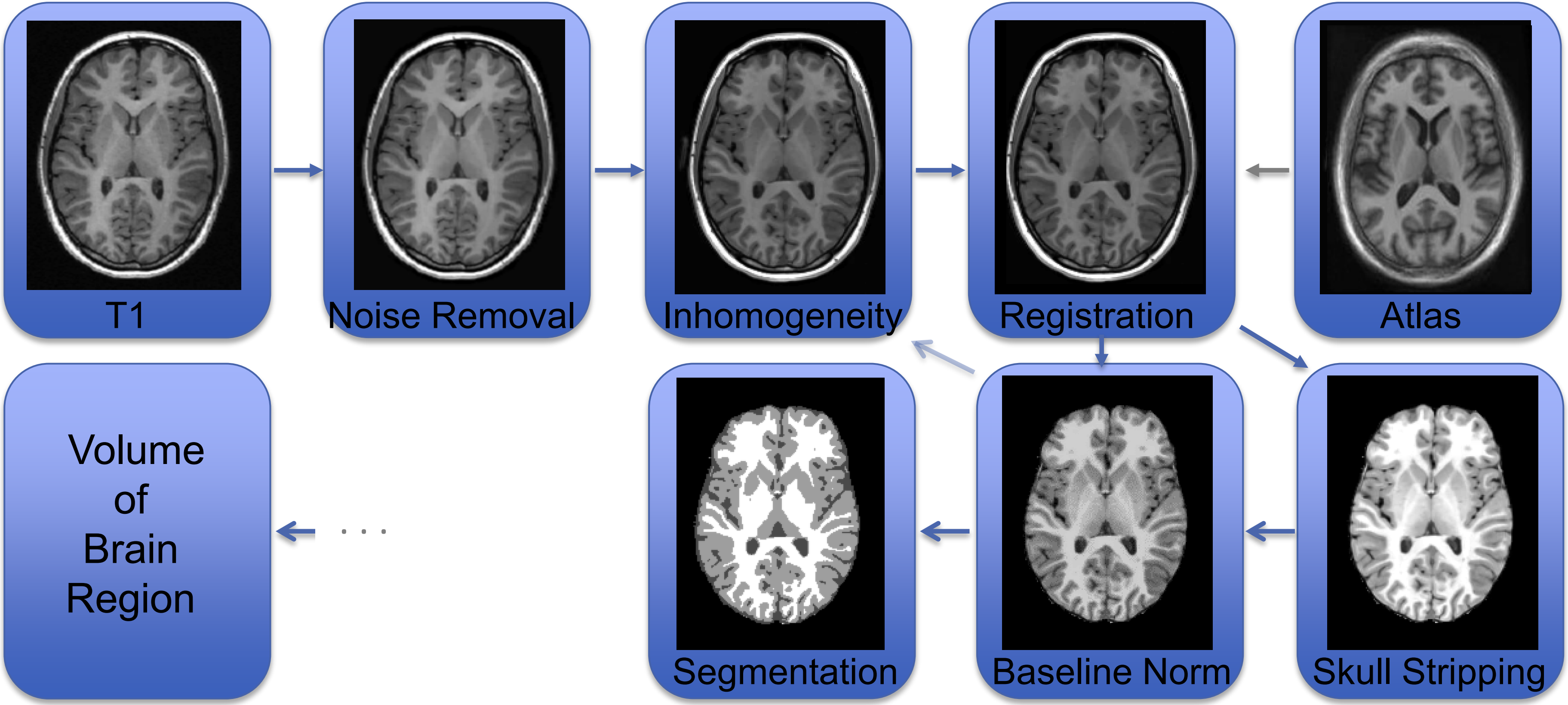
Spatial Atlas



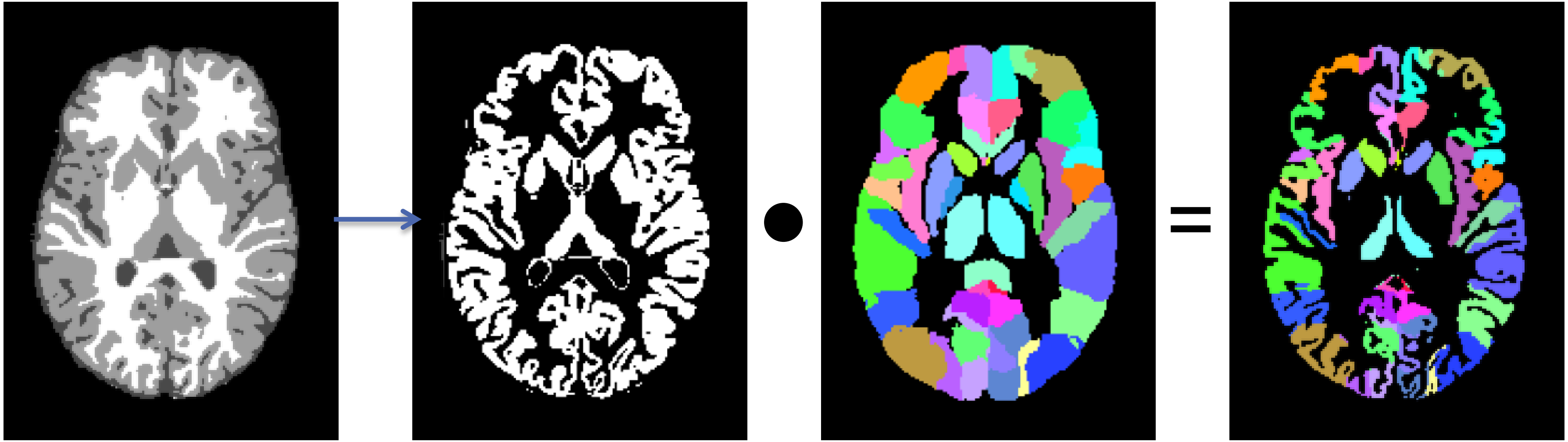


Pohl, Prior Information for Brain Parcellation, 2005

Why thresholding fails ?

