Vendredi 11 Décembre 13:30 – 15:30
First INT Technical Lecture

Part 1 : Magnetic Resonant (MR) Imaging of cerebral structure

Thanks to the organizers Nicolas WANAVERBECQ & Ivo VANZETTA

Thanks to the speakers and those who helped to prepare this session :
Jean-Luc ANTON, Guillaume AUZIAS, Olivier COULON,
Julien LEFEVRE, Kep Kee LOH & Julien SEIN

Institut de Neurosciences de la Timone (UMR 7289) & Centre IRM-INT@CERIMED

- The three main parts of a MR system
- Introduction to MRI acquisition (Julien Sein)
- Analyses of cerebral anatomy (Olivier Coulon, Julien Lefèvre, Kep Kee Loh)
- Diffusion imaging (Julien Sein, Olivier Coulon)
- Quantitative measurements (Julien Sein)

Modalities of the session :

microphones off, questions in the chat, discussion at the end … ;-)

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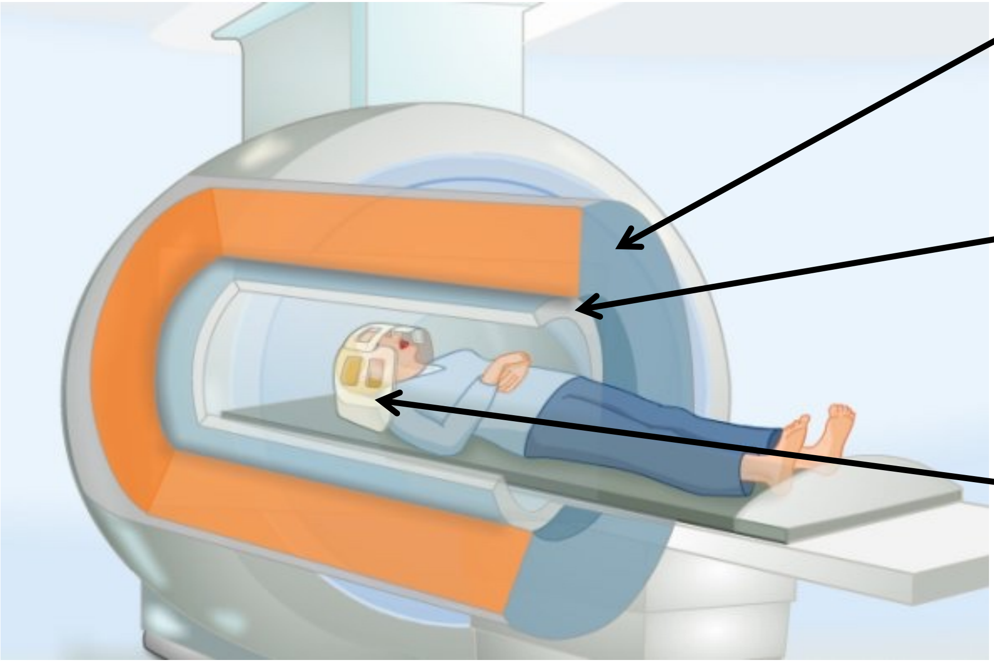
The three main parts of a MR system



The supraconductor magnet

→ B0 main magnetic field

(0.5 Tesla … 11.7 Tesla)

The gradients system

→ spatial modulation of B0 for coding the space

→ diffusion imaging …

The radio-frequency system

- RF transmission coils (excitation)
- Receiving RF coils (signal acquisition)

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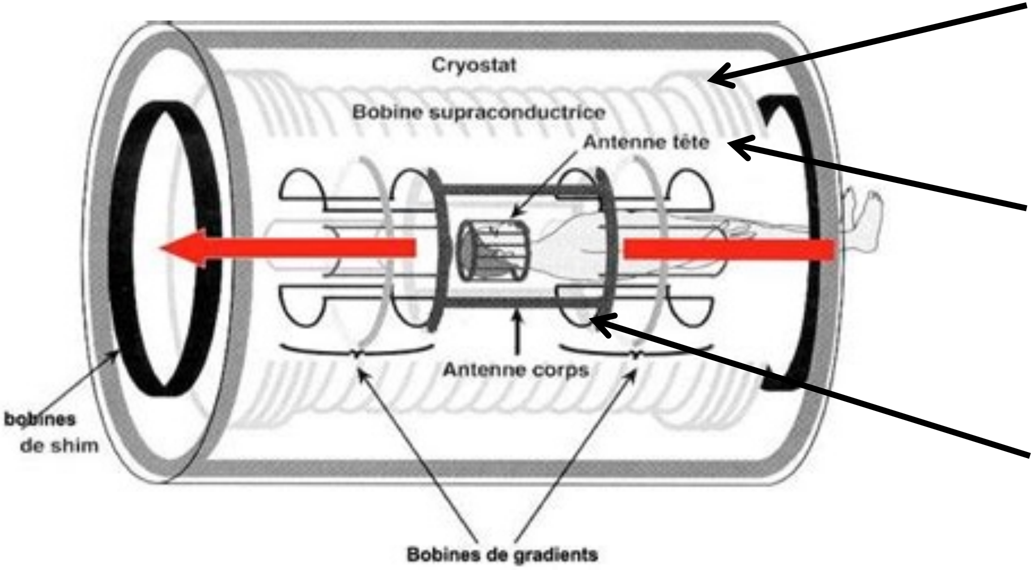
IRMf

The three main parts of a MR system



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→ diffusion imaging …

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Our very first (the 2nd 3T in France) :
Bruker Medspec 30/80
(2000 – 2015)

- **B0 = 3T**
- **Gradients : 45mT/m**
- **Head RF coil : bird cage (2 channels)**

Now, the best of the 3T :
Siemens Magnetom - Prisma (2016 – . . .)

- B0 = 3T
- Gradients : 80mT/m
- RF coils :
  - body coil (TX)
  - many receiver coils (up to 64 channels)

  → parallel imaging, multiband acceleration

Outline

MRI acquisition Principles
Different types of contrats
Example of standard sequences (T1w, T2w, FLAIR)
Advanced technics : Acquisition robust to head movements (v-Nav, Fat-Nav, ultra-fast : Compress sensing)

A little bit of history

1937 Discovery of the magnetic resonance principle by Isaac Rabi (Nobel prize of Physics in 1944).

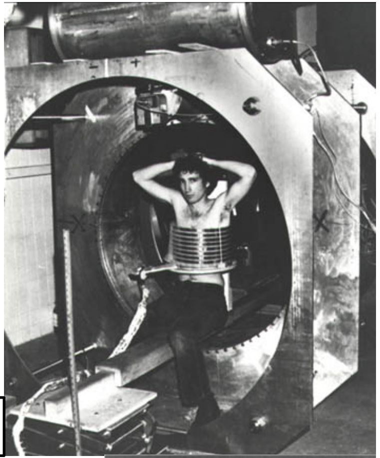
1946 Behavior of the proton in a magnetic field by physicists Félix BLOCH and Edward M. PURCELL (Nobel Prize in Chemistry in 1952).

1966 Relationship between NMR and Fourier Transform R. Ernst (Nobel Prize in Chemistry en 1991).

1973 First images of test tube by Paul LAUTERBUR

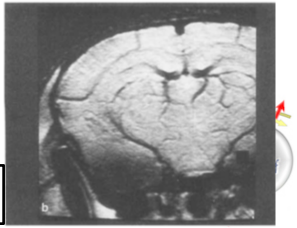
1984 MRI of human brain in vivo

1990 BOLD experiment on rat (Ogawa et al.)



1st in vivo MRI

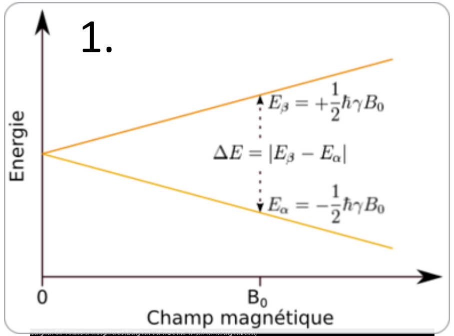
Rat breathing 100% oxygen

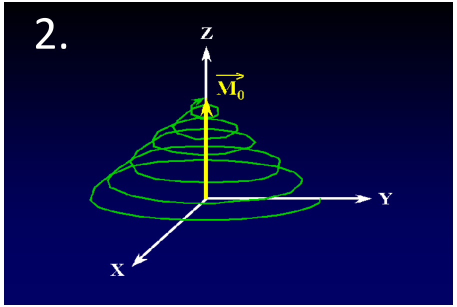


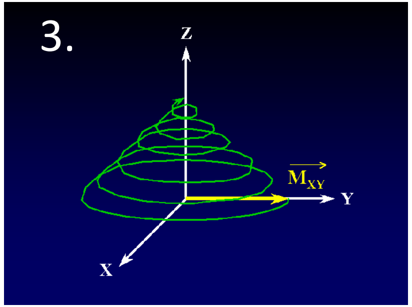
Rat breathing normal air

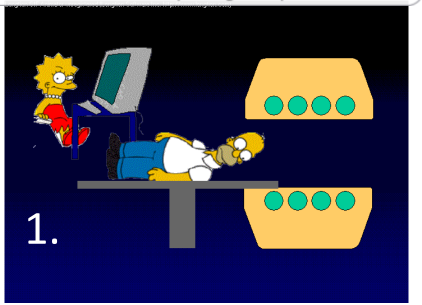
Signal:

1. Polarization
2. Resonance
3. Relaxation









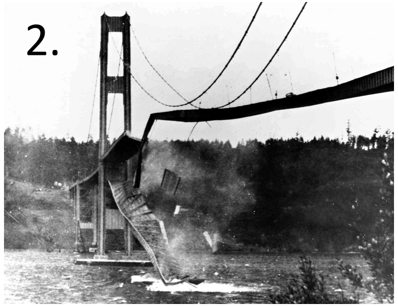
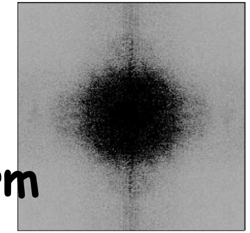


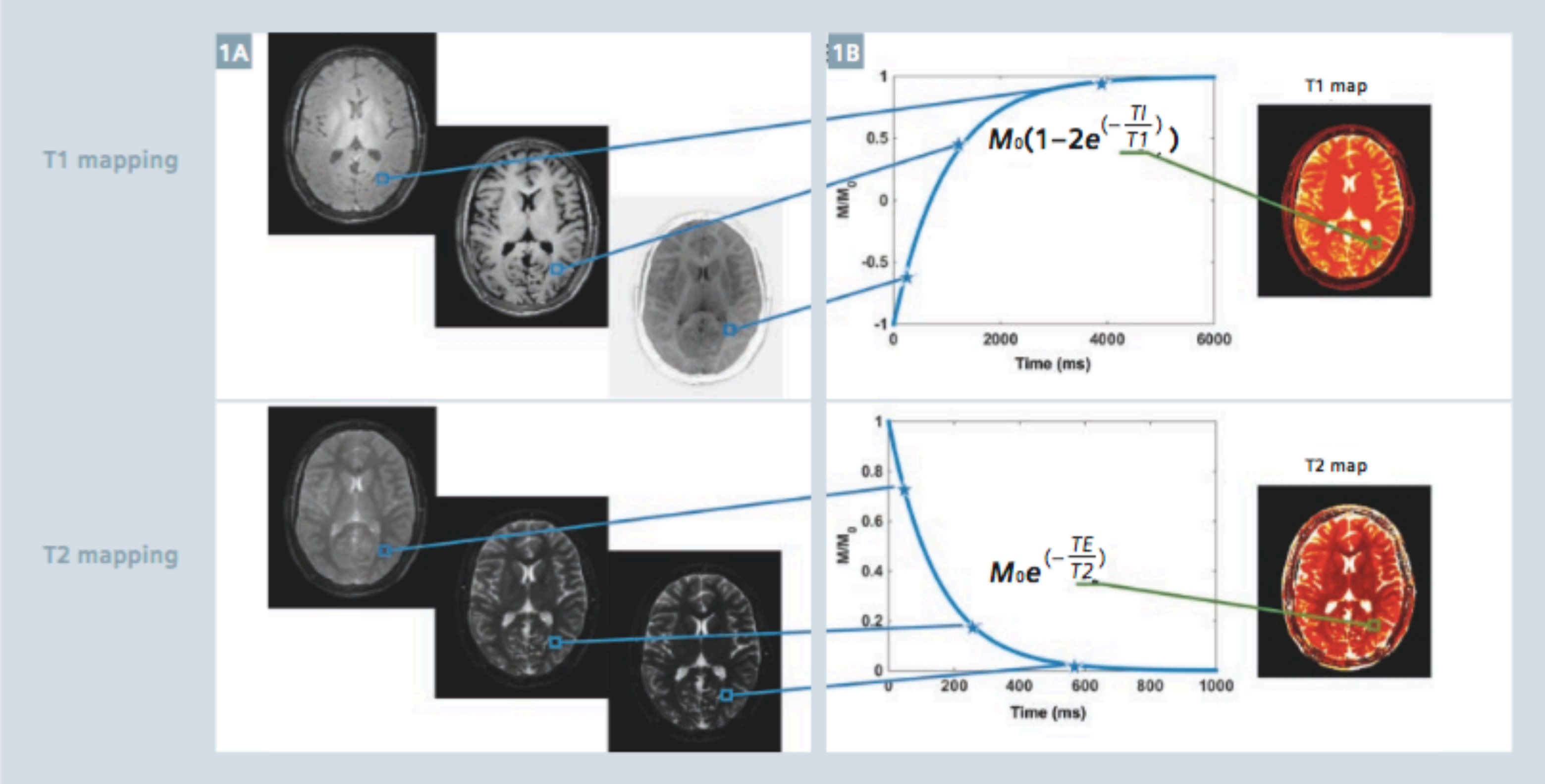
Image:

1. ADC
2. Fourier Transform



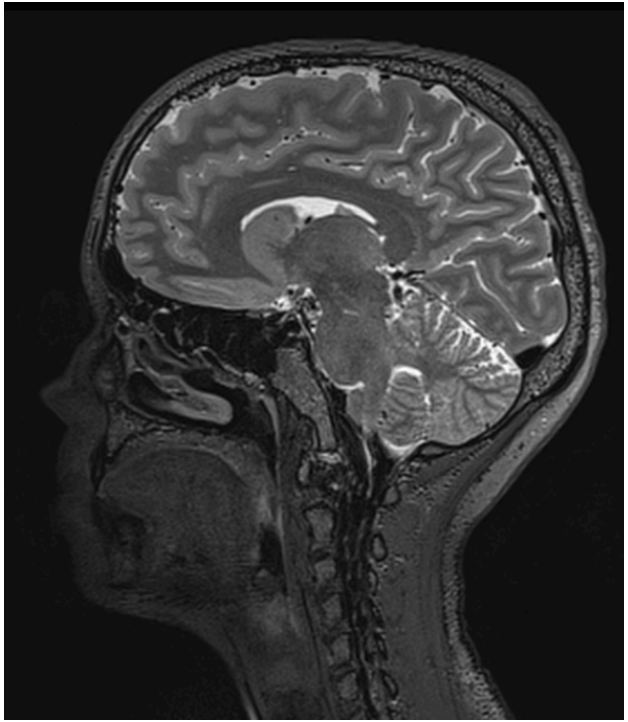
FT

Different kind of contrasts



T1-weighted image

@ 3T	T1 (ms)	T2 (ms)	DP
Matière Blanche	832 ∓ 10	79.6 ∓ 0.6	71 %
Matière Grise	1331 ∓ 13	110 ∓ 2	83 %
LCR	4163 ∓ 263	500-2200	100 %



T2-weighted image

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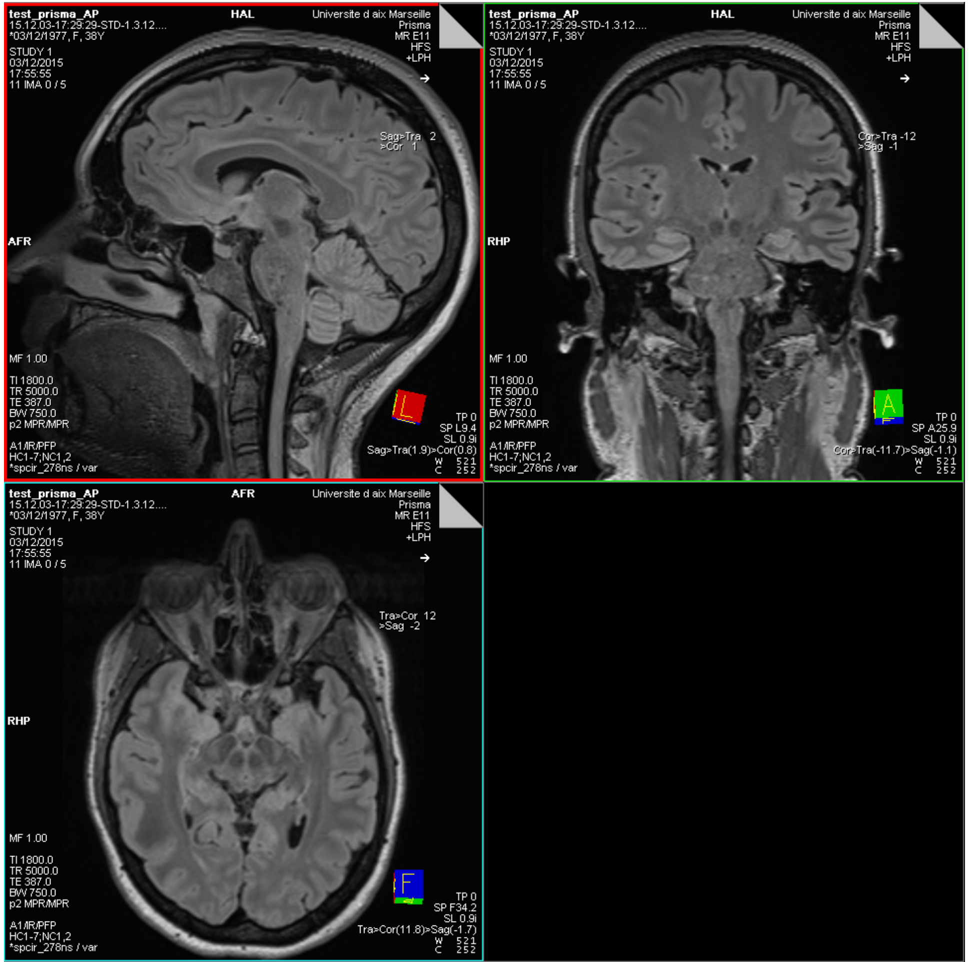
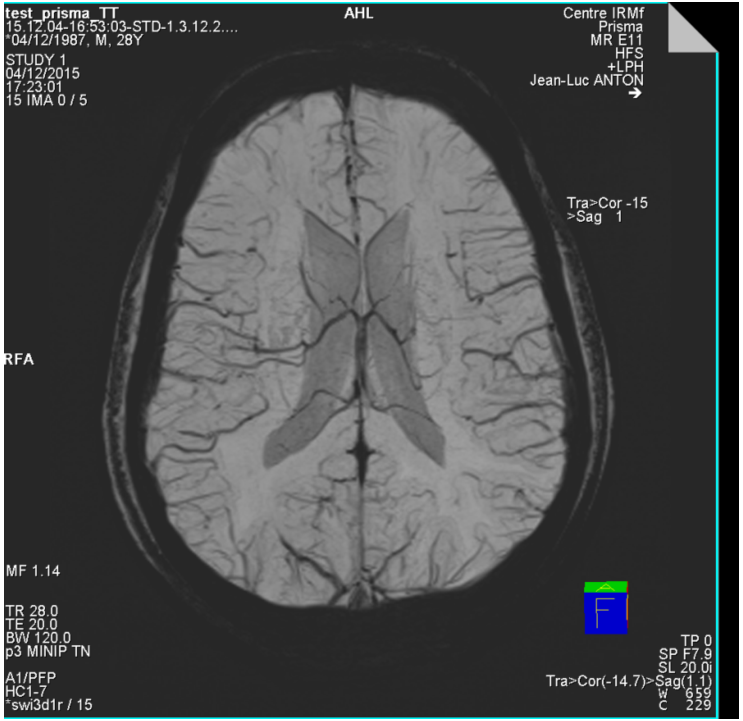
MRI sequence : FLAIR

