An introduction to brain image processing and it's softwares
(with a focus on MRI tools)

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Outline

- **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

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

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

fMRI

DTI

**T1 weighted
magnetic resonance image**

**Functional magnetic
resonance imaging**

**Diffusion tensor
imaging**

MRI-T1

FMRI

DTI

MRI-T1
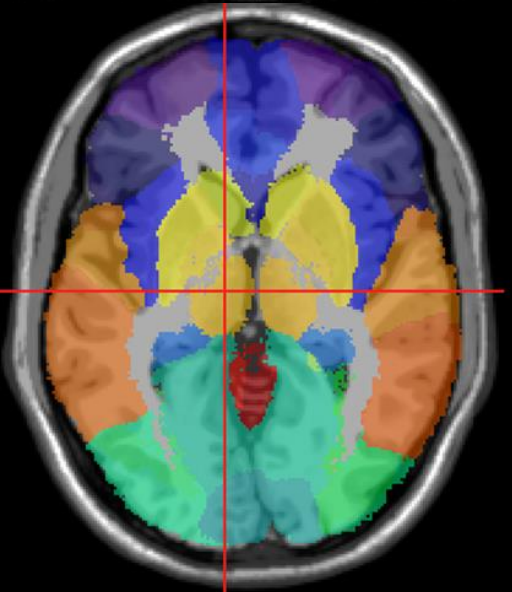
fMRI

DTI

MRS
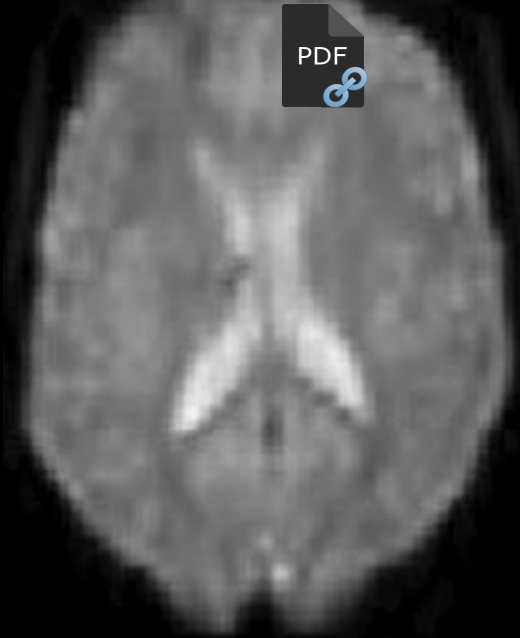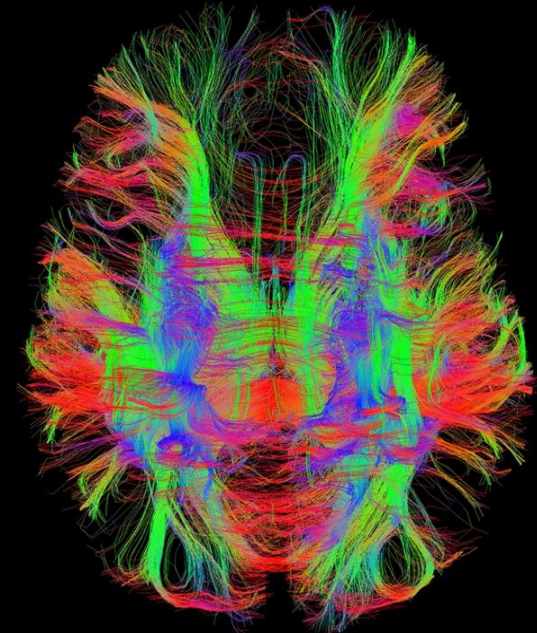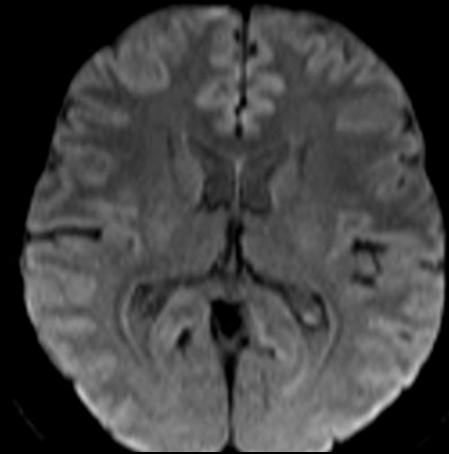
Magnetic Resonance Spectroscopy
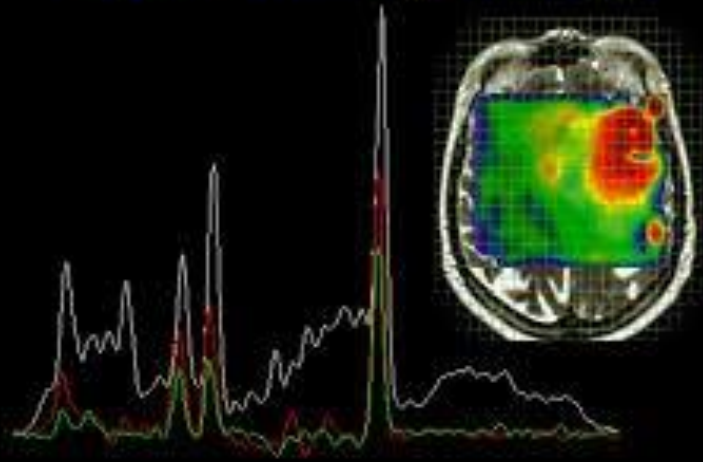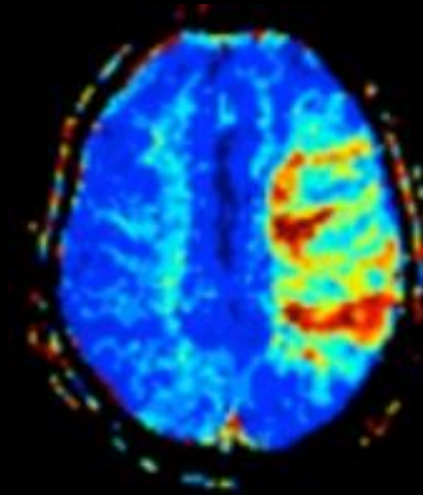
PWI

Perfusion-weighted imaging

MRS

PERFUSION

sagittal   # axial   # cronal

SAG

PDF

Slice Thickness
e.g., 6 mm

VOXEL
(Volumetric Pixel)

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

3 mm

6 mm

3 mm
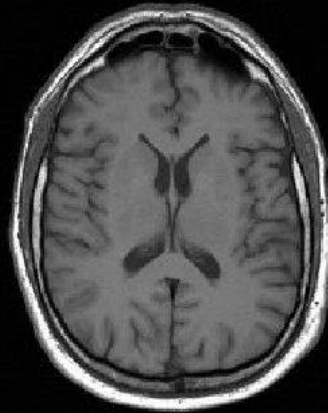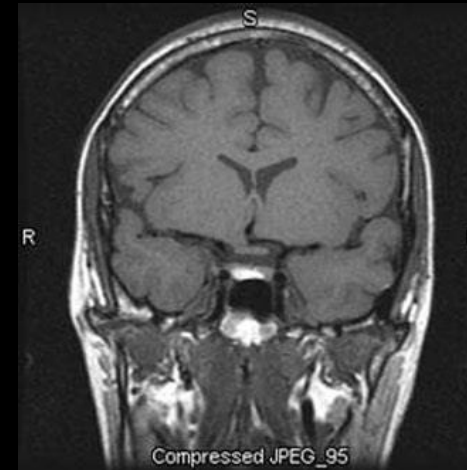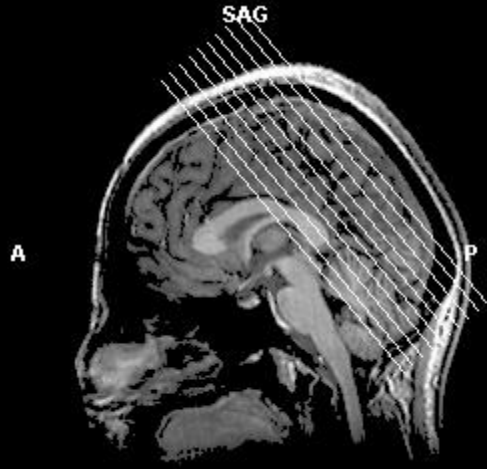
SAGITTAL SLICE
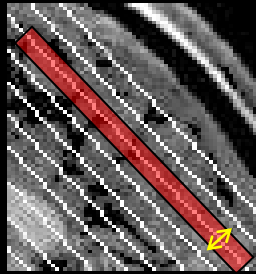
IN-PLANE SLICE

Number of Slices
e.g., 10

Matrix Size
e.g., 64 x 64

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

SAG

NBML

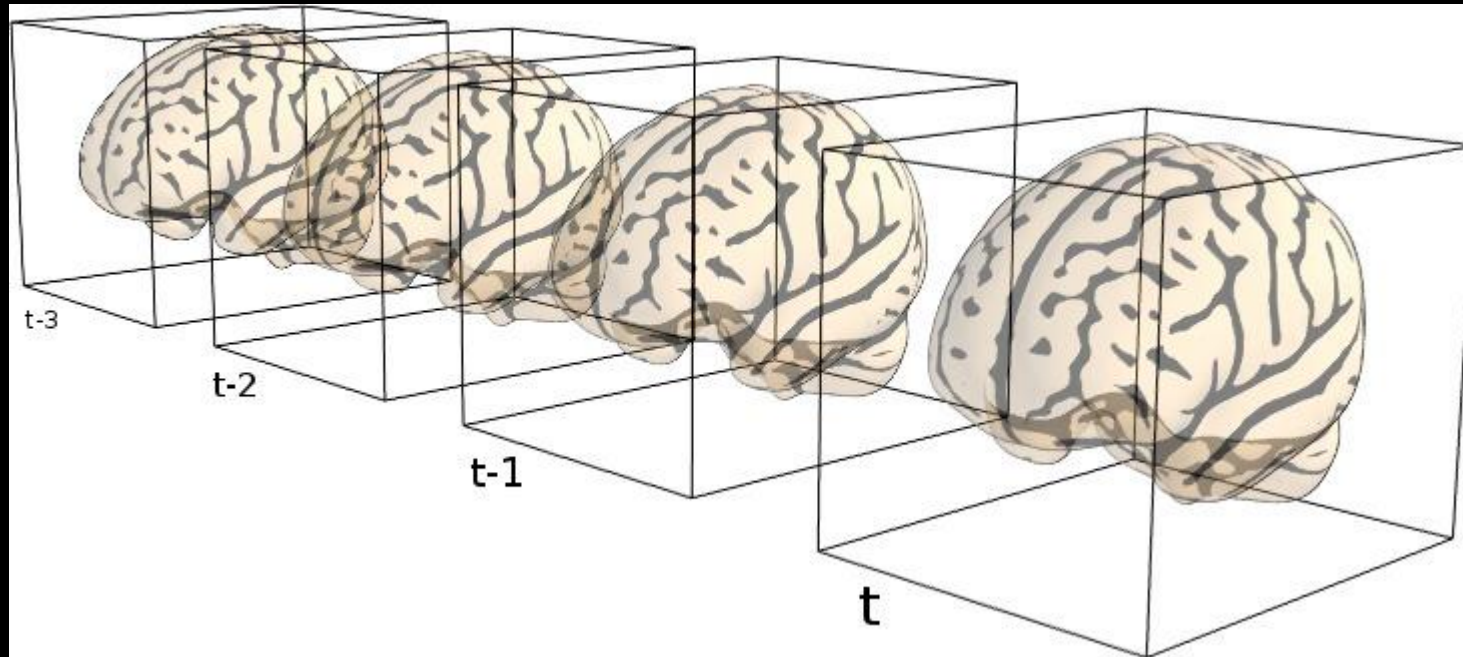# fMRI
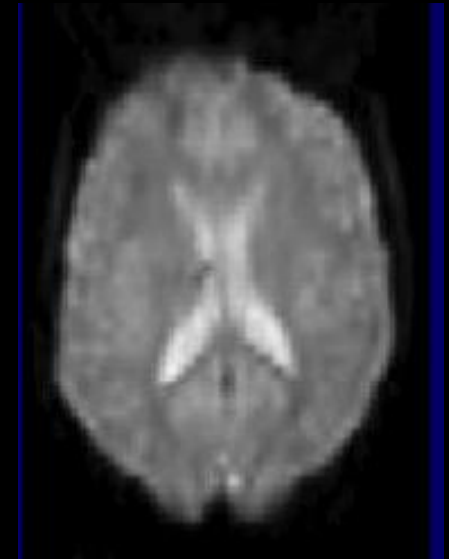
MRI-T1

T1 weighted
magnetic resonance image

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

Ales Bartos[a,b,*], David Gregus[a,b], Ibrahim Ibrahim[c], Jaroslav Tintěra[a,c]

[a] National Institute of Mental Health, Topolová 748, Klecany 250 67, Czechia
[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
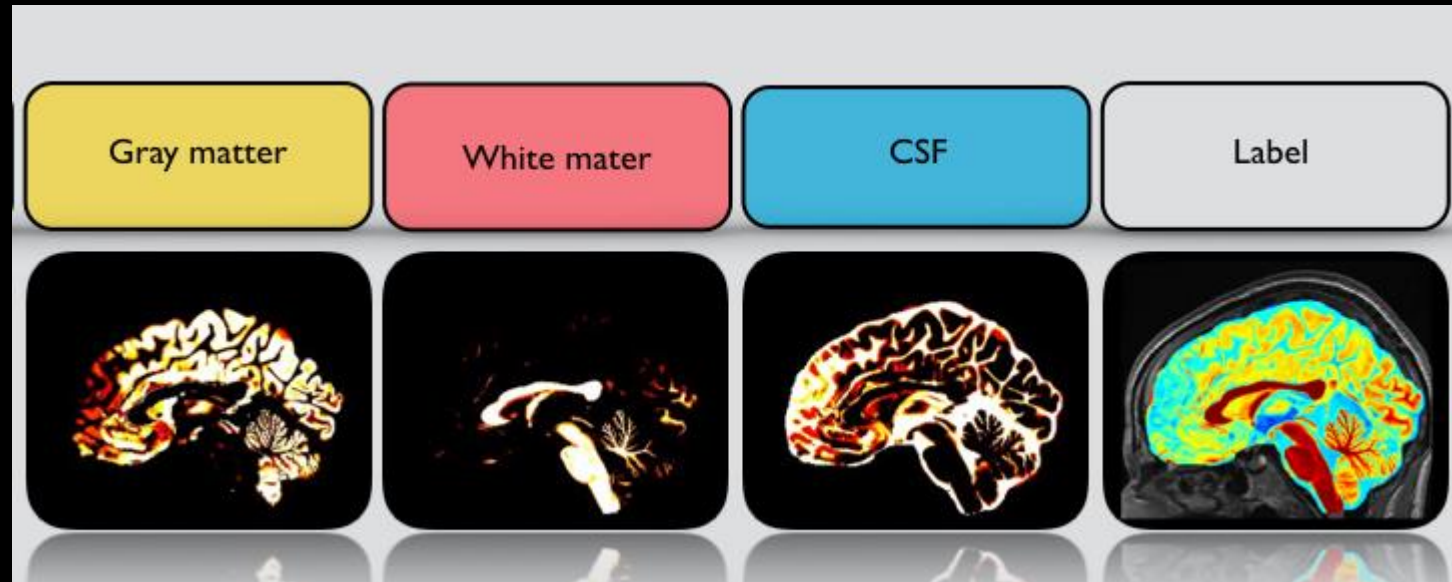
Morphometric analysis