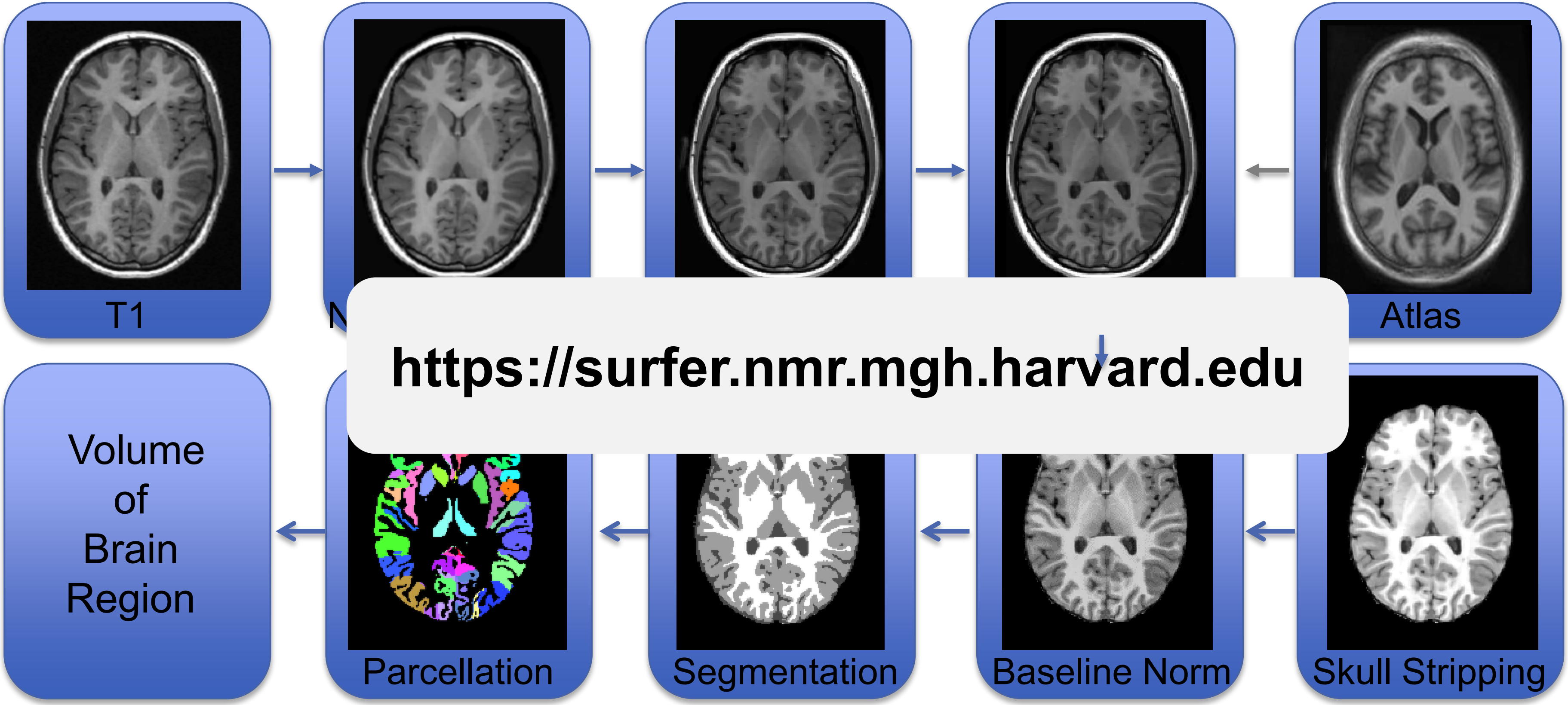


Brain Parcellation



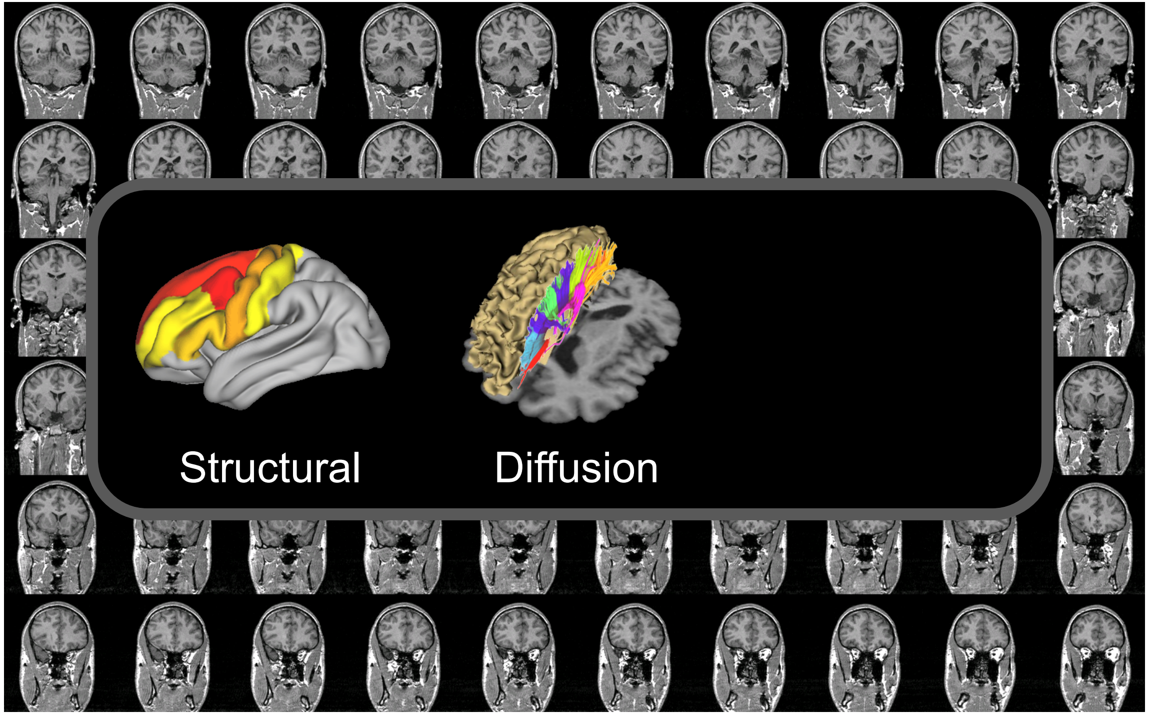
GM Mask ROI Atlas Parcellation

Processing of Structural MRI

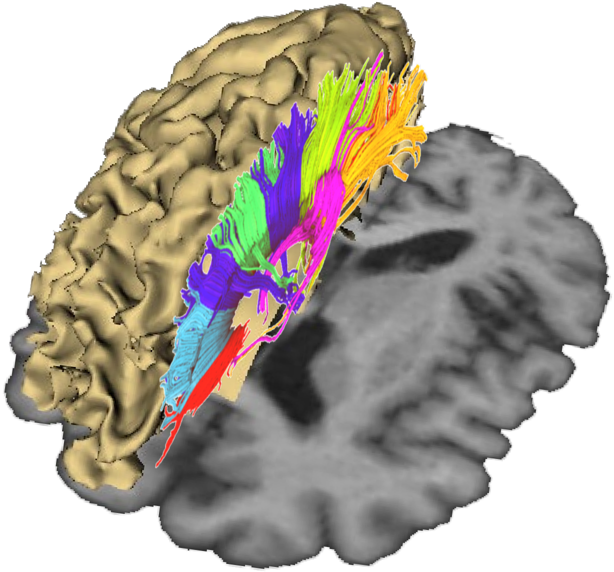


https://surfer.nmr.mgh.harvard.edu

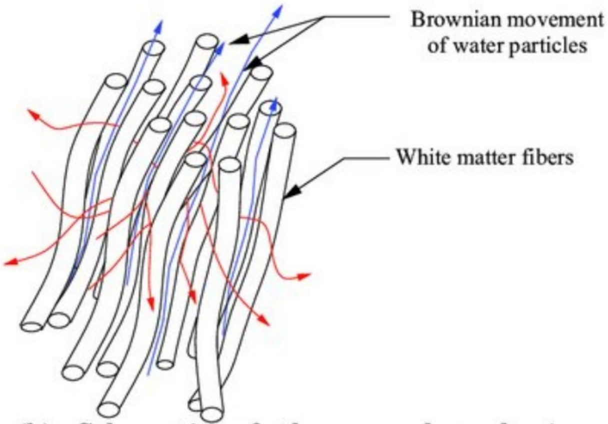
Processing by MRI Type



Fiber Bundles



White matter contains axons that group together to bundles connecting gray matter regions



(b) Schematic of the axonal packaging within a voxel [Poupon: 1999]

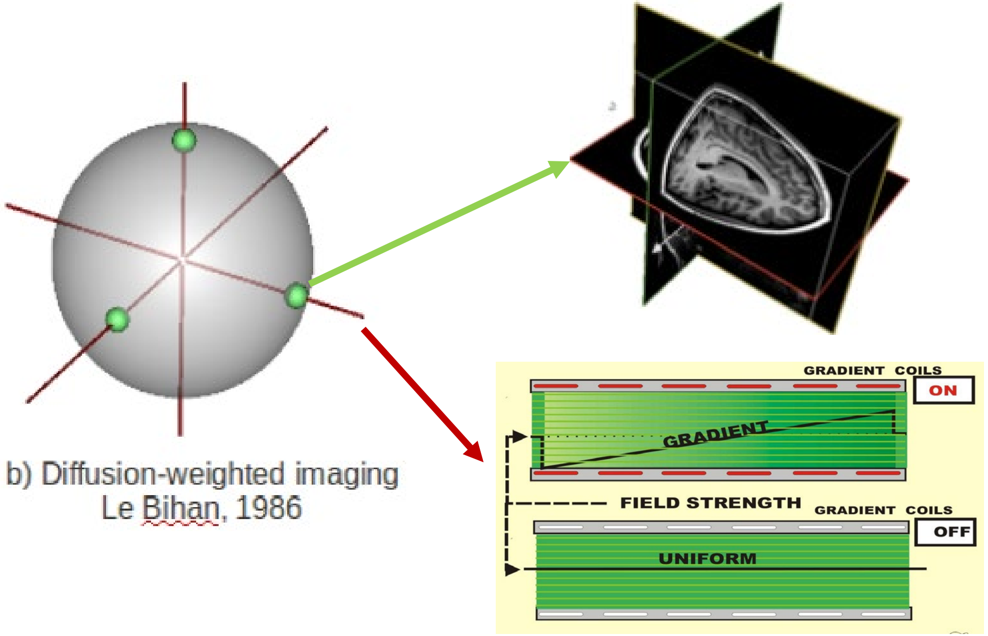
Fiber bundles restrict diffusion of water molecules

Mathematically represented by a tensor $\mathbf{D} = \begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ \cdot & D_{yy} & D_{yz} \\ \cdot & \cdot & D_{zz} \end{pmatrix}$

Descoteaux, Poupon: Comprehensive Biomedical Physics, Vol 3, Chapter 6, 2014

Diffusion Weighted Imaging (DWI)

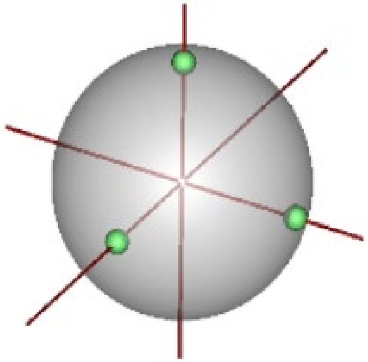
Measure the rate of diffusion within white matter
by varying gradient direction of scanner's magnetic field



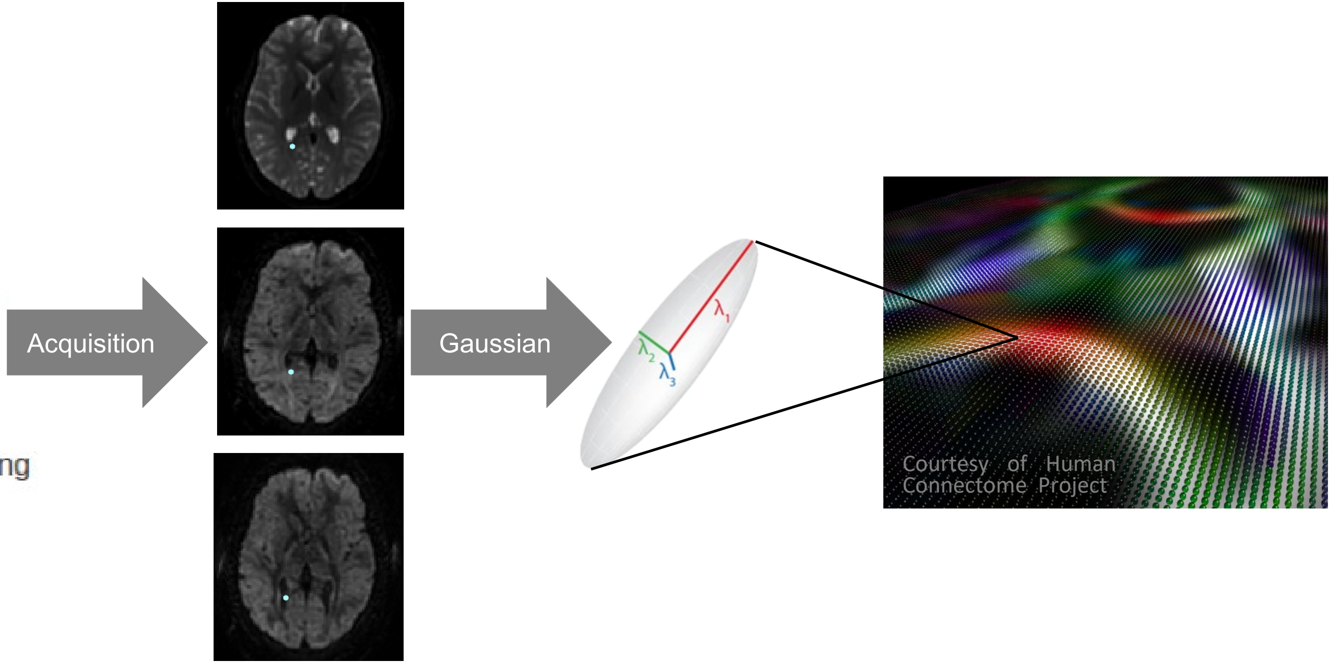
b) Diffusion-weighted imaging
Le Bihan, 1986

Diffusion Weighted Imaging (DWI)

Measure the rate of diffusion within white matter
by varying gradient direction of scanner’s magnetic field

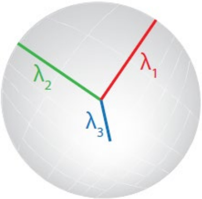


b) Diffusion-weighted imaging
Le Bihan, 1986

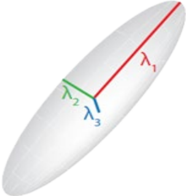


Fractional Anisotropy (FA)