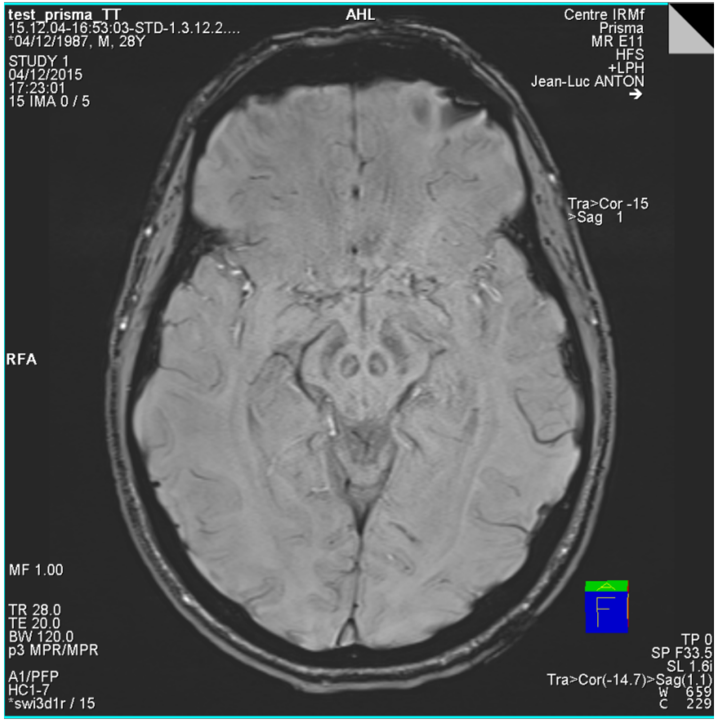
T2 FLAIR à 0.9mm
For diagnostic imaging



Susceptibility weighted Imaging

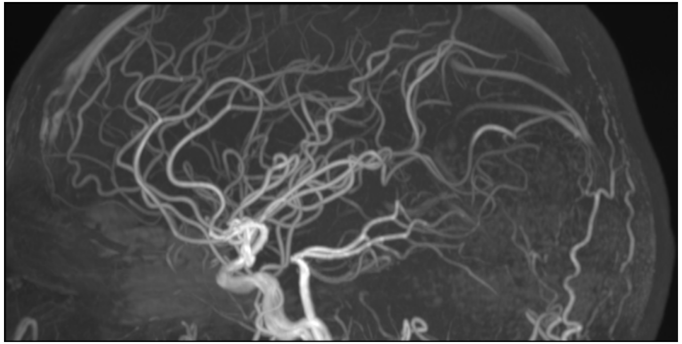


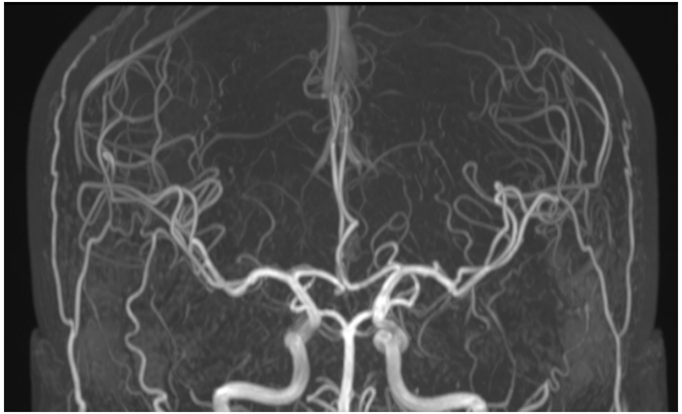
Vizualisation of veins



Vizualisation of iron-rich structures
Substancia nigra, red nuclei..

Angiogram: Time-of-flight sequence

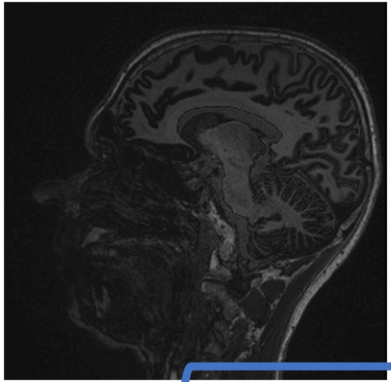




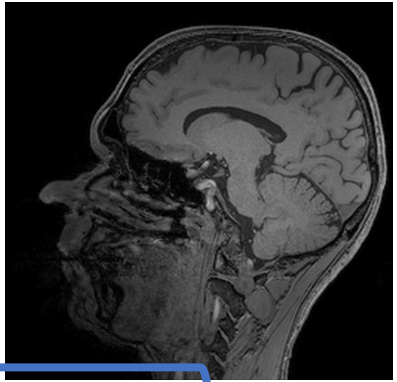
TA = 6:40min
0.6 mm iso

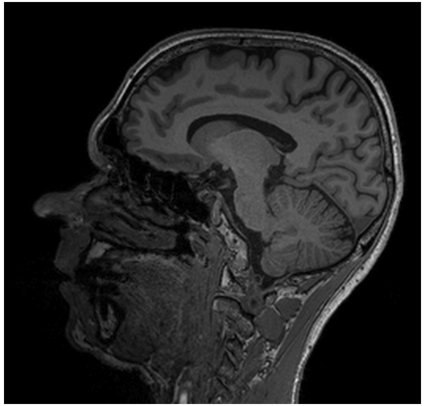
Playing with contrasts: MP2RAGE sequence

Contrast 1:
« indian ink »

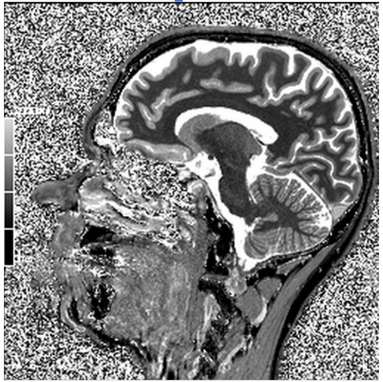


Contrast 2
PD -like





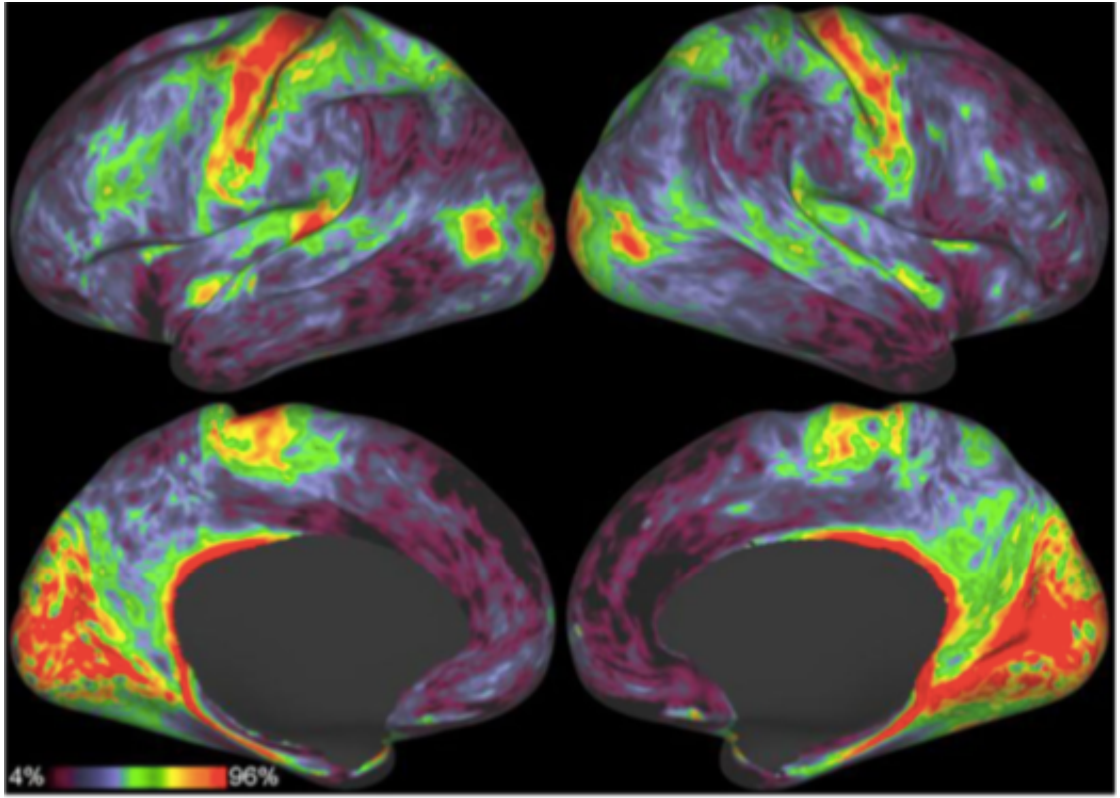
« Classic »T1w image



T1 map

« Uniform » T1w image

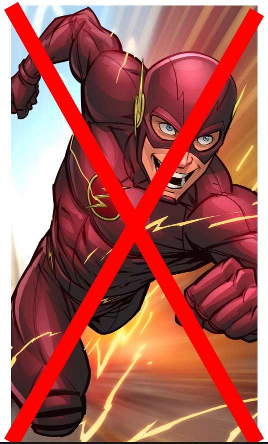
T1w/T2w ratio image use to contruct a "myelin map" of cortical surface
=> See talk of Olivier for surface generation from MRI image ;-)

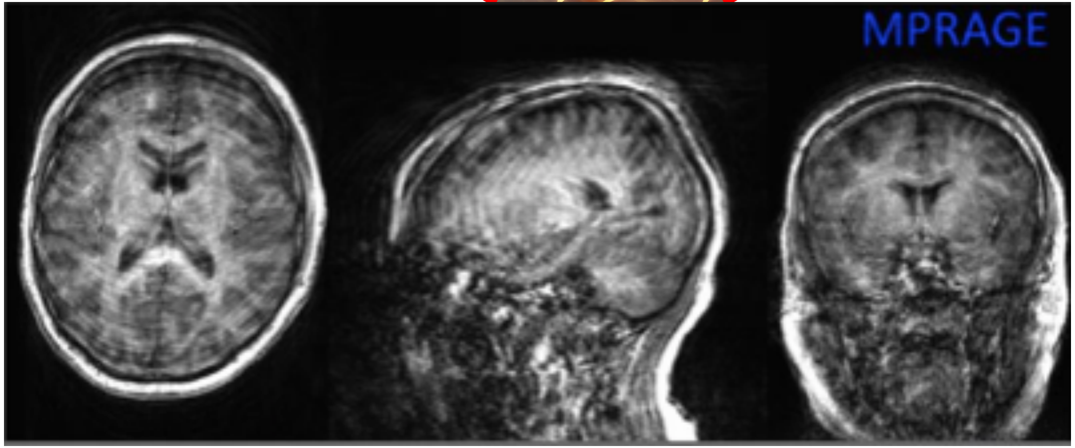


Glasser, Van Essen et al. NeuroImage (2014)

MRI can go wild !

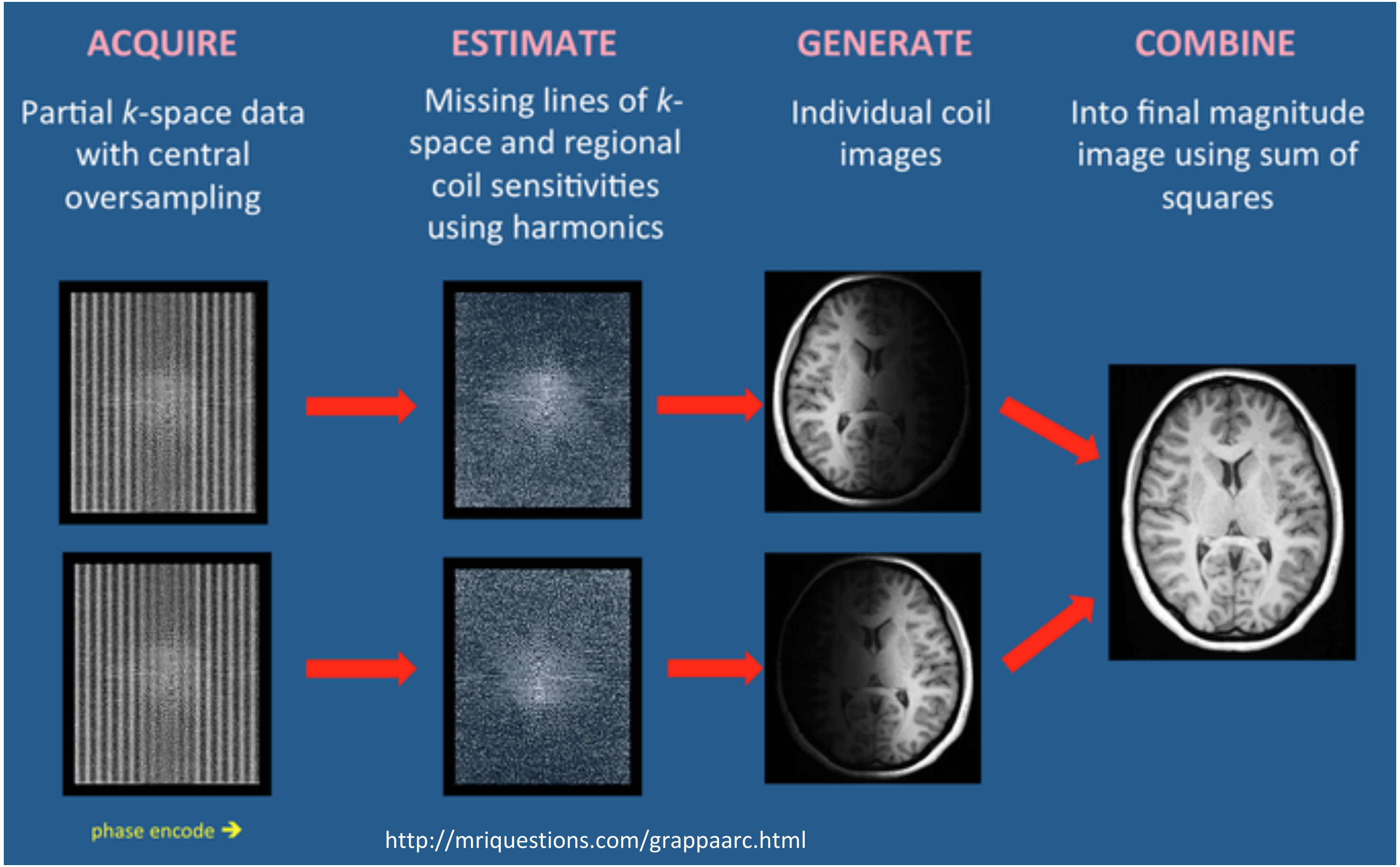
- Beautiful images but not in a flash!
- It takes several minutes to get a HR anatomical image
- Subject need to be compliant and stay still!
- Acquisitions can go wrong…





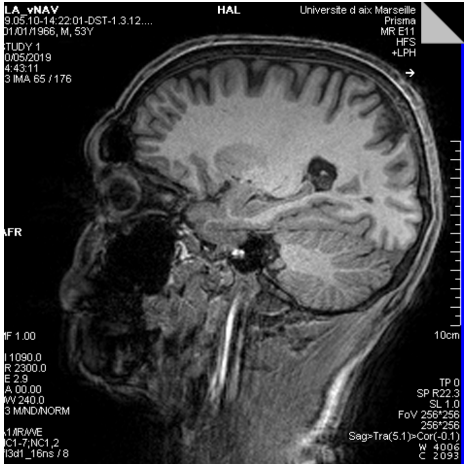
Craddock et al. 2020

Parallel acceleration (GRAPPA)



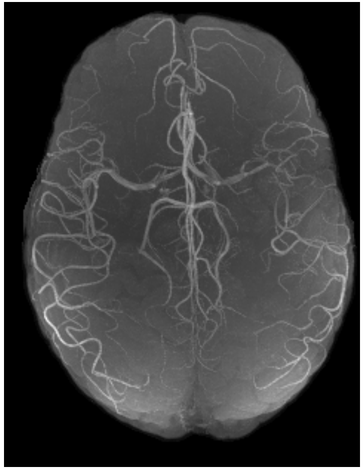
Motion correction for anatomical MRI

Prospective
MOCO off



Prospective
MOCO on

Retrospective
MOCO off



Retrospective
MOCO on

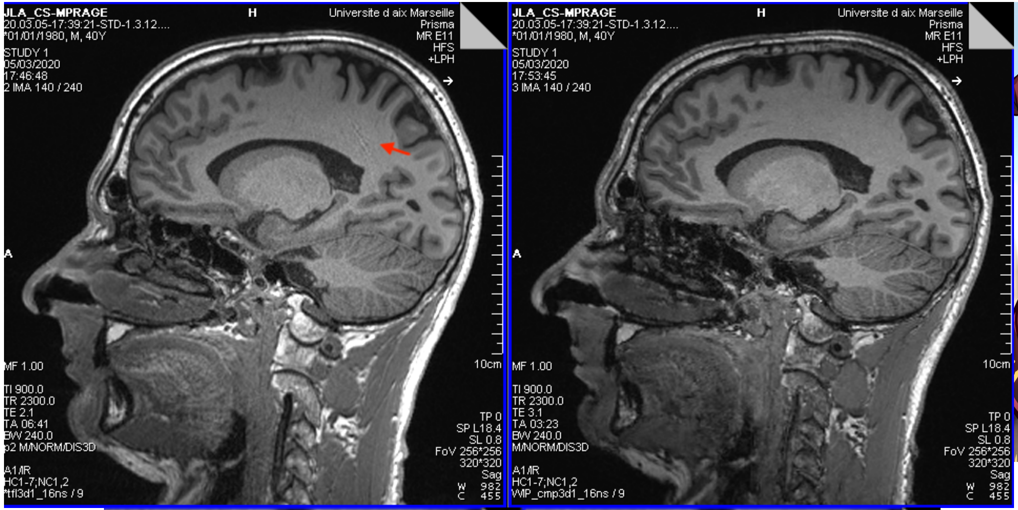
Volumetric navigators

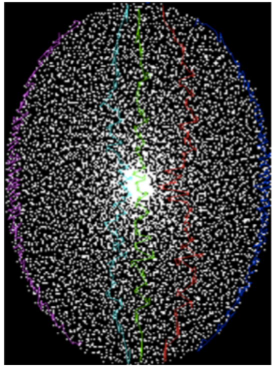
Faster acquisition!