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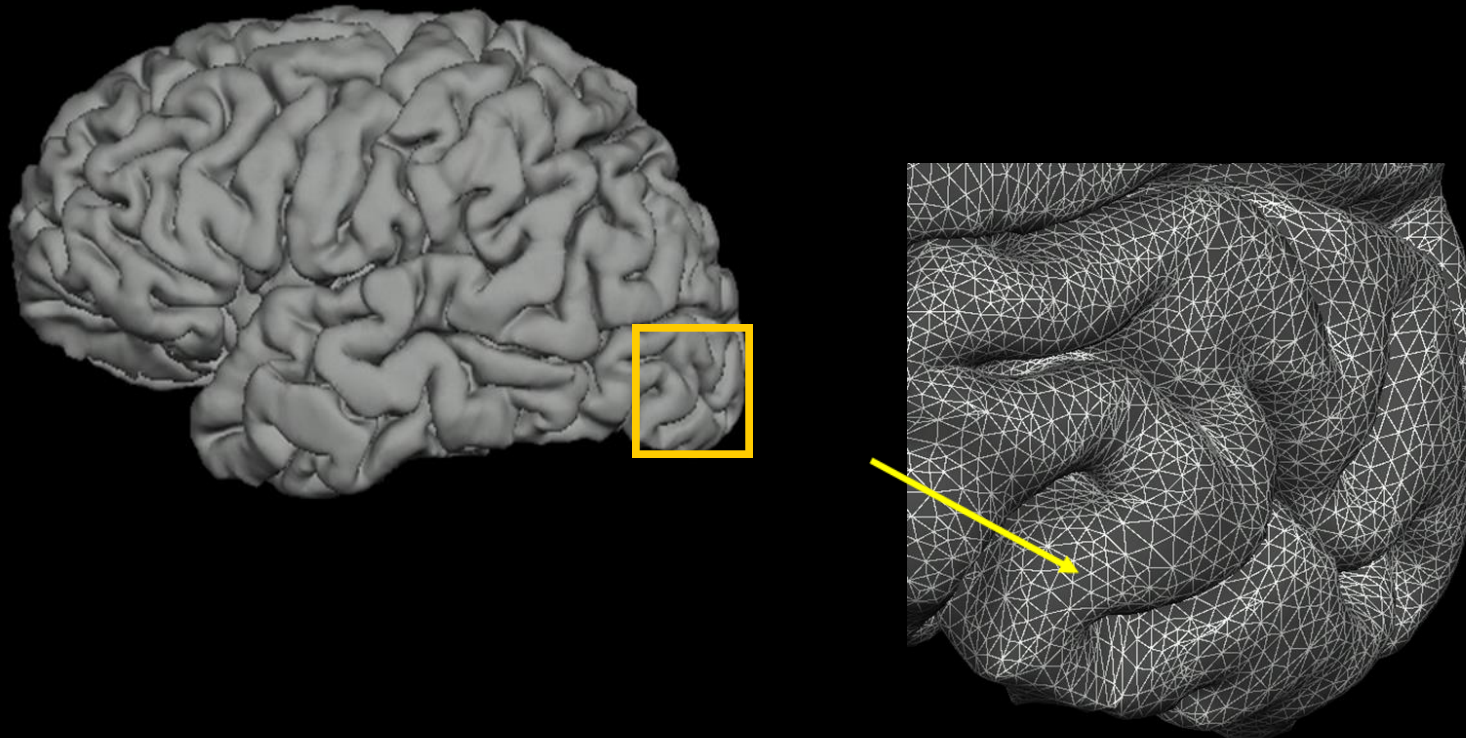
Voxel-based morphometry (VBM)

- **VBM provides the voxel-wise estimation of the local amount or volume of a specific tissue compartment**
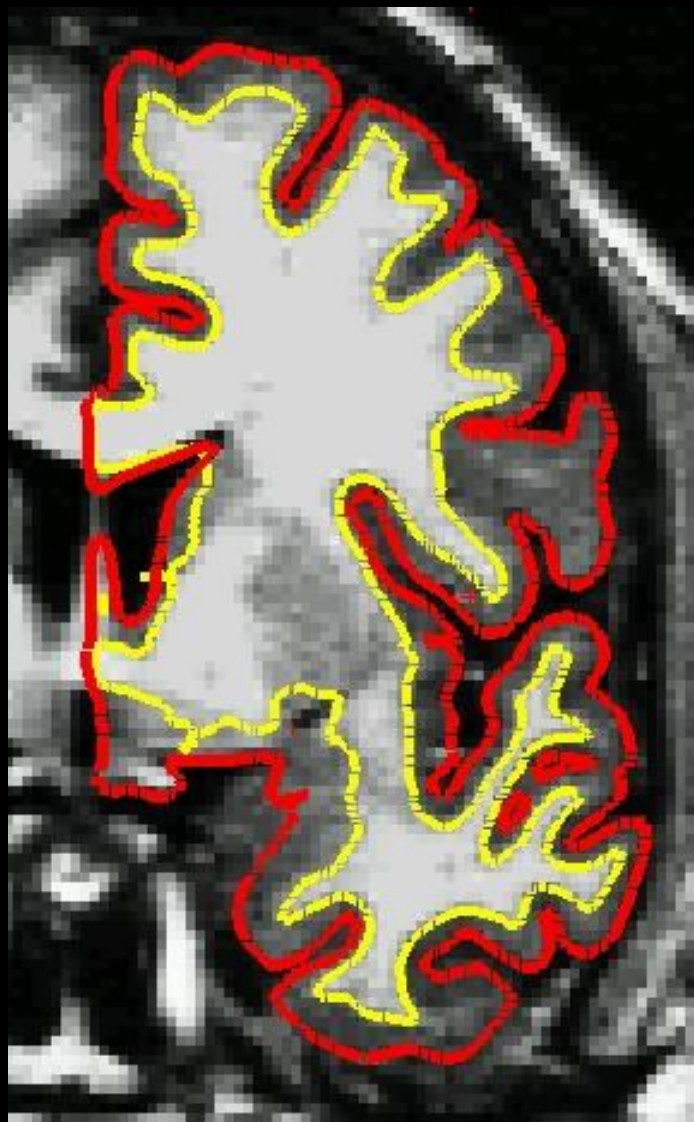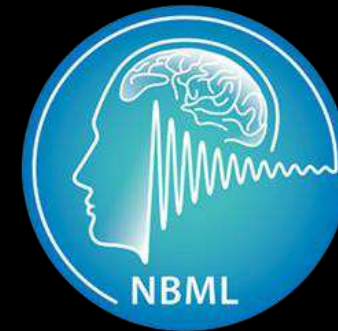
Surface-based morphometry (SBM)

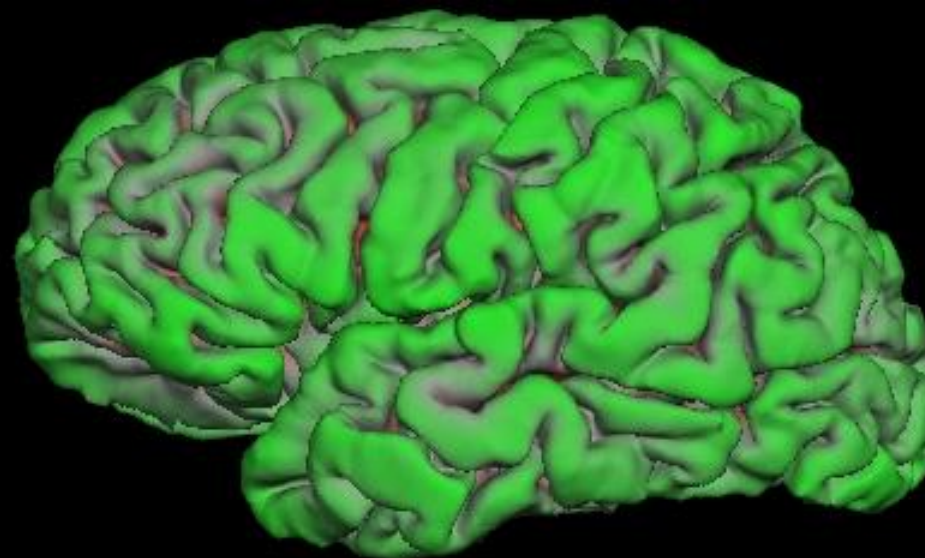- **Estimation of the cortical thickness and central surface of the left and right hemisphere.**

Surface-based morphometry (SBM)

Surface reconstruction

Deformation-based morphometry (DBM)

- **DBM is based on the application of non-linear registration procedures to spatially normalise one brain to another one.**
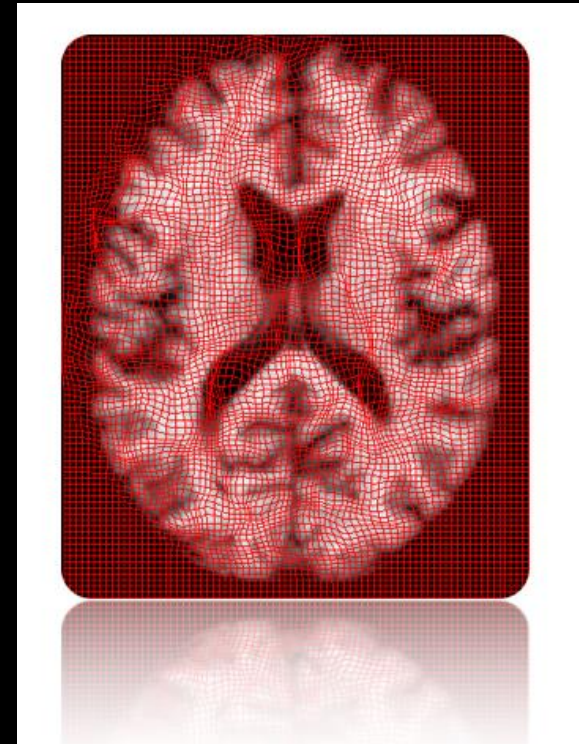
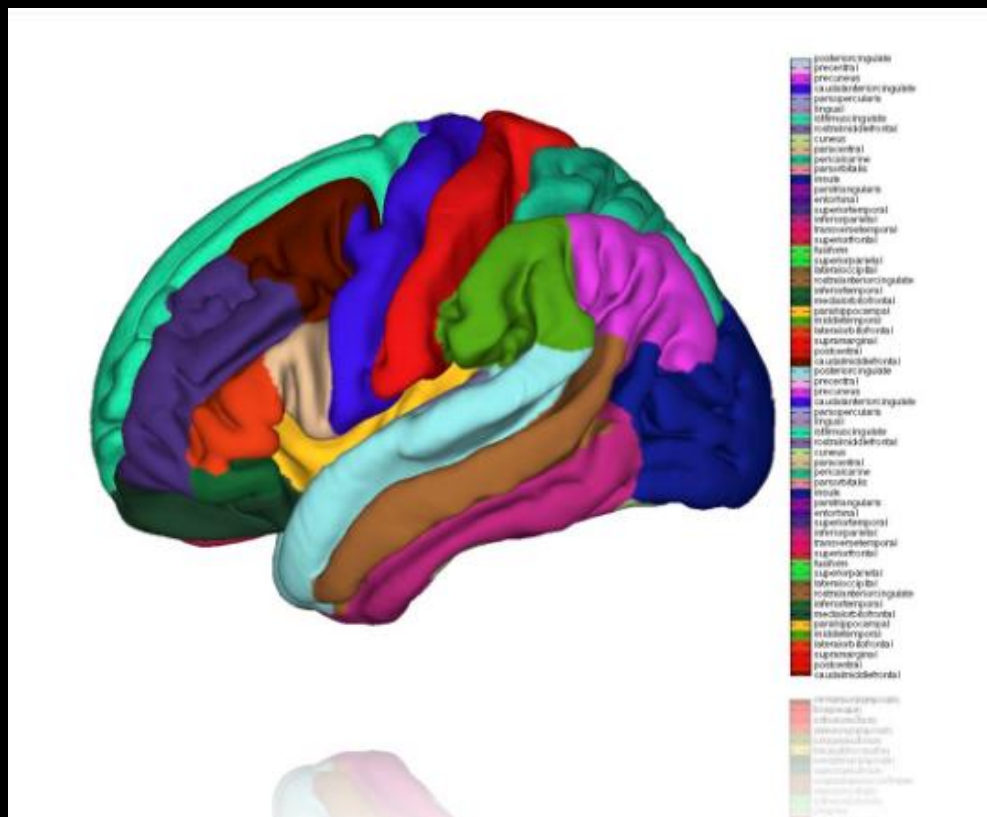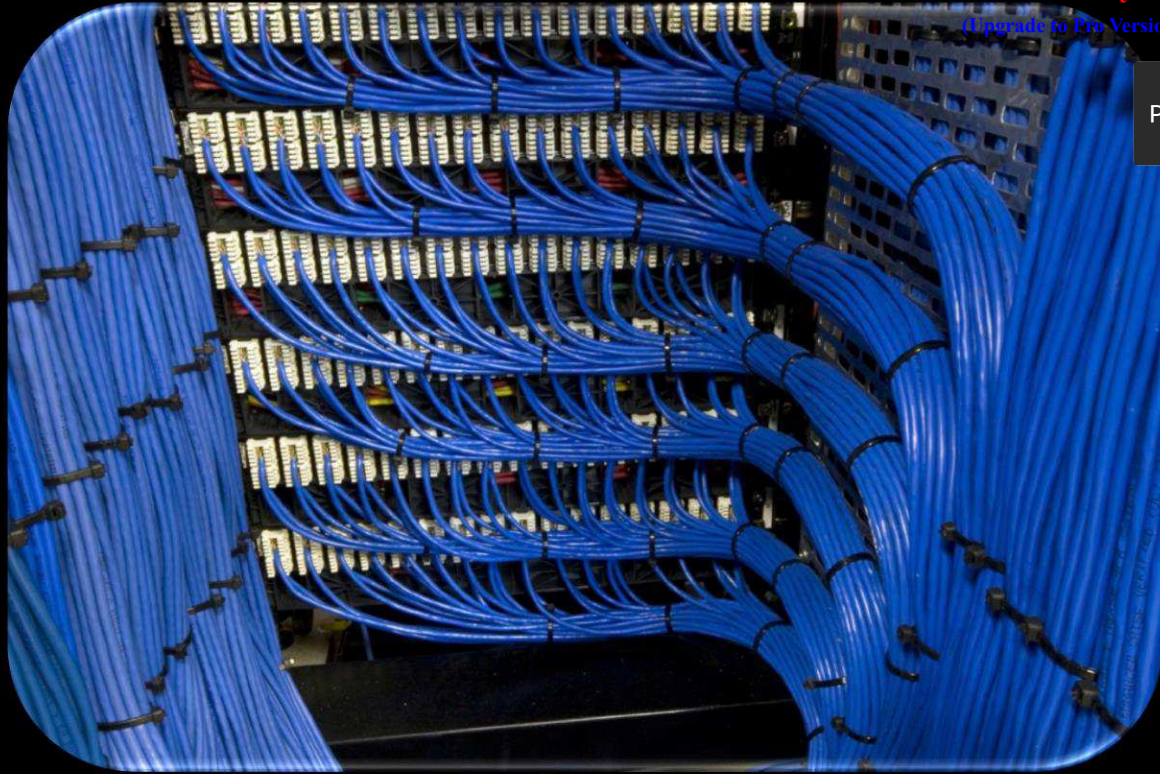# Region- or label-based morphometry (RBM)

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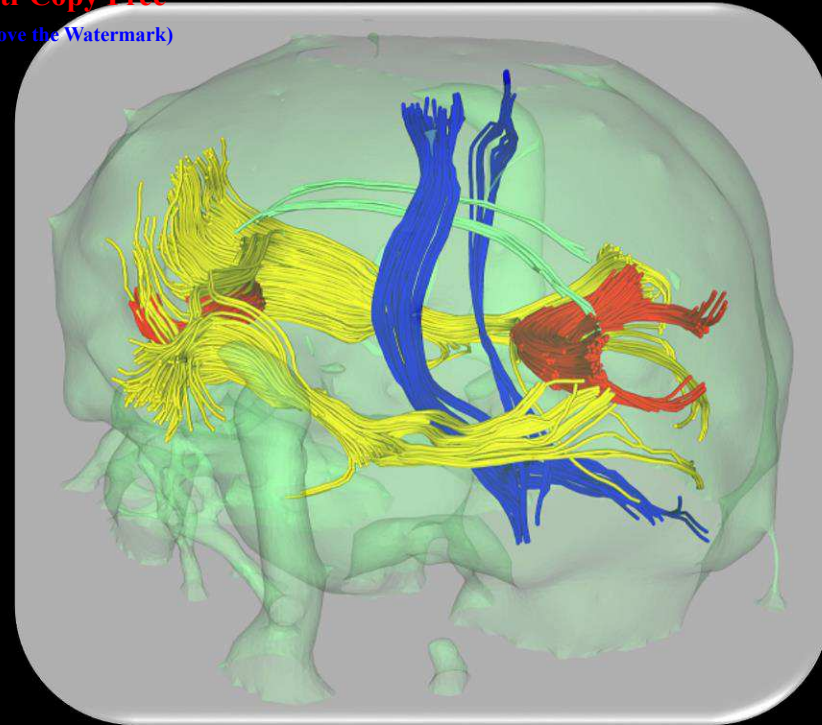
DTI:

UNC Computer Science: Network wire cabinets

An introduction to diffusion tensor image analysis-lauren-2011

Diffusion Tensor Imaging (DTI)

