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AAIC>23

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JULY 16-20 > AMSTERDAM, NETHERLANDS, AND ONLINE

ISTAART Neuroimaging PIA
THE BASICS OF NEUROIMAGING SEMINAR SERIES

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The Basics of Neuroimaging Series

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BASICS OF NEUROIMAGING
DIFFUSION MRI

DR ALEXA PICHET BINETTE
LUND UNIVERSITY, LUND, SWEDEN

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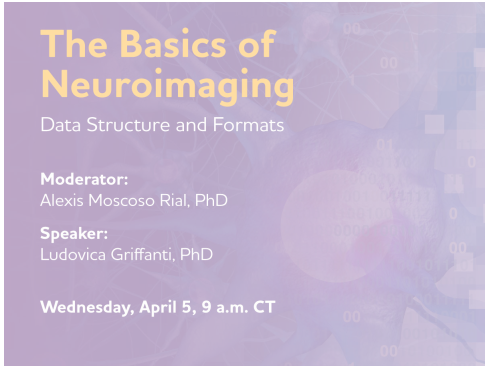
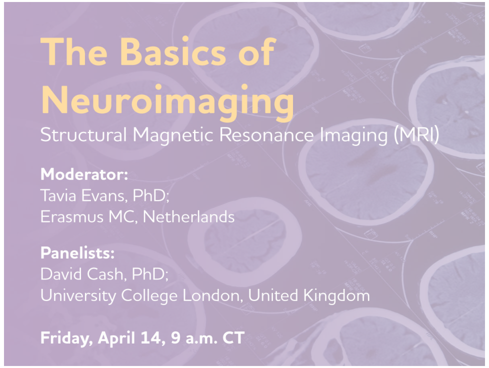
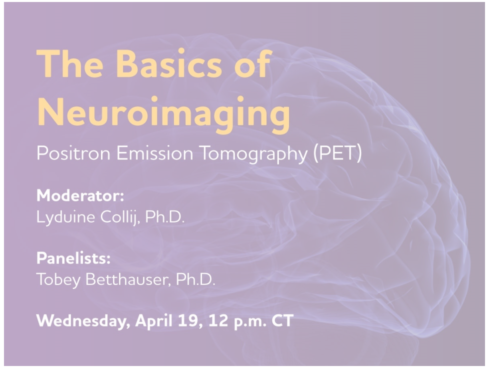
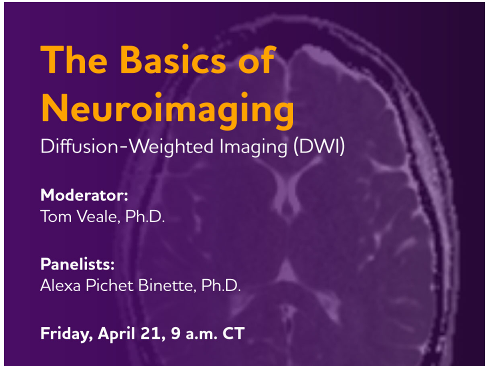
BASICS OF NEUROIMAGING

Available on demand very soon!









Place for Luigi ☺

GOALS

By the end of this session, you should be able to:

- Understand the acquisition and data structure of diffusion MRI
- Outline the basic preprocessing steps needed for diffusion MRI data and how to look for issues in the data and processing
- Describe the main outputs from diffusion tensor models

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NEUROIMAGING DATA ANALYSIS: A BLUEPRINT FOR DIFFUSION MRI

1. Data acquisition

Aim: obtain good quality and consistent data

2. Data preprocessing

Aim: Reduce noise and prepare data for further analyses

3. Single-subject analysis

Aim: Obtain measure of interest for each subject (often an image)

4. Group-level analysis

Aim: Compare single-subject results across groups

5. Statistical inference

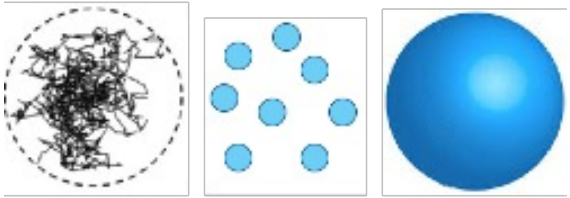
Aim: test reliability of results and generalizability to the general population

Blueprint courtesy Ludovica Griffanti, University of Oxford

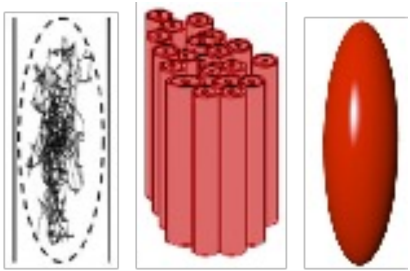
DIFFUSION IMAGING: KEY PRINCIPLES

1. Data acquisition

Basic principles of diffusion:



Free diffusion – Isotropy (in CSF)



Restricted diffusion – Anisotropy (in WM)

We are measuring the movement of water molecules along certain directions in the brain.

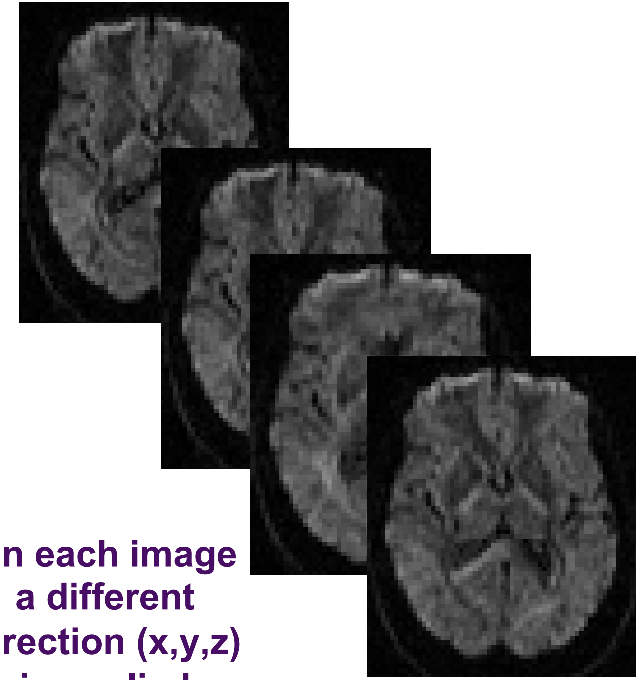
Descoteaux, *HARDI Chapter in Wiley Encyclopedia*, 2015

DIFFUSION IMAGING: KEY PRINCIPLES ORIENTATION

1. Data acquisition

Orientation is key in DWI. We measure the diffusion of water molecules along different directions

The diffusion-weighting signal varies according to the gradient direction in which it measures the image. If the gradient direction is aligned with the underlying white matter structure, the signal in the image is attenuated. It is weaker.

