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An introduction to brain image processing and it's softwares

(with a focus on MRI tools)

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Outline

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- **The purpose is to study:**
 - ✓ How are the healthy brain functions
 - ✓ How cognitive states are encoded in the brain activities
 - ✓ How different diseases affect the brain functions
 - ✓ How healthy brain function is recovered after damage
 - ✓ How drugs can control the diseases effect on the brain activity
- Which MRI modality should I use?
- To answers these questions we require some softwares to extract information about the different stimuli
- There is no single package that can provide all the necessary analyses



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- **There is no single package that can provide all the necessary analyses**



Motivation

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- There are many ways of examining the brain .Depends on:
 - The question you want to ask
 - The data you have
 - The available software



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Outline

- The research groups prefer to consider “**which available software package will be useful for their needs?**”
- The features of software package that must be considered :
 - ✓ Address/availability
 - ✓ Platform/operating system
 - ✓ Input of data
 - ✓ Preprocessing
 - ✓ Image display
 - ✓ Region of interest (ROI) analysis
 - ✓ Statistical model

MRI-T1

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fMRI



DTI



T1 weighted
magnetic resonance image

Functional magnetic
resonance imaging

Diffusion tensor
imaging

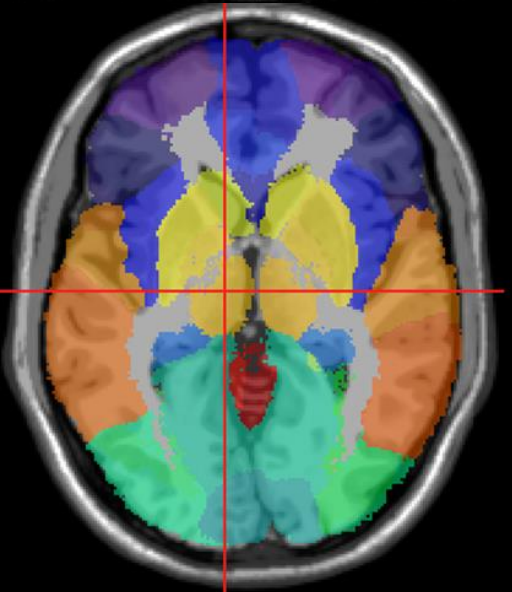


MRI-T1

fMRI

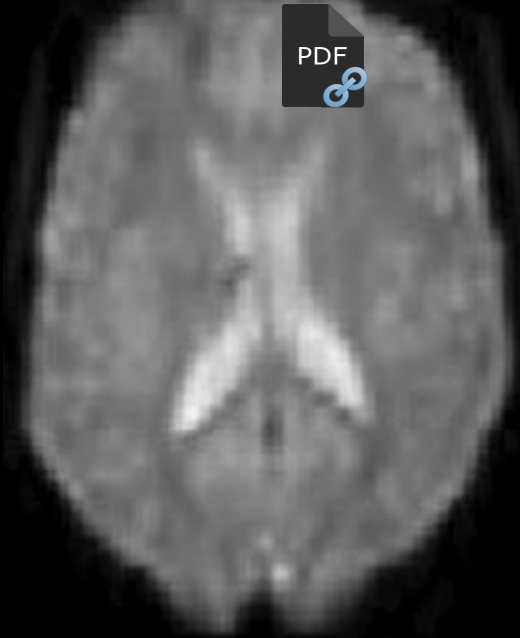
DTI

MRI-T1

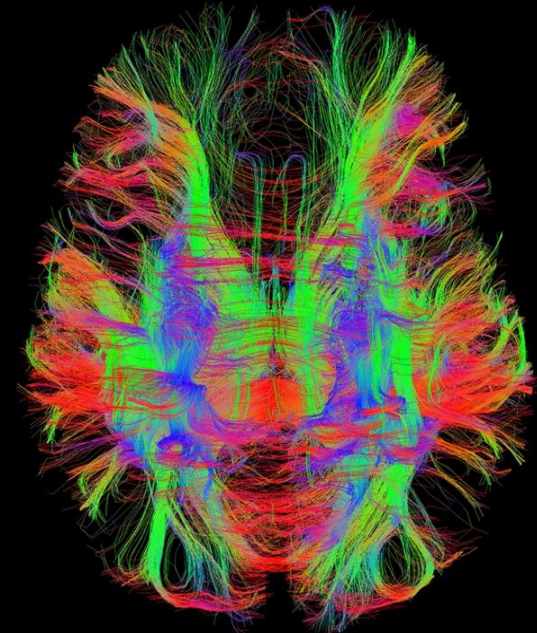
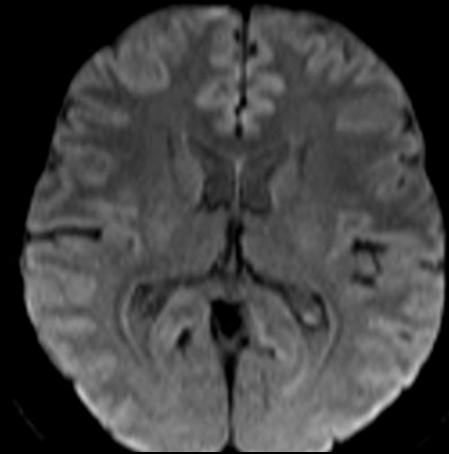


fMRI

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DTI



MRS

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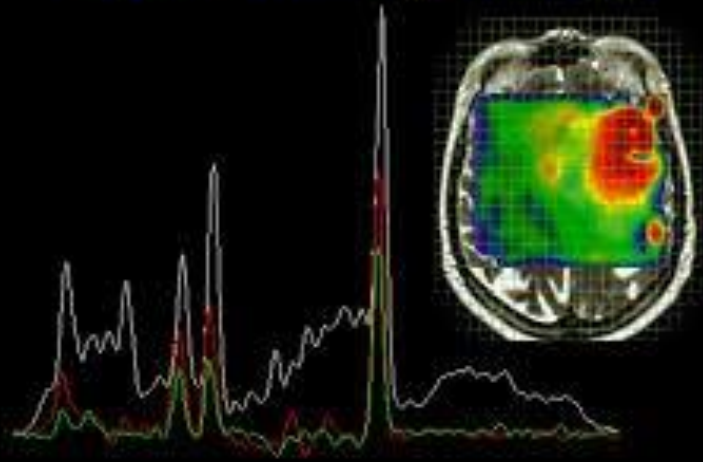
PWI



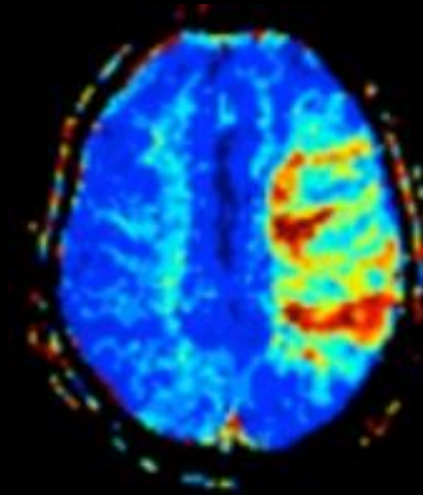
Magnetic Resonance Spectroscopy

Perfusion-weighted imaging

Magnetic Resonance Spectroscopy



MRS



PERFUSION

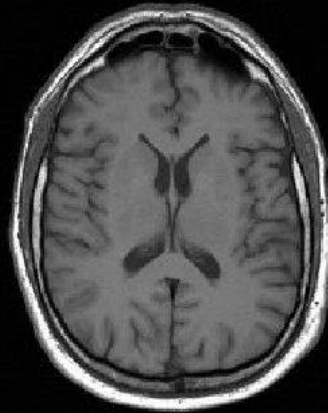
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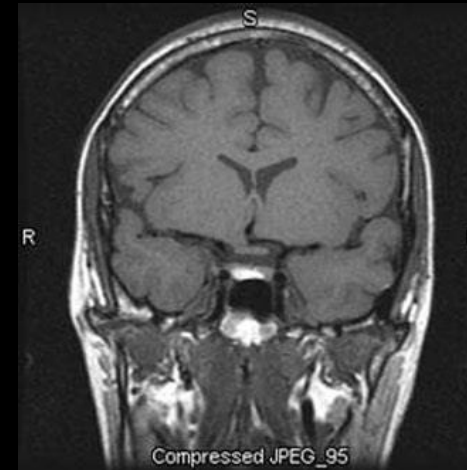
sagittal



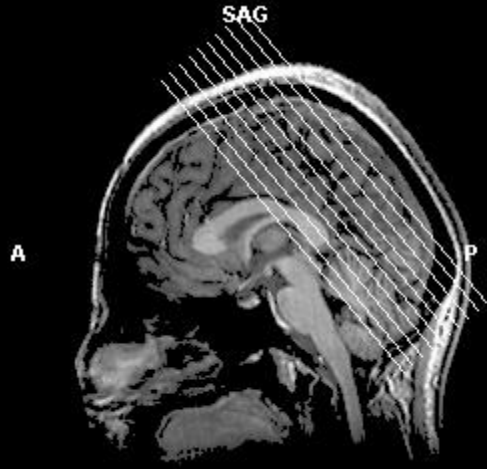
axial



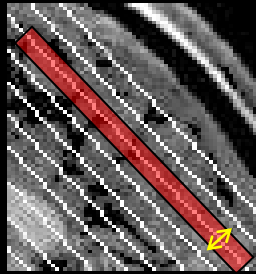
cronal



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SAGITTAL SLICE



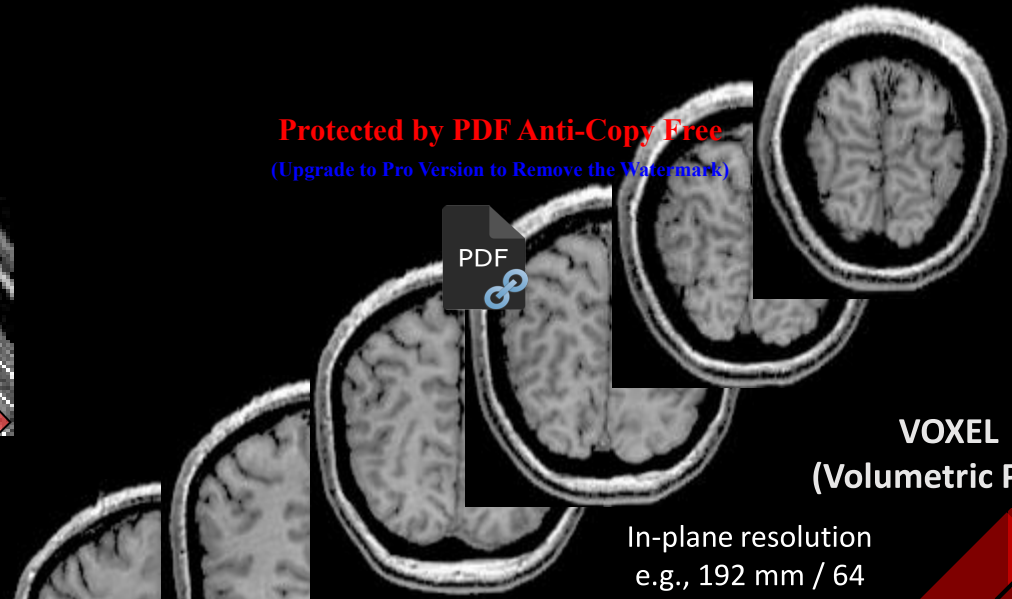
Slice Thickness
e.g., 6 mm

Number of Slices
e.g., 10



Matrix Size
e.g., 64 x 64

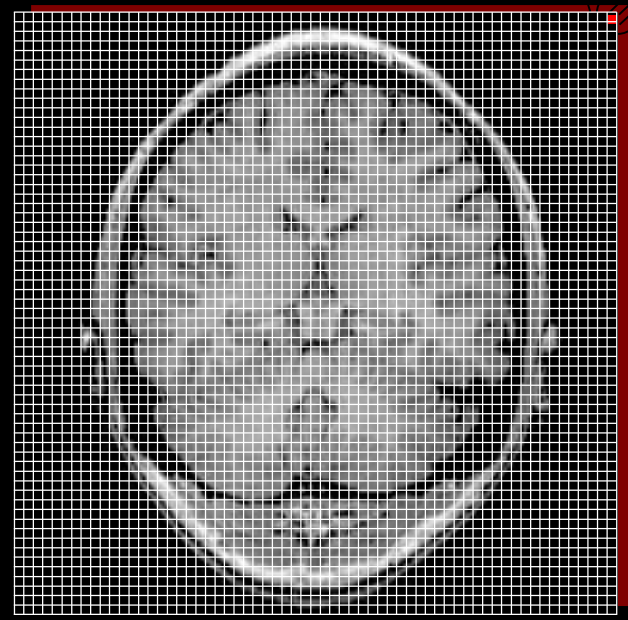
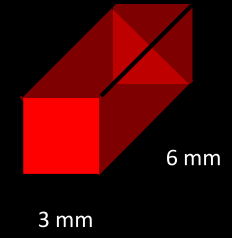
Field of View (FOV)
e.g., 19.2 cm



IN-PLANE SLICE

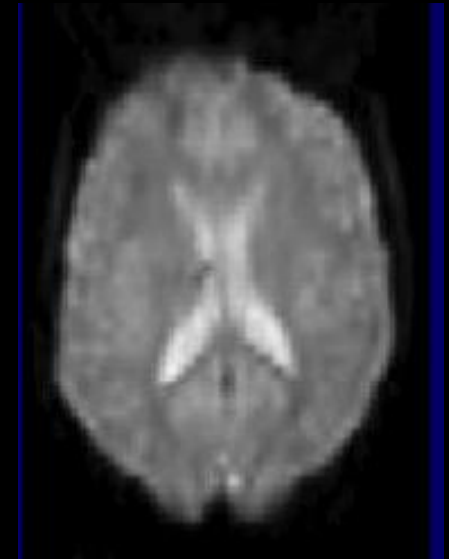
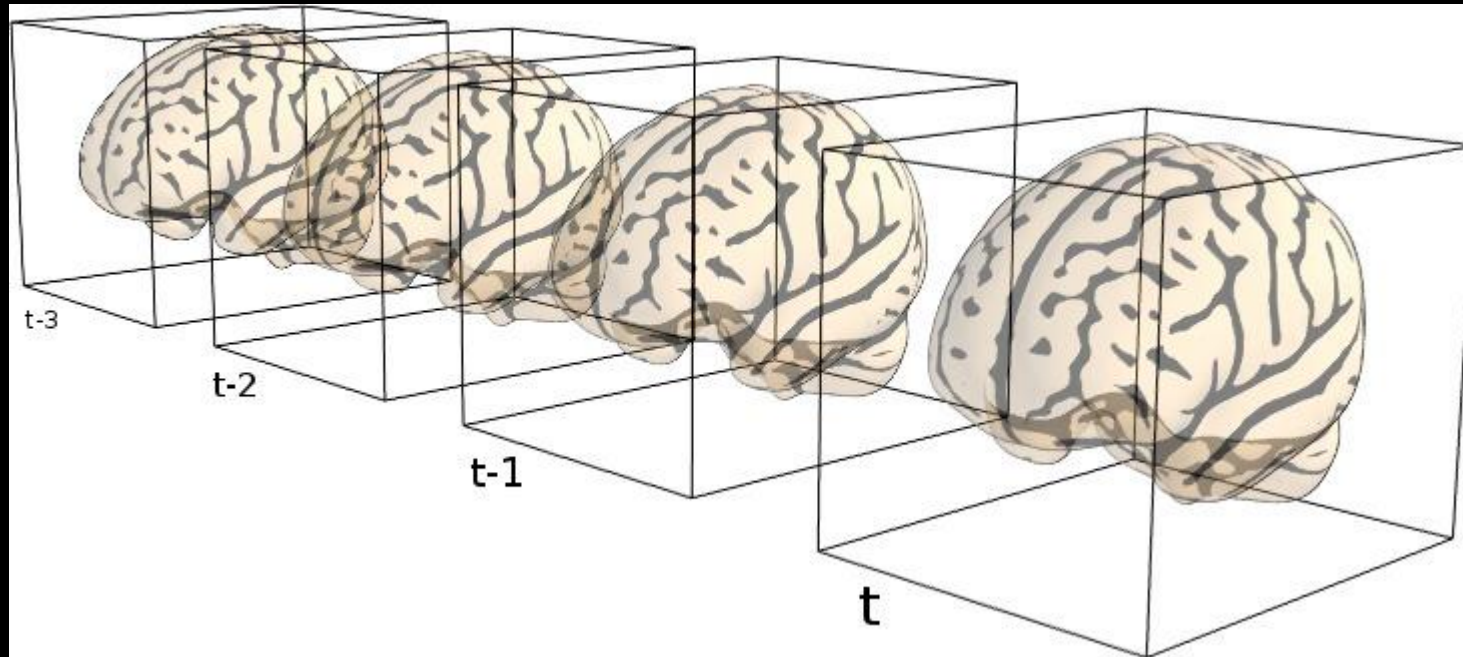
In-plane resolution
e.g., 192 mm / 64
= 3 mm

**VOXEL
(Volumetric Pixel)**



fMRI

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MRI-T1

T1 weighted
magnetic resonance image

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Psychiatry Research: Neuroimaging 287 (2019) 70–74



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Psychiatry Research: Neuroimaging

journal homepage: www.elsevier.com/locate/psychresns



Brain volumes and their ratios in Alzheimer's disease on magnetic resonance imaging segmented using Freesurfer 6.0



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^b Charles University, Third Faculty of Medicine, University Hospital Královské Vinohrady, Department of Neurology, AD Center, Šrobárova 50, 100 34 Prague 10, Czechia

^c Institute of Clinical and Experimental Medicine, Czechia



Morphometric analysis

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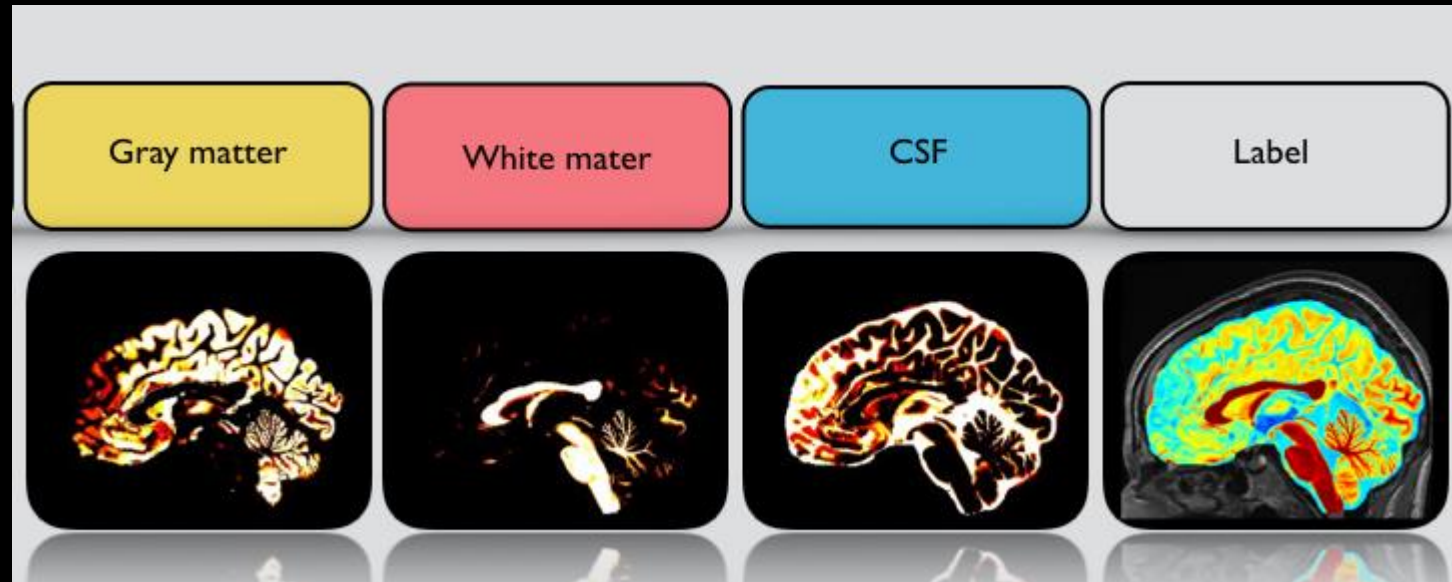