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
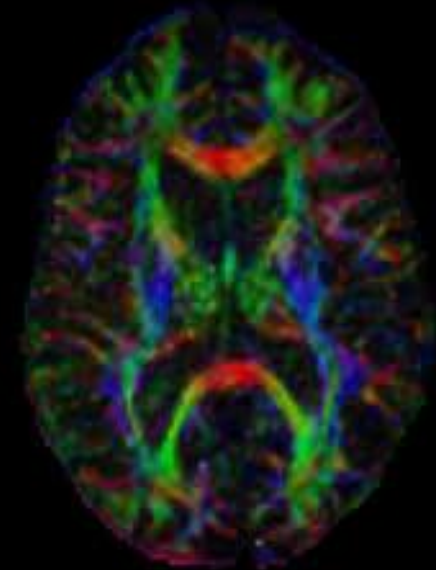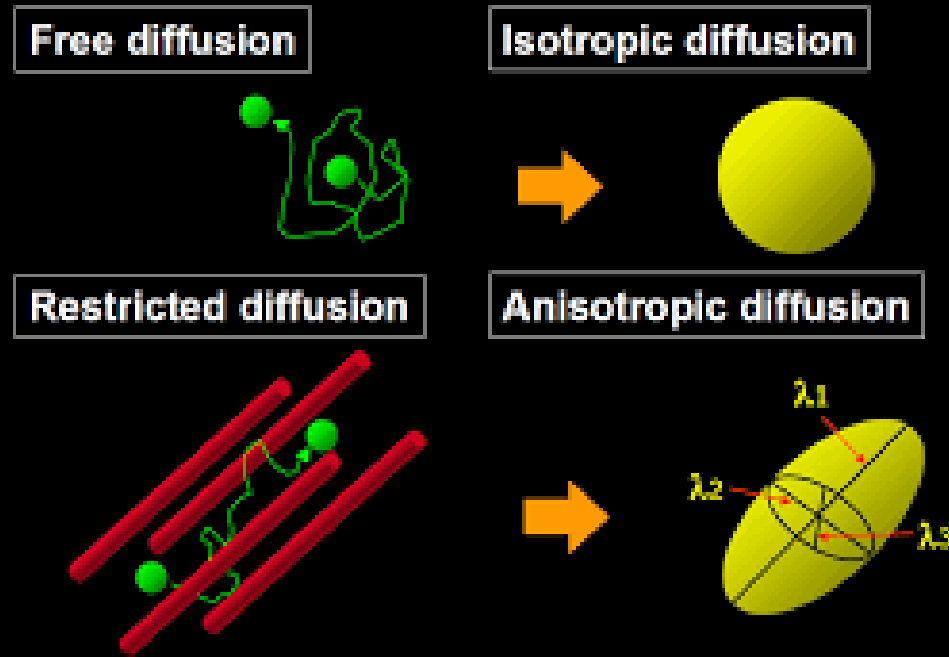[d]Institute of Neurology, Catholic University, Rome, Italy
[e]Department of Neuroscience, Brighton and Sussex Medical School, University of Sussex, Falmer, East Sussex, UK

diffusion tensor imaging (DTI)

- DTI is a special kind of DWI

- To map **white matter tractography** in the brain

Free diffusion

Isotropic diffusion

Restricted diffusion

Anisotropic diffusion

λ_1
λ_2
λ_3

colored fractional anisotropy map
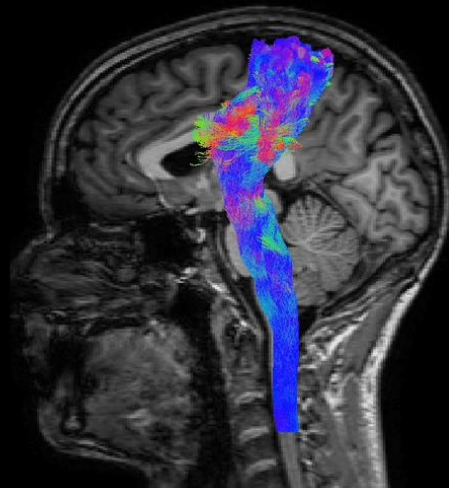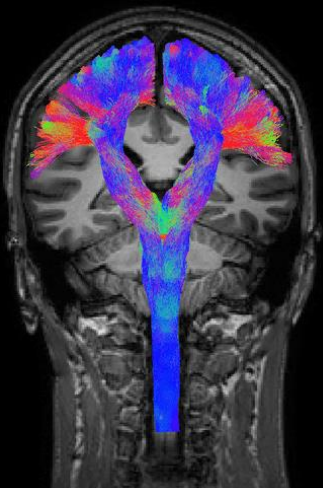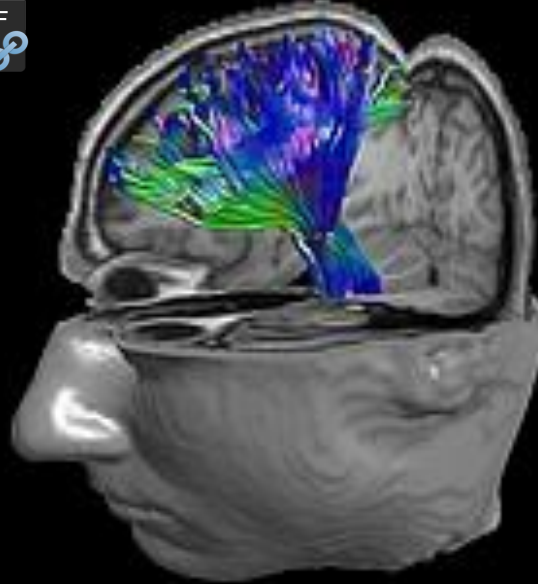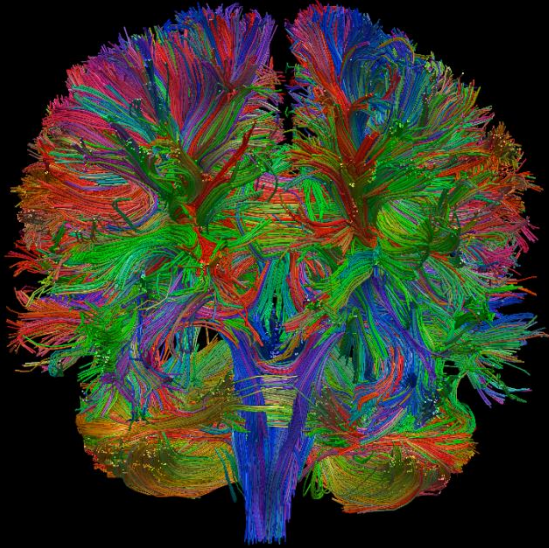
Diffusion tensor imaging (DTI)

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

$$FA = \sqrt{\frac{(\lambda_1-\lambda_2)^2+(\lambda_2-\lambda_3)^2+(\lambda_1-\lambda_3)^2}{2(\lambda_1^2+\lambda_2^2+\lambda_3^2)}}$$
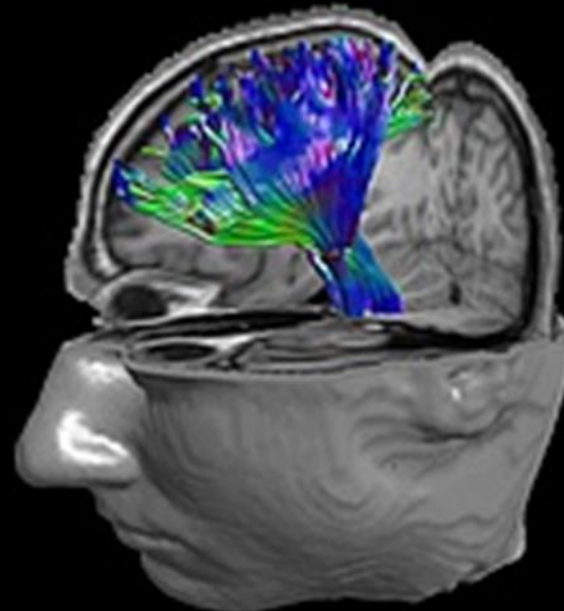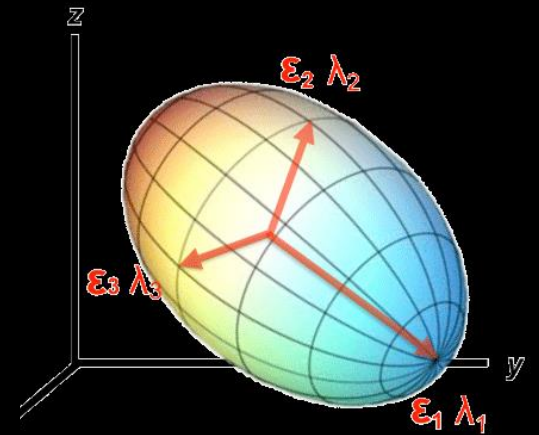
24

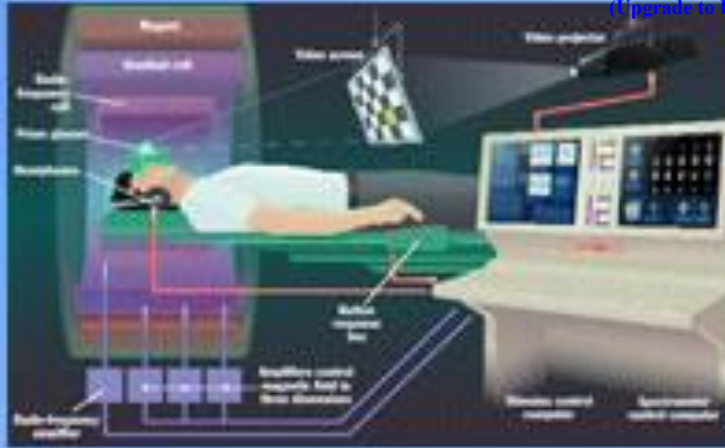# Diffusion tensor imaging (DTI)
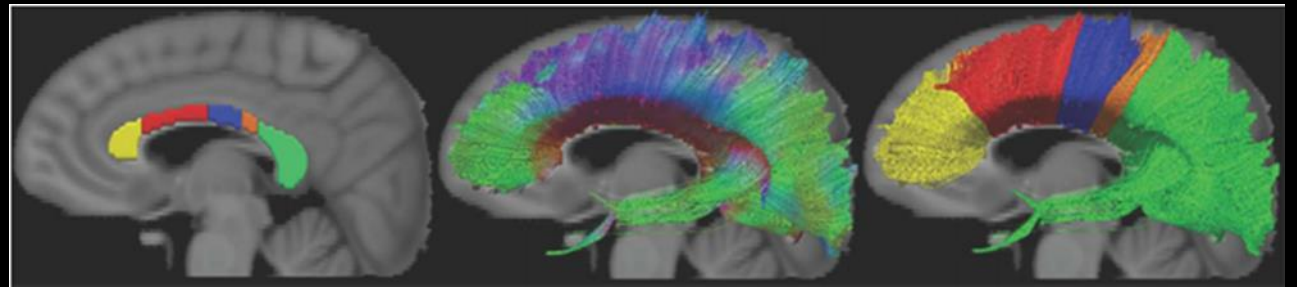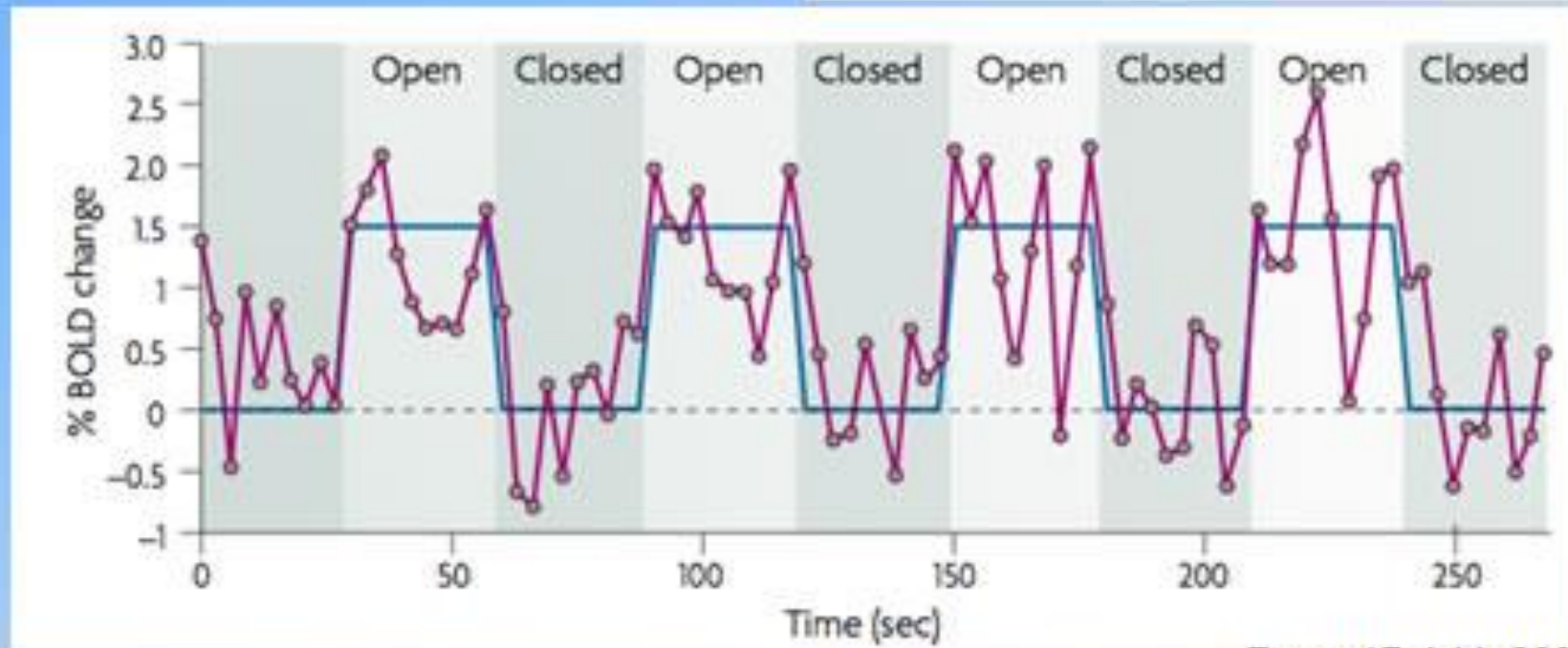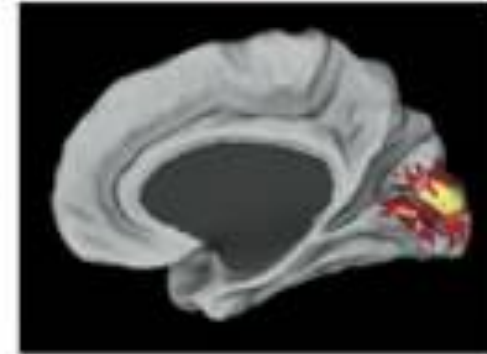
Functional MRI

Fox and Raichle 2007

Functional magnetic resonance imaging (fMRI)

Neurobiology of Aging 32 (2011) S37–S43

ELSEVIER

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
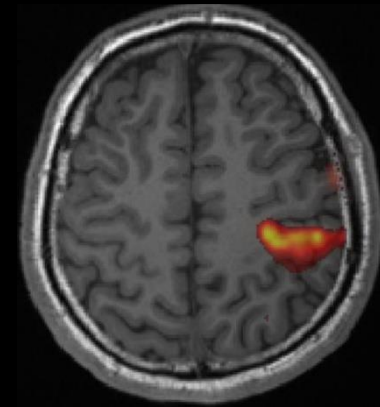   - Directs cortical stimulation
    - Near-infrared spectroscopy (NIRS)

Functional magnetic resonance imaging (fMRI)

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

Functional magnetic resonance imaging (fMRI)