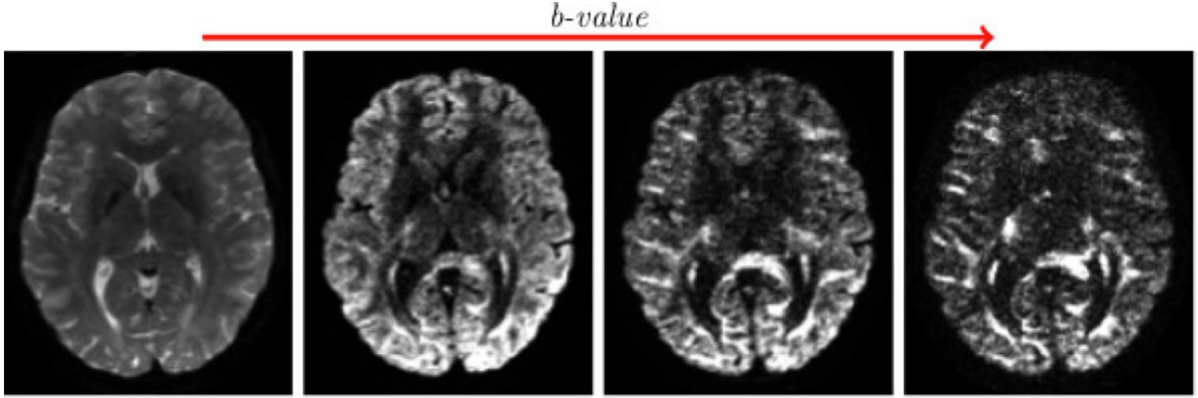


On each image a different direction (x,y,z) is applied

DIFFUSION IMAGING: KEY PRINCIPLES
B-VALUE

1. Data acquisition

Another key aspect is the **b-value**, which is related to the strength and duration of the gradients used to generate diffusion-weighted images.



(a) $b = 0\ s/mm^2$ (b) $b = 1000\ s/mm^2$ (c) $b = 2000\ s/mm^2$ (d) $b = 3000\ s/mm^2$

Higher b-values = "longer time to let molecules **to diffuse"**

b=1000 is standard is most basic research MRI sequence

Descoteaux, *HARDI Chapter in Wiley Encyclopedia*, 2015

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DIFFUSION IMAGING: DATA ORGANIZATION

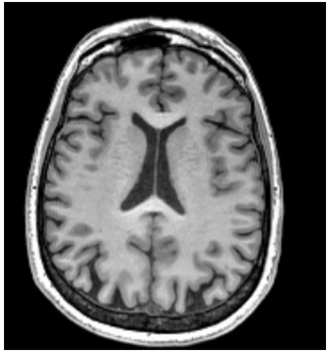
1. Data acquisition

1.b Data organization

BIDS
BRAIN IMAGING DATA STRUCTURE
https://bids.neuroimaging.io

- my_dataset/
  - participants.tsv
  - sub-01/
    - anat/
      - sub-01_T1w.nii.gz
    - func/
      - sub-01_task-rest_bold.nii.gz
      - sub-01_task-rest_bold.json
    - dwi/
      - sub-01_dwi.nii.gz
      - sub-01_dwi.json
      - sub-01_dwi.bval
      - sub-01_dwi.bvec

T1-Weighted



April 14 webinar

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DIFFUSION IMAGING: DATA ORGANIZATION

1. Data acquisition

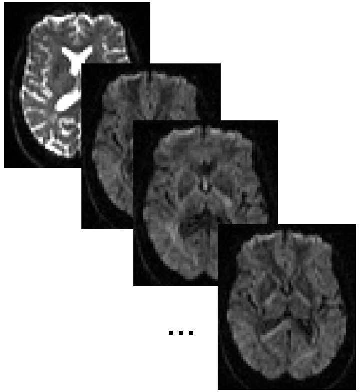
1.b Data organization

BIDS
BRAIN IMAGING DATA STRUCTURE
https://bids.neuroimaging.io

4-D file where each image has a specific diffusion gradient and orientation

```
my_dataset/
    participants.tsv
    sub-01/
        anat/
            sub-01_T1w.nii.gz
        func/
            sub-01_task-rest_bold.nii.gz
            sub-01_task-rest_bold.json
        dwi/
            sub-01_dwi.nii.gz
            sub-01_dwi.json
            sub-01_dwi.bval
            sub-01_dwi.bvec
```

DWI scan



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DIFFUSION IMAGING: DATA ORGANIZATION

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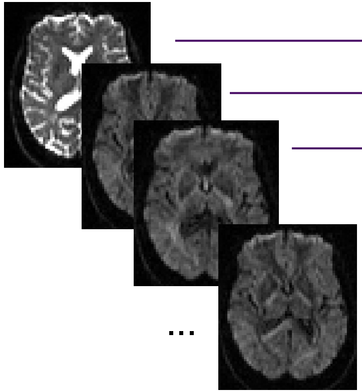
      - sub-01_task-rest_bold.json
    - dwi/
      - sub-01_dwi.nii.gz
      - sub-01_dwi.json
      - sub-01_dwi.bval
      - sub-01_dwi.bvec

Vectors of length equal to the total number of directions of the diffusion scan

DWI scan



	b-values	Orientation (x,y,z)
	bval	bvec
	0	0, 0, 0
	1000	0.999, -0.003, -0.003
	1000	0.001, 0.999, -0.003
	…	…
	…	…
…	1000	0.265, 0.960, 0.082

DIFFUSION IMAGING: PREPROCESSING

1. Data acquisition

↓

2. Data preprocessing

Key steps:

-Correcting for susceptibility-induced distortions

- Correcting for eddy currents and movement

DIFFUSION IMAGING: SUSCEPTIBILITY-INDUCED ARTEFACTS

1. Data acquisition

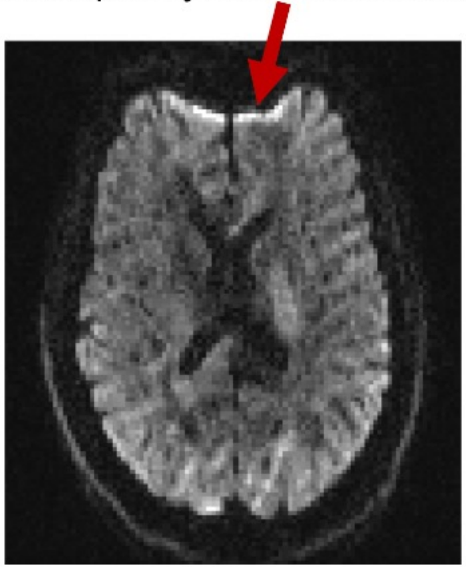
2. Data preprocessing

Key steps:

-Correcting for susceptibility-induced distortions

- Correcting for eddy currents and movement

Susceptibility induced distortions



Source: FSL Diffusion Toolbox

Some parts of the brain can appear distorted depending on their magnetic properties.

One common way to correct the distortions with DWI data is by acquiring a b0 image acquired with a different phase-encoding, and merging the two types of images running TOPUP.

DIFFUSION IMAGING: SUSCEPTIBILITY-INDUCED ARTEFACTS

1. Data acquisition

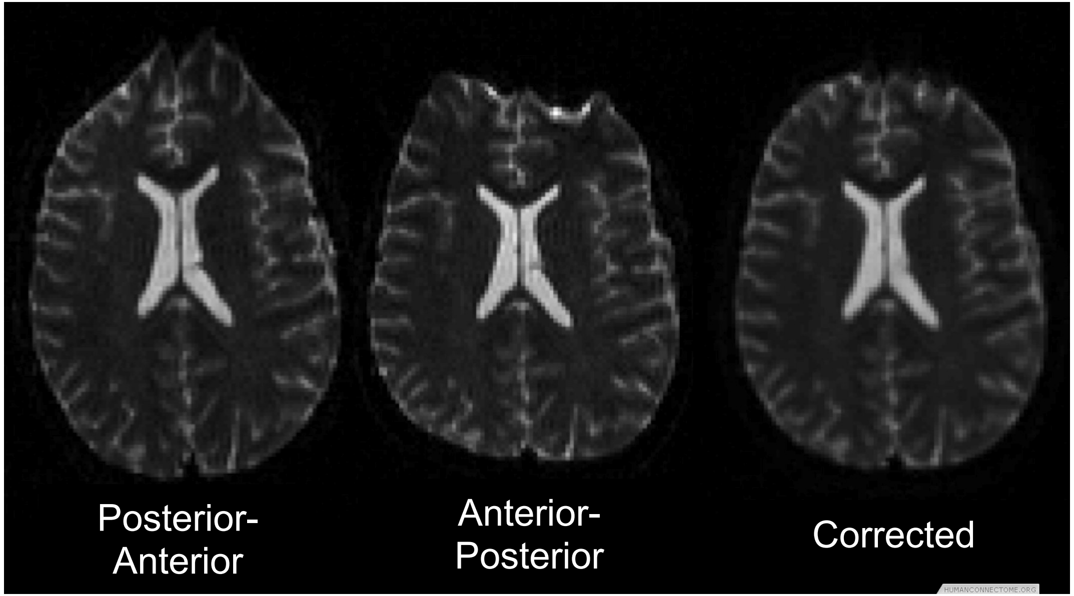
2. Data preprocessing

Key steps:

