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JÜLICH FORSCHUNGSZENTRUM

Diffusion MRI

Overview

Part 1

- Diffusion: Overview
- Diffusion MRI

Part 2

- Anisotropic Diffusion
- Diffusion Tensor Imaging
- Fibre Tracking
- Restricted diffusion

Part 3

- Clinical use
- Advanced Diffusion MRI

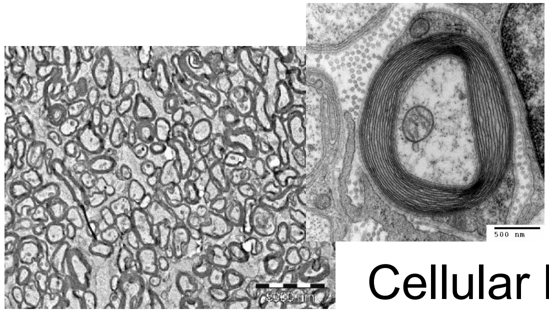
Acknowledgement: Dr. Ezequel Farrher for provided figures/pictures

Diffusion MRI is a unique modality of brain MRI

We can non-invasively examine

- Tissue microstructure

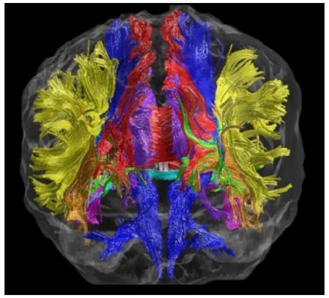
  (~ 1-10 μm)



Cellular level

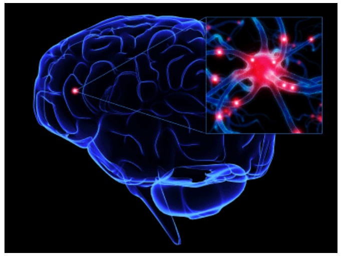
- Global white matter organization

  (~ 0.1 - 10 cm)



Whole brain

- Brain function and connectivity



Whole brain

Ultimate goals

- to provide biomarkers of tissue condition

- neurodegenerative pathologies (Alzheimer's and Parkinson's diseases, etc.)
- development and aging
- stroke
- tumours
- neurosurgical planning

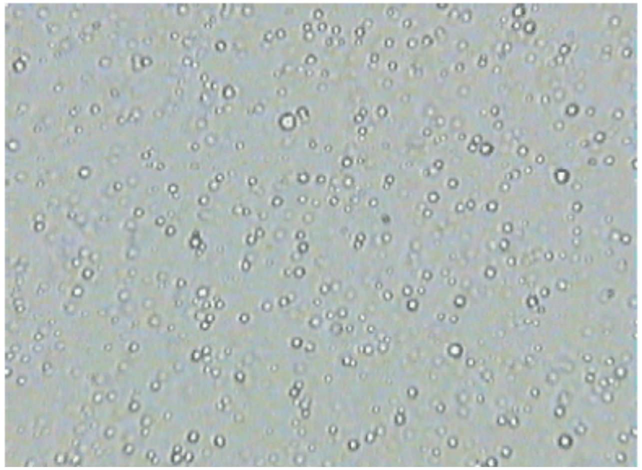
- to explore biophysical mechanisms of diffusion

Observation of Diffusion

• 1828 – “A brief Account of Microscopic Observations” Robert Brown described a phenomenon which is now known as “Brownian Motion”

