

BCC

Brain Connectivity Center

I.R.C.C.S. C. Mondino – Pavia



UNIVERSITÀ
DI PAVIA

RISONANZA MAGNETICA: DAGLI SPIN ALLE NEUROSCIENZE

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Incontri del martedì, Pavia, 8 marzo 2016

Outline

- Magnetic Resonance history
- From signal to image: the physics of MRI
- What can we measure with MRI?
- Brain metabolites
- Brain microstructural architecture
- Brain functionality
- Neurological applications

MAGNETIC RESONANCE HISTORY

1930 – Isidor Rabi

Resonance method for recording the magnetic properties of atomic nuclei.

Nobel Prize 1944
Physics

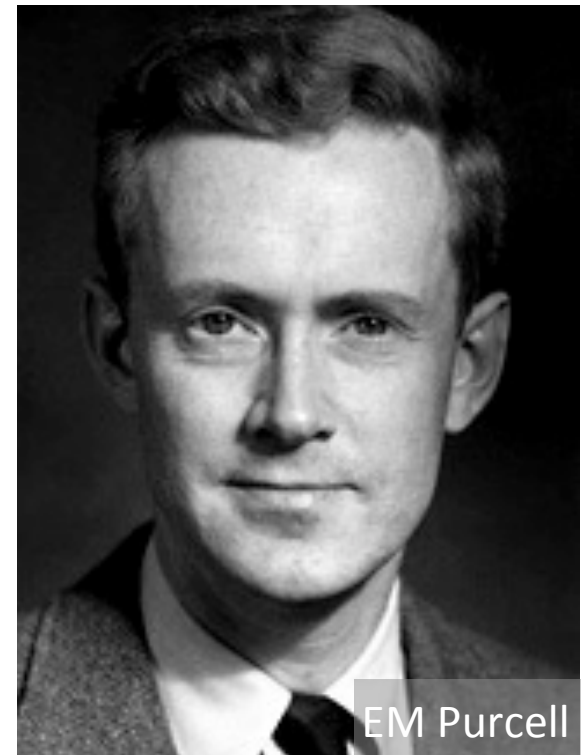


1946 - Felix Bloch and Edward M. Purcell

Certain nuclei in a magnetic field absorbed energy and re-emitted this energy when they returned to their original state.

Nobel Prize 1952

Physics



1974 – Paul Lauterbur and Peter Mansfield

Magnetic field gradients can be used for spatial localization of NMR signals (2D NMR)

back-projection approach & slice selection

Nobel Prize 2003

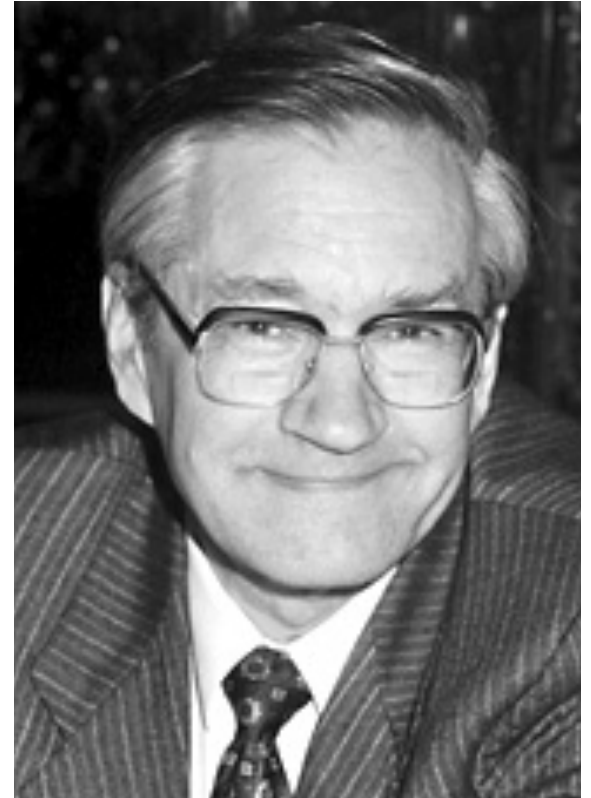
Medicine



1975 – Richard Ernst

Two-dimensional Fourier Transform (2D-FT) to reconstruct 2D images, i.e. 2D spatial encoding.

Nobel Prize 1991
Chemistry

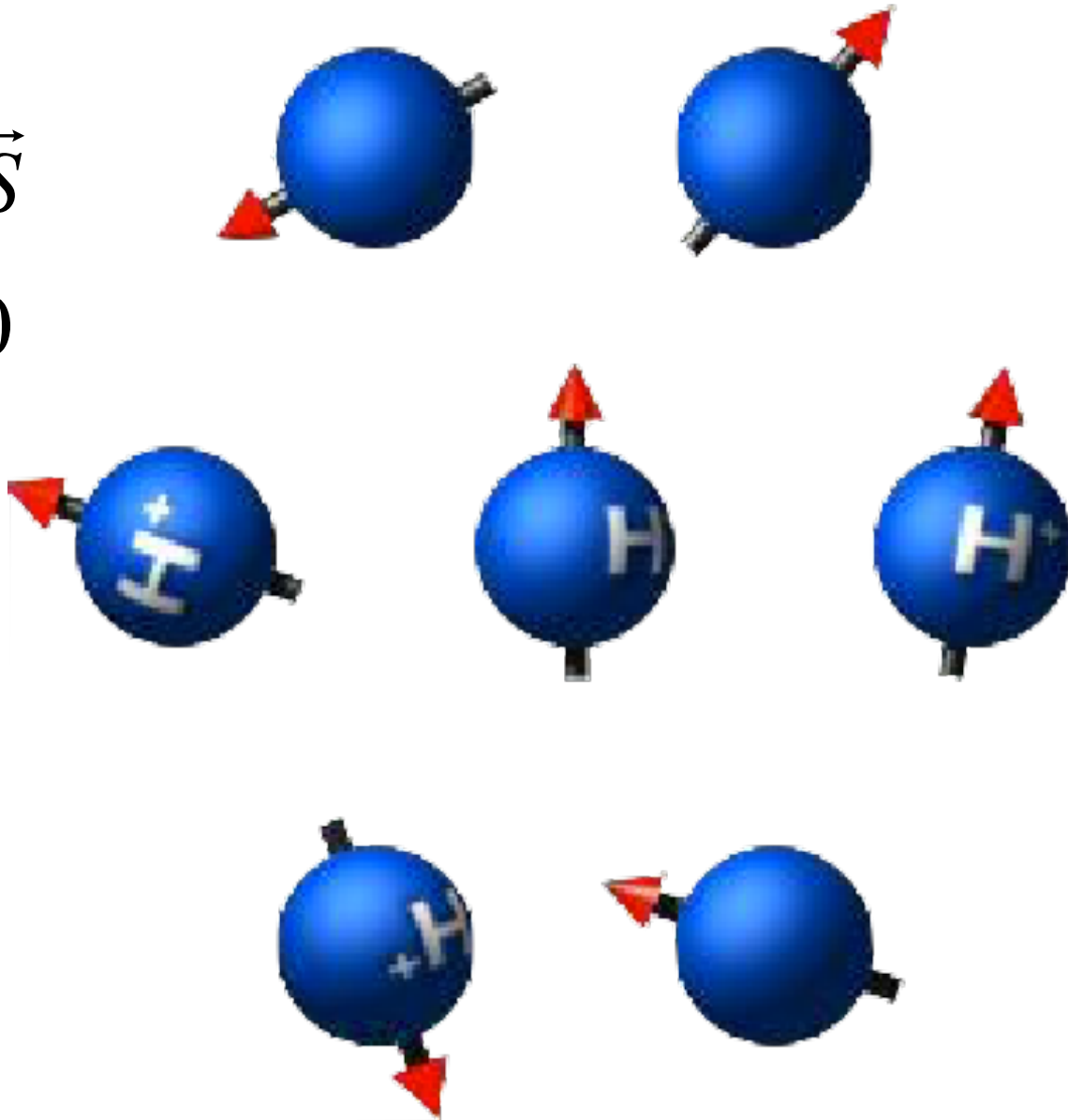


FROM SIGNAL TO IMAGE: THE PHYSICS OF MRI

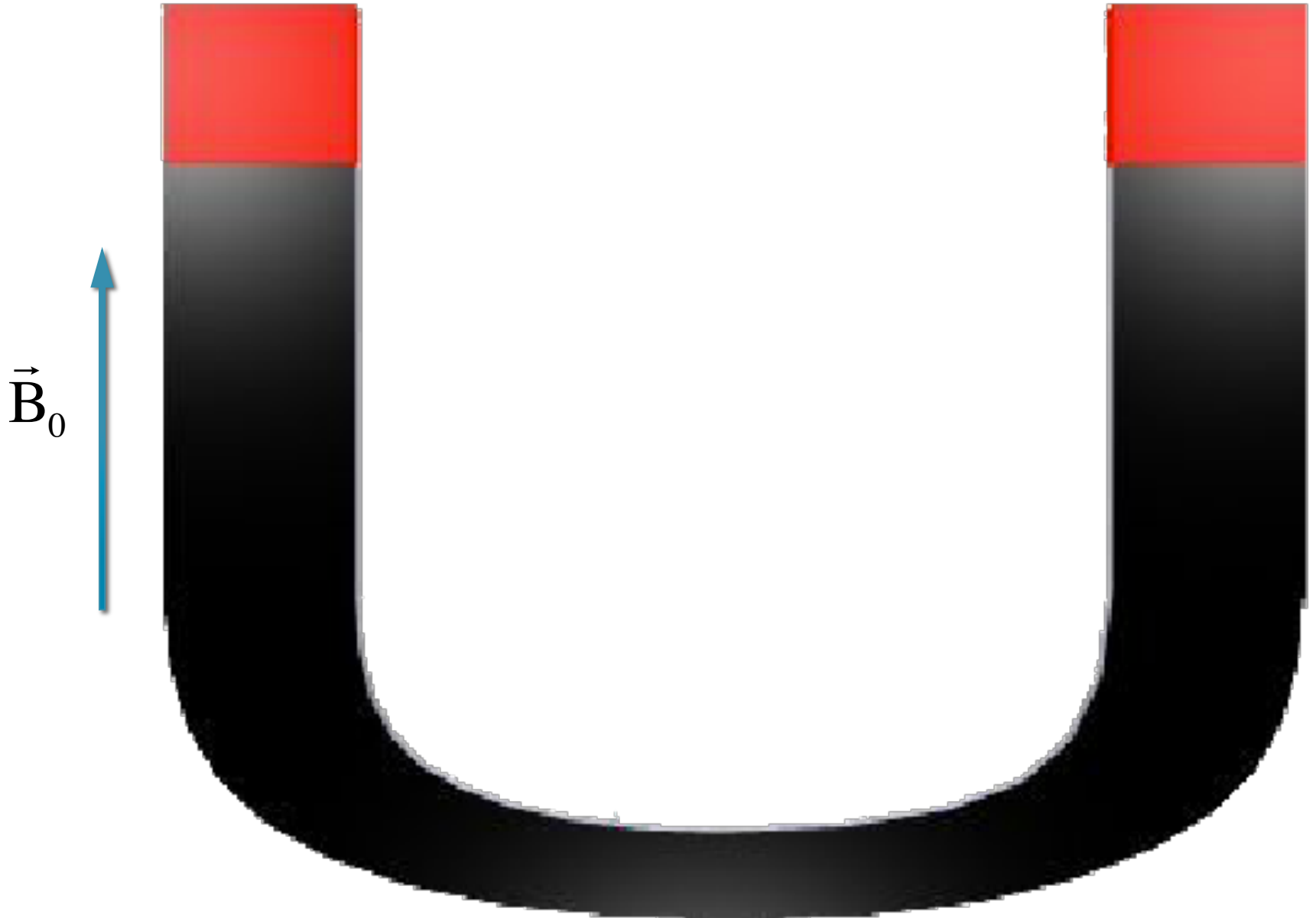
Basic Principles – Nuclear spins

$$\vec{\mu} = \gamma \vec{S}$$

$$\vec{M} = 0$$



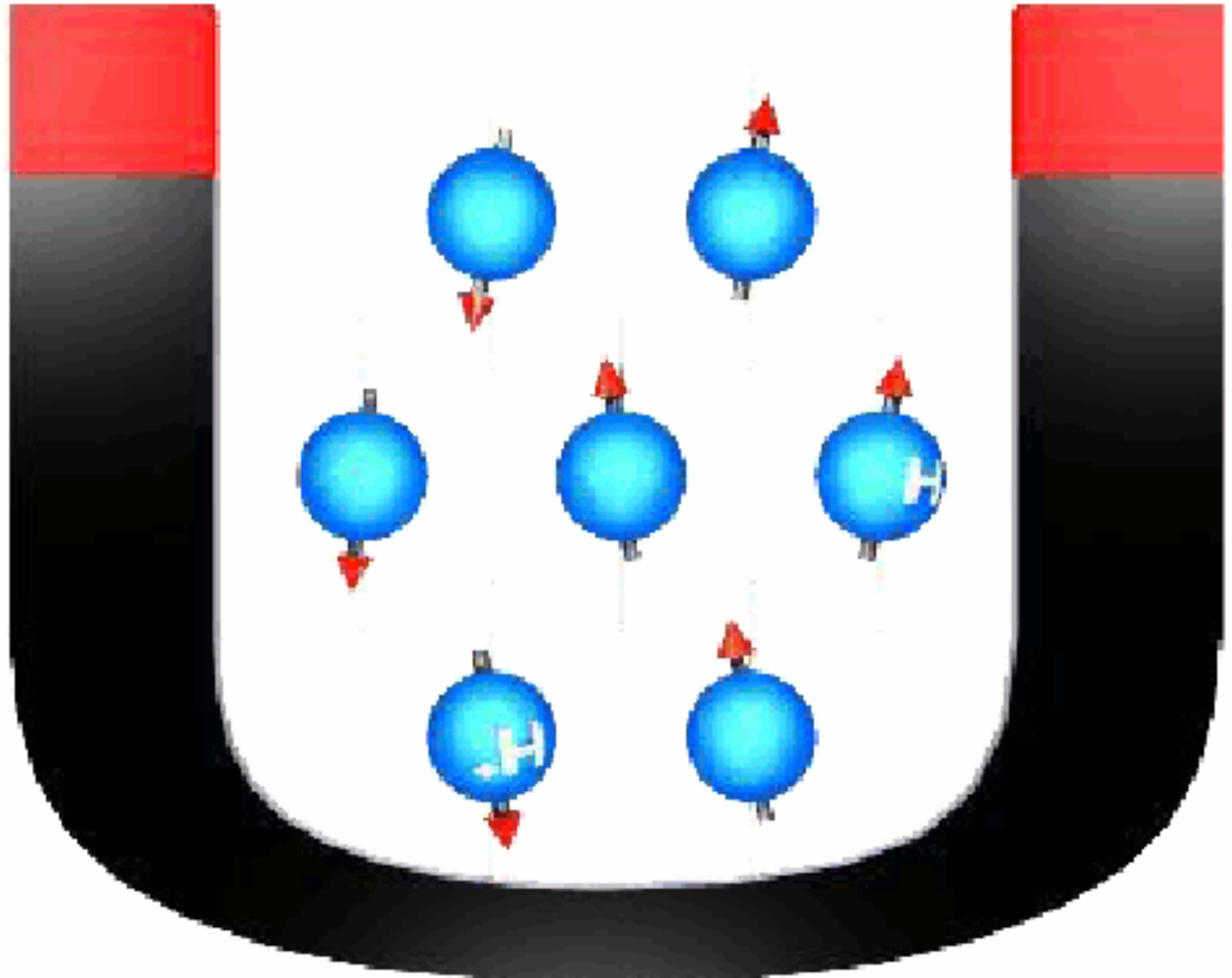
Basic Principles – Static magnetic field



Basic Principles – Nuclear magnetization

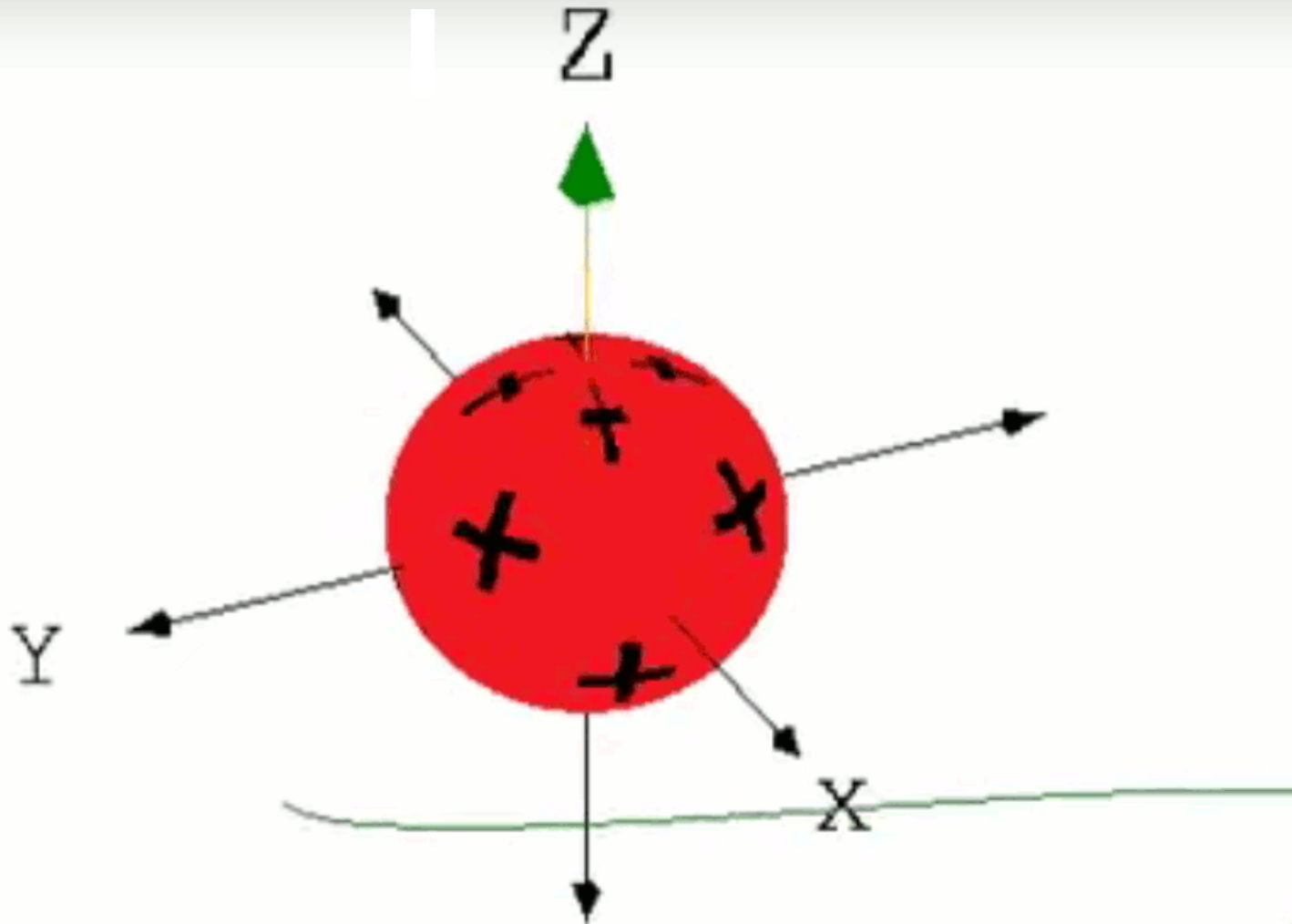
$$\vec{\omega}_L = \gamma \cdot \vec{B}_0$$

$$\vec{M} = \sum \vec{\mu}_i$$



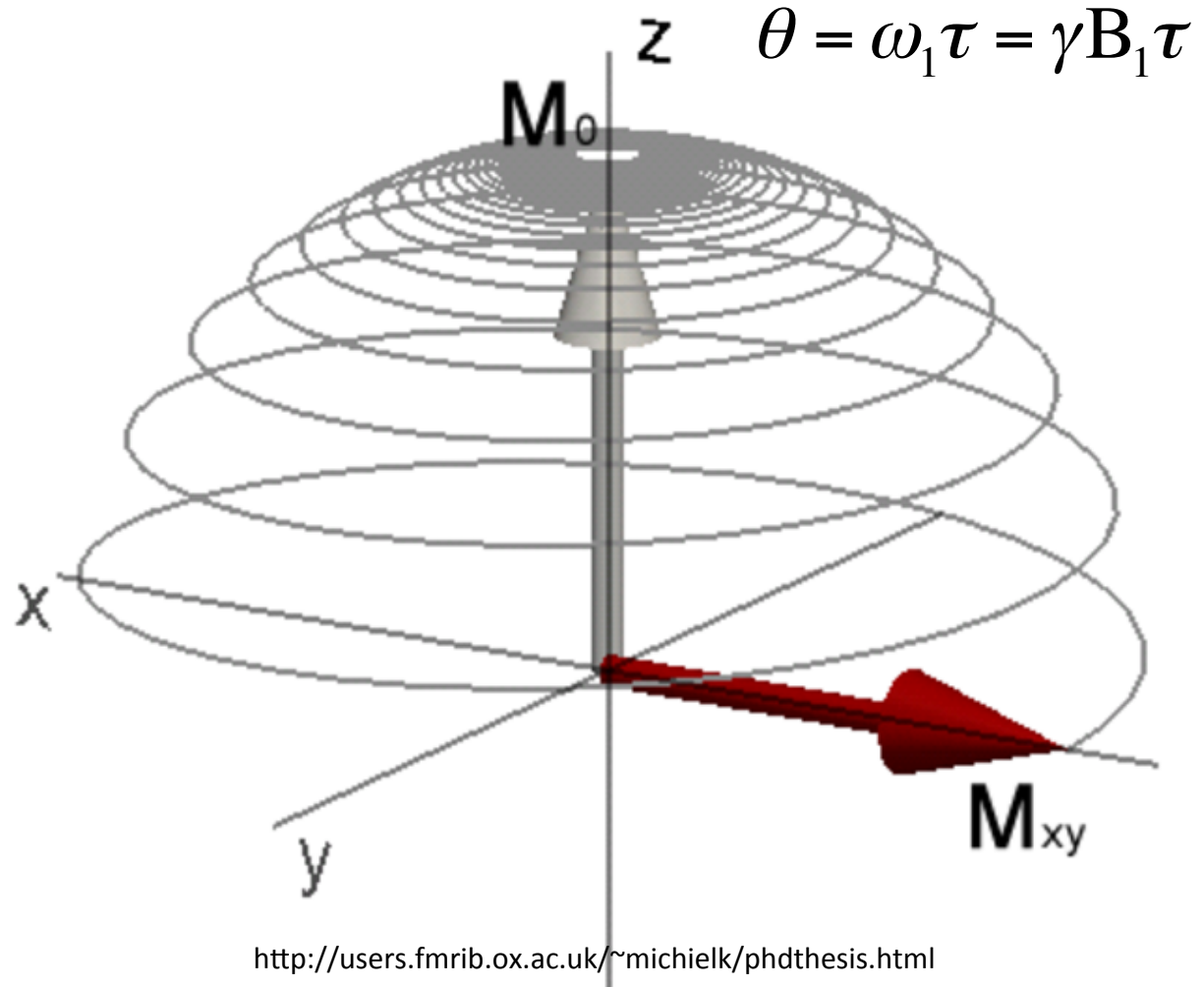
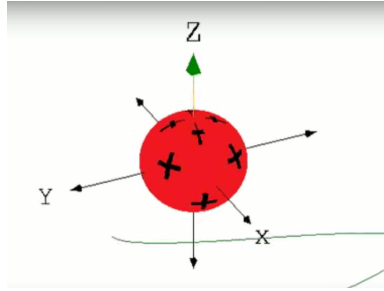
Basic Principles – RF magnetic field

\vec{B}_1 oscillating with $\omega = \omega_L$ for τ seconds



Basic Principles – RF magnetic field

\vec{B}_1 oscillating with $\omega = \omega_L$ for τ seconds



Time evolution and Relaxation

Bloch equations

$$\frac{dM_z}{dt} = \gamma (\vec{M} \times \vec{B}_0)_z + \frac{M_0 - M_z}{T_1}$$

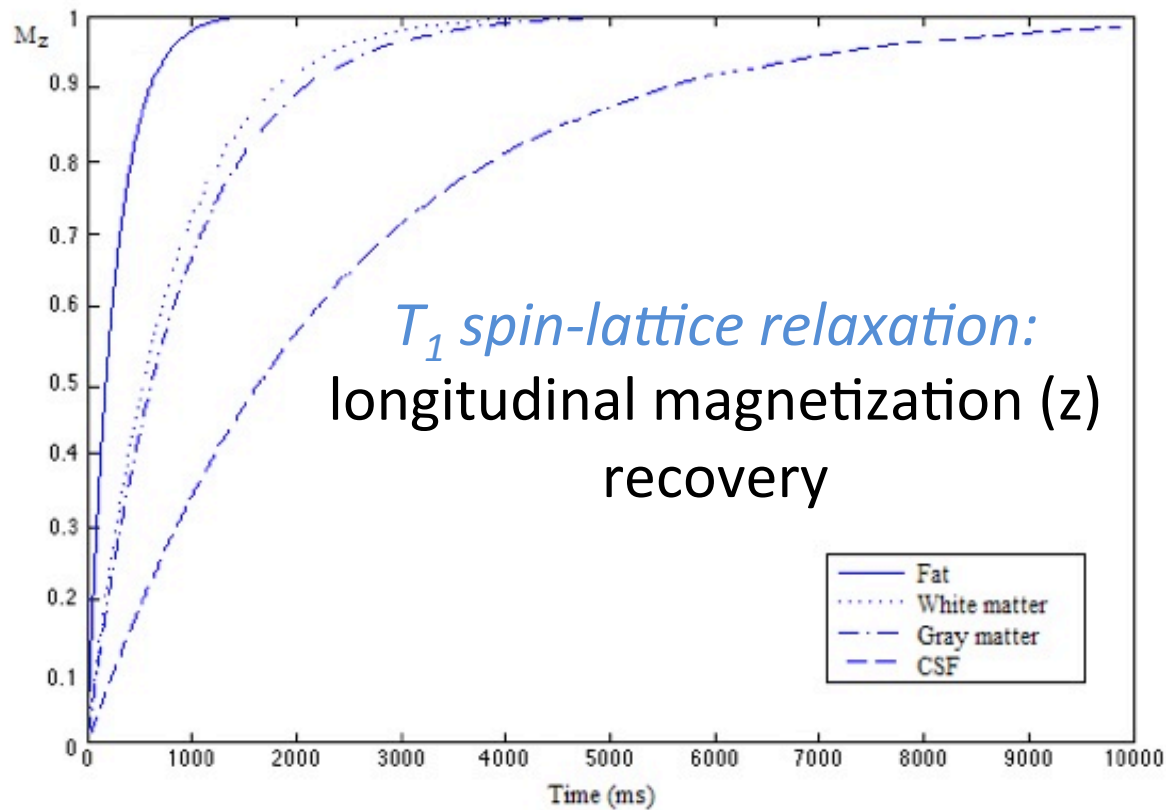
$$\frac{dM_{xy}}{dt} = \gamma (\vec{M} \times \vec{B}_0)_{xy} + \frac{M_{xy}}{T_2}$$

Time evolution and Relaxation

Bloch equations

$$\frac{dM_z}{dt} = \gamma(\vec{M} \times \vec{B}_0)_z + \frac{M_0 - M_z}{T_1}$$

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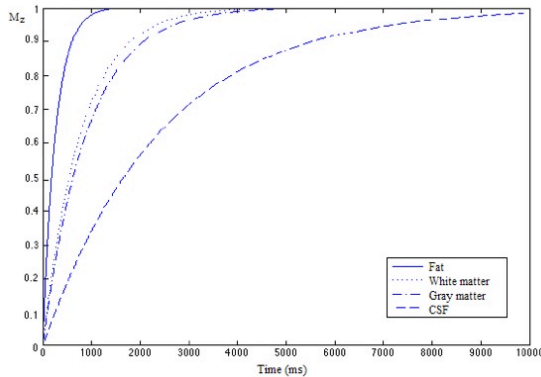


Time evolution and Relaxation

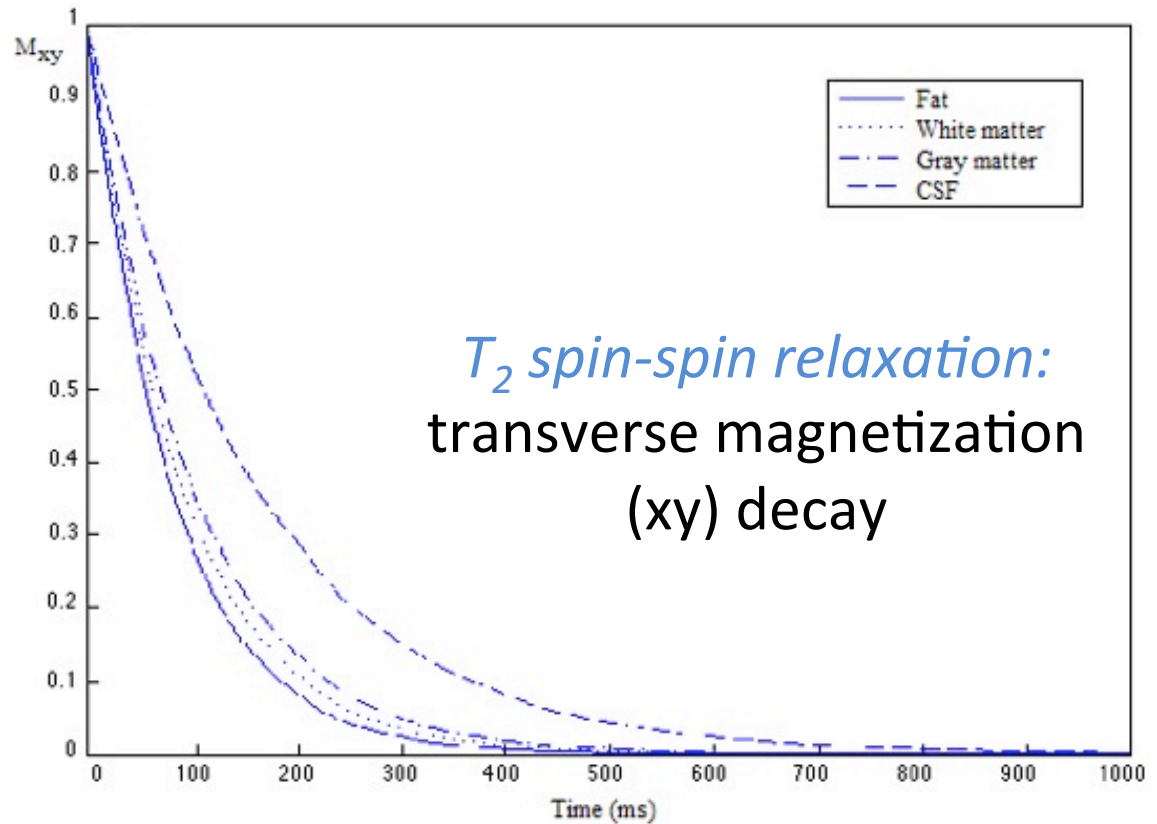
Bloch equations

$$\frac{dM_z}{dt} = \gamma(\vec{M} \times \vec{B}_0)_z + \frac{M_0 - M_z}{T_1}$$

$$\frac{dM_{xy}}{dt} = \gamma(\vec{M} \times \vec{B}_0)_{xy} - \frac{M_{xy}}{T_2}$$