- **Morphometric methods :**
 - ✓ **Voxel-based morphometry (VBM)**
 - ✓ **Surface-based morphometry (SBM)**
 - ✓ **Deformation-based morphometry (DBM)**
 - ✓ **Region- or label-based morphometry (RBM)**

Voxel-based morphometry (VBM)



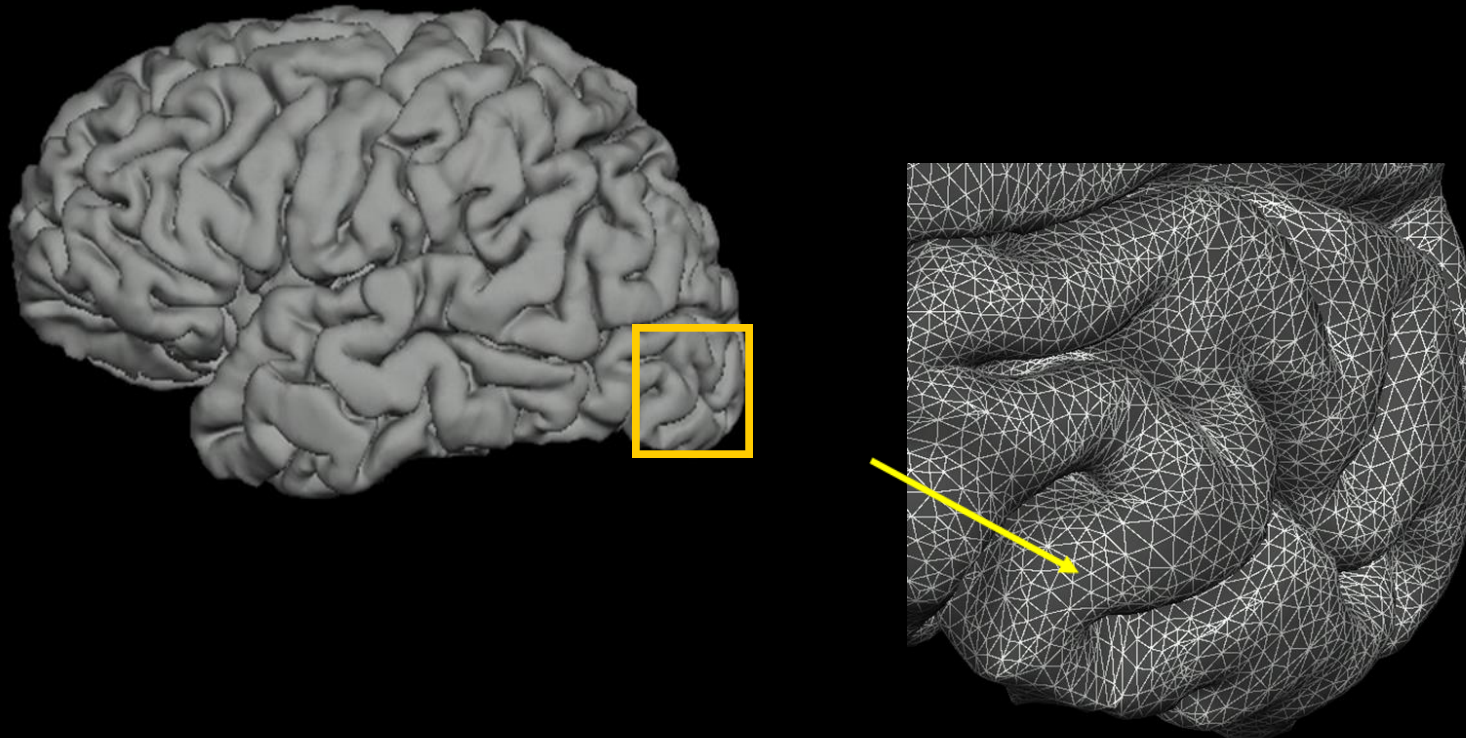
- VBM provides the voxel-wise estimation of the local amount or volume of a specific tissue compartment



Surface-based morphometry (SBM)

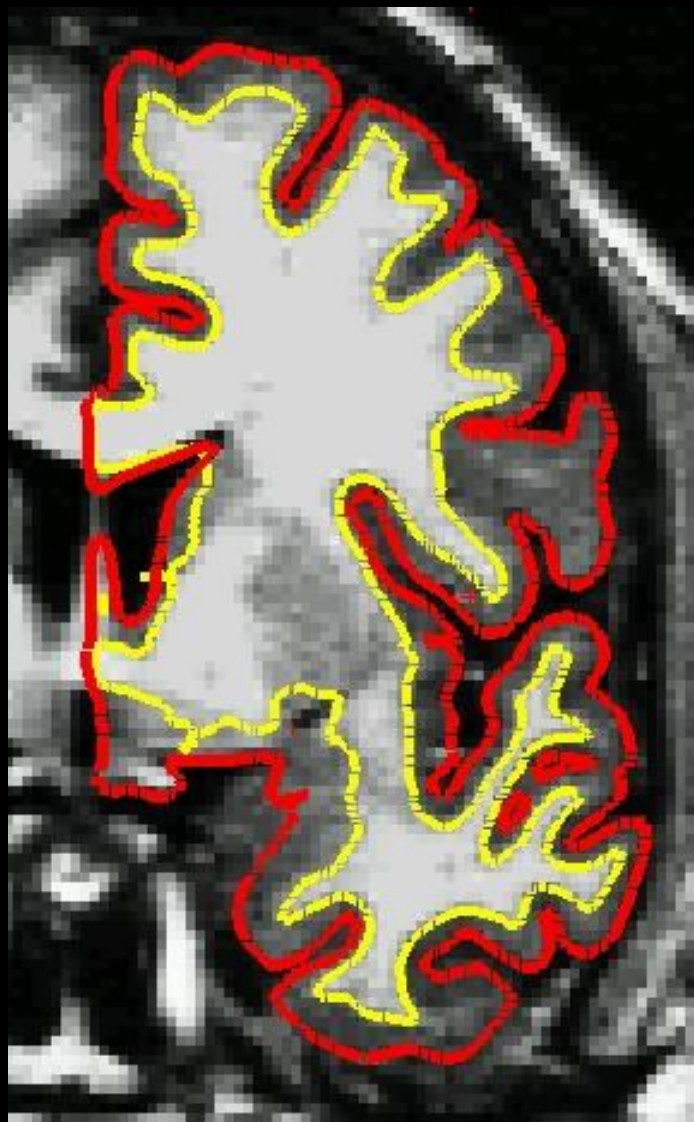
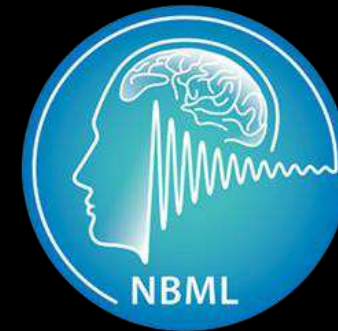


- Estimation of the cortical thickness and central surface of the left and right hemisphere.

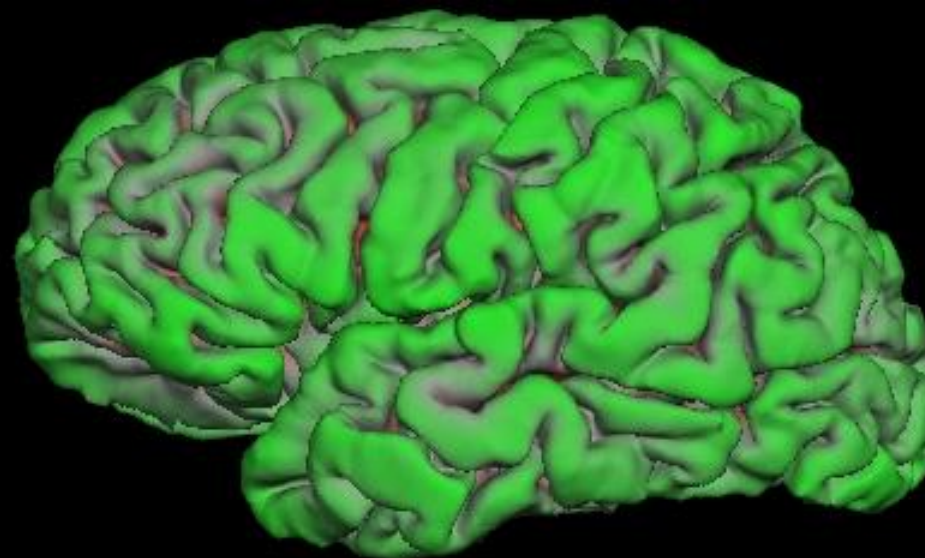


Surface-based morphometry (SBM)

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Surface reconstruction



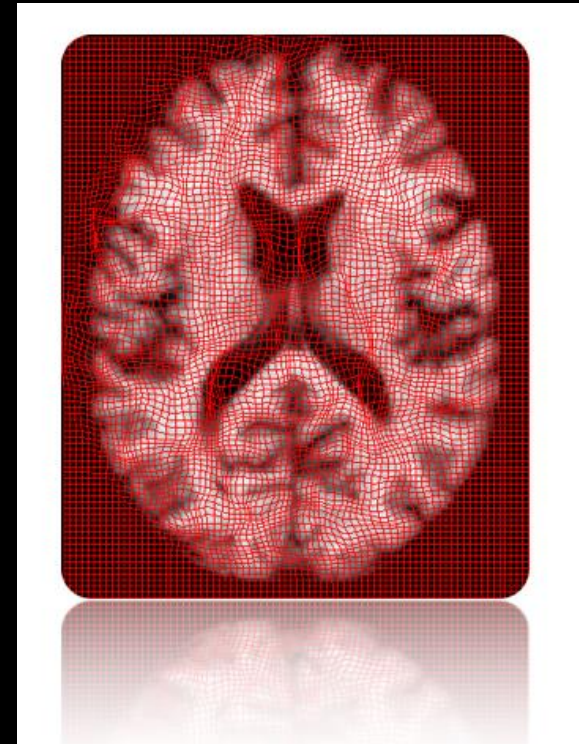


Deformation-based morphometry (DBM)

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- DBM is based on the application of non-linear registration procedures to spatially normalise one brain to another one.





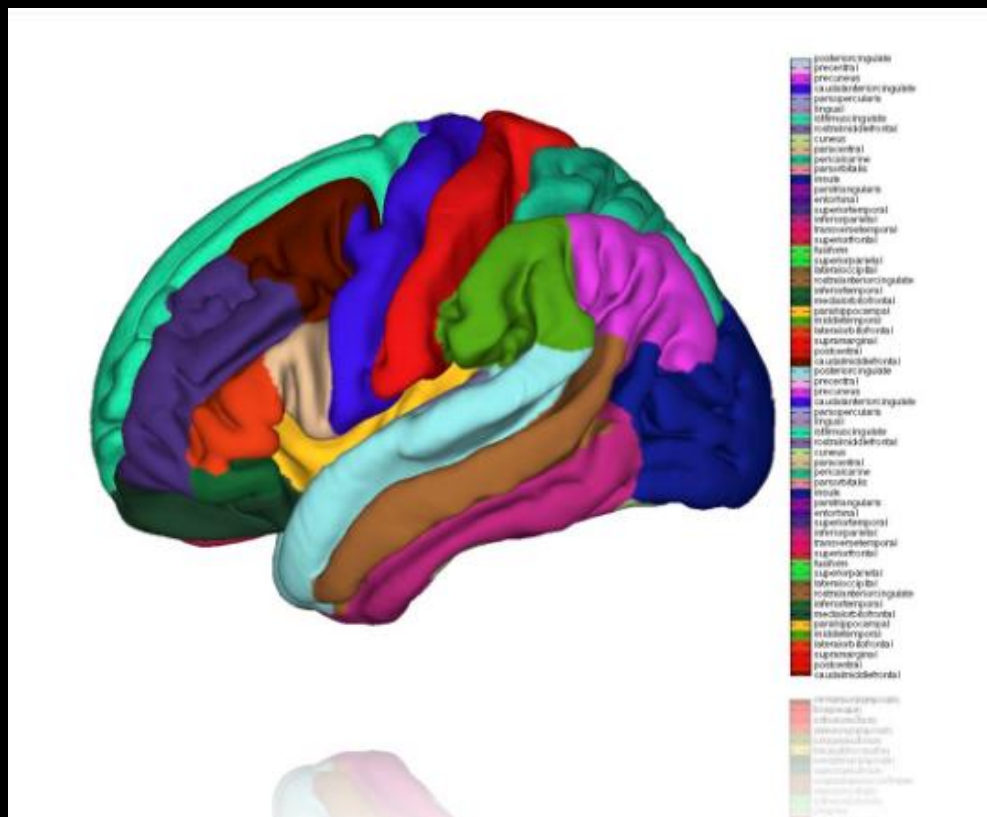
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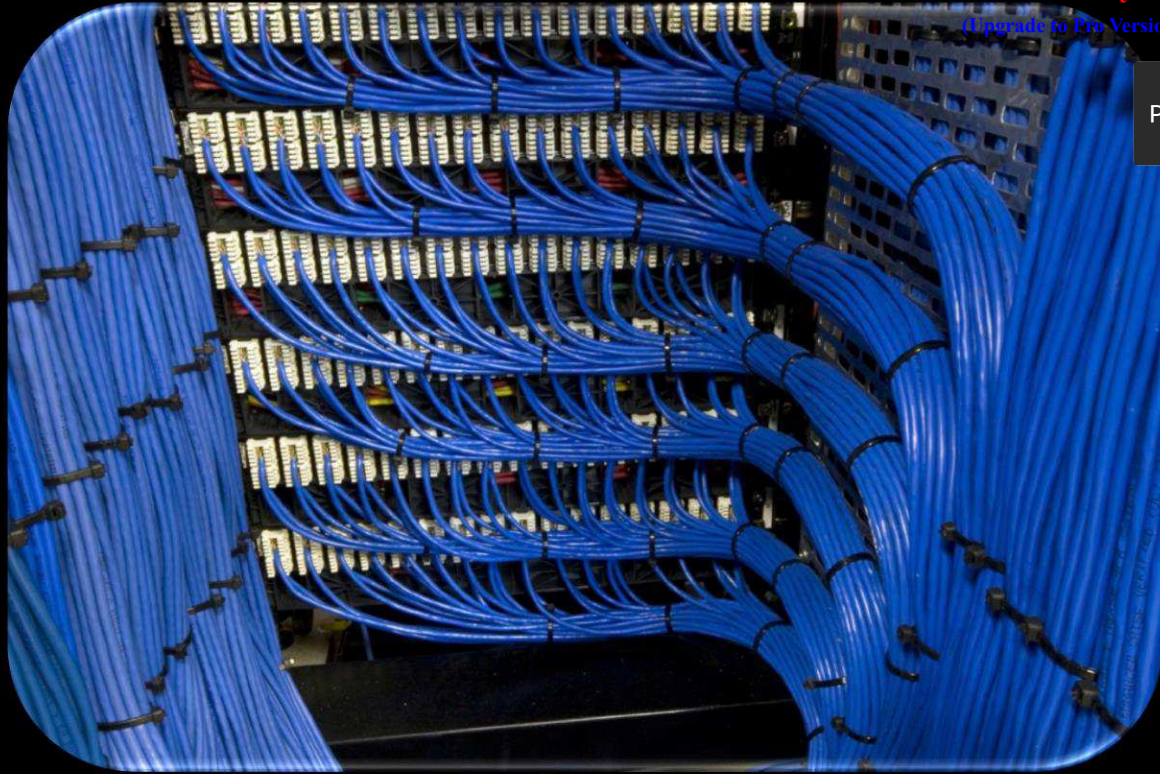
Region- or label-based morphometry (RBM)



- Estimation of regional tissue volumes (and optionally cortical thickness values) for different volume and surface-based atlas maps

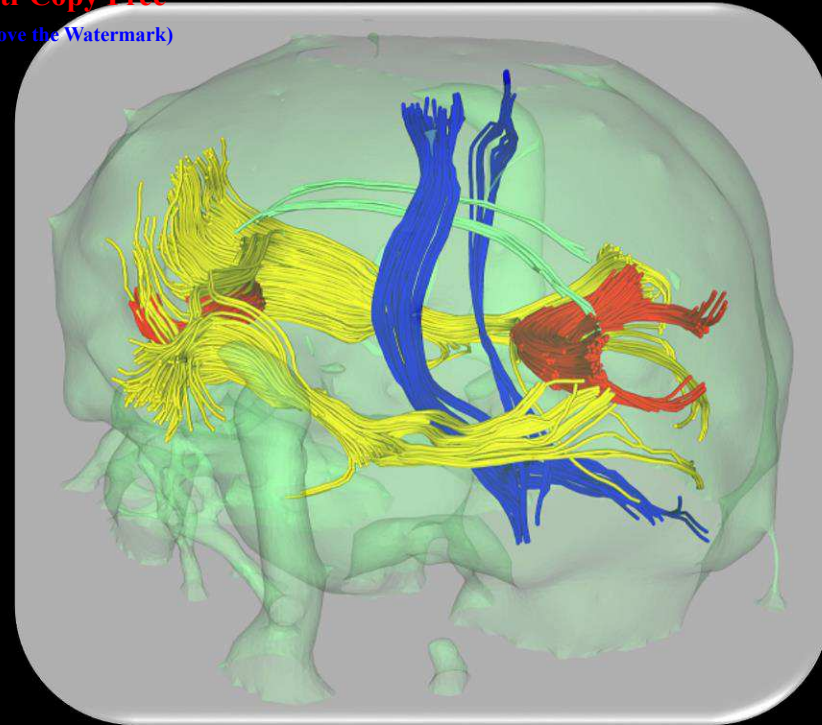


DTI:



UNC Computer Science: Network wire cabinets

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An introduction to diffusion tensor image analysis-lauren-2011

Diffusion Tensor Imaging (DTI)

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IOS Press

Accepted 13 January

Cerebellar White Matter Disruption in Alzheimer's Disease Patients: A Diffusion Tensor Imaging Study

Sofia Toniolo^{a,b}, Laura Serra^a, Giusy Olivito^a, Carlo Caltagirone^{b,c}, Nicola B. Mercuri^b, Camillo Marra^d, Mara Cercignani^e and Marco Bozzali^{a,e,*}

^a*Neuroimaging Laboratory, Fondazione Santa Lucia, IRCCS, Rome, Italy*

^b*Department of Neuroscience, University of Rome 'Tor Vergata', Rome, Italy*

^c*Department of Clinical and Behavioural Neurology, Fondazione Santa Lucia, IRCCS, Rome, Italy*