Robert Brown
1828

Brownian Motion

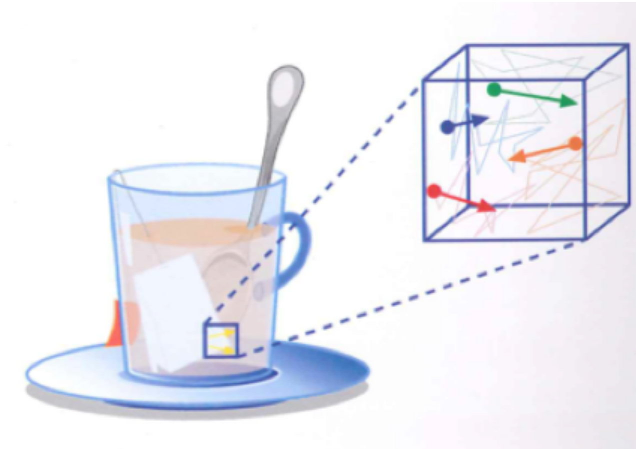


Random particle movements of pollen grains on the water surface

Scottish botanist Robert Brown was first to observe spontaneous vibration of pollen particles under the microscope in 1827.

Diffusion

- **Diffusion** refers to the random, microscopic movement of water and other small molecules due to thermal collisions.
- The rate of diffusion depends on temperature, viscosity of the fluid and the size (mass) of the particles.



Two ways to introduce **diffusion**:

a) Phenomenological approach based on Fick's laws of diffusion

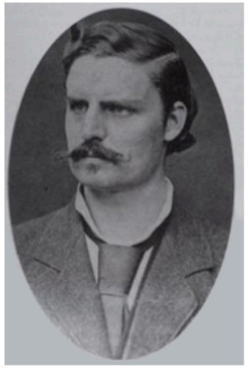
b) Atomistic approach based on the random walk model of diffusion

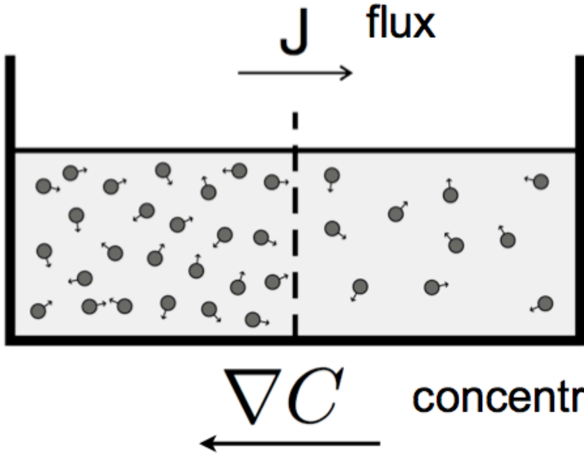
Diffusion

Fick's First Law

Adolf Fick

1855





concentration gradient

Diagram: Diffusion MRI textbook, Johansen-Berg and Behrens.

Flux of particles is proportional to concentration gradient.

$$J = -D\nabla C$$

from high to low concentration

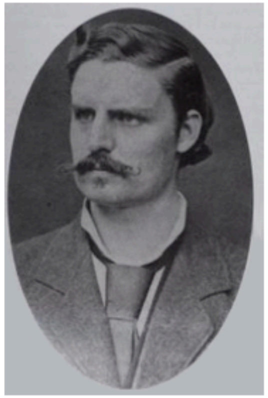
Diffusion coefficient

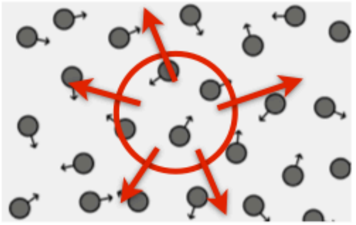
Diffusion

Fick's Second Law

Adolf Fick

1855





For an elemental volume:

Rate of change in concentration is equal to the net flux across its boundaries.

$$\frac{\partial C}{\partial t} = -\nabla \cdot J$$

$$(J = -D\nabla C)$$

$$\boxed{\frac{\partial C}{\partial t} = D\nabla^2 C}$$

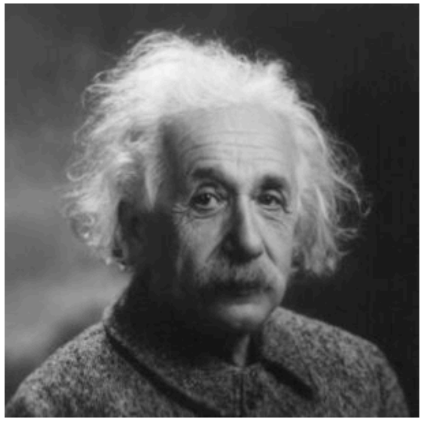
The rate of change of concentration at a point in space is proportional to the second derivative of concentration with space.