-Correcting for susceptibility-induced distortions

- Correcting for eddy currents and movement

Example from HCP:



Source: https://www.humanconnectome.org/study/hcp-young-adult/project-protocol/mr-preprocessing

DIFFUSION IMAGING: SUSCEPTIBILITY-INDUCED ARTEFACTS

1. Data acquisition

2. Data preprocessing

Key steps:

-Correcting for susceptibility-induced distortions

- Correcting for eddy currents and movement

Eddy currents arise from electric current due to strong and fast changing gradients.

FSL's eddy is a tool to correct for eddy current-induced distortions and movement on the image. It also does outlier detection and will replace signal loss by non-parametric predictions.

DIFFUSION IMAGING: EDDY CURRENTS

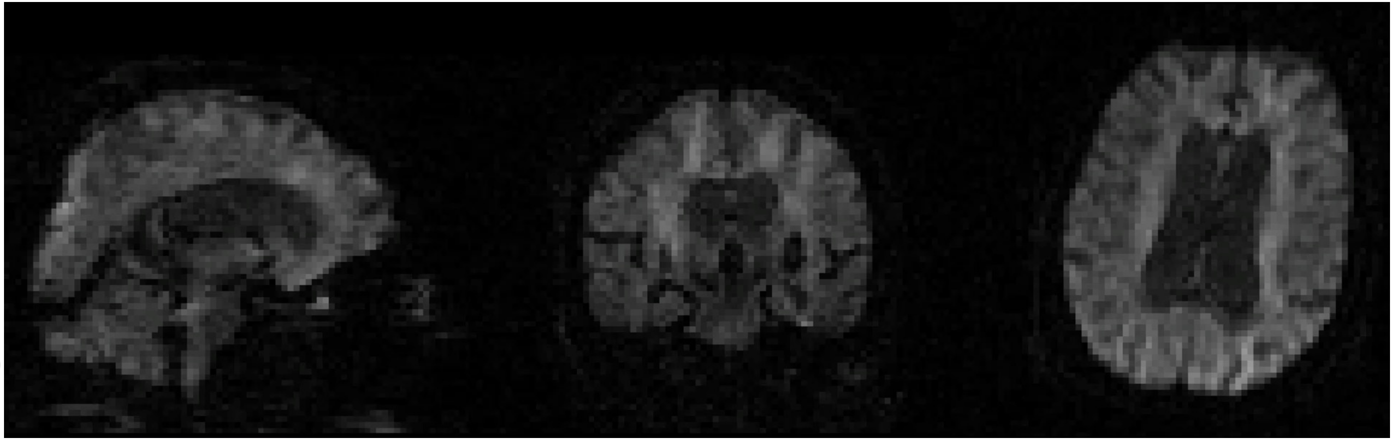
1. Data acquisition

2. Data preprocessing

Key steps:

-Correcting for susceptib distortions

- Correcting for eddy currents and movement



Example of diffusion scan with artefact

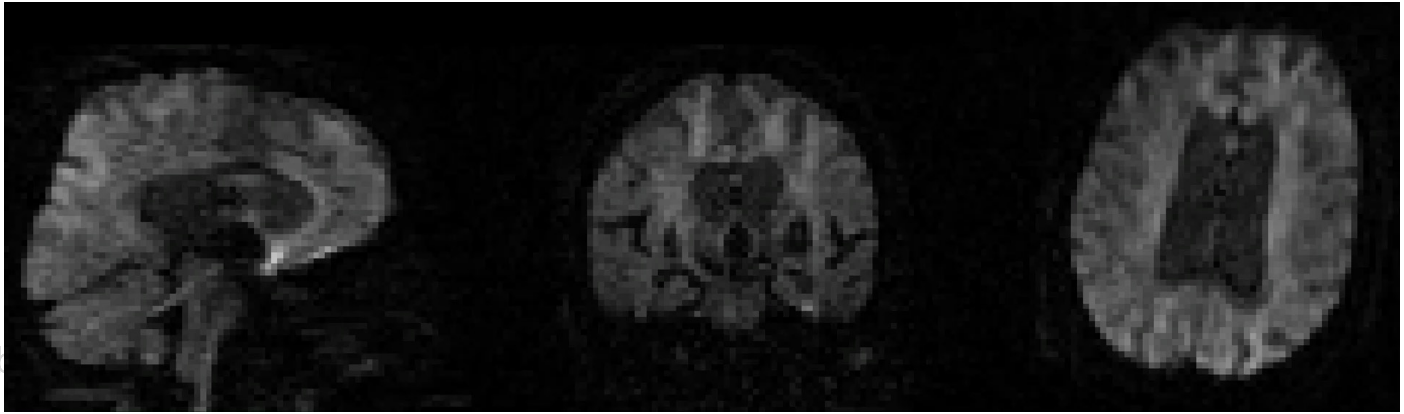
DIFFUSION IMAGING: EDDY CURRENTS

1. Data acquisition

2. Data preprocessing

Key steps:

-Correcting for susceptibility distortions



After eddy correction

- Correcting for eddy currents and movement

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DIFFUSION IMAGING: EDDY CURRENTS

1. Data acquisition

2. Data preprocessing

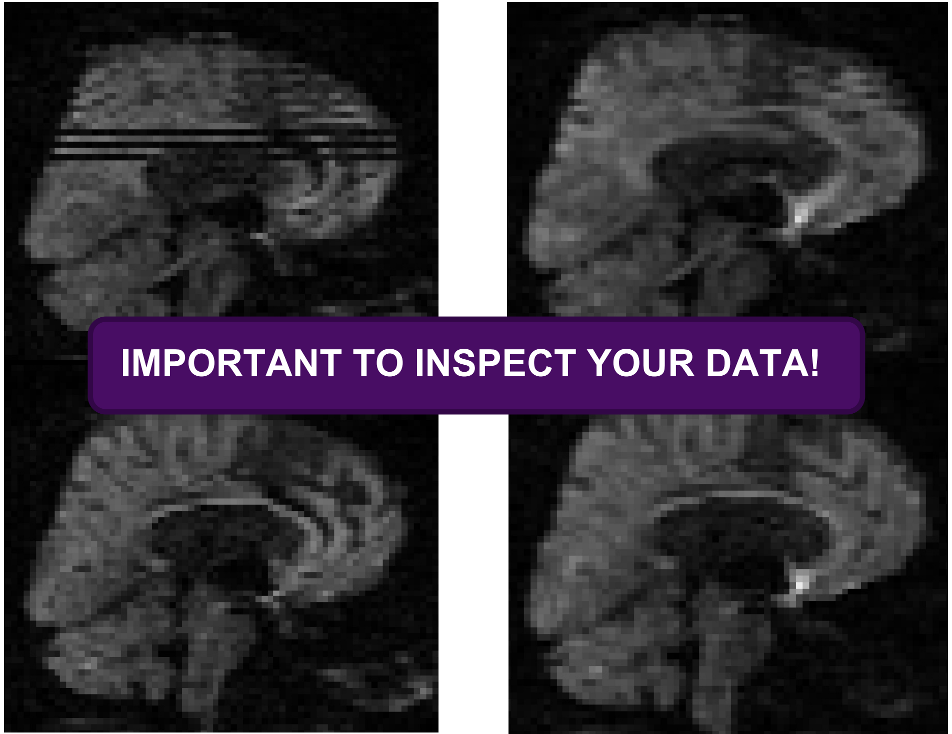
Key steps:

-Correcting for susceptibility-induced distortions

- Correcting for eddy currents and movement

Raw data

After eddy correction

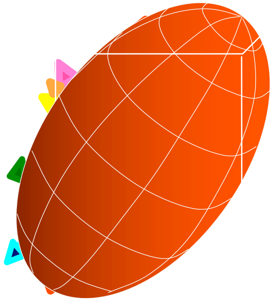


FROM THE DIFFUSION SCAN TO SUBJECT-LEVEL MEASURES

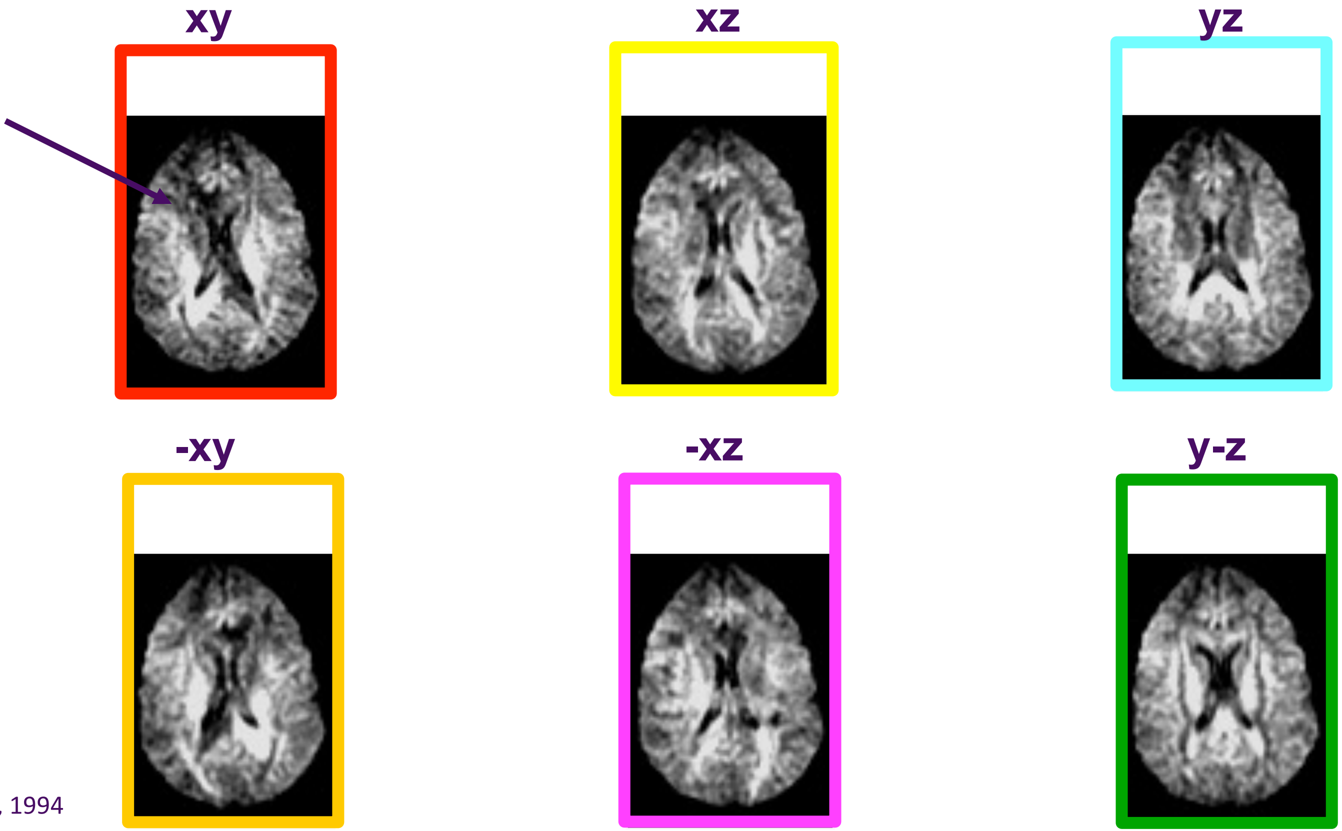
1. Data acquisition
2. Data preprocessing
3. Single-subject analysis

How to go from the diffusion scan to representing the underlying white matter microstructure organization?

TENSOR TO REPRESENT DIFFUSION SIGNAL



Basser et al, 1994



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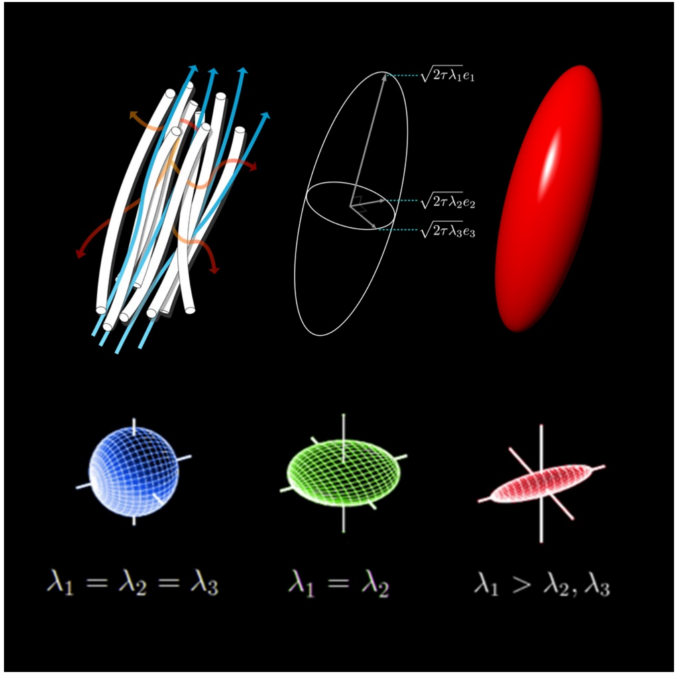
DIFFUSION TENSOR MODEL

1. Data acquisition
2. Data preprocessing
3. Single-subject analysis

We can represent the diffusion direction in each voxel using **tensors.**

Each tensor is described by 3 eigen vectors which represent diffusivity along 3 axes, with the first eigenvalue being the main diffusion axis.

The **diffusion tensor model** is the most common way to fit diffusion data. It is often a prerequisite for any diffusion imaging analysis pipeline.