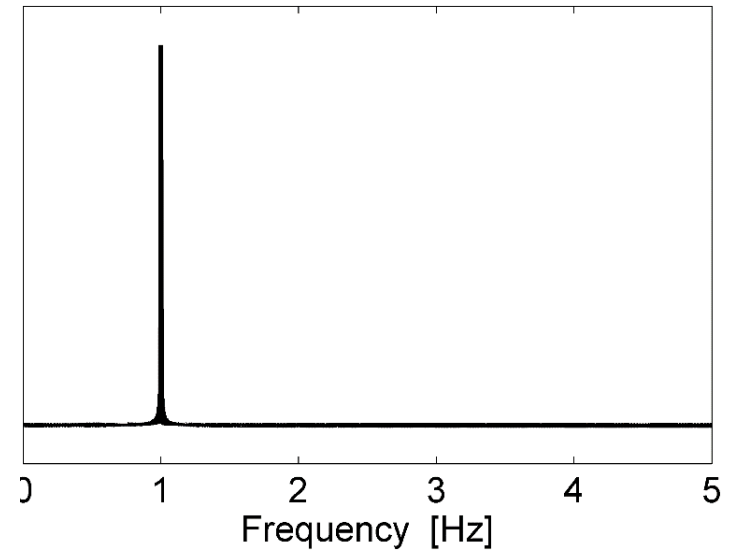
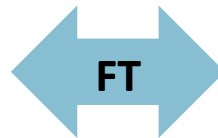
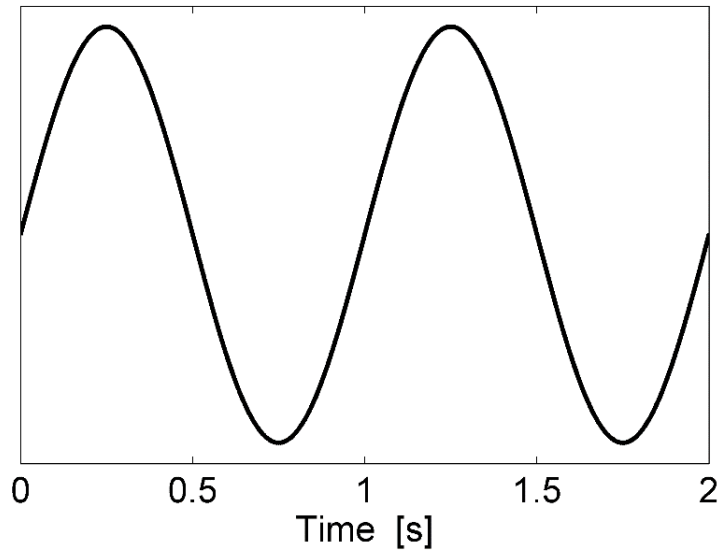
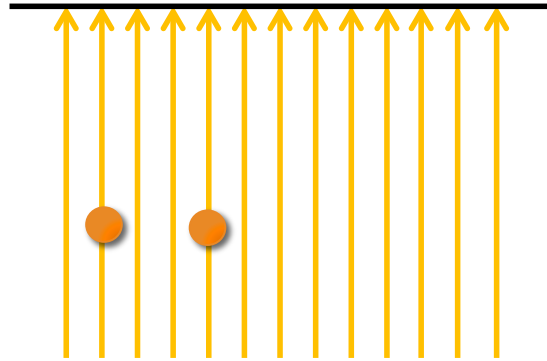
T_1 spin-lattice relaxation:
longitudinal magnetization (z)
recovery



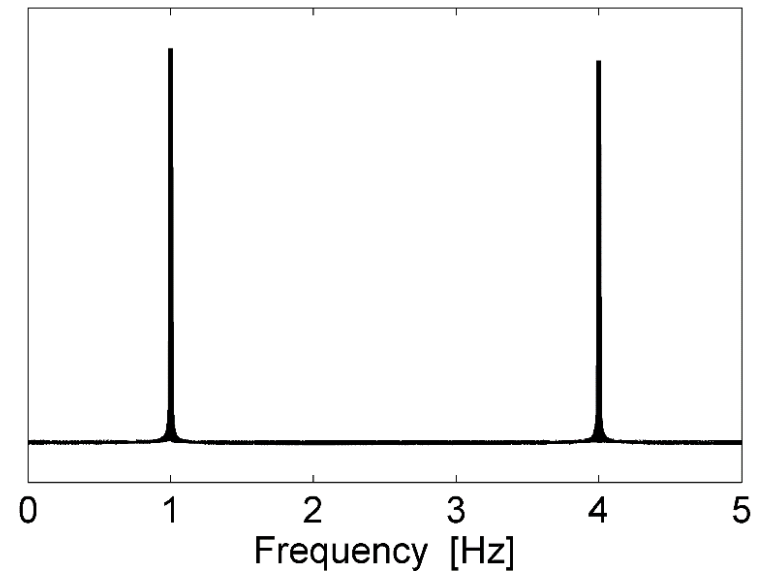
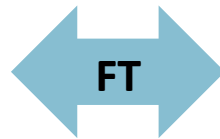
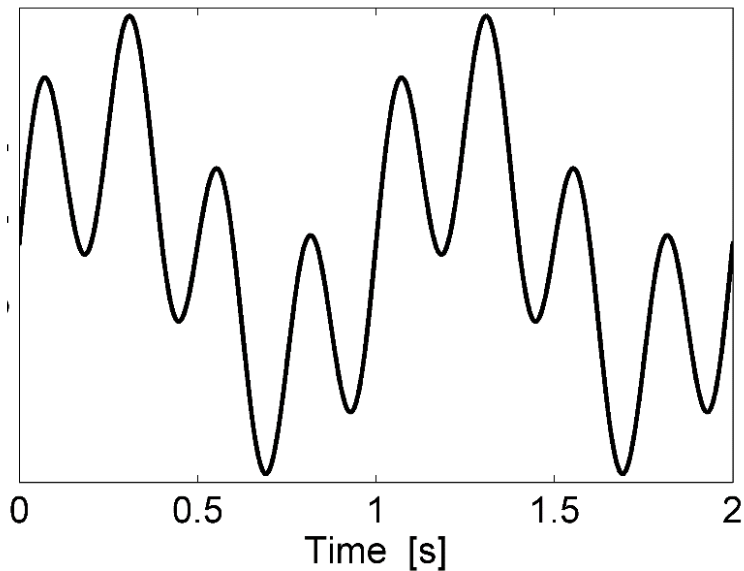
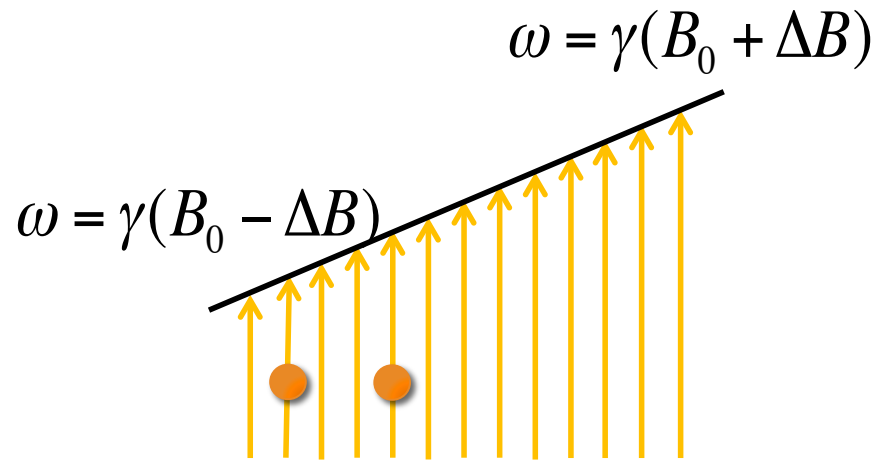
T_2 spin-spin relaxation:
transverse magnetization
(xy) decay

From signal to image

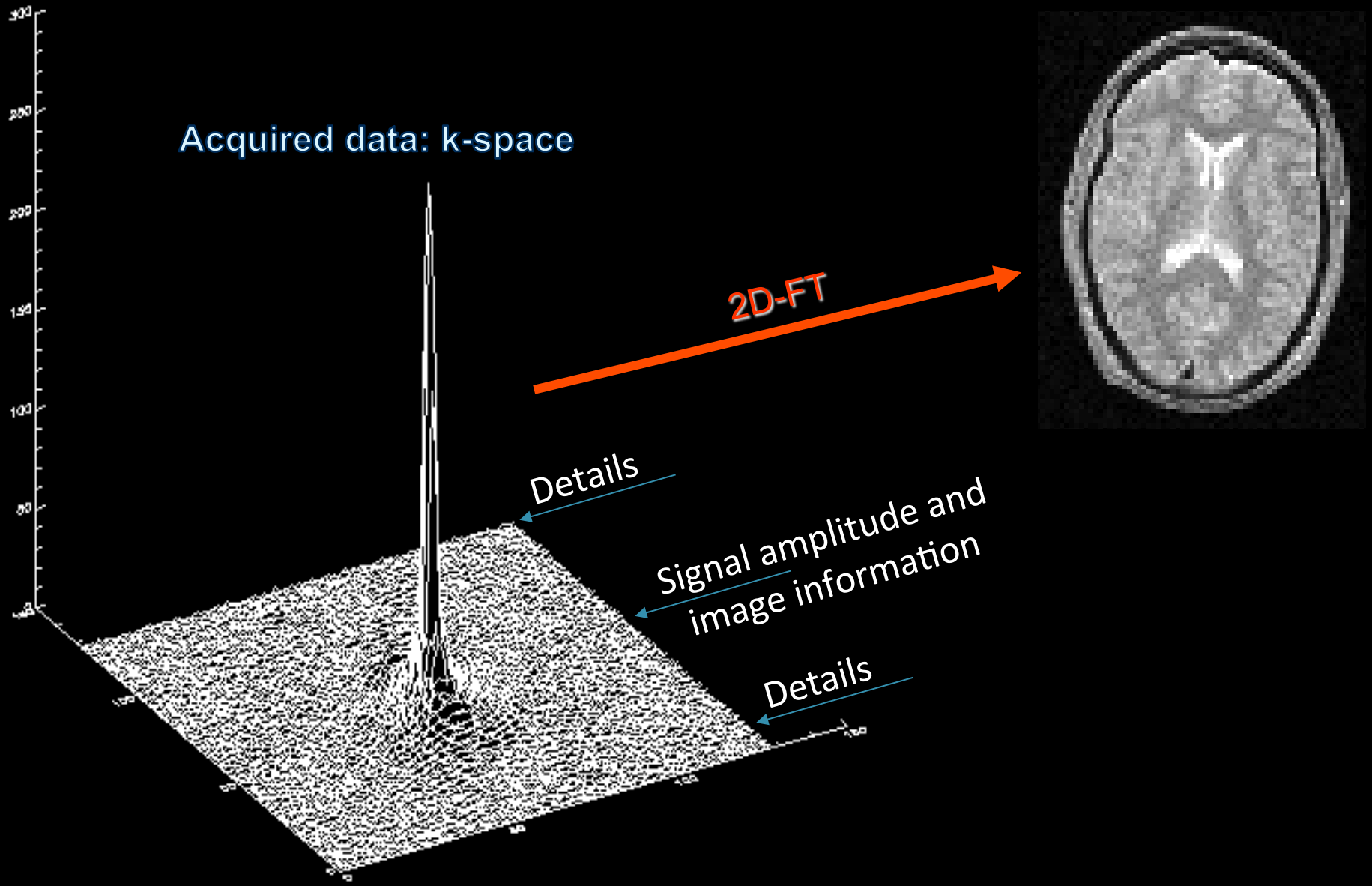
$$\omega = \gamma \cdot B_0$$



From signal to image – Spatial localization



From signal to image



WHAT CAN WE MEASURE WITH MRI?

Why is it widely used in medicine?

What makes MRI so powerful is ...

Really exquisite soft tissue, and anatomic, detail

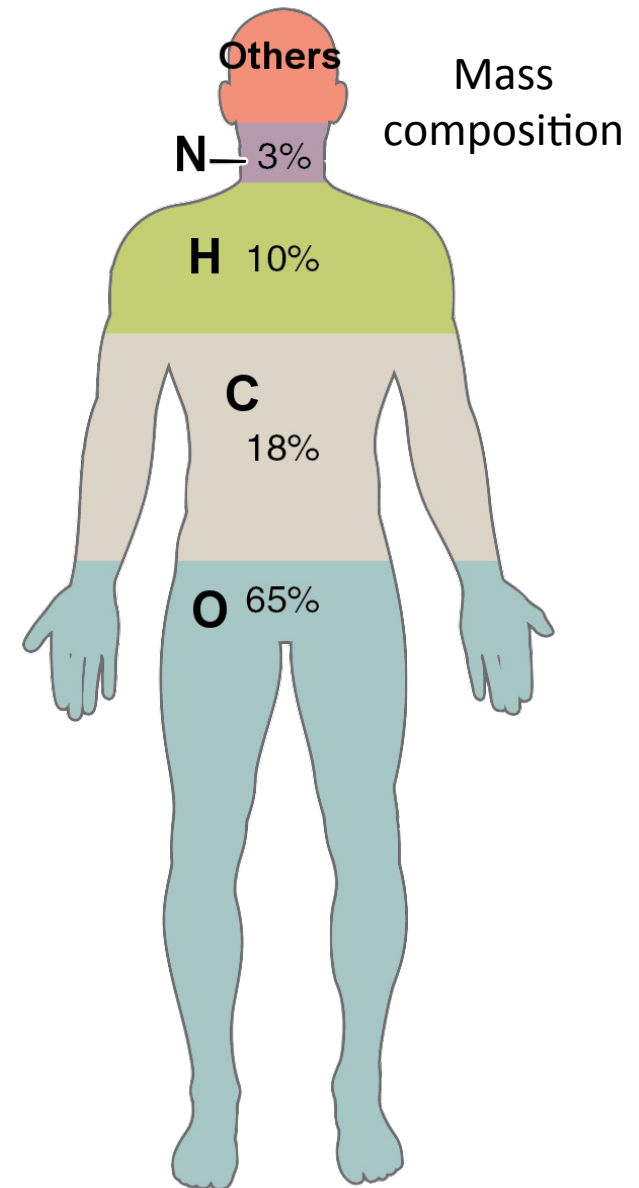
Doesn't use ionizing radiation
(opposite to X-ray, CT)

No adverse effects have been demonstrated

Any kind of magnetic metal implant poses a hazard

Elements abundance *in vivo*

Nucleus	Net Spin	γ (MHz/T)	Natural abundance (%)
^1H	1/2	42.58	99.98
^{31}P	1/2	17.25	100
$^{23-31}\text{Na}$	3/2	11.27	100
^{14}N	1	3.08	99.60
^{13}C	1/2	10.71	1.11
$^{19-23}\text{F}$	1/2	40.08	100



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Hydrogen is used typically in *in vivo* experiments.

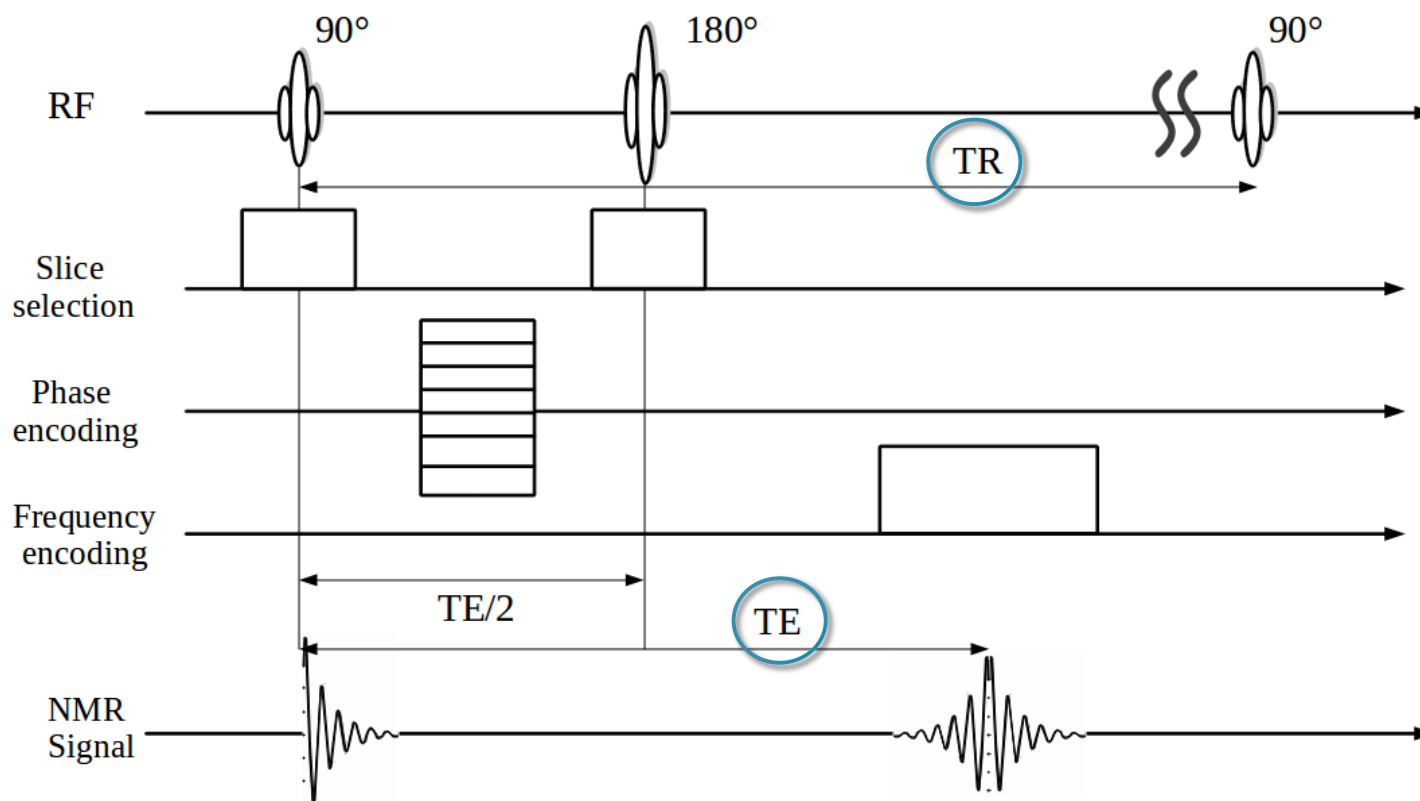


MRI acquisition – Sequences

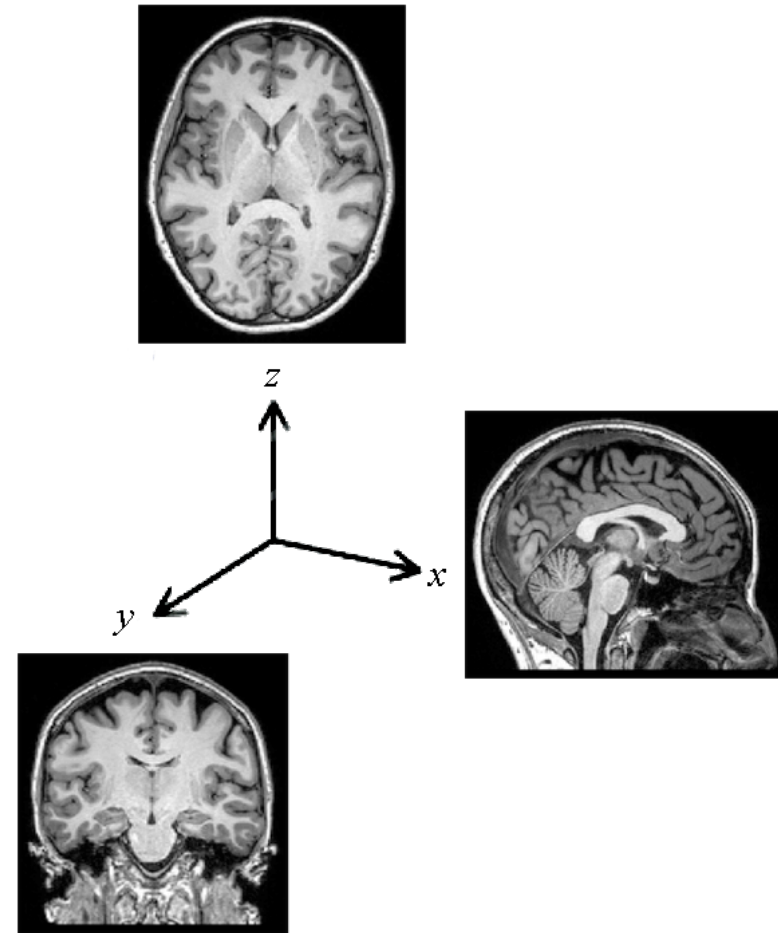
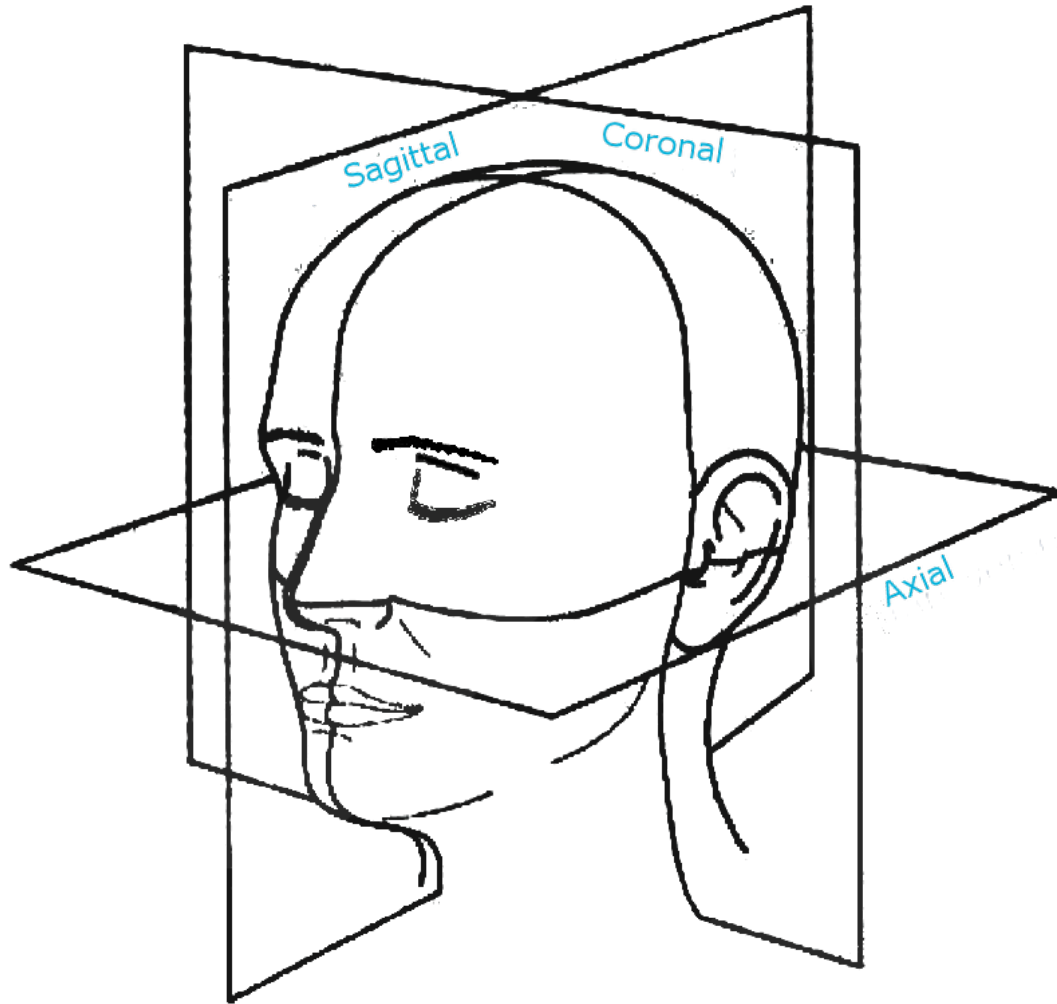
Train of radiofrequency pulses

Fundamental parameters are

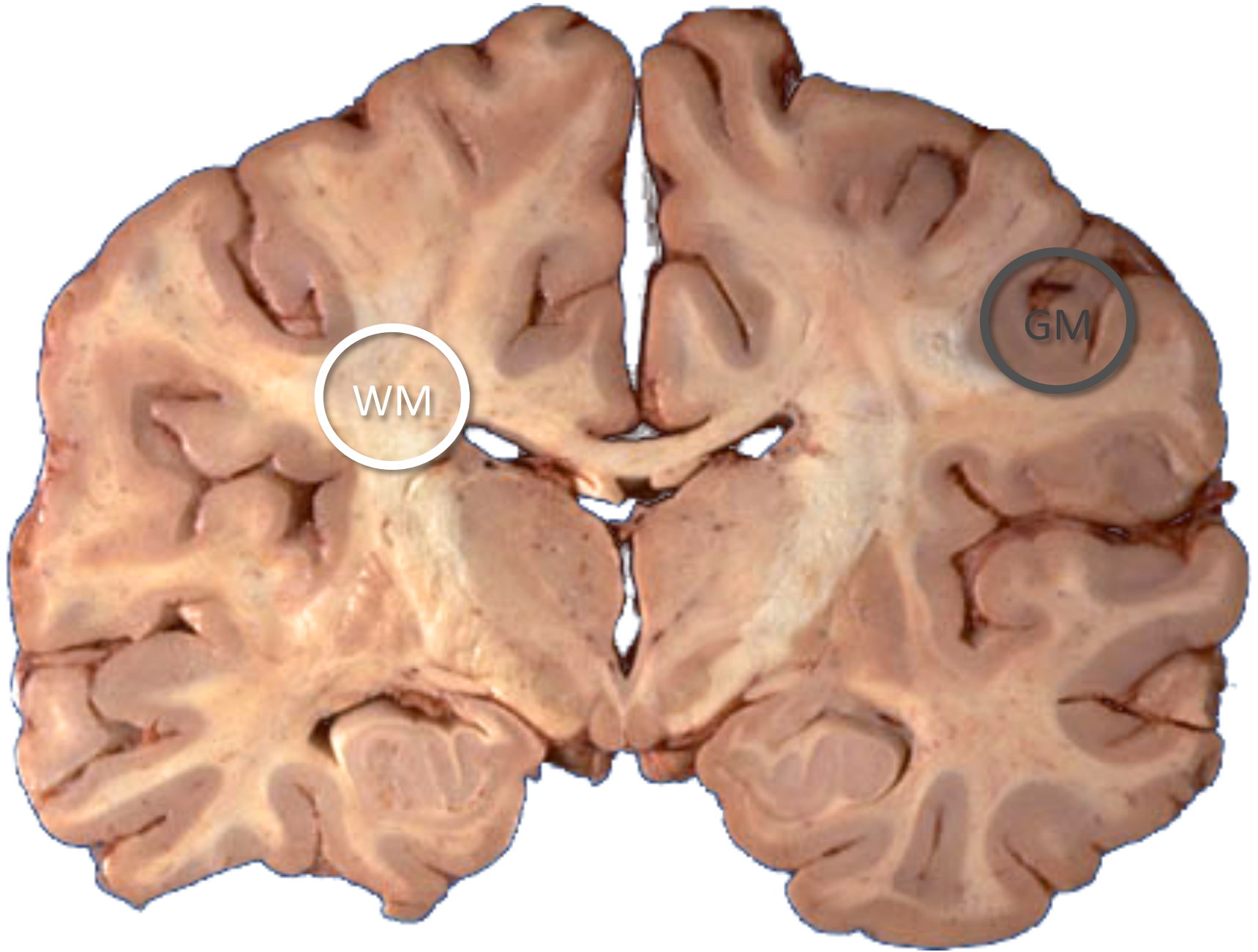
TR = Repetition time & **TE** = Echo time