Self-diffusion

Self-Diffusion and Probabilities

Albert Einstein

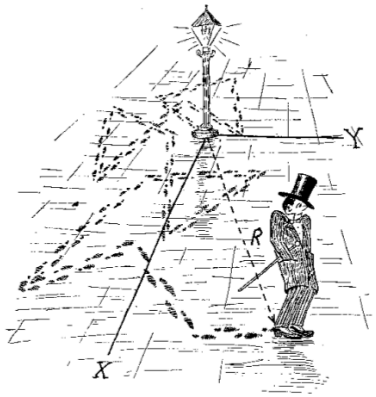
1905

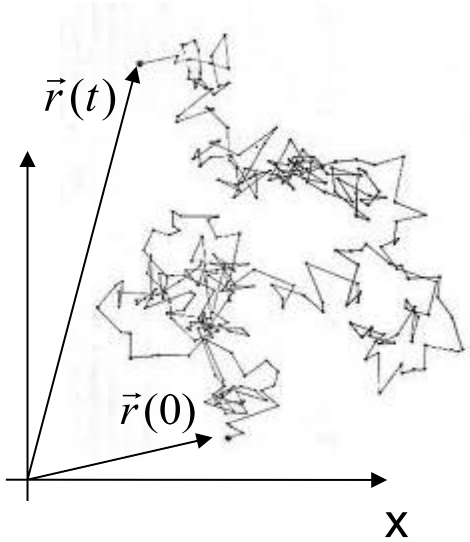


- Fick's Laws describe particles drifting from higher to lower concentration (***mutual diffusion***).
- Einstein applied the same idea to the case without a macroscopic concentration gradient (***self-diffusion***).
- Einstein ascribed Fick's Laws an interpretation based on probabilities.

“Random walk” model

- 1905 – Einstein provided a statistical description of diffusion.





$$\left\langle \left| \vec{r}(t) - \vec{r}(0) \right|^2 \right\rangle = 6Dt$$

Mean Square Displacement at the time *t* (averaged over the particle ensemble). What we measure with MRI.

Diffusion Coefficient

We can estimate *D* by measuring MRI signal

„Quantum Cloud“

Antony Gormley, London

Free diffusion in isotropic media

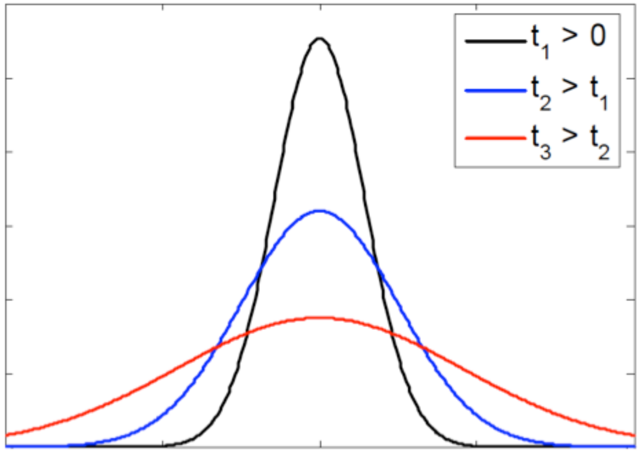
(isotropic, homogeneous, infinite)