^d*Institute of Neurology, Catholic University, Rome, Italy*

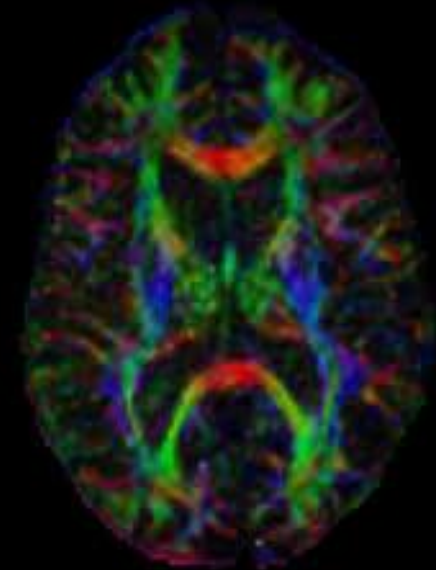
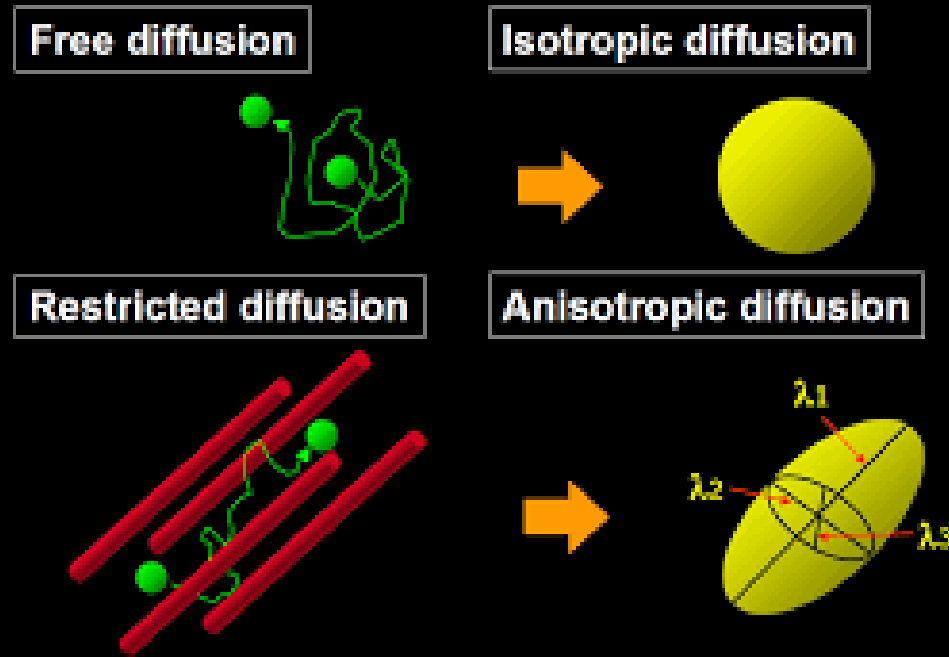
^e*Department of Neuroscience, Brighton and Sussex Medical School, University of Sussex, Falmer, East Sussex, UK*

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diffusion tensor imaging (DTI)



- DTI is a special kind of DWI
- To map white matter tractography in the brain



colored fractional anisotropy map



Diffusion tensor imaging (DTI)

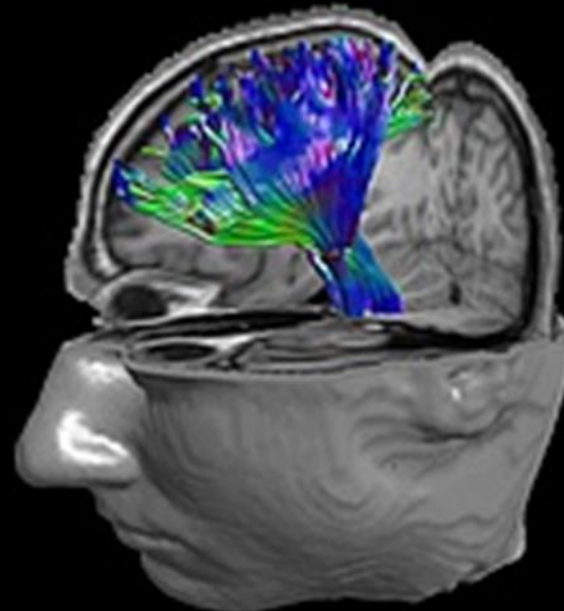
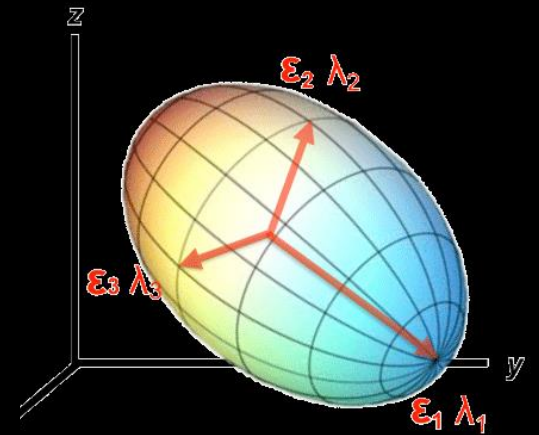
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PDF



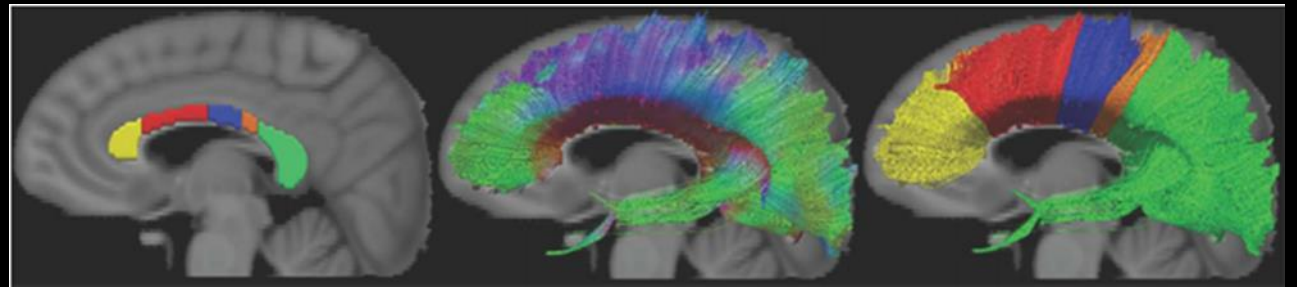
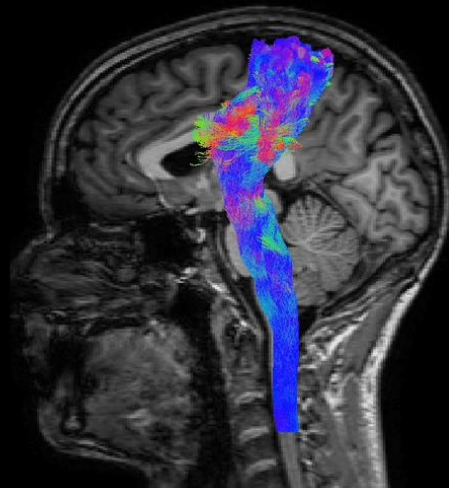
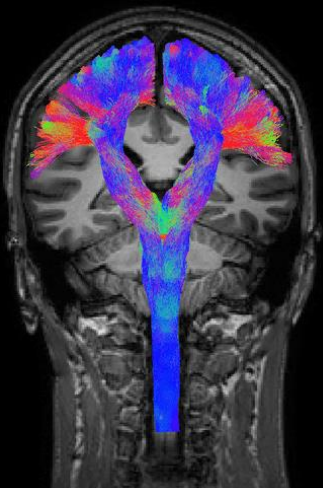
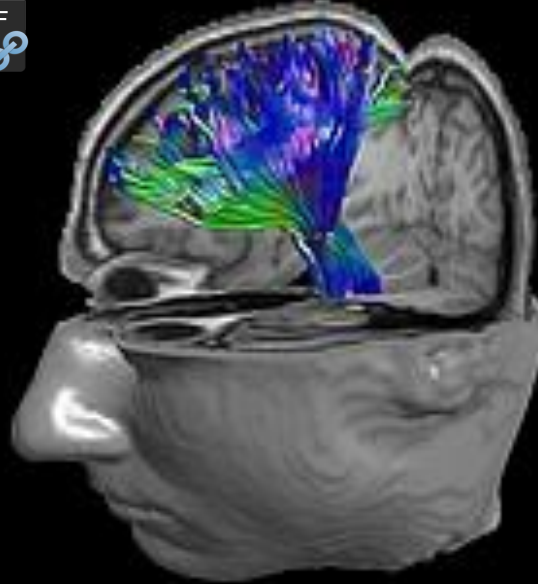
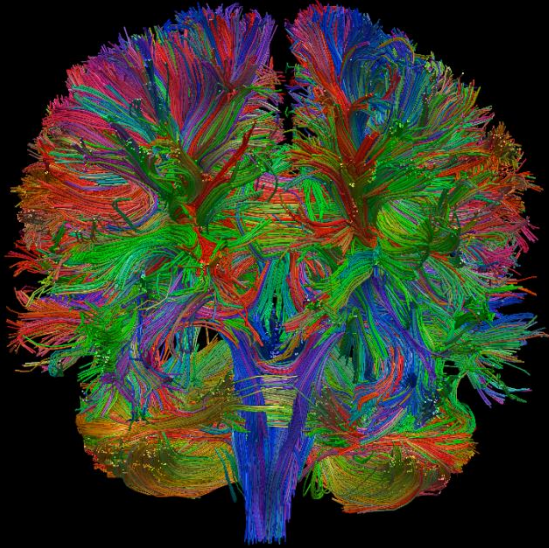
- Fractional anisotropy (FA) is an index for the amount of diffusion asymmetry within a voxel, defined in terms of its eigenvalues:

$$FA = \sqrt{\frac{(\lambda_1 - \lambda_2)^2 + (\lambda_2 - \lambda_3)^2 + (\lambda_1 - \lambda_3)^2}{2(\lambda_1^2 + \lambda_2^2 + \lambda_3^2)}}$$



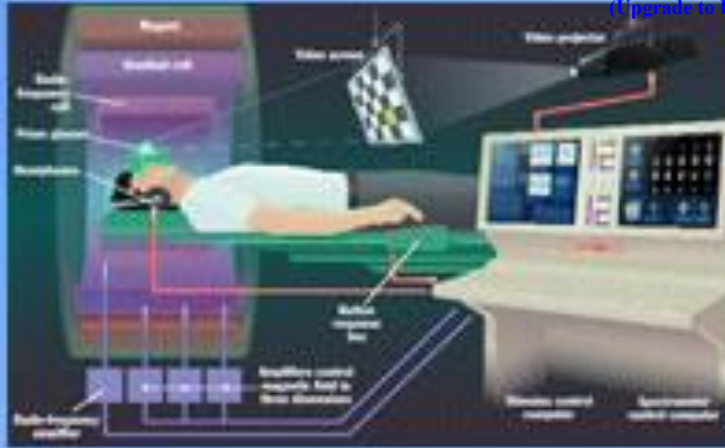
Diffusion tensor imaging (DTI)

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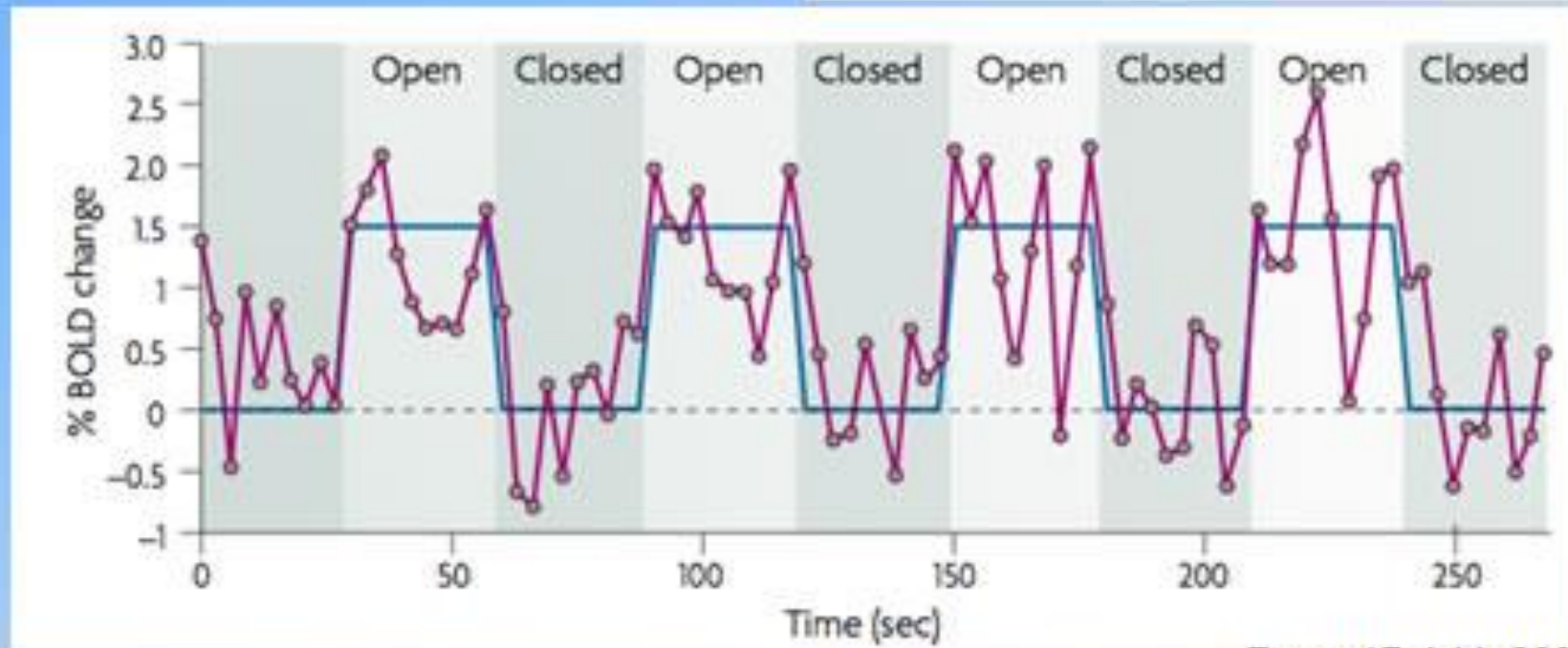
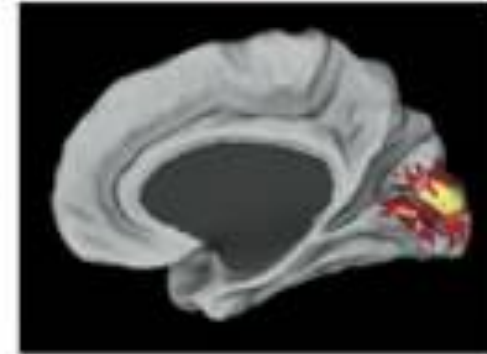


Functional MRI

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Open - Closed =



Fox and Raichle 2007



Functional magnetic resonance imaging (fMRI)

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PDF



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Neurobiology of Aging 32 (2011) S37–S43

*NEUROBIOLOGY
OF
AGING*

www.elsevier.com/locate/neuaging

The potential of functional MRI as a biomarker in early Alzheimer's disease

Reisa Sperling

*Center for Alzheimer Research and Treatment, Brigham and Women's Hospital,
Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA*



Functional magnetic resonance imaging (fMRI)



- fMRI measures brain activity by detecting changes associated with **blood flow**
- Combining with other methods
 - **Physiological measures :**
 - heart rate, breathing, skin conductance (rate of sweating), and eye movements
 - Other brain-imaging techniques :
 - ✓ EEG
 - ✓ Transcranial stimulation
 - ✓ Directs cortical stimulation
 - ✓ Near-infrared spectroscopy (NIRS)

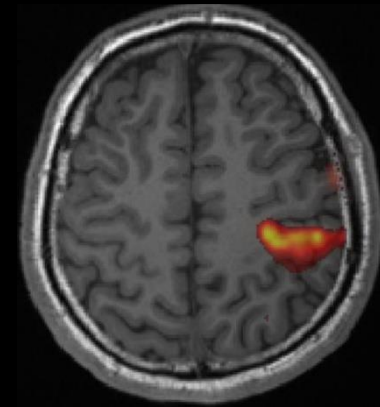


Functional magnetic resonance imaging (fMRI)

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- Issues in fMRI:
 - Task Design
 - Block versus event-related design
 - Artifacts





Functional magnetic resonance imaging (fMRI)

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- **Analysis Steps”**

- **Temporal Processing:**

- ✓ Slice timing

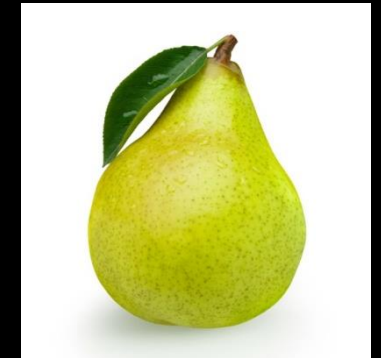
- **Spatial Processing:**

- Realign
 - Co-registration
 - Segmentation
 - Normalization
 - Smoothing

- **fMRI Statistics**

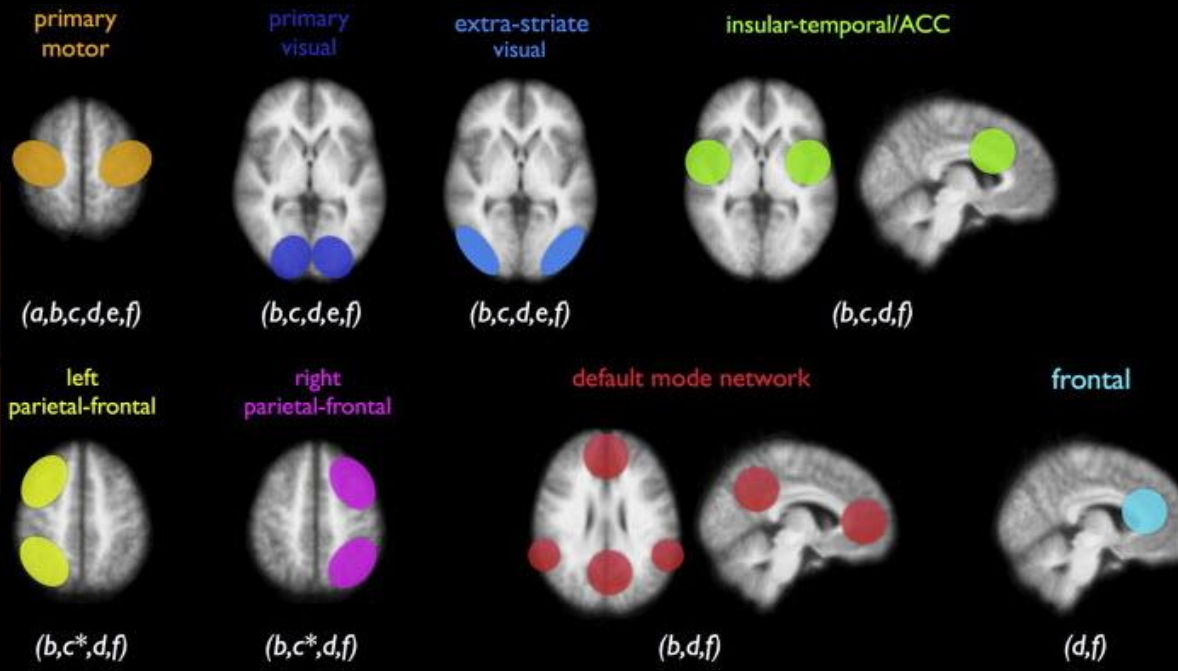
- ✓ fMRI model specification: GLM (spm: using classical or Bayesian approaches)
 - ✓ fMRI model estimate

Normalization



rest fMRI

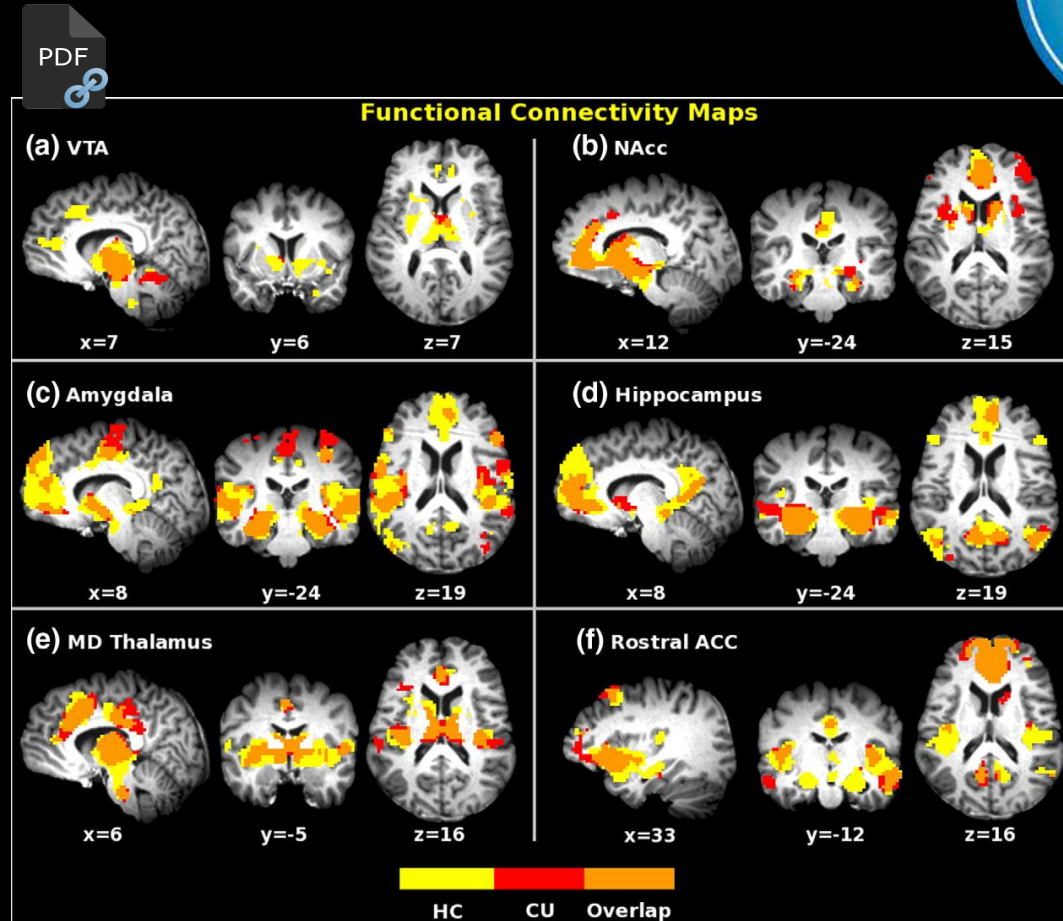
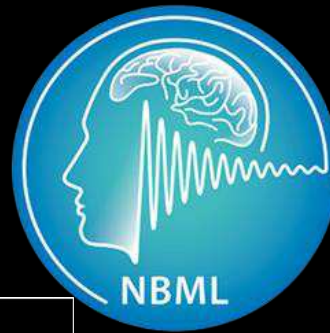
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rest fMRI

Reduced rsFC strength in **cocaine-users** relative to matched non-using controls

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Gu, Hong, et al. , Neuroimage, 2010.