Compute from Diffusion Tensor the Fractional Anisotropy, i.e., $FA = \frac{1}{2}\frac{\sqrt{(\lambda_1-\lambda_2)^2+(\lambda_1-\lambda_3)^2+(\lambda_2-\lambda_3)^2}}{\lambda_1^2+\lambda_2^2+\lambda_3^2}$



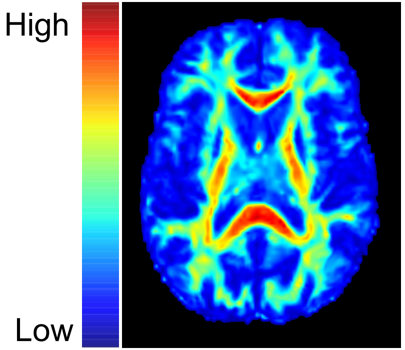
FA=0



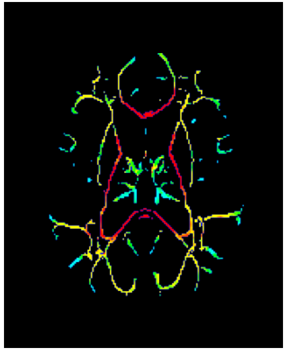
FA=0.8

Apply to each voxel of the 3D volume

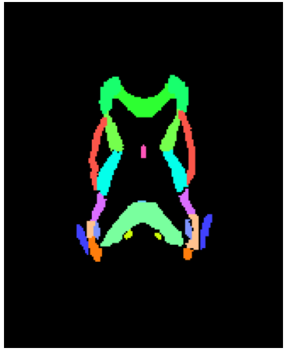
FA Maps



Skeletonize[1]



JHU-DTI Atlas[2]



Average

ROI Scores

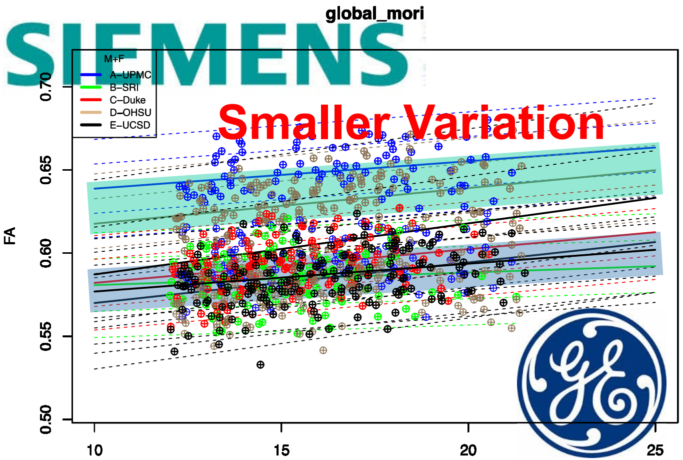
High FA confined to WM

[1] https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/TBSS

[2] https://neurovault.org/collections/264

Other processing issues

- Accounting for scanner differences in multi-site studies
  Pohl et al., *NeuroImage*, 2016

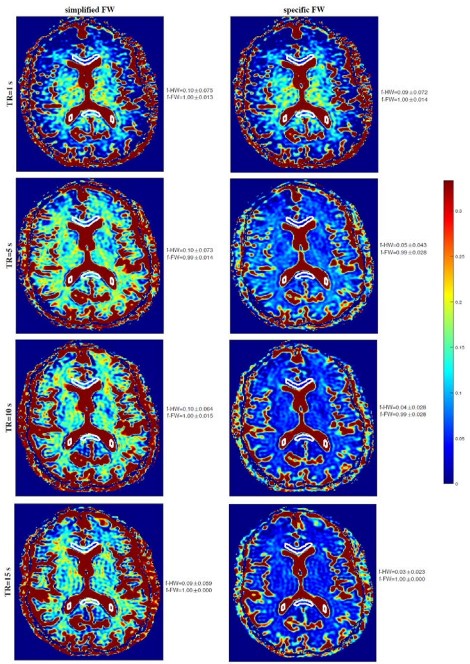


Use data from 3 human phantoms to correct scanner differences

Other processing issues

- Accounting for scanner differences in multi-site studies
  Pohl et al., *NeuroImage*, 2016

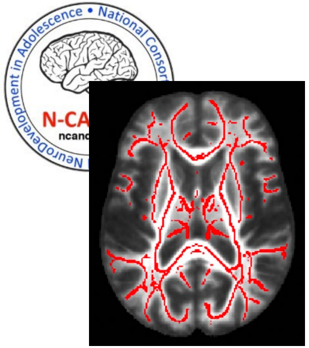
- Accurately estimating “free water”
  Ferizi et al., Physics in Medicine and Biology, 2023
- ….



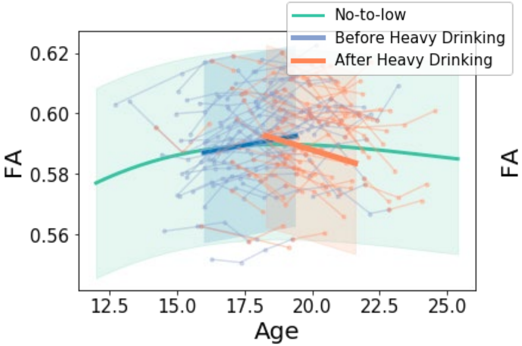
Recent Findings

Alcohol Disrupts Microstructural Development

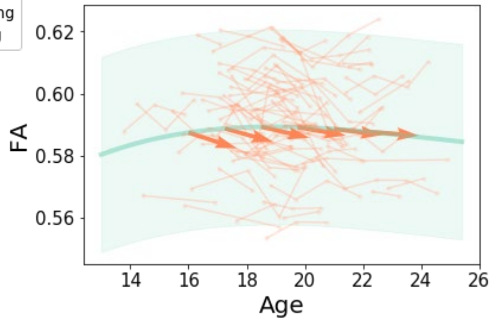
Zhao et al., JAMA Psychiatry, 2021



FA Skeleton



291 no-to-low drinkers
63 no-to-low to heavy drinking transitioners

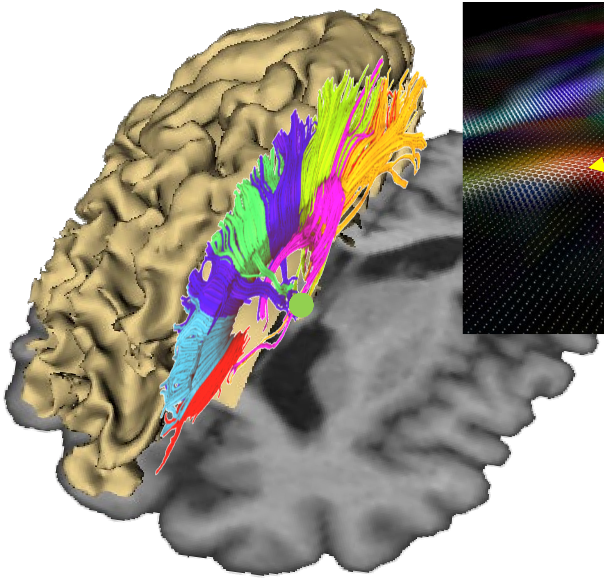


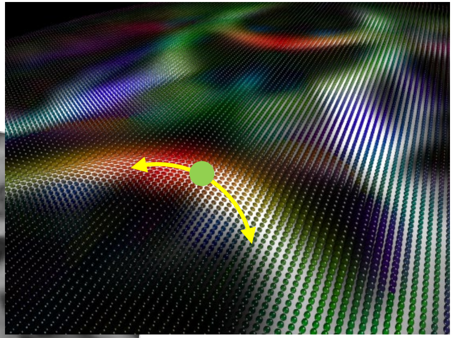
291 no-to-low drinkers
78 heavy drinkers

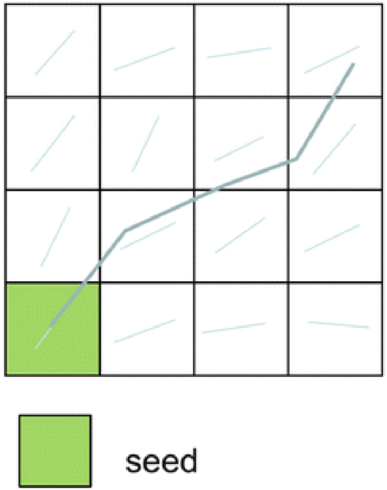
Direct in vivo evidence of disruption due to alcohol on white matter microstructural development during adolescence

Medscape Healio

How to (deterministically) extract fibers



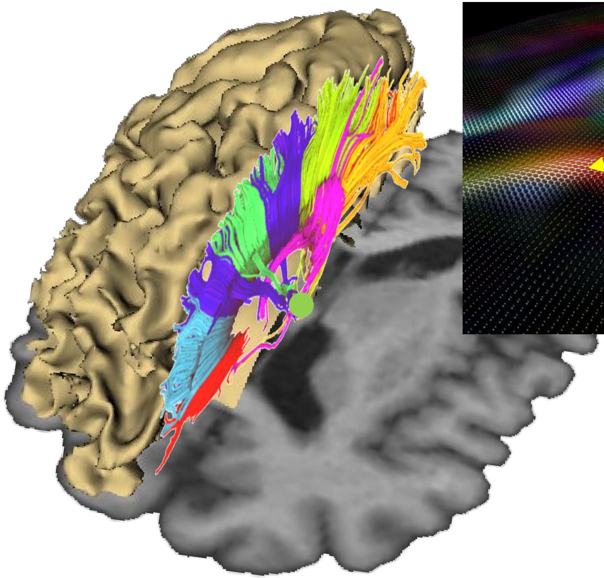


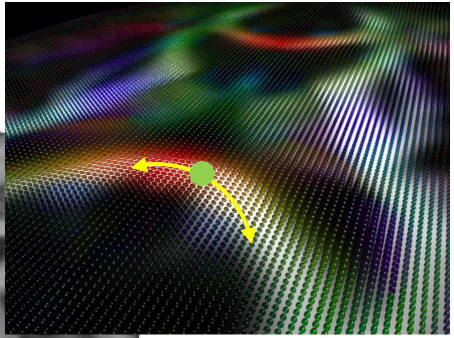


https://radiologykey.com/dti-analysis-methods-fibre-tracking-and-connectivity

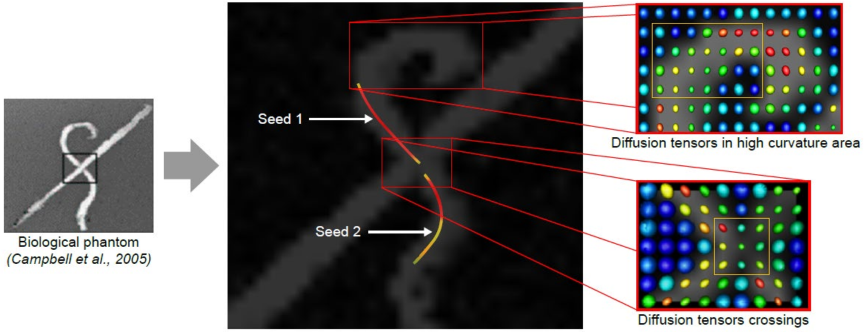
Software for extracting fibers
https://dipy.org/documentation/1.4.1./interfaces/tracking_flow