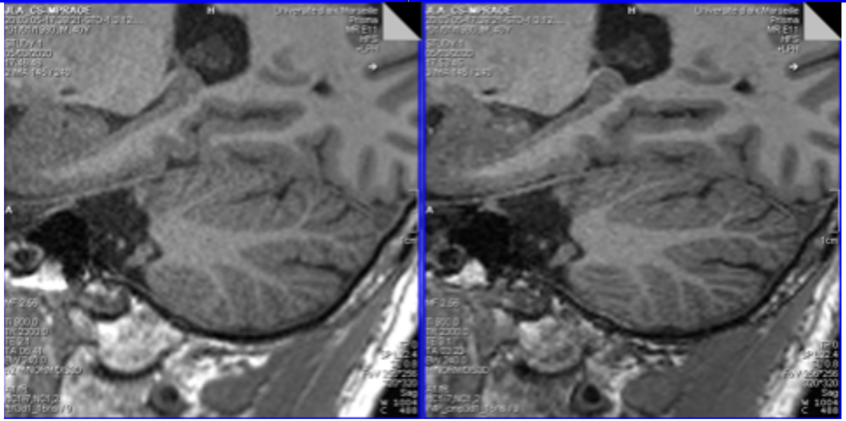
Compress Sensing acquisition:
Sparse sampling

TA: 6min43-> 3min23

T1w @ 0.8mm iso

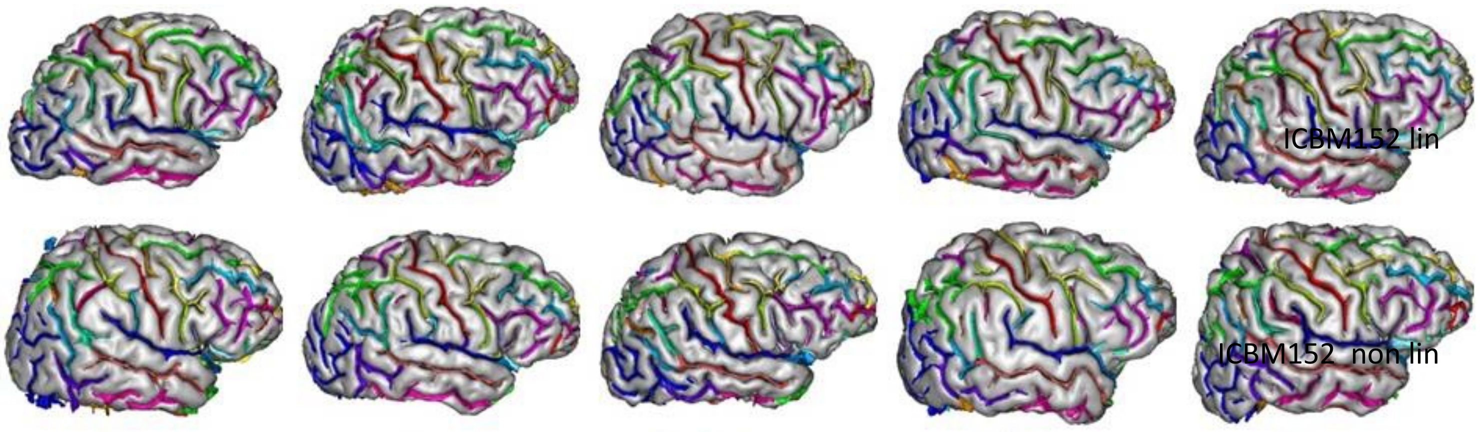


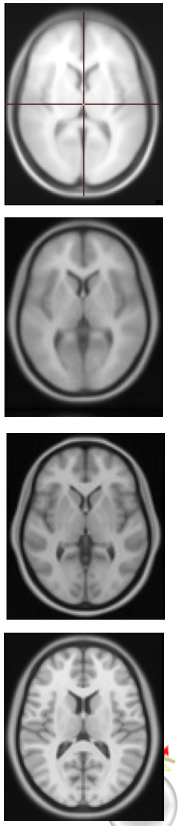




MRI and Brain Anatomy

- In order to compare individuals, images must be transformed to match eachother.
- This process is known as **registration**.
- All subject’s anatomies are registered to the same template in a standard space.





MNI305

ICBM152 lin

ICBM152 non lin

ICBM152 non lin 2009

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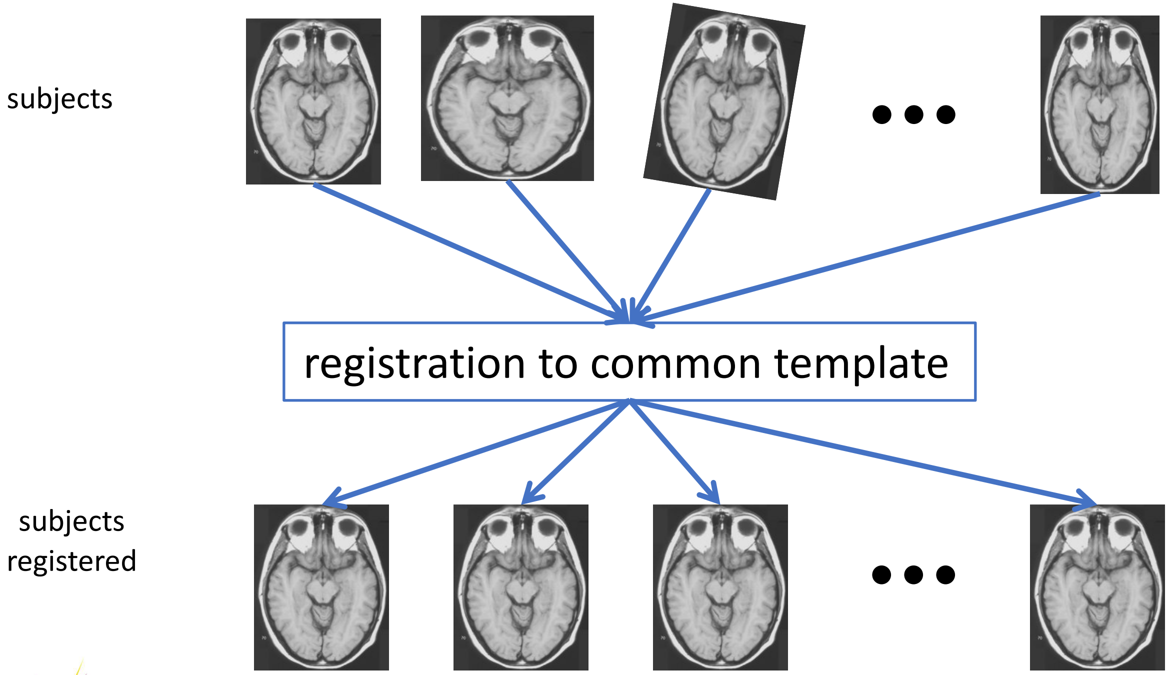

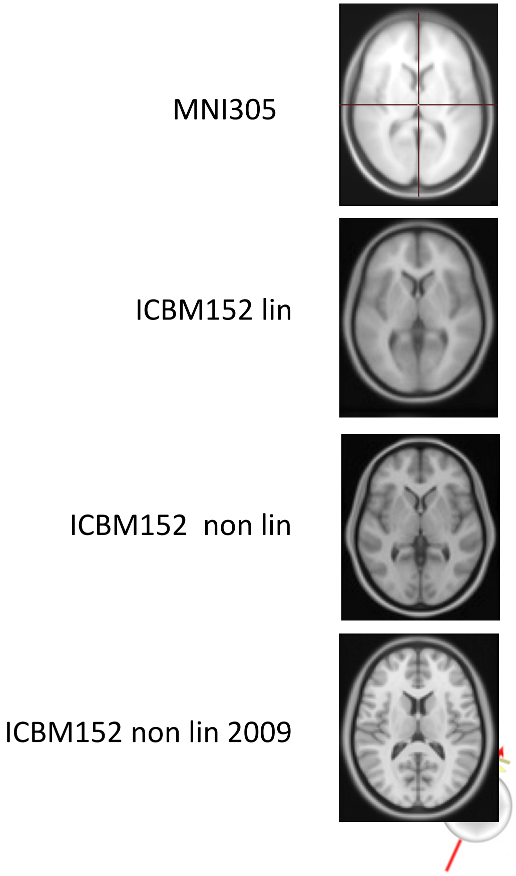

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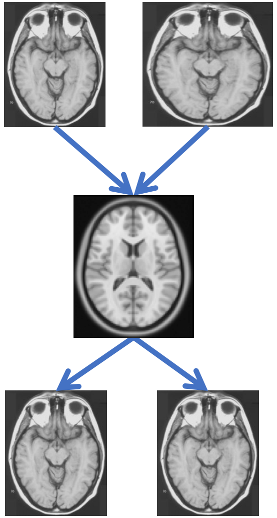
Several major software available (at INT) to perform such registration

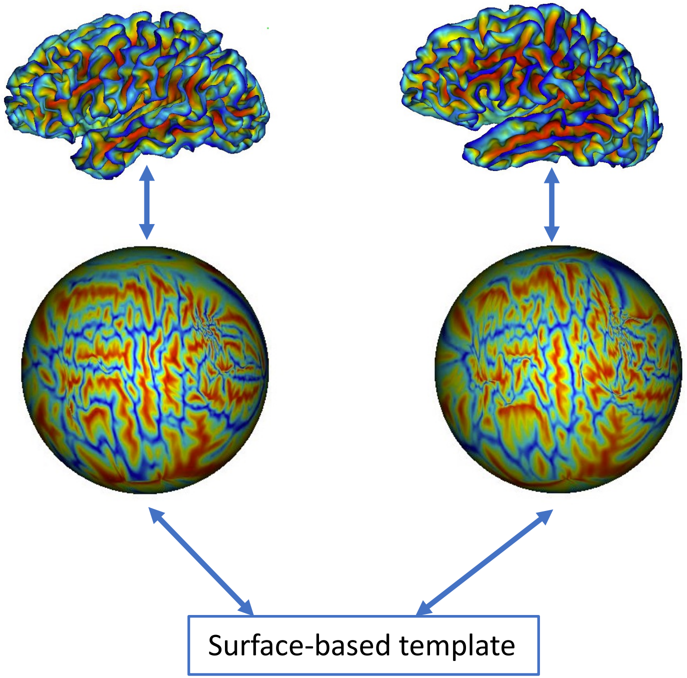
Volume based



SPM

FSL

Surface based



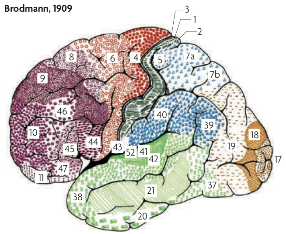
Brain Visa

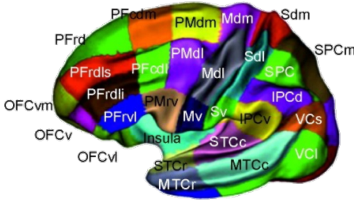
FreeSurfer

- Inter-subject registration is traditionnally done based on intensities (volume), shape (surface), or explicit landmarks such as sulci (volume and surface).
- Recent advances allow the use of other information such as grey-matter myelin content, function, or connectivity.

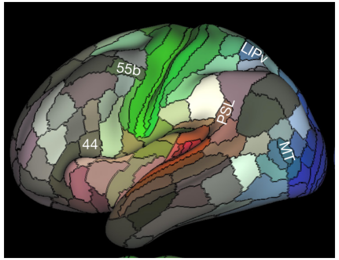
- It is assumed that after group registration images or surfaces correspond point-to-point:
  - This is wrong (but it is an approximation)
  - Quality is not uniform: some areas are easier to register than others.

- A classic side-product of registering all images on a template is that a parcellation defined on the template can be then projected on registered images.

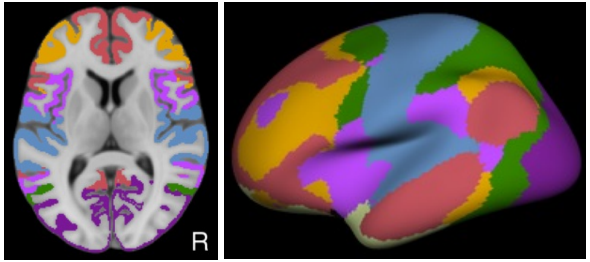




(Auzias et al. , 2015)

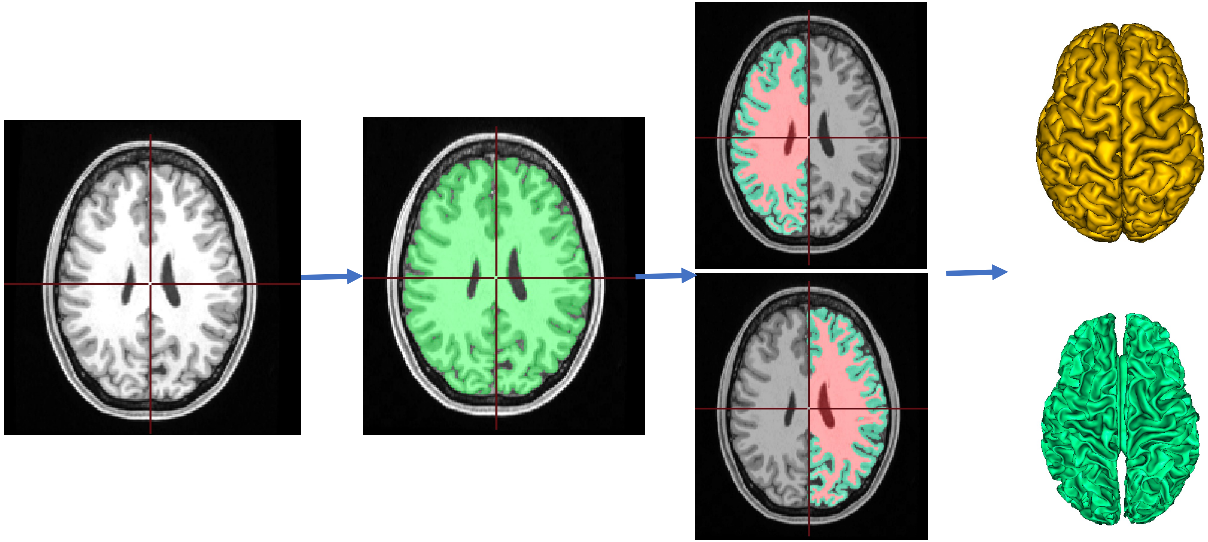


(Glasser et al. , 2016)



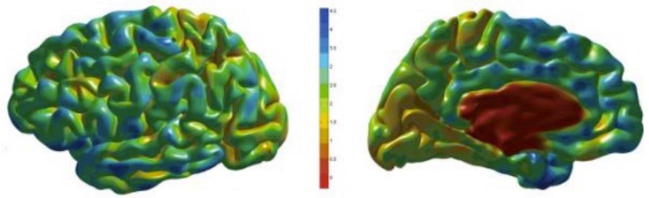
(Yeo et al. , 2006)

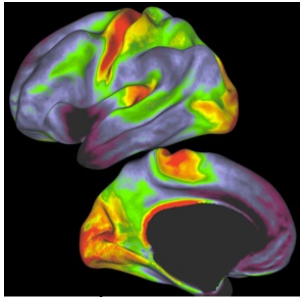
From MRI to tissues: segmentation and surface modeling



- The more atypical, the more difficult to find a good segmentation method (babies, unsual NHPs, pathological images…)
- Modern evolution will lead to refined segmentations: cortical layers, subdivision of subcortical structures…

- Measurements can be performed at a global, regional or local level, both in the volume or on the cortical surface:
    - Grey matter volume
    - Tissue surface area
    - Cortical thickness
    - Cortical myelination



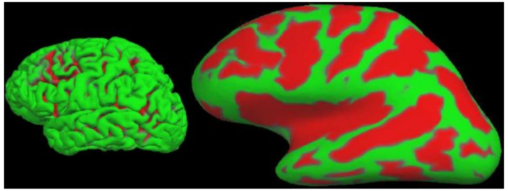


- Methods have been developed to study specifically these measures and provide statistical comparisons across populations
    - Voxel-based morphometry (SPM, CAT12, FSL)
    - Surface-based morphometry (Freesurfer)
    - Machine learning-based methods.
- Such methods are often used to study:
    - Pathologies -> finding biomarkers
    - Inter-hemispheric asymetries and/or functional specificities (e.g. anatomical correlates of handedness).
    - Changes in time:
        - Developmental trajectories
        - Aging
        - Plasticity
        - Recovery

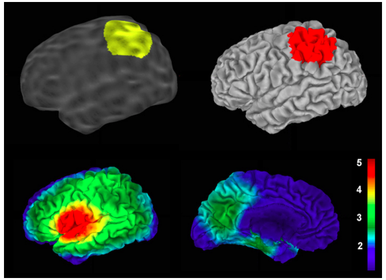
Cortical shape analysis (1)

- Surface based approaches (Image-like): freesurfer and beyond

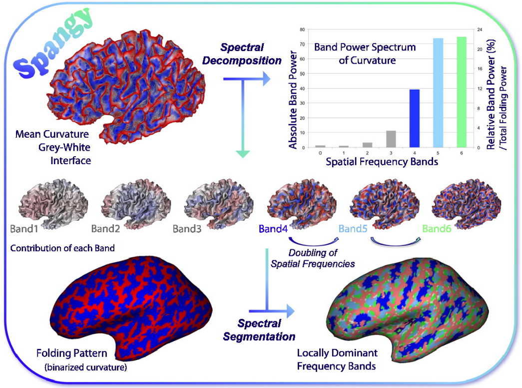
Convexity (Freesurfer)



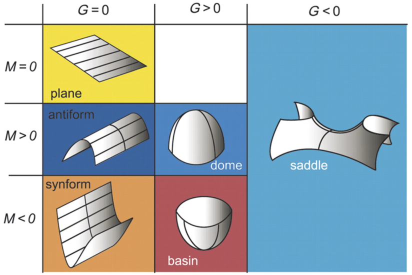
Local gyrification index (Freesurfer)



Spectral Analysis of Gyrification (primary, secundary, tertiary folding)



(A lot of) curvatures (slam)

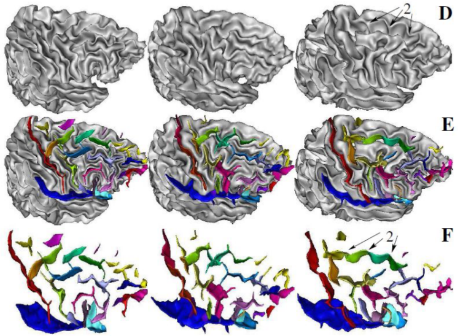


Depth potential function (Brainvisa)

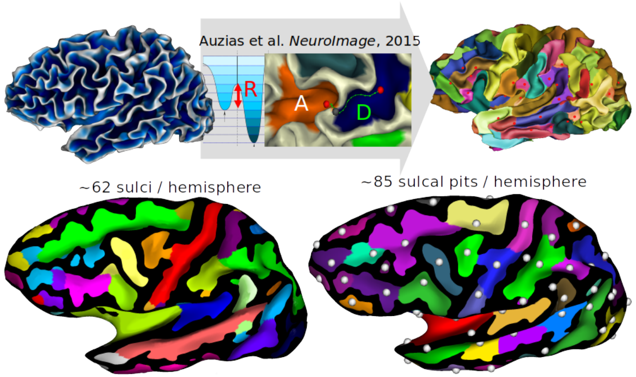
Personal advice: Be careful with physical units/influence of brain size (allometry) !