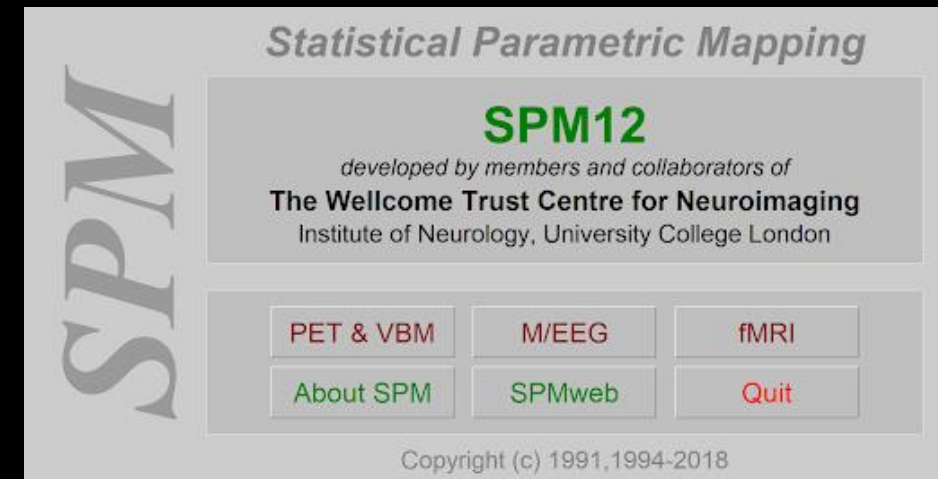


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SPM (Statistical Parametric Mapping)



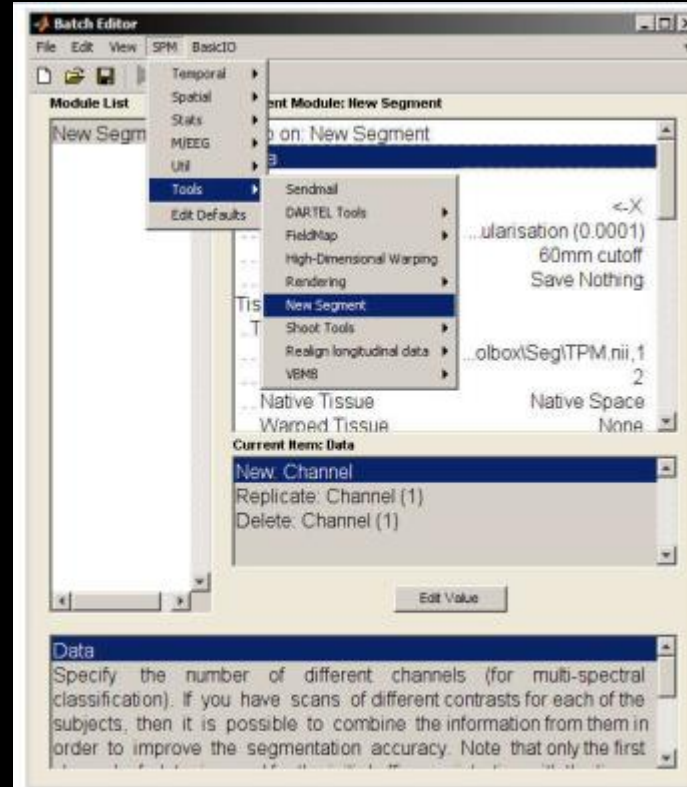
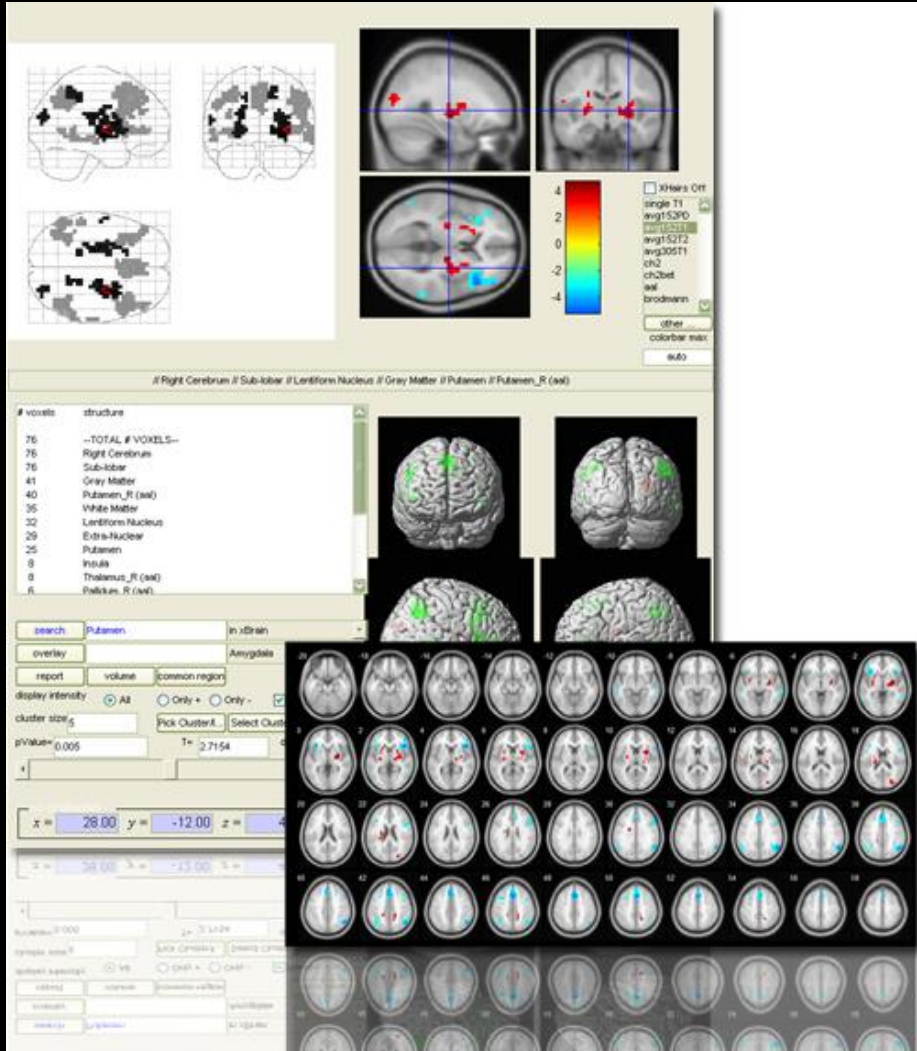
- Developed by at the Functional Imaging Laboratory at University College London.
- Freely available
- Matlab based: Both 32 and 64 bit version of MATLAB
- This package is designed for the analysis of
 - ✓ PET
 - ✓ VBM
 - ✓ MEG
 - ✓ EEG
 - ✓ fMRI





SPM (Statistical Parametric Mapping)

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CAT (Computational Anatomy Toolbox)

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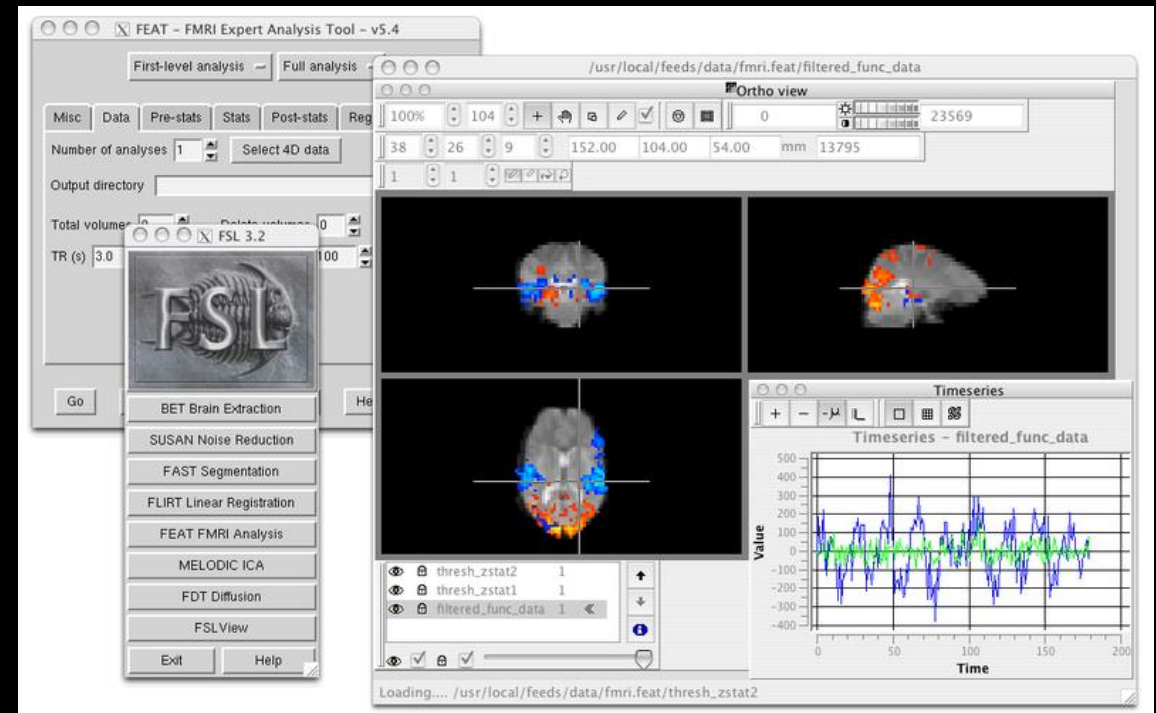
- CAT is an extension to SPM12
- For computational anatomy
- Covers diverse morphometric methods such as:
 - ✓ Voxel-based morphometry (VBM)
 - ✓ Surface-based morphometry (SBM)
 - ✓ Deformation-based morphometry (DBM)
 - ✓ Region- or label-based morphometry (RBM)

FSL (FMRIB Software Library)

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- Written by FMRIB (Functional Magnetic Resonance Imaging of the Brain) Analysis Group, Oxford University, UK.
- Freely available
- Operating system : Linux and Windows (via a Virtual Machine)
- Including statistical tools for
 - ✓ fMRI
 - ✓ MRI
 - ✓ DTI

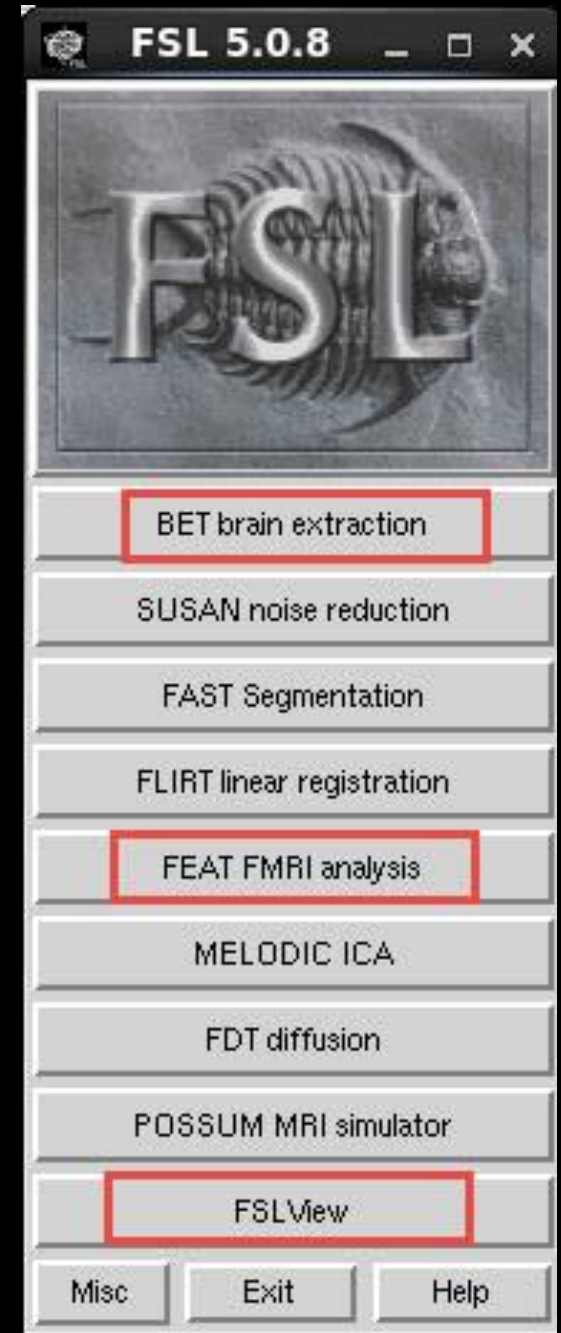


FSL (FMRIB Software Library)

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- FSL functions:
- **BET** (brain extraction tool)
- **SUSAN** (nonlinear noise reduction)
- **FAST** (FMRIB's automated segmentation tool)
- **FLIRT** (FMRIB's linear image registration tool)
- **FEAT** (Model-based fMRI analysis)
- **MELODIC** (Model-free fMRI analysis using probabilistic independent component analysis)

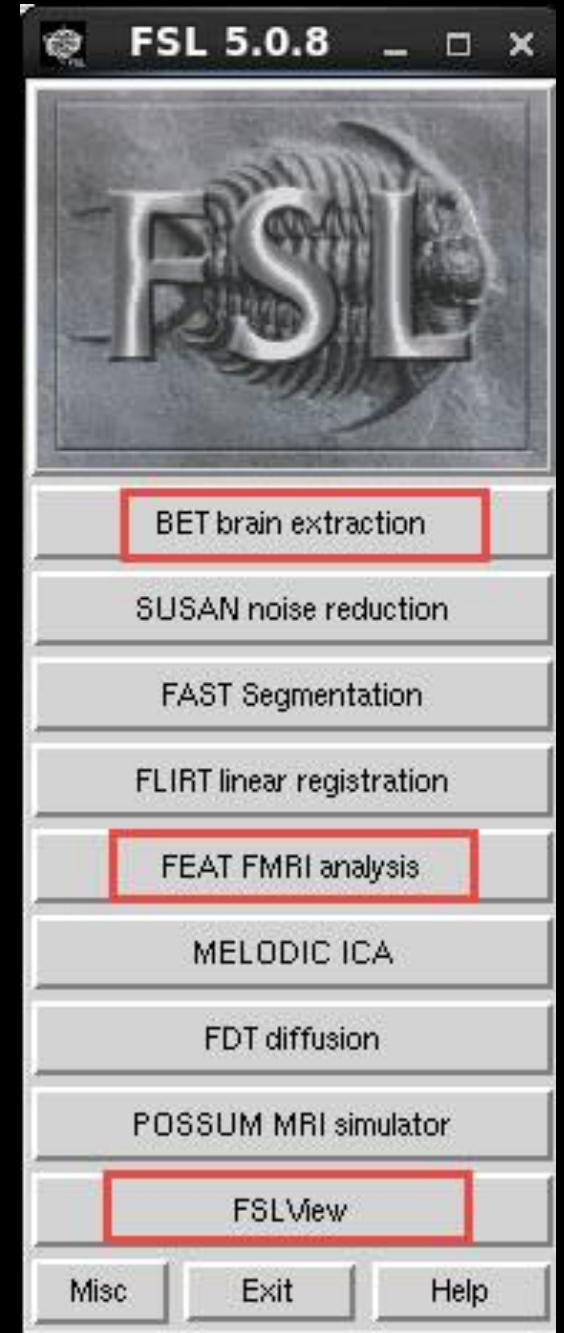


FSL (FMRIB Software Library)

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- **FSL functions:**
- **FDT** (FMRIB's diffusion toolbox), TBSS (tract-based spatial statistics) for diffusion MRI
- **POSSUM** (Physics-Oriented Simulated Scanner for Understanding MRI)
- **FSLeyse**(Interactive display tool for 3D and 4D data.)



FEAT Report



/home/fsl/Desktop/test/output/poststats.html
Finished at Mon Nov 13 15:40:24 GMT 2017

[Registration](#) - [Pre-stats](#) - [Stats](#) - [Post-stats](#) - [Log](#)



Post-stats

Analysis methods

FMRI data processing was carried out using FEAT (FMRI Expert Analysis Tool) Version 6.00, part of FSL (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl). Z (Gaussianised T/F) statistic images were thresholded using clusters determined by $Z > 2.3$ and a (corrected) cluster significance threshold of $P = 0.05$ [Worsley 2001].

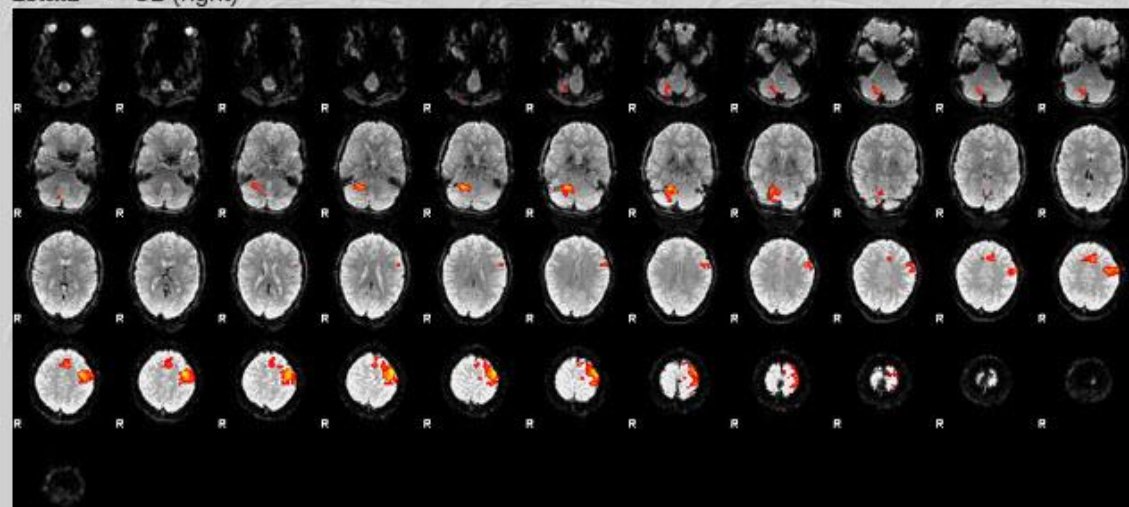
References

[Worsley 2001] K.J. Worsley. Statistical analysis of activation images. Ch 14, in Functional MRI: An Introduction to Methods, eds. P. Jezzard, P.M. Matthews and S.M. Smith. OUP, 2001.