How to (deterministically) extract fibers



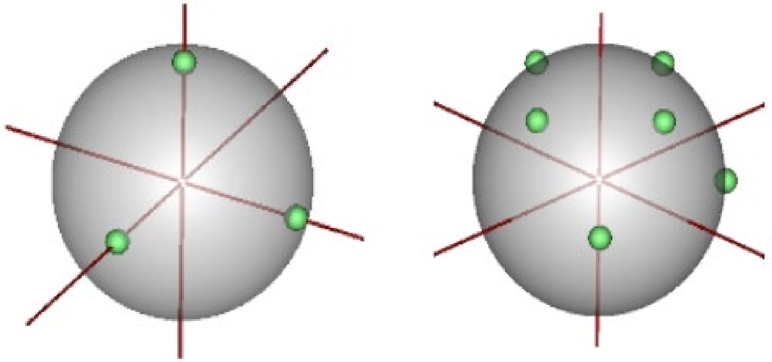


Problem: Crossing Fibers



Diffusion Tensor Imaging (DTI)

Measure the rate of diffusion within white matter
by varying gradient direction of scanner's magnetic field
and removing Gaussian Assumption



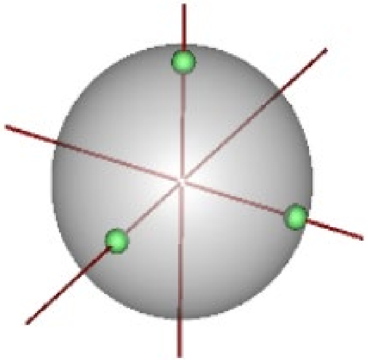
b) Diffusion-weighted imaging
Le Bihan, 1986

d) Diffusion tensor imaging
Basser, 1994

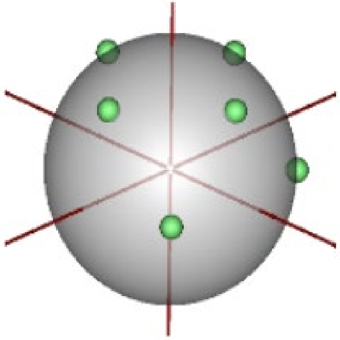
Does not solve problem with crossing fibers !

High Angular Resolution Diffusion Imaging (HARDI)

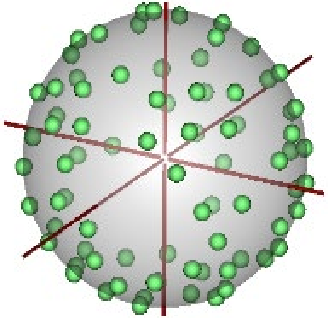
Measure the rate of diffusion within white matter
by varying gradient direction of scanner’s magnetic field
so that q-space is densely sampled



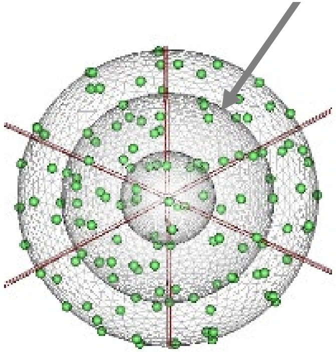
b) Diffusion-weighted imaging
Le Bihan, 1986



d) Diffusion tensor imaging
Basser, 1994

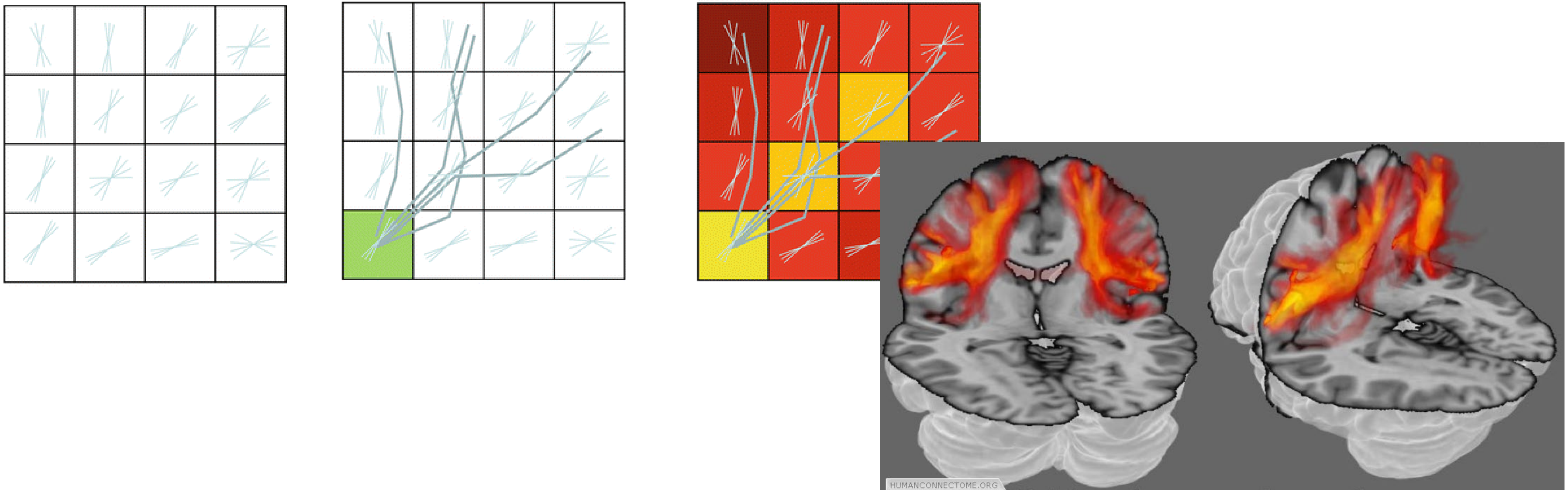


f) Single-Shell High Angular Resolution Diffusion Imaging
2000-2008



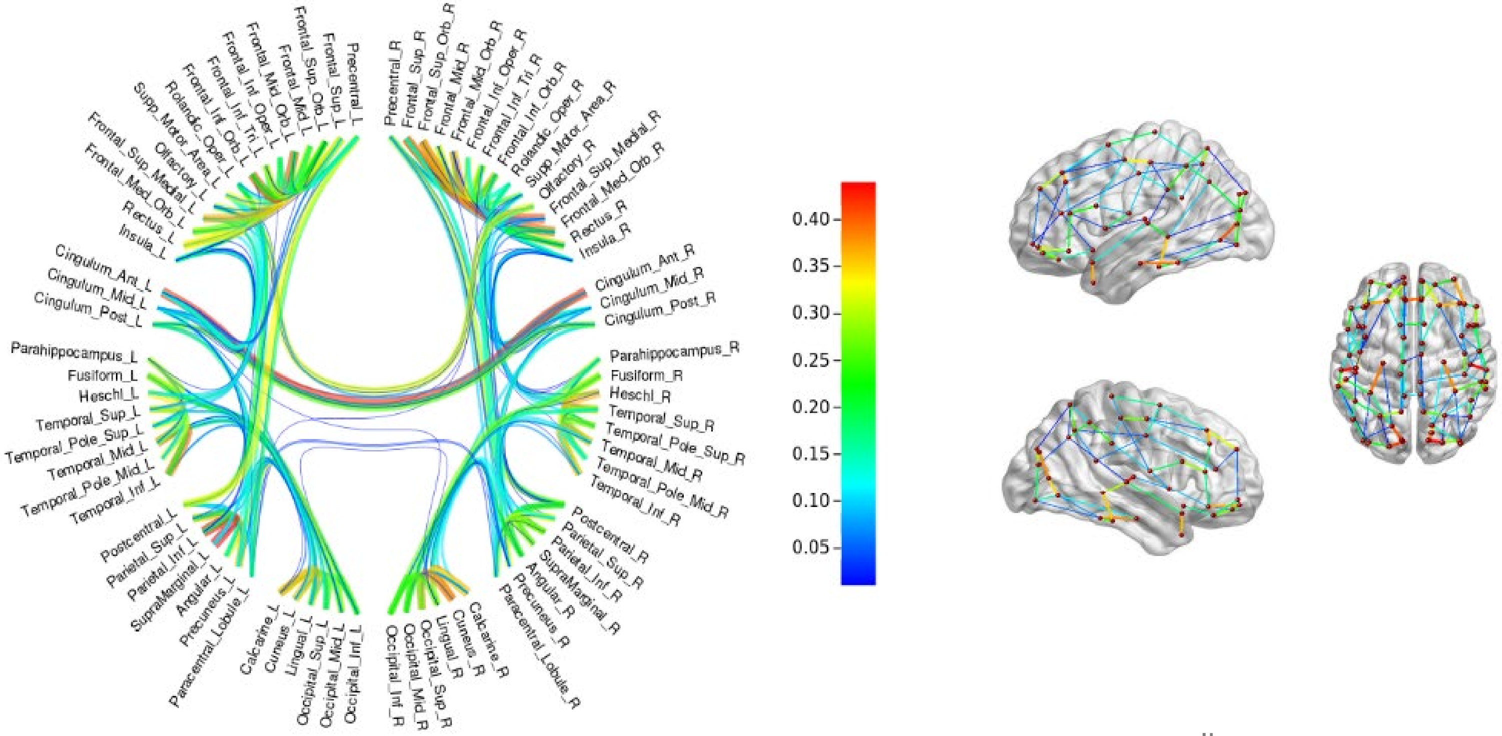
h) Multiple-Shell, sparse Hybrid Diffusion Imaging
2008-now