Diffusion equation (initial conditions $P(r,0) = \delta(r=0)$)

$$\frac{\partial}{\partial t} P(r,t) = D\nabla^2 P(r,t)$$

D - diffusion coefficient

$$\boxed{P(r,t) = \frac{1}{(4\pi Dt)^{3/2}} \exp\left\{-\frac{r^2}{4Dt}\right\}}$$



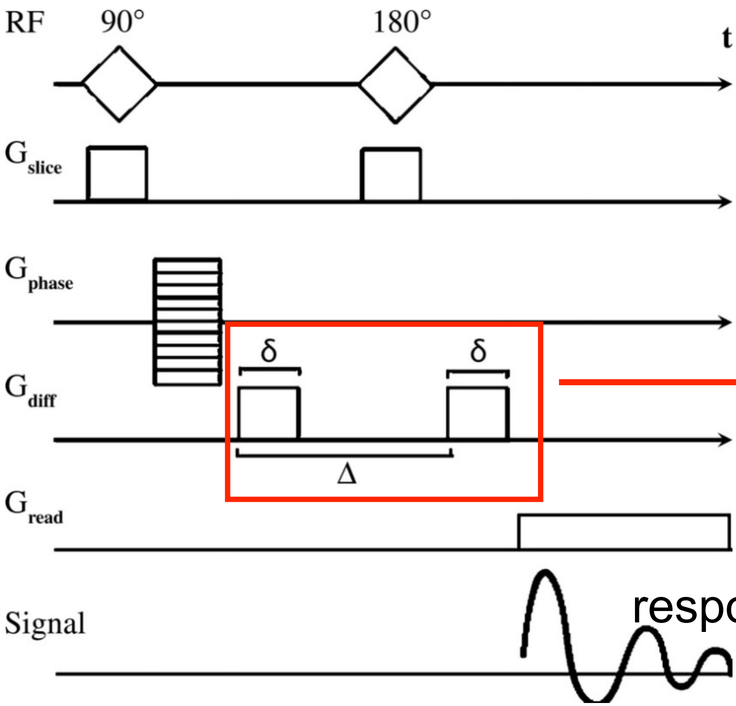
The propagator here is Gaussian

$$\boxed{\langle r^2 \rangle = 6Dt}$$

„normal" or Gaussian diffusion

Mean squared displacement

Diffusion MRI: pulsed field gradients