Thresholded activation images

2.3  8.6

zstat1 - C1 (right)



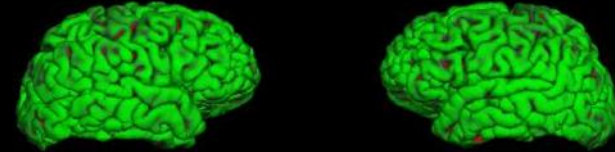


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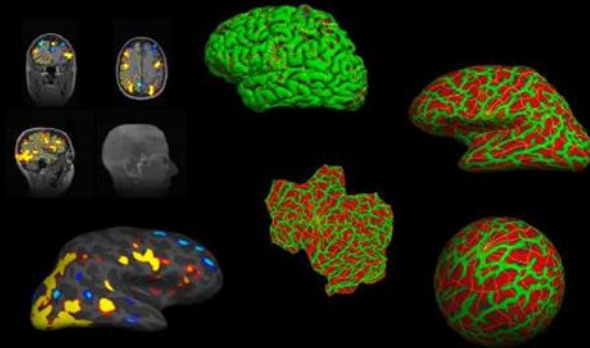
FreeSurfer:



- Developed by Martinos Center for Biomedical Imaging
- Freely available
- Operating system : Linux , Mac OS X and Windows (via a Virtual Machine)
- Including statistical tools for
 - ✓ fMRI
 - ✓ VBM, SBM
 - ✓ DTI



FreeSurfer



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

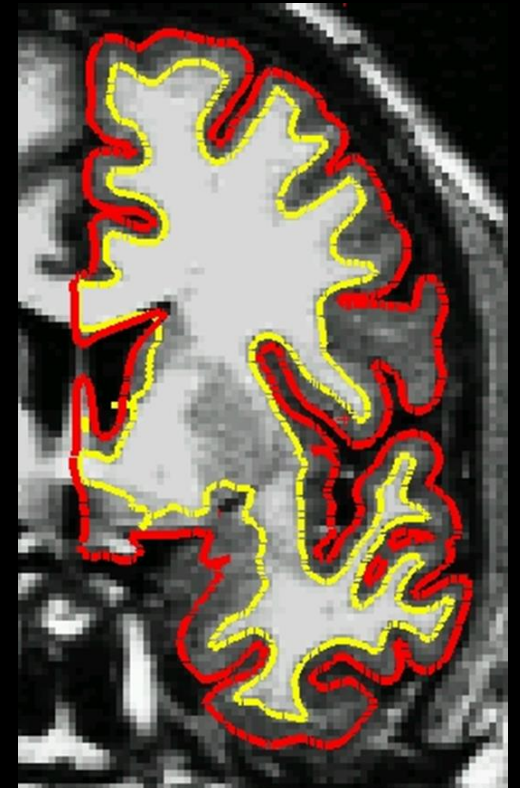
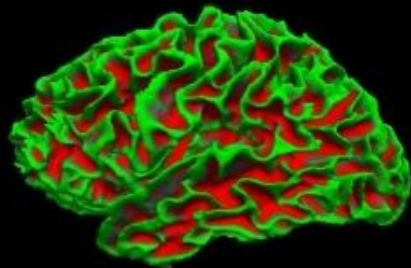
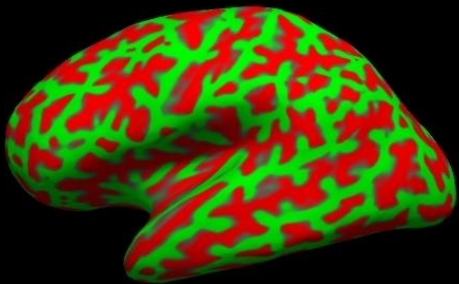


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FreeSurfer

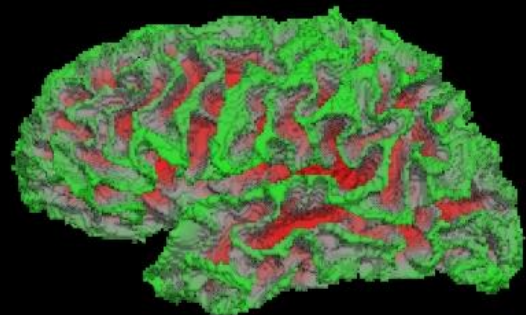
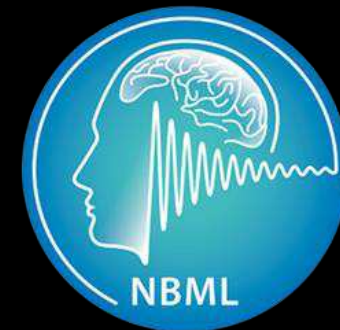


- Contains tools to conduct both volume based and **surface based analysis**.
- Includes tools for the reconstruction of models of :
 - ✓ Both the gray/white and pial surfaces
 - ✓ Measuring cortical thickness, surface area and folding
 - ✓ **Computing inter-subject registration based on the pattern of cortical folds.**

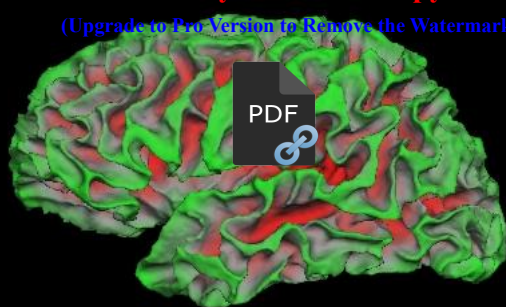


FreeSurfer

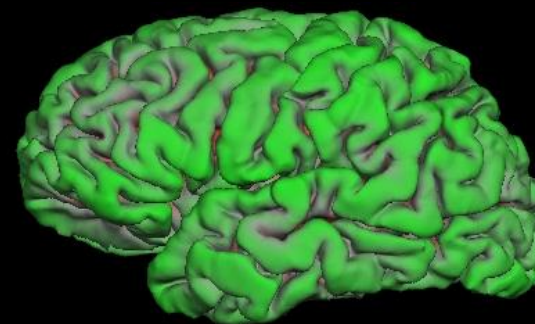
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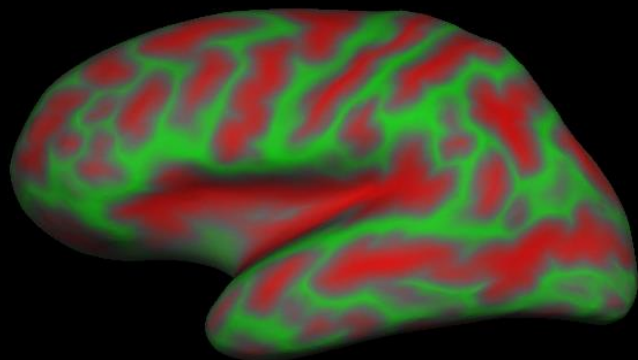
orig



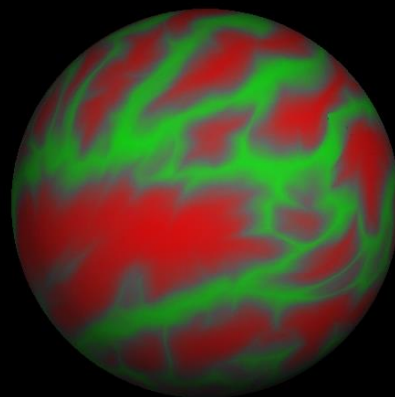
white



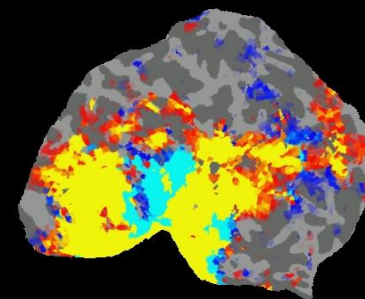
pial



inflated



sphere,sphere.reg



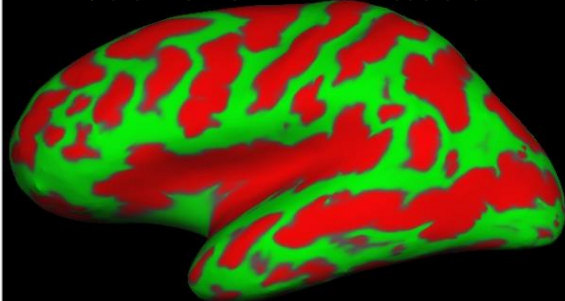
flat

FreeSurfer

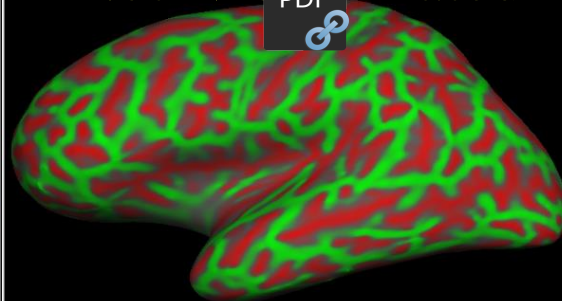
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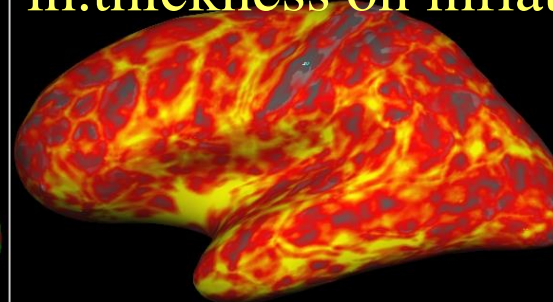
lh.sulc on inflated



lh.curv on inflated



lh.thickness on inflated



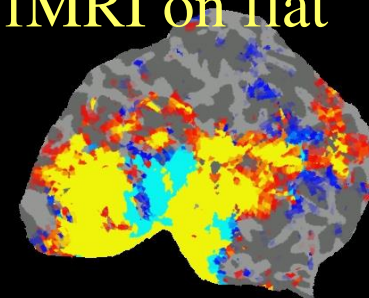
lh.sulc on pial



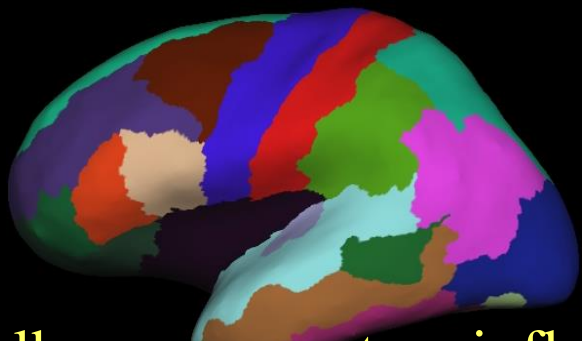
lh.curv on inflated



fMRI on flat



lh.aparc.annot on inflated



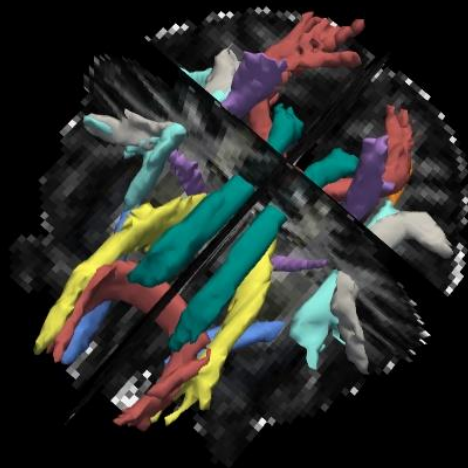


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FreeSurfer

- Freesurfer packages:

- ✓ FreeView: a tool to visualize FreeSurfer output, can also display common MRI image formats
- ✓ TRACULA: a tool to construct white matter tract data from diffusion images
- ✓ FSFAST: a tool for analysis of functional MRI data



AFNI (Analysis of Functional NeuroImages)

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- Developed by the NIMH Scientific and Statistical Computing Core
- Runs under many Unix-like operating systems that provide X11 and Motif libraries, including IRIX, Solaris, Linux, FreeBSD and OS X (a set of C programs)
- For fMRI and DTI analysis

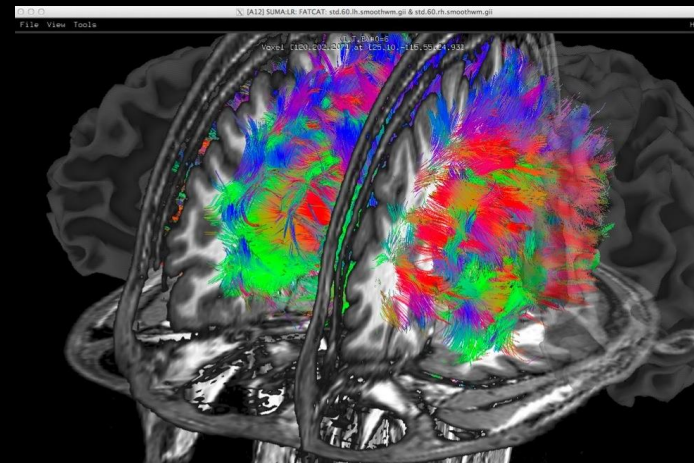
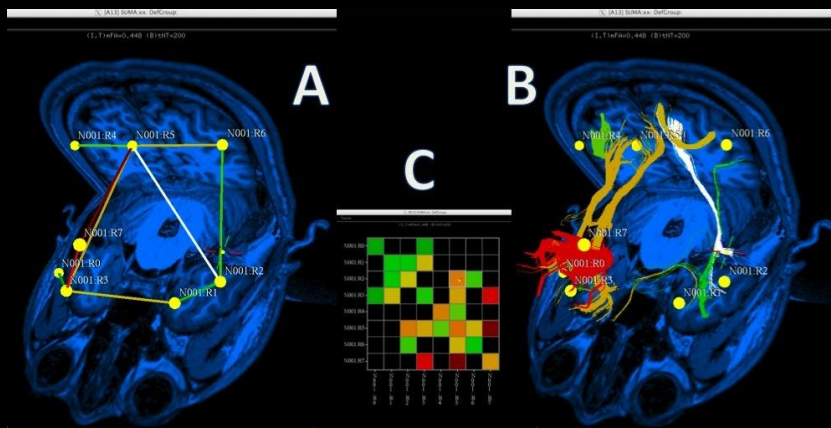
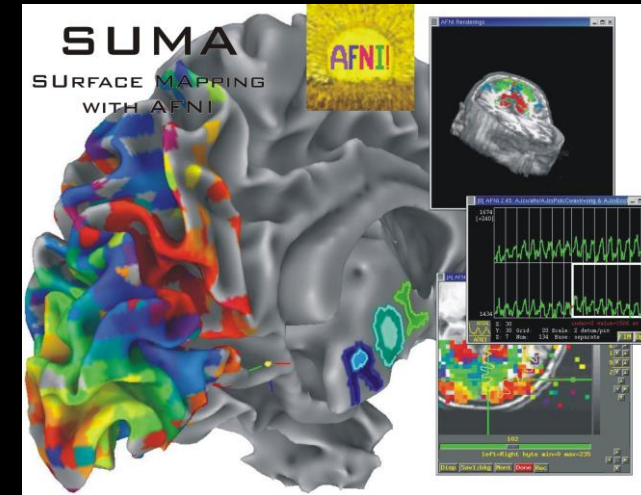


AFNI (Analysis of Functional NeuroImages)

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- SUMA:
- It is a program that adds cortical surface based functional imaging analysis to the AFNI suite of programs
- Allows display and manipulation of matrices for various flavors of connectivity data, tractography results from AFNI's FATCAT toolbox

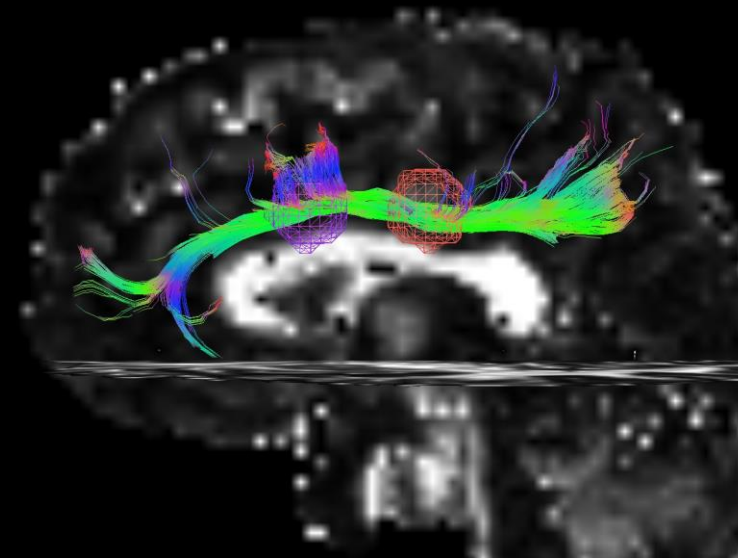


AFNI (Analysis of Functional NeuroImages)

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- **FATCAT:** The Functional And Tractographic Connectivity Toolbox
- combining fMRI and diffusion-based data
- Statistics
 - ✓ Multivariate modeling approach for group analysis
 - ✓ Linear Mixed-Effects Modeling
 - ✓ Mixed-Effects Meta Analysis (MEMA)



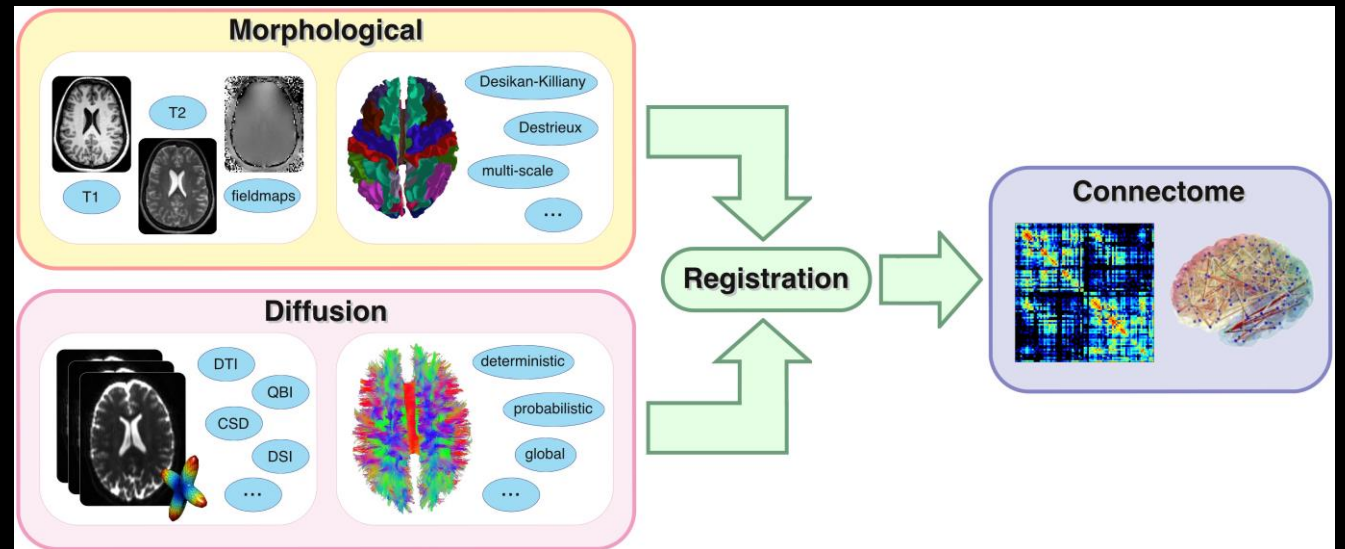


The Connectome Mapper

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- An Open-Source Processing Pipeline (Python)
- Full diffusion MRI processing pipeline, from raw Diffusion/T1/T2 data to multi-resolution connection matrices
- DTI, QBI and DSI & resting-state fMRI data processing
- Combining modules:
 - FSL
 - Freesurfer
 - DIFFUSION TOOLKIT (trackvis)