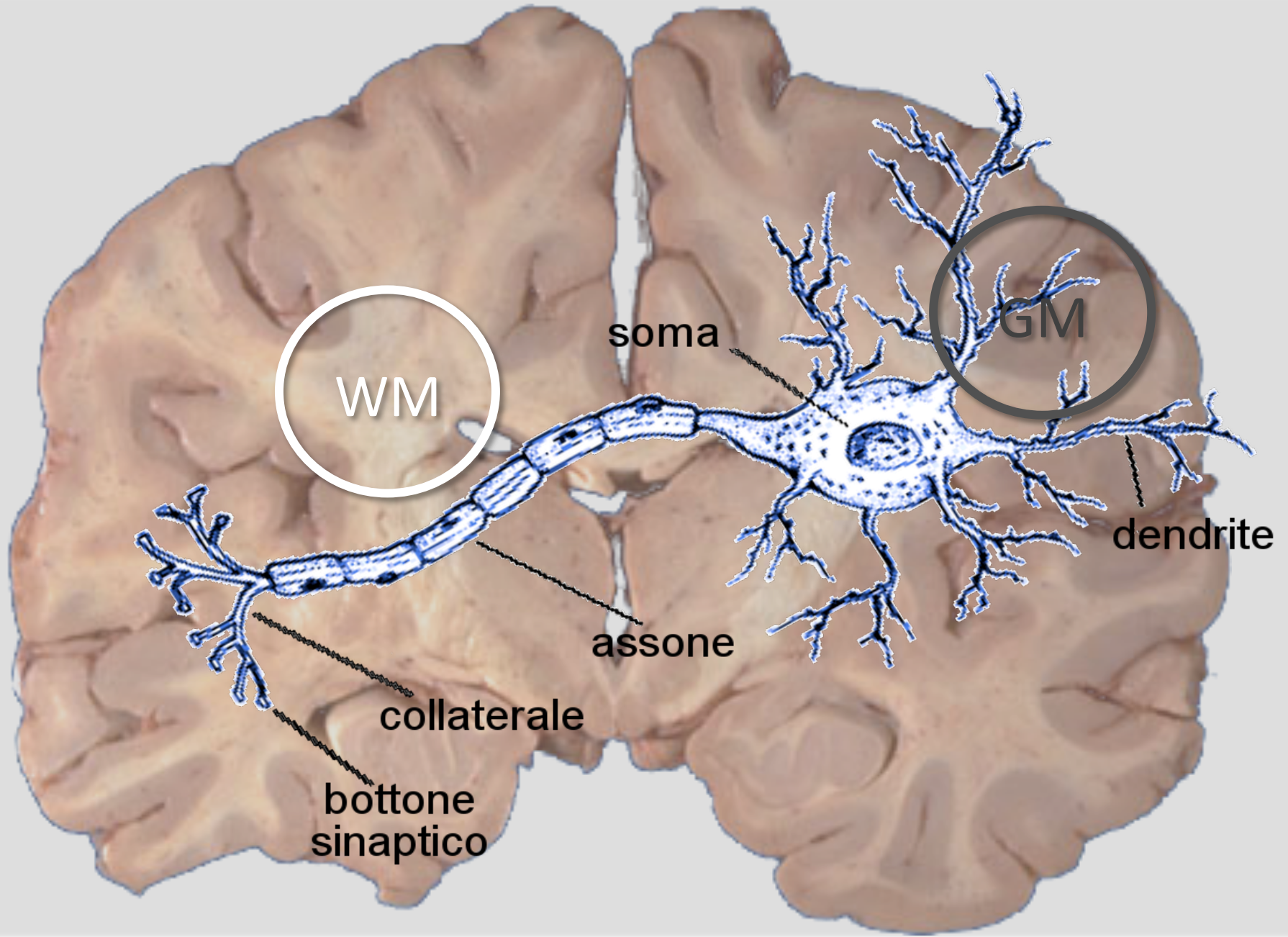
MRI acquisition – Slice orientation



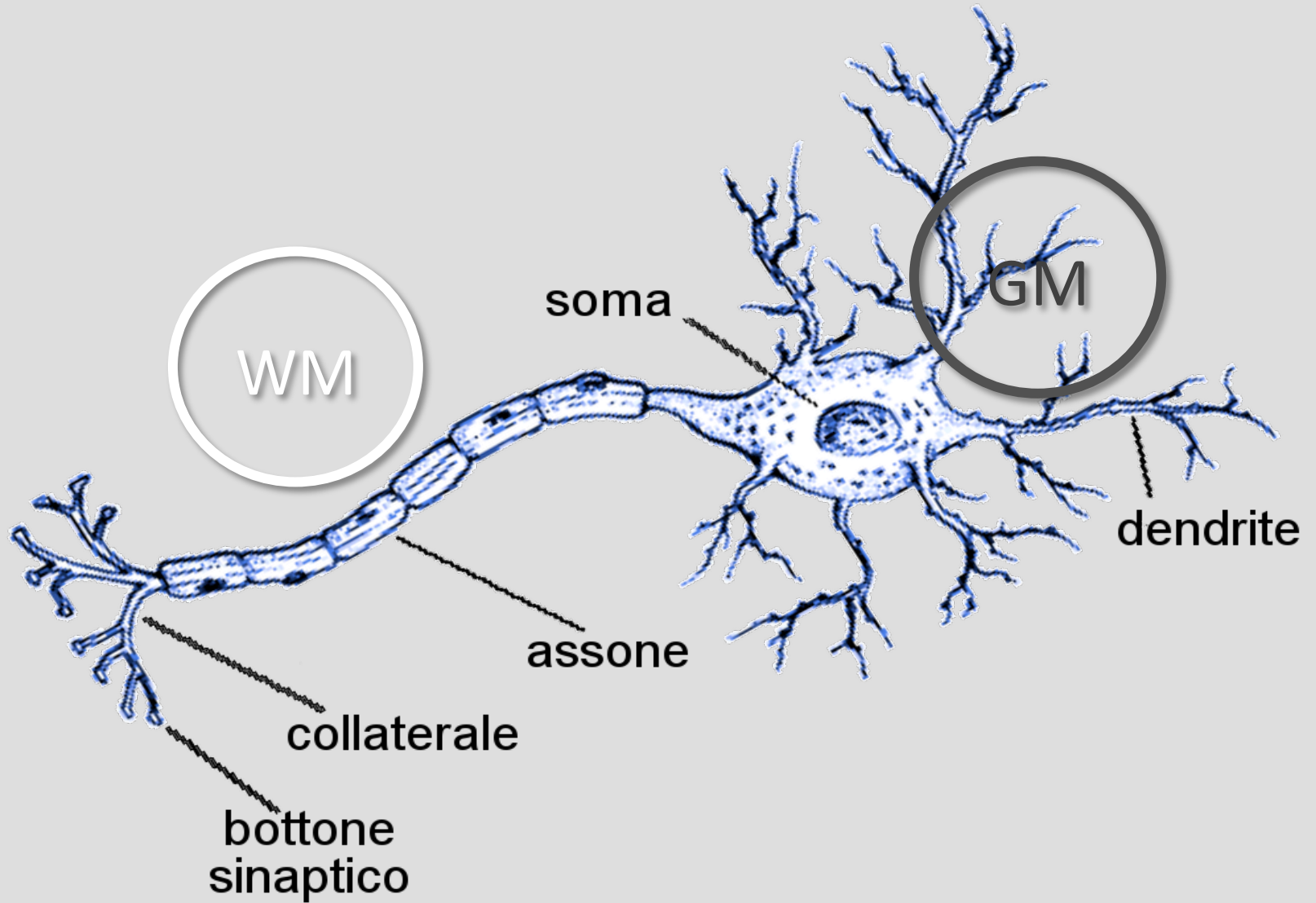
Nervous system



Nervous system



Nervous system



What information can we infer with MRI?

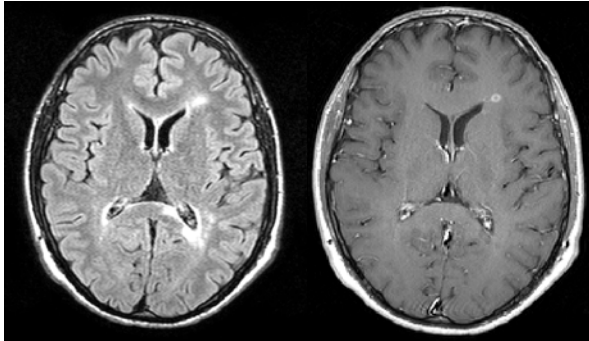


What information can we infer with MRI?

Structural imaging

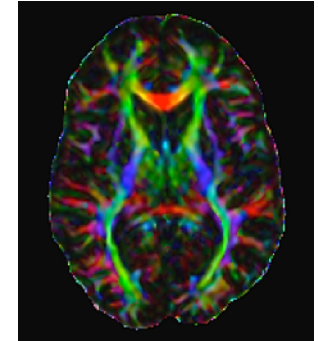
FLAIR

T1 gad

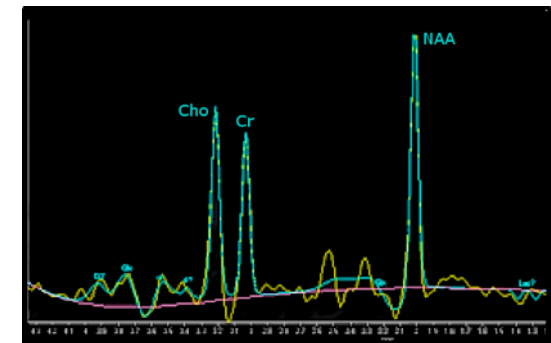


Quantitative imaging

White matter fibres

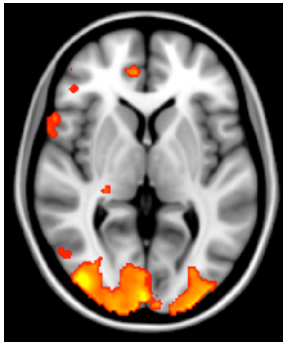


Spectroscopy (MRs)

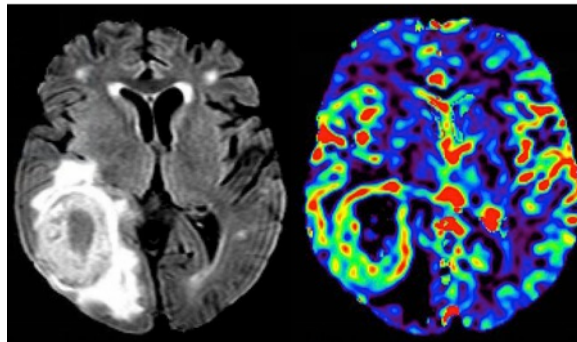


“Physiological” imaging

fMRI



Perfusion (PWI)



MRI acquisition – Image contrast

$$S_0 \propto \rho(H) \cdot e^{-TE/T_2} \left(1 - e^{-TR/T_1} \right)$$

MRI acquisition – Image contrast

$$S_0 \propto \rho(H) \cdot e^{-TE/T_2} \left(1 - e^{-TR/T_1} \right)$$

Inversion Recovery

Short TR and TE: T1-weighted images (T1W)

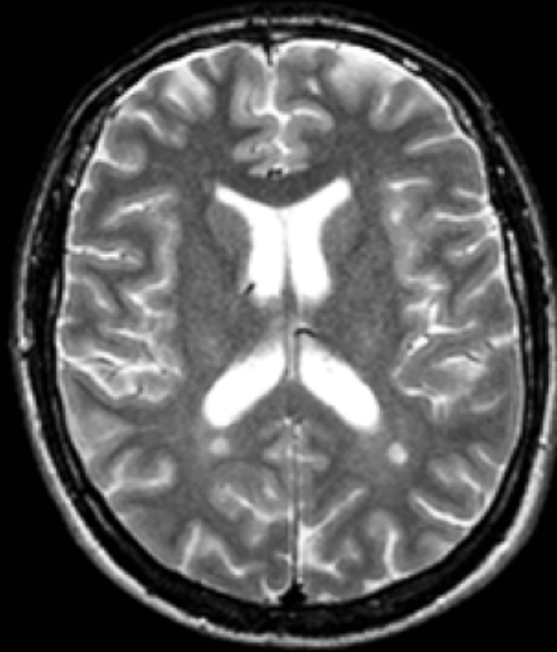
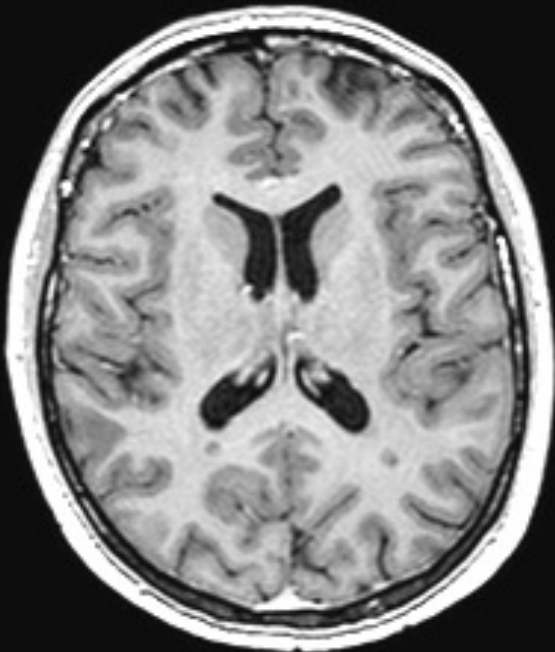


MRI acquisition – Image contrast

$$S_0 \propto \rho(H) \cdot e^{-TE/T_2} \left(1 - e^{-TR/T_1} \right)$$

Spin Echo

Long TR and TE: T2-weighted images (T2W)

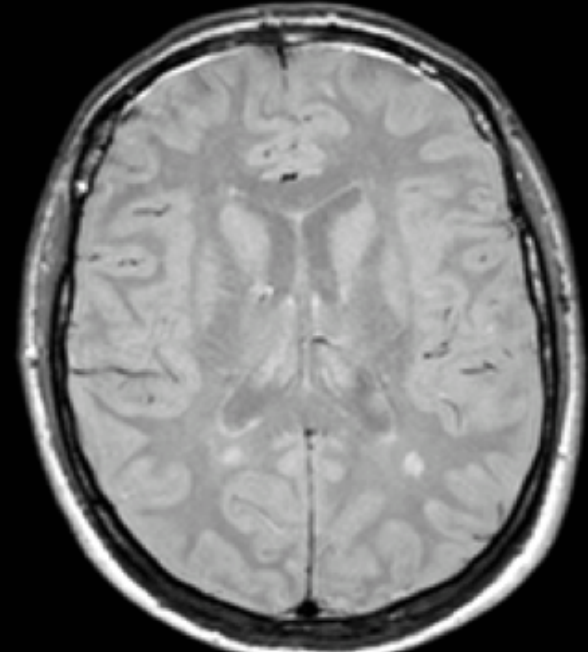
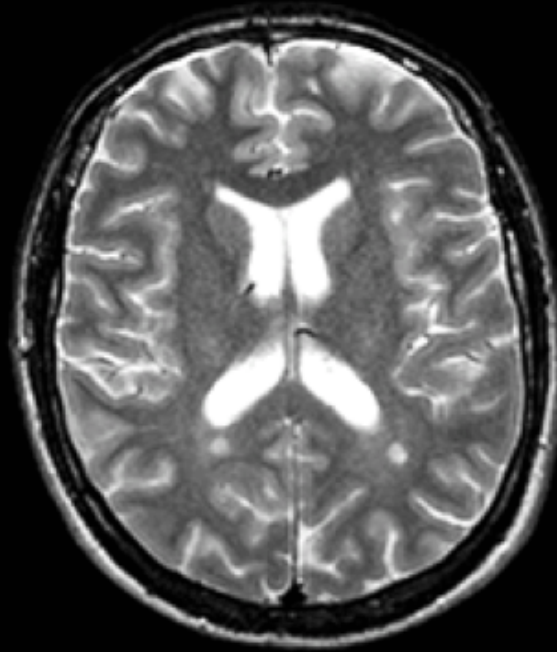


MRI acquisition – Image contrast

$$S_0 \propto \rho(H) \cdot e^{-TE/T_2} \left(1 - e^{-TR/T_1} \right)$$

Spin Echo

Long TR and short TE: PD-weighted images (PDW)



SPECTROSCOPY

Metabolites quantification

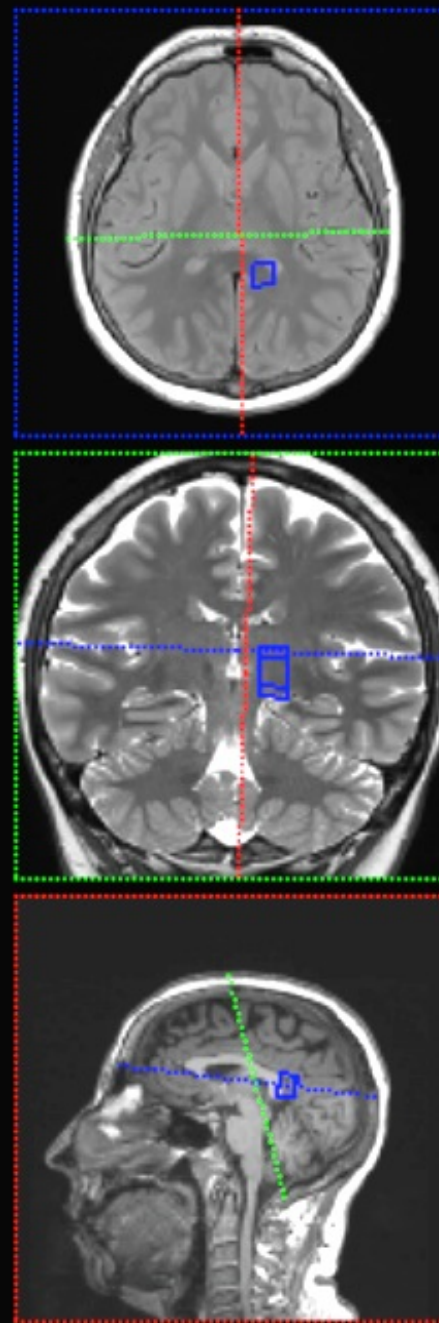
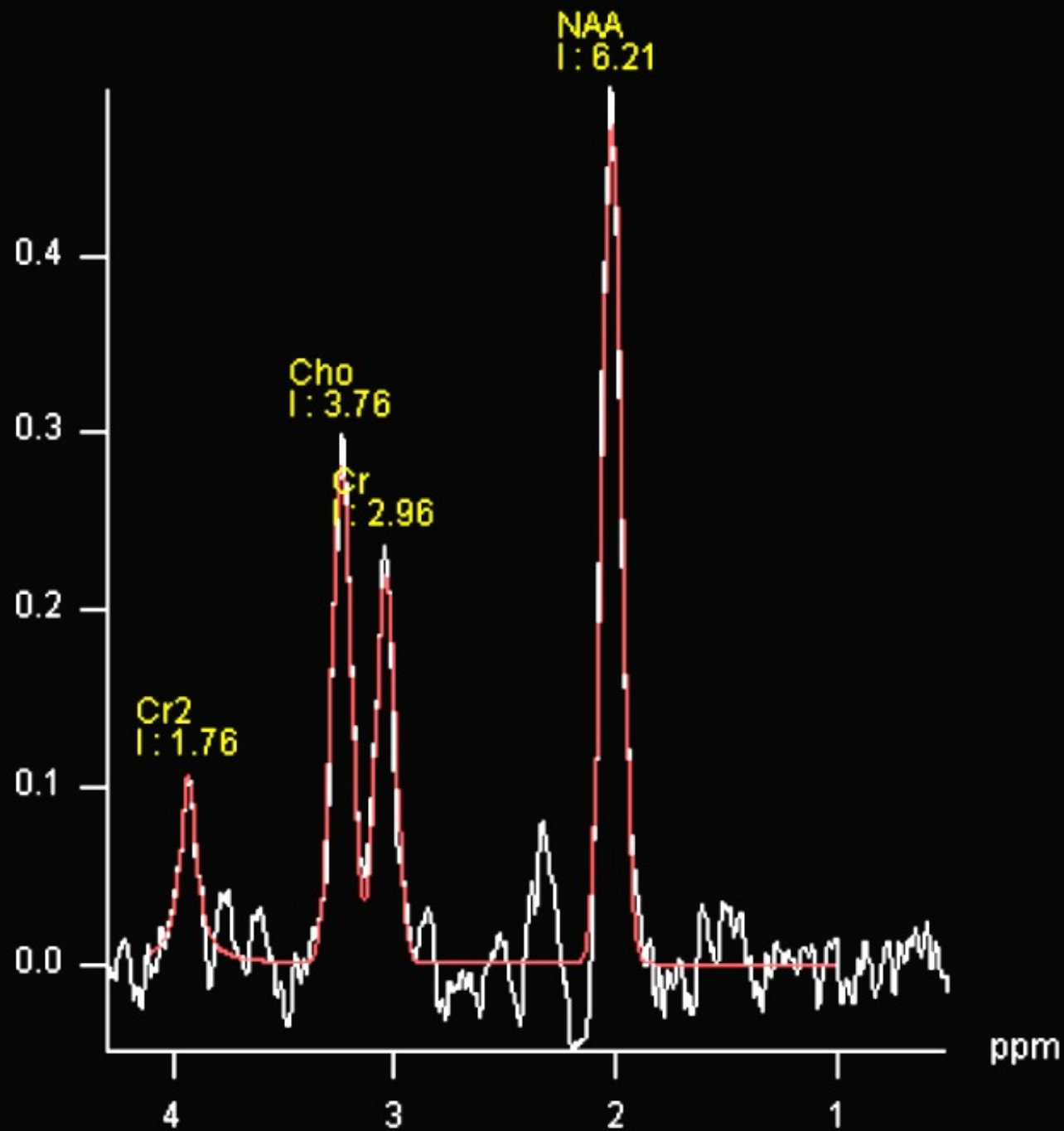
Chemical environment

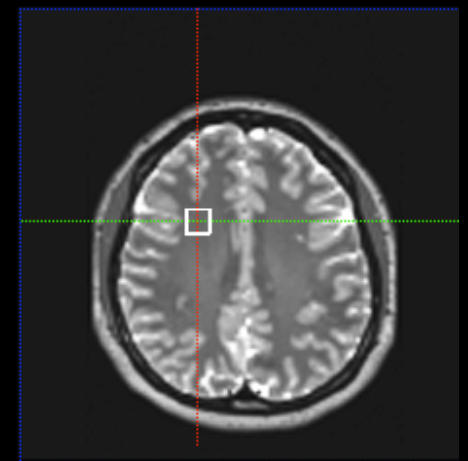
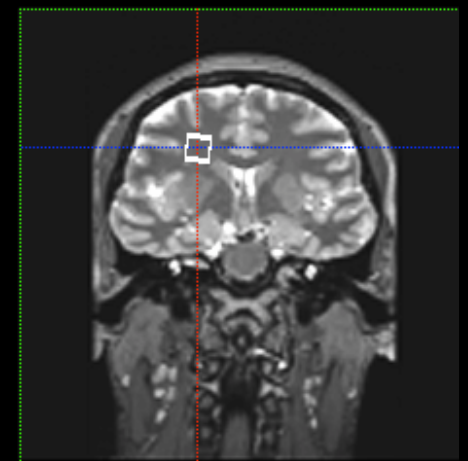
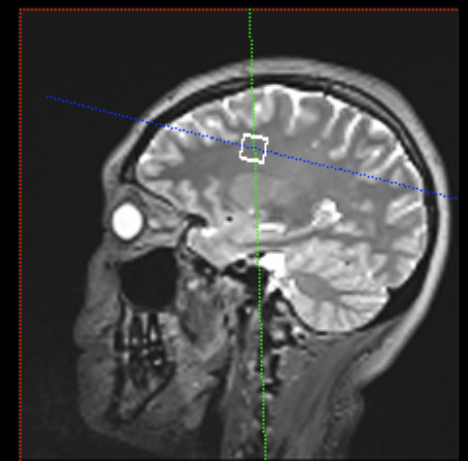
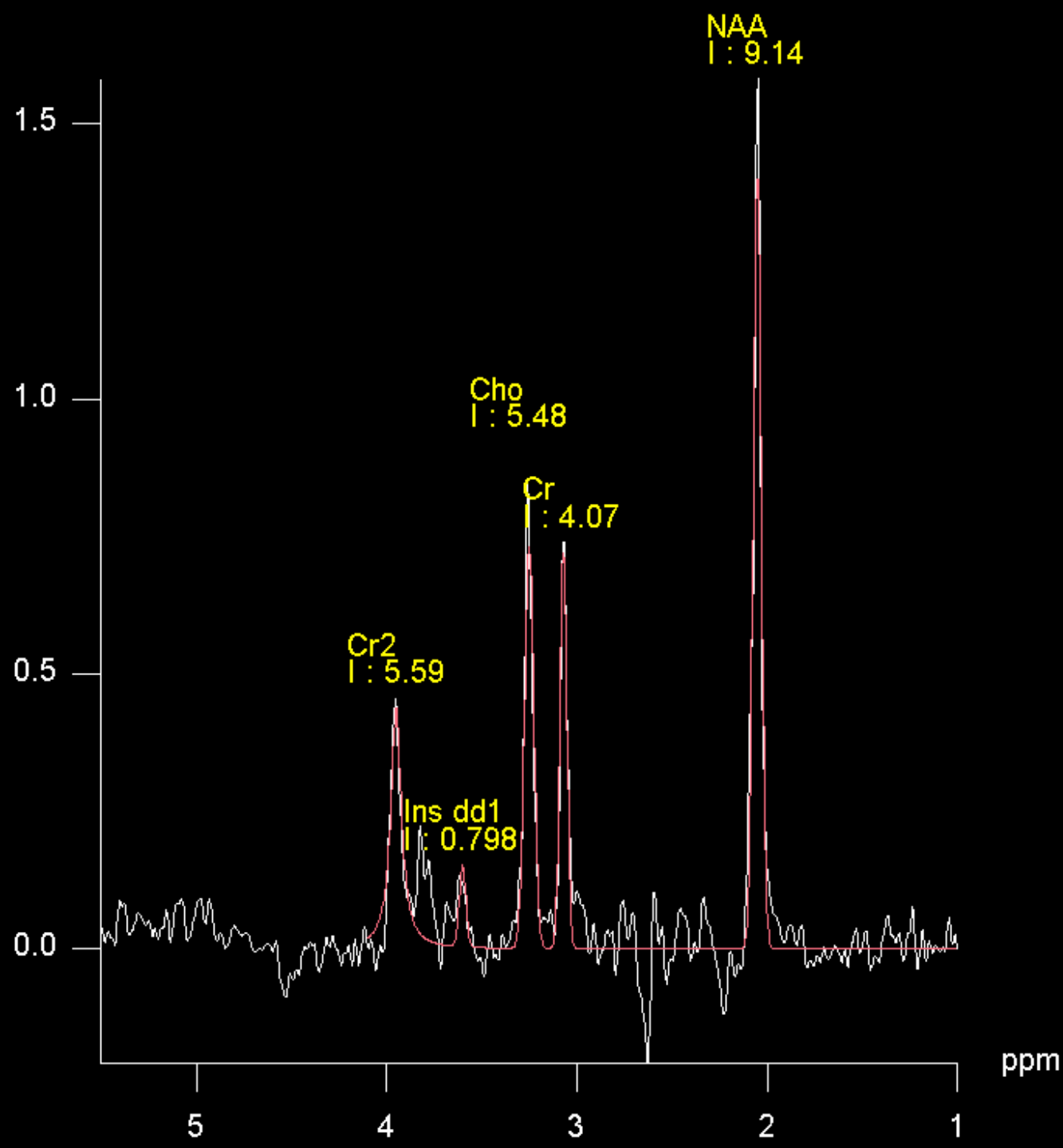
1-D Fourier transform of the NMR signal

Chemical Shift:

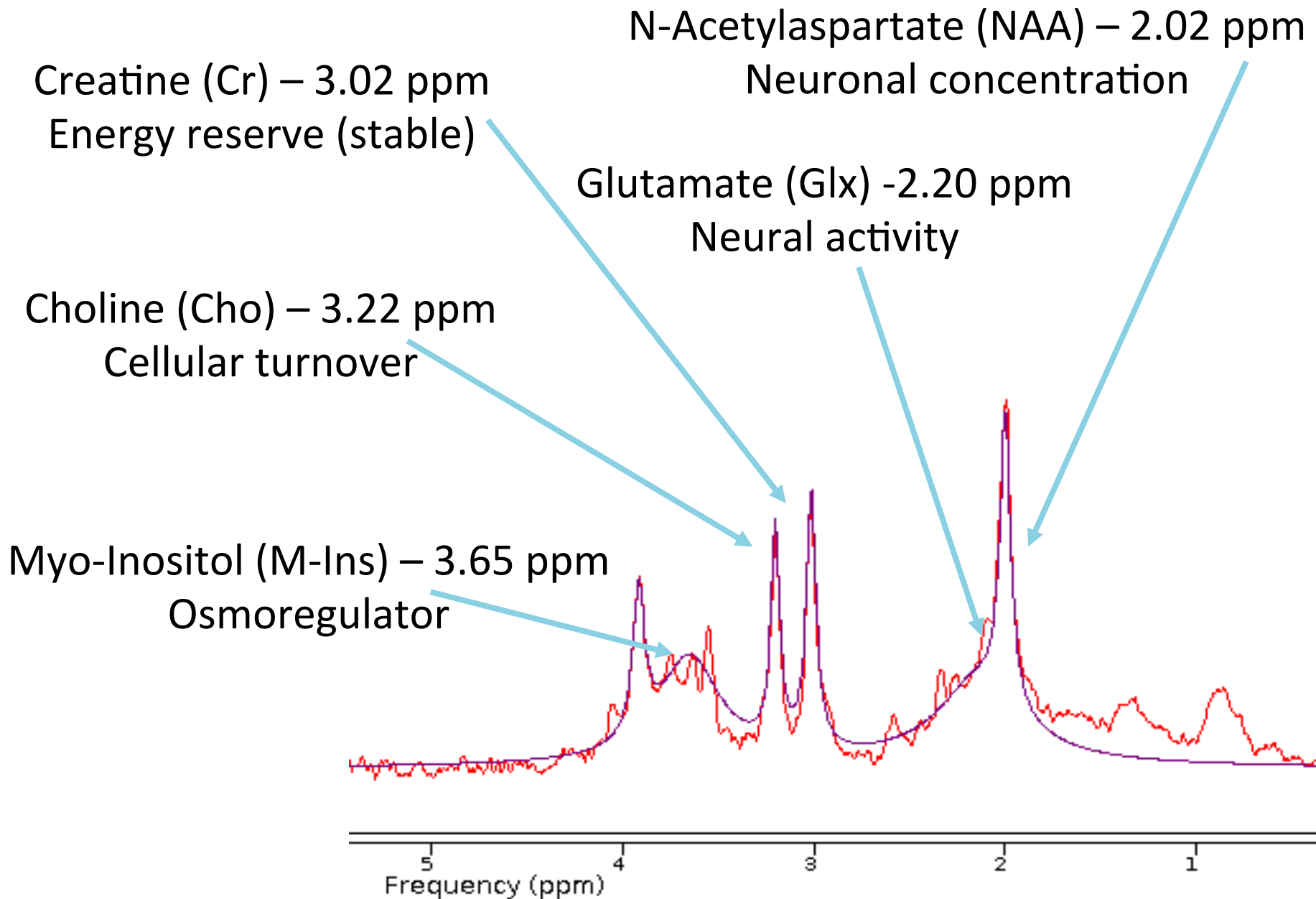
Each peak corresponds to a metabolite

Metabolite concentration = peak area





Brain metabolites

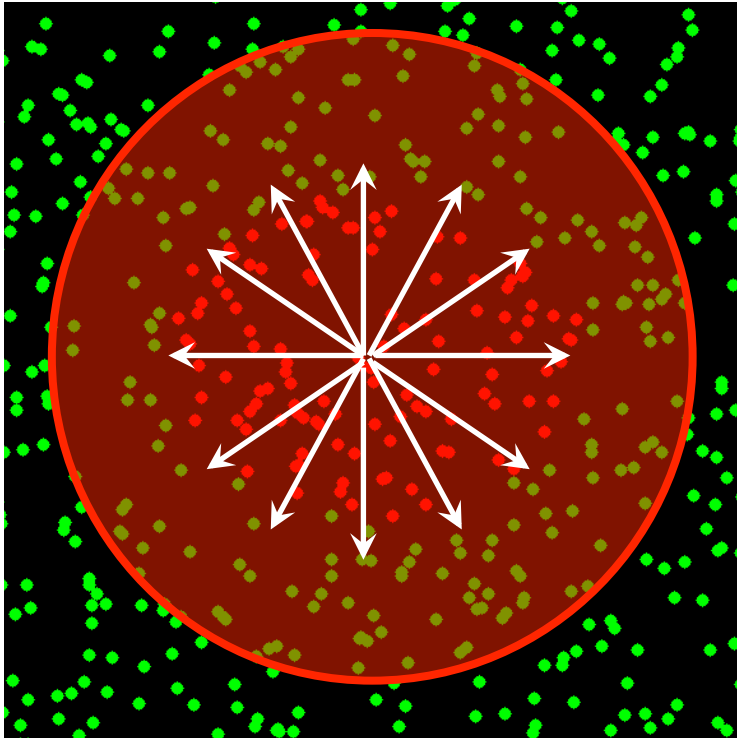


DIFFUSION IMAGING

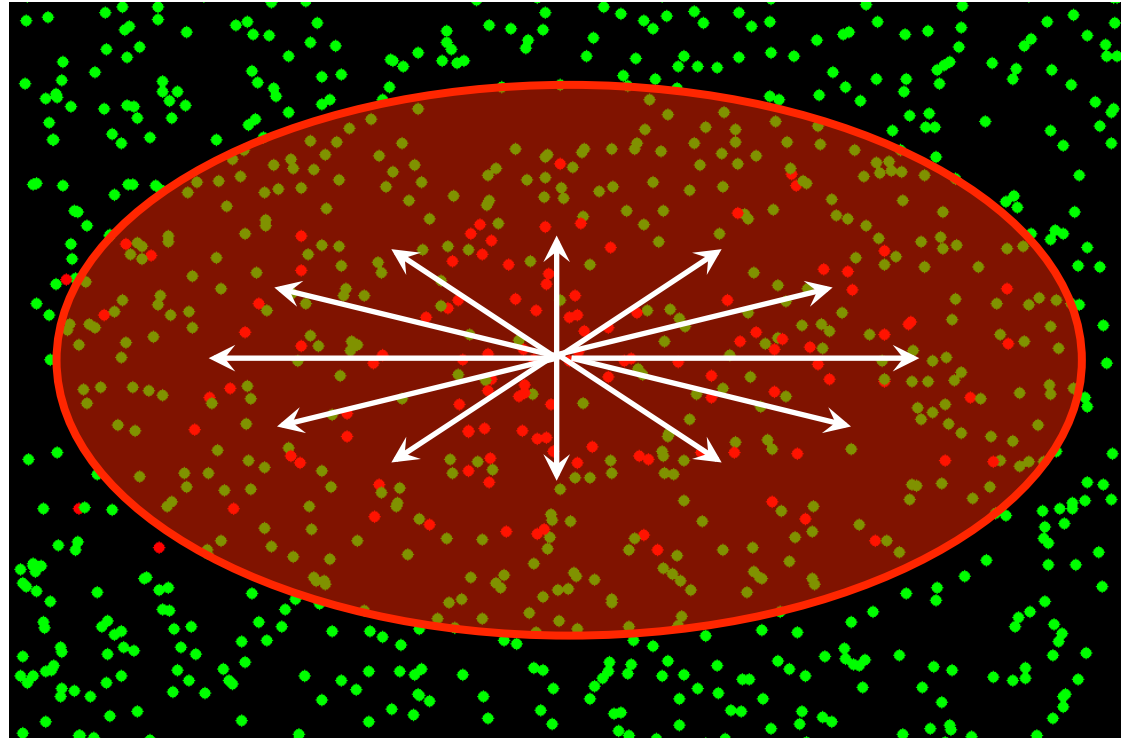
Structural Imaging

Diffusion – Brownian motion

Isotropic

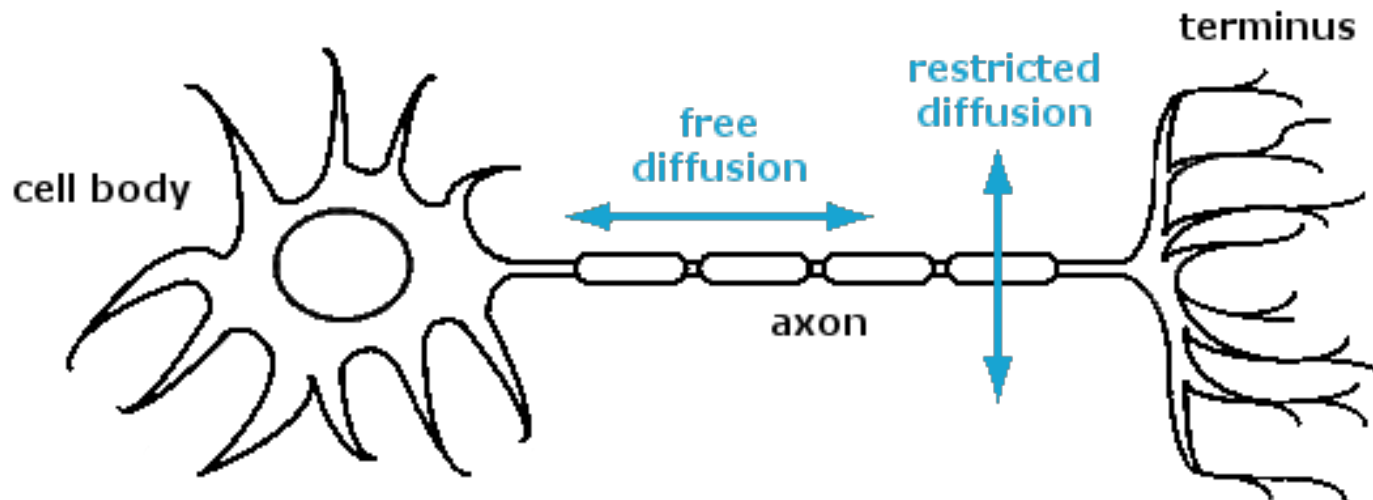


Anisotropic



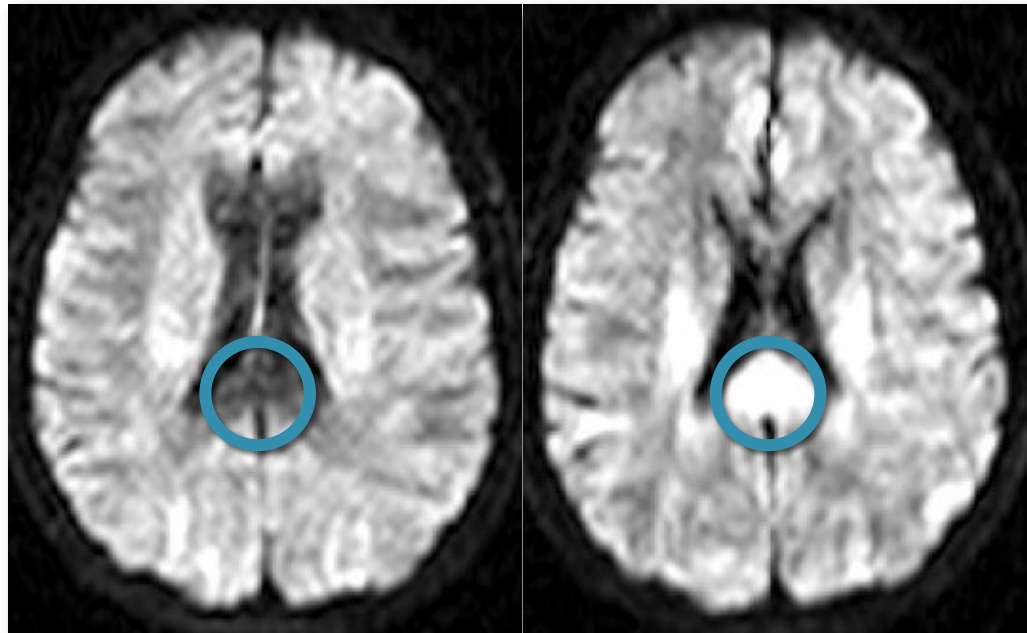
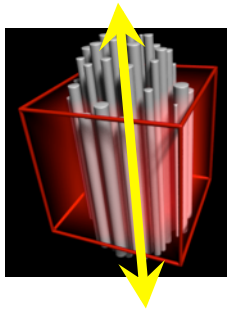
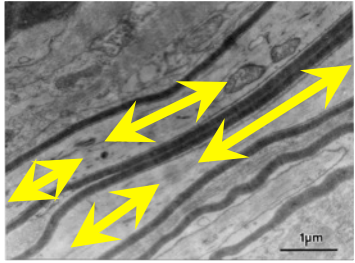
Why “diffusion” help us?

The *in vivo* sample is an anisotropic system



→ Diffusion gives indirect information about the underlying structure.

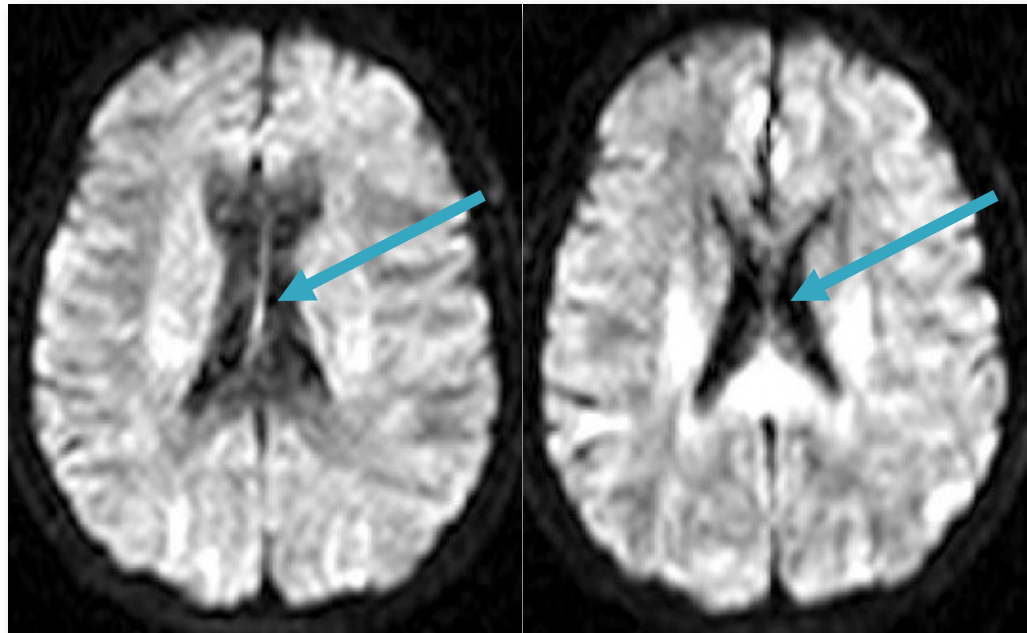
Why "diffusion" help us?



x-direction: R-L

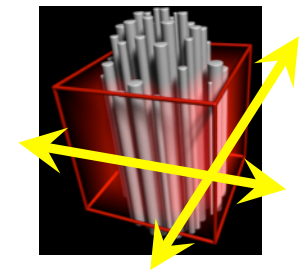
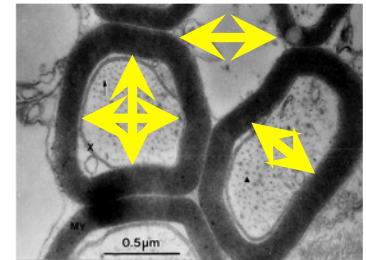
y-direction: A-P

Why "diffusion" help us?



x-direction: R-L

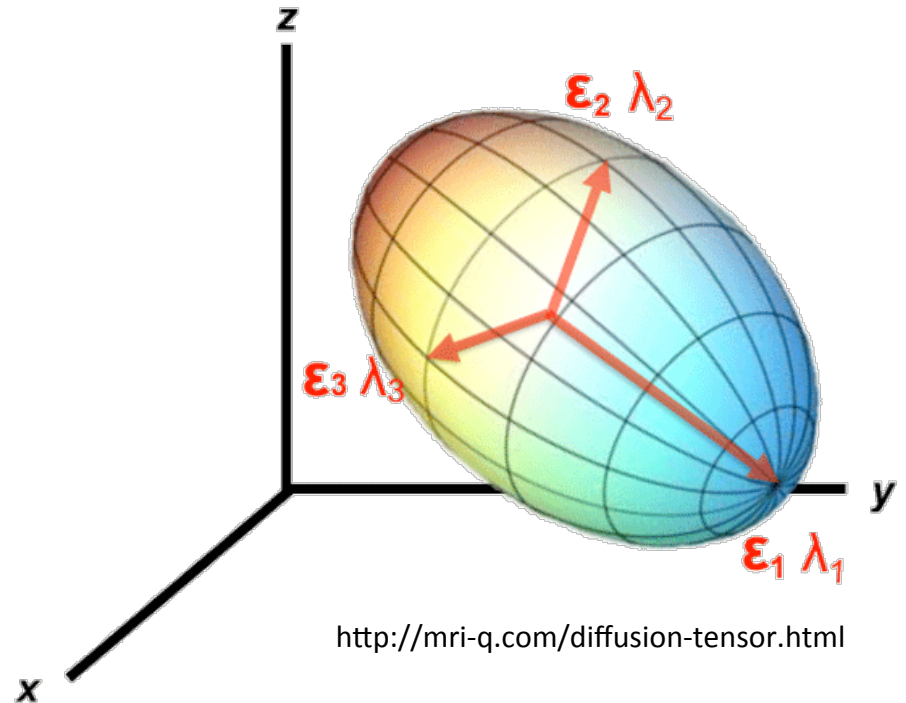
y-direction: A-P



Eigen-system and Diffusion Tensor

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

$$\mathbf{D} = \begin{pmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{pmatrix}$$

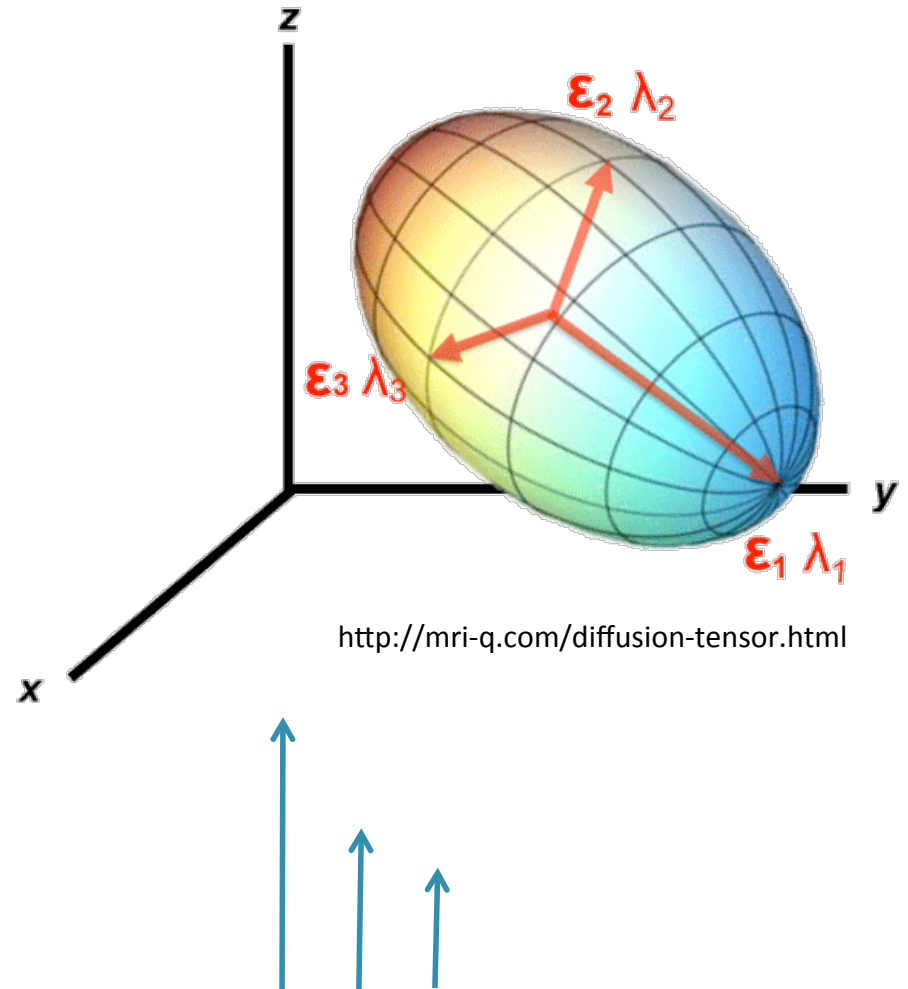


Eigen-system and Diffusion Tensor

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Eigenvalues

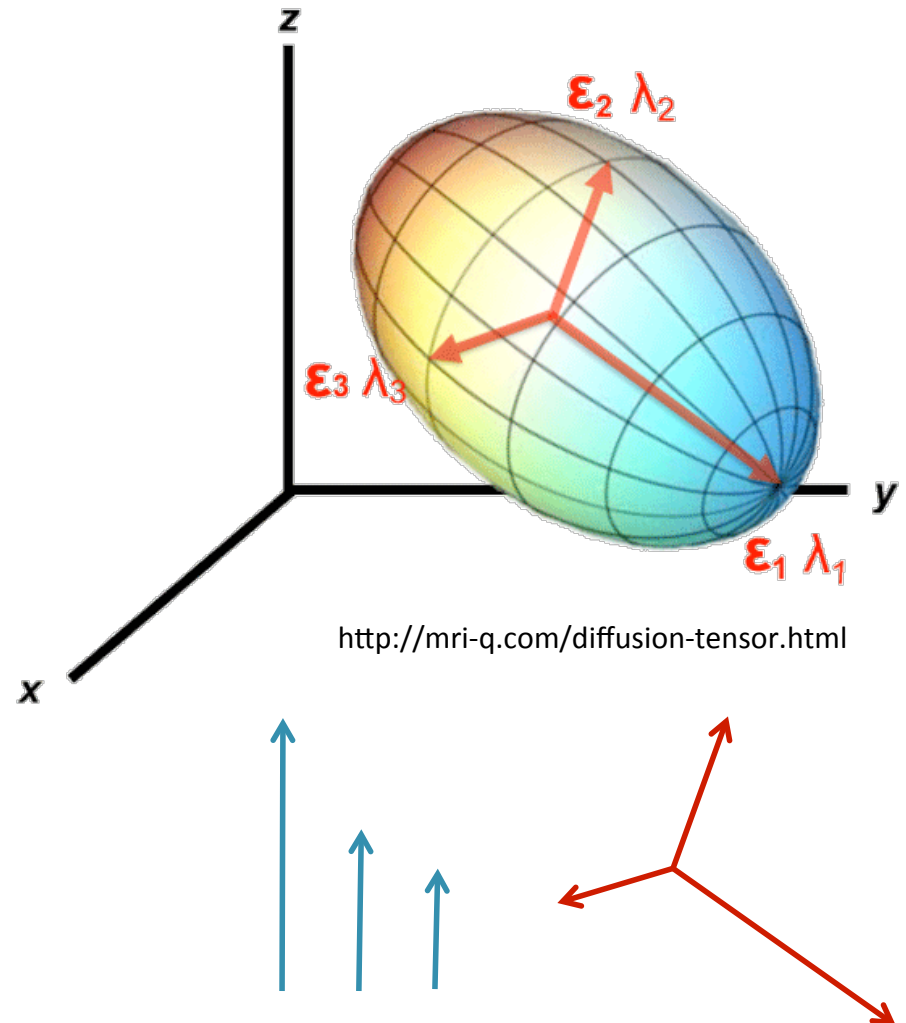


Eigen-system and Diffusion Tensor

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$$\mathbf{D} = \begin{pmatrix} \boxed{\lambda_1} & \boxed{0} & \boxed{0} \\ \boxed{0} & \boxed{\lambda_2} & \boxed{0} \\ \boxed{0} & \boxed{0} & \boxed{\lambda_3} \end{pmatrix}$$

Eigenvectors

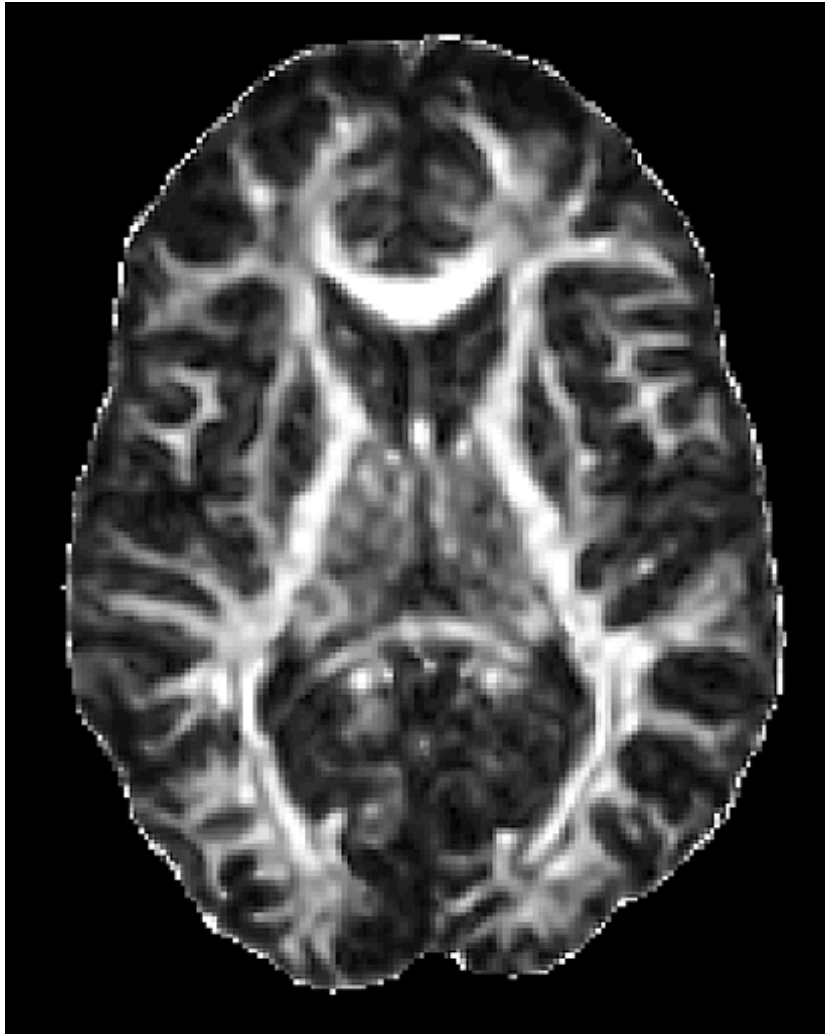


Fractional Anisotropy and Mean Diffusivity

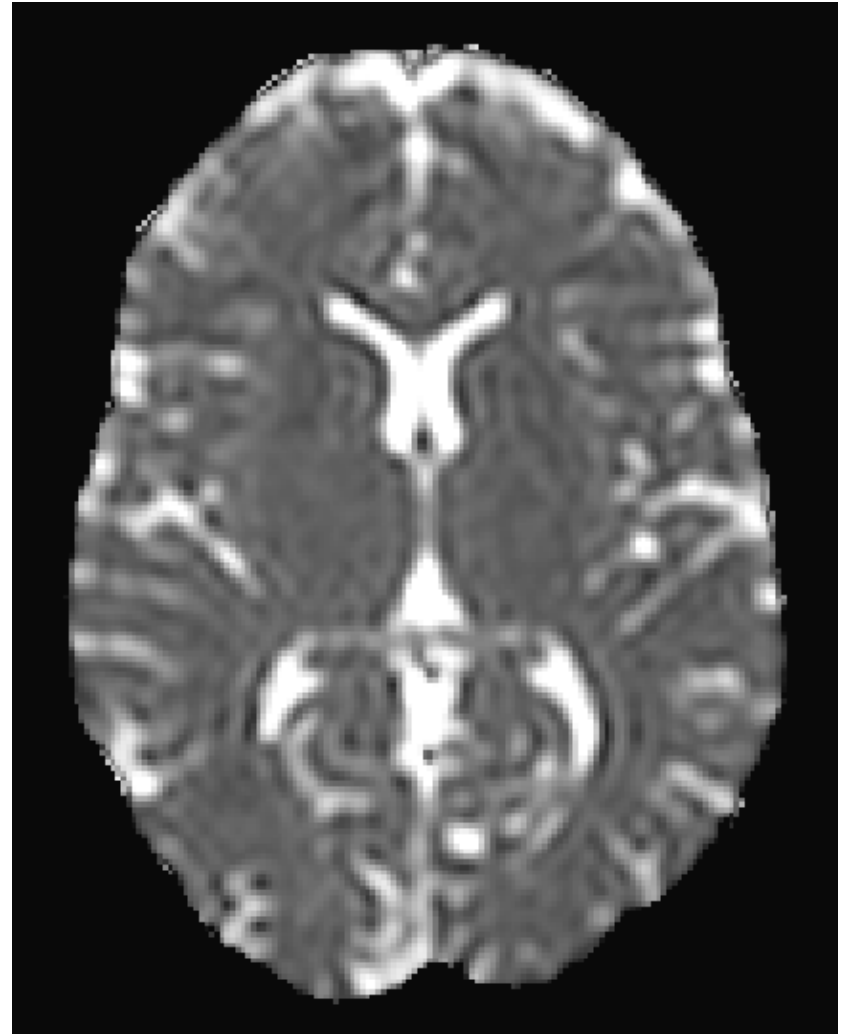
Measure intrinsic properties
of tissues and
characterize their microstructure

Fractional Anisotropy and Mean Diffusivity

Degree of anisotropy for each voxel

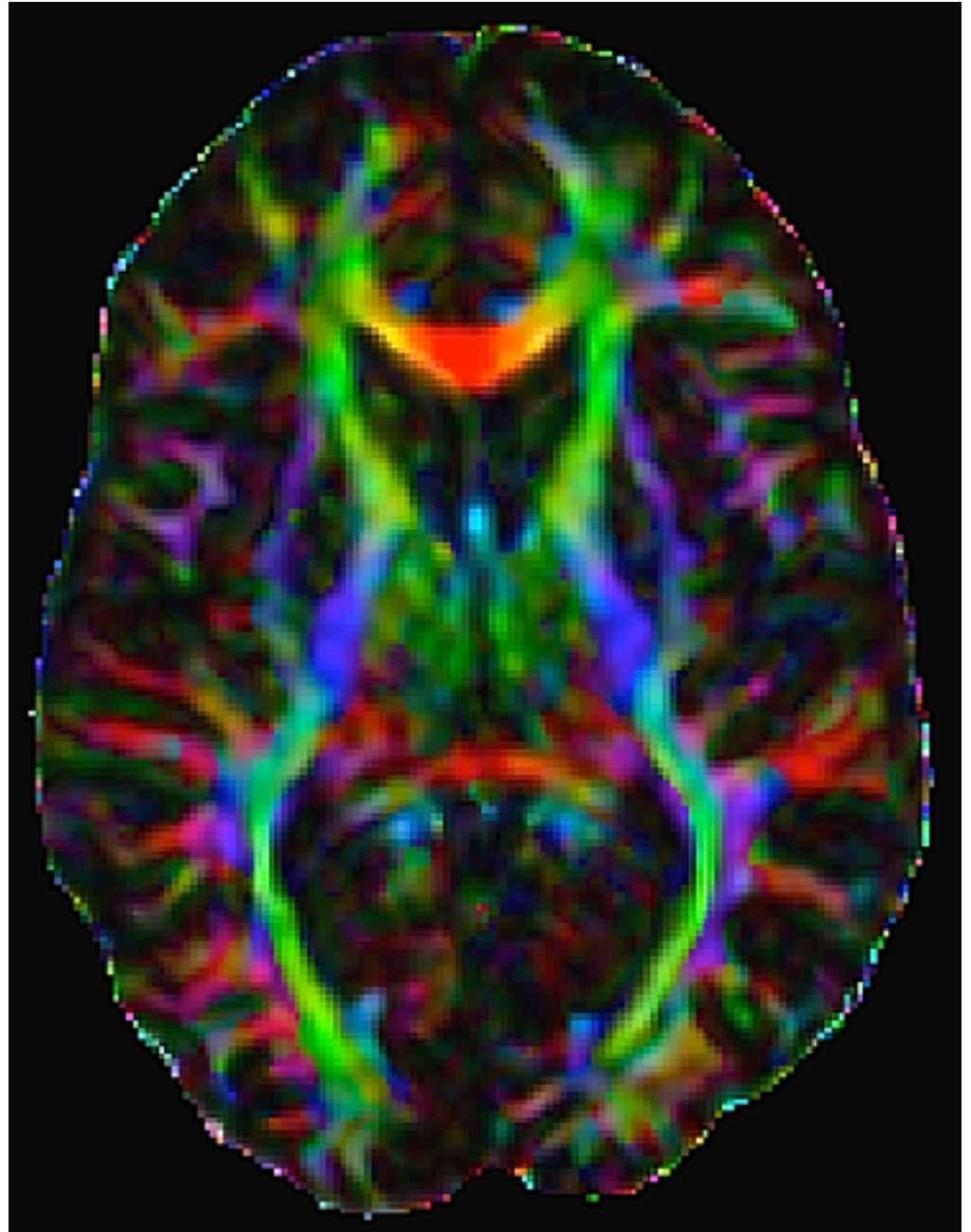
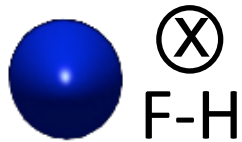
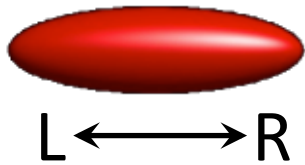
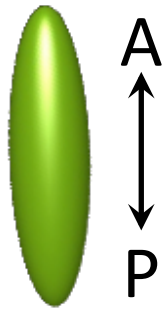