- Object-based approaches: isolated anatomical entities can be obtained

BrainVisa sulci (anatomical nomenclature)

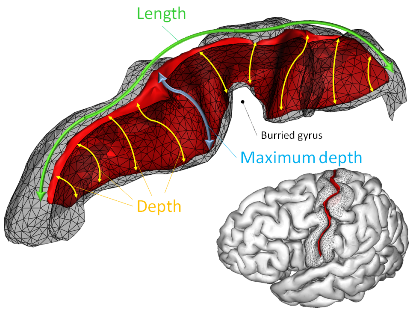


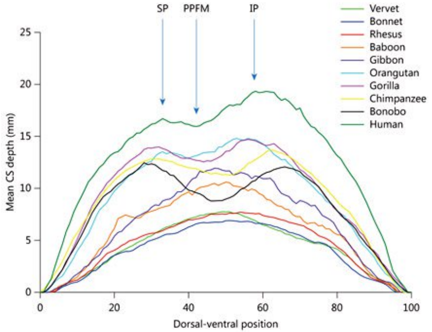
Sulcal pits/ sulcal bassins (developmental hypothesis)



- For each object, a set of measurements/stats can be proposed

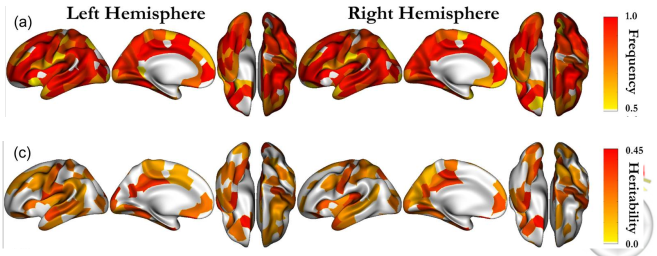
length, width, depth, area





(Hopkins et al. , 2014)

heritability

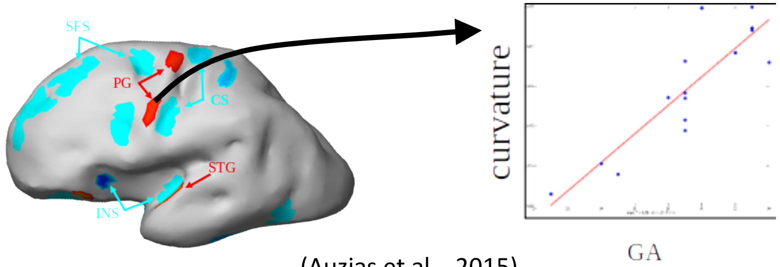


(Le Guen et al. , 2018)

Trajectories of development/aging

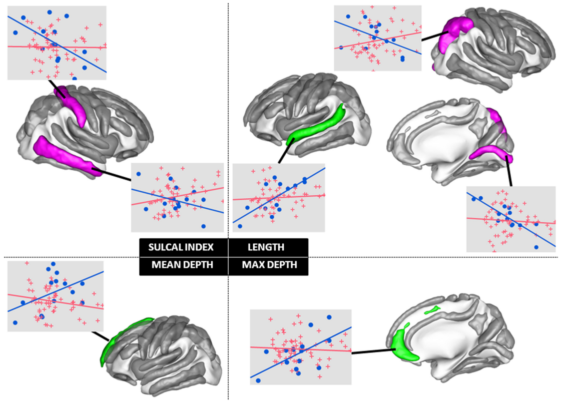
- Importance of the temporal models
  - Linear models
  - Polynomial models
  - Gompertz models

Local evolution of curvature at fetal stage

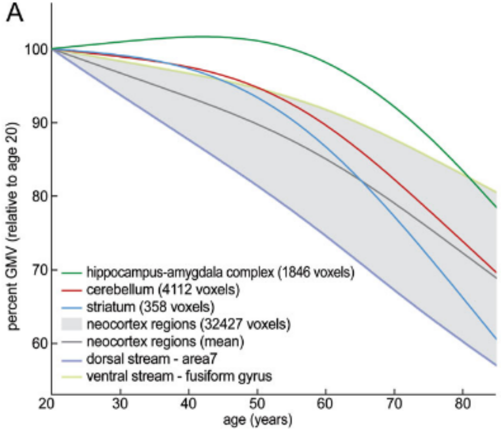


(Auzias et al. , 2015)

Abnormal trajectories in ASD

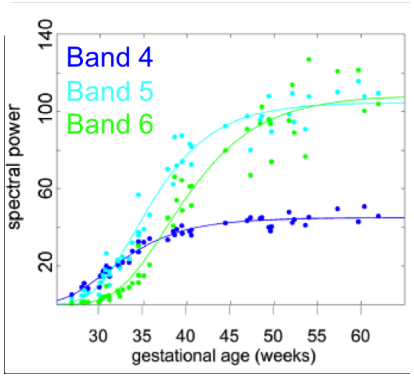


(Auzias et al. , 2014)



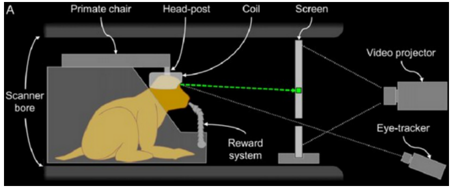
(Ziegler et al, 2012)

Spectral analysis reveals primary, secundary, tertiary folding

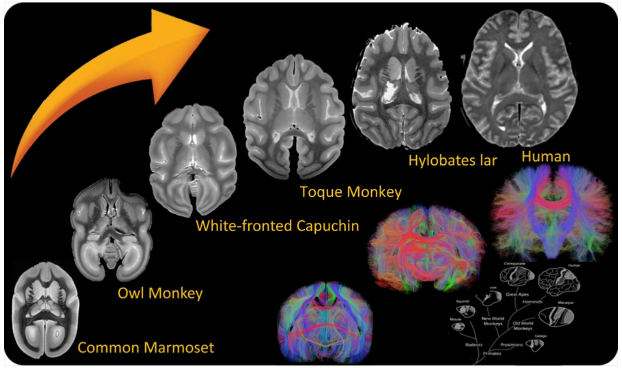


(Dubois et al. , 2018)

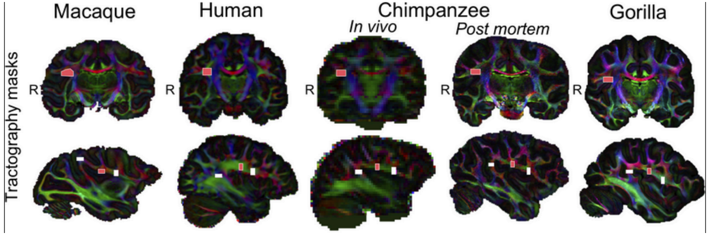
- **Comparative neuroimaging -> using MRI for brain comparisons across species.**
- Compared to traditional neuroscience techniques, MRI has the **advantages** of:
    1. **Less invasive...**
    2. **Repeatable measurements across individuals and species**
    3. **Multimodal - gives a complete picture of the brain.. (structure, connections, function)**
    4. **Digital – data-sharing, public databases, big data..**
- Provides an important window to study the **evolution of the human brain and its functions**.



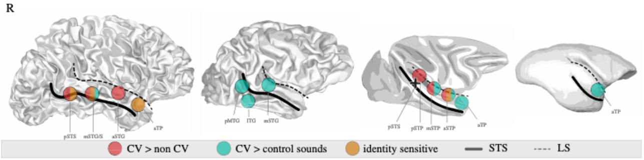
typical monkey MRI setup



T2-weighted and Diffusion-weighted images across primate species

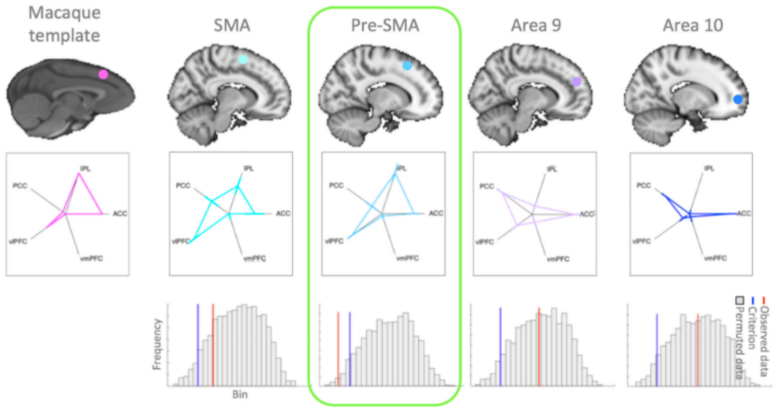


White matter tract comparisons

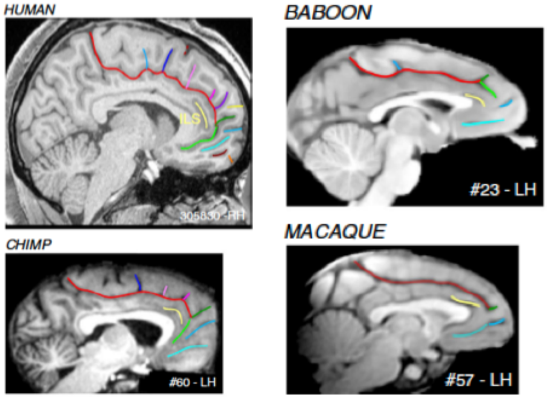


Functional comparisons

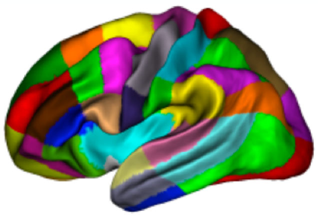
- Across species, brains can differ in many ways (e.g. connectional or areal changes).
- Common **approaches** for interspecies brain comparisons:
  1. Comparing brains via **Connectivity Fingerprints**
  2. Comparing brains via **Common Sulci**



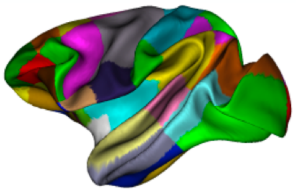
Human-Macaque Region Matching via Connectivity Fingerprints



Human MarsAtlas



MarsAtlas on Macaque

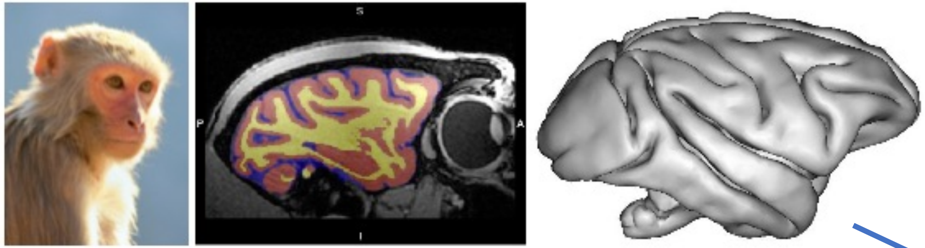


Human-Macaque Surface Mapping via Common Sulci

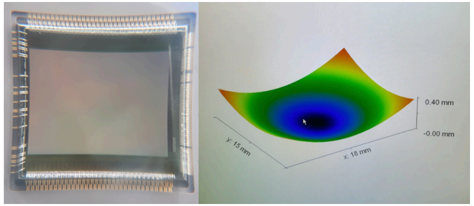
In humans, brain imaging has been used for localization of specific areas :

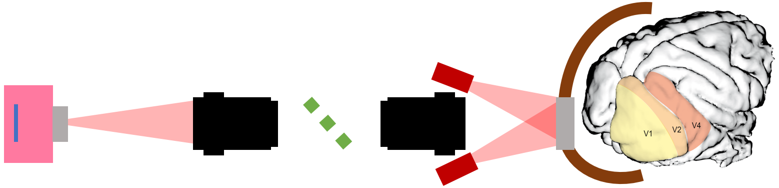
- surgical planning (resection of a specific zone)
- TMS target localization
- functional localizers.
- electrode implantation

At INT, it can be used with NHPs for interventional planning



Optimising chamber and electrode implantation

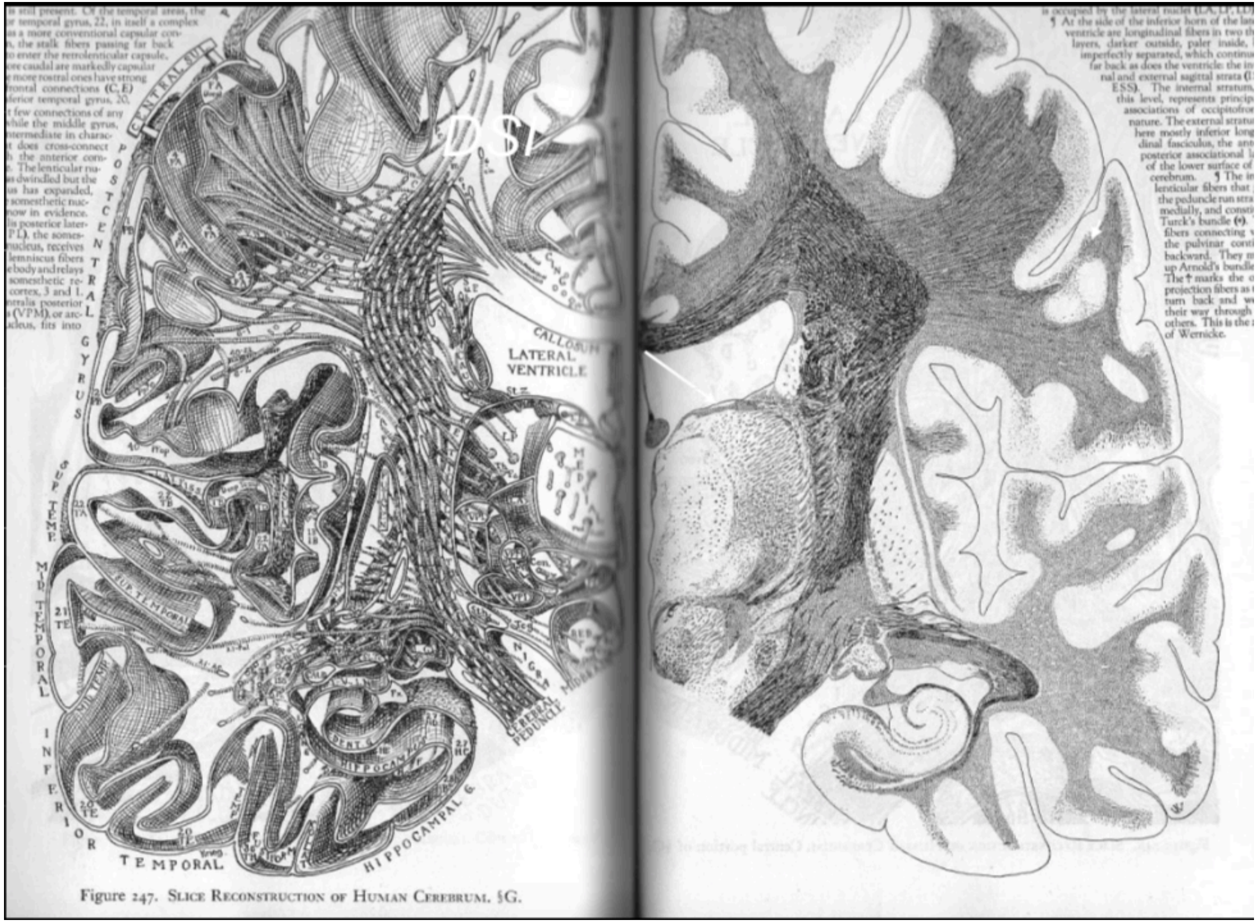




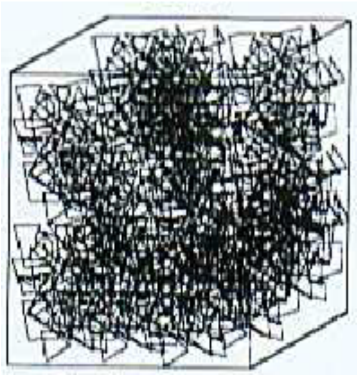
Improving the effective field of view by using a curved detector