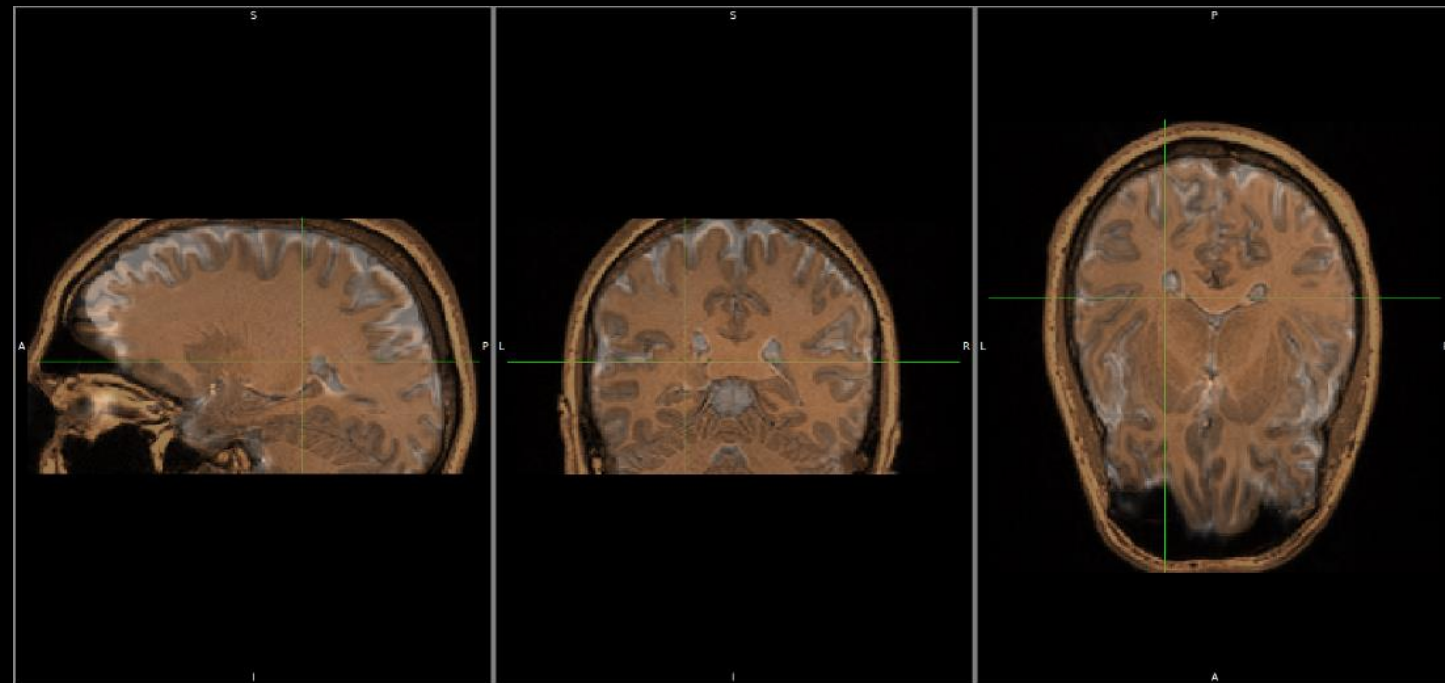


The Connectome Mapper

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- **Registration**
- Registration of T1 to Diffusion space (b0). T1 in copper overlaid to the b0 image.



The Connectome Mapper

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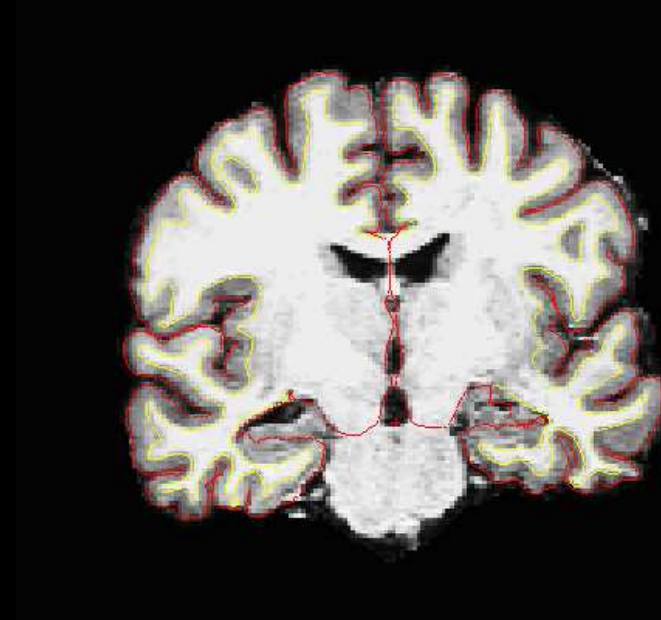
- Segmentation



T1 is segmented using Freesurfer



Surfaces are extracted using Freesurfer

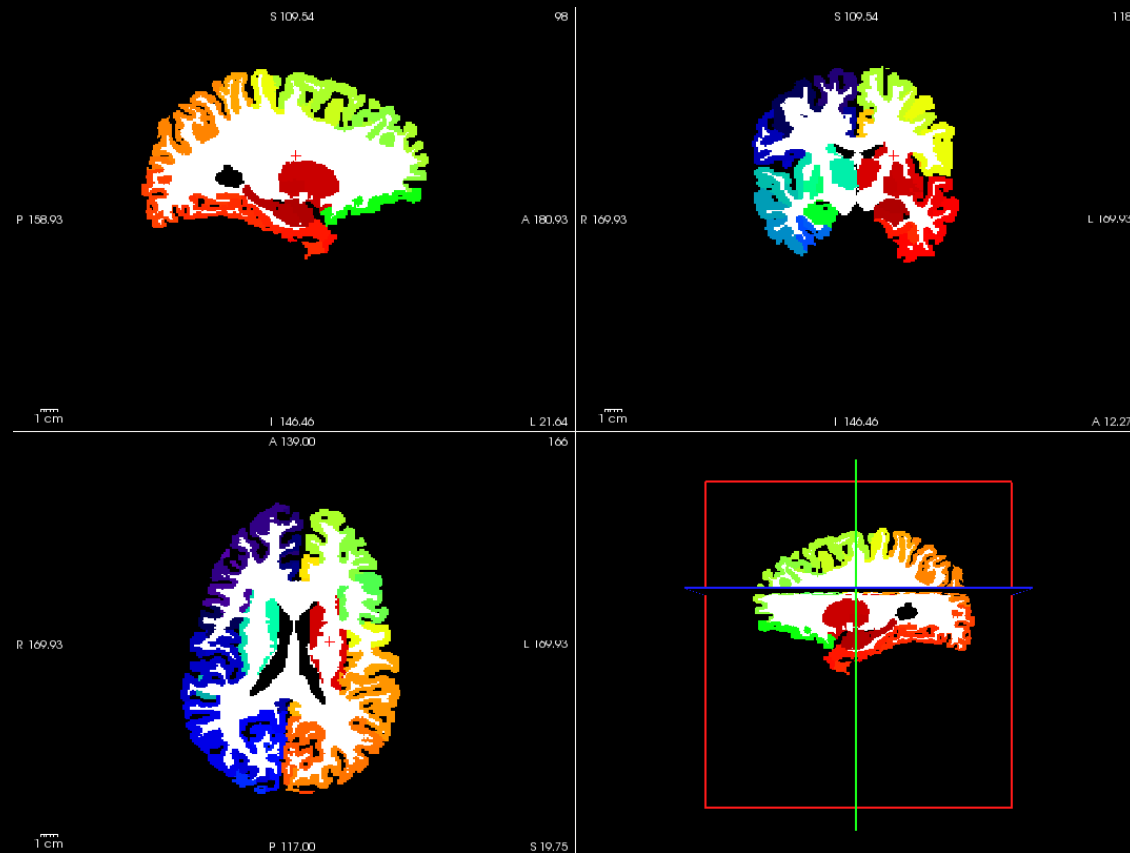


The Connectome Mapper

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- **Parcellation**
- Cortical and subcortical parcellation are shown with Freeview



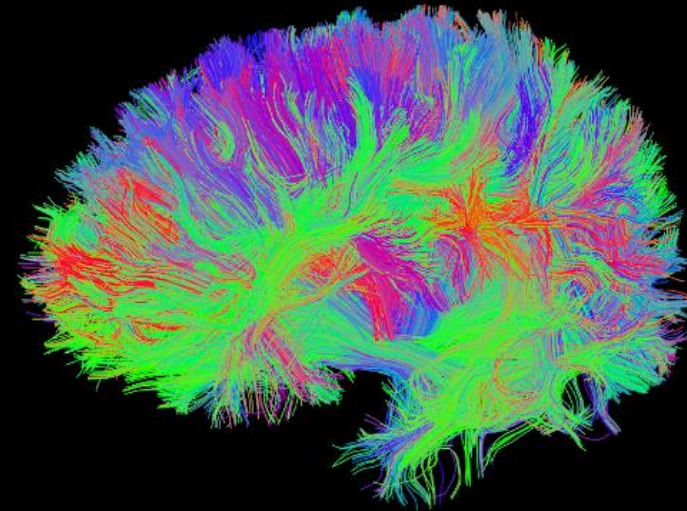
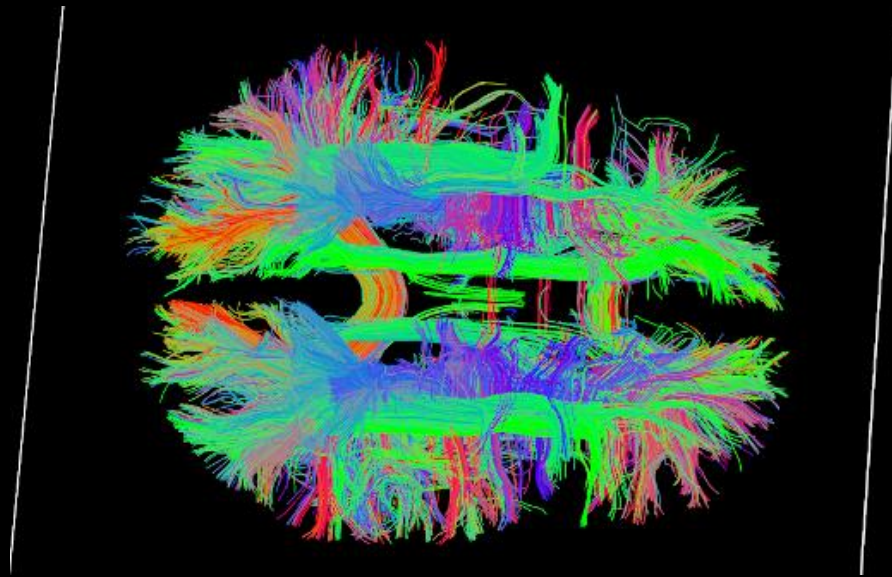


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The Connectome Mapper



- **Tractography**
- DSI Tractography results are displayed with TrackVis



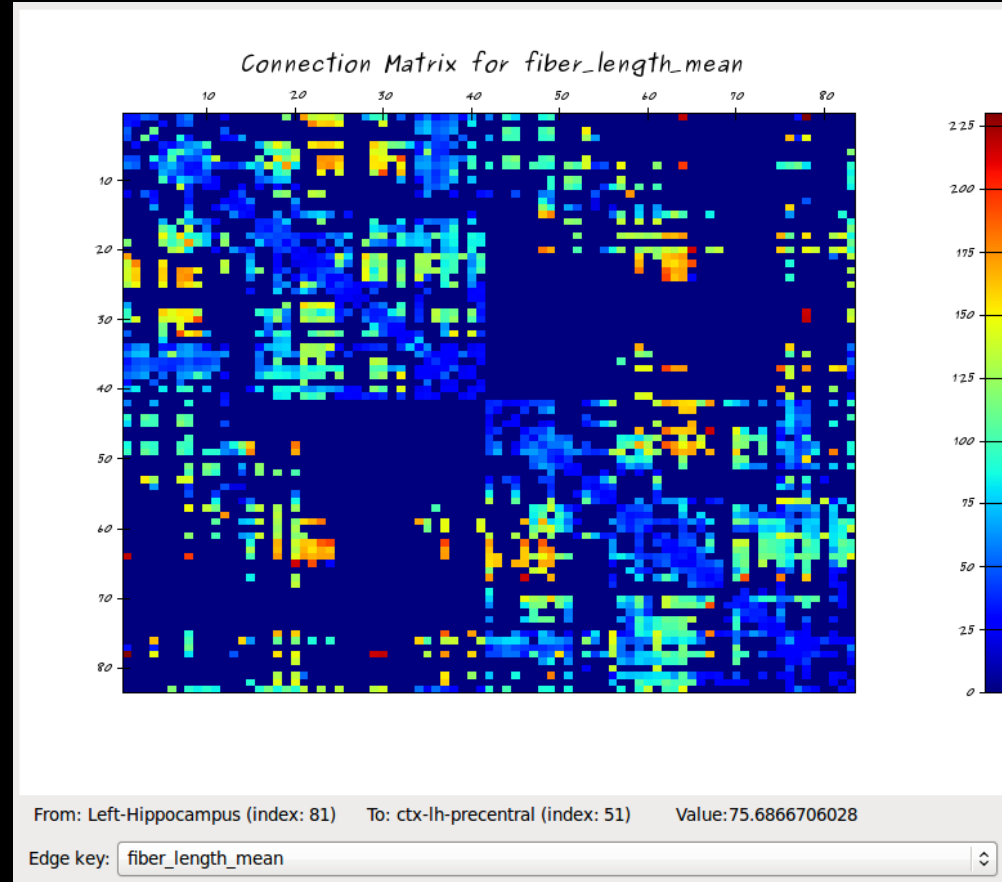


The Connectome Mapper

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- Connection Matrix Creation

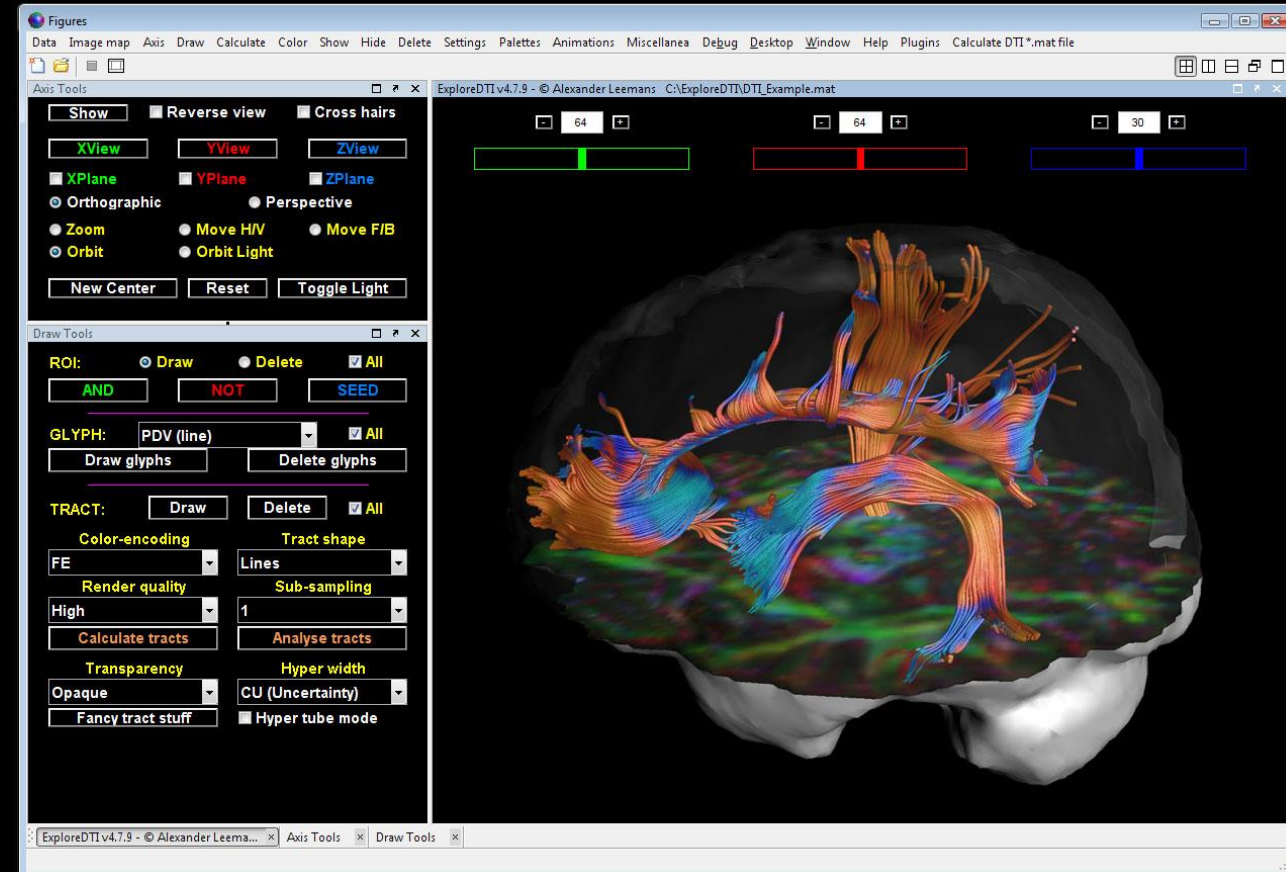


Explore DTI

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- A graphical toolbox for
 - ✓ Processing
 - ✓ Analyzing
 - ✓ Visualizingdiffusion MR data
- Written in Matlab
- Works across multiple platforms:
 - ✓ Windows PC, Unix, Mac



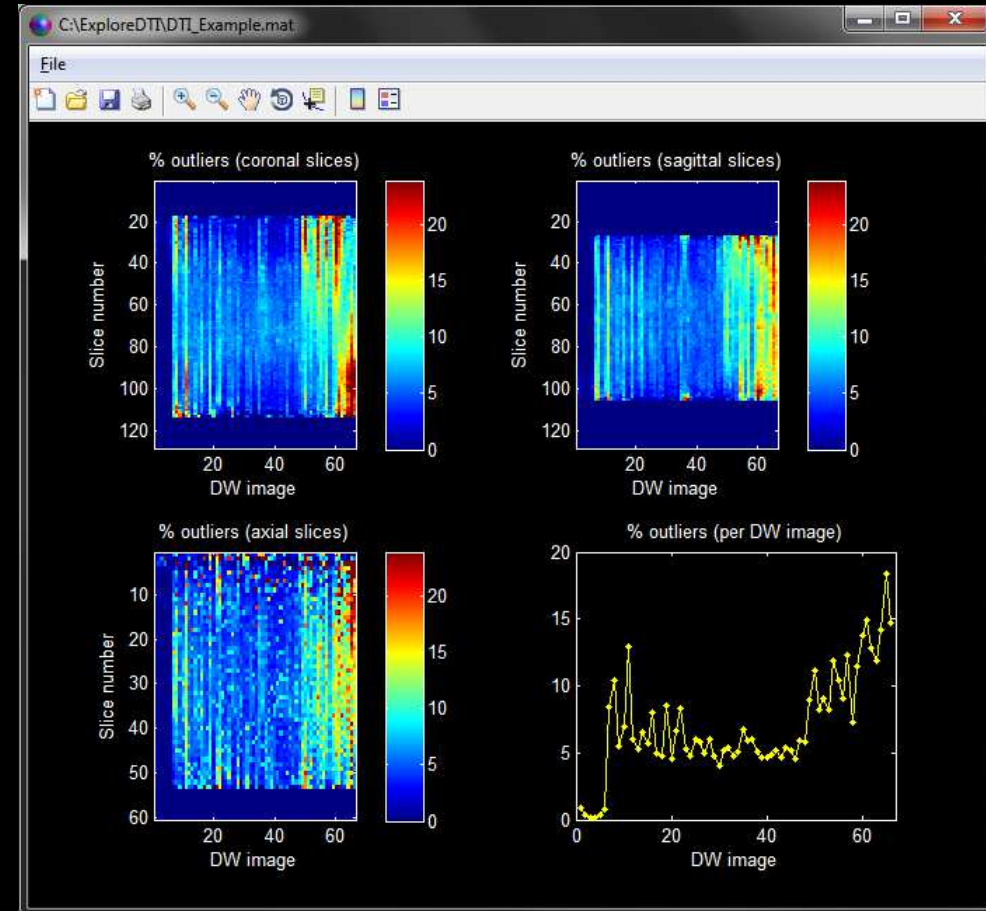
Explore DTI

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- **Key features :**

- *Data Reconstruction*
- *Motion / Eddy Current Correction*
- ***Quality Assessment Tools***
- *Fiber tractography*
- *Automated “atlas based” tractography*
- *Tract-specific measurements*
- *Tract-segment analysis*
- *Along-tract analysis*
- *Visualizations*
- *Making animations*
- *Network analysis tools*