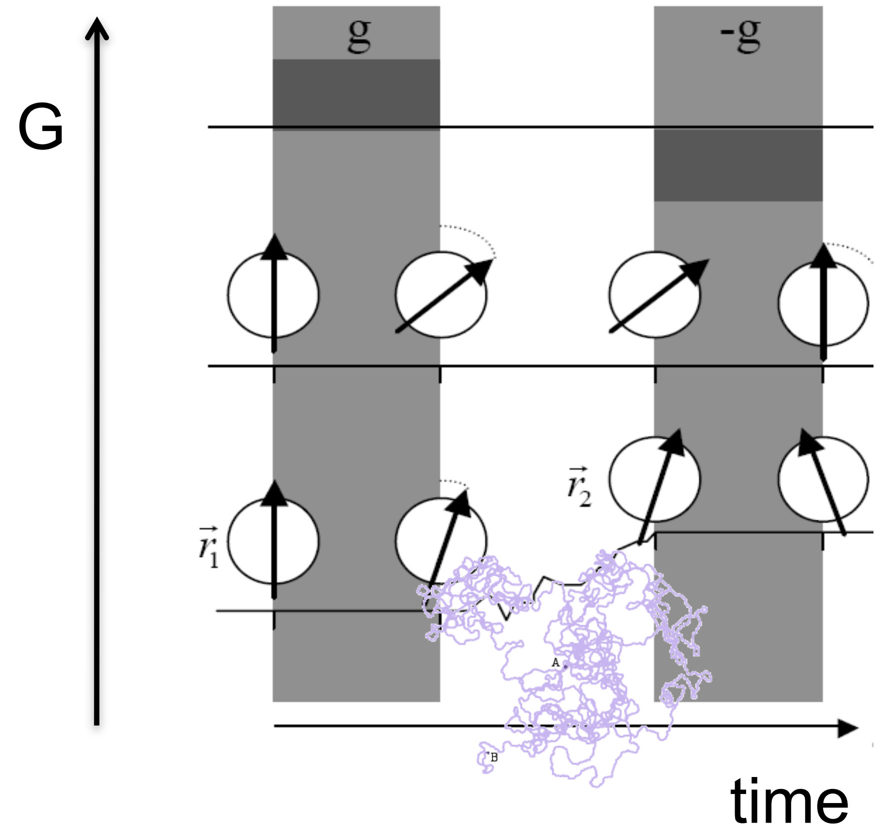
Diffusion weighting

response signal

propagator

$$\psi_{diff} = \int P(z,t)\, e^{i\gamma G\delta z}\, dz$$

Diffusion MRI: pulsed field gradients



In absence of diffusion:

$$z(t) = const$$

If diffusion occurs:

$$z(t) \neq const$$

$$\Delta\varphi = \gamma G \delta \Delta z$$

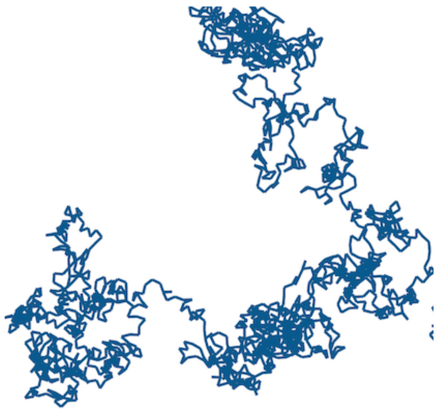
Echo amplitude is attenuated by diffusion