Diffusion imaging

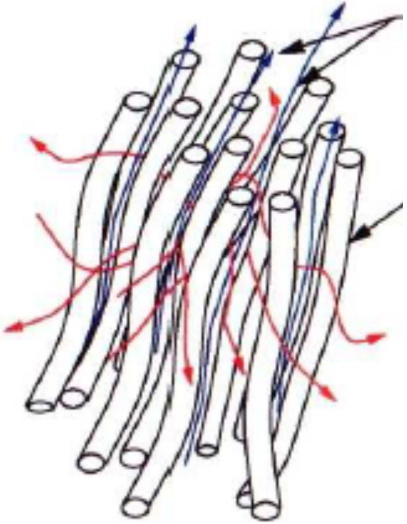
Wendell Krieg
1963



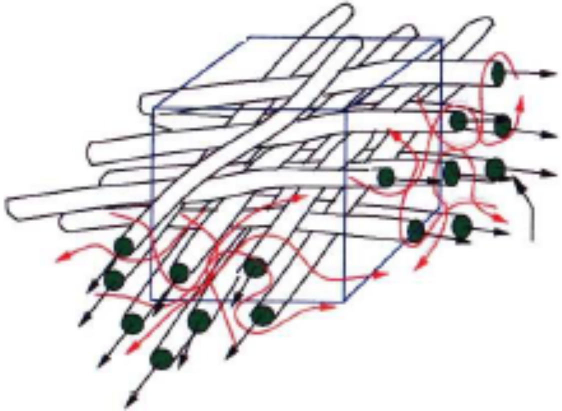
Random motions



1 privileged direction of diffusion



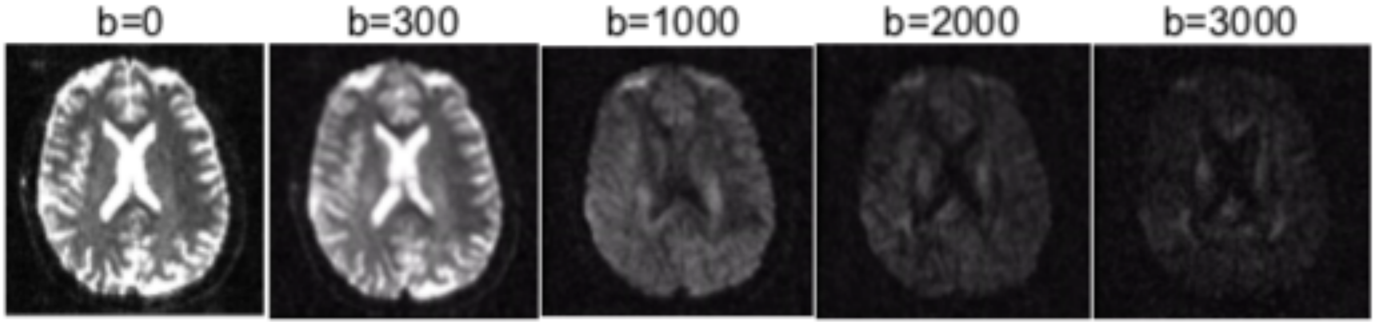
2 privileged direction of diffusion



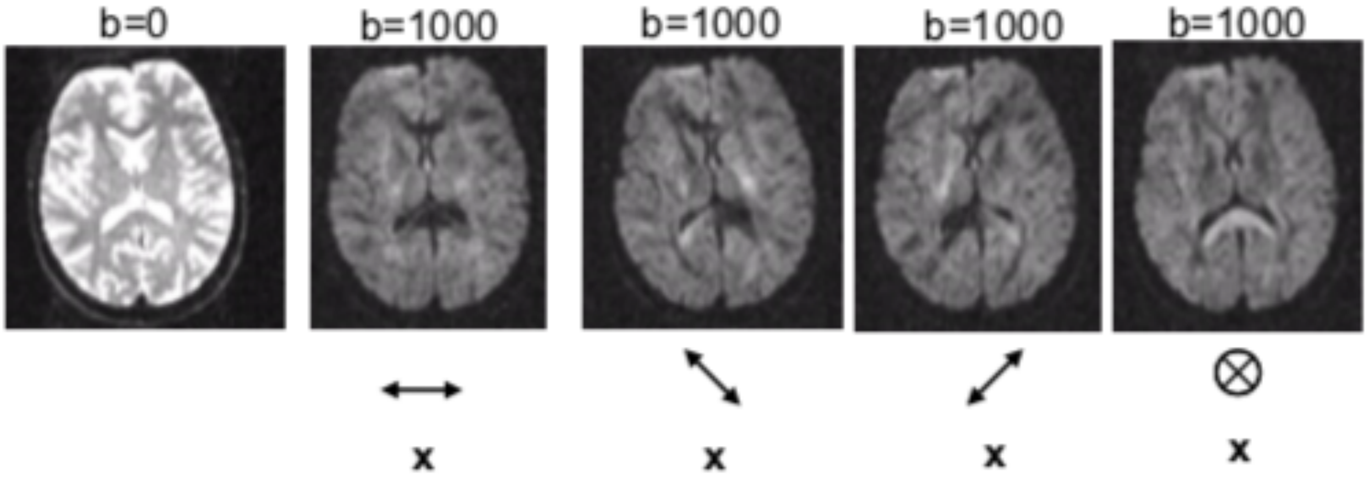
Diffusion sensitive MRI sequences

Contrast dependent on:

- **Strength** of diffusion gradient



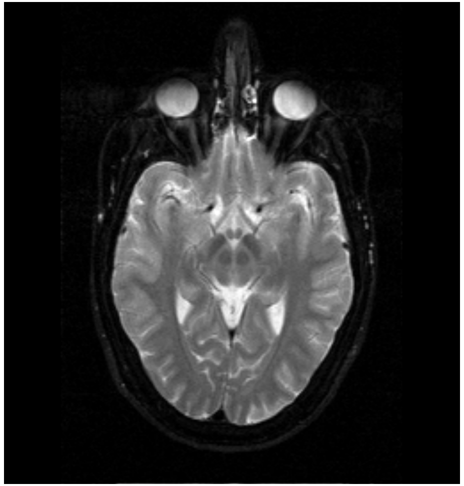
- **Direction** of diffusion gradient



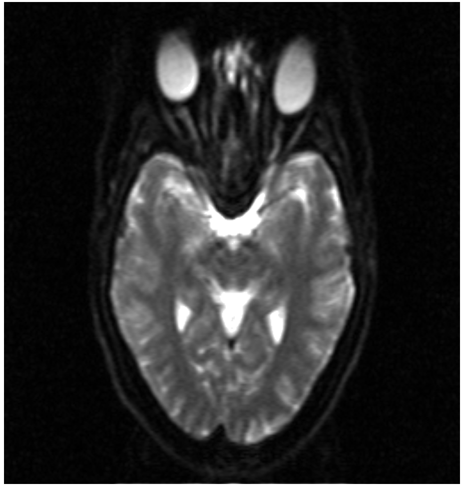
=> Need to acquire many direction! (depending on the application)

EPI readout (after the diffusion weighting part)

- **Faster** than anatomical images (5-8 s vs 5-8 min)
- **Lower** spatial resolution (1.5 -2 mm iso vs 0.8 -1mm iso)
- **Geometric distortions**
- **Gibbs ringing artefacts**

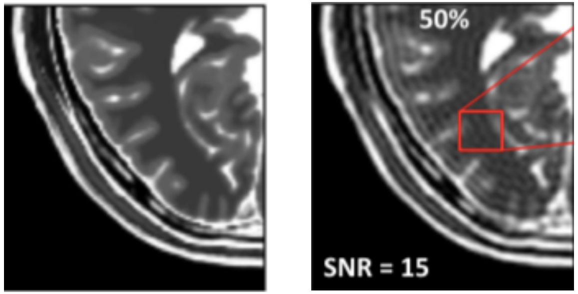


SE sequence (anatomical imaging)



SE-EPI sequence (diffusion)

Ground truth



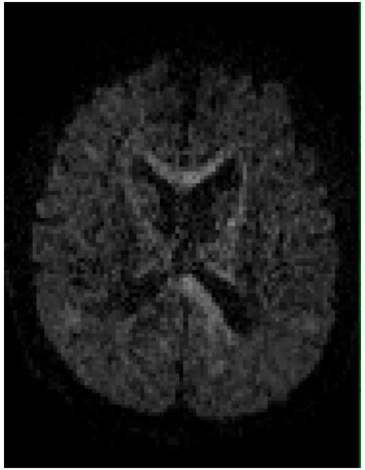
Perrone et al. (2015)

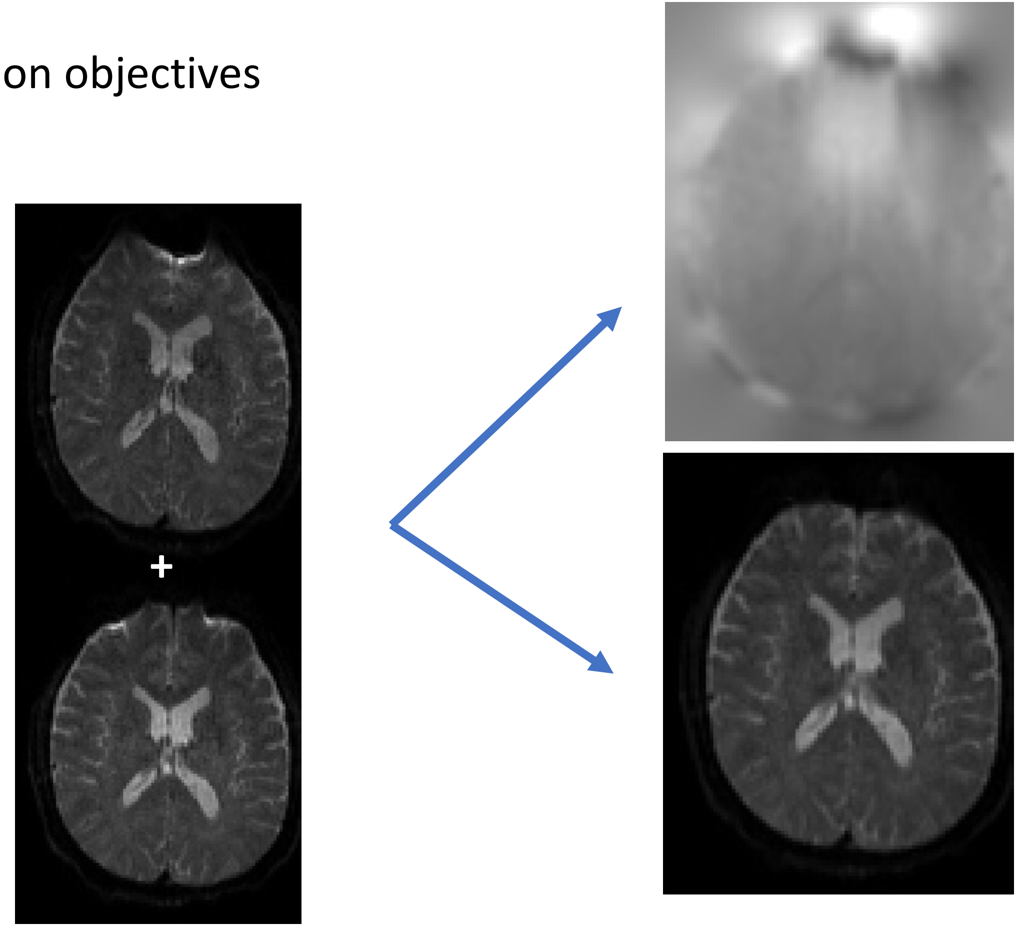
Gibbs ringing

Acquisition strategy for Diffusion imaging

- Several volumes acquired:
from 3 to more than 500 depending on objectives

- Acquire at least some volumes with reversed phase encoding direction



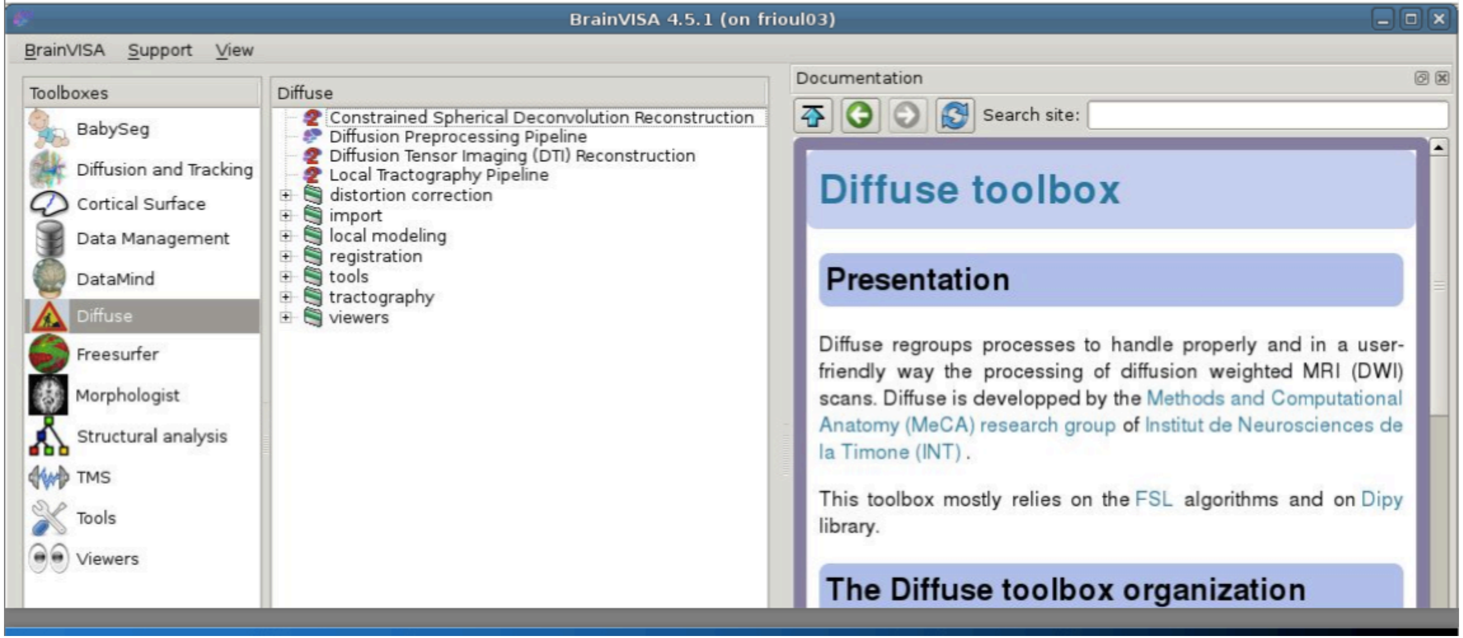


- Denoising
- Degibbs
- Topup (correct geometric distorsions)
- Eddy (motion and eddy current correction)
- Bias correction
- Fiber orientation distribution
- Whole brain Tractogram
- Connectome

Toolbox Diffuse developed at INT !!!

- Toolbox for processing Diffusion MRI
  - Guided and adapted for each acquisition type
  - Automated
  - Allowing interface with anatomical data

http://brainvisa.fr/web/index.html



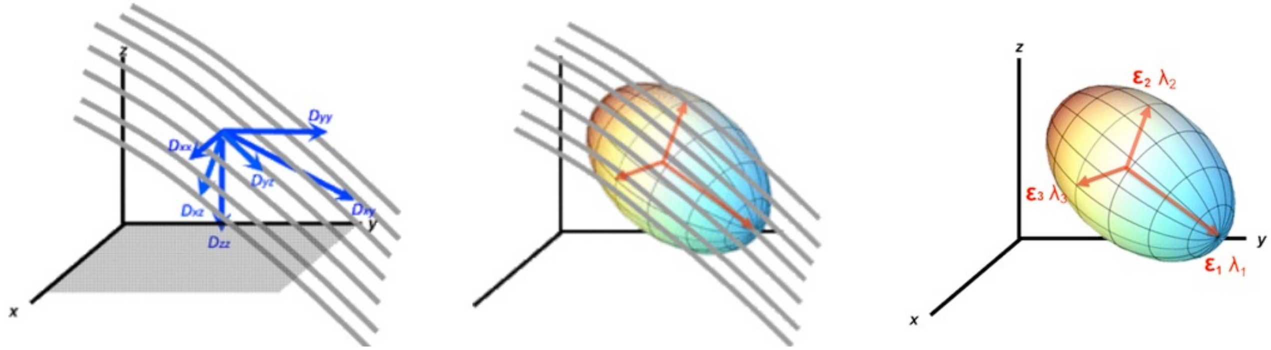
Lucile Brun, Alexandre Pron, Julien Sein, Christine Deruelle and Olivier Coulon (2019)

Local models: the diffusion tensor

To estimate diffusion properties, a model of diffusion is fitted to the data at every voxel

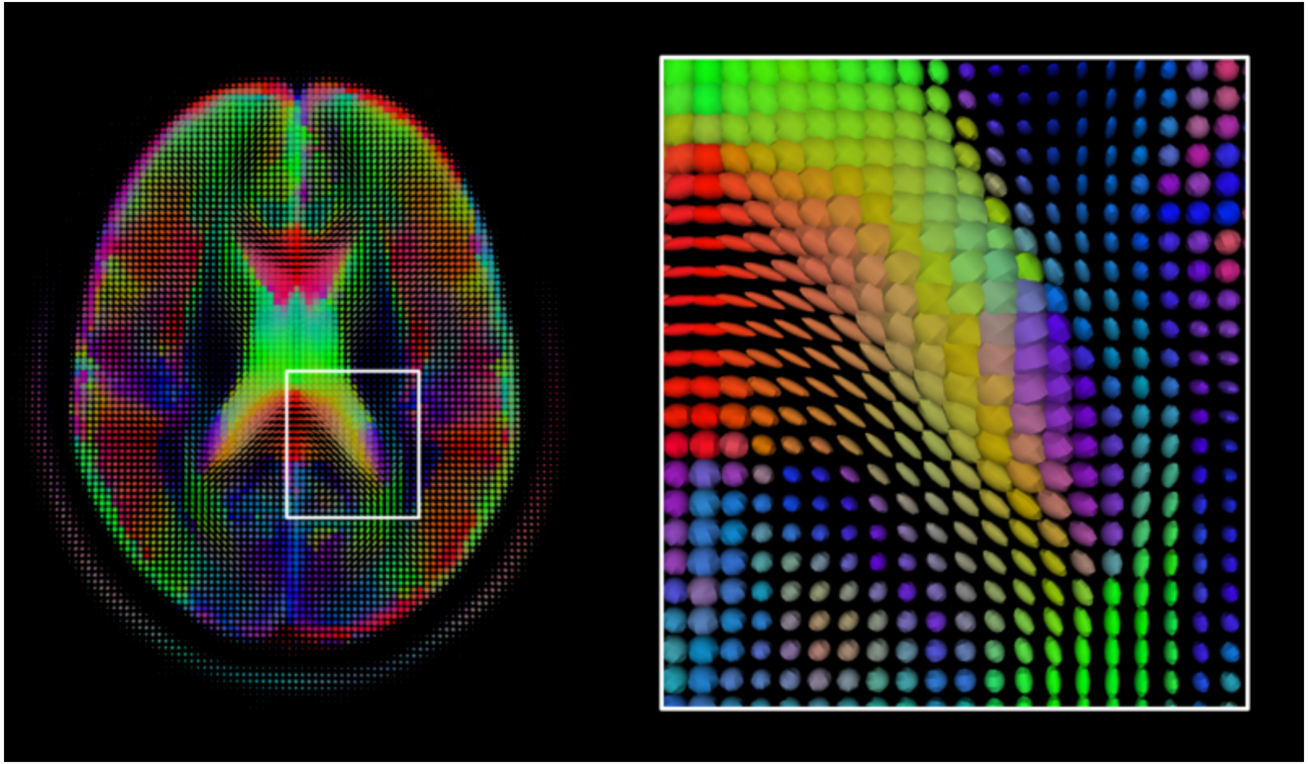
The diffusion tensor is the simplest historical (Gaussian) model (Basser et al. 1994).