Mean diffusivity for each voxel

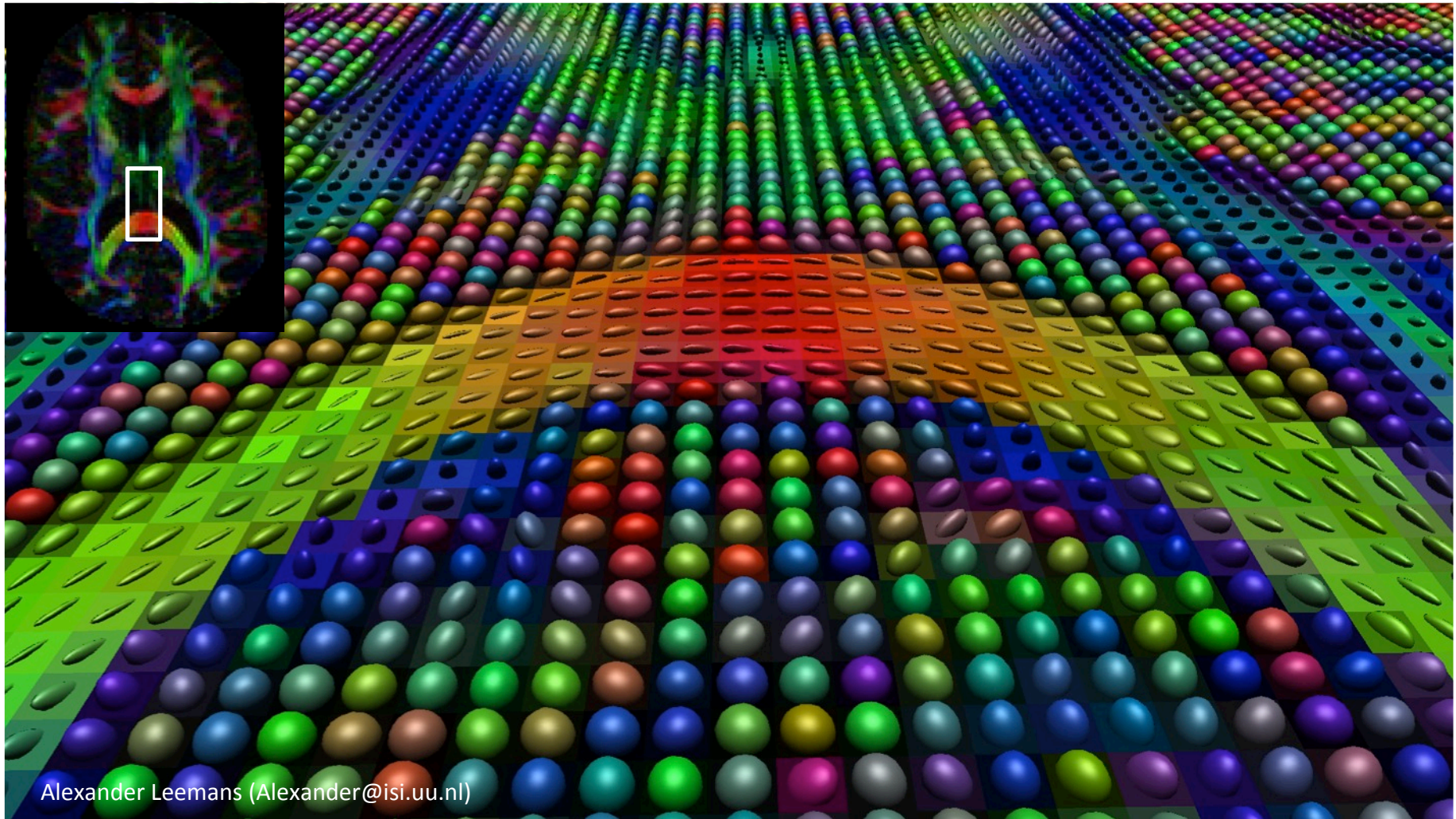


Directions information

color

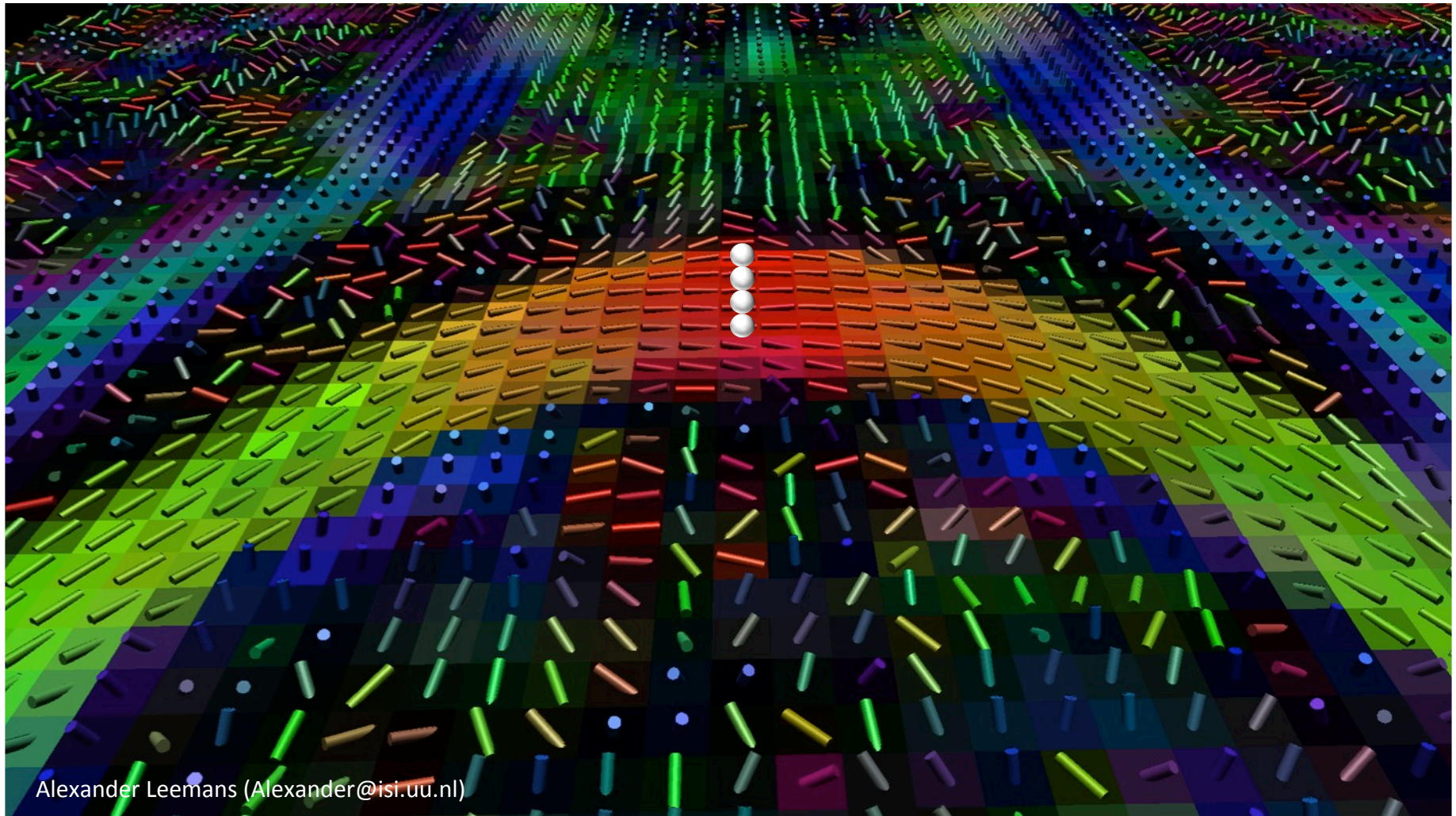


Diffusion tractography



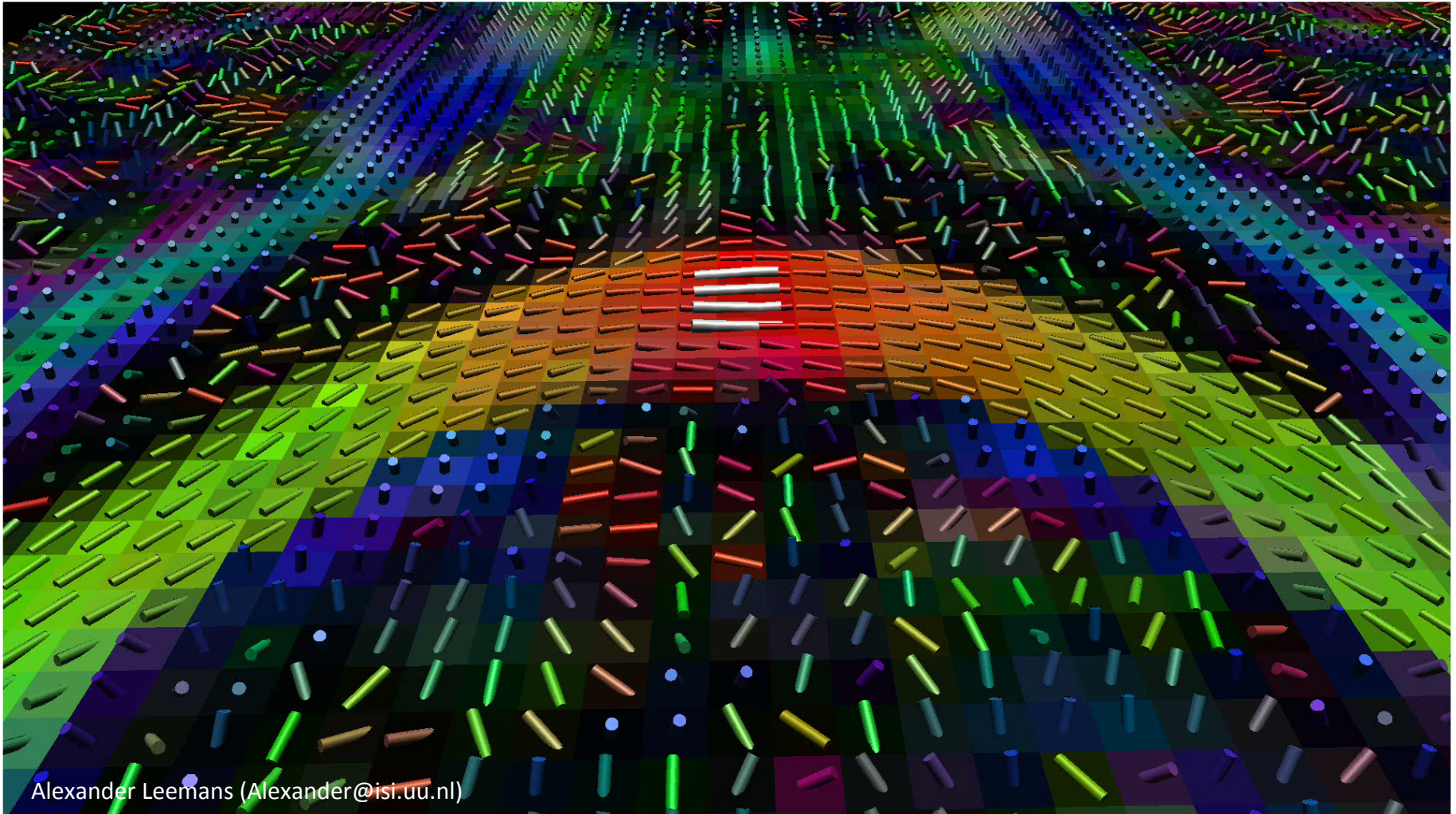
“connecting neighbouring ellipsoids”

Diffusion tractography



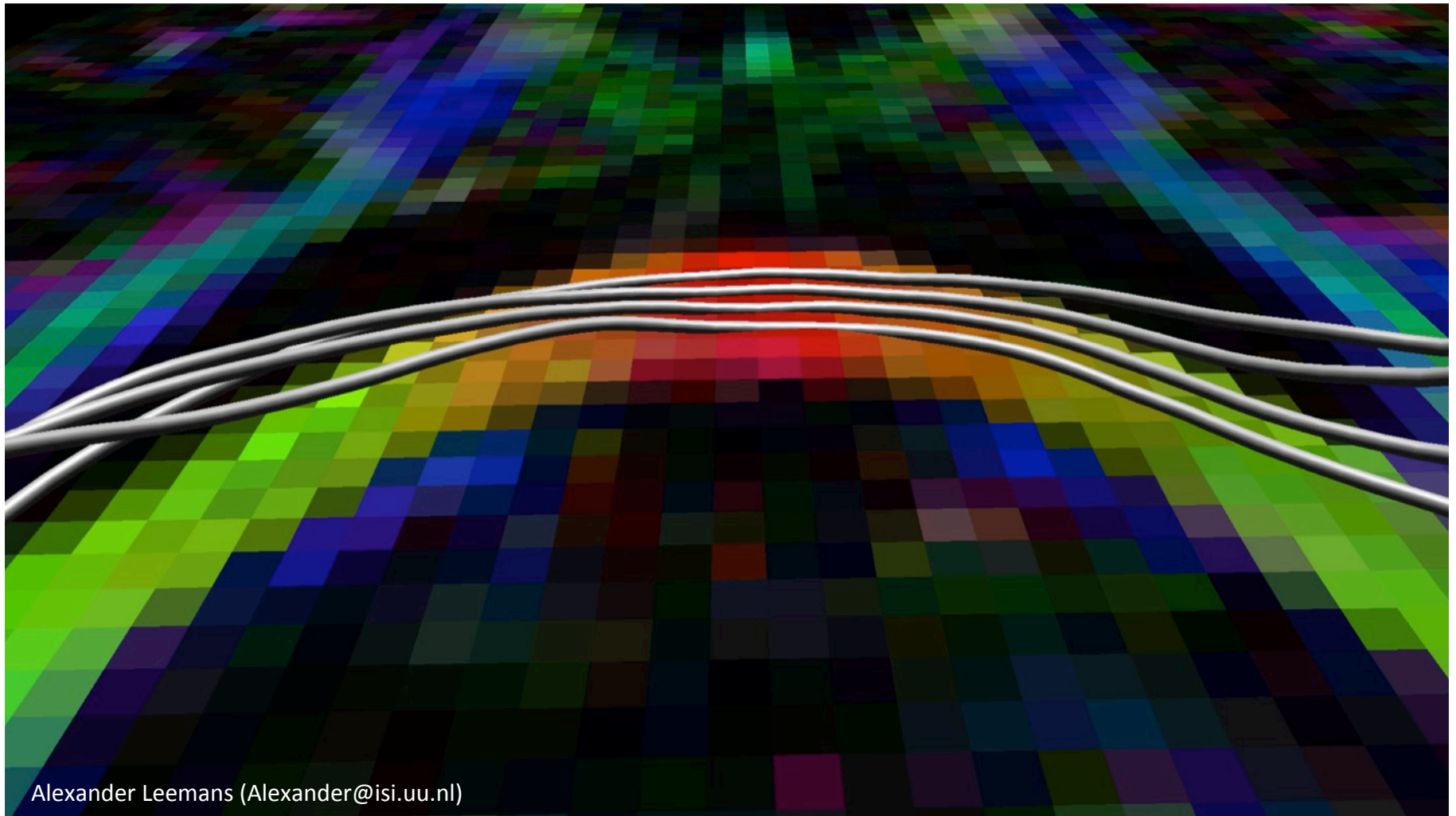
“connecting neighbouring ellipsoids”

Diffusion tractography



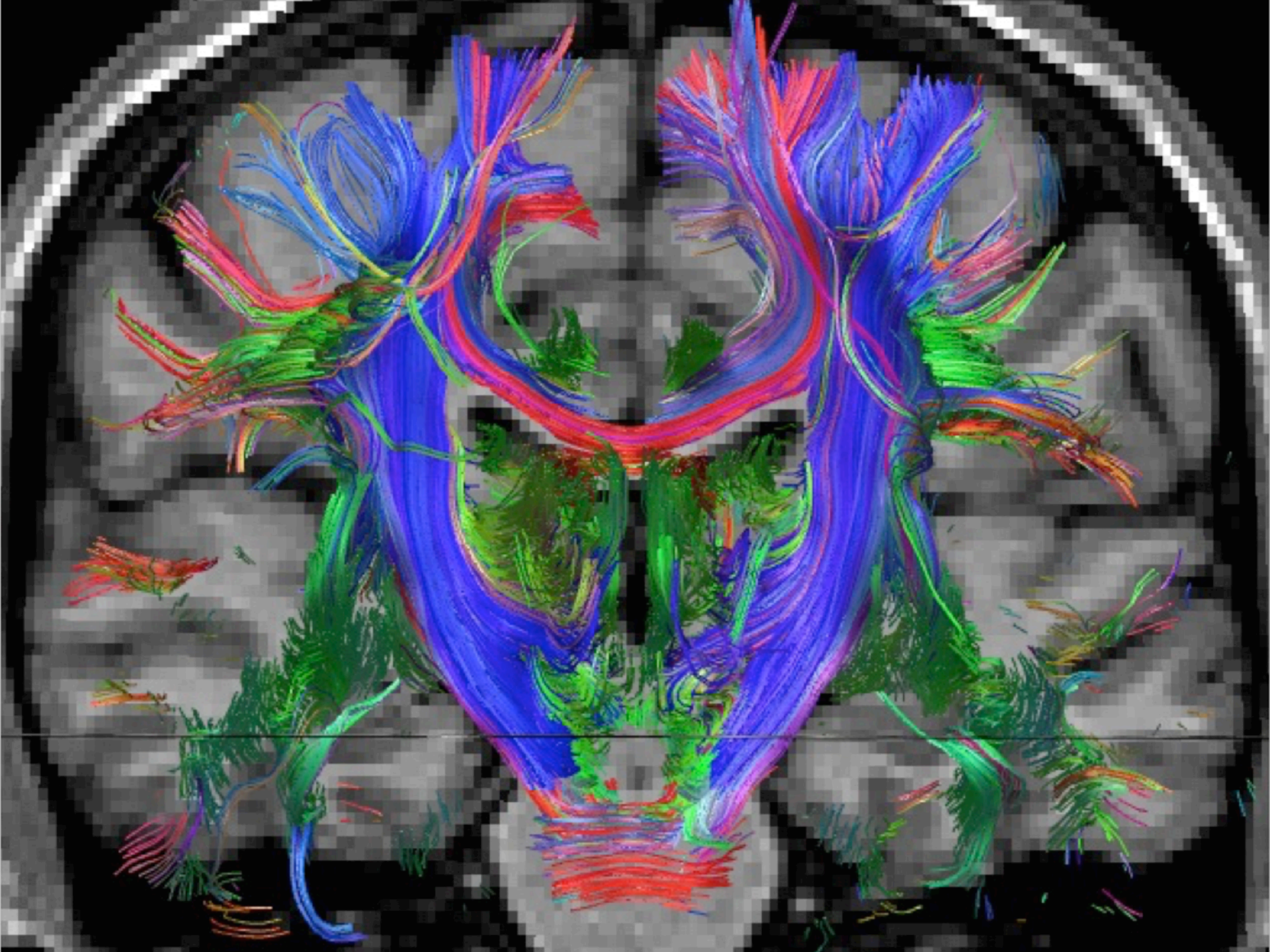
“connecting neighbouring ellipsoids”

Diffusion tractography



Alexander Leemans (Alexander@isi.uu.nl)

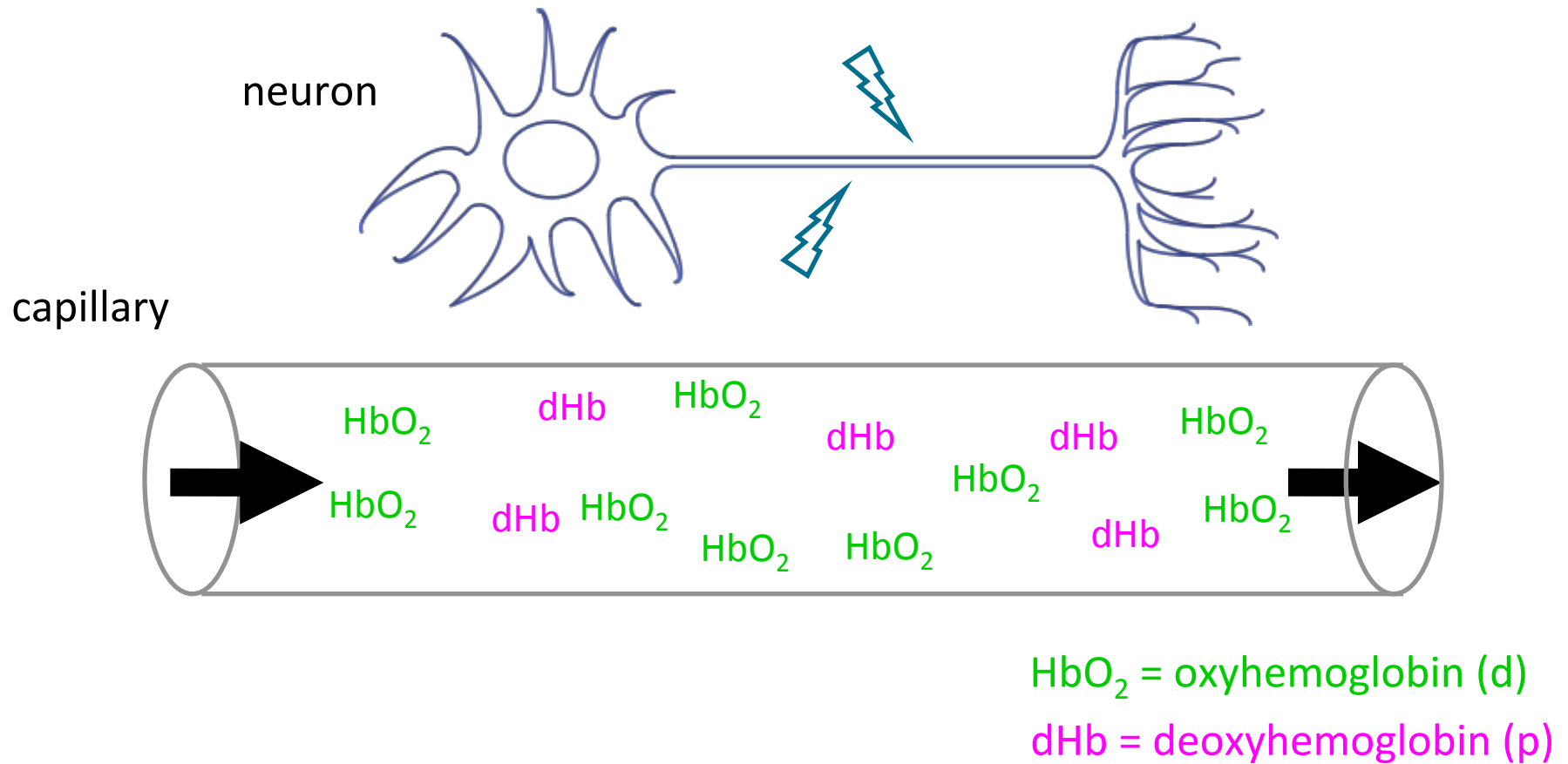
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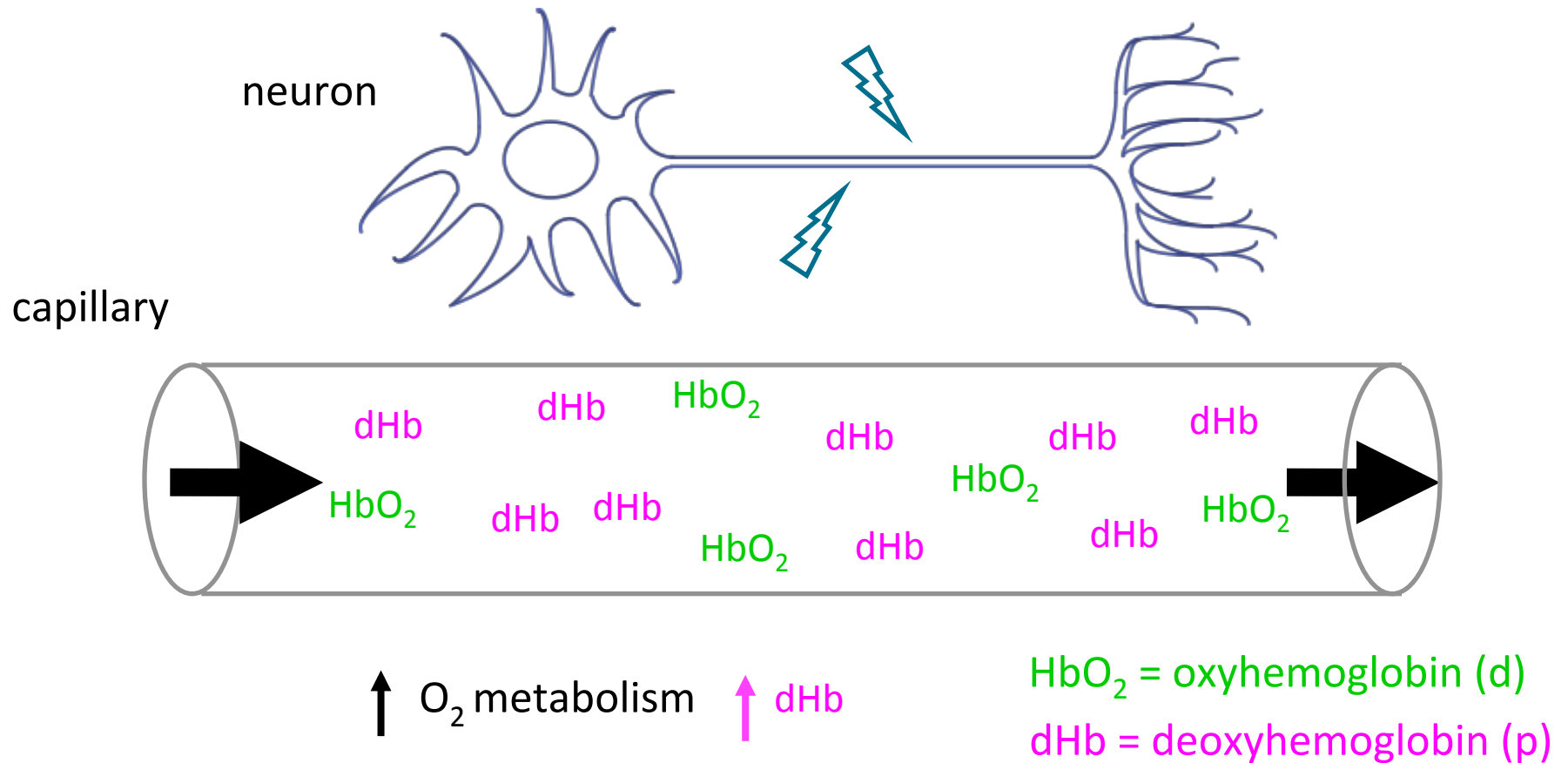
FUNCTIONAL IMAGING