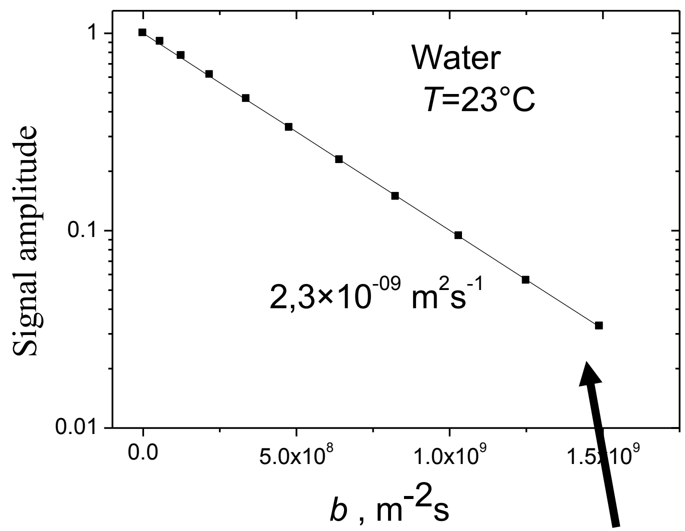
Gaussian diffusion

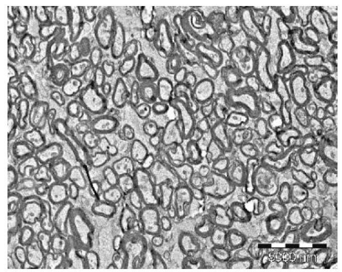
$$S(b) = S_0 e^{-b \cdot D}$$

$$b = (\gamma g \delta)^2 \left(\Delta - \frac{\delta}{3} \right)$$

D – diffusivity
b – "b-factor", i.e. diffusion weighting

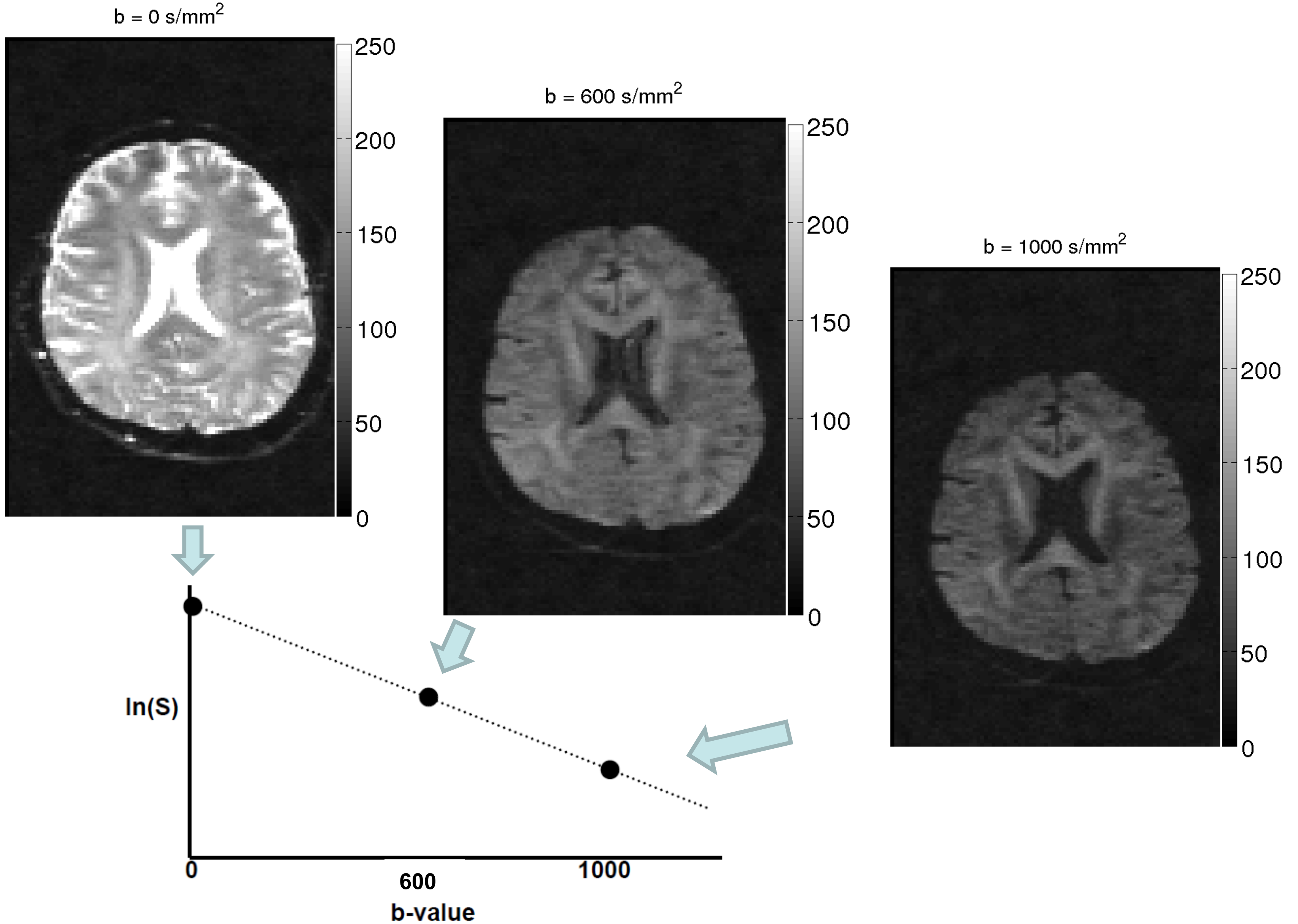






Mono-exponential function

Diffusion weighted imaging (DWI) in the human brain.