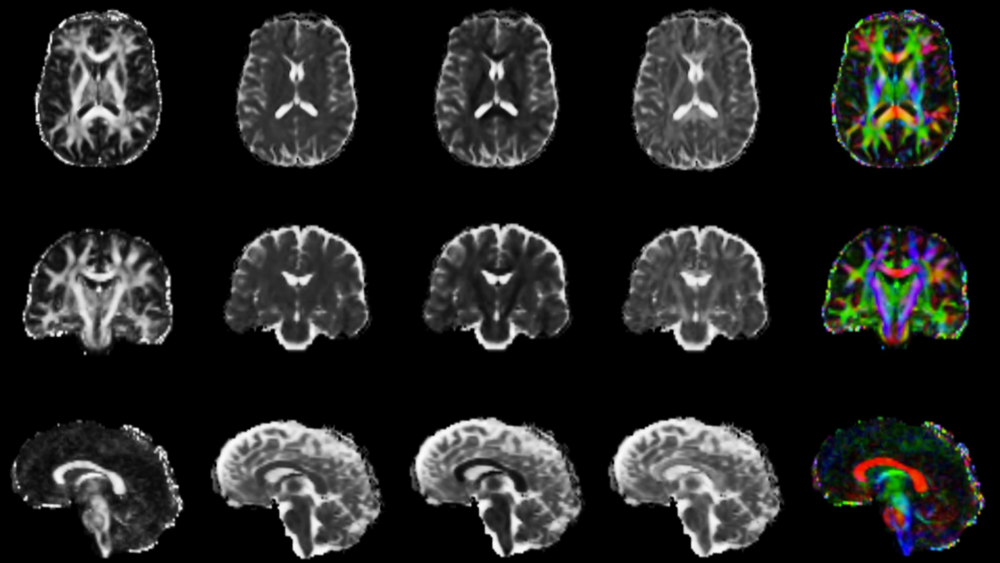
Descoteaux, *HARDI Chapter in Wiley Encyclopedia*, 2015

DIFFU

1. Data acquisition
2. Data preprocessing
3. Single-subject analysis

There are key measures that can be derived from the diffusion tensor model, namely:

- **Fractional anisotropy (FA)**
- **Mean, Radial and Axial diffusivities**

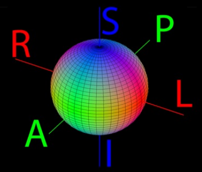


$$\text{FA}: \frac{3}{2} \cdot \sqrt{\frac{(\lambda_1-\lambda_2)^2+(\lambda_1-\lambda_3)^2+(\lambda_2-\lambda_3)^2}{\lambda_1^2+\lambda_2^2+\lambda_3^2}}$$

$$\text{Mean}: \frac{\lambda_1+\lambda_2+\lambda_3}{3}$$

$$\text{Radial}: \frac{\lambda_2+\lambda_3}{2}$$

$$\text{Axial}: \lambda_1$$



Descoteaux, *HARDI Chapter in Wiley Encyclopedia*, 2015

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DIFFUSION TENSOR MODEL

1. Data acquisition
2. Data preprocessing
3. Single-subject analysis

There are key measures that can be derived from the diffusion tensor model, namely:

- **Fractional anisotropy (FA)**
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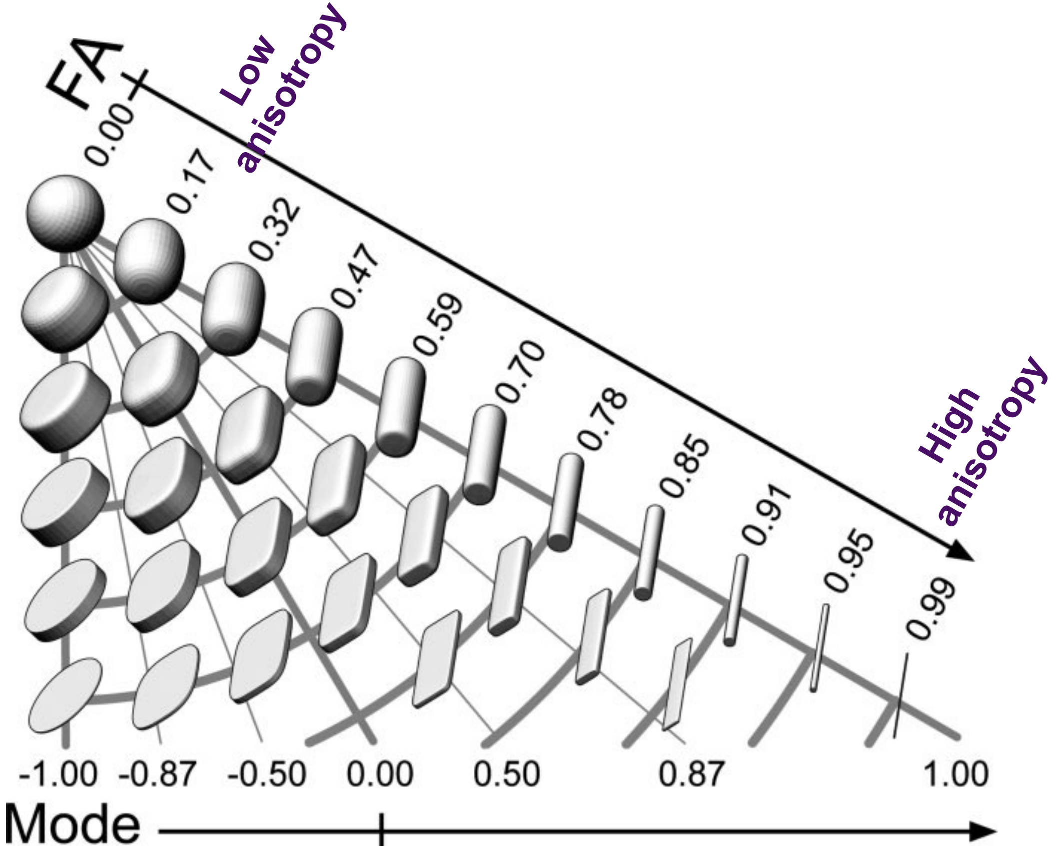


GROUP-LEVEL ANALYSIS OF DIFFUSION DATA

1. Data acquisition
2. Data preprocessing
3. Single-subject analysis
4. Group-level analysis
5. Statistical inference

- **Numbers** fed into ‘classic’ stats software

- **Images** require specific stats (usually within imaging software tools)
- Input = Single subject image
- Output = Statistical maps in pseudocolours shows **significant voxels,** overlaid on template.

- **Atlases** can help interpreting results

GROUP-LEVEL ANALYSIS OF DIFFUSION DATA – NUMERICAL VALUES

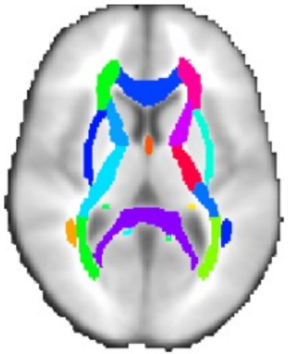
1. Data acquisition
2. Data preprocessing
3. Single-subject analysis
4. Group-level analysis
5. Statistical inference

- **Numbers** fed into ‘classic’ stats software

  Example: We can extract diffusion measures (FA, MD, …) for each participant in known white matter tract
  Each label corresponds to a white matter tract.

- **Atlases** can help interpreting results

JHU DTI Atlas
John Hopkins University



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GROUP-LEVEL ANALYSIS OF DIFFUSION DATA – IMAGES AS INPUT

1. Data acquisition
2. Data preprocessing
3. Single-subject analysis
4. Group-level analysis
5. Statistical inference

- **Numbers** fed into 'classic' stats software

- **Images** require specific stats (usually within imaging software tools)
- Input = Single subject image
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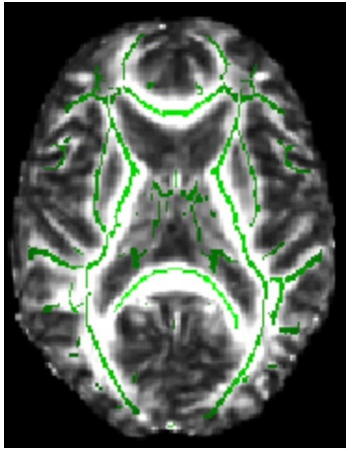
GROUP-LEVEL ANALYSIS OF DIFFUSION DATA – IMAGES AS INPUT

1. Data acquisition
2. Data preprocessing
3. Single-subject analysis
4. Group-level analysis
5. Statistical inference

Example: Tract-Based Spatial Statistics

All participants' FA maps are aligned into a common space

A mean FA skeleton which represents all tracts common to the group is created.