Physiological Imaging

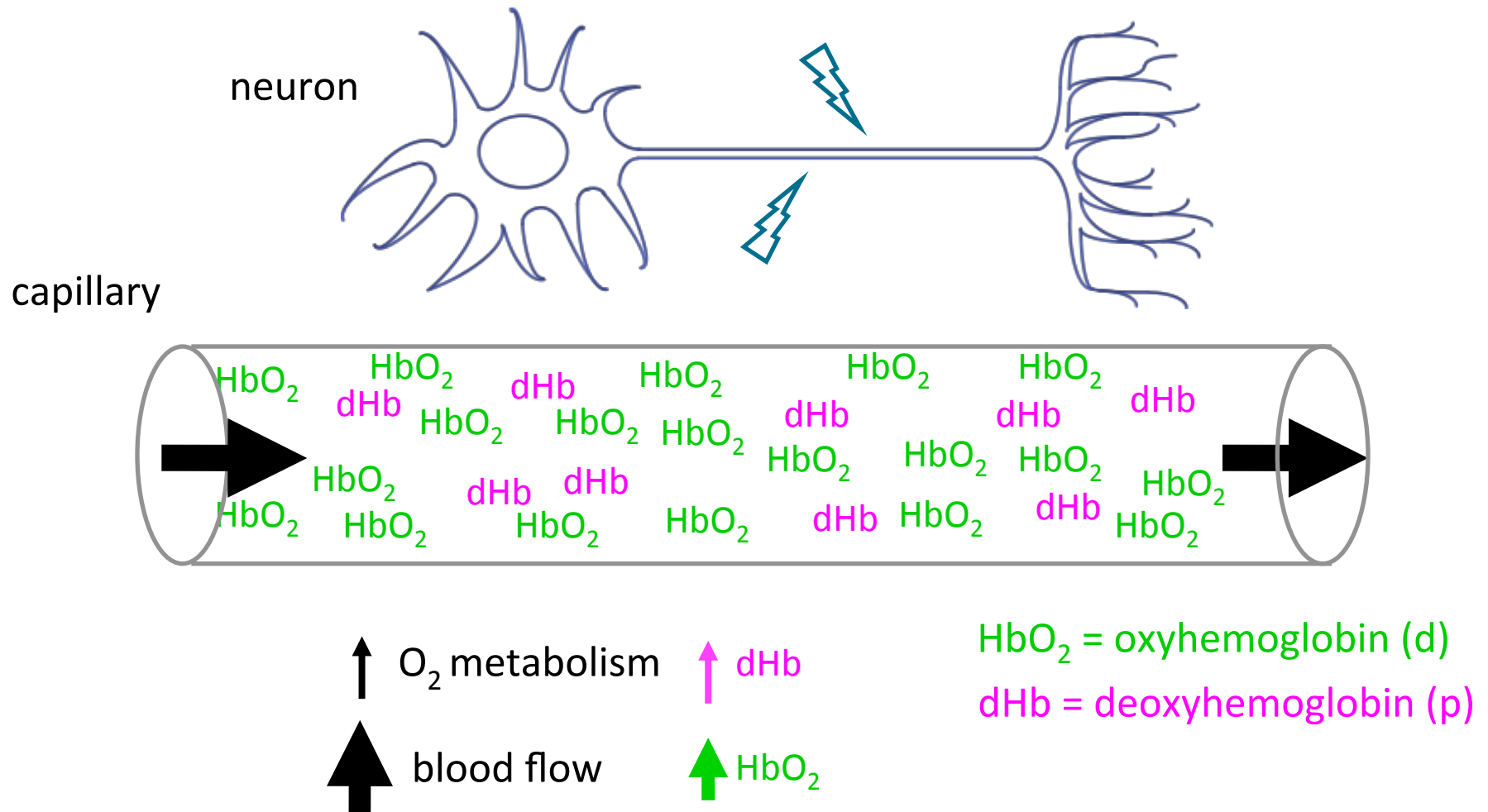
Vascular Response to Activation



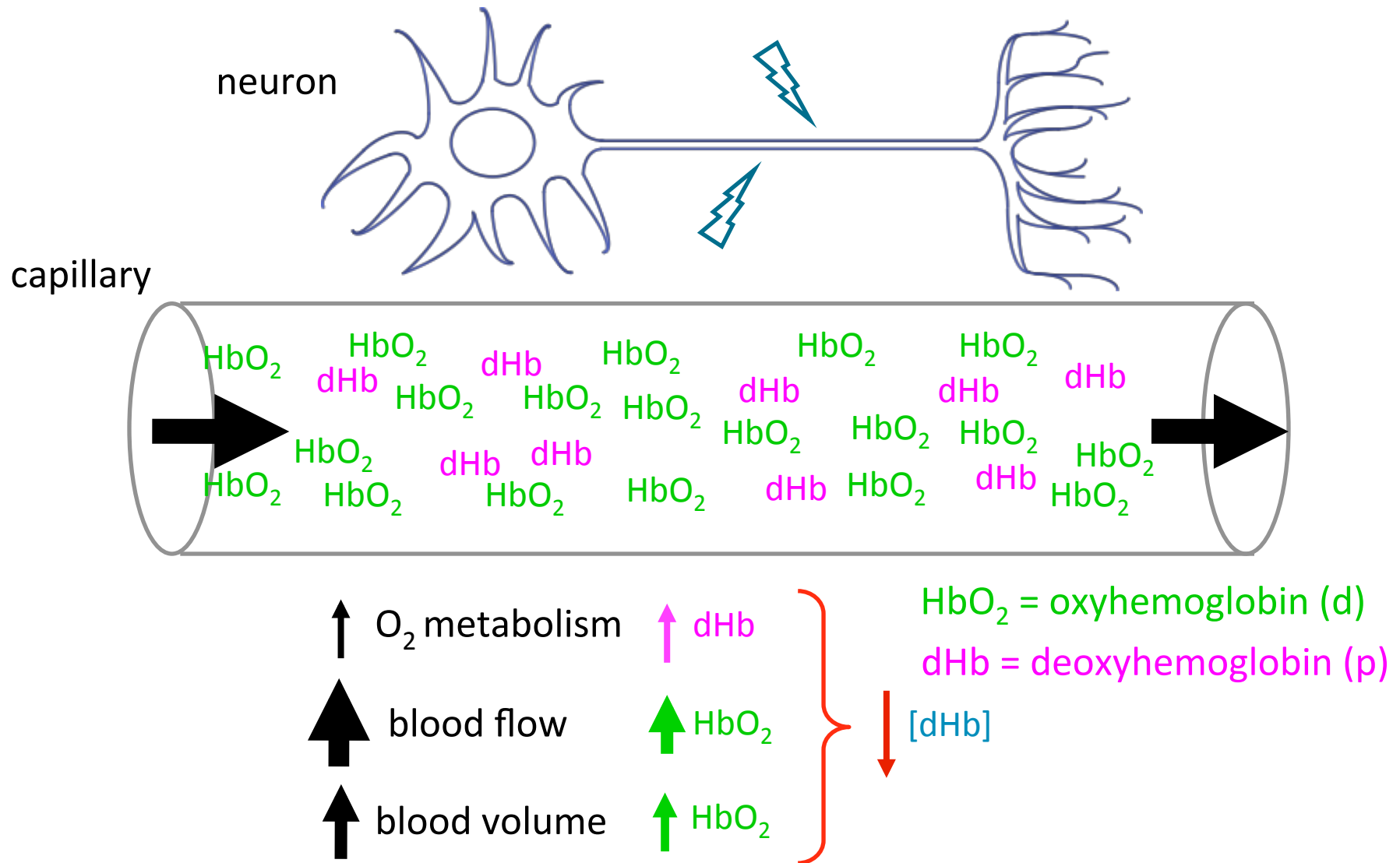
Vascular Response to Activation



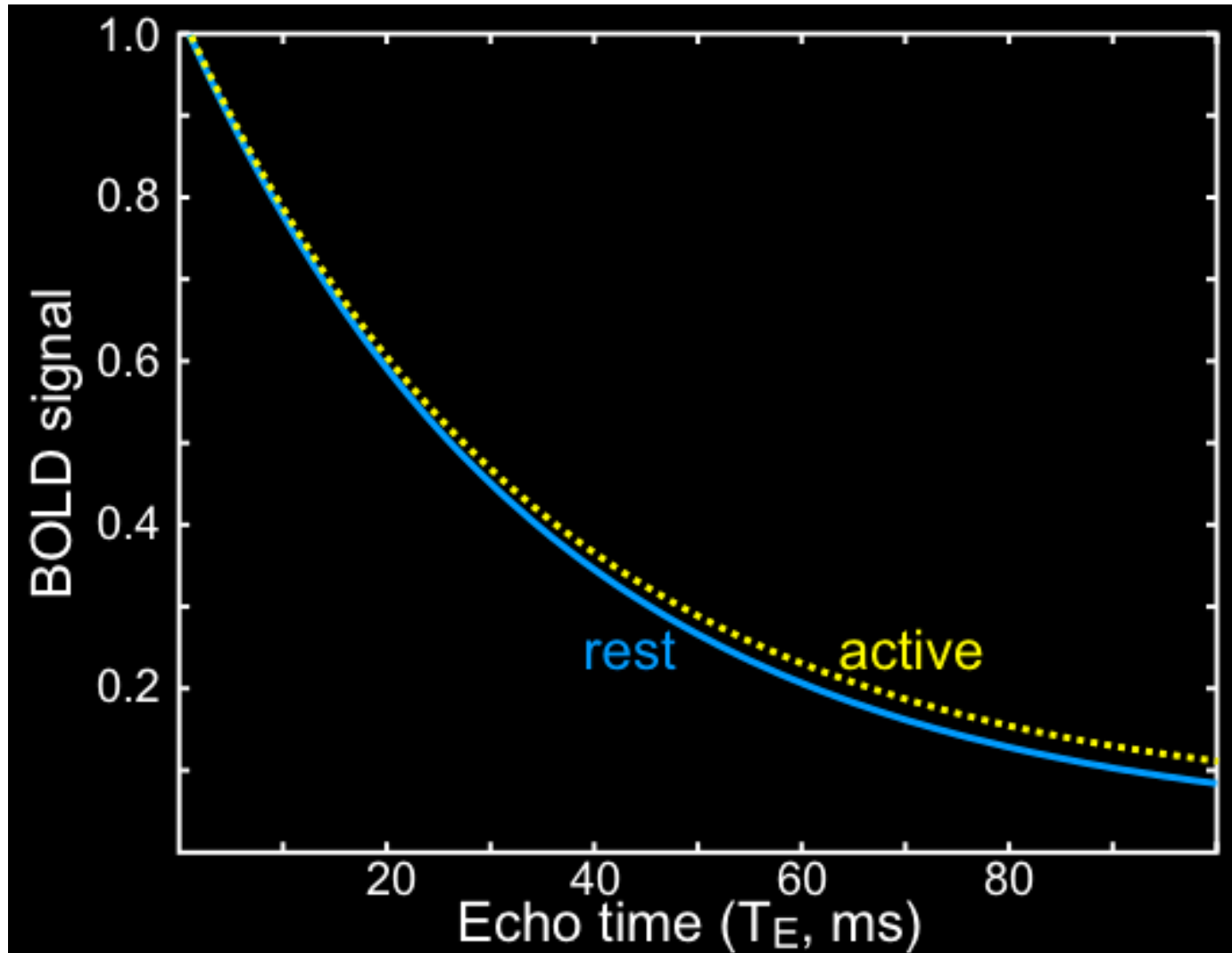
Vascular Response to Activation



Vascular Response to Activation



BOLD Contrast

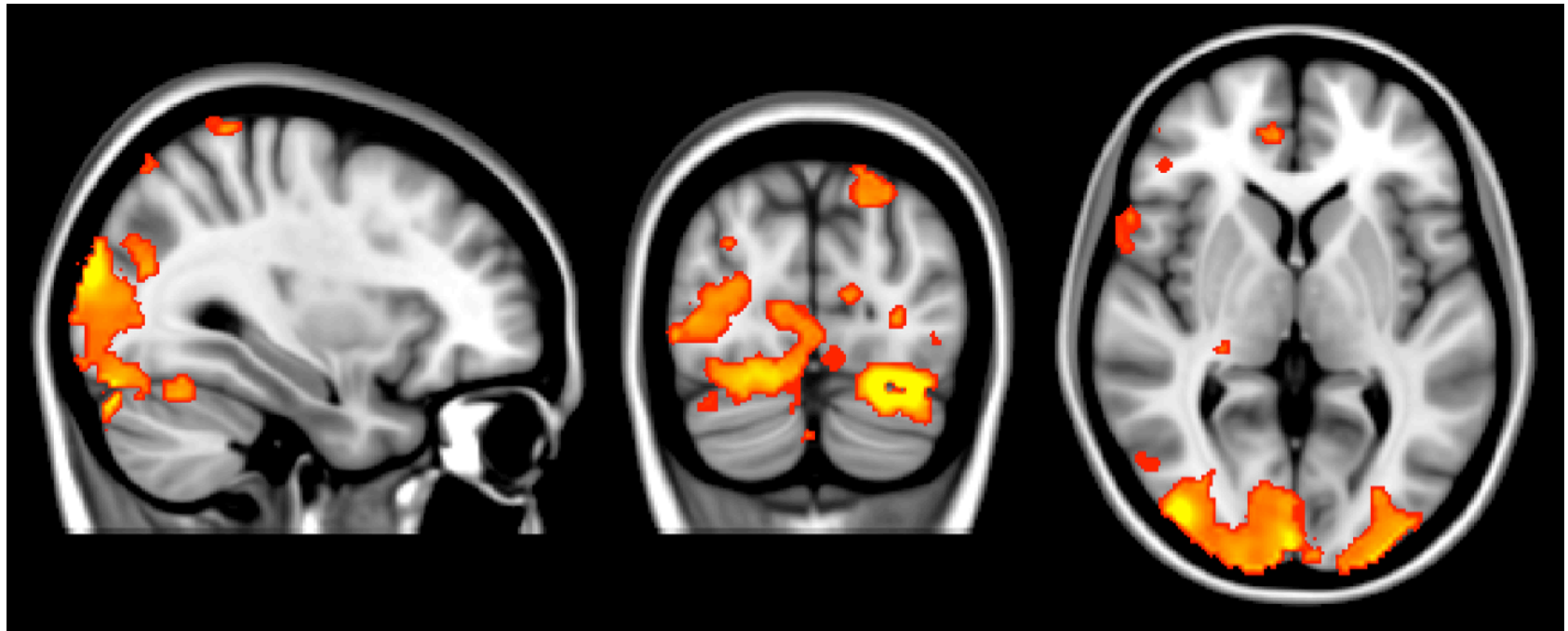
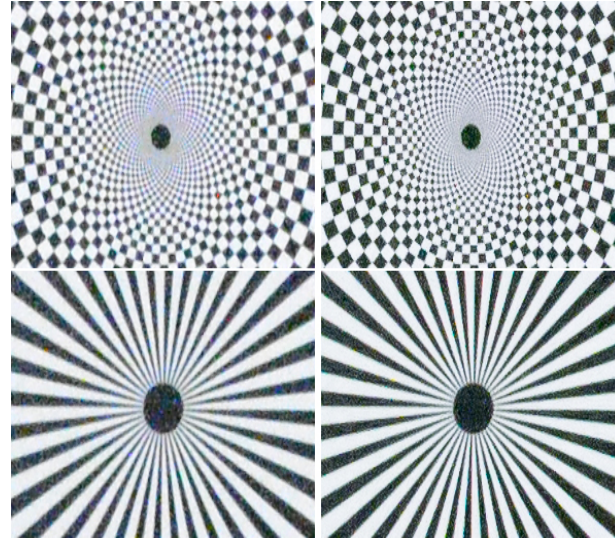


Signal increases during activation (less decay)
1–5% signal change

BOLD signal

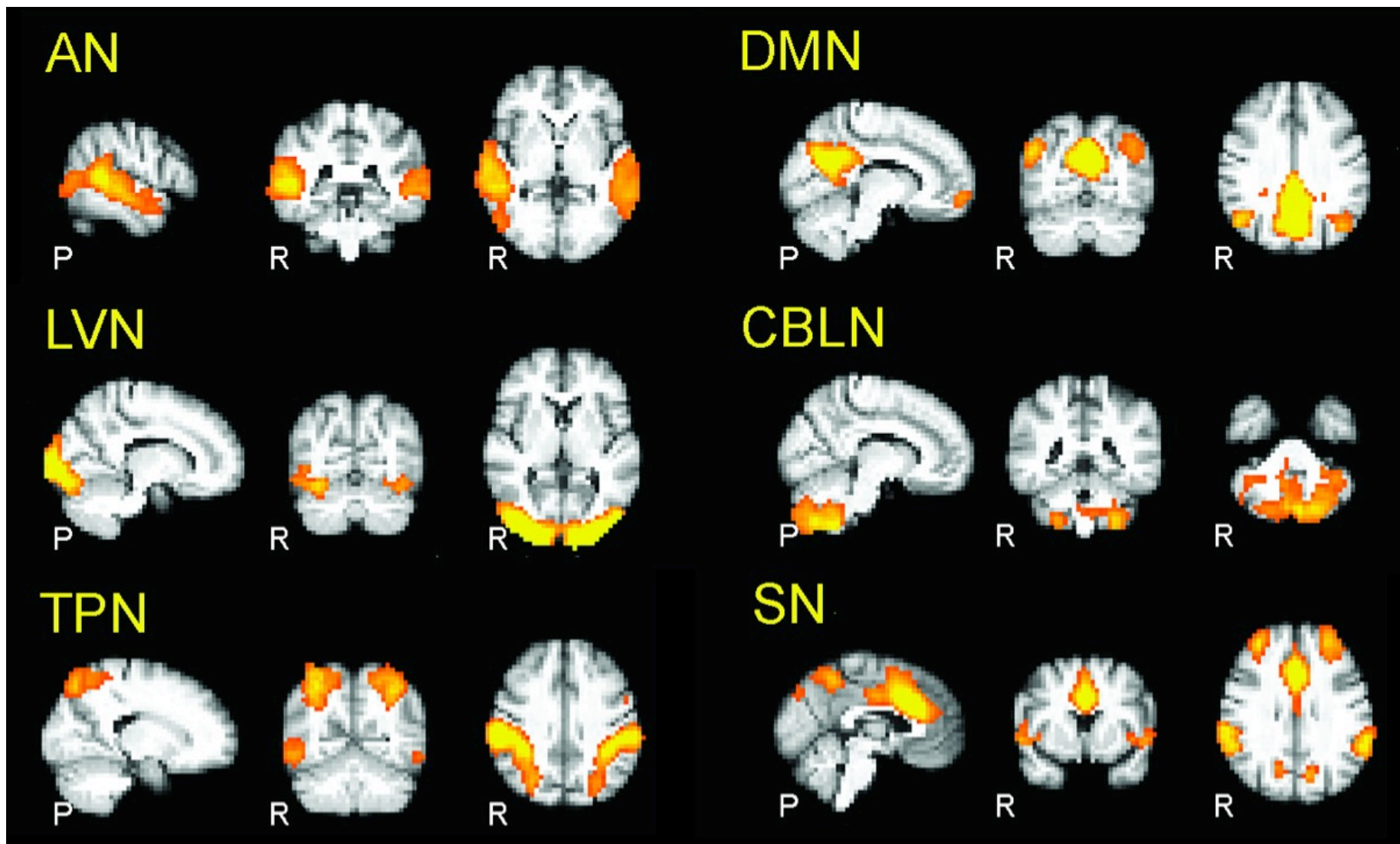
Measures activity of neurons
indirectly

Task-related fMRI – Visual task



Resting state fMRI

Networks found by correlation analysis of signal variation at low frequencies (0.01 – 0.05 Hz).

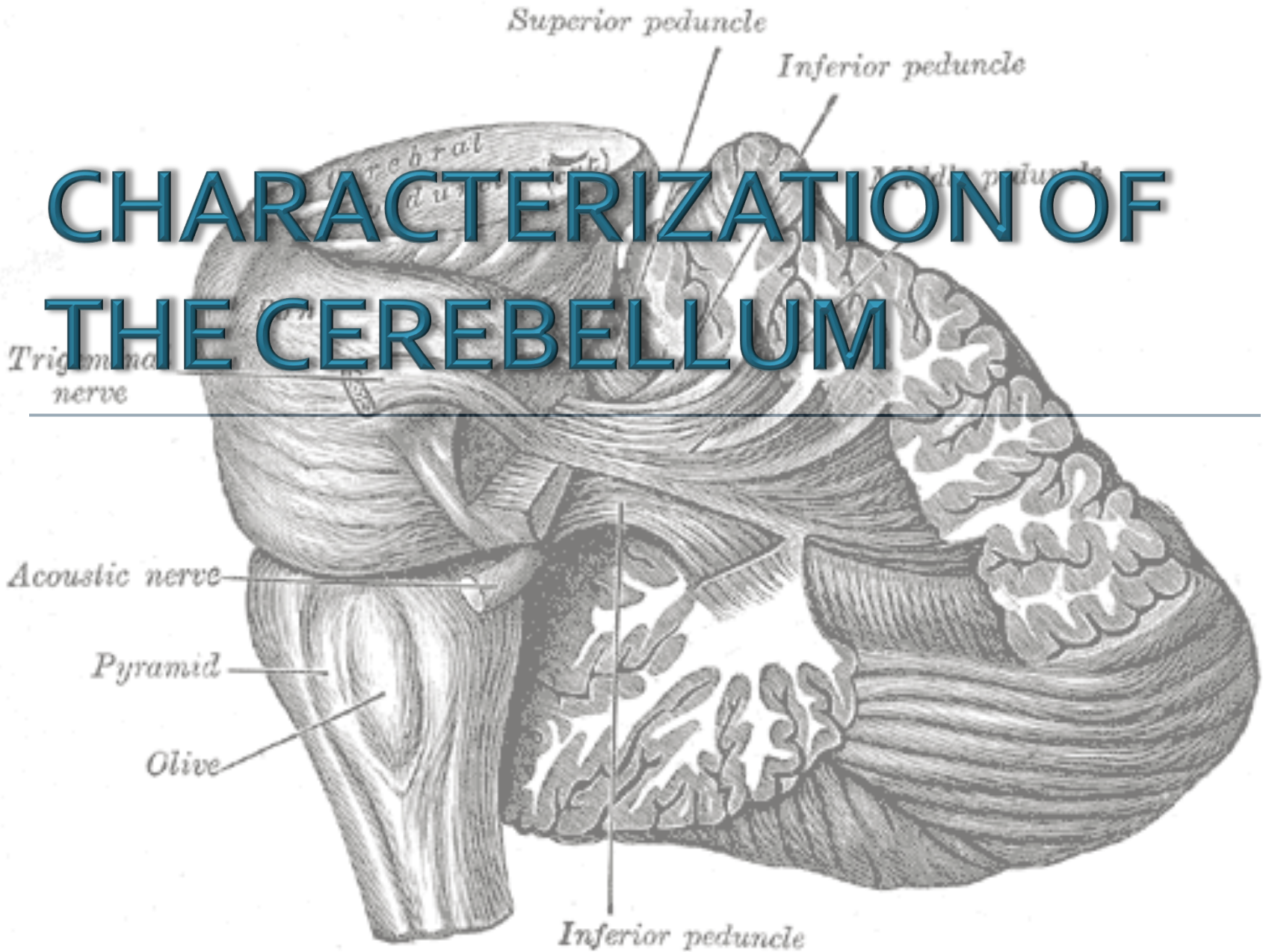


Courtesy of Gloria Castellazzi

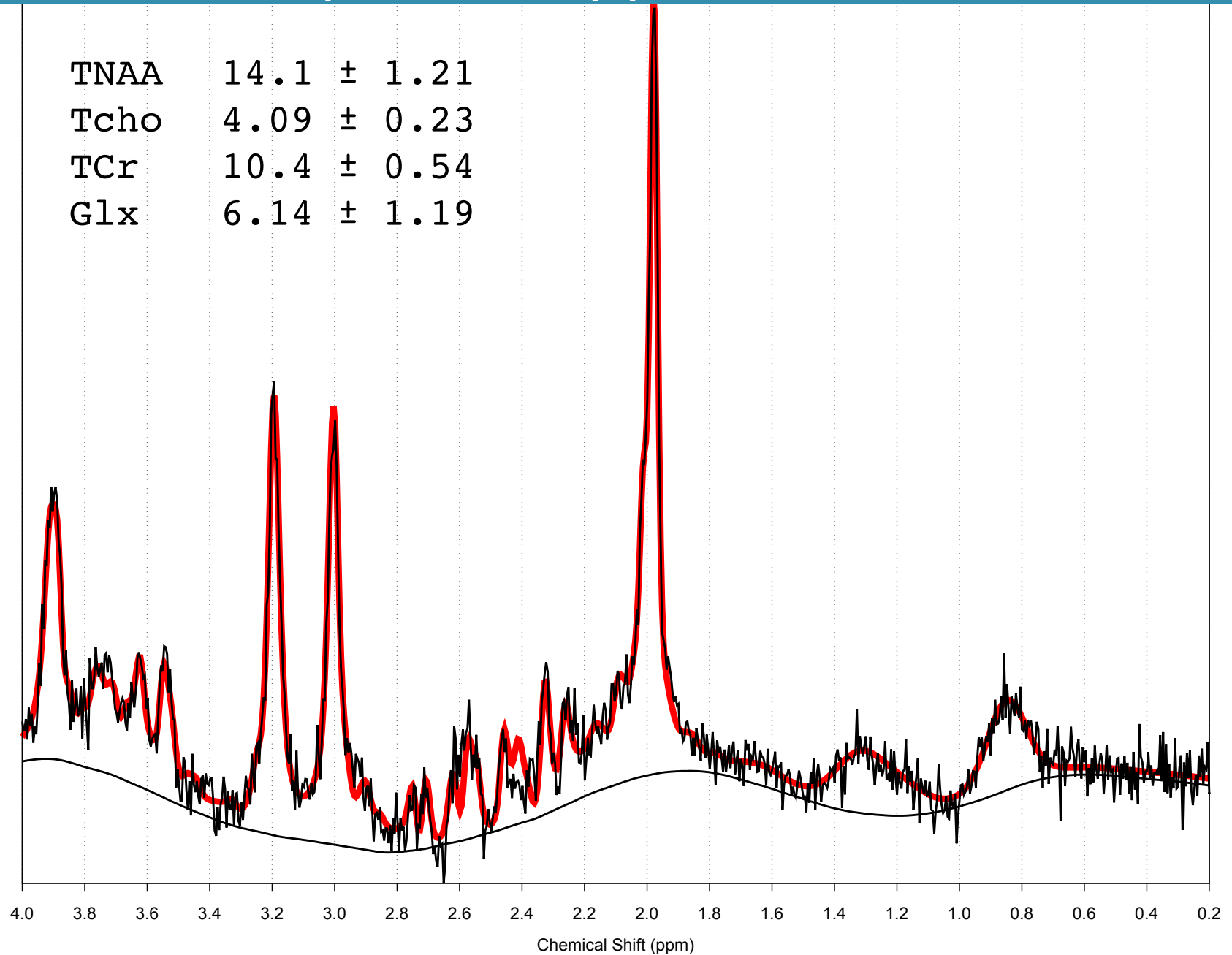
NEUROLOGICAL APPLICATIONS

What can we know about anatomy and diseases?

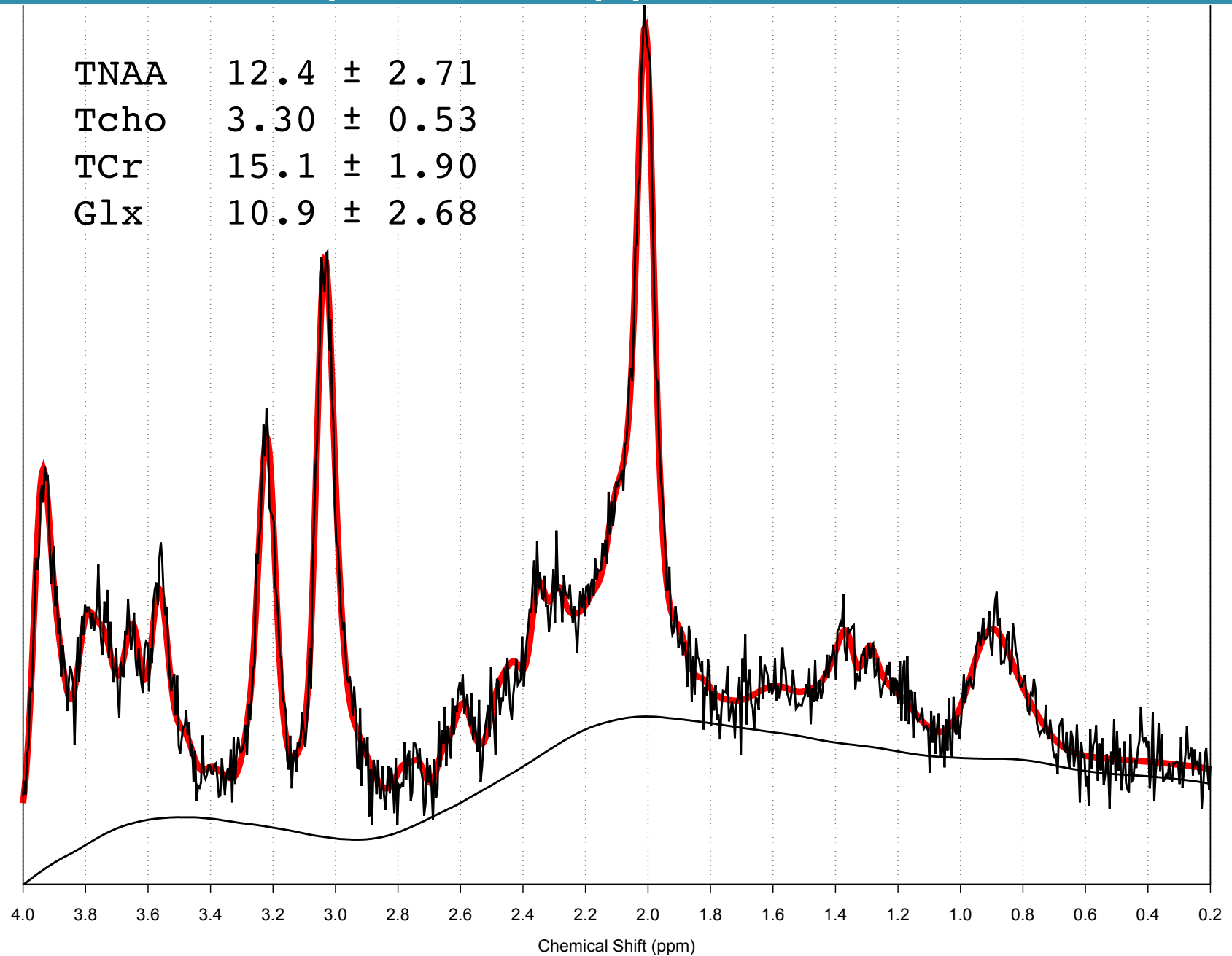
CHARACTERIZATION OF THE CEREBELLUM



Cerebellar Spectroscopy – WM brain

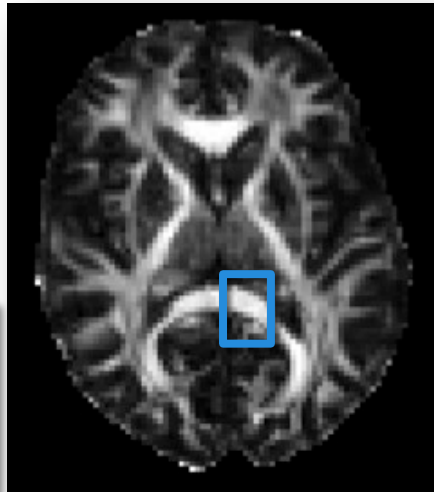


Cerebellar Spectroscopy – GM cerebellum

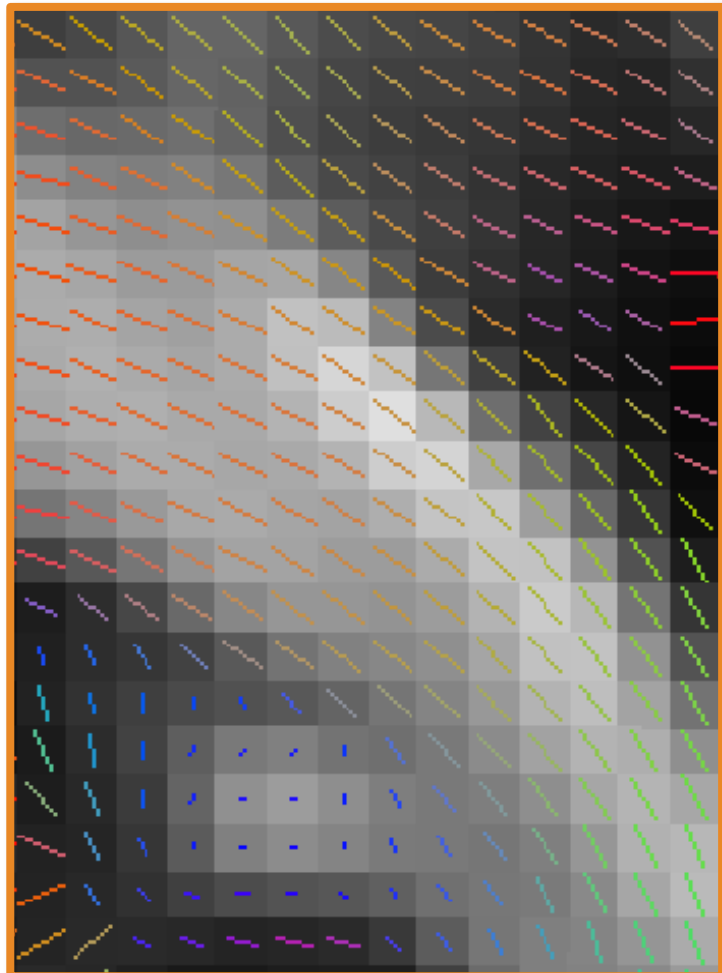
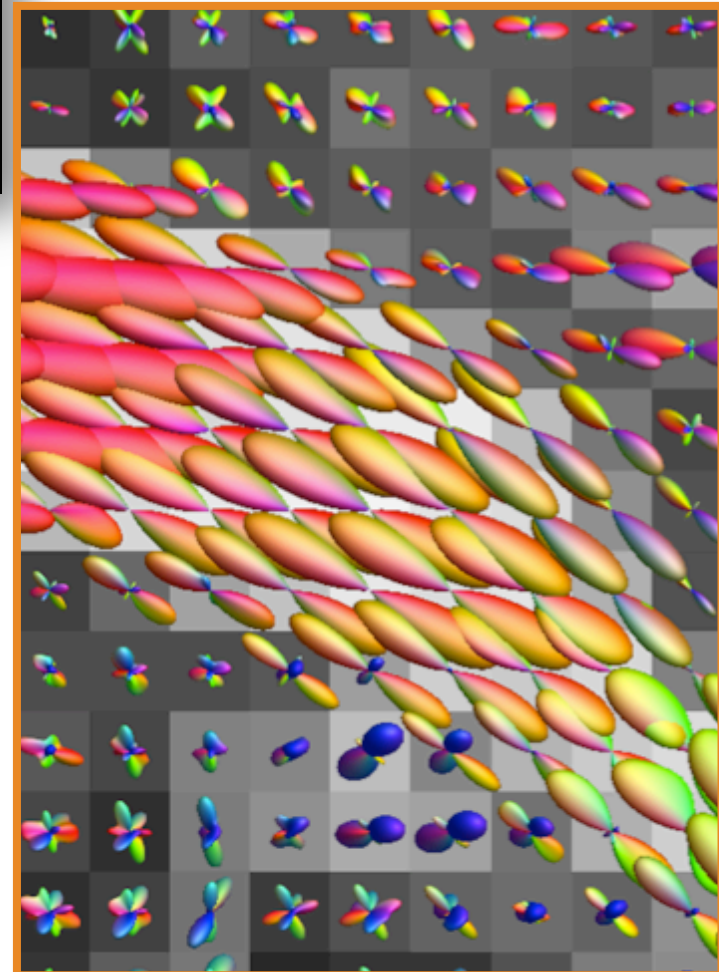