Diffusion in the brain tissue

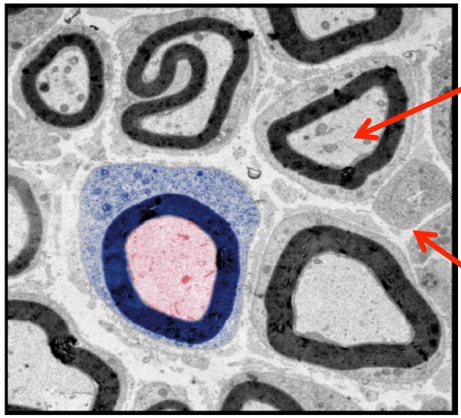
- Restricted
- Anisotropic

Courtesy of Dr. Ezequiel Farrher

Restricted diffusion

$$\langle x^2 \rangle = const$$

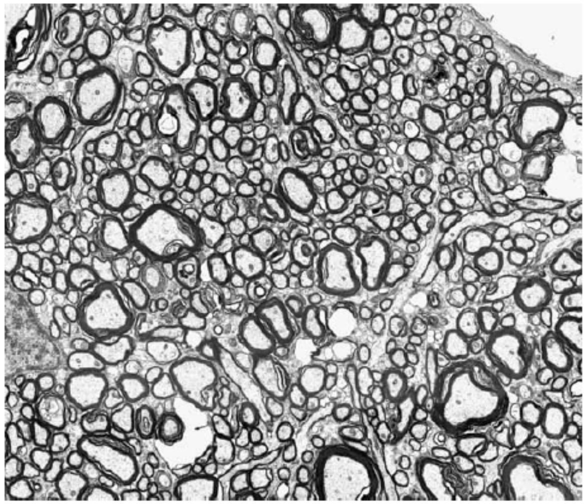
... determined by the pore or cell size



intra-cellular space (ICS) → ... restricted (in-plane) and might be localised

extra-cellular space (ECS) → ... restricted but not localised

Apparent Diffusion Coefficient (ADC)



Bundles of axons in the corpus callosum in the human brain.

Signal amplitude

$$S(b) = S_0 e^{-b \cdot ADC}$$

If diffusion is not free, but influenced by restrictions, what we measure is not intrinsic diffusion coefficient of water

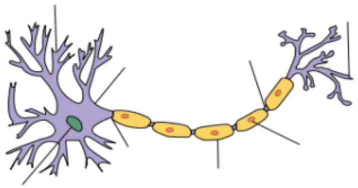
ADC is a phenomenological parameter

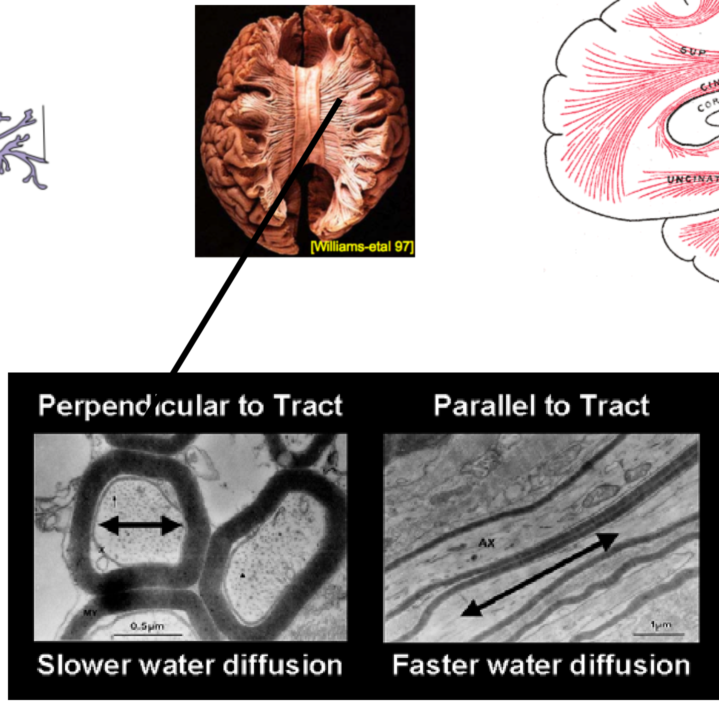
- integrative information on the tissue microstructure
- is a very important biomarker of various pathologies