- **Analysis Steps"**
  - ➤ **Temporal Processing:**
    - ✓ **Slice timing**
  - ➤ **Spatial Processing:**
    - ➤ **Realign**
    - ➤ **Co-registration**
    - ➤ **Segmentation**
    - ➤ **Normalization**
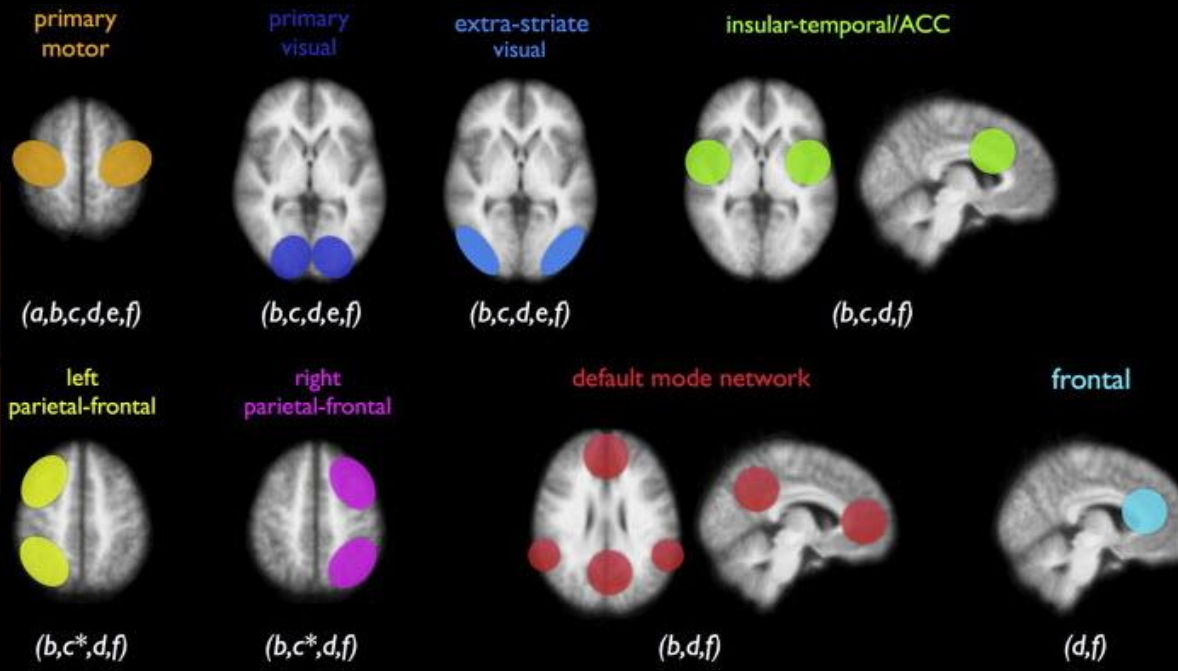   - ➤ **Smoothing**
  - ➤ **fMRI Statistics**
    - ✓ **fMRI model specification: GLM (spm:** using classical or Bayesian approaches **)**
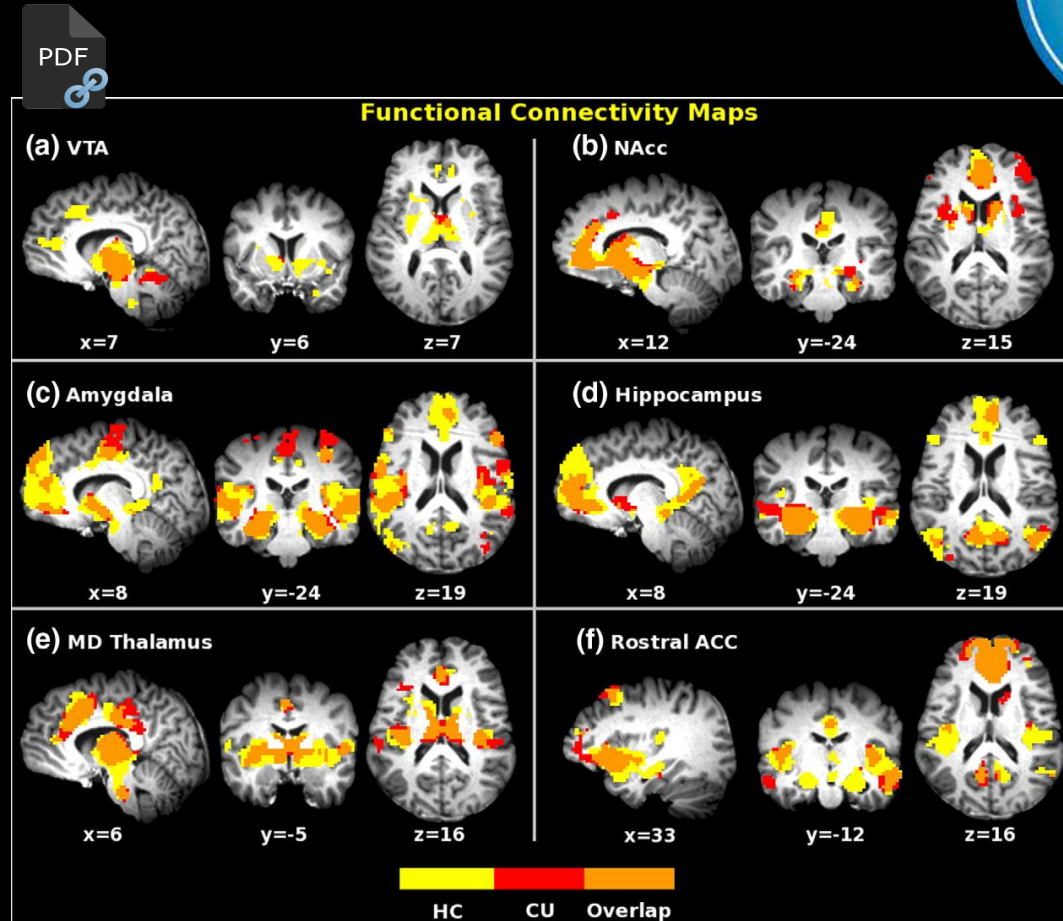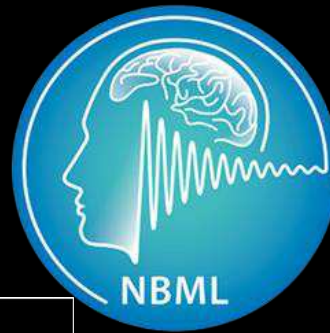   - ✓ **fMRI model estimate**

Normalization
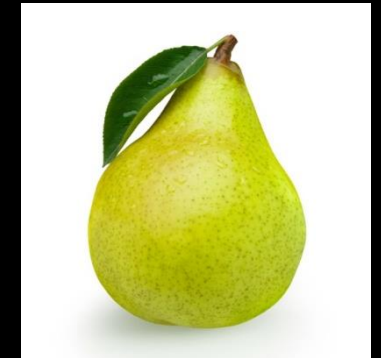
rest fMRI

rest fMRI

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

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

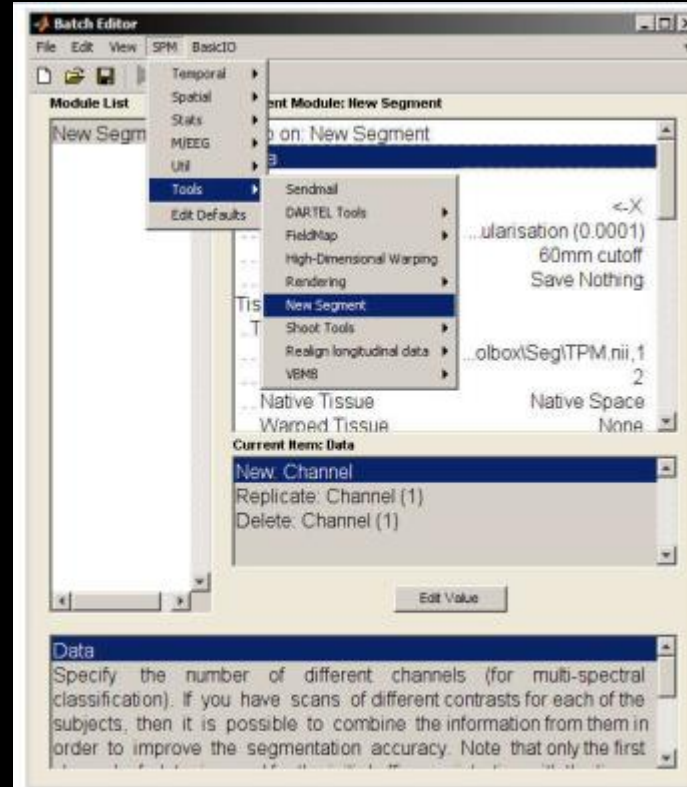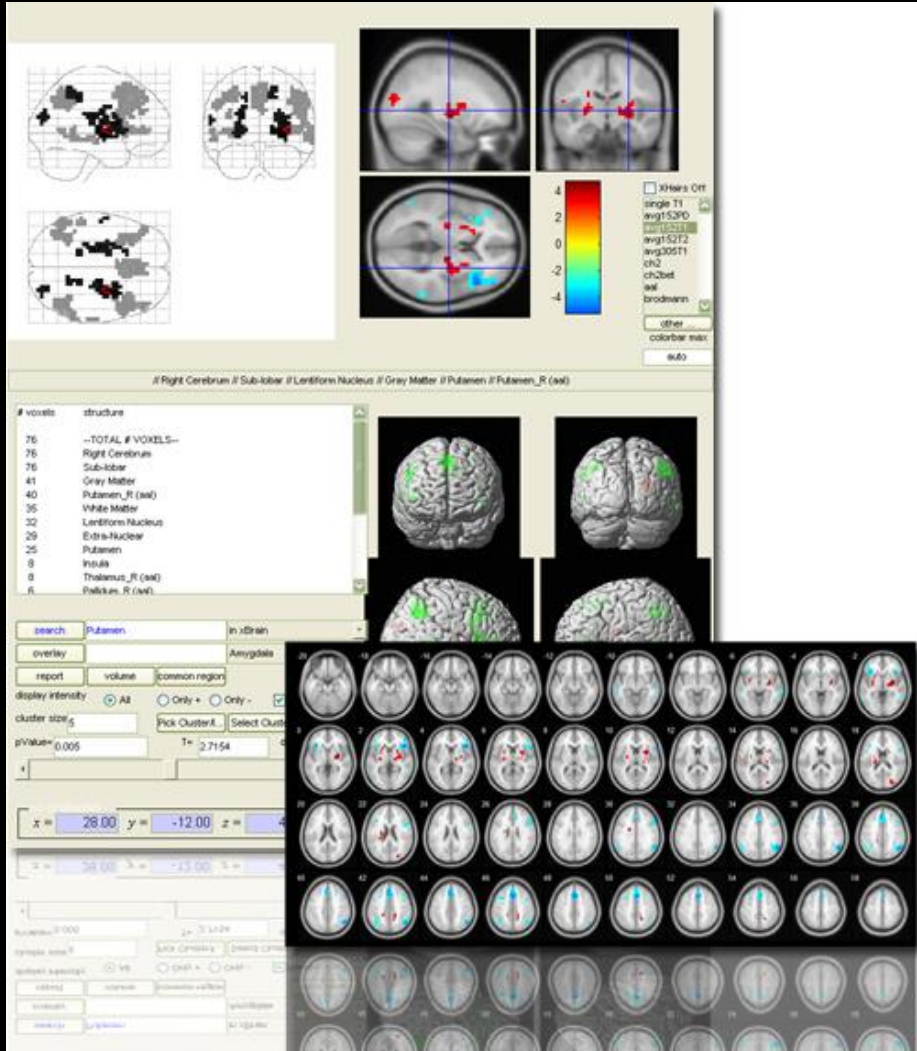# SPM (Statistical Parametric Mapping)

- 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
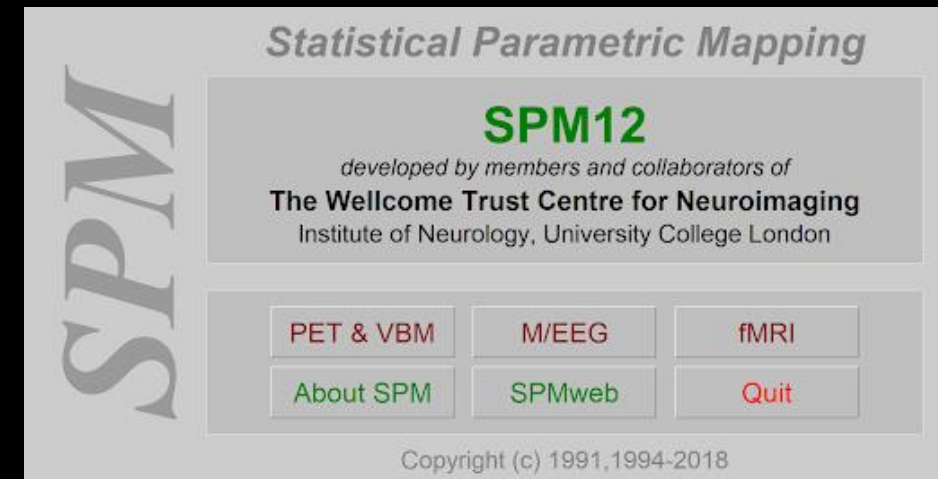
Statistical Parametric Mapping

SPM12
developed by members and collaborators of
The Wellcome Trust Centre for Neuroimaging
Institute of Neurology, University College London

| PET & VBM | M/EEG | fMRI |
| About SPM | SPMweb | Quit |

Copyright (c) 1991,1994-2018

SPM (Statistical Parametric Mapping)

# CAT (Computational Anatomy Toolbox)

- 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)

- 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
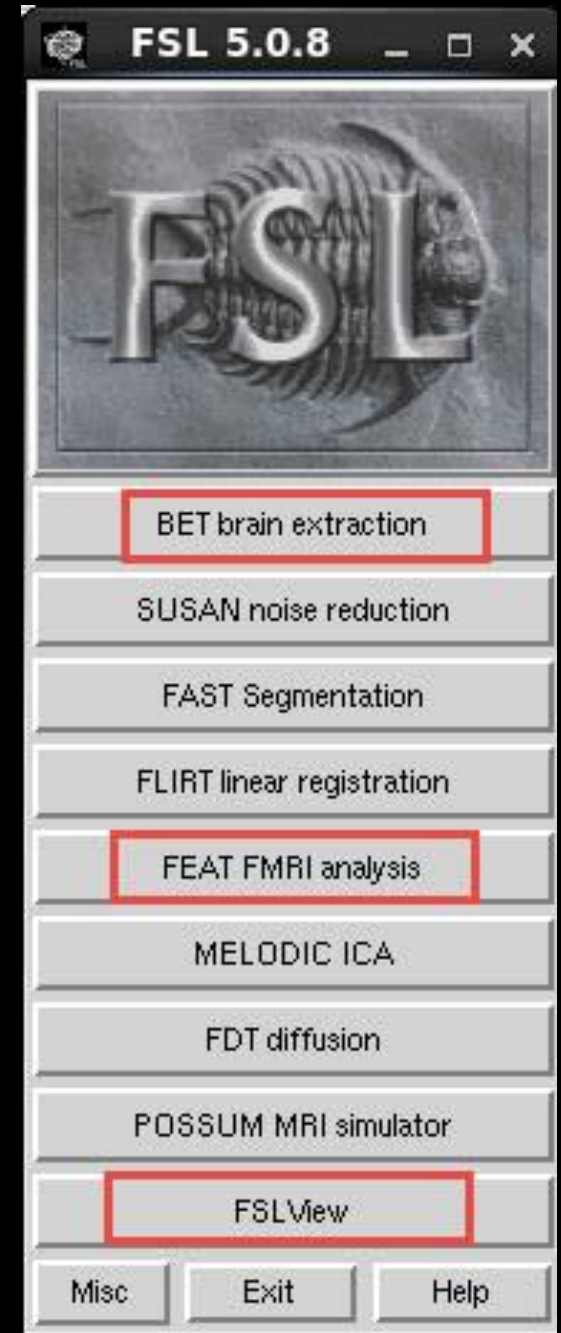 - ✓ fMRI
  - ✓ MRI
  - ✓ DTI
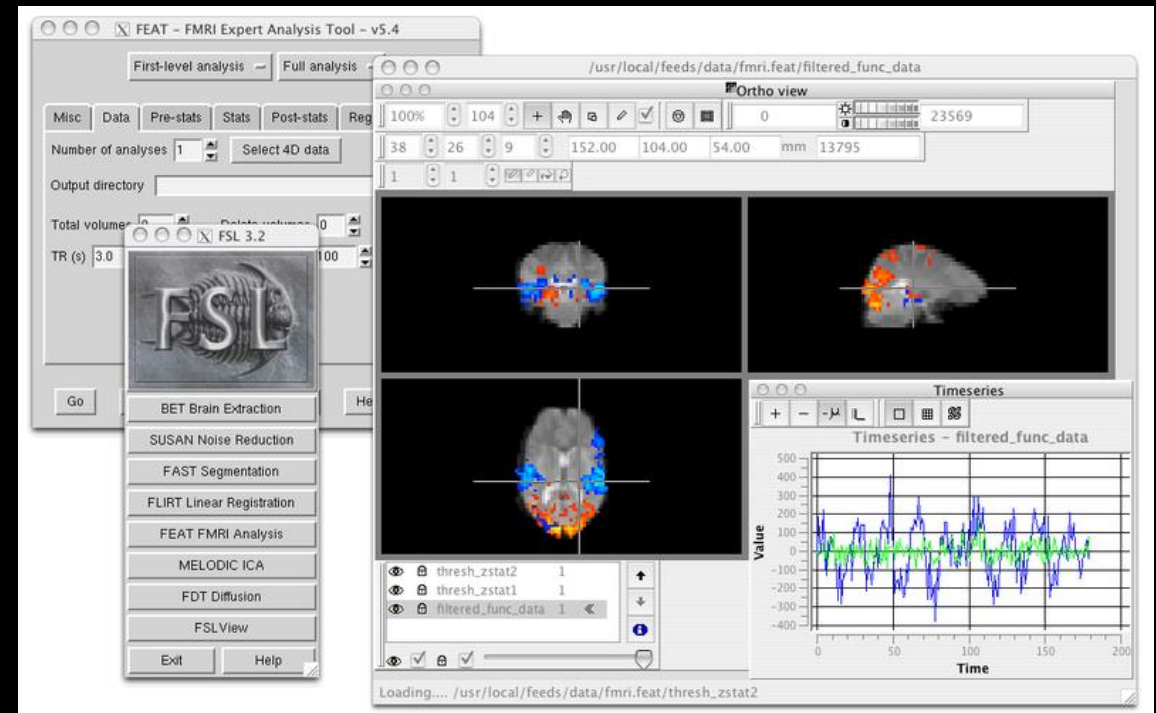
FSL (FMRIB Software Library)