Probabilistic Tractography



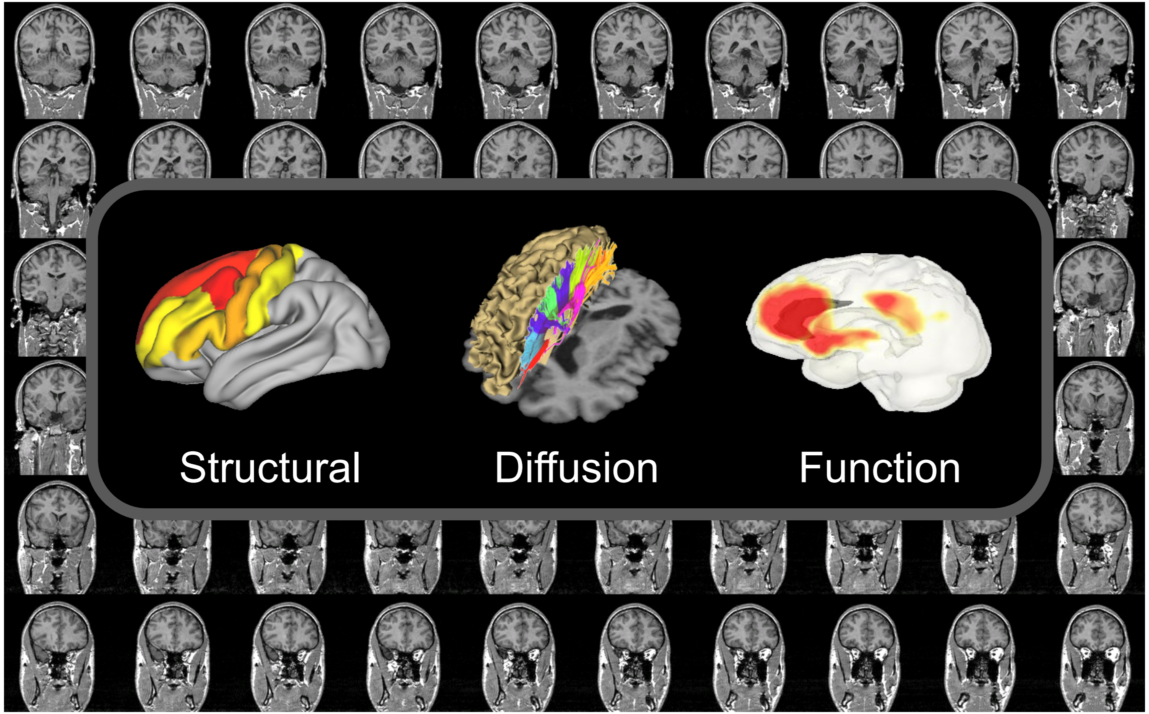
https://radiologykey.com/dti-analysis-methods-fibre-tracking-and-connectivity

Connectome



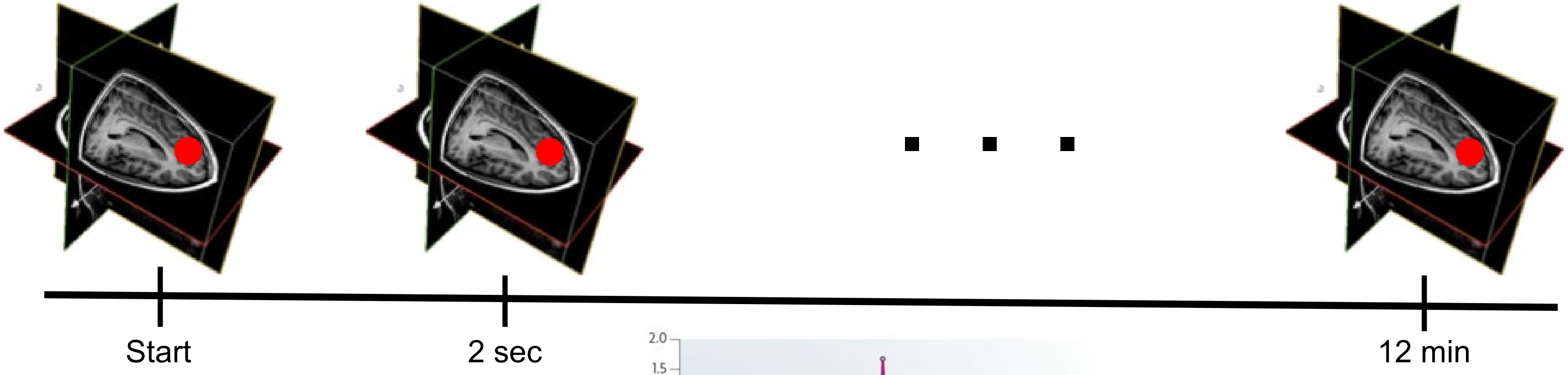
slicer.org

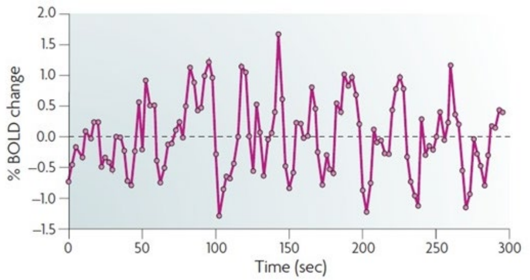
Processing by MRI Type



How Does Functional MRI (fMRI) Work ?

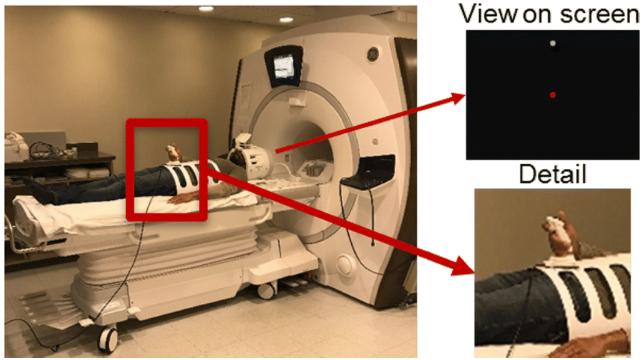
When a brain ROI is more active it consumes more oxygen, which causes more blood to flow to the active area. These changes in blood oxygenation and flow are recorded by fMRI by acquiring a MRI every couple seconds.





Type of fMRI

Task fMRI

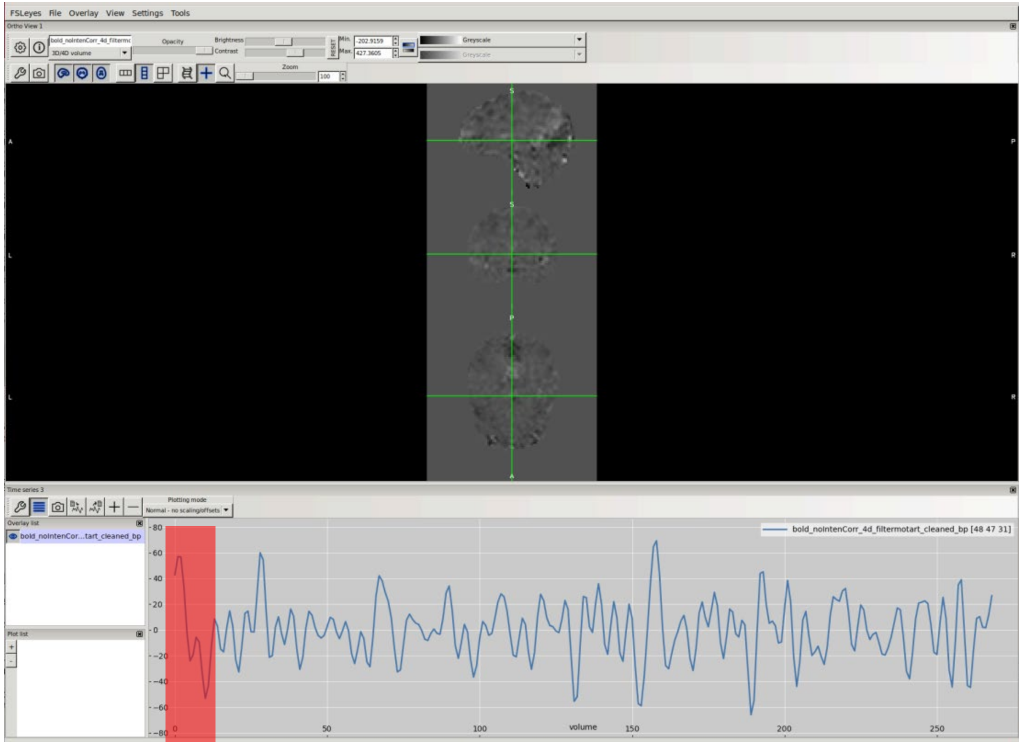


Resting-state fMRI (rs-fMRI)

Problem: fMRI is very noisy
How to Improve SNR ?

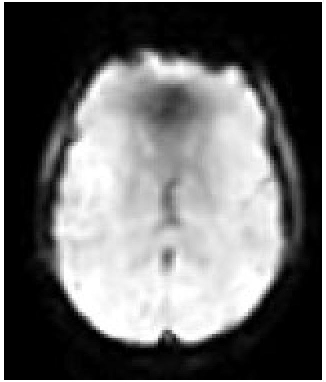
Excellent Tutorial:
http://www.newbi4fmri.com