Source: FSL TBSS User Guide

GROUP-LEVEL ANALYSIS OF DIFFUSION DATA – IMAGES AS INPUT

1. Data acquisition
2. Data preprocessing
3. Single-subject analysis
4. Group-level analysis
5. Statistical inference

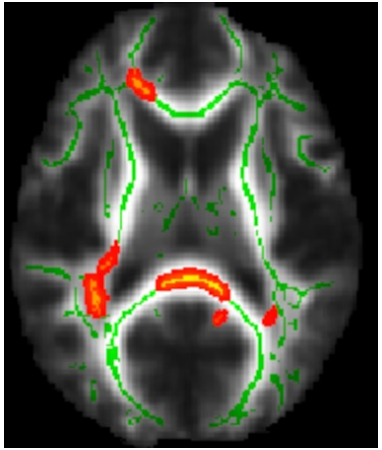
Example: Tract-Based Spatial Statistics

All participants' FA maps are aligned into a common space

A mean FA skeleton which represents all tracts common to the group is created.

Each participant's aligned FA data is then projected onto this skeleton.

Voxelwise analyses can then be performed across participants.



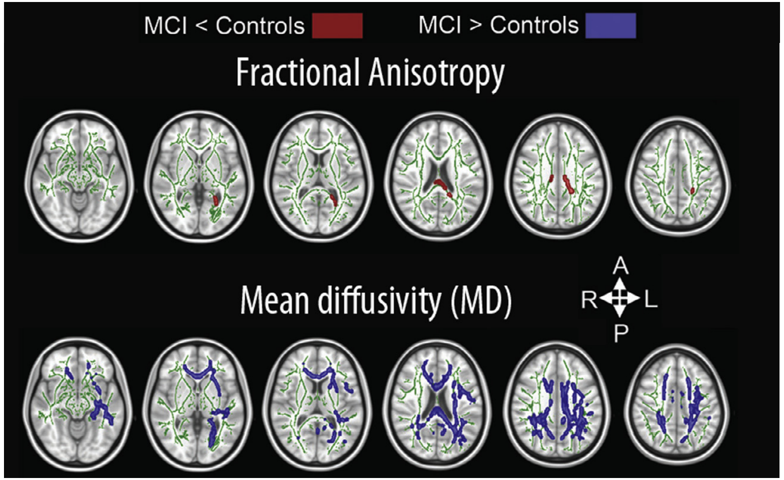
Signicant voxels that are different between two groups, related to a variable of interest, etc

Source: FSL TBSS User Guide

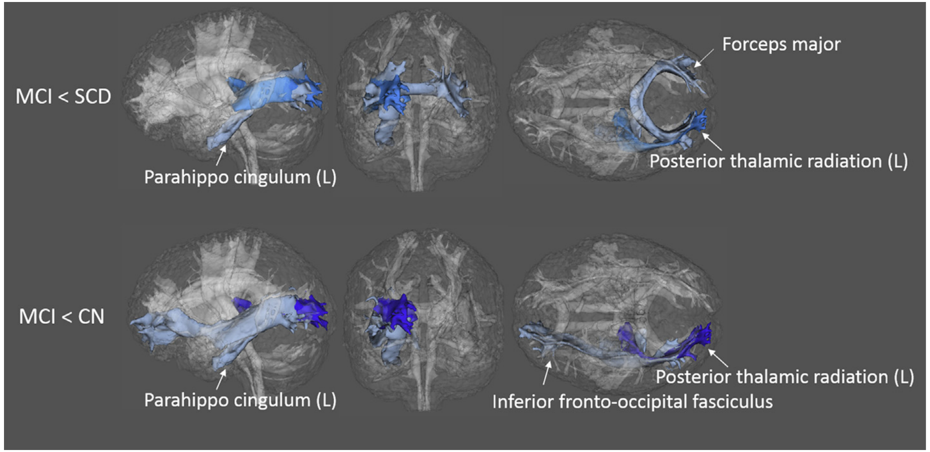
DIFFERENCES IN DIFFUSION MEASURES ACROSS THE AD CONTINUUM

Differences in white matter microstructure across diagnostic groups

↓FA and ↑MD across the AD spectrum



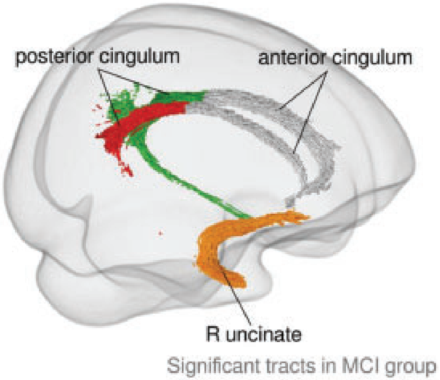
Amlien et al., *Radiology*, 2013



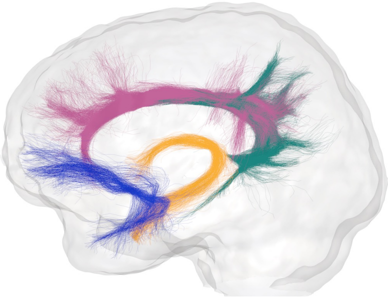
Wen et al., *Alz Dem: DADM*, 2019

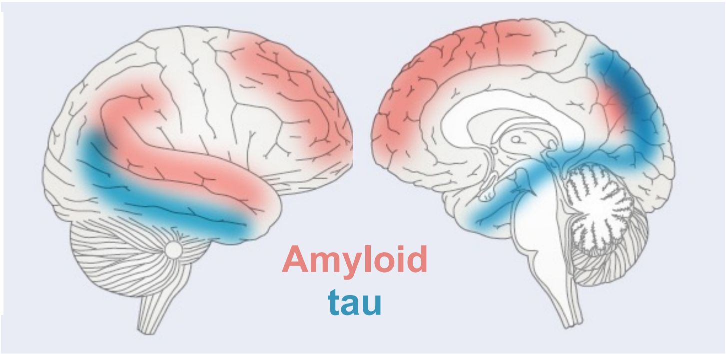
DIFFUSION MEASURES IN RELATION WITH AD PATHOLOGY IN VIVO

There are commonly affected white matter bundles in AD … that connect regions where AD pathological proteins accumulate



Mito et al., *Brain*, 2018
Jacobs et al., *Nature Neuro*, 2018





Jagust, *Nature Reviews*, 2018

DIFFUSION MEASURES IN RELATION WITH AD PATHOLOGY IN VIVO

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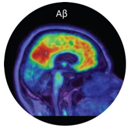
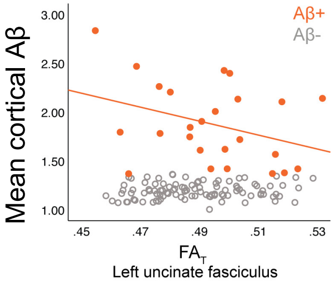
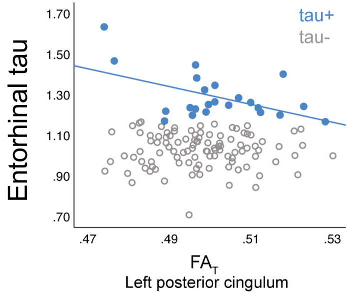
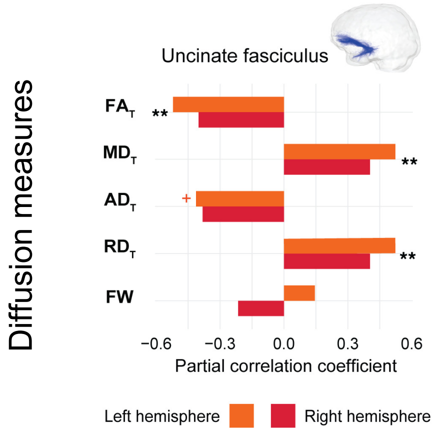
PREVENT-AD Research Group