- **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)
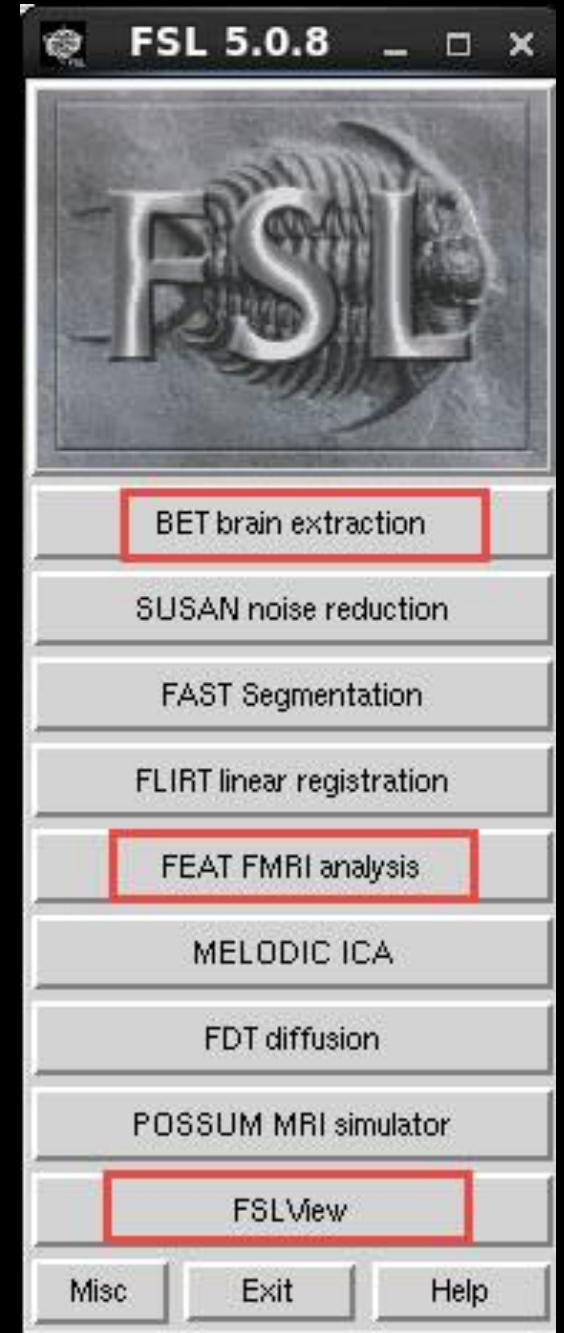
FSL (FMRIB Software Library)

- **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.feat

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)
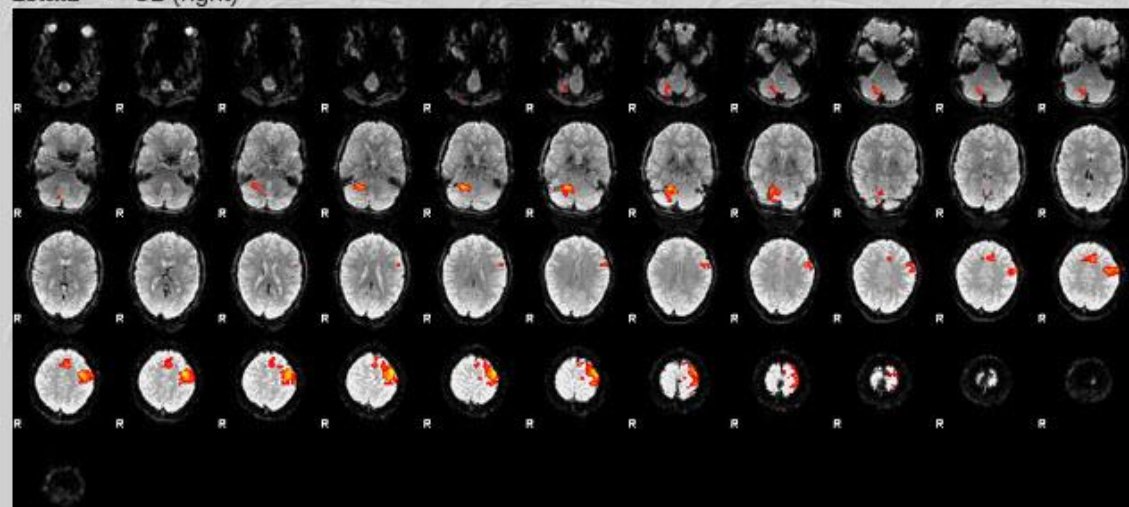
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FreeSurfer:

- 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
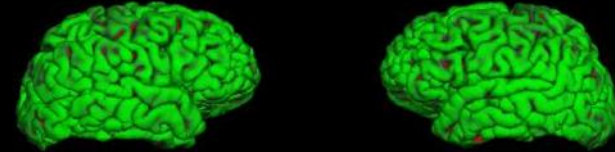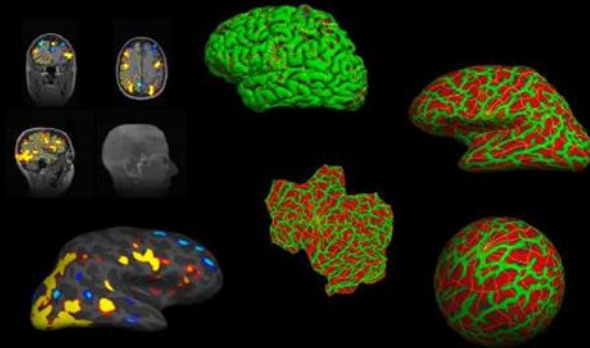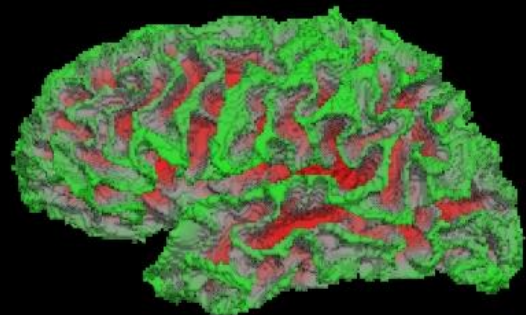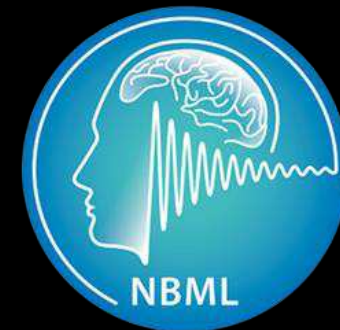
http://surfer.nmr.mgh.harvard.edu

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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.
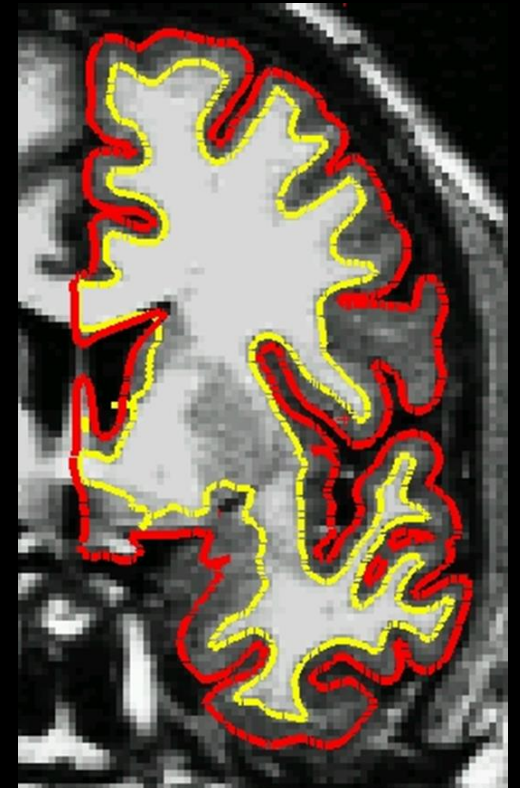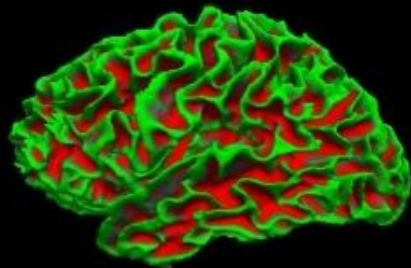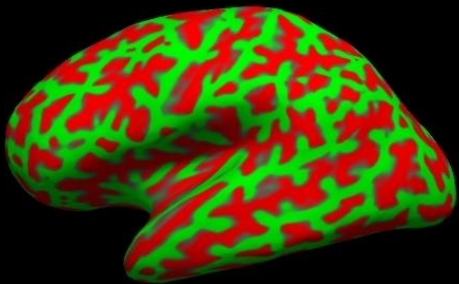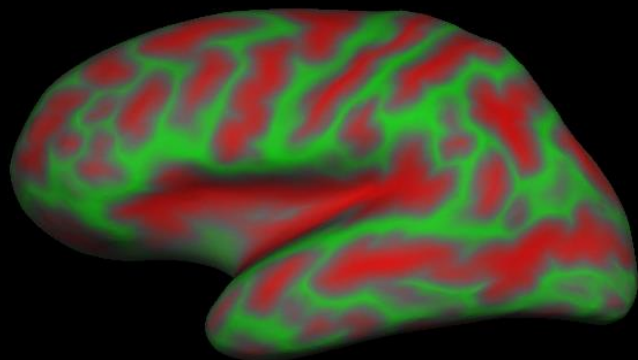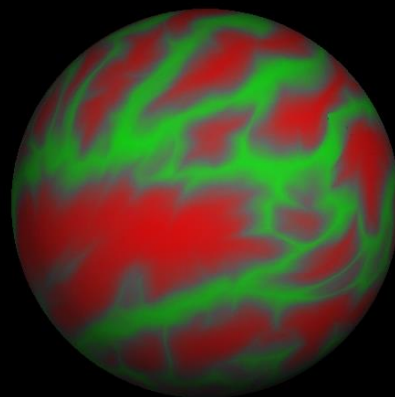
FreeSurfer
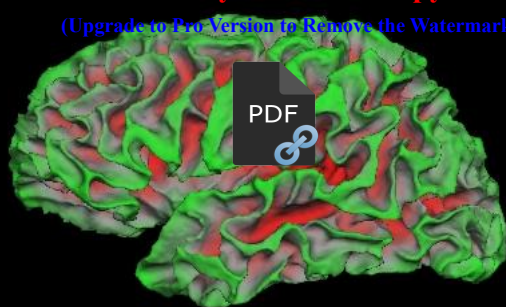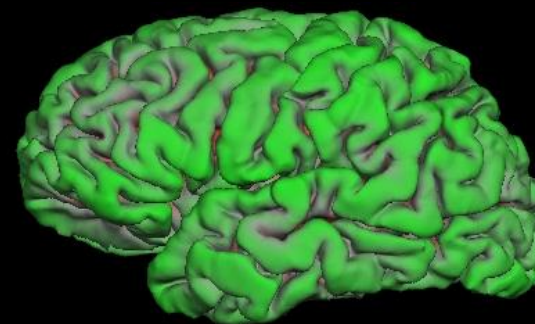
orig   white   pial

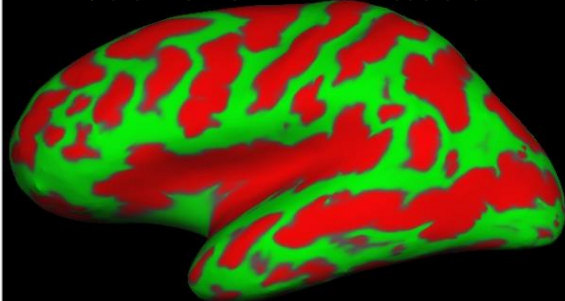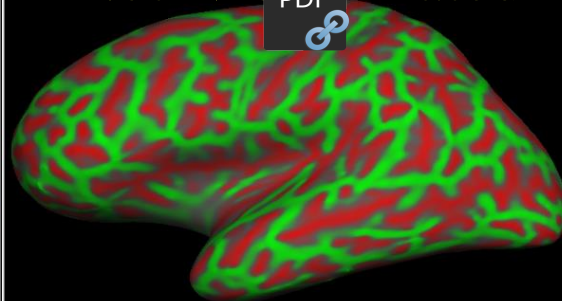inflated   sphere,sphere.reg   flat
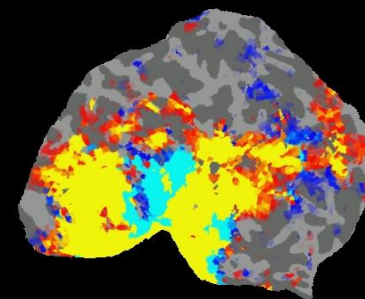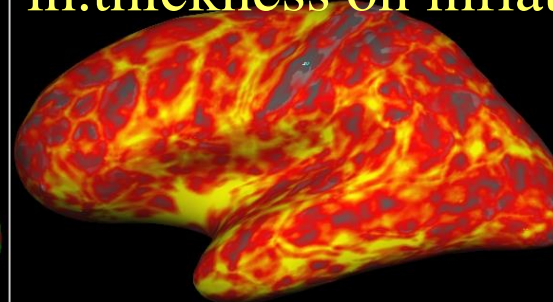
FreeSurfer

lh.sulc on inflated

lh.curv on inflated

lh.thickness on inflated

lh.sulc on pial

lh.curv on inflated

fMRI on flat
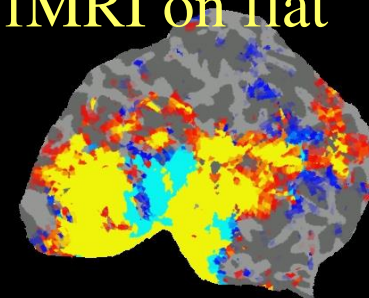
lh.aparc.annot on inflated
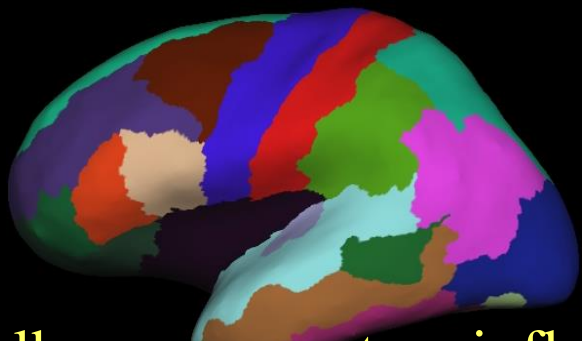
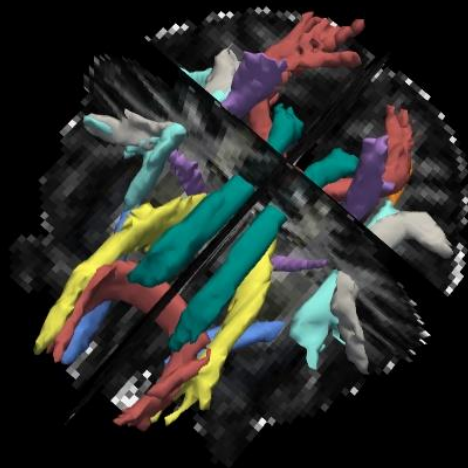# FreeSurfer

- 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)