Cerebro-cerebellar loop – Tractography

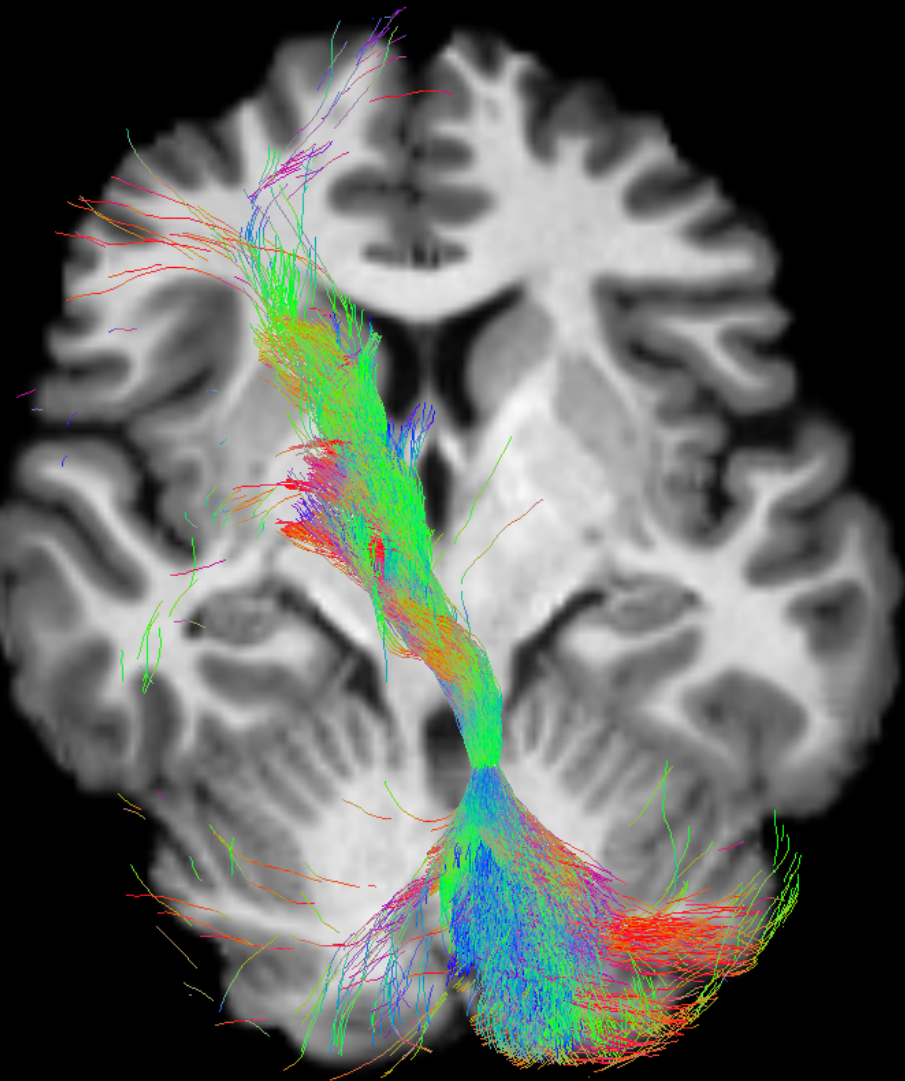
Diffusion Tensor



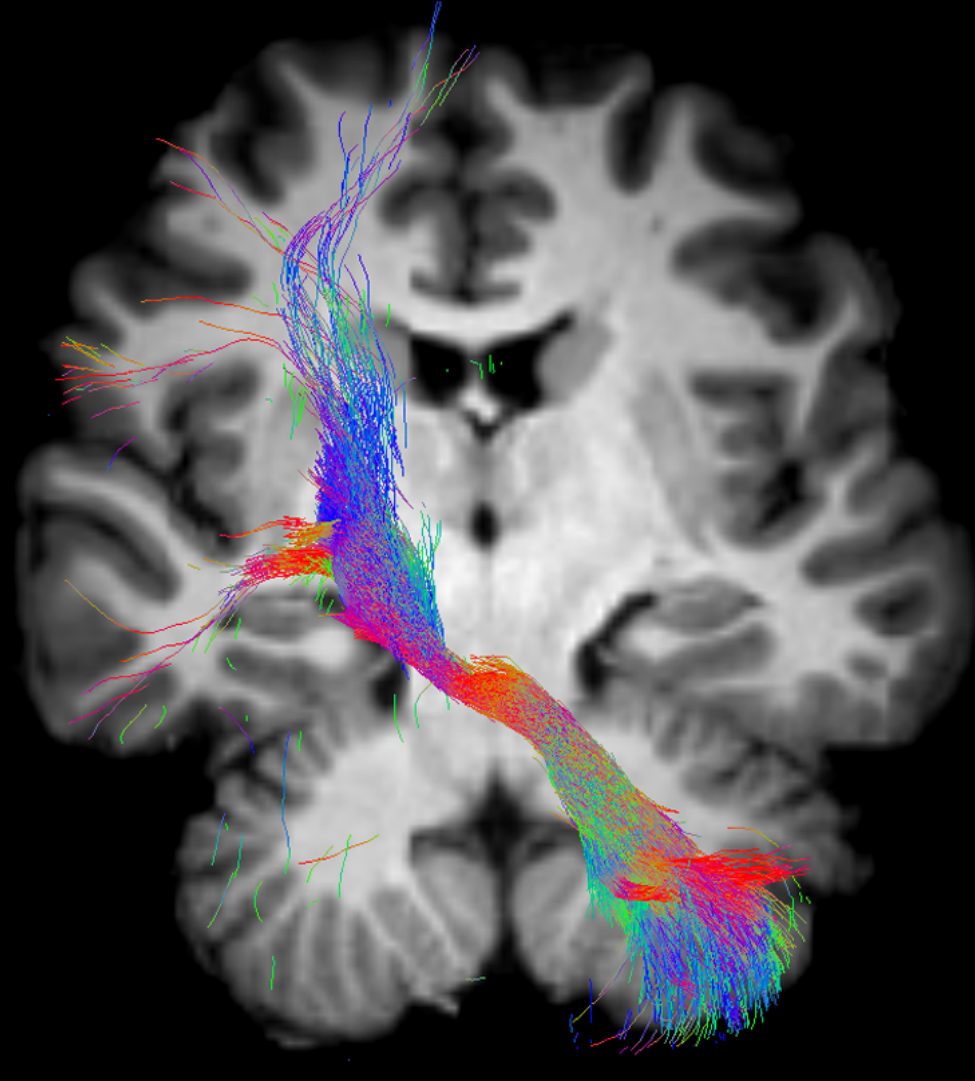
Constrained Spherical Deconvolution



Cerebro-cerebellar loop

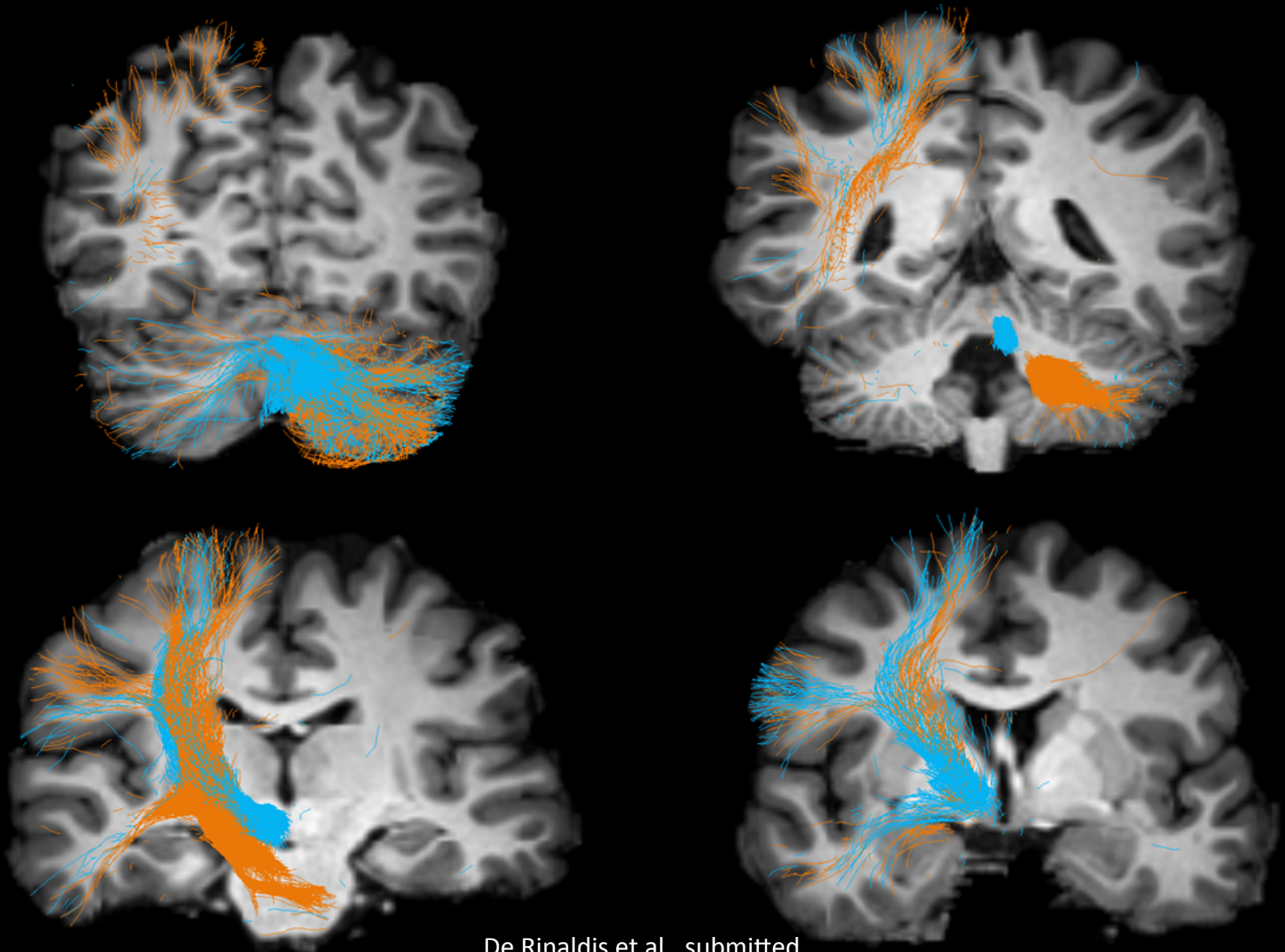


Left SCP

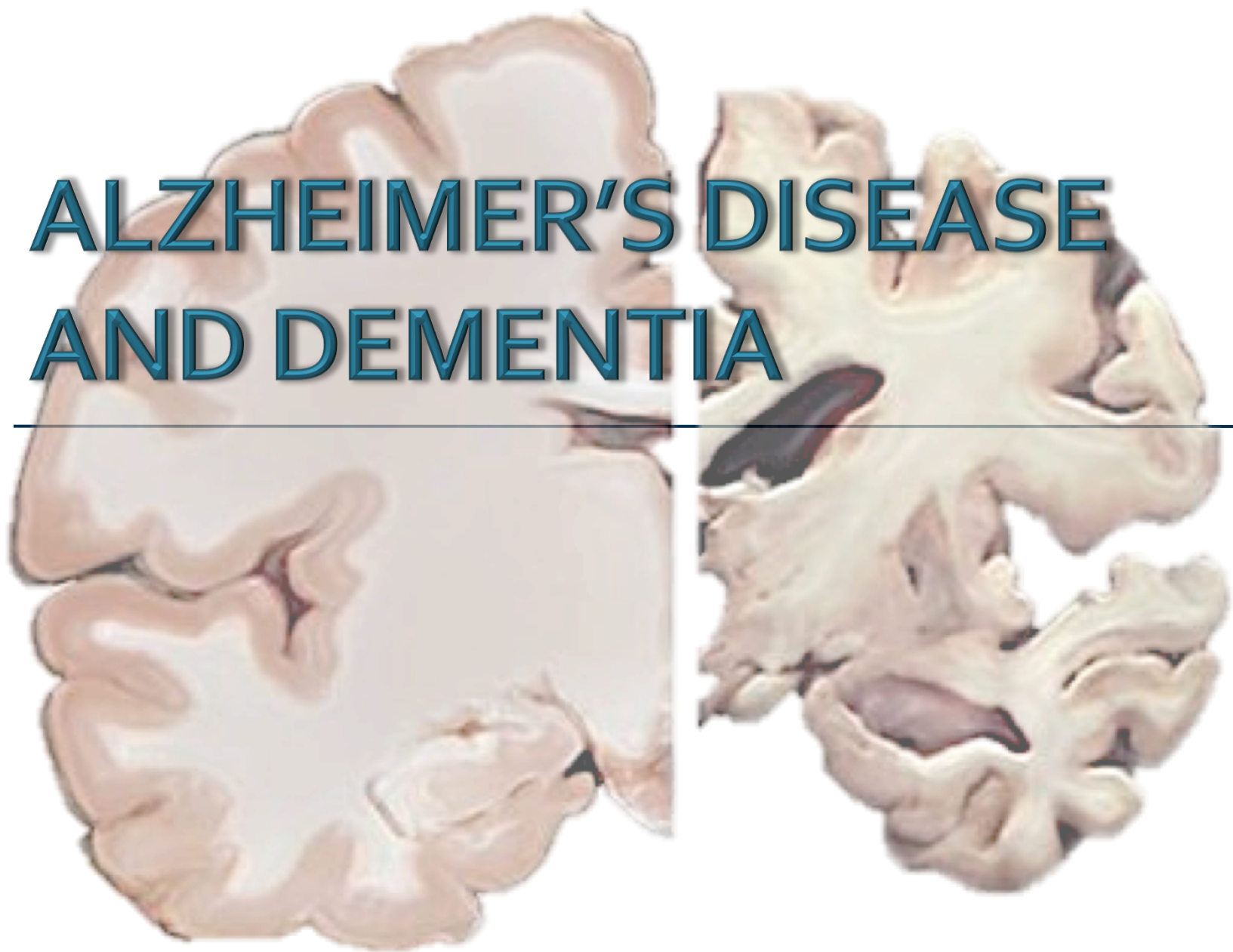


Left MCP

Cerebro-cerebellar loop

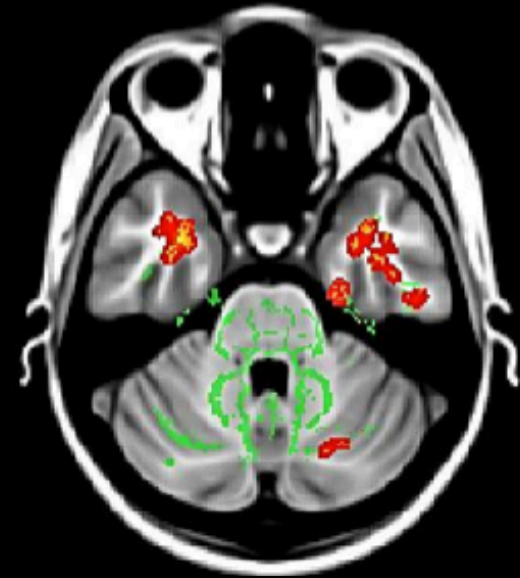
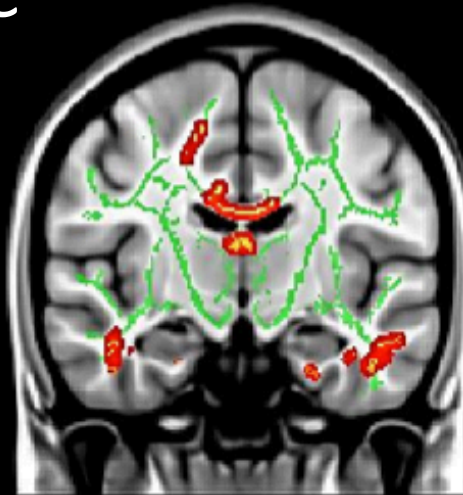
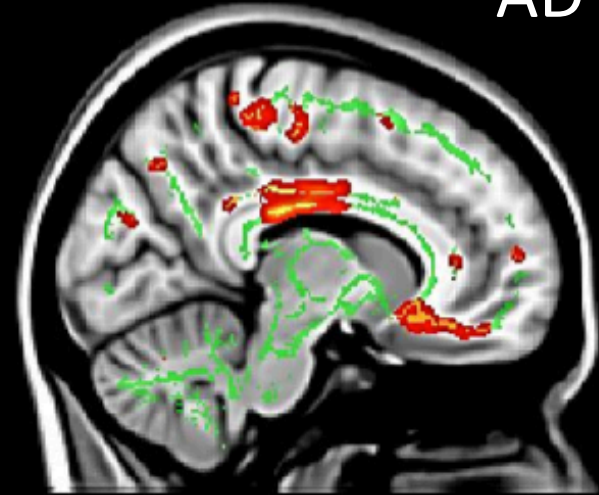


ALZHEIMER'S DISEASE AND DEMENTIA

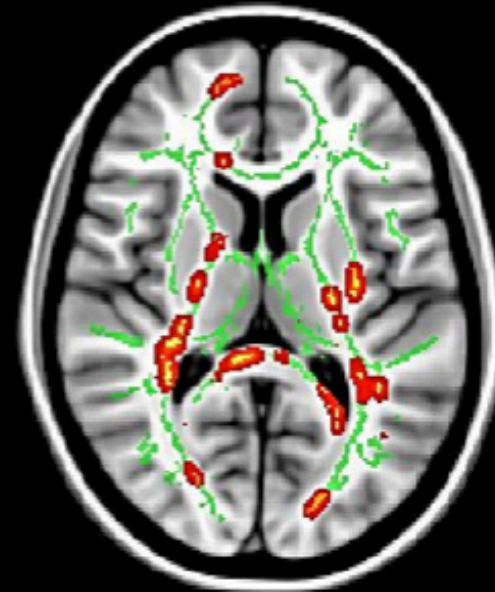
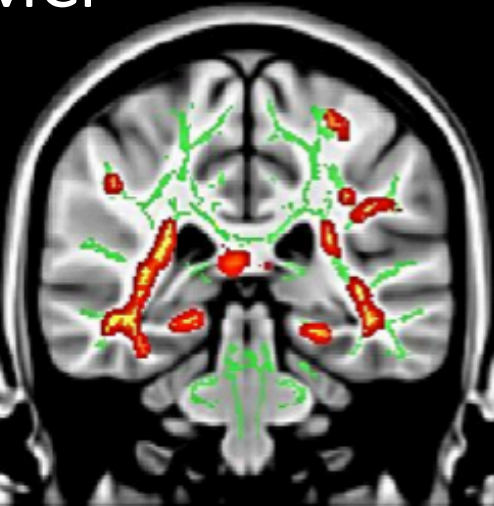
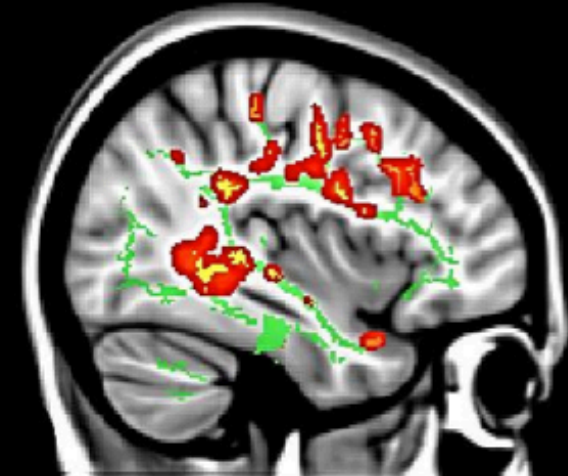


Alzheimer's disease & mild cognitive impairment – FA reduction

AD < HC



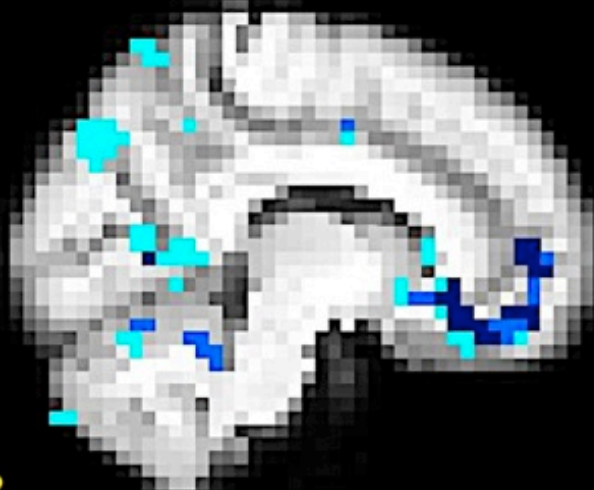
cMCI < ncMCI



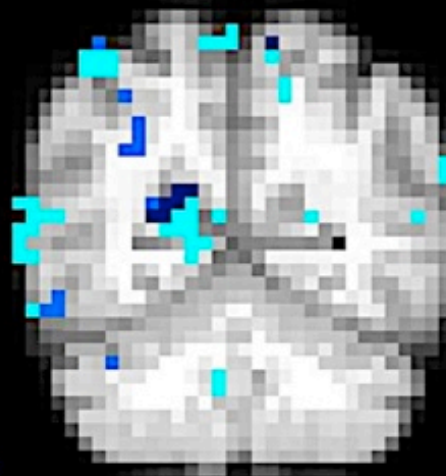
Courtesy of Letizia Casiraghi

Alzheimer's disease & mild cognitive impairment – functional connectivity alterations

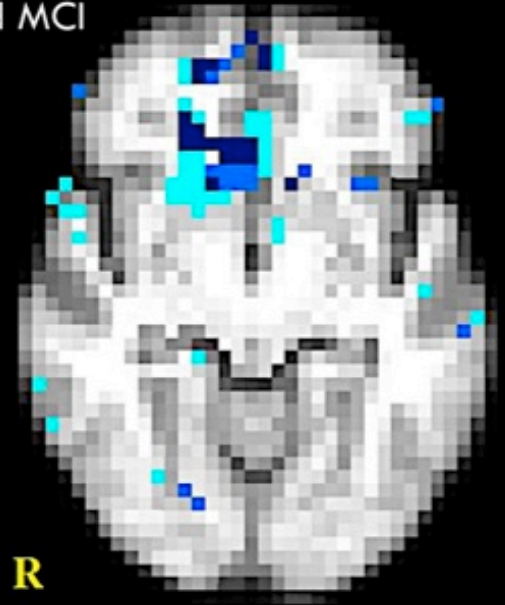
■ reduced FC in AD ■ reduced FC in MCI ■ reduced FC in both AD and MCI



P

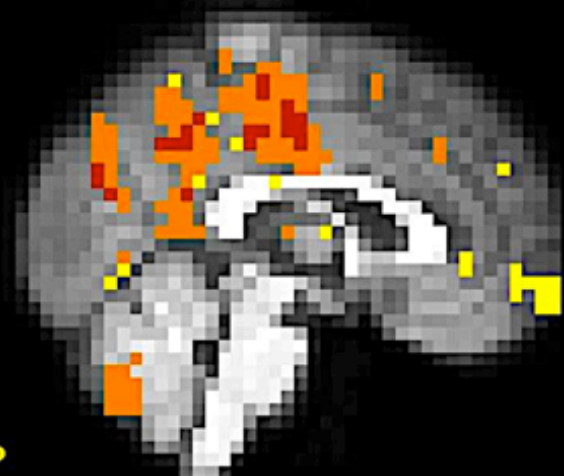


R

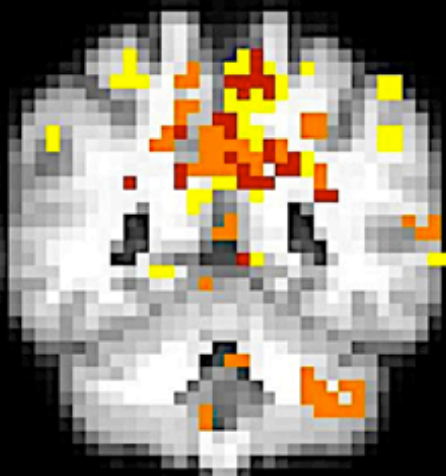


R

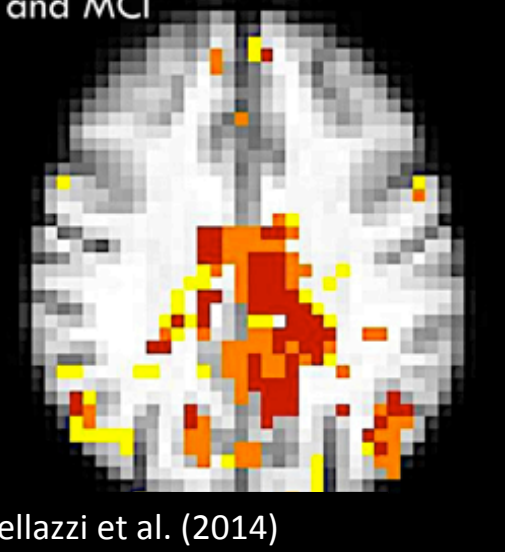
■ increased FC in AD ■ increased FC in MCI ■ increased FC in both AD and MCI



P

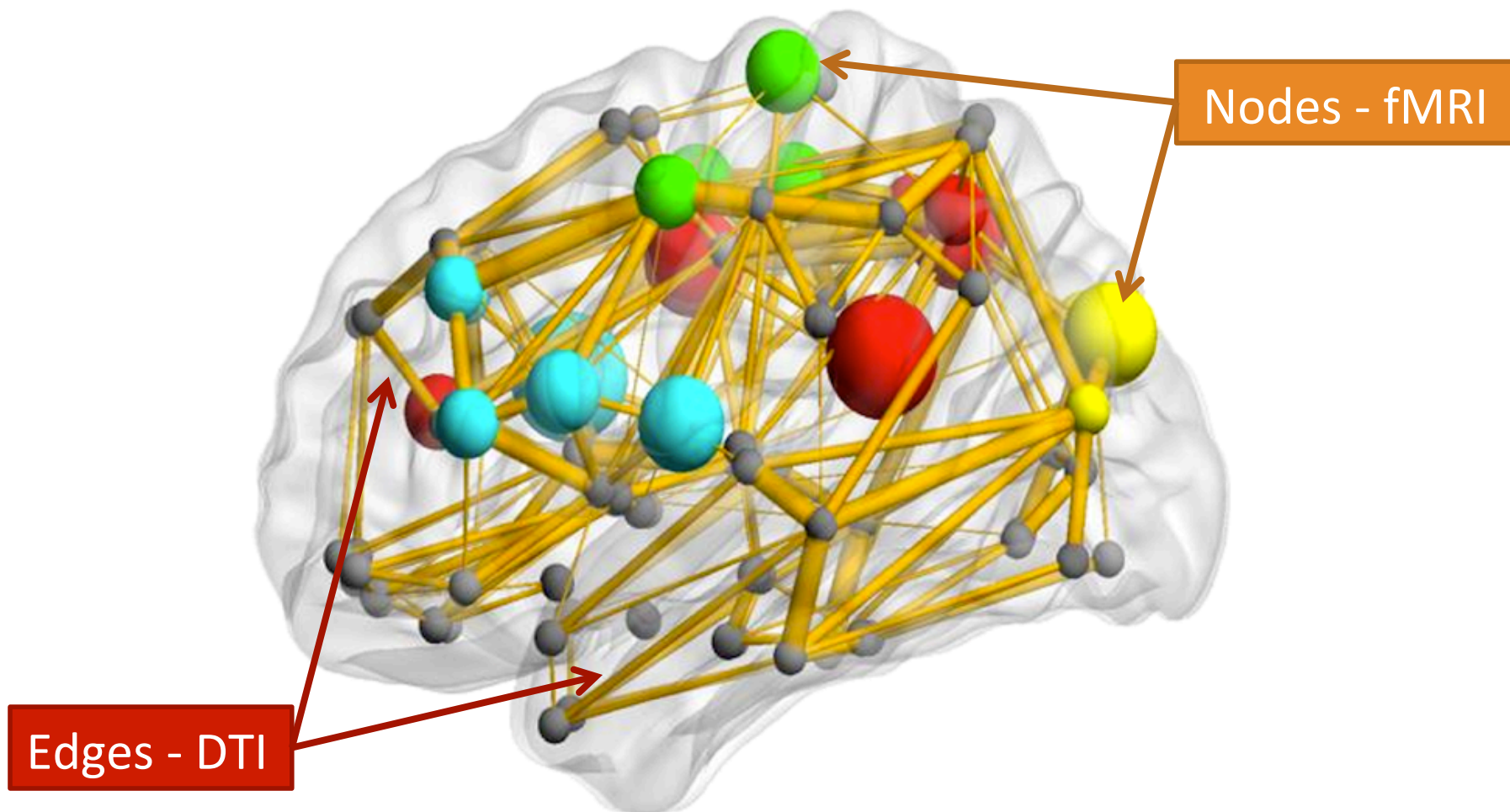


R

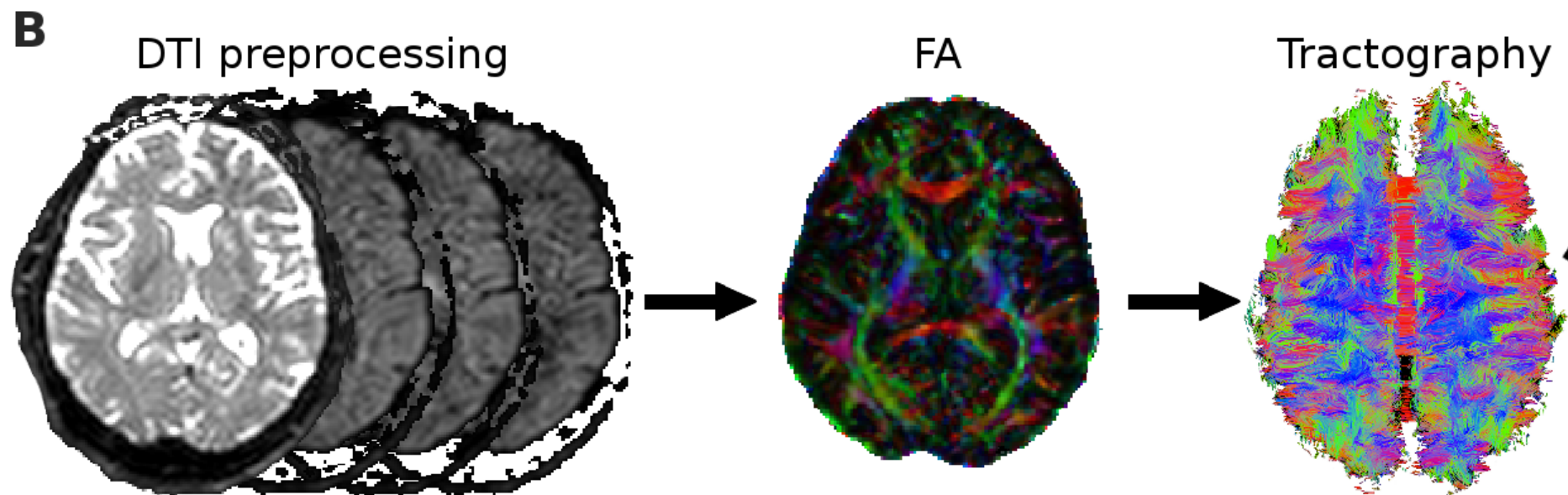
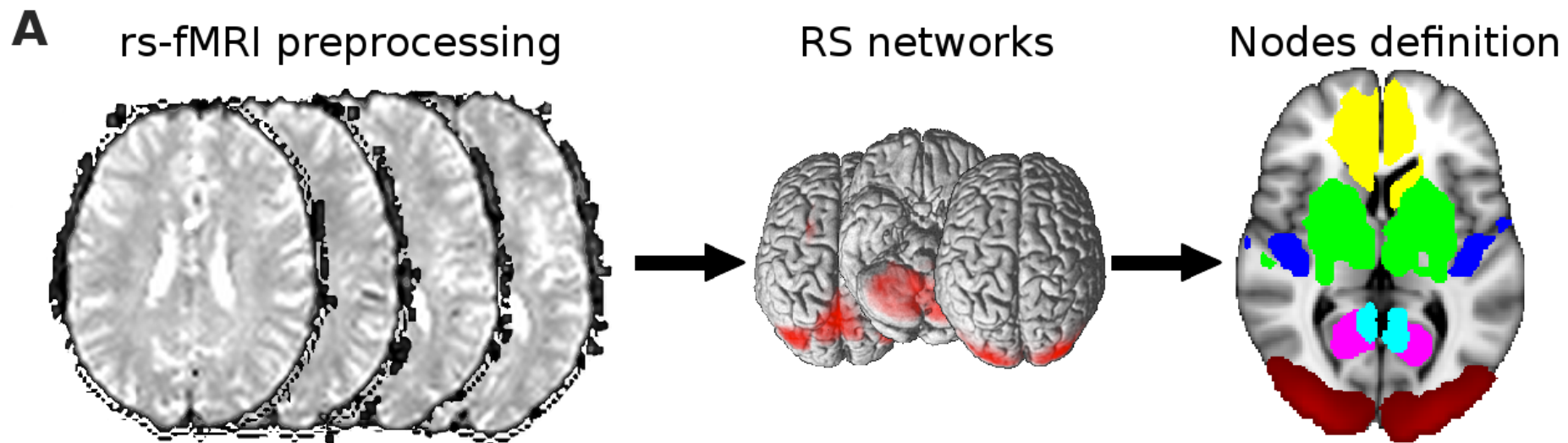