Omit first N Time Points

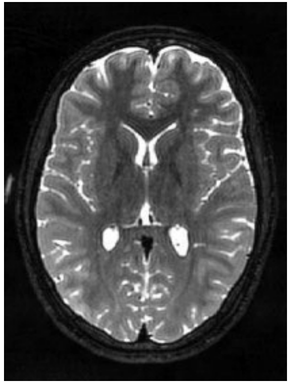


Brain Tissue Segmentation

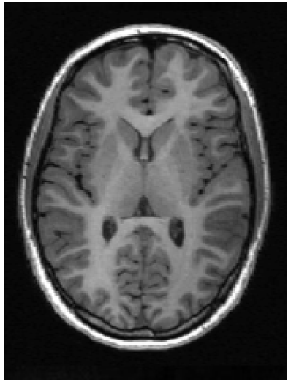
Register



Mean B0

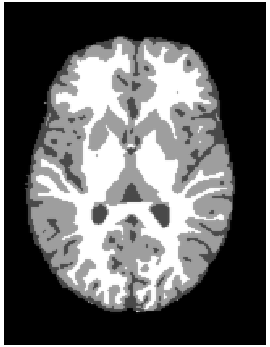


T2w



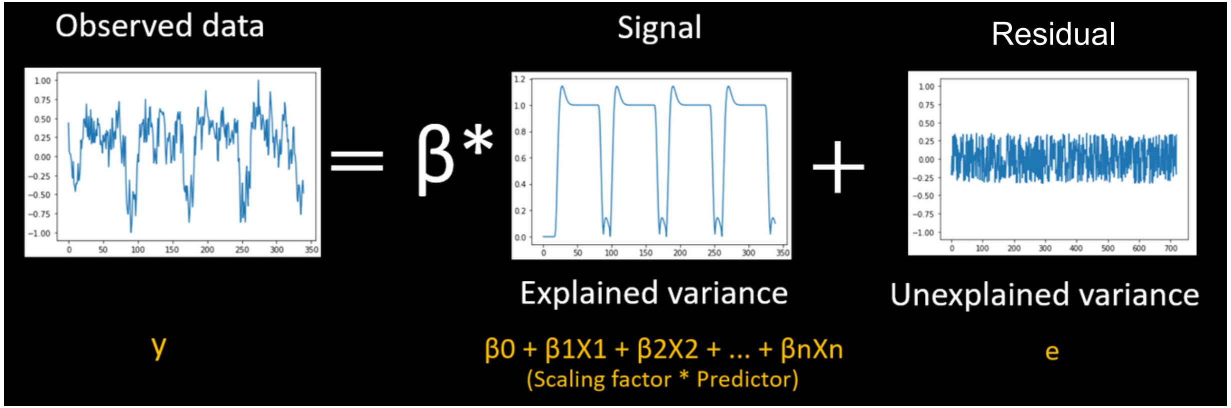
T1w

Transform

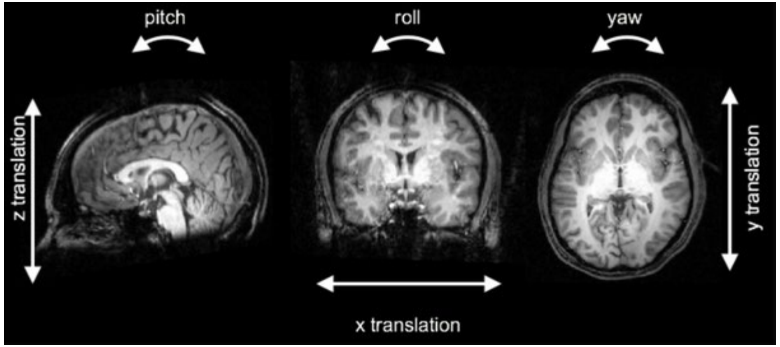


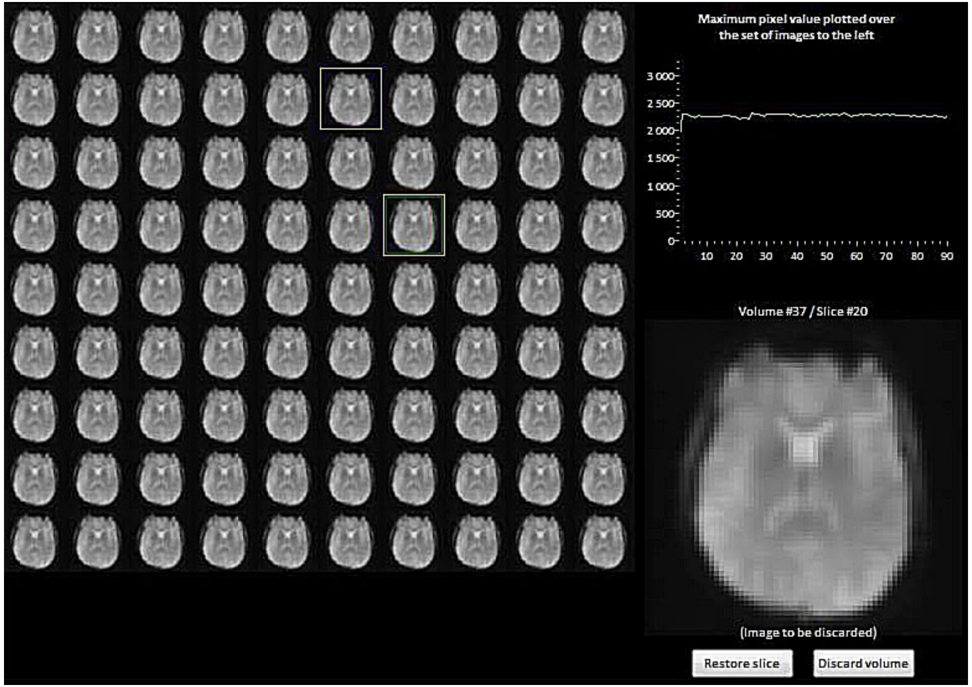
Remove Physiological Noise

- factors related to the participant such as head and body motion, breathing and cardiac pulsations, as well as performance factors such as fluctuations in alertness.
- Factors removed by fitting General Linear Model



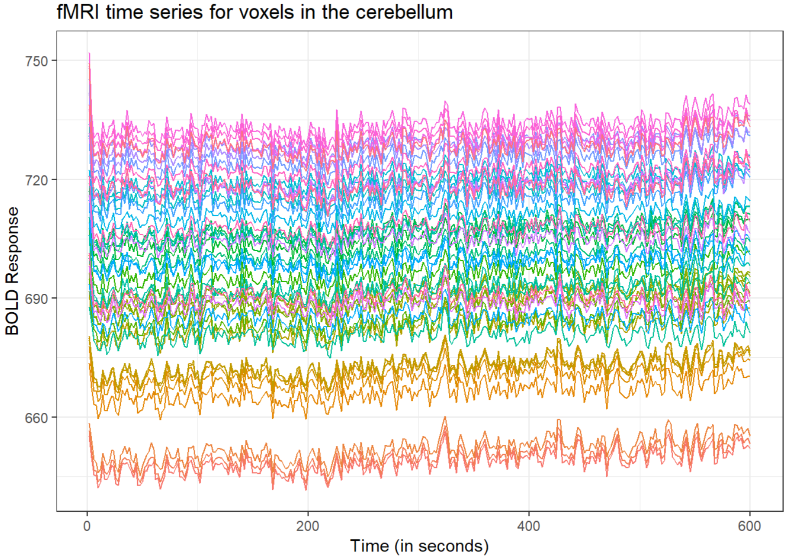
Detect Motion Outliers





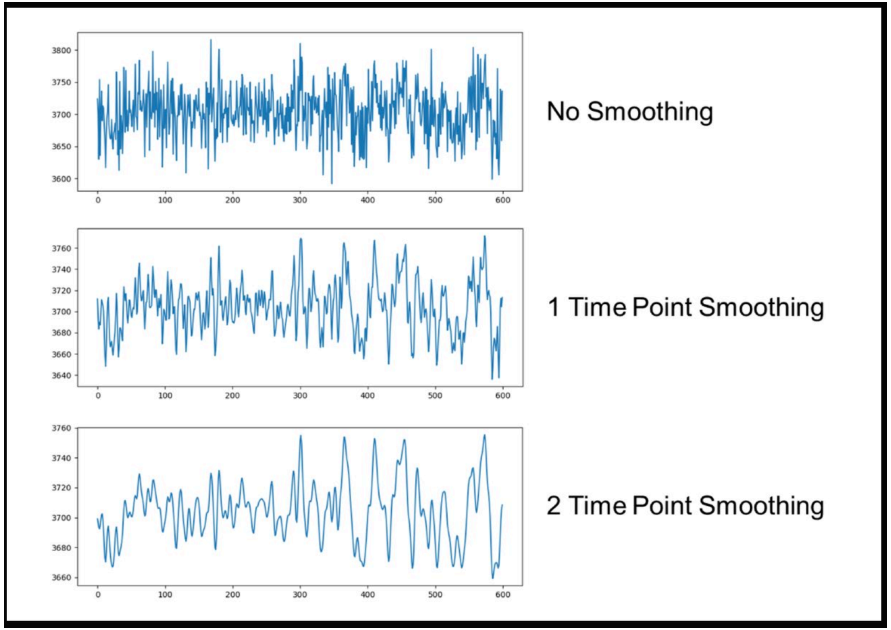
Detrending

Removes linear and polynomial drift possible arising from scanner instability



[Demo]

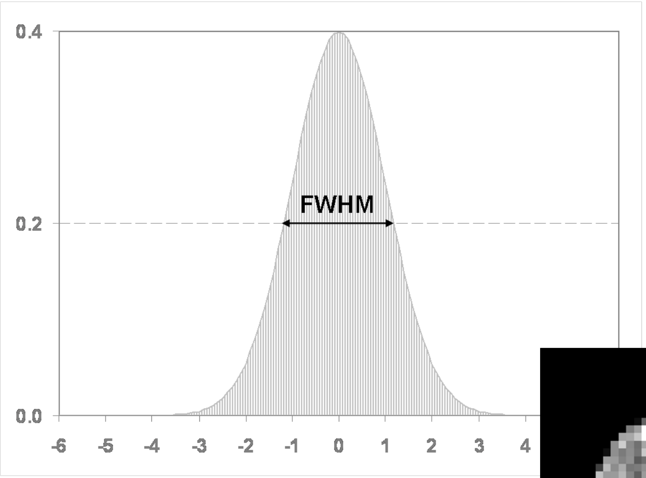
Temporal Smoothing



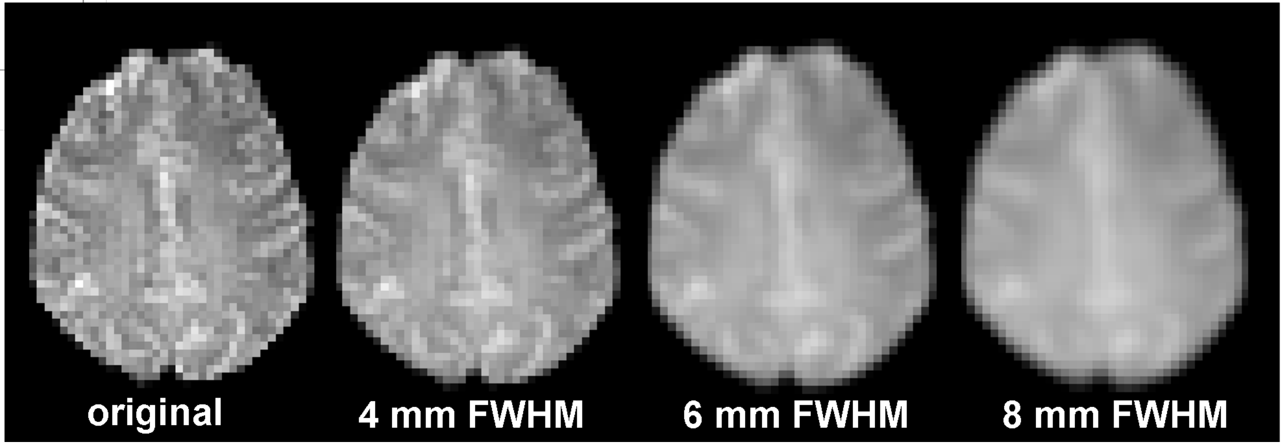
http://www.newbi4fmri.com/tutorial-6-filtering