- 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)
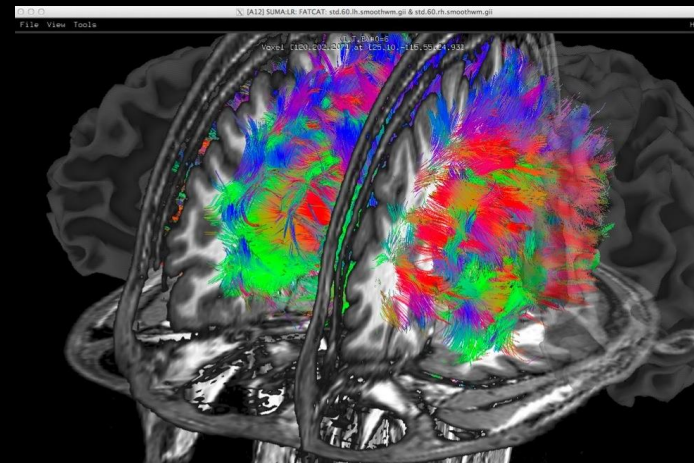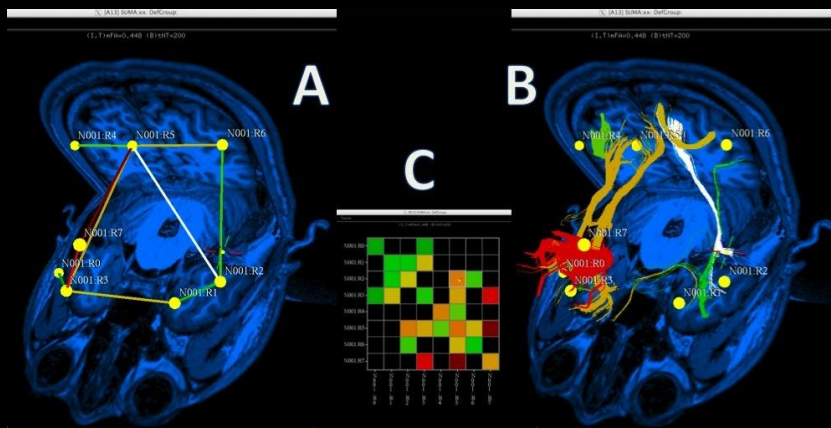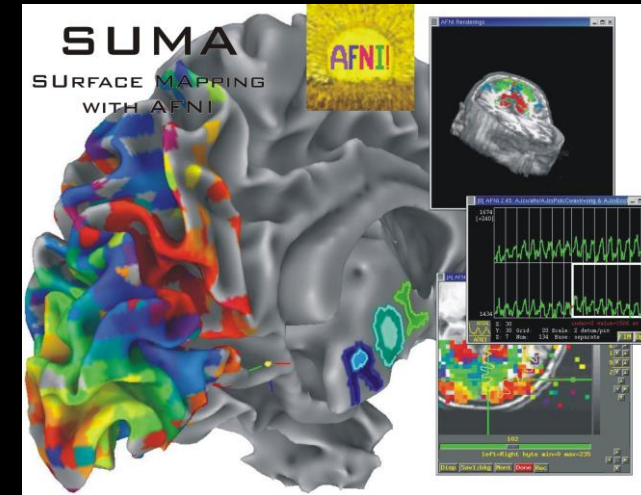
- For fMRI and DTI analysis

AFNI (Analysis of Functional NeuroImages)

- ## 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
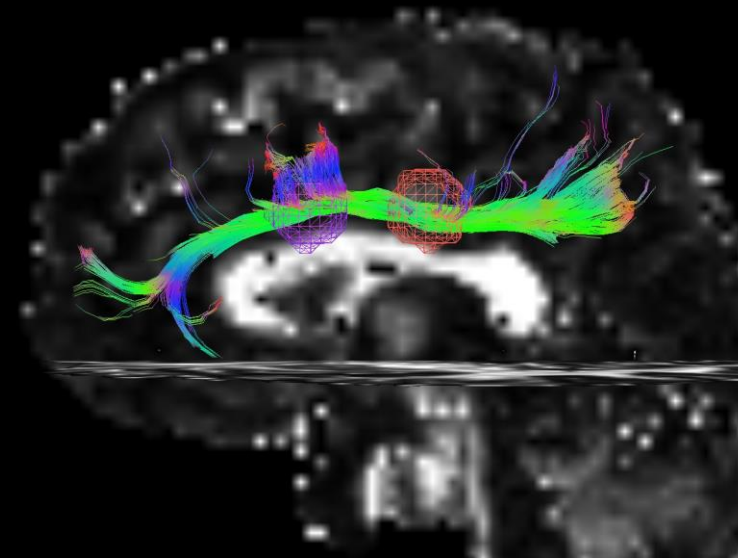
AFNI (Analysis of Functional NeuroImages)

- **FATCAT:** The Functional And Tractographic Connectivity Toolbox

- combining FMRI and diffusion-based data

- Statistics
  - ✓ **Multivariate modeling approach for group analysis**
  - ✓ **Linear Mixed-Effects Modeling**
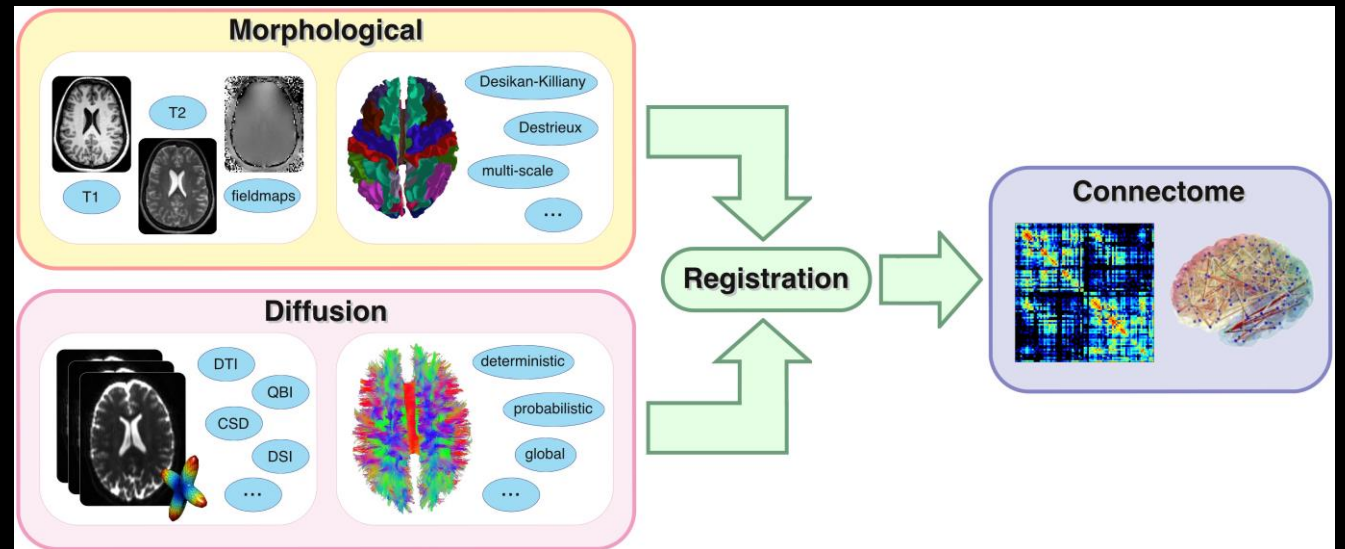 - ✓ **Mixed-Effects Meta Analysis (MEMA)**

The Connectome Mapper

- 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:
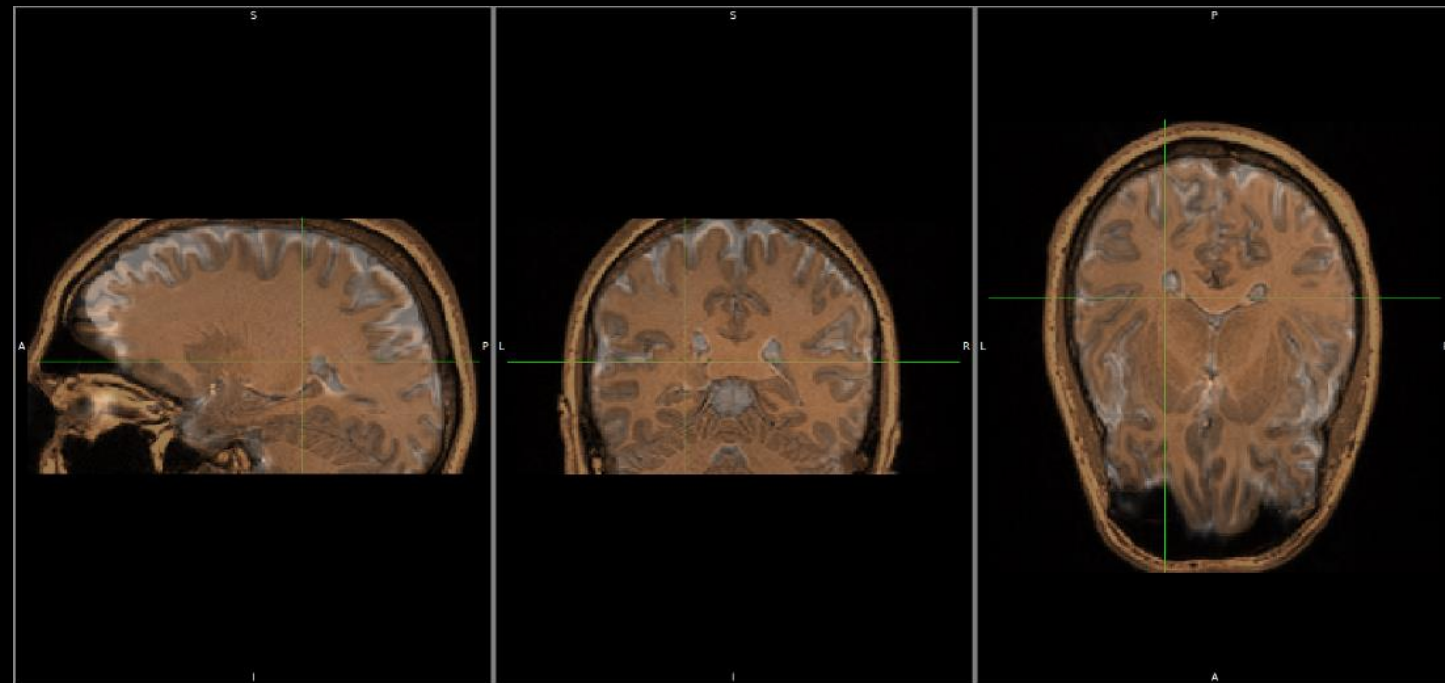 - FSL
  - Freesurfer
  - DIFFUSION TOOLKIT (trackvis)

The Connectome Mapper

- **Registration**

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

The Connectome Mapper

- **Segmentation**

T1 is segmented using Freesurfer

Surfaces are extracted using Freesurfer
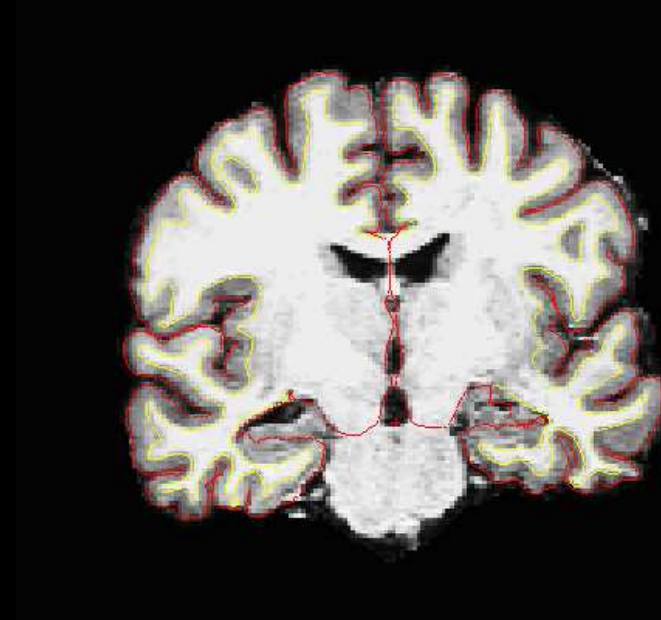
The Connectome Mapper

- **Parcellation**

- Cortical and subcortical parcellation are shown with Freeview
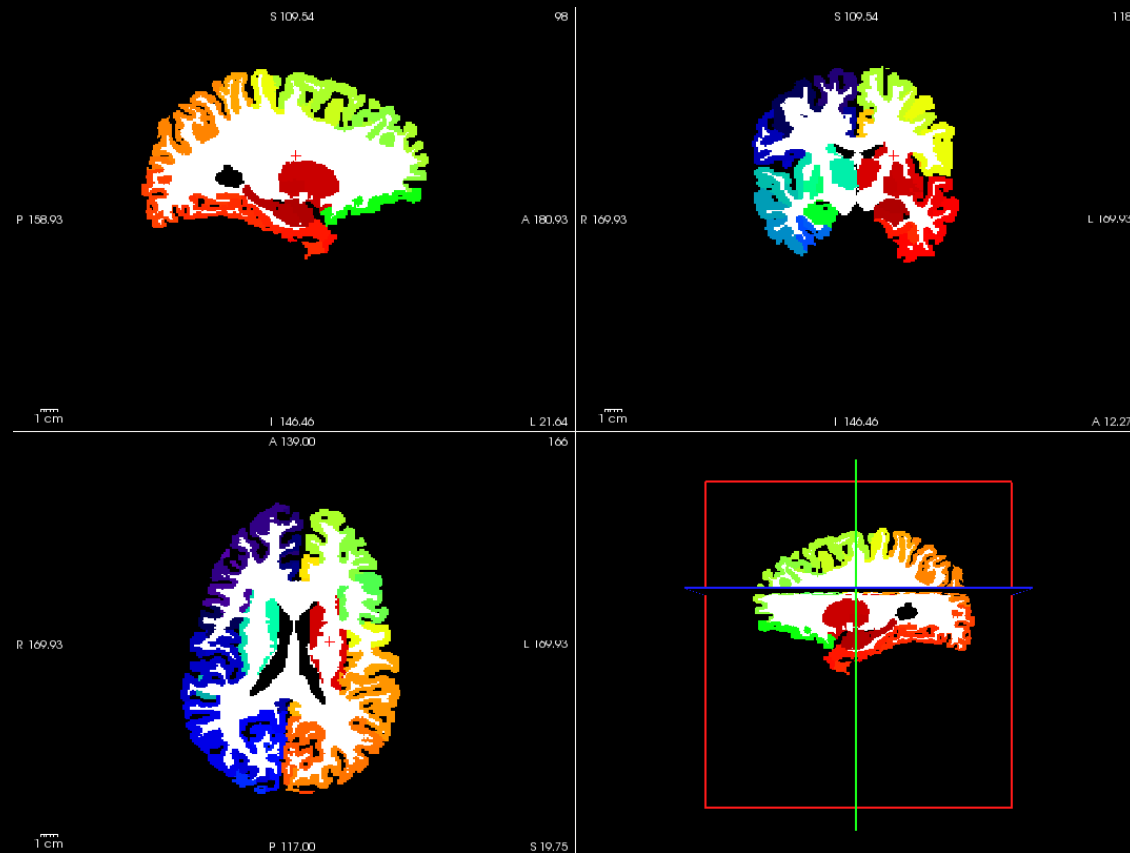
The Connectome Mapper

- **Tractography**

- DSI Tractography results are displayed with TrackVis
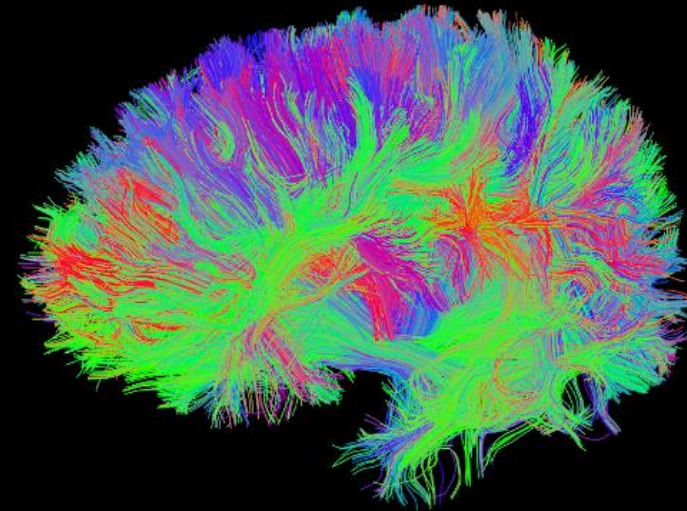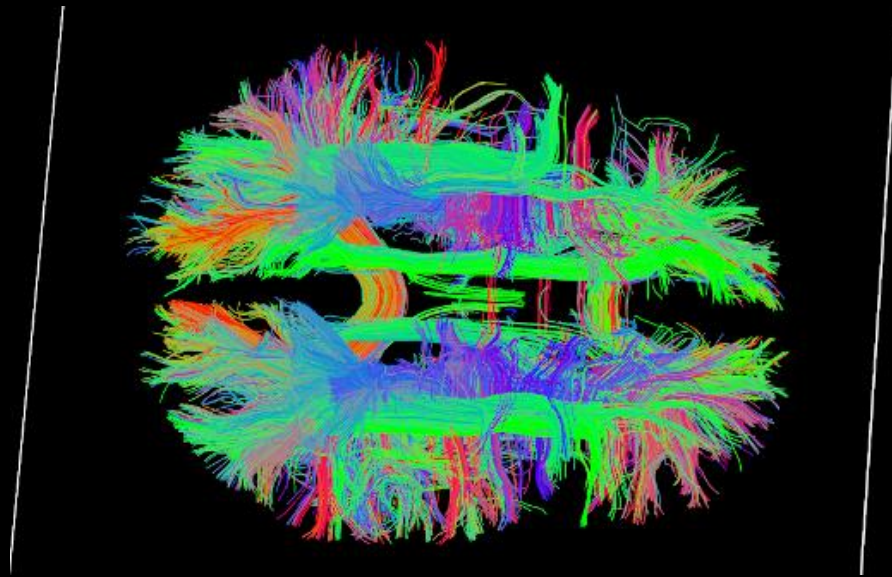
The Connectome Mapper