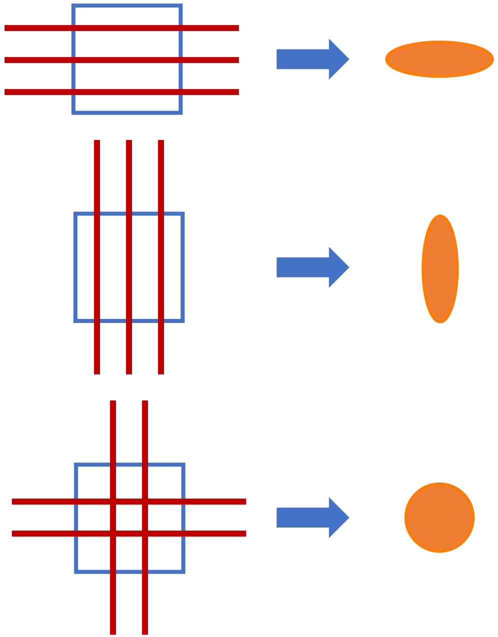
$$\mathcal{D} = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix}$$



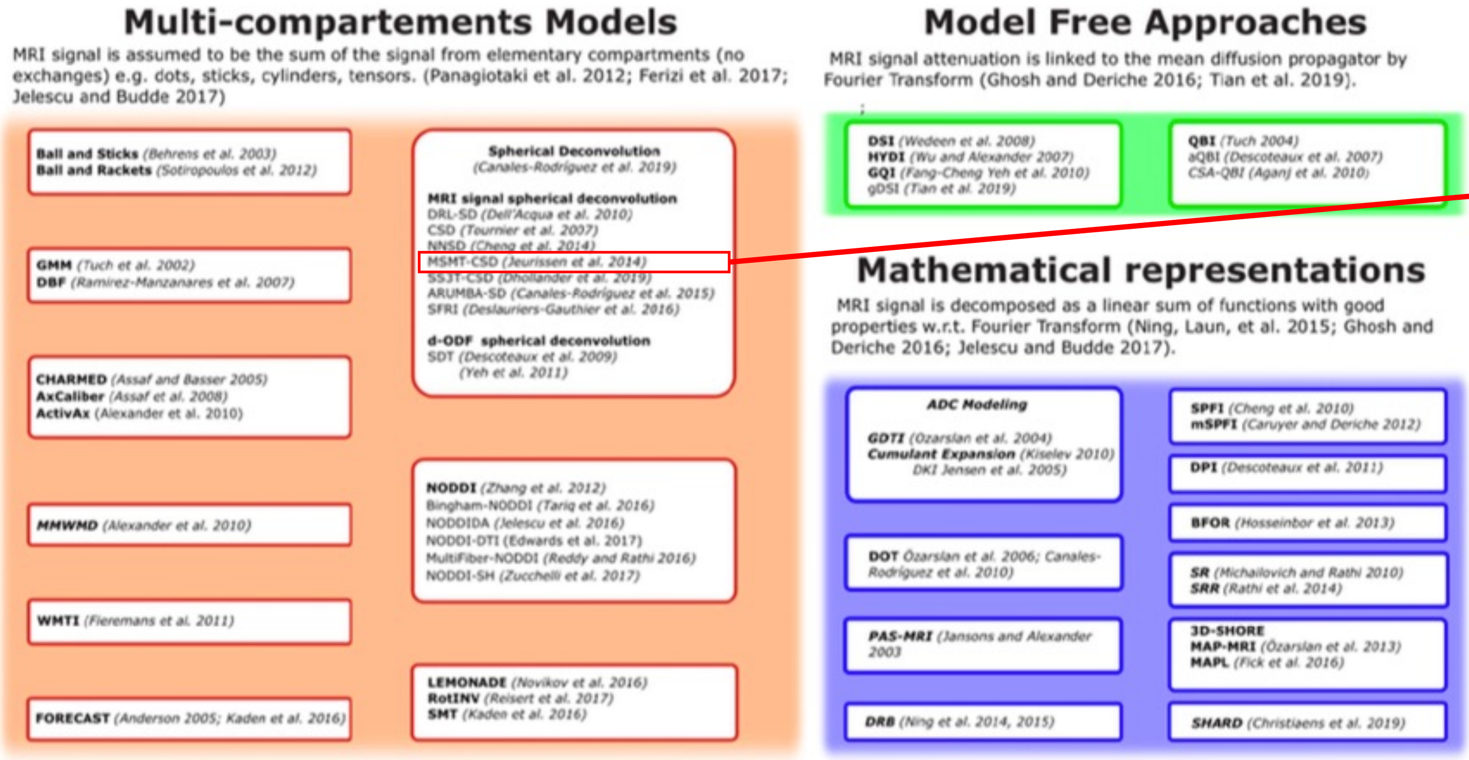
(from http://www.mri-q.com/dti-tensor-imaging.html)

Local models: the diffusion tensor



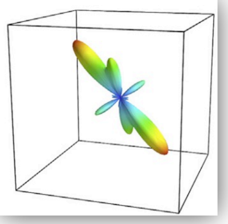


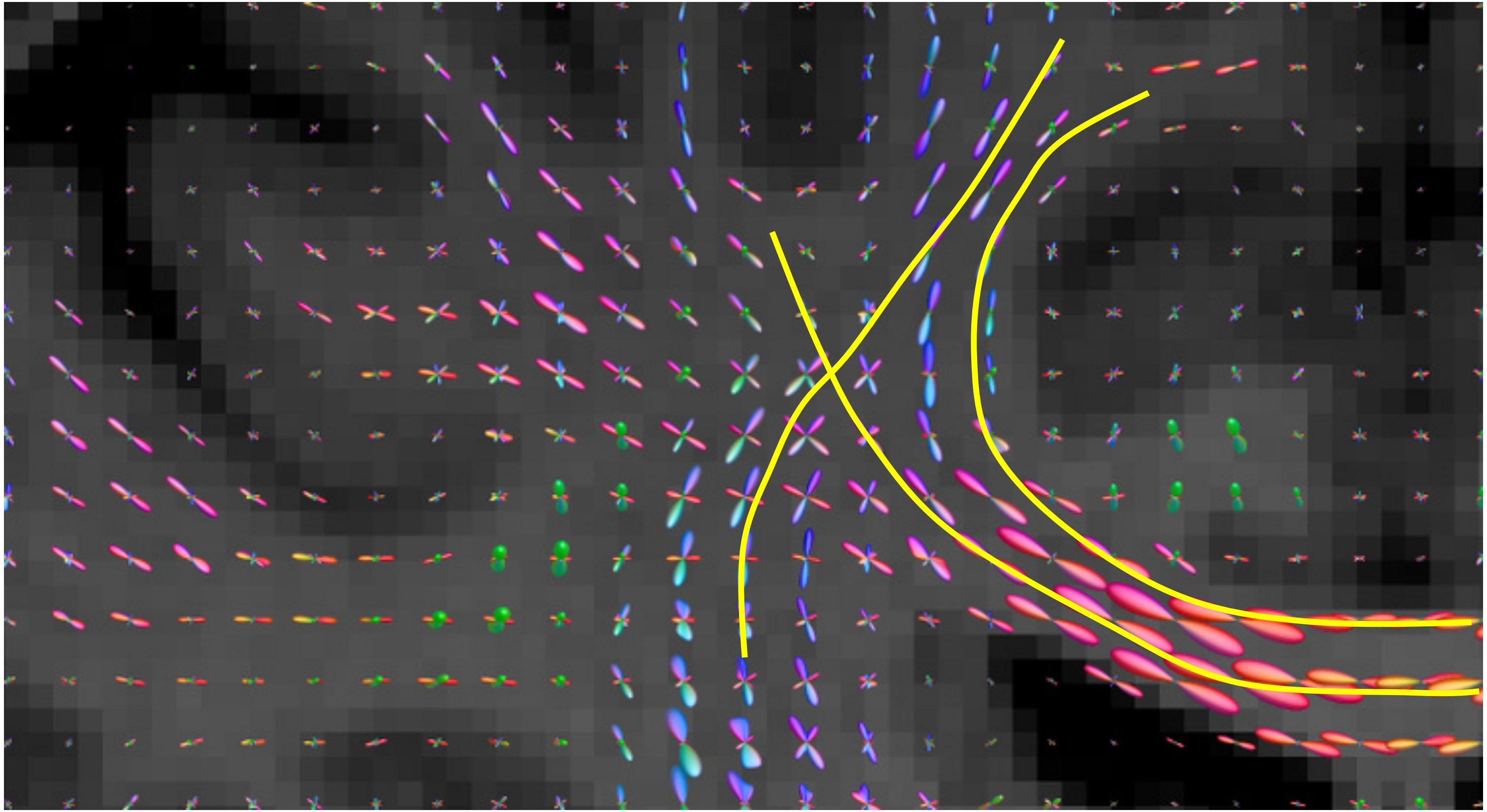
Local models: higher order



(Pron, 2020)

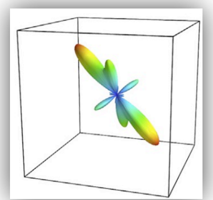
Multi-shell multi-tissue CSD (MRTrix software)





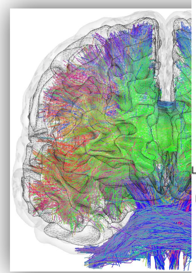
Fiber structure is apparent, and fiber crossing becomes explicit

Tractography

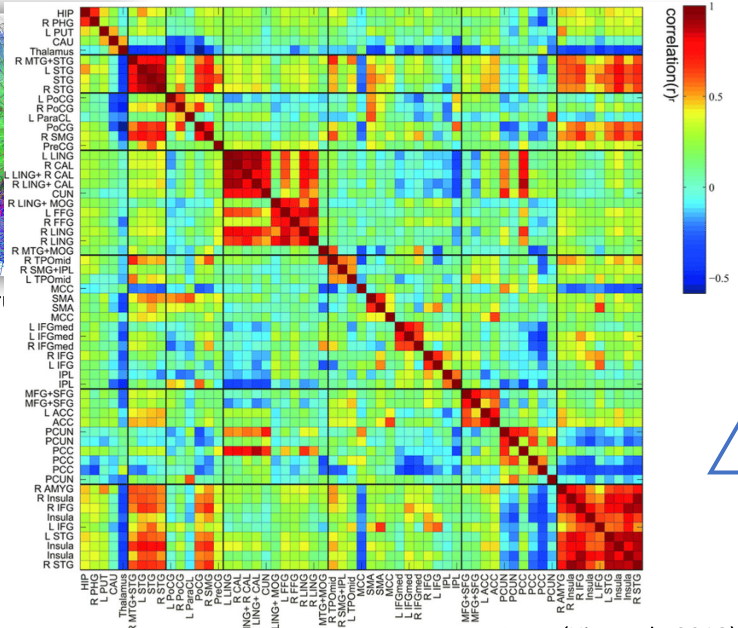


Approximate macroscopic reconstruction of white matter fiber trajectory = Reconstruction of streamlines that represent group of white matter fibers

One can either specifically look for tracts passing through specific seeds or initiate seeds in all white matter voxels (or all WM surface vertices) to get a whole brain tractogram



© Lucile bru



From (Xia et al., 2018)

Such a tractograms can then also be represented as a connectivity matrix indicating the strength of the connection between pairs of points, voxels, or regions.

! No directionality

Tractography: what is it good for ?

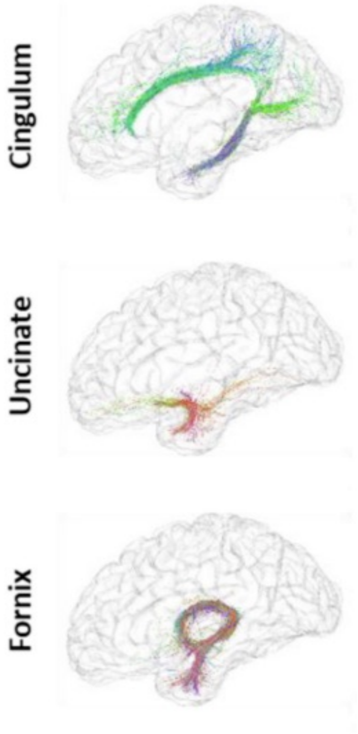
Expliciting white matter organization: what is connected to what ? And how ?

Applications:

- Segmenting white matter, e.g. *‘where is the uncinate fasciculus ?’*
- Finding markers of pathologies: different connectivity (or connectivity strength) ? (psychiatric diseases, epilepsy,…)
- Pre-surgical planning
- Comparing species (see Kep Kee’s slides earlier)
- …

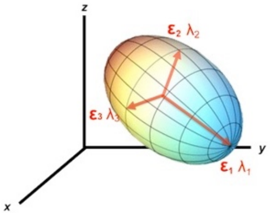
- To some extent: quantifying connections (streamline density, volume of bundles)

Current biases of tractography limit possible studies, but this is changing fast.



(brun et al., 2019)

Don’t throw away the tensor: it’s not all about connectivity

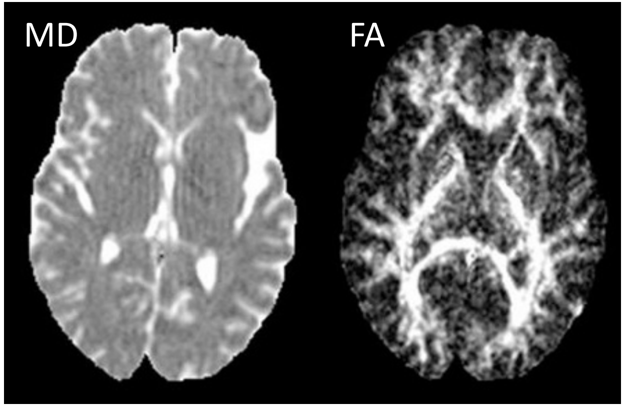


Mean diffusivity

$$MD = \frac{\lambda_1 + \lambda_2 + \lambda_3}{3}$$

Fractional anisotropy

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



MD and FA are often uses as proxies for tissue microstructure.

As such, their variations are relevant (across time, or between groups).

They have been found markers for:

- pathologies (Parkinson disease, multiple sclerosis,…)
- development (e.g. prenatal cortical maturation)
- plasticity
- …

Careful with interpretation !

Don’t throw away the tensor: it’s not all about connectivity

	FA	MD	AD	RD
		$(\lambda_1+\lambda_2+\lambda_3)/3$	λ_1	$(\lambda_2+\lambda_3)/2$
	FA is a summary measure of microstructural integrity. While FA is highly sensitive to microstructural changes, it is less specific to the type of change.	MD is an inverse measure of the membrane density, is very similar for both GM and WM and higher for CSF. MD is sensitive to cellularity, edema, and necrosis.	AD tends to be variable in WM changes and pathology. In axonal injury AD decreases. The ADs of WM tracts have been reported to increase with brain maturation.	RD increases in WM with de- or dys-myelination. Changes in the axonal diameters or density may also influence RD.
Gray Matter	↓	–	↓	↑
White Matter	↑	–	↑	↓
CSF	↓	↑	↑	↑
High myelination	↑	↓	–	↓
Dense axonal packing	↑	↓	–	↓
WM Maturation	↑	↓	↑	↓
Axonal degeneration	↓	↑	↓	↑
Demyelination	↓	↑	–	↑
Low SNR	↓	↑	↓	–

(from https://www.diffusion-imaging.com/2013/01/relation-between-neural-microstructure.html)

Tools

Centre IRM - INT

La plateforme de recherche en Imagerie par Résonance Magnétique de l'Institut de Neurosciences de la Timone (INT) installée au sein du Centre Européen de Recherche en Imagerie Médicale (CERIMED – Campus Santé Timone, Marseille)

FSL

State-of-the-art preprocessing algorithms
WM atlases

DIPY

DIPY is a **free** and **open source** software project for computational neuroanatomy, focusing mainly on **diffusion** *magnetic resonance imaging* (dMRI) analysis. It implements a broad range of algorithms for denoising, registration, reconstruction, tracking, clustering, visualization, and statistical analysis of MRI data.

Brain Visa

DIFFUSE

Diffuse is a BrainVISA toolbox designed to process diffusion-weighted MRI (DWI) data with state-of-the-art algorithms in a user-friendly way. Diffuse is currently developed at the Institut de Neurosciences de la Timone (INT), Marseille, France by both MeCA and SCaLP research teams. Diffuse mainly relies on FSL and Dipy for DWI processing.

MRtrix3

Advanced tools for the analysis of diffusion MRI data

int institut de neurosciences de la timone

DSI Studio

SlicerDMRI

PANDA

Pipeline for Analysing braiN Diffusion imAges

PANDA

Version 1.1.0 (released 2012)

CID - Artefact correction in diffusion MRI

What is ACID?

The Artefact correction in diffusion MRI (ACID) toolbox is an academic software toolkit for pre-processing of diffusion MRI data, estimation of DTI indices and spatially normalisation of DTI index maps, which fully integrates into the batch system of SPM8. The methods used in the ACID tools have been reviewed by experts in their field and are published in methodological recognized journals (see section "Referencing"). These tools are made for users familiar with the underlying statistical, mathematical and image processing concepts. The ACID toolbox provides the option to write the estimated diffusion tensor in the format of the DTI and Fibertools Software Package.

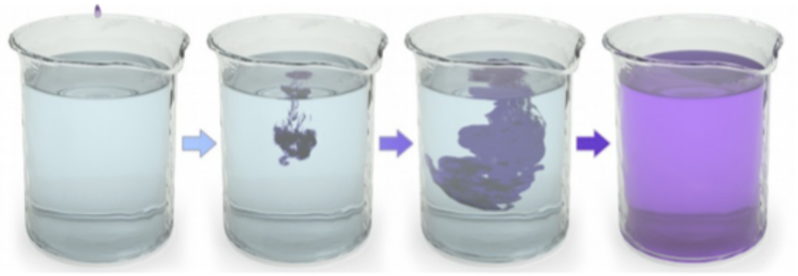
UCL Camino Diffusion MRI Toolkit

Camino is an open-source software toolkit for diffusion MRI processing. The toolkit implements standard techniques, such as diffusion tensor fitting, mapping fractional anisotropy and mean diffusivity, deterministic and probabilistic tractography. It also contains more specialized and cutting-edge techniques, such as Monte-Carlo diffusion simulation, multi-fibre and HARDI reconstruction techniques, multi-fibre PICo, compartment models, a axon density and diameter estimation.