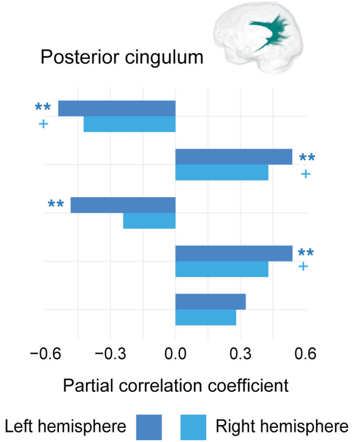
At risk of sporadic AD





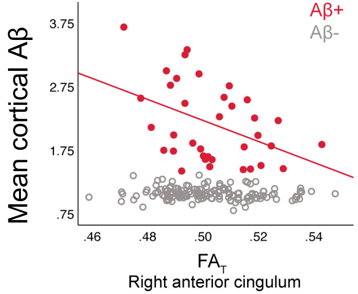


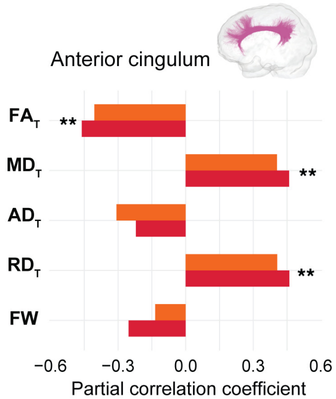




DIAN
Dominantly Inherited Alzheimer Network

Presymptomatic ADAD



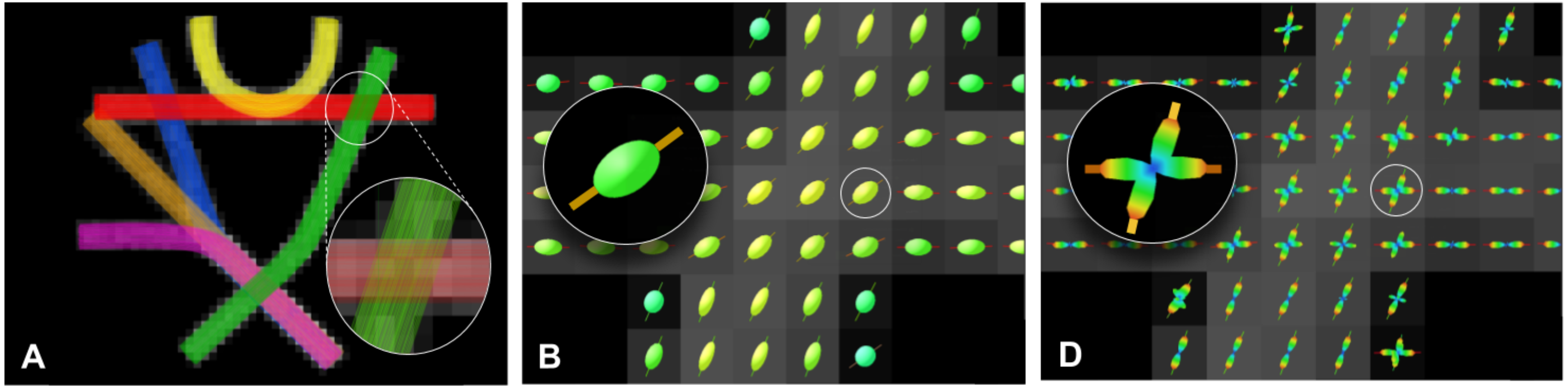


Pichet Binette et al, *eLife*, 2021

BEYOND THE DIFFUSION TENSOR MODEL

- Advanced diffusion model:

There are limitations to the diffusion tensor models, and another commonly used model that can better recapitulate crossing fibers are the **fiber orientation distribution functions (fODF)**



Tensor

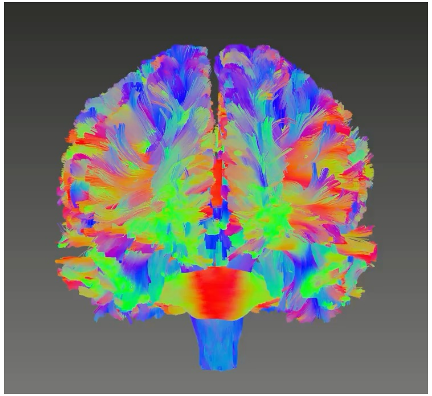
Fiber orientation distribution function (fODf)

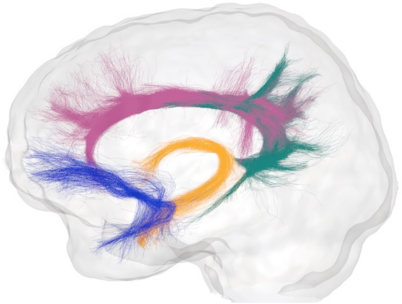
BEYOND THE DIFFUSION TENSOR MODEL

- Tractography

After fitting the data to a model, another possibility is to do tractography.

Tractography is a way to "reconstruct" the white matter fibers to generate a whole-brain tractogram.





We can extract known anatomical white matter bundles from the tractogram

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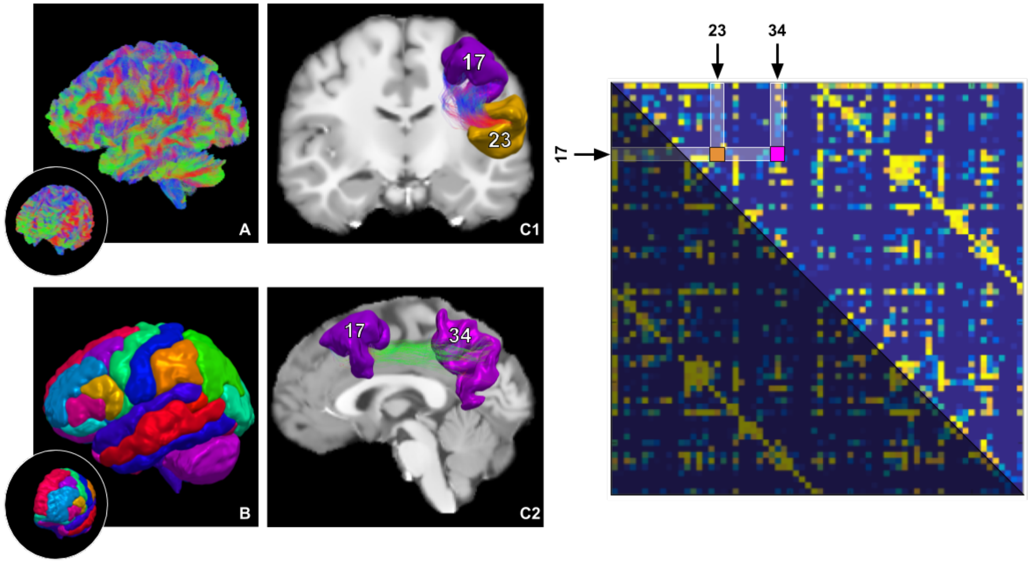
BEYOND THE DIFFUSION TENSOR MODEL

- Structural connectivity

After fitting the data to a model, another possibility is to do tractography.