- Connection Matrix Creation
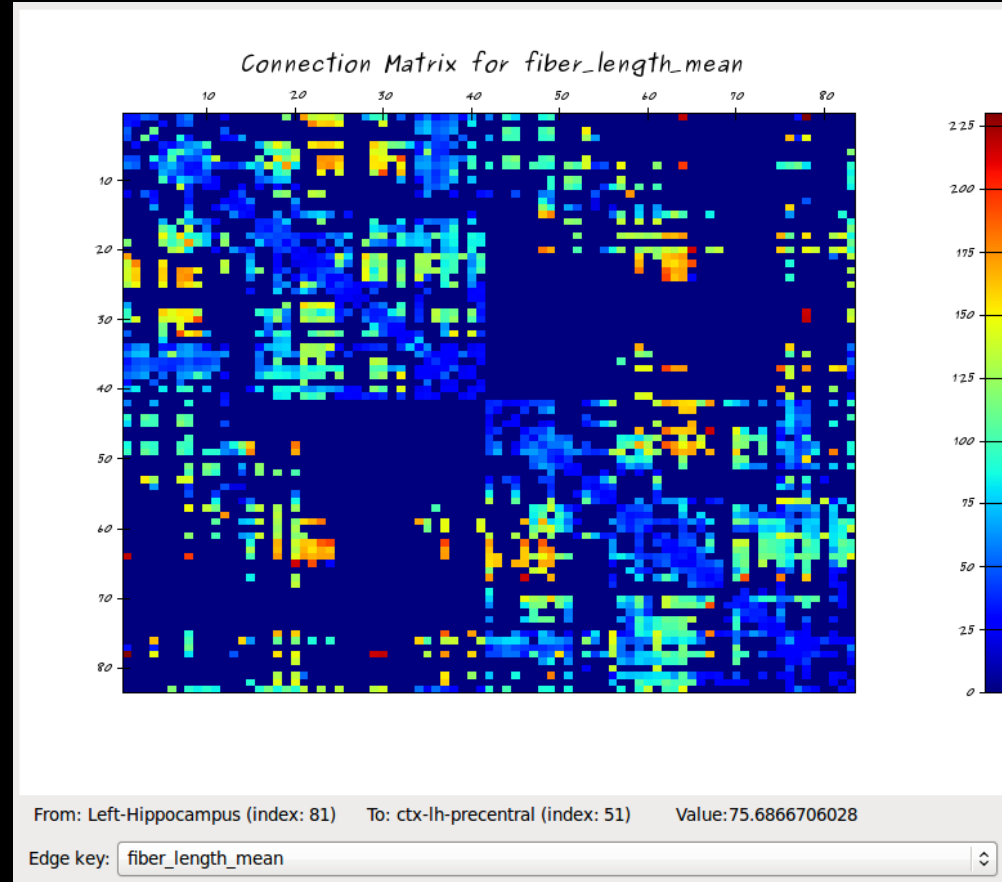
Connection Matrix for fiber_length_mean

From: Left-Hippocampus (index: 81)   To: ctx-lh-precentral (index: 51)   Value:75.6866706028

Edge key: fiber_length_mean

Explore DTI

- A graphical toolbox for
  - ✓Processing
  - ✓Analyzing
  - ✓Visualizing

  diffusion MR data

- Written in Matlab

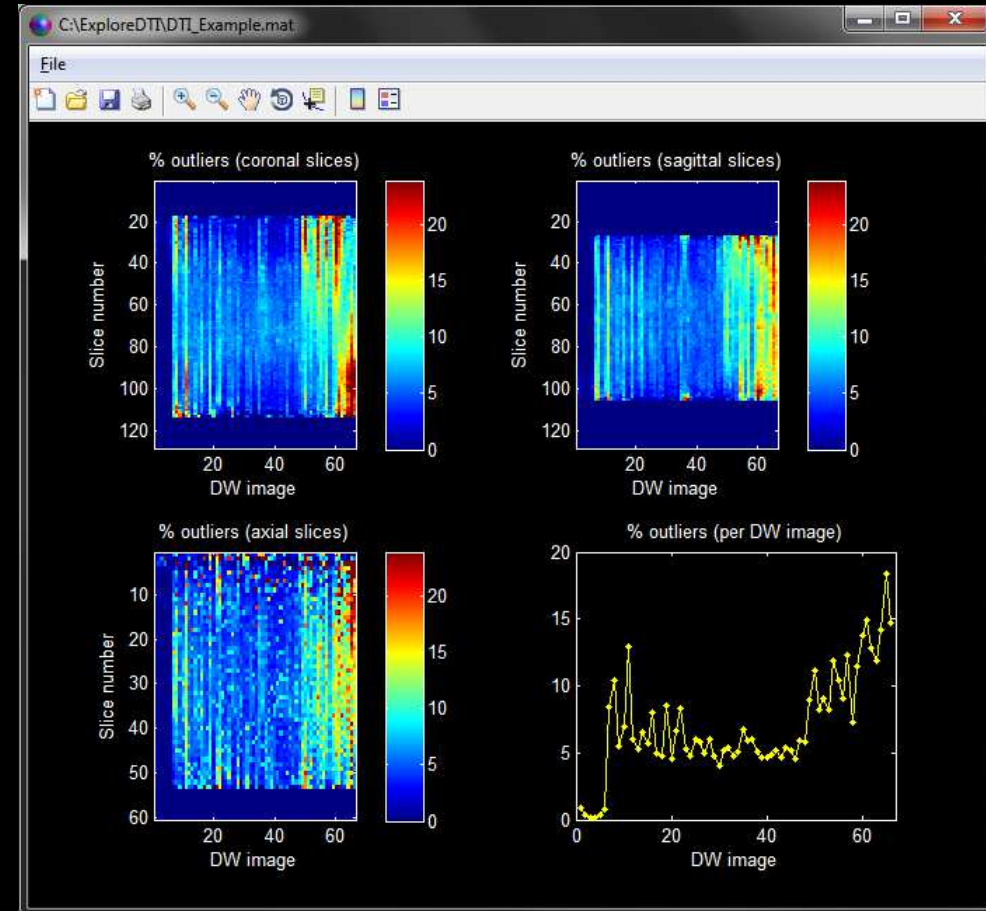- Works across multiple platforms:
  - ✓Windows PC, Unix, Mac

Explore DTI

- **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*
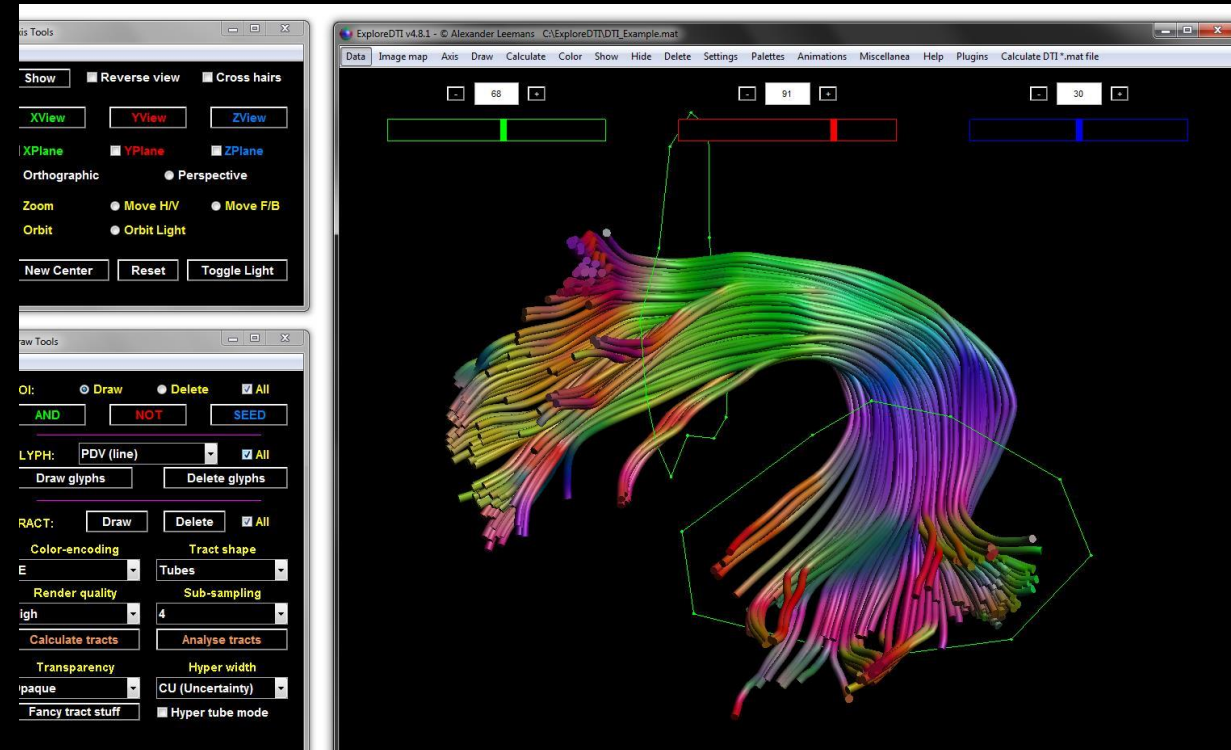 - *Making animations*
  - *Network analysis tools*

Explore DTI

- **Key features** :
  - *Data Reconstruction*
  - *Motion / Eddy Current Correction*:
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  - *Fiber tractography*
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  - Tract-segment analysis
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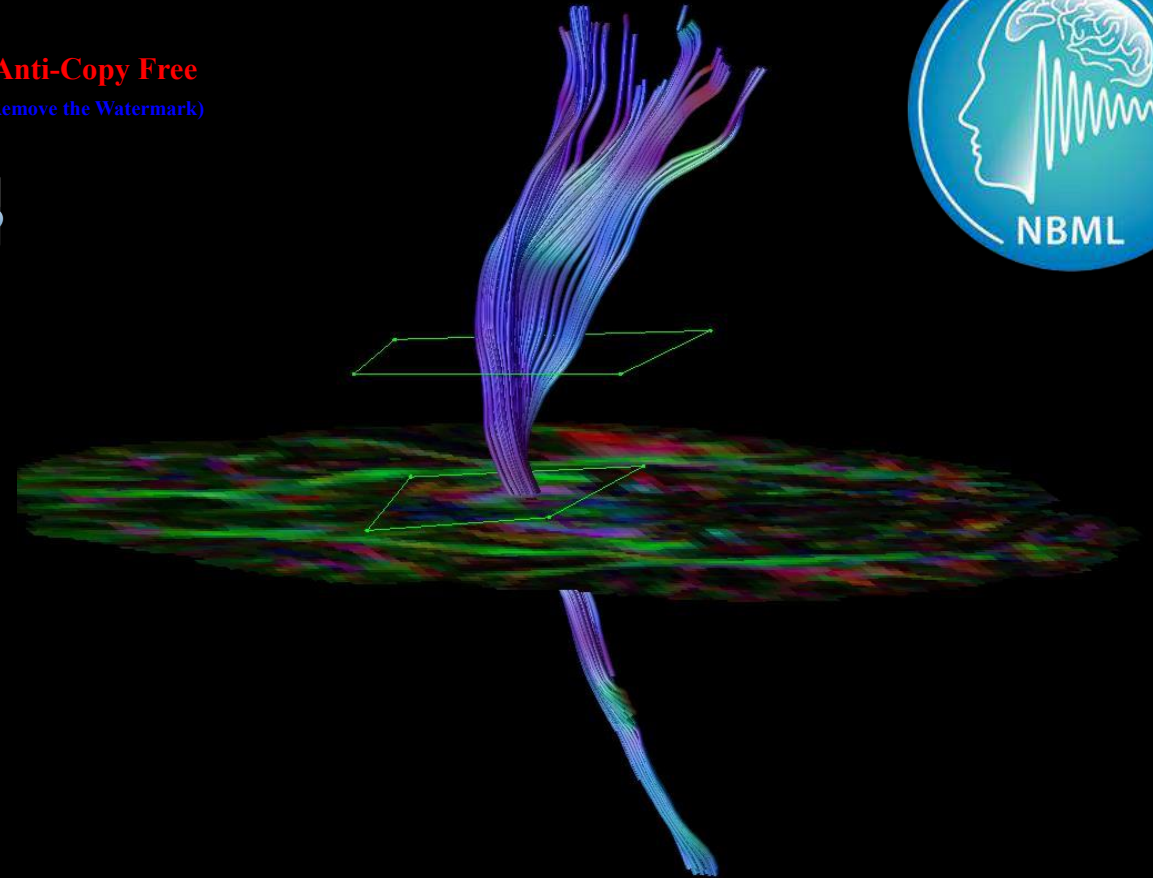 - *Making animations*
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Explore DTI

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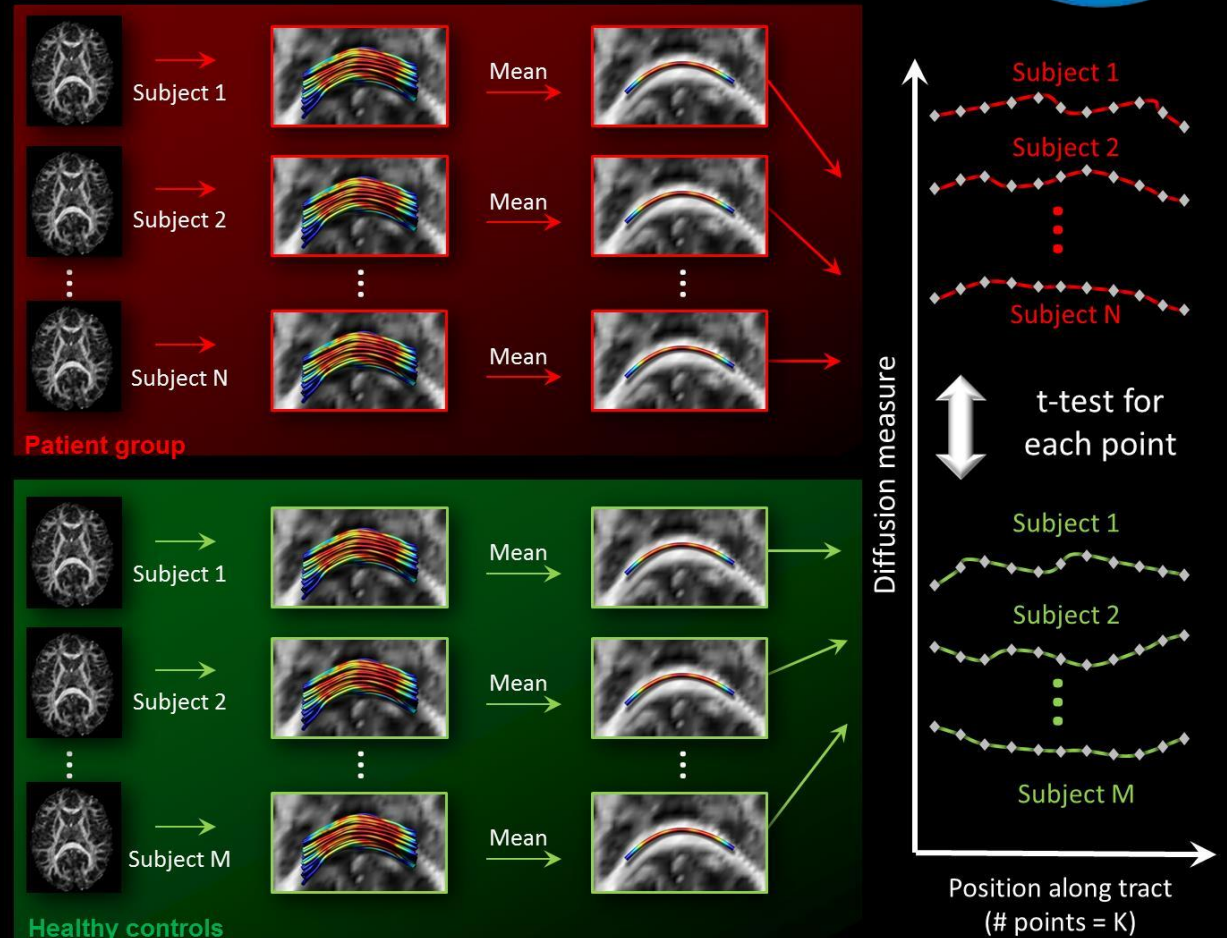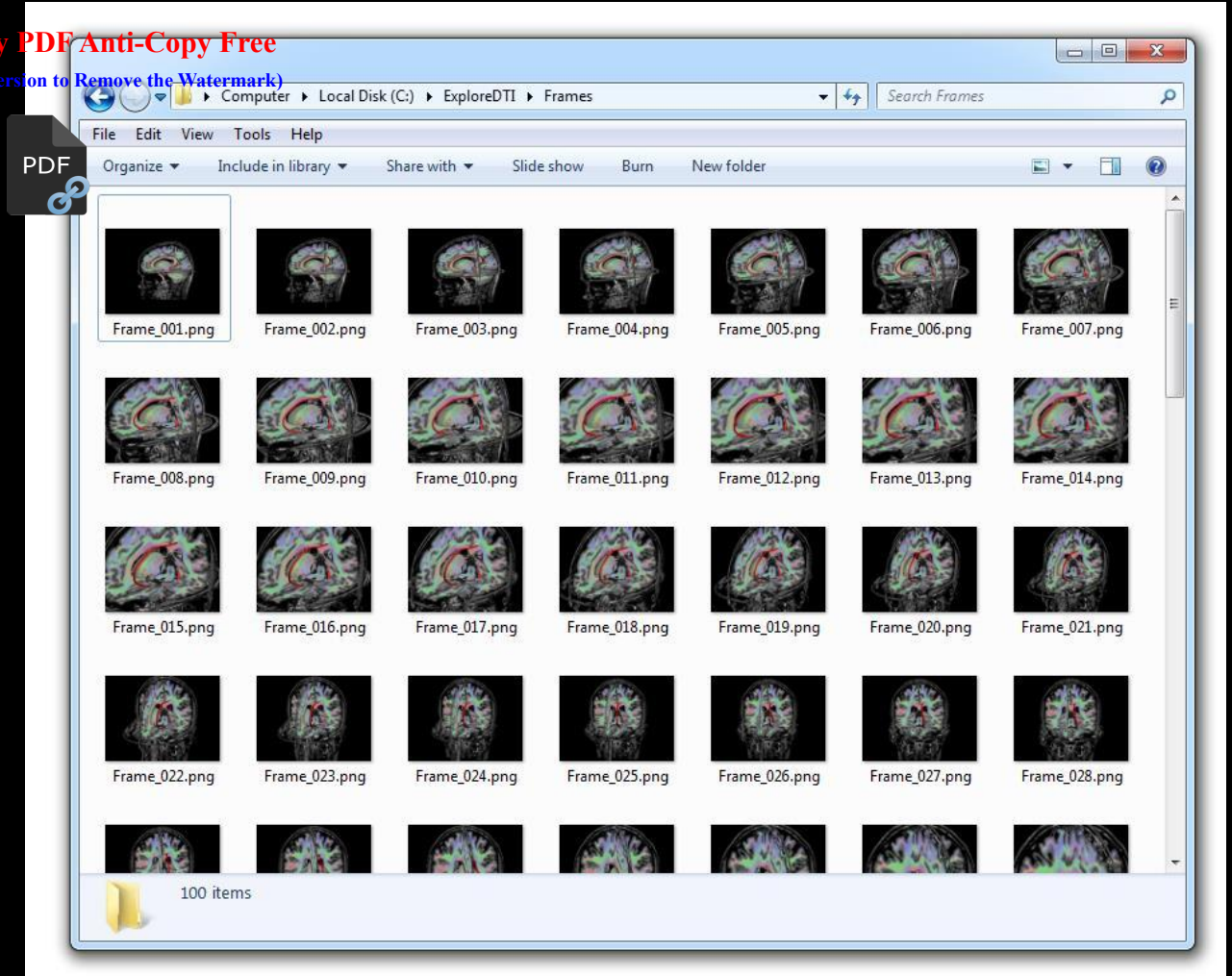 - *Making animations*
  - *Network analysis tools*
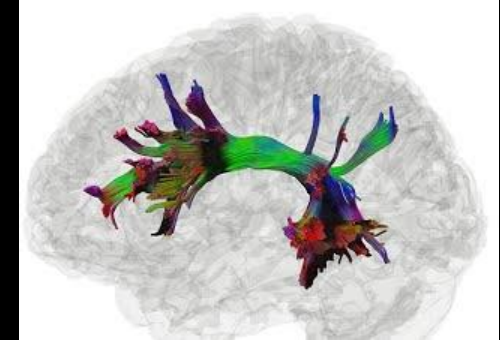
Explore DTI