Demo

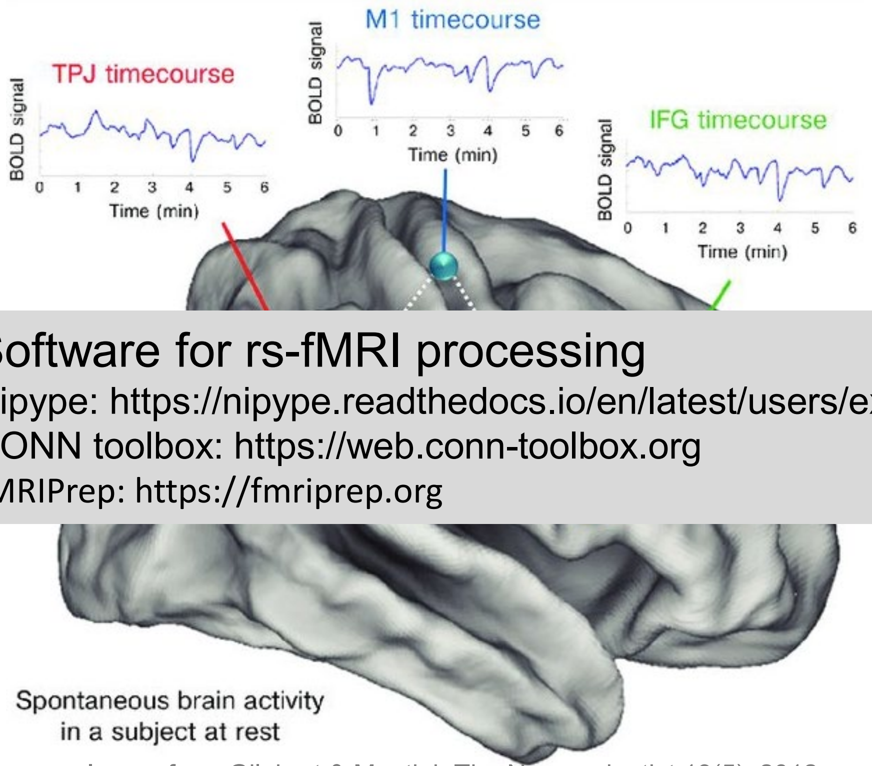
Spatial Smoothing

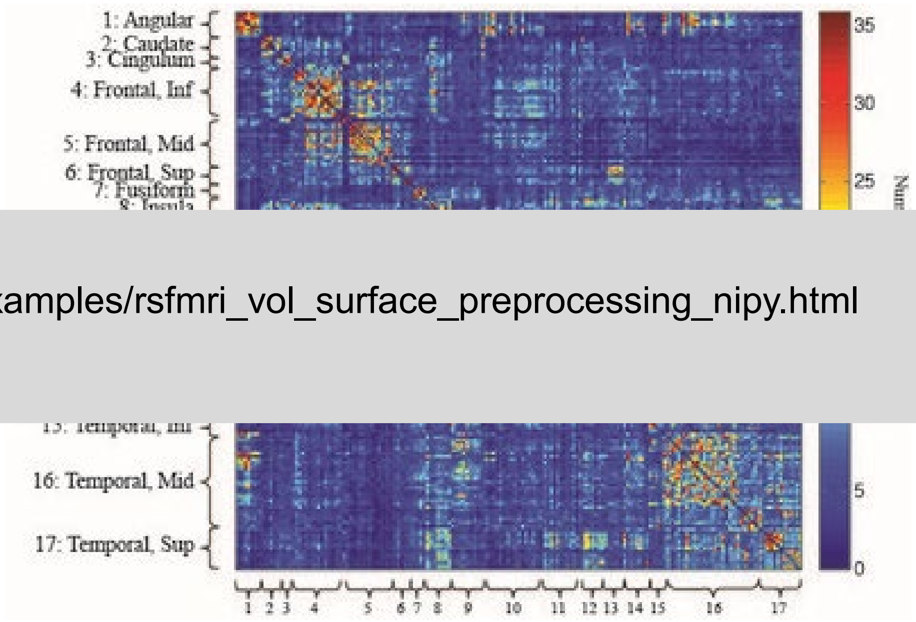


Full Width at Half Maximum



Correlate ROI Bold Signals





Software for rs-fMRI processing

Nipype: https://nipype.readthedocs.io/en/latest/users/examples/rsfmri_vol_surface_preprocessing_nipy.html
CONN toolbox: https://web.conn-toolbox.org
fMRIPrep: https://fmriprep.org

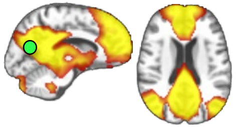
Image from Gilebert & Mantini, The Neuroscientist 19(5), 2012

Problems with rs-fMRI Processing

- Harmonizing functional connectivity across scanners

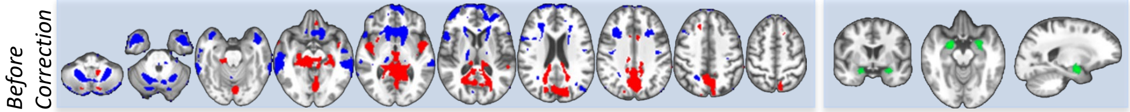
EM Müller-Oehring et al. *Cerebral Cortex*, 2018

Default Mode Network (DMN)



Posterior Cingulate Cortex (PCC) seed

Manufacturer **Alcohol**



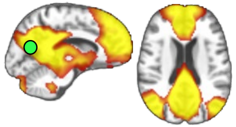
Manufacturer	GE > Siemens	Siemens > GE
Alcohol	no/low > exceeds	exceeds > no/low alcohol

Problems with rs-fMRI Processing

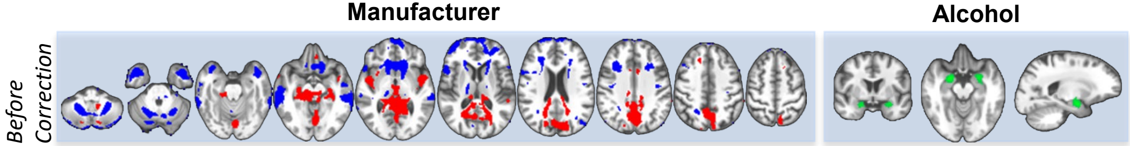
- Harmonizing functional connectivity across scanners

EM Müller-Oehring et al. *Cerebral Cortex*, 2018

Default Mode Network (DMN)



Posterior Cingulate Cortex (PCC) seed



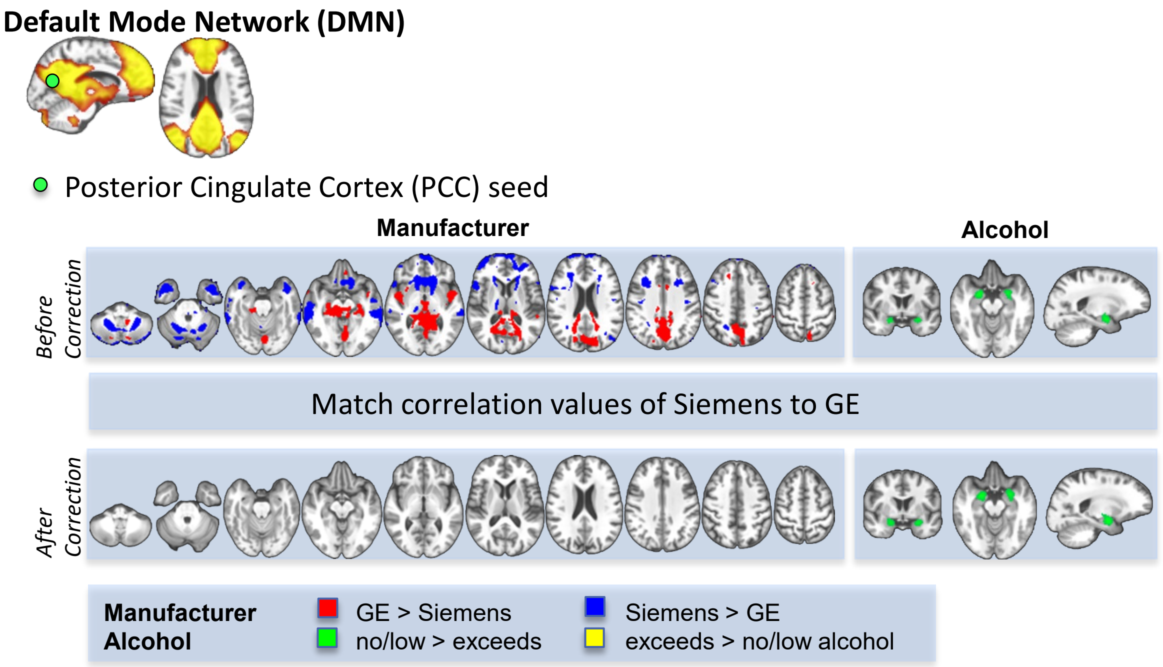
Match correlation values of Siemens to GE

Manufacturer	GE > Siemens	Siemens > GE
Alcohol	no/low > exceeds	exceeds > no/low alcohol