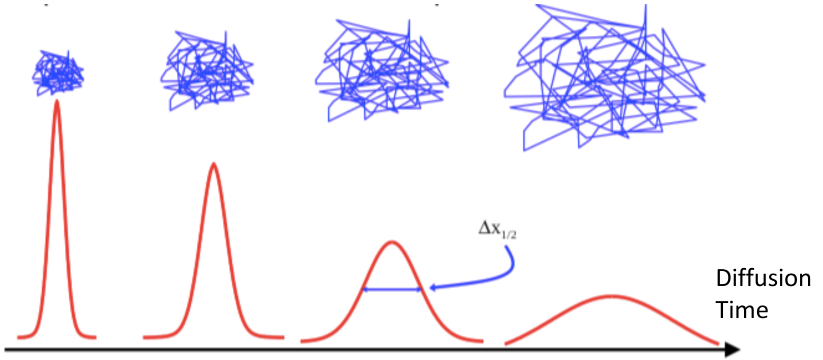
BrainSuite

TractoFlow

Diffusion to probe microstructure



Process of free diffusion



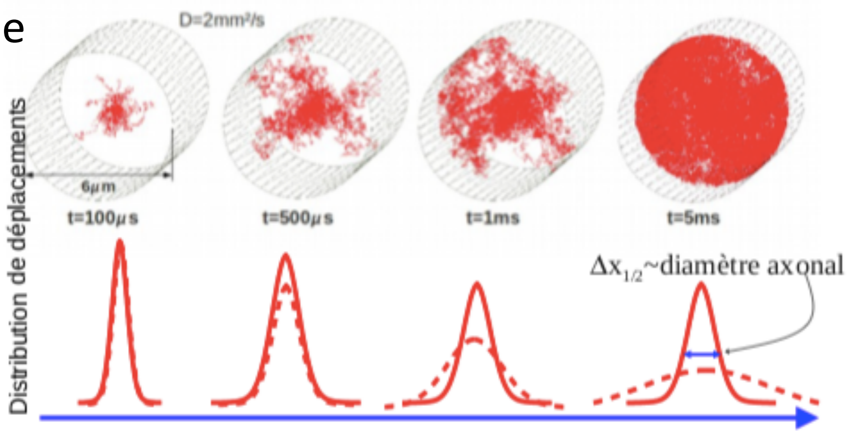
Distribution of displacements as function of diffusion time

Angular distribution of displacements = tissue **orientation**

Amplitude of displacements = **size** of cells !

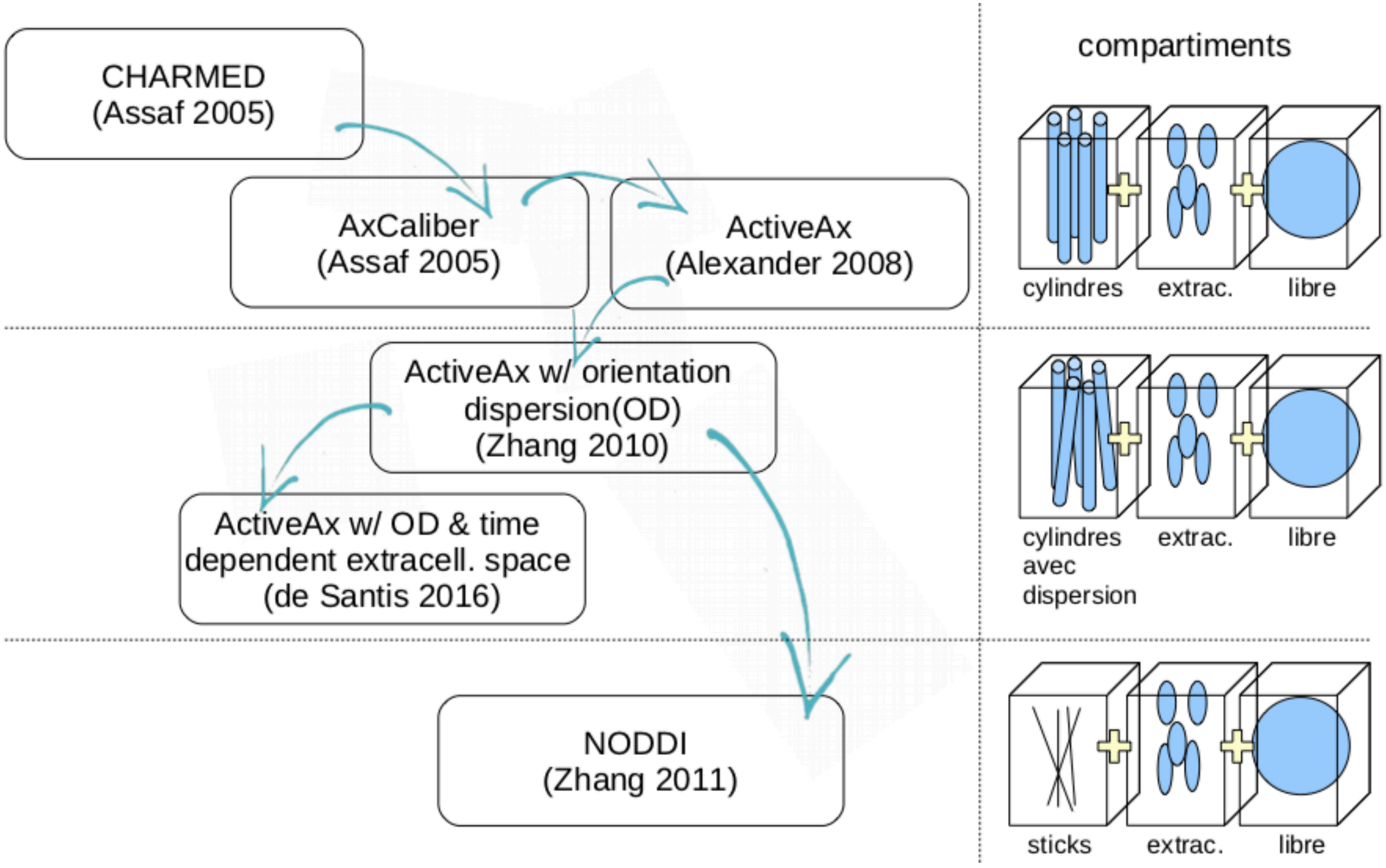
Fingerprint of cells through diffusion signal

=> Diffusion MRI can become a **microscope**!



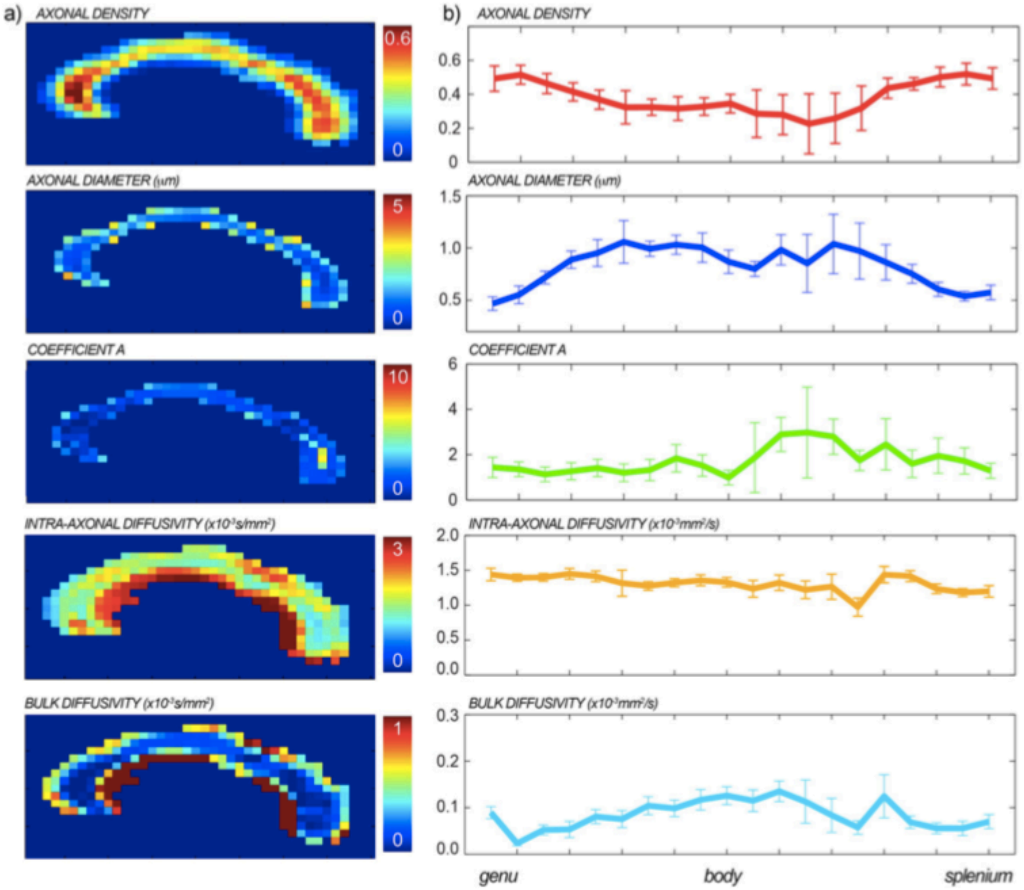
Adapted from C. Poupon, Diffusion formation in Marseille (2016)

Multi - compartment models of white matter



Adapted from C. Poupon, Diffusion formation in Marseille (2016)

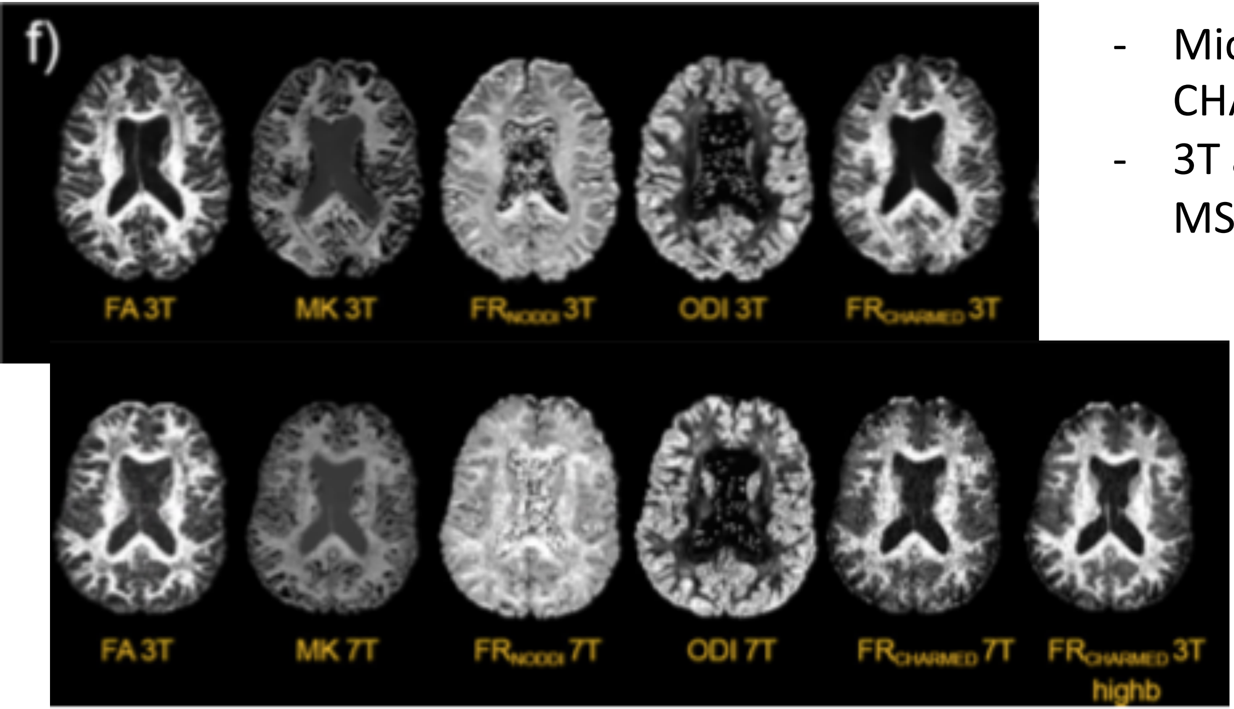
Microstructure cartography of the corpus callosum



In vivo cartography of the microstructure of corpus callosum

7T
2mm isotropic
25 min acquisition time

De Santis et al. *NeuroImage* (2016)



- Microstructure maps from DKI, CHARMED, and NODDI models
- 3T and 7T acquisition on healthy and MS patients

=> Microstructure maps proves to be valuable biomarker of NAWM and NAGM MS lesions at 3T and 7T.

De Santis et al. *Neuroscience* (2018)

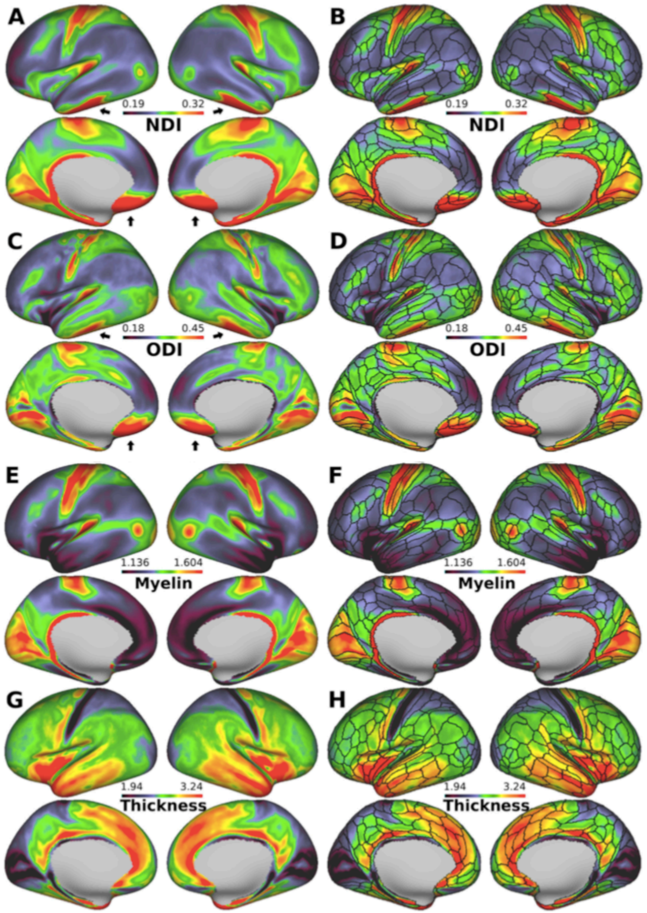
int institut de neurosciences de la timone

Neurite measurement on cortex

Neurite: any projection from neuron body: dendrite and axon

HCP 3T data, 1.25mm resolution
NODDI model
ODI: Orientation Dispertion Index
NDI: Neurite Density Index

NODDI provides valuable Information about microarchitecture of myelinated neurites in the cortex

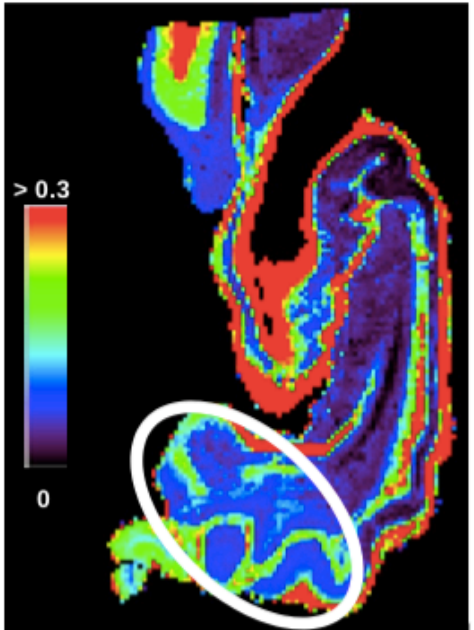


Group Neurite maps

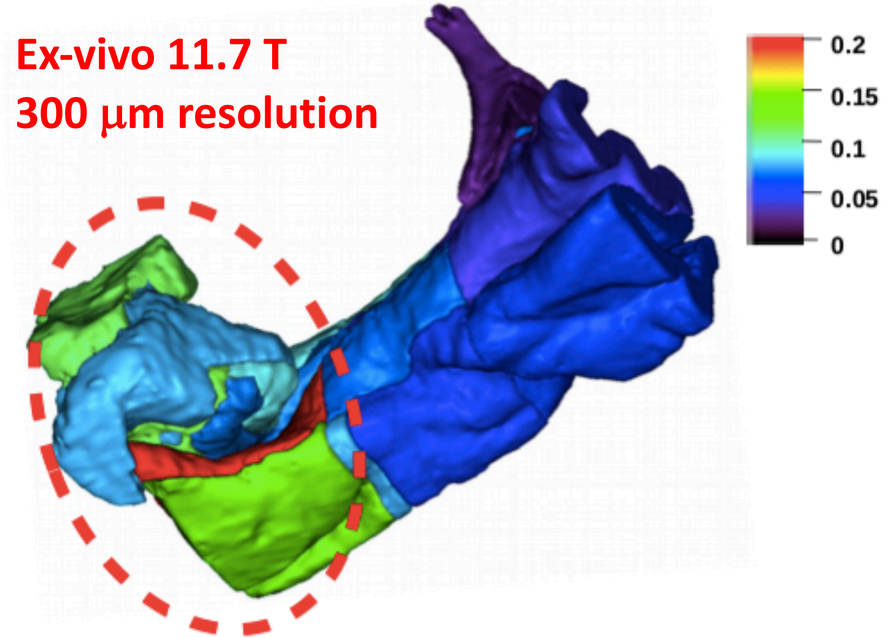
Group Myelin maps

Fukutomi et al. (2018)