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Explore DTI

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Explore DTI

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  - Tract-segment analysis
  - *Along-tract analysis*
  - *Visualizations*
  - *Making animations*
  - **Network analysis tools**

DTI studio & MRtrix

- 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

- **Brain Connectivity Toolbox (BCT):**

- A Matlab toolbox (http://www.brain-connectivity-toolbox.net)
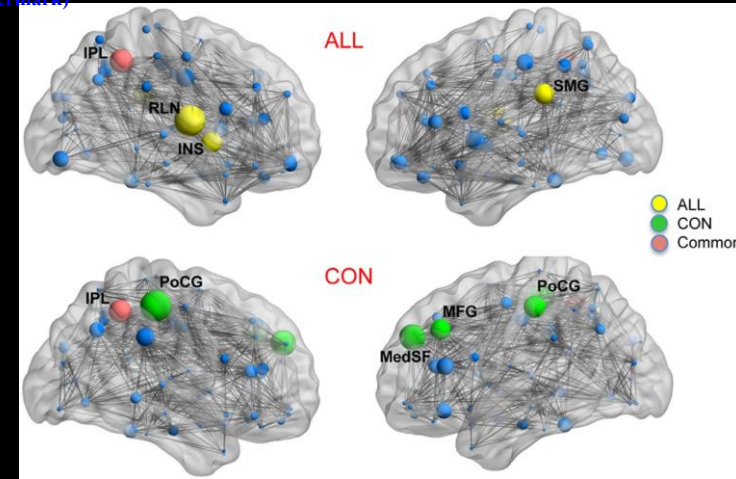
Graph Theory Softwares

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

Hosseini, SM Hadi, Fumiko Hoeft, and Shelli R. Kesler,PloS one,2012.
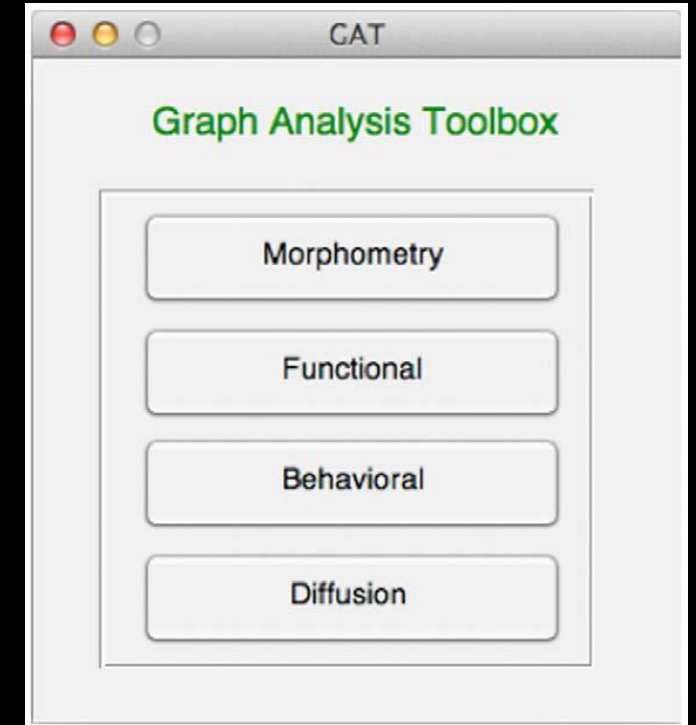
Graph Theory Softwares

- GAT (graph-analysis toolbox)

- Matlab-based software

- Integrates the:
  - ✓ Brain Connectivity Toolbox
  - ✓ REX toolbox
  - ✓ BrainNet Viewer
  - ✓ Original code
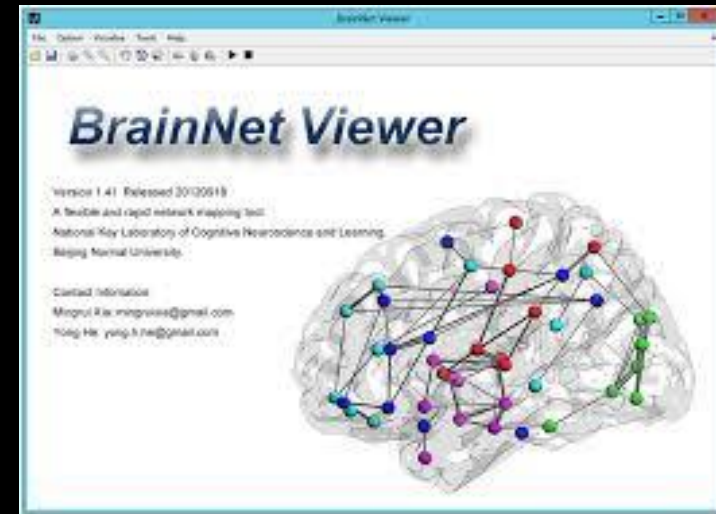
Hosseini, SM Hadi, Fumiko Hoeft, and Shelli R. Kesler,PloS one,2012.

Graph Theory Softwares

- **CONN:**

- Matlab-based (SPM8/SPM12)

- For the <u>computation</u>, <u>display</u>, and <u>analysis</u> 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

Rubinov, Mikail, and Olaf Sporns. *Neuroimage* (2010)

Graph Theory Softwares

- **CONN:**

Rubinov, Mikail, and Olaf Sporns. *Neuroimage* (2010)

Graph Theory Softwares

- **CONN:**

Rubinov, Mikail, and Olaf Sporns. *Neuroimage* (2010)

Graph Theory Softwares

- **CONN:**

- Is vailable 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
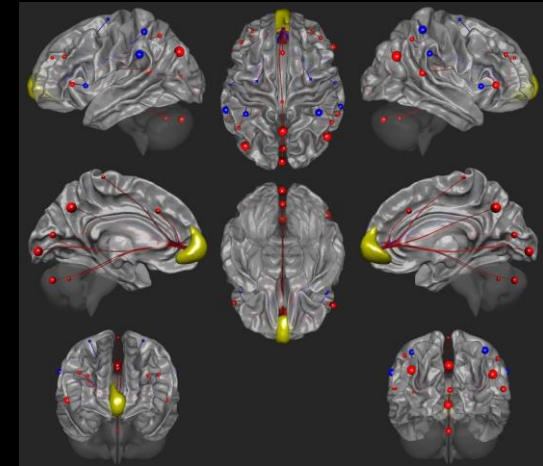
Rubinov, Mikail, and Olaf Sporns. *Neuroimage* (2010)

Graph Theory Softwares

- **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

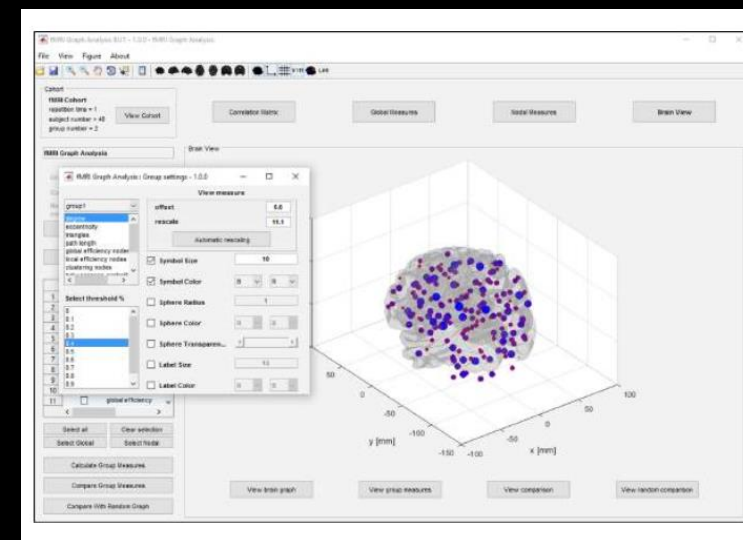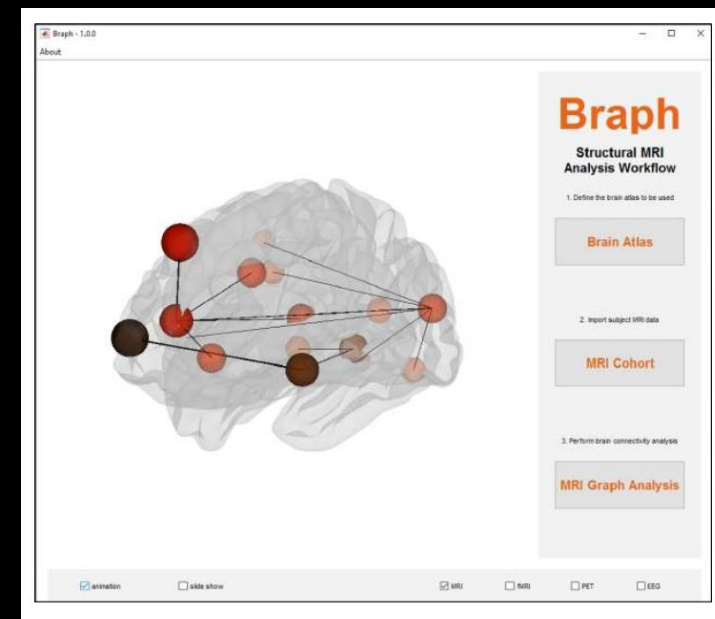- Statistical analysis (GLM and Machine Learning)

(GraphVar 2.0)
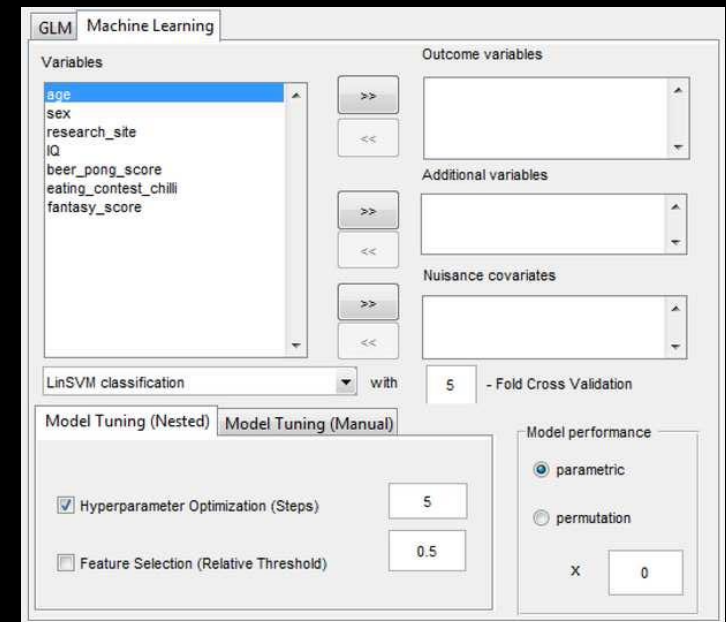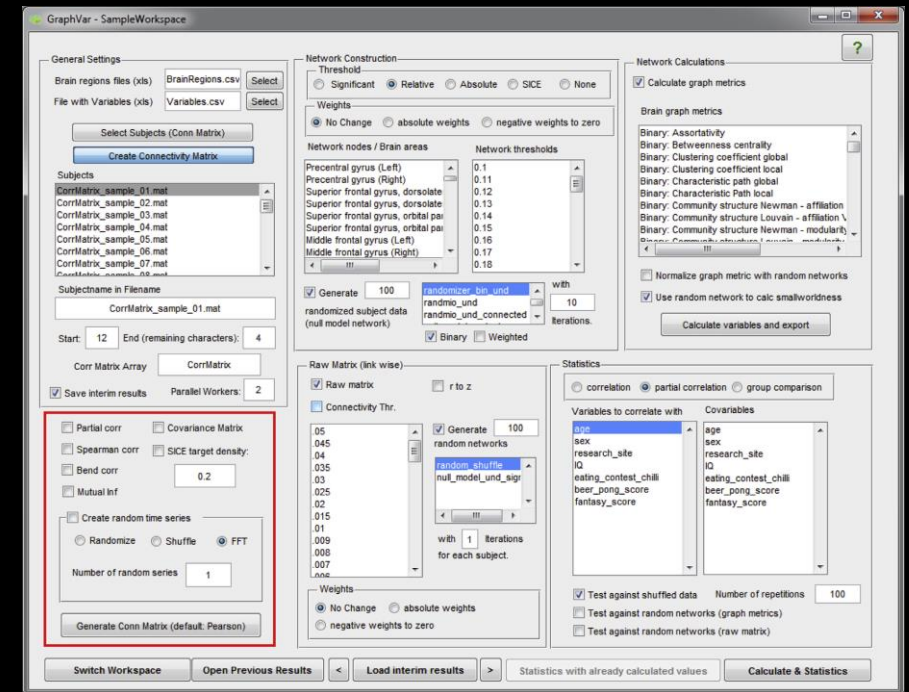
Kruschwitz, J. D., et al. *Journal of neuroscience methods* ,2015.
Waller, Lea, et al. *Journal of neuroscience methods*,2018.

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.

Mijalkov, Mite, et al. 2017. *PloS one* (2017).

Multimodal Analysis

Future Works

Dynamic graph metrics: Tutorial, toolbox, and tale

Ann E. Sizemore [a], Danielle S. Bassett [a,b,*]

[a] Department of Bioengineering, University of Pennsylvania, Philadelphia, PA, 19104, USA
[b] Department of Electrical and Systems Engineering, University of Pennsylvania, Philadelphia, PA, 19104, USA

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ANY QUESTIONS?