Tractography is a way to "reconstruct" the white matter fibers to generate a whole-brain tractogram.



We can generate a structural connectivity matrix from the tractogram

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SOFTWARE TO PROCESS DIFFUSION IMAGING

FMRIB SOFTWARE LIBRARY

FSL
Diffusion
Toolbox

dMRIprep

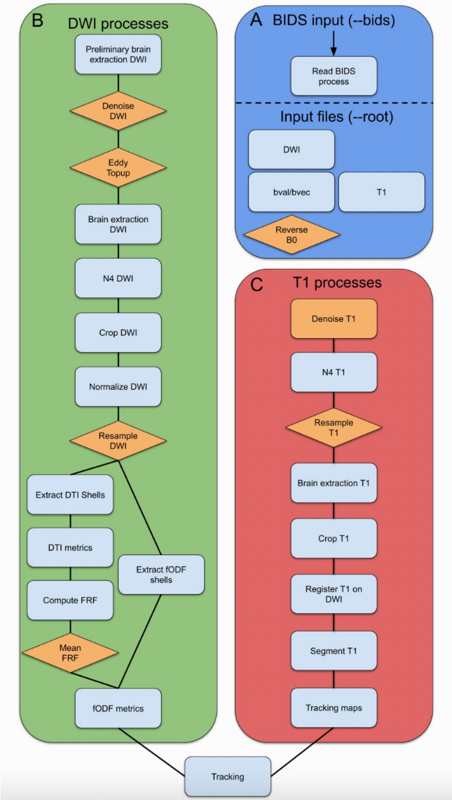
https://www.nipreps.org/dmriprep/index.html

Basic preprocessing steps such as head-motion correction, susceptibility-derived distortion correction, eddy current correction, etc. providing outputs that can be easily submitted to a variety of diffusion models.

DIPY

Diffusion in Python
dipy.org

TractoFlow



https://tractoflow-documentation.readthedocs.io/en/latest/

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NEUROIMAGING DATA ANALYSIS: A BLUEPRINT FOR DIFFUSION MRI

1. Data acquisition	**Aim**: obtain good quality and consistent data	**Diffusion sequence has different b-values and each image has a specific gradient direction.** Data includes diffusion scan, bvec and bval vectors. Optimize protocol for research aim.
2. Data preprocessing	**Aim**: Reduce noise and prepare data for further analyses	**Susceptibility-induced and eddy curents distortions:** correct for magnetic field inhomogeneities, eddy-induced currents, motion and signal loss. Requires careful checking.
3. Single-subject analysis	**Aim**: Obtain measure of interest for each subject (often an image)	**Image of different diffusion measures: Fractional anisotropy, Mean diffusivity, Axial diffusivity, Radial diffusivity, …** Examples limited to DTI, other measure can be derived from other models.
4. Group-level analysis	**Aim**: Compare single-subject results across groups	**Voxelwise analyses with images** **Individual numerical values from regions of interest can be extracted**
5. Statistical inference	**Aim**: test reliability of results and generalizability to the general population	**Comparisons between groups** **Associations of diffusion measures with other clinical data**

Blueprint courtesy Ludovica Griffanti, University of Oxford

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POP QUIZ!

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QUESTION 1

What is the signal that is acquired on a diffusion MRI scan?

a) The orientation of white matter fibers
b) The movement of water molecules
c) The white matter density
d) All of the above

QUESTION 2

What do the main preprocessing steps in diffusion MRI try to account for?

a) Eddy currents, movement, and registration
b) Susceptibility-induced distortions, movement and registration
c) Susceptibility-induced distortions, eddy currents and movement

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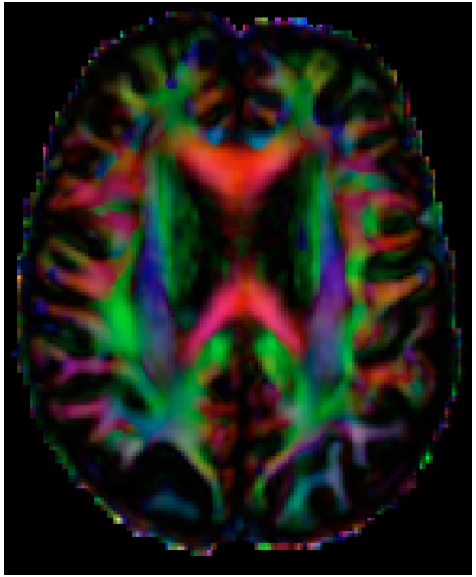
QUESTION 3

On this map, what do the colors represent?



a) The strength of structural connectivity
b) Mean diffusivity
c) Length of the white matter fibers
d) The main direction of the white matter fibers

QUESTION 4

If we compare cognitively unimpaired participants to patients with AD dementia, the fractional anisotropy will be:

a) Lower in the AD patients
b) Lower in the cognitively unimpaired participants
c) Unchanged between the two groups

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Neuroimaging PIA: Advanced MR imaging in Alzheimer's disease and related dementias

Recorded: April 21, 2022

The basic principles and latest advances in arterial spin labelling and diffusion weighted imaging discussed in the context of neurodegenerative diseases. The application of these techniques, focusing on scientific research is covered.

Neuroimaging PIA: Getting started with connectomics analysis

Recorded: May 12, 2022

This webinar is a primer on how to setup, generate, review and interpret structural and functional connectivity analyses. Speakers go over best practices and what pitfalls to watch out for with their work.

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ISTAART Neuroimaging PIA

The Basics of Neuroimaging Series

@NeuroimagingPIA

THANK YOU!

On demand at https://training.alz.org/:

Basics of Neuroimaging: Data structure and formats by Ludovica Griffanti
Basics of Neuroimaging: Structural Magnetic Resonance Imaging (MRI) by David Cash
Basics of Neuroimaging: Positron emission tomography (PET) by Tobey Betthauser

Next up!
Basics of Neuroimaging: Functional Magnetic Resonance Imaging (FMRI) by Luigi Lorenzini
26 April, 2023; 10AM – 11AM CT

GETTING STARTED WITH NEUROIMAGING WORKSHOP Friday July 14 8:00-12:00 Amsterdam

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LUND UNIVERSITY

alzheimer's association

BrightFocus Foundation

Fonds de recherche Santé Québec

Fièrement propulsée par les FRQ

ALZHEIMER'S IMAGING CONSORTIUM (AIC) – JULY 15, 2023

Alzheimer's Association International Conference®

July 16-20, 2023
Amsterdam, Netherlands and Online

NEW THIS YEAR AT AIC!

>> Panel discussion: **The Role of Brain Imaging in the Era of disease modifying treatments** moderated by Phillip Scheltens with panelists Emily Collins, Gil Rabinovici, Kacie Deters, Oskar Hansson, Reisa Sperling and Sylvia Villeneuve

>> Lunchtime mentoring session for trainees

PLENARY SESSIONS:

>> Year in Review: What have we learned? by **Indira Turney**

>> Sporadic Early-Onset Alzheimer's Disease in the Spotlight: Results from iLeads by **Liana Apostolova**

SCIENTIFIC SESSIONS:

>> 3 oral sessions, datablitz presentations and a dedicated poster session!

- *Beyond volume and thickness: Imaging of microstructure in ADRD*
- *Imaging neuroinflammation and synaptic density*
- *Neuroimaging genetic correlates*