Increased neurite density in hippocampus head



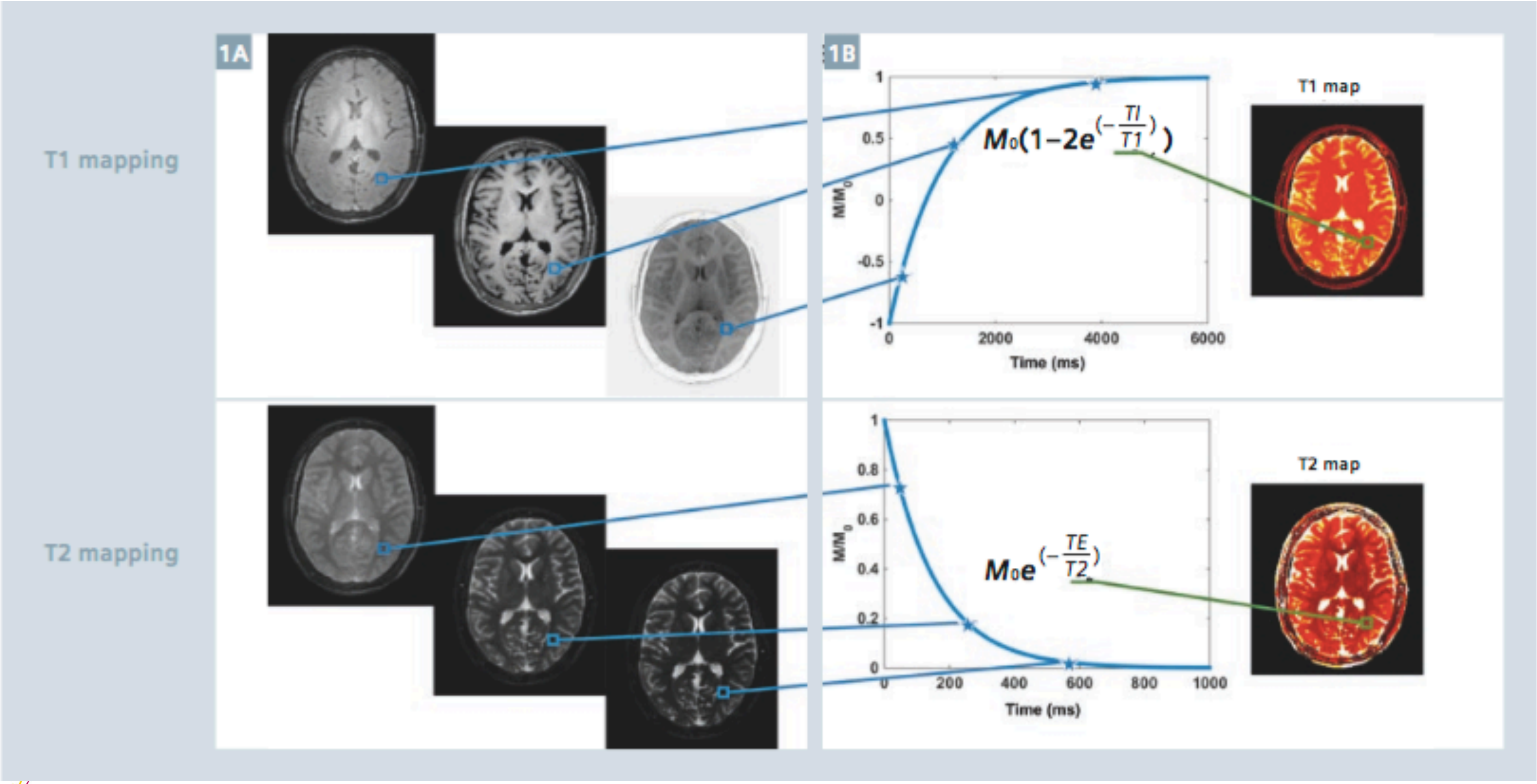
A. Hippocampal intracellular volume fraction obtained with NODDI



B. Color-encoded main intracellular volume fraction per grey matter region

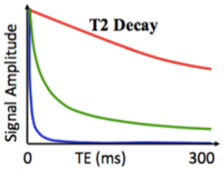
Beaujoin et al, 2016

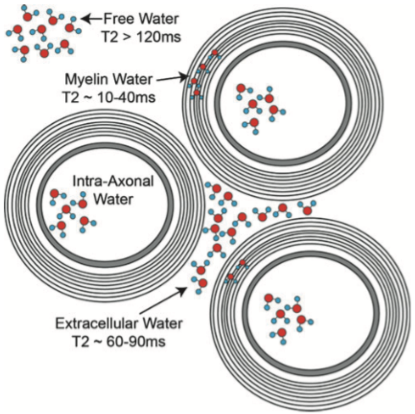
Quantitative measurements

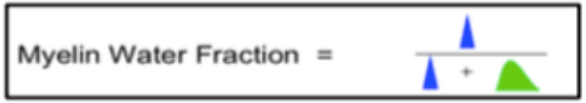


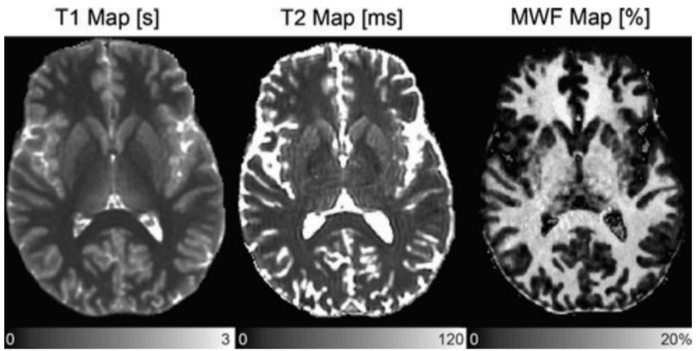
Coppo et al. Magnetom FLASH 2016

- T1 and T2map are quantitative measures but not specific: several compartments per voxel but a single T1 or T2 value
- Multicompartment fit: **M**yelin **W**ater **F**raction (**MWF**) or **M**yelin **V**olume **F**raction (**MVF**)



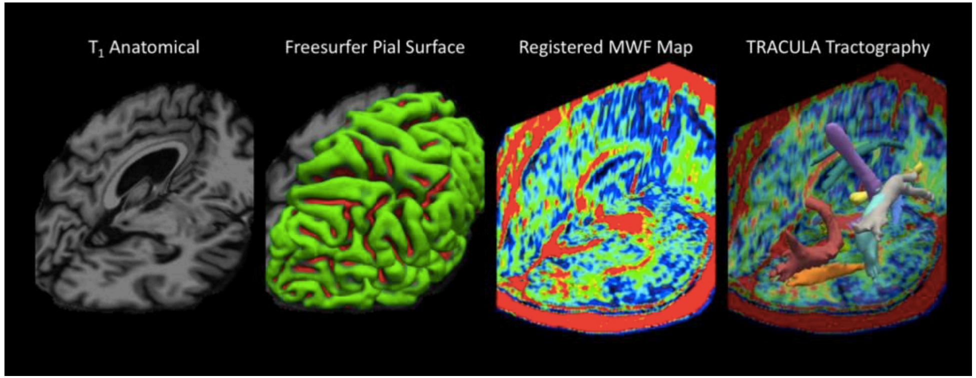






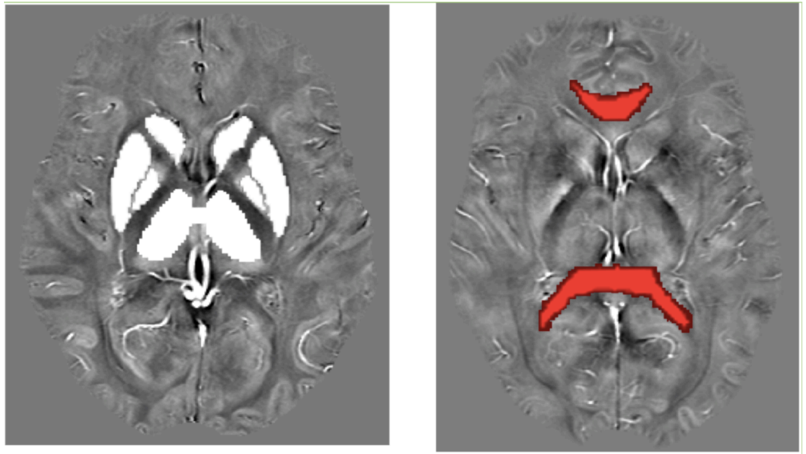
Alexander et al. (2011)

Application to characterize **stroke** lesions: **MWF** more sensitive to myelin integrity than Diffusion

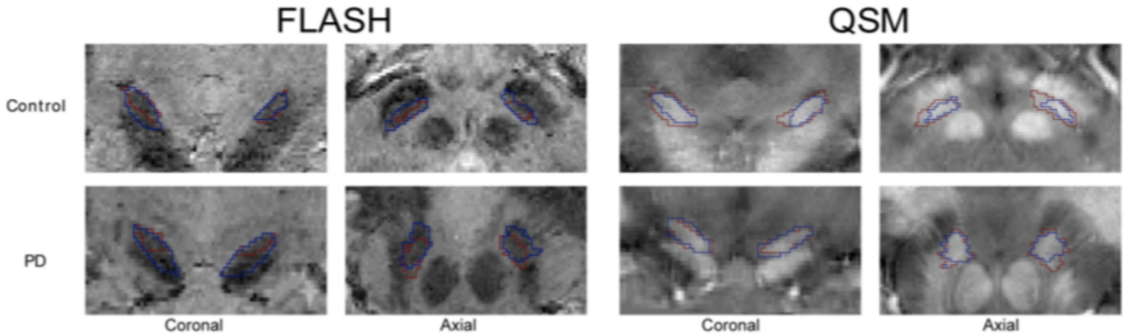


Lakhani et al. OHBM (2017)

QSM for evaluation of consequence of mild traumatic injuries in hockey players
=> Assessment of myelin integrity



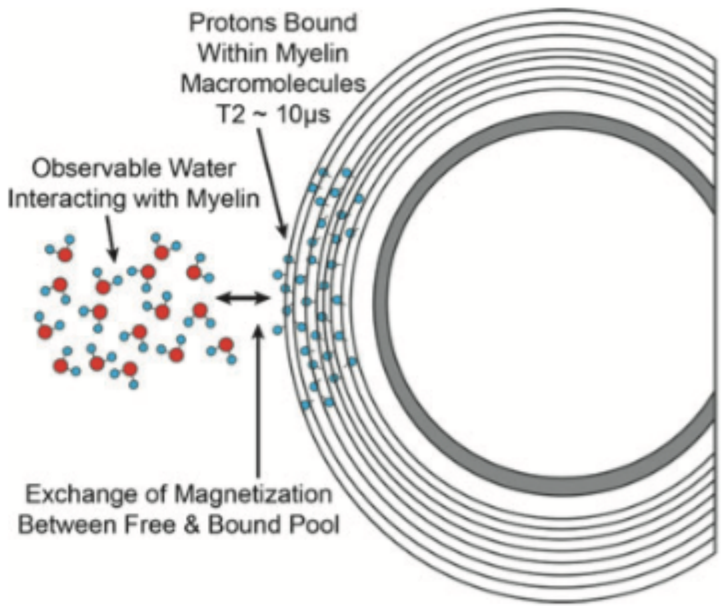
Pukropski et al. OHBM (2017)

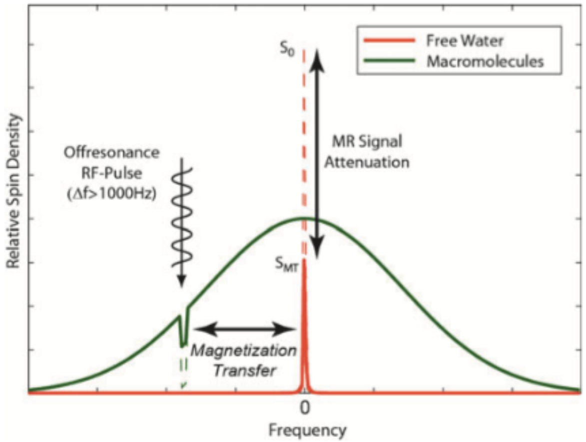


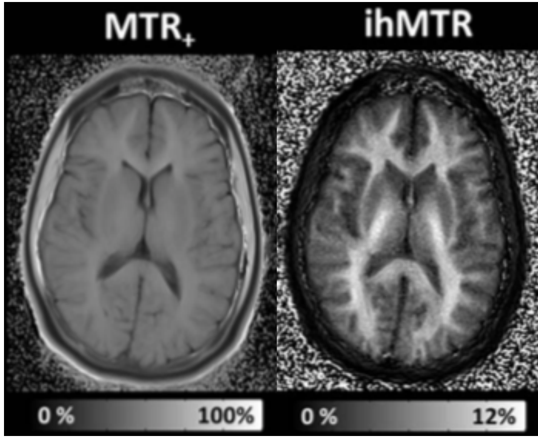
Alkemade et al. PLoS ONE (2017)

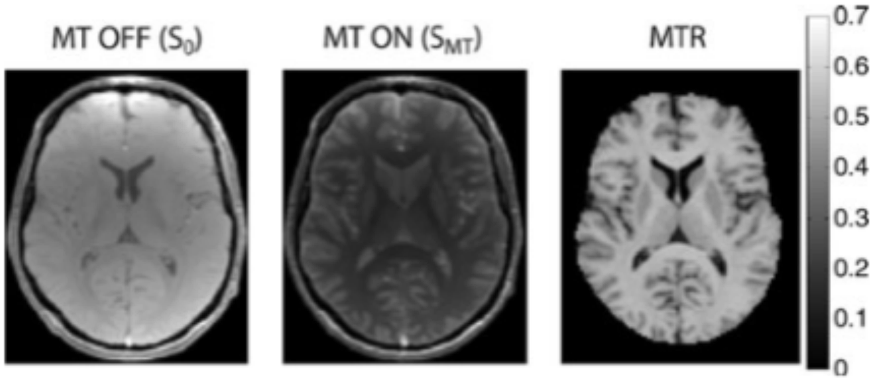
Delineation of STN: comparision between T2*w and QSM
=> Better accuracy with QSM for DBS

Magnetization Transfer (homegeneous or not)



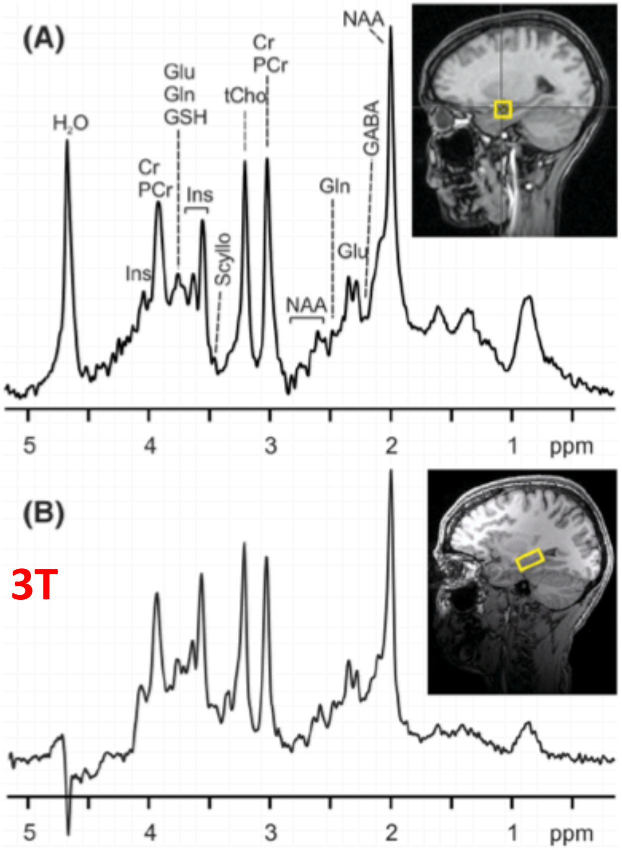




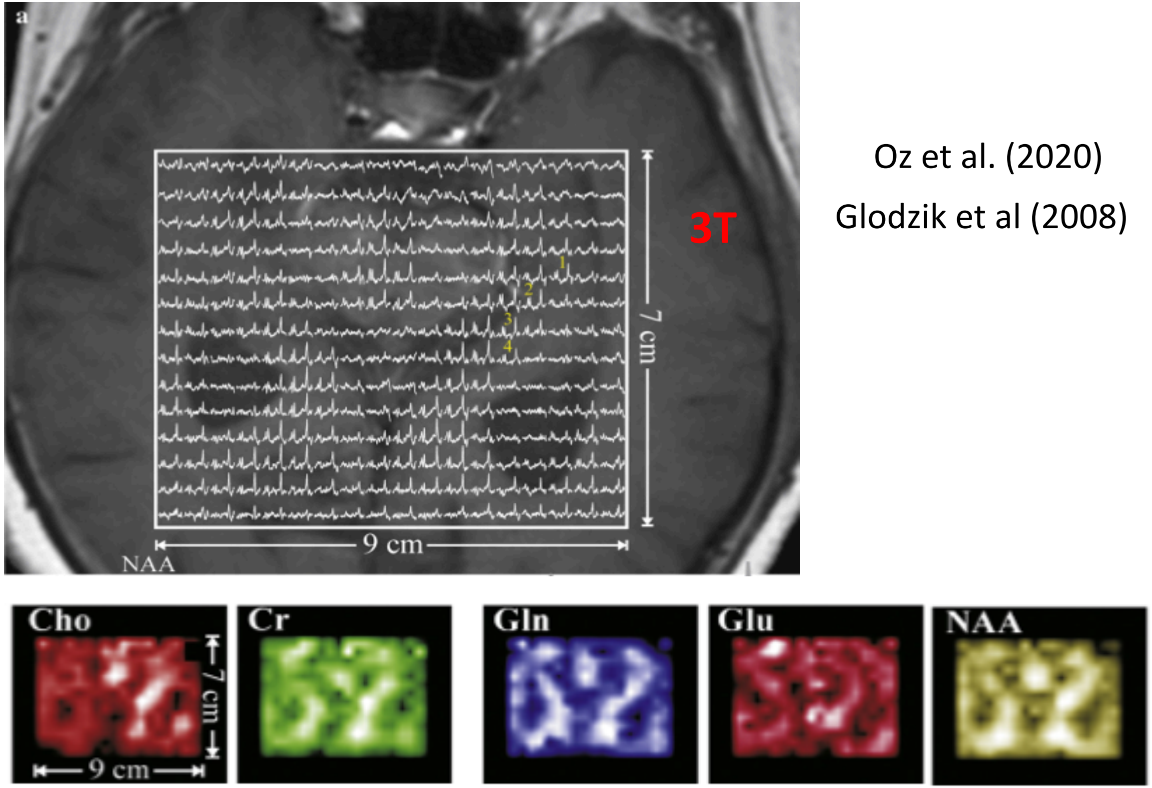


Alexander et al., *Brain Connectivity*, (2011)
Girard et al. *MRM* (2015)
Duhamel et al. *NeuroImage* (2019)

Magnetic Resonance Spectroscopy (MRS)



Single voxel spectroscopy (SVS)



Oz et al. (2020)

Glodzik et al (2008)

Chemical shift Imaging (CSI)

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Thank you for your attention !!!

Questions ???