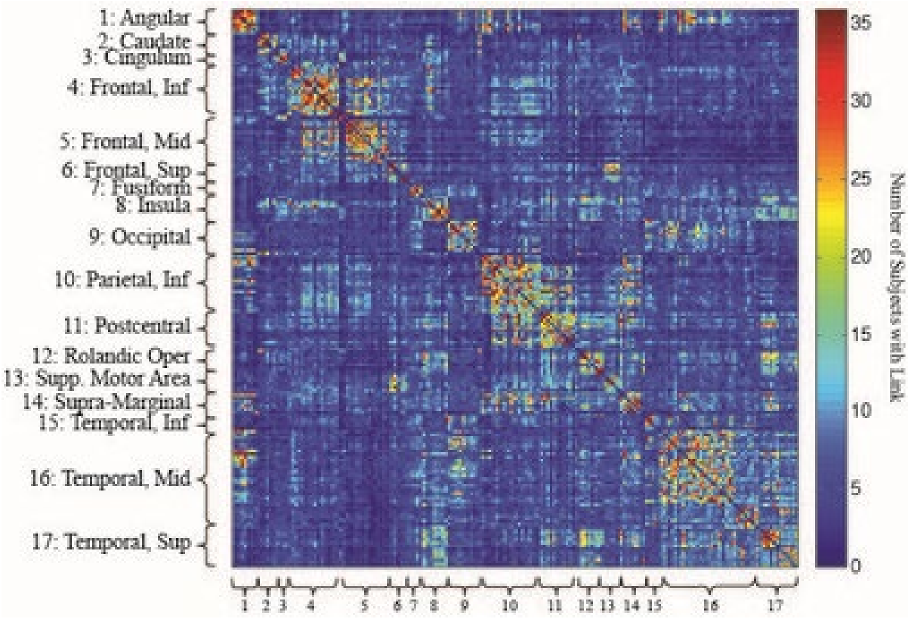
Problems with rs-fMRI Processing

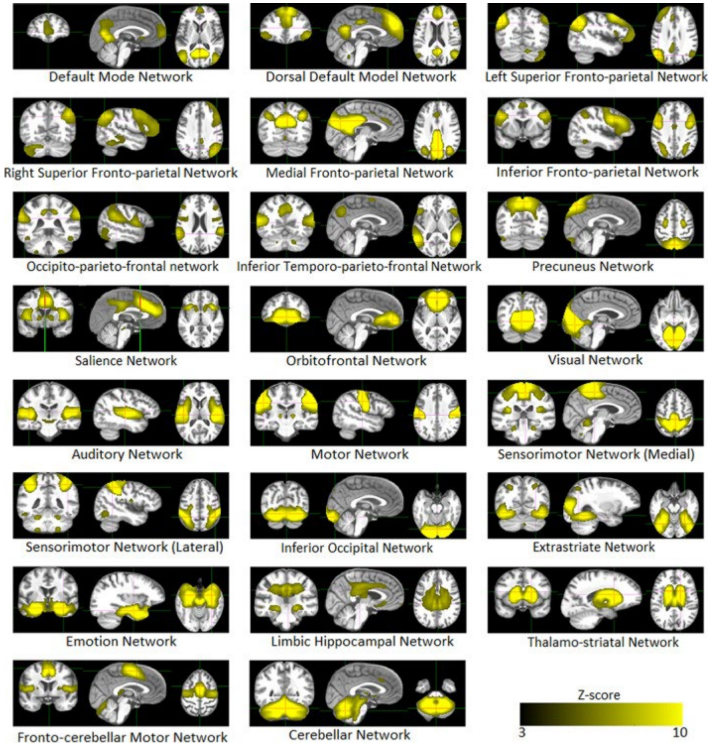
- Harmonizing functional connectivity across scanners

  EM Müller-Oehring et al. *Cerebral Cortex*, 2018

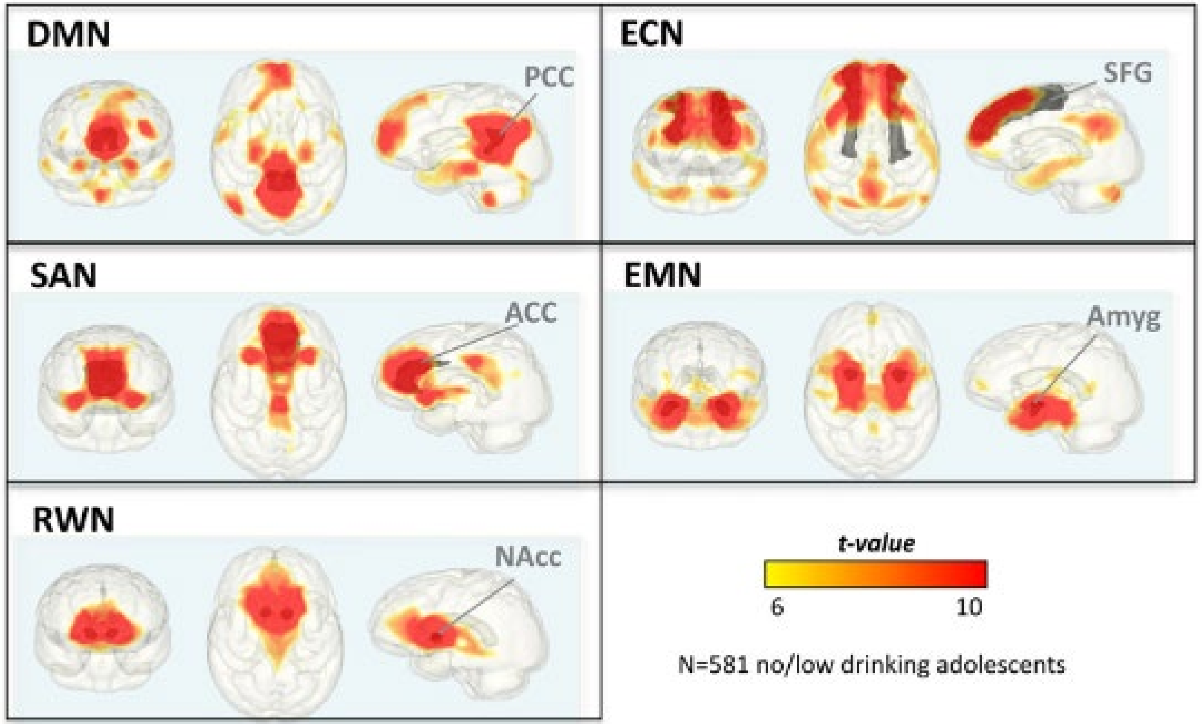


Identify Networks (via ICA)



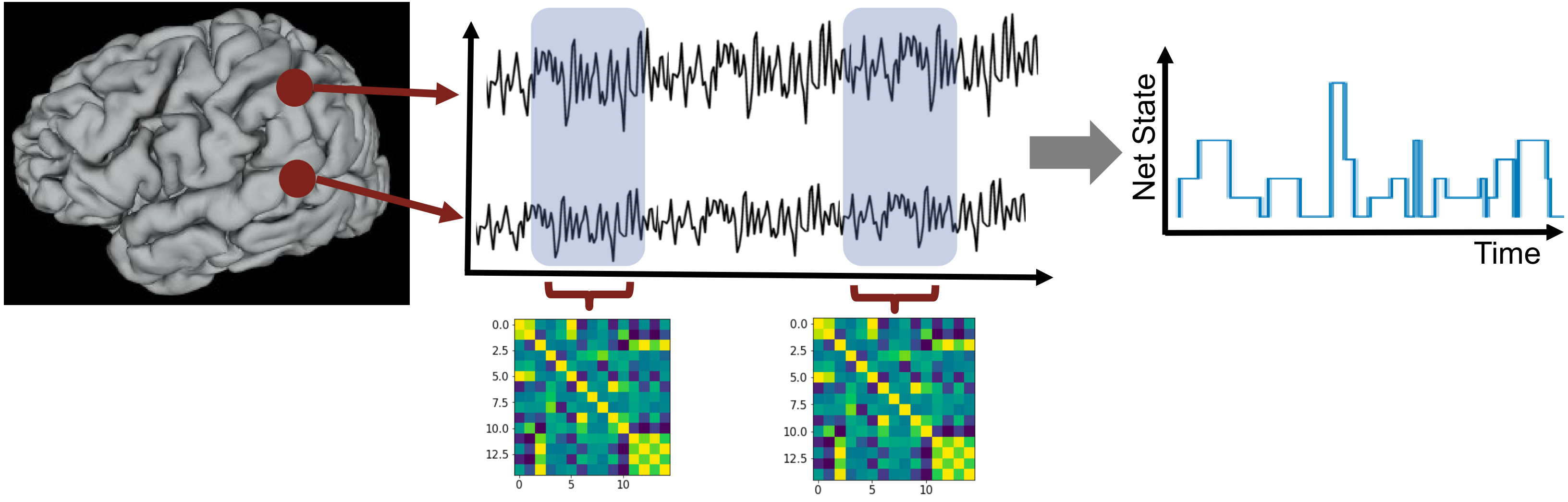


Select Specific Seed Regions



Dynamic Functional Networks

So far assumed networks are co-existing and stable during scan
A network is dominant for only short period of time



Today…

- MRI Processing
- Tools for Processing

Python

- Nipy.org: 0verview of neuroimage analysis packages
    - nibabel : Read / write common neuroimaging file formats
    - nipype: Neuroimaging pipelines and interfaces
    - nipy : Analysis of functional MRI
    - dipy: Analysis of diffusion MRI
    - nilearn: Fast and easy statistical learning on neuroimaging data (have not used it myself)
    - tutorial: https://nipy.org/nibabel/coordinate_systems.html#introducing-someone

- Machine/deep learning packages
    - tensorflow: end-to-end deep learning platform with excellent visualization
    - pytorch: popular deep learning platform
    - keras: high-level neural network library that runs on top of TensorFlow
    - scikit-learn: traditional machine learning models

- Miscellaneous:
    - pandas: data analysis and manipulation tool
    - numpy: basic operations such as sorting, indexing, and elementary mathematical functions on arrays
    - scipy: algorithms for optimization, interpolation, statistics and many other classes of problems
    - matplotlib: plotting graphs
    - math: simple mathematical operations
    - os: operating system interface

Other Software Packages

- C++ :
  - VTK: visualization toolkit
  - ITK: extensive suite of software tools for image analysis
- Matlab:
  - SPM: software package designed for the analysis of brain imaging data (www.fil.ion.ucl.ac.uk/spm/)
- Command line tools for processing and visualization:
  - ITKSnap : (interactive) segmentation tool for structural MRIs
  - Mango: viewer for medical research images.
  - 3DSlicer: Visualization and editing tool
  - Freesurfer: analysis and visualization of structural, functional, and diffusion neuroimaging data
  - FSL: analysis and visualization of structural, functional, and diffusion neuroimaging data
  - ANTS: state-of-the-art medical image registration and segmentation toolkit (http://stnava.github.io/ANTs)
  - AFNI: analysis and visualization of structural, functional, and diffusion neuroimaging data
  - Convert3D: a command-line image processing tool offering complementary features to ITK-SNAP
  - Camino: toolkit for diffusion MRI processing
  - CMTK: analysis and visualization of structural neuroimaging data

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Extra Class Session (4 Unit Students)

And the winner is …

Thursdays 5 - 6:20 pm

Thank you!

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