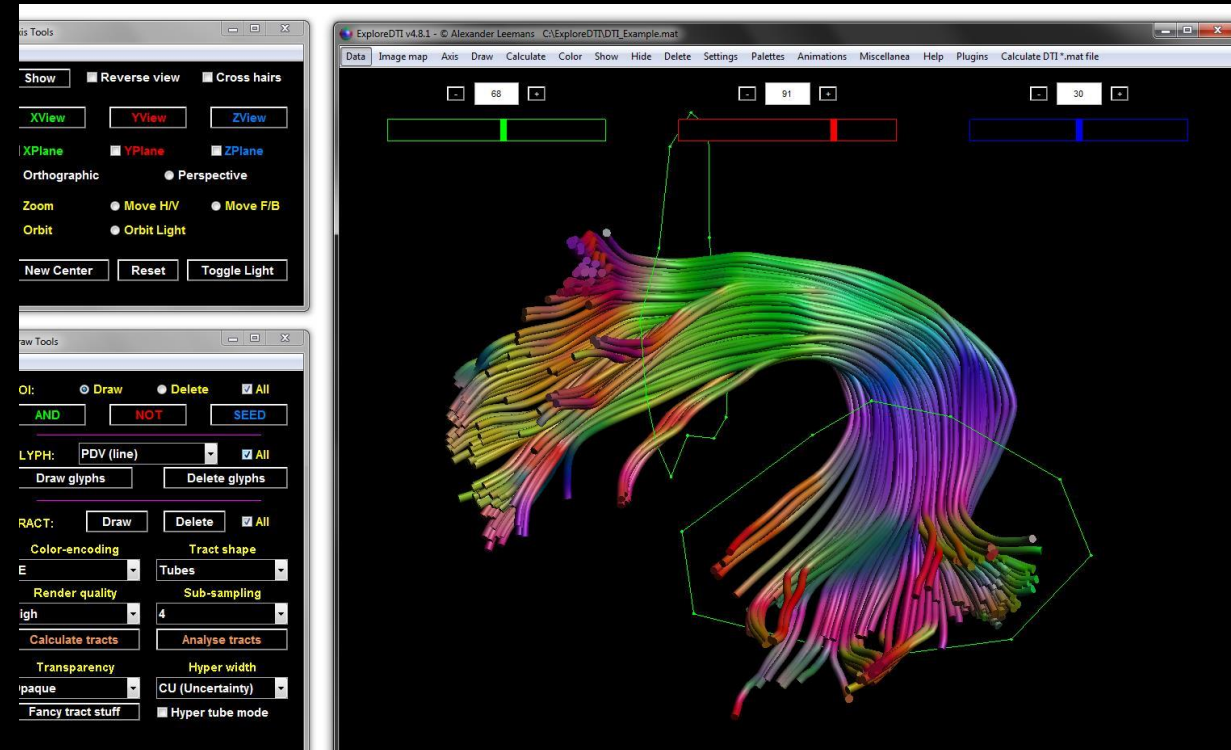
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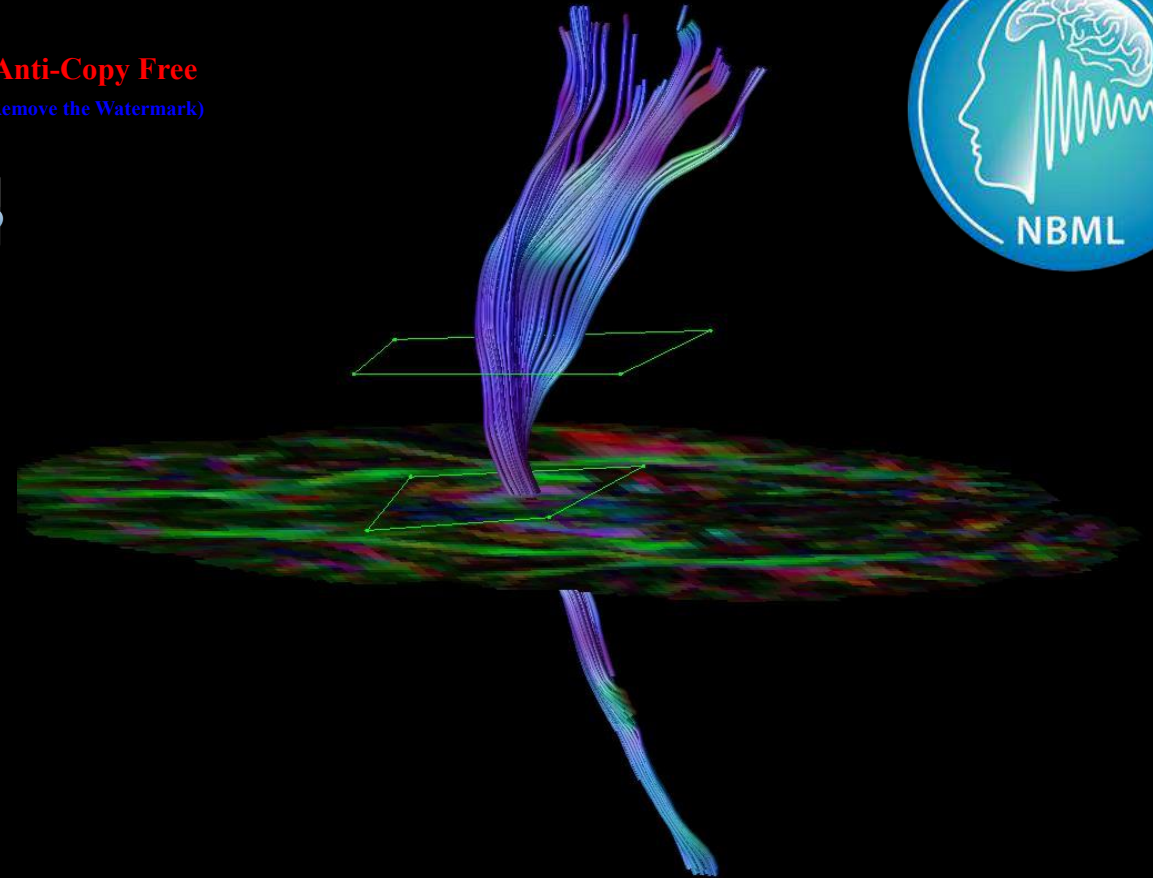
Explore DTI

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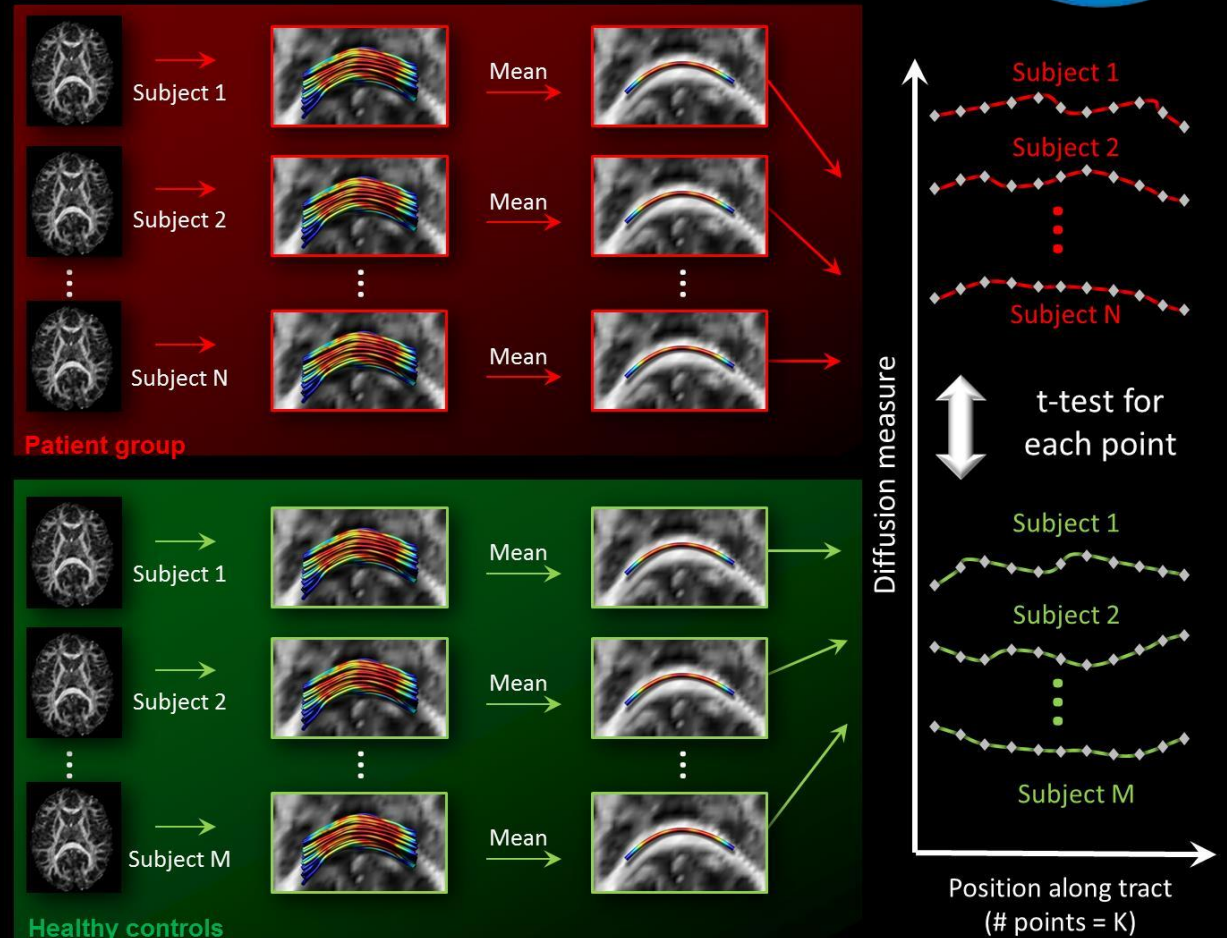
Explore DTI

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• Key features :

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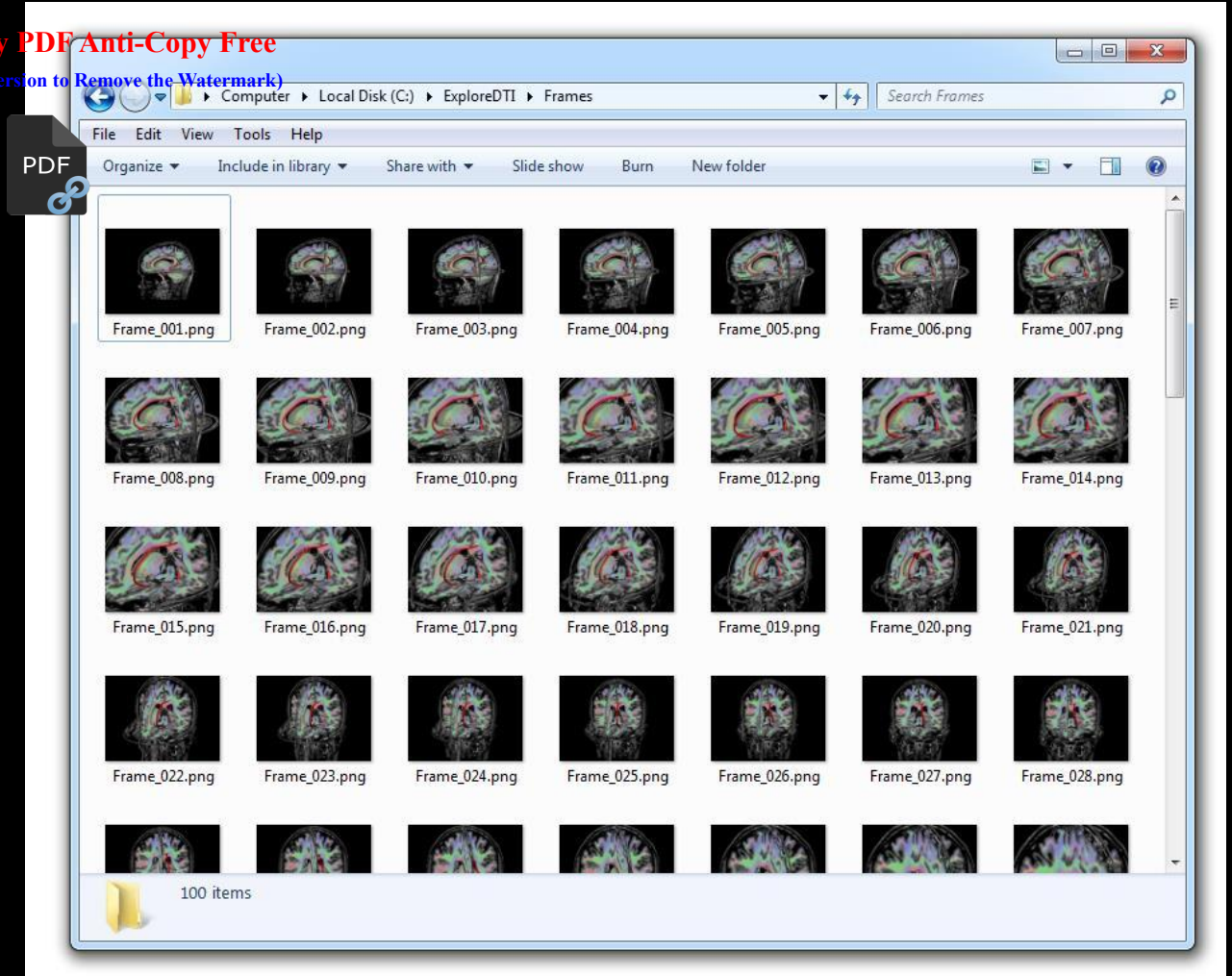


Explore DTI

- **Key features :**

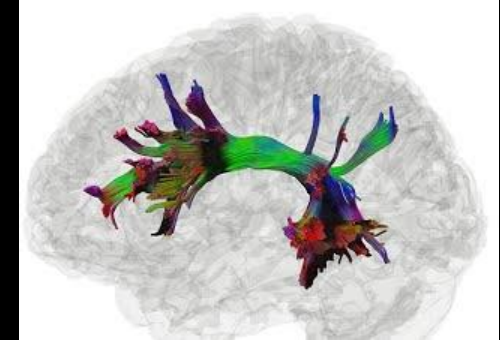
- *Data Reconstruction*
- *Motion / Eddy Current Correction:*
- *Quality Assessment Tools*
- *Fiber tractography*
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- *Tract-segment analysis*
- *Along-tract analysis*
- ***Visualizations***
- ***Making animations***
- *Network analysis tools*

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DTI studio & MRtrix

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- DSI Studio:

- Robust to crossing fibres, using constrained spherical deconvolution (CSD) and probabilistic streamlines.
- Including :DTI , diffusion MRI connectometry, and generalized deterministic fiber tracking

- MRtrix:

- Provides various forms of tractography through to next-generation group-level analyses, quantitative structural connectivity analysis
- written from scratch in C++



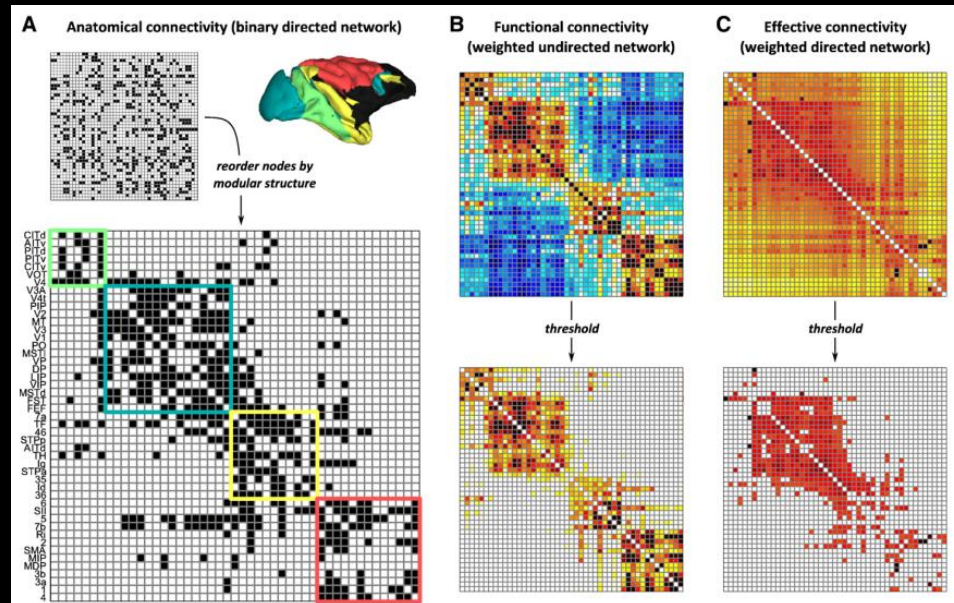


Graph Theory Softwares

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- Brain Connectivity Toolbox (BCT):
- A Matlab toolbox (<http://www.brain-connectivity-toolbox.net>)



NeuroImage 52 (2010) 1059–1069

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Complex network measures of brain connectivity: Uses and interpretations

Mikail Rubinov^{a,b,c}, Olaf Sporns^{d,*}

^a Black Dog Institute and School of Psychiatry, University of New South Wales, Sydney, Australia
^b Mental Health Research Division, Queensland Institute of Medical Research, Brisbane, Australia
^c CSIRO Information and Communication Technologies Centre, Sydney, Australia
^d Department of Psychological and Brain Sciences, Indiana University, Bloomington, IN 47405, USA

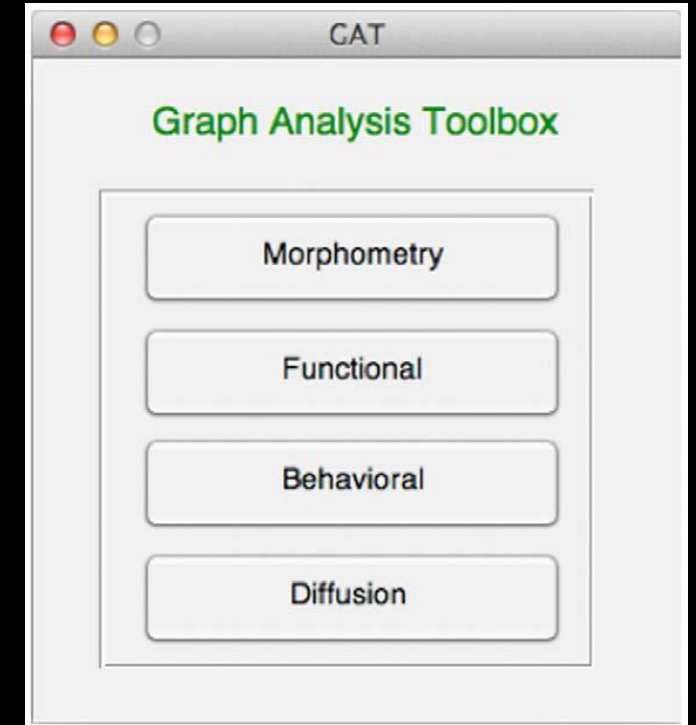


Graph Theory Softwares

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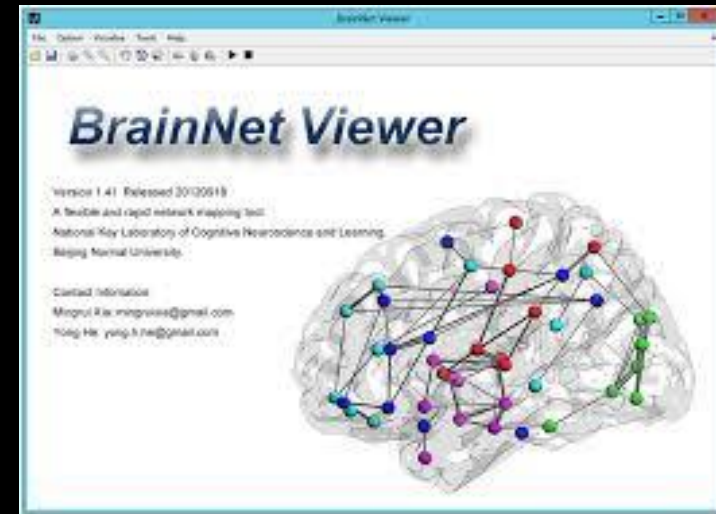
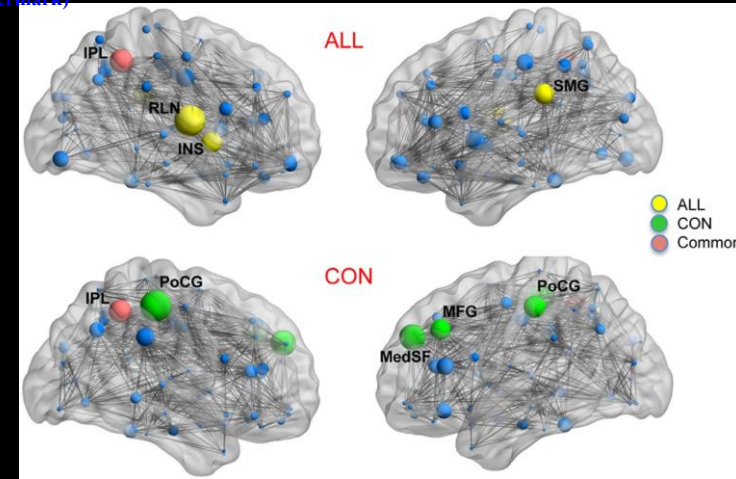
- GAT (graph-analysis toolbox)
- You can analyze **structural/functional networks** constructed from
 - ✓ VBM
 - ✓ Free Surfer data
 - ✓ resting state/task fMRI
 - ✓ DTI
 - ✓ MRS
 - ✓ Behavioral data