Overview structure and function of the brain

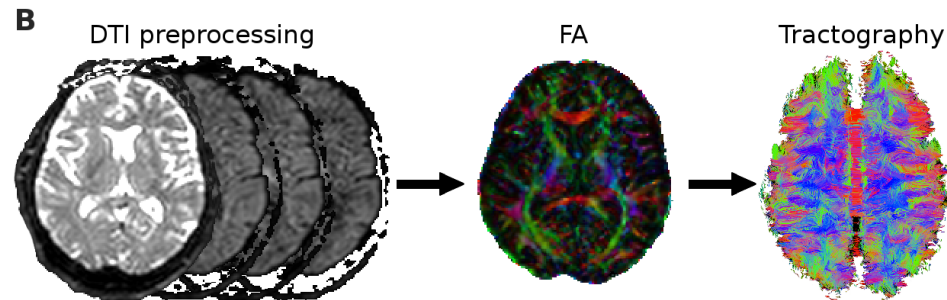
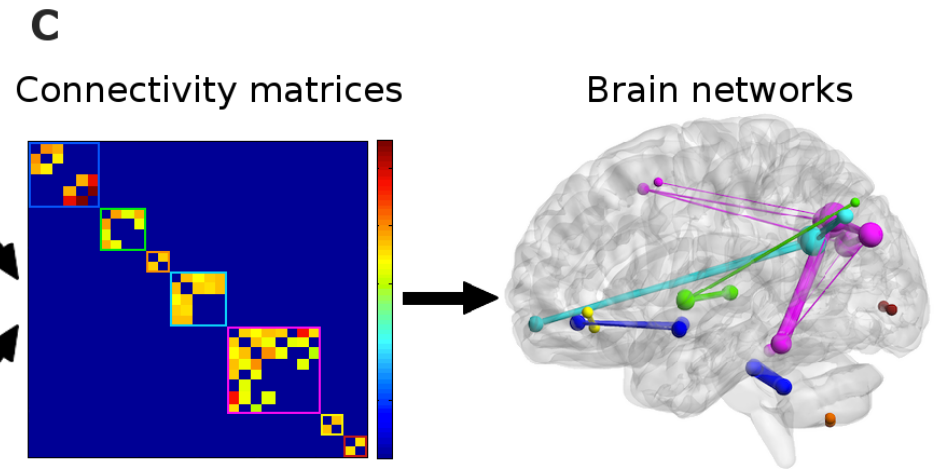
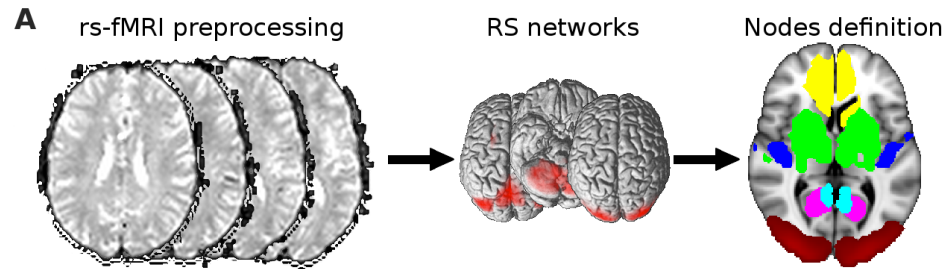
Combined MRI modalities to assess structure/function relationship



Workflow

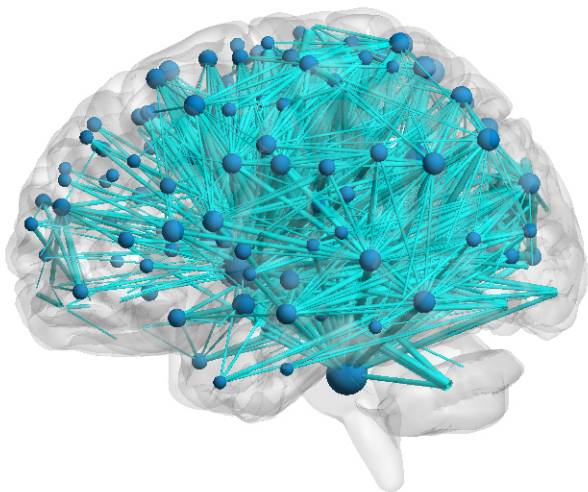


Workflow

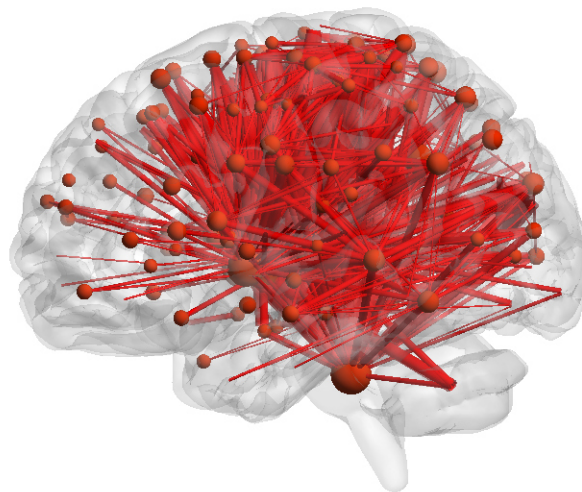


Alzheimer's disease & Vascular dementia

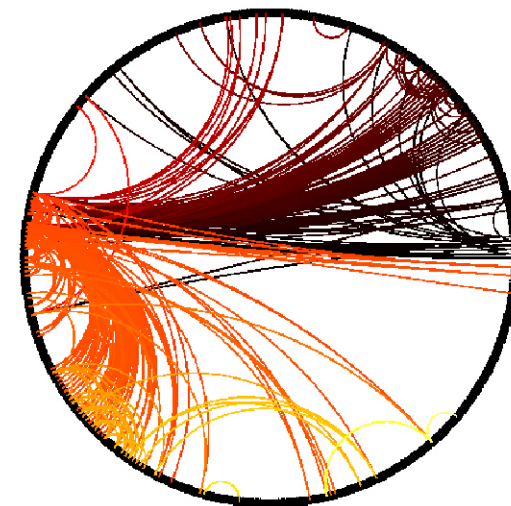
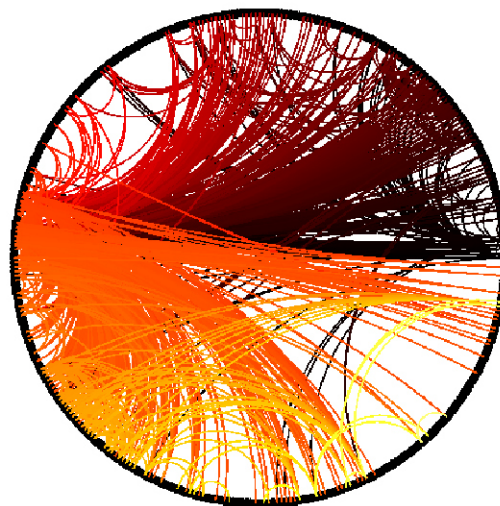
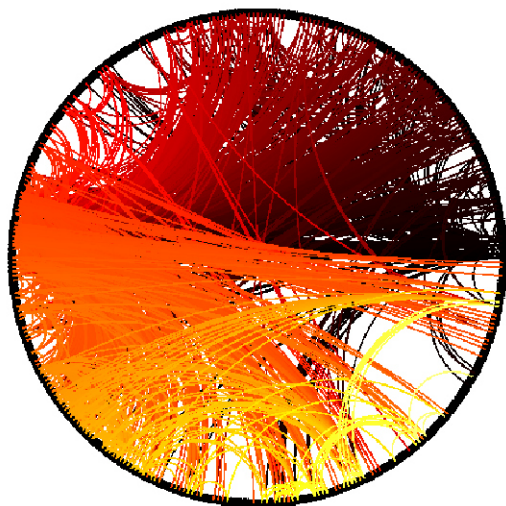
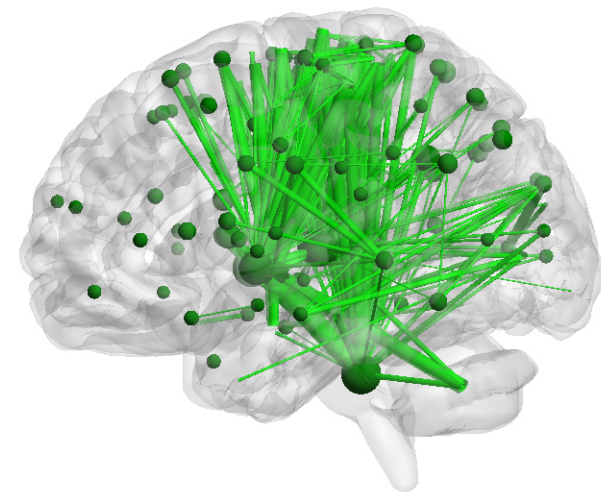
HC



AD



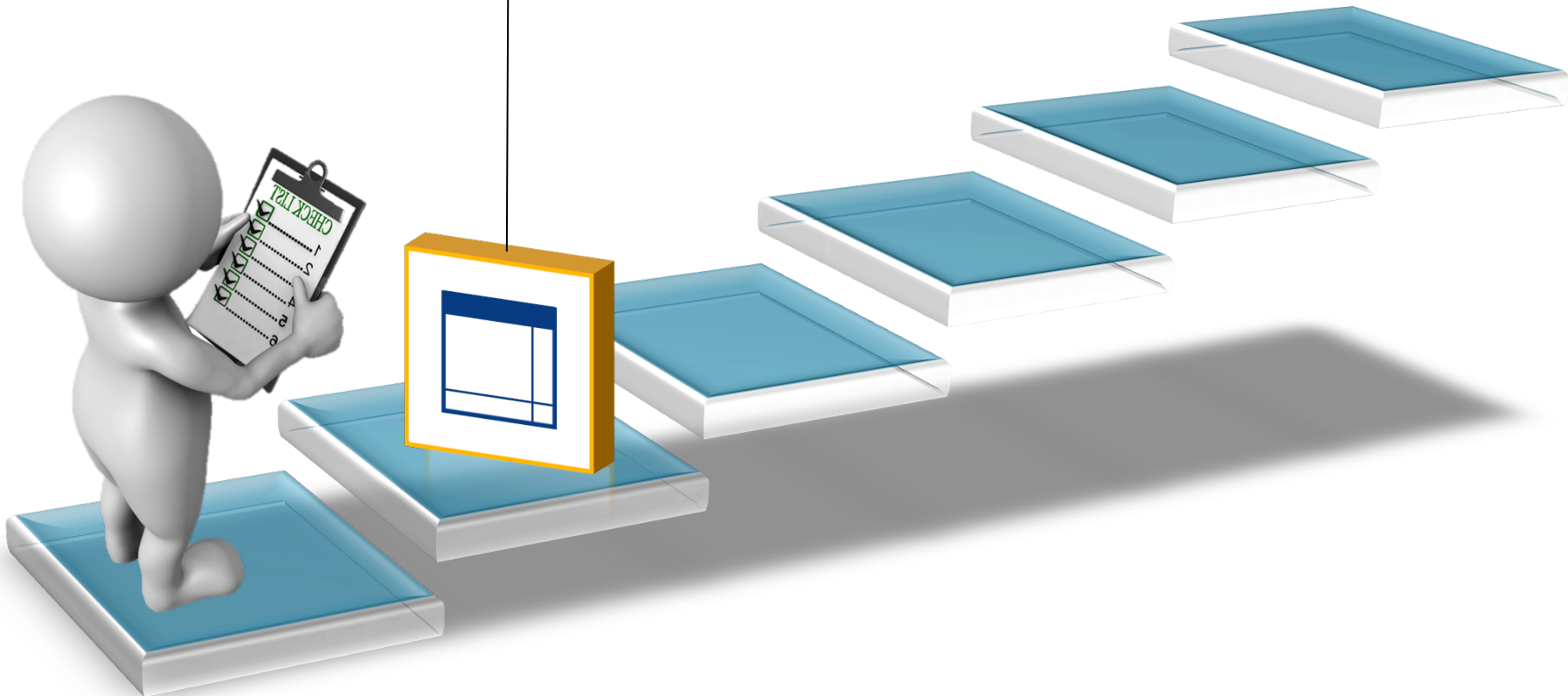
VaD



Beyond groups – Single subject classification

Dataset

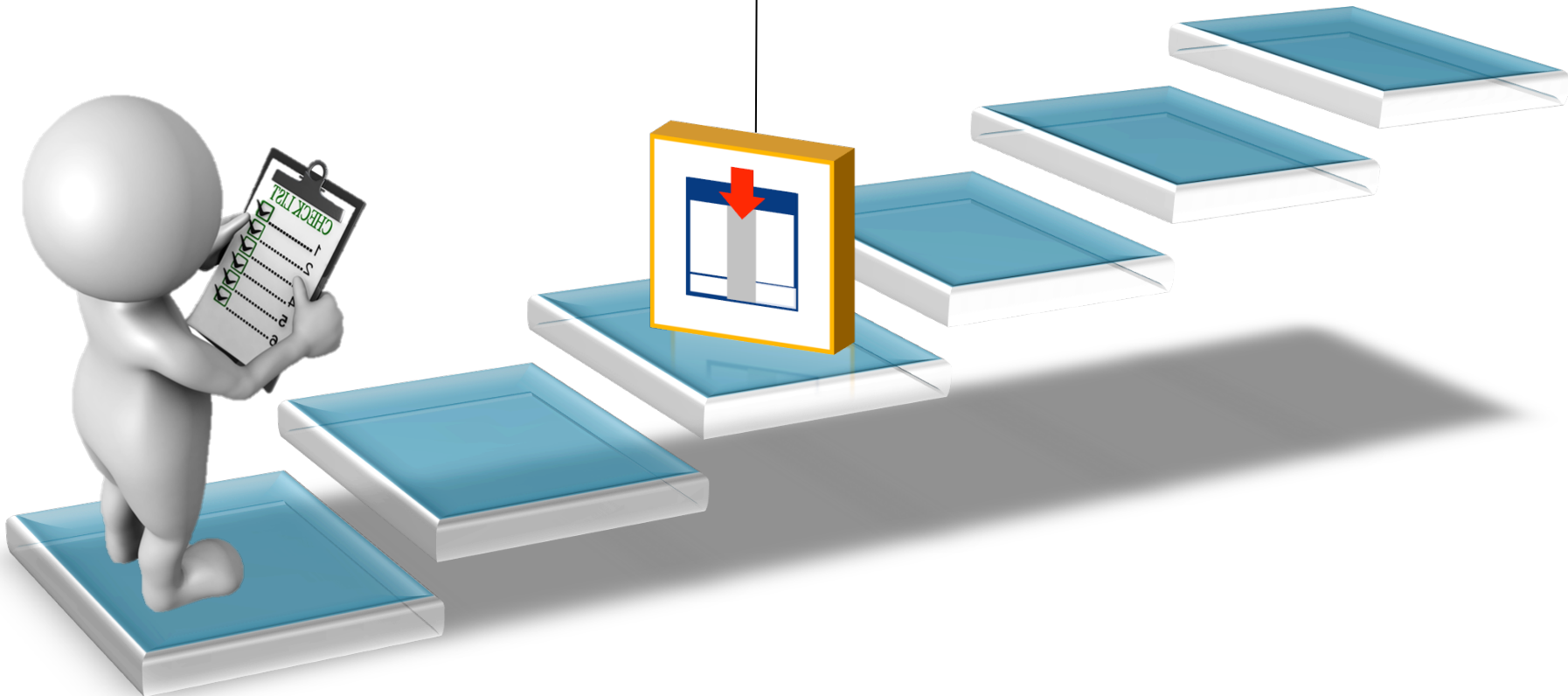
Quantitative indices from
clinical tests and MRI



Beyond groups – Single subject classification

Feature Selection

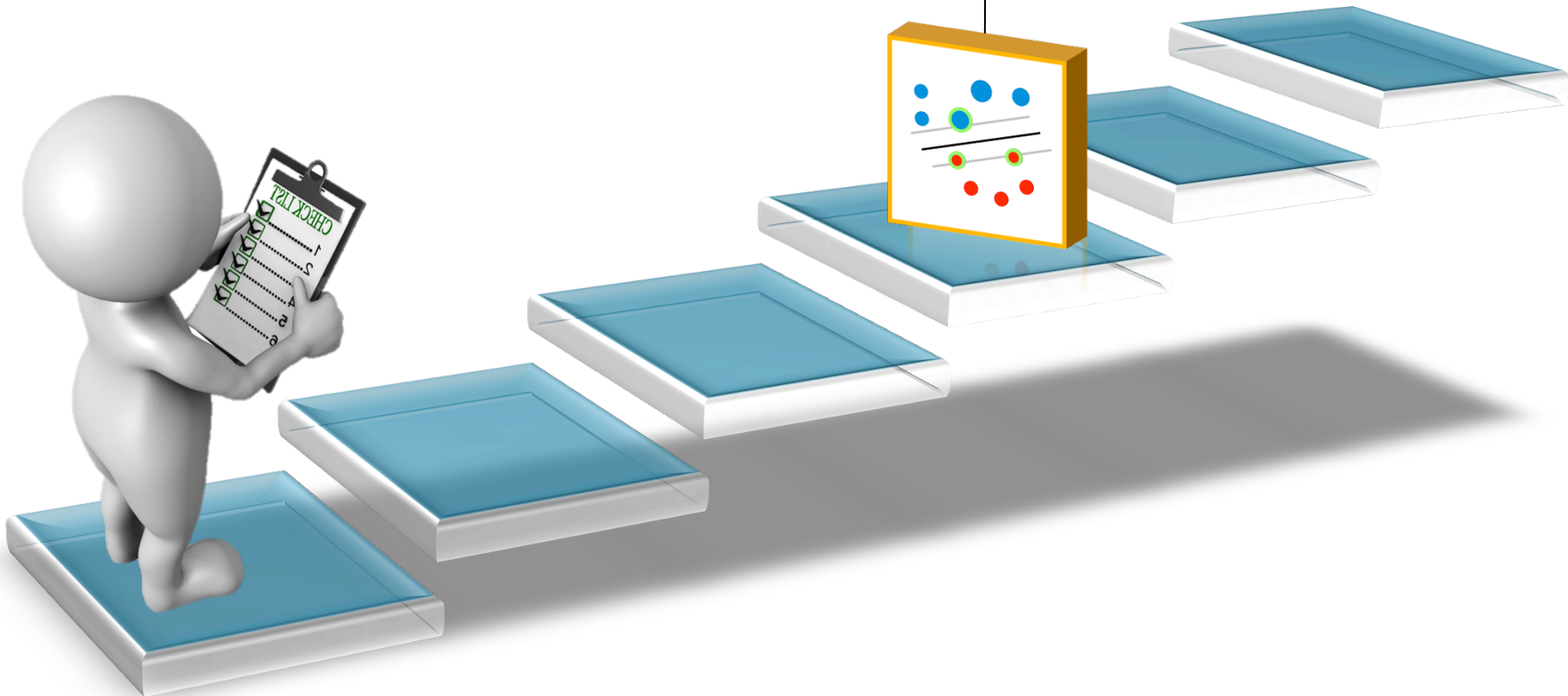
- Kruskal-Wallis test
- Relief algorithm



Beyond groups – Single subject classification

Classification

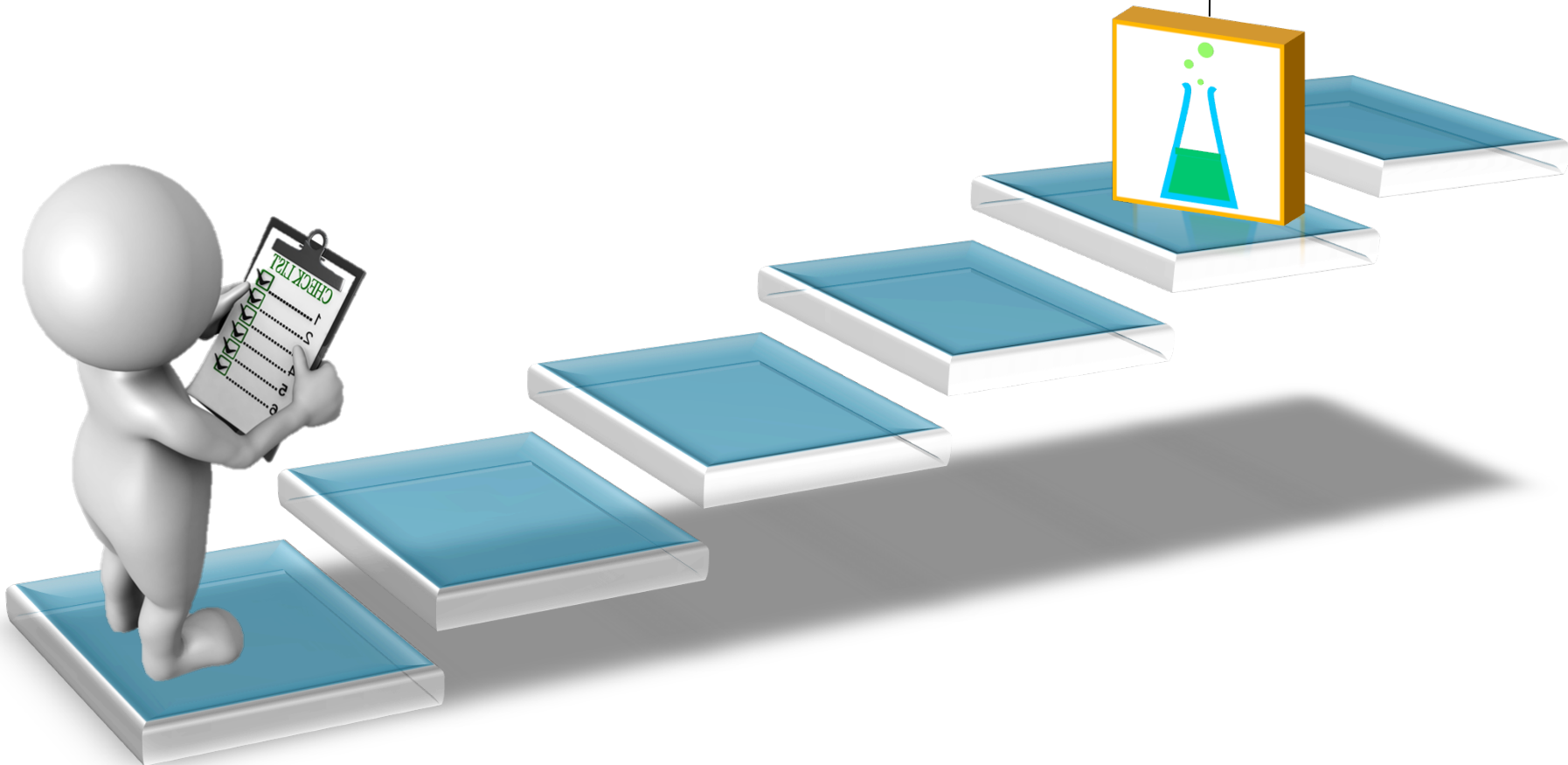
- Support Vector Machine (SVM)
- RBF kernel ($C=1.0$, $v=0.5$)
- SVM Training



Beyond groups – Single subject classification

Validation

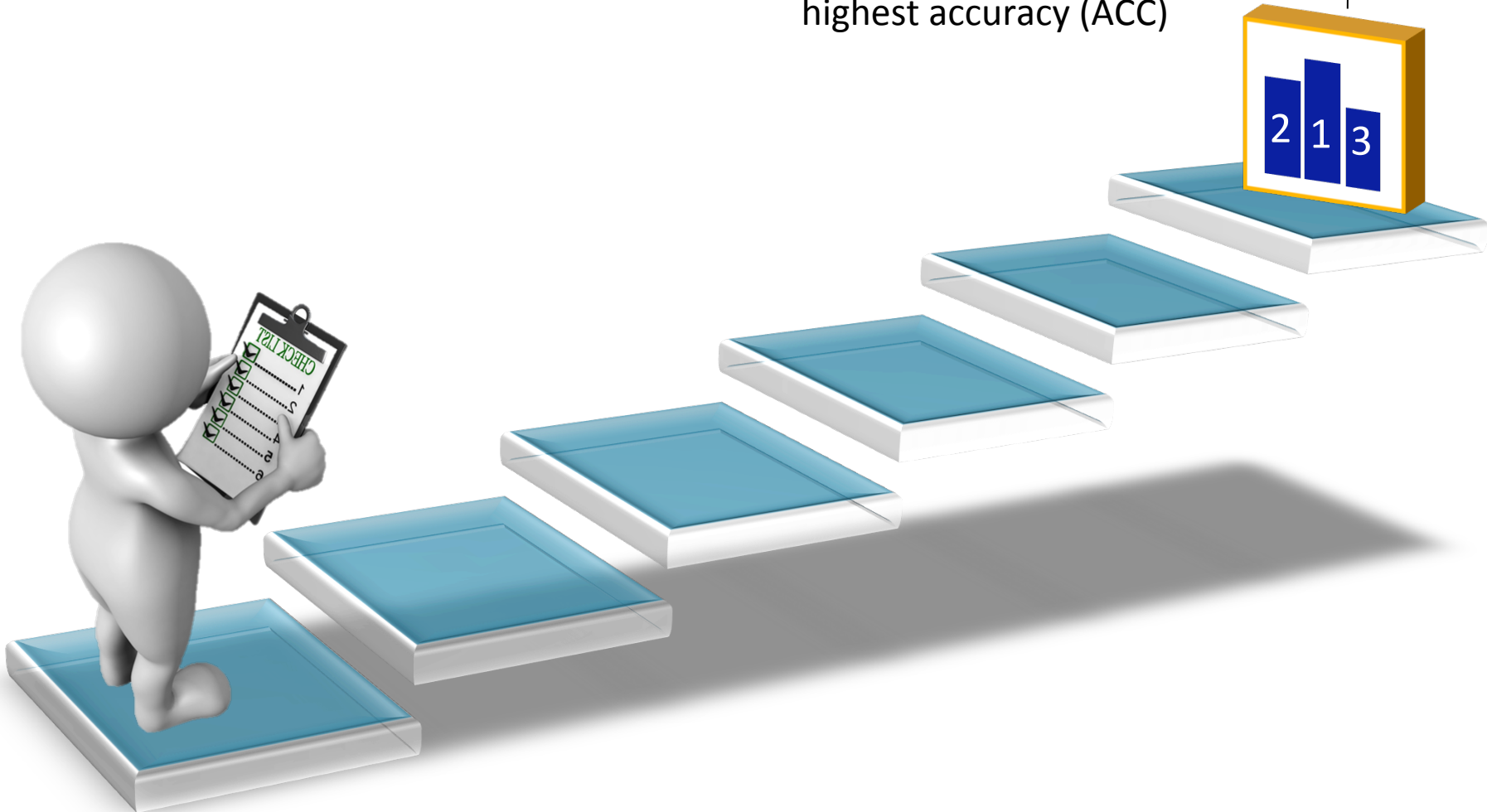
- SVM test



Beyond groups – Single subject classification

Best features

Pool of the most informative features to discriminate between two groups with the highest accuracy (ACC)



Converter MCI vs non converter MCI

Conversion to AD is predicted

with an accuracy of 77%

using multi-modality (rs-fMRI + DTI + NPS + sMRI)