Graph Theory Softwares



- GAT (graph-analysis toolbox)
- Matlab-based software
- Integrates the:
 - ✓ Brain Connectivity Toolbox
 - ✓ REX toolbox
 - ✓ BrainNet Viewer
 - ✓ Original code



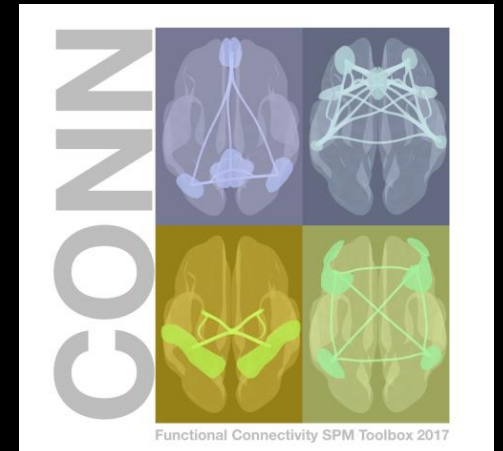


Graph Theory Softwares

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- **CONN:**
- Matlab-based (SPM8/SPM12)
- For the computation, display, and analysis of functional connectivity in fMRI
- Includes a rich set of connectivity analyses
 - ✓ ROI-to-ROI analyses (ROI-to-ROI functional connectivity matrices)
 - ✓ Seed-to-Voxel analyses (functional connectivity maps)
 - ✓ Voxel-to-Voxel analyses
 - ✓ ICA analyses
 - ✓ Dynamic ICA analyses



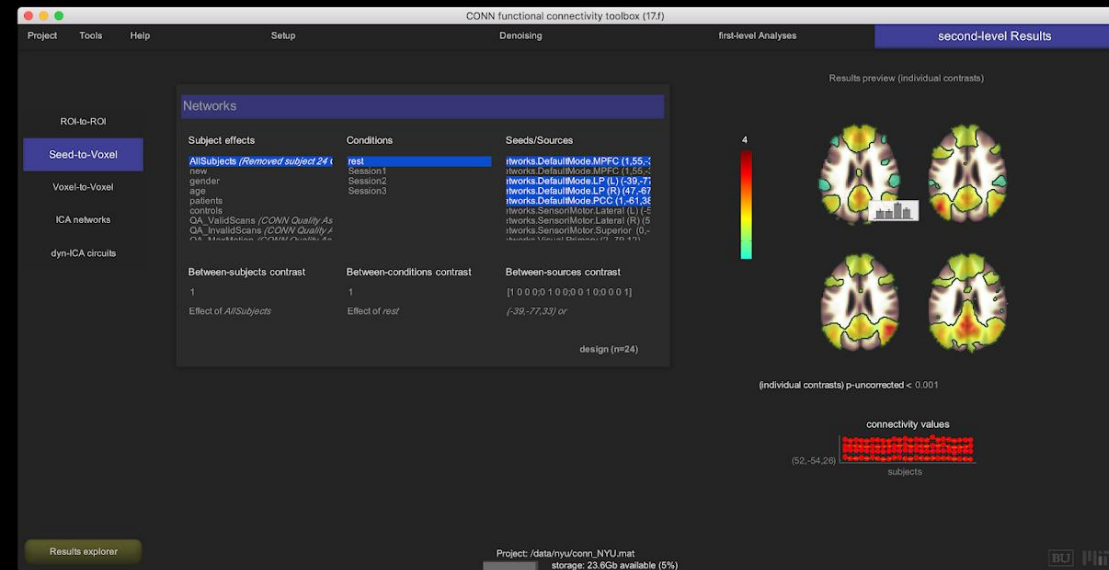


Graph Theory Softwares

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• CONN:





Graph Theory Softwares

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• CONN:

Project Tools Help Setup Denoising first-level Analyses **second-level Results**

ROI-to-ROI

Seed-to-Voxel

Voxel-to-Voxel

ICA networks

dyn-ICA circuits

Second-level design

newdenoising

Subject effects	Conditions	Seeds/Sources
AllSubjects	rest	dmm.MPFC
age	Pre	dmm.PCC
gender	Post_A	dmm.LLP
male	Post_B	dmm.RLP
female		atlas.FP.r (Frontal Pole Right)
controls		atlas.FP.l (Frontal Pole Left)
patients		atlas.IC.r (Insular Cortex Right)
symptoms		atlas.IC.l (Insular Cortex Left)
sum scrubbing at rest		atlas.SFG.r (Superior Frontal Gyrus)
ageCentered		atlas.SFG.l (Superior Frontal Gyrus)
max(abs(d#)) realignment at rest.r		atlas.MidFG.r (Middle Frontal Gyrus)
max(abs(d#)) realignment at rest.r		atlas.MidFG.l (Middle Frontal Gyrus)
max(abs(d#)) realignment at rest.r		atlas.IFG.tr (Inferior Frontal Gyrus)
max(abs(d#)) realignment at rest.r		atlas.IFG.tr.l (Inferior Frontal Gyrus)

Between-subjects contrast	Between-conditions contrast	Between-sources contrast
1	1	1
Effect of AllSubjects	Effect of rest	Effect of dmm.LLP

- contrast tools

Analysis results

Targets	beta	T(24)	p-unc	p-FDR
atlas.pITG.l (Middle Tempwefl)	0.47	9.93	0.000000	0.000000
atlas.Cereb2.l (Cerebellumwefl)	0.24	9.45	0.000000	0.000000
atlas.pITG.l (Inferior Tempwefl)	0.30	9.35	0.000000	0.000000
atlas.sLOC.r (Lateral Occipit)	0.29	9.07	0.000000	0.000000
atlas.pITG.l (Inferior Tempwefl)	0.32	8.50	0.000000	0.000000

ROI-to-ROI effects: -35.05 35.05

Define connectivity matrix:

Targets are source ROIs only (connectivity matrix: 136x136 ROIs)

Select seed ROI(s):

- atlas.Ver7 (Vermis 7) (132)
- atlas.Ver8 (Vermis 8) (134)
- atlas.Ver9 (Vermis 9) (135)
- atlas.Ver10 (Vermis 10) (136)

Select all

Define thresholds:

threshold ROI-to-ROI connections (by intensity)

1e-8 p-FDR (seed-level correction) two-sided

threshold seed ROIs (F-test)

0.05 p-FDR

Enable permutation tests

Analysis Unit	Statistic	p-unc	p-FDR	p-FWE
Seed LG.r	F(1)(20) = 75.93	0.0000	0.0000	
Intensity = 288.60				
Size = 19				
LG.r - LG.l	T(24) = 30.10	0.0000	0.0000	
LG.r - ICC.r	T(24) = 27.08	0.0000	0.0000	
LG.r - ICC.l	T(24) = 24.18	0.0000	0.0000	
LG.r - Cuneal.l	T(24) = 20.07	0.0000	0.0000	
LG.r - Cuneal.r	T(24) = 18.08	0.0000	0.0000	
LG.r - SCC.r	T(24) = 18.03	0.0000	0.0000	
LG.r - TOFusC.r	T(24) = 17.75	0.0000	0.0000	
LG.r - OFusG.r	T(24) = 14.41	0.0000	0.0000	
LG.r - TOFusC.l	T(24) = 13.05	0.0000	0.0000	
LG.r - SCC.l	T(24) = 12.86	0.0000	0.0000	
LG.r - OFusG.l	T(24) = 12.79	0.0000	0.0000	
LG.r - PP.l	T(24) = 10.79	0.0000	0.0000	
LG.r - OFusG.l	T(24) = 10.40	0.0000	0.0000	



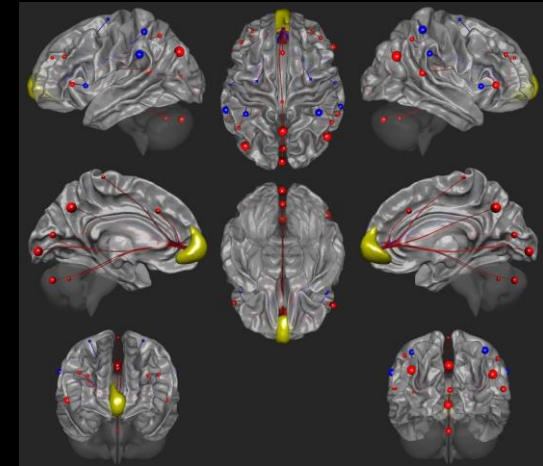
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Graph Theory Softwares



- **CONN:**

- Is available for resting state data (rsfMRI) and task-related designs.
- Covers the entire pipeline from raw fMRI data to hypothesis testing
- Highlights:
 - ✓ Comprehensive quality assurance methods/measures/displays
 - ✓ Connectome-wide analyses (ICA, MVPA)
 - ✓ Dynamic connectivity analyses (dyn-ICA)
 - ✓ Non-parametric cluster-level statistics (permutation tests)
 - ✓ ANOVA, regression, longitudinal, and mixed designs

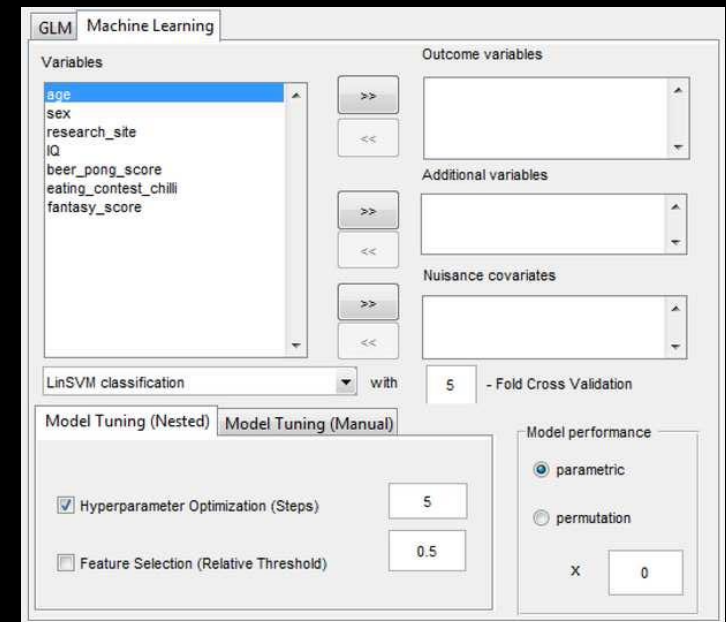
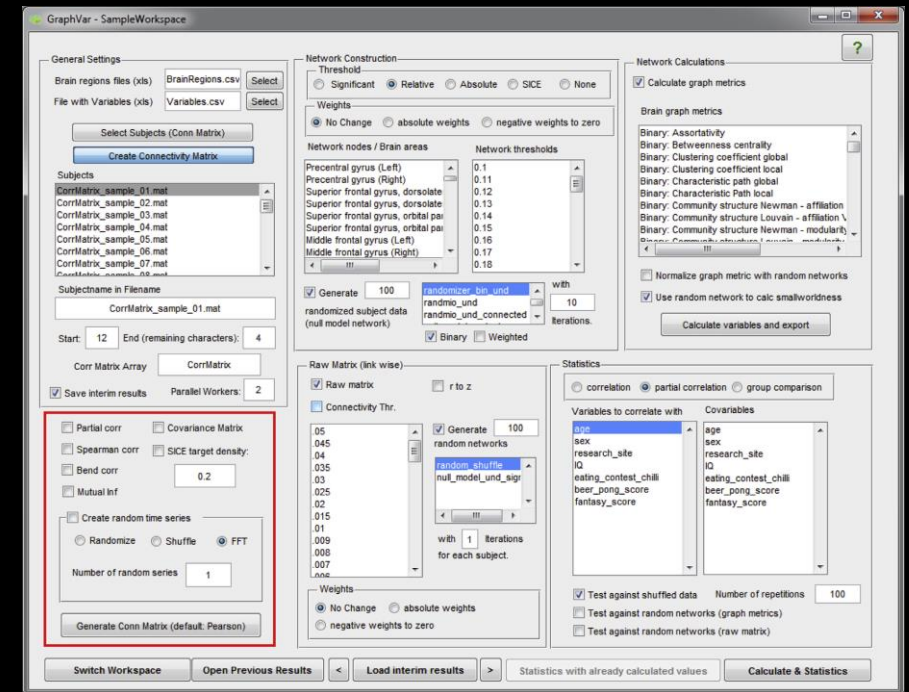


Graph Theory Softwares

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- **Graphvar:**
- For functional brain connectivity
- GUI-based toolbox (matlab)
- One single toolbox by combining features across:
 - ✓ Brain Connectivity Toolbox (BCT)
 - ✓ Graph Analysis Toolbox (GAT)
 - ✓ Network Based Statistic Toolbox (NBS)
 - ✓ BrainNetClass
- Statistical analysis (GLM and Machine Learning)
(GraphVar 2.0)

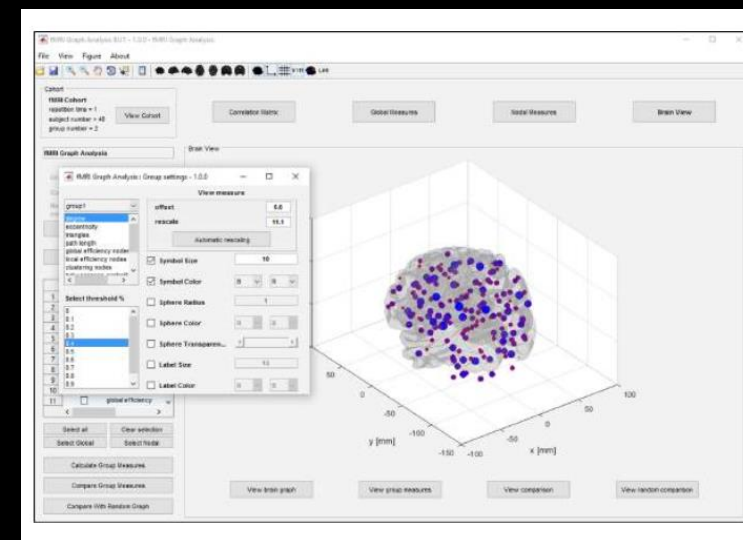
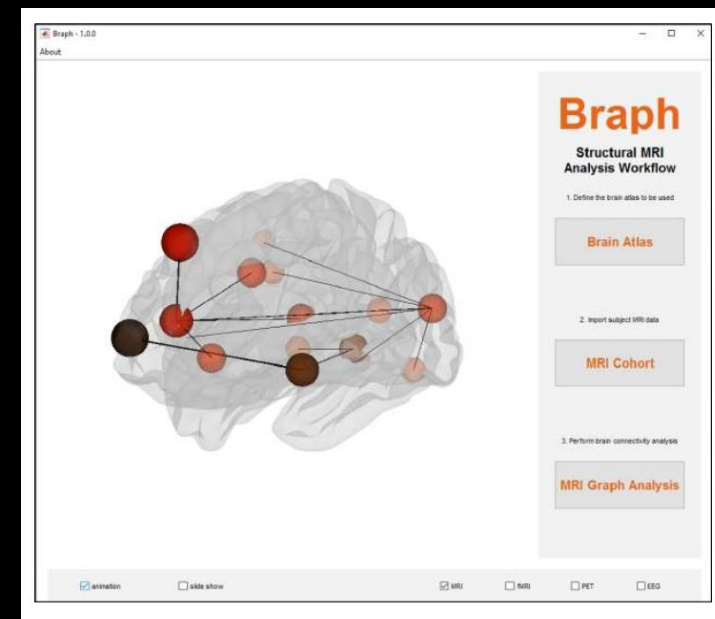


Kruschwitz, J. D., et al. *Journal of neuroscience methods*, 2015.
Waller, Lea, et al. *Journal of neuroscience methods*, 2018.

Graph Theory Softwares



- **BRAPH** (BRain Analysis using graPH theory)
- Freeware MatLab-based software
- For connectivity analysis of brain networks derived from
 - ✓ MRI
 - ✓ fMRI
 - ✓ PET
 - ✓ EEG
 - ✓ No DTI
- By contrast to other toolboxes, it allows **performing longitudinal comparisons of the same patients across different points in time.**



Multimodal Analysis

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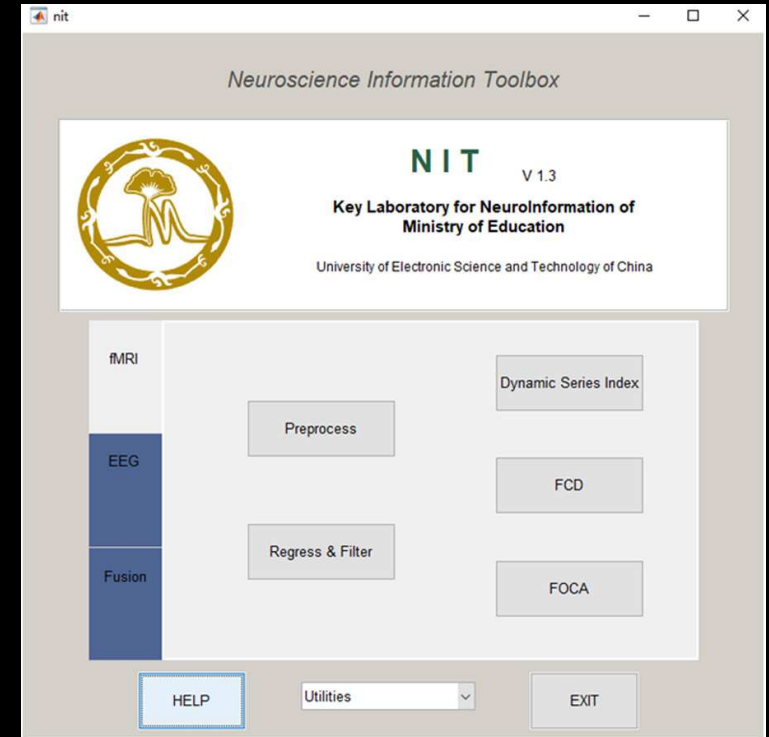
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Neuroscience Information Toolbox: An Open Source Toolbox for EEG–fMRI Multimodal Fusion Analysis

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Future Works

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Dynamic graph metrics: Tutorial, toolbox, and tale

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