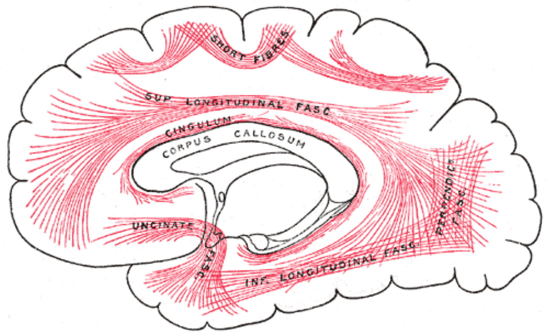
Diffusion "probes" the microstructure

Length scale: a few microns

Neuron cell





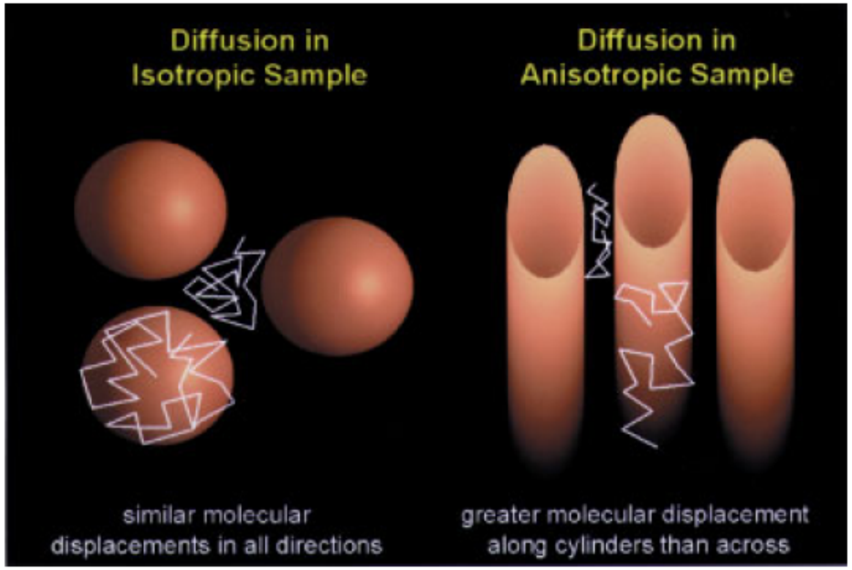


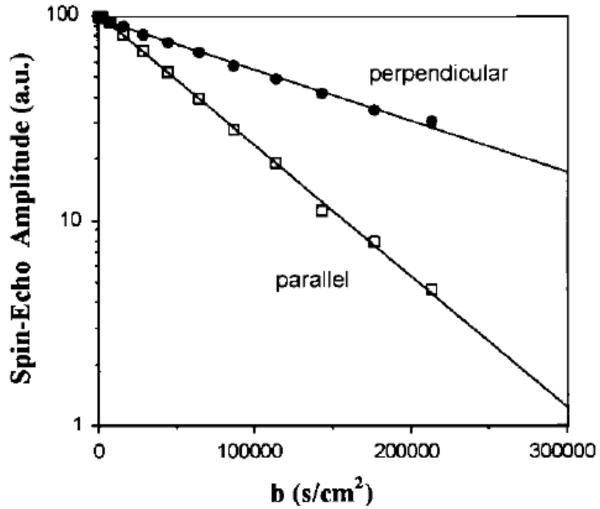
In the brain tissue, water diffusion is <u>anisotropic</u> and <u>restricted</u>

The measured diffusivity is NOT intrinsic ("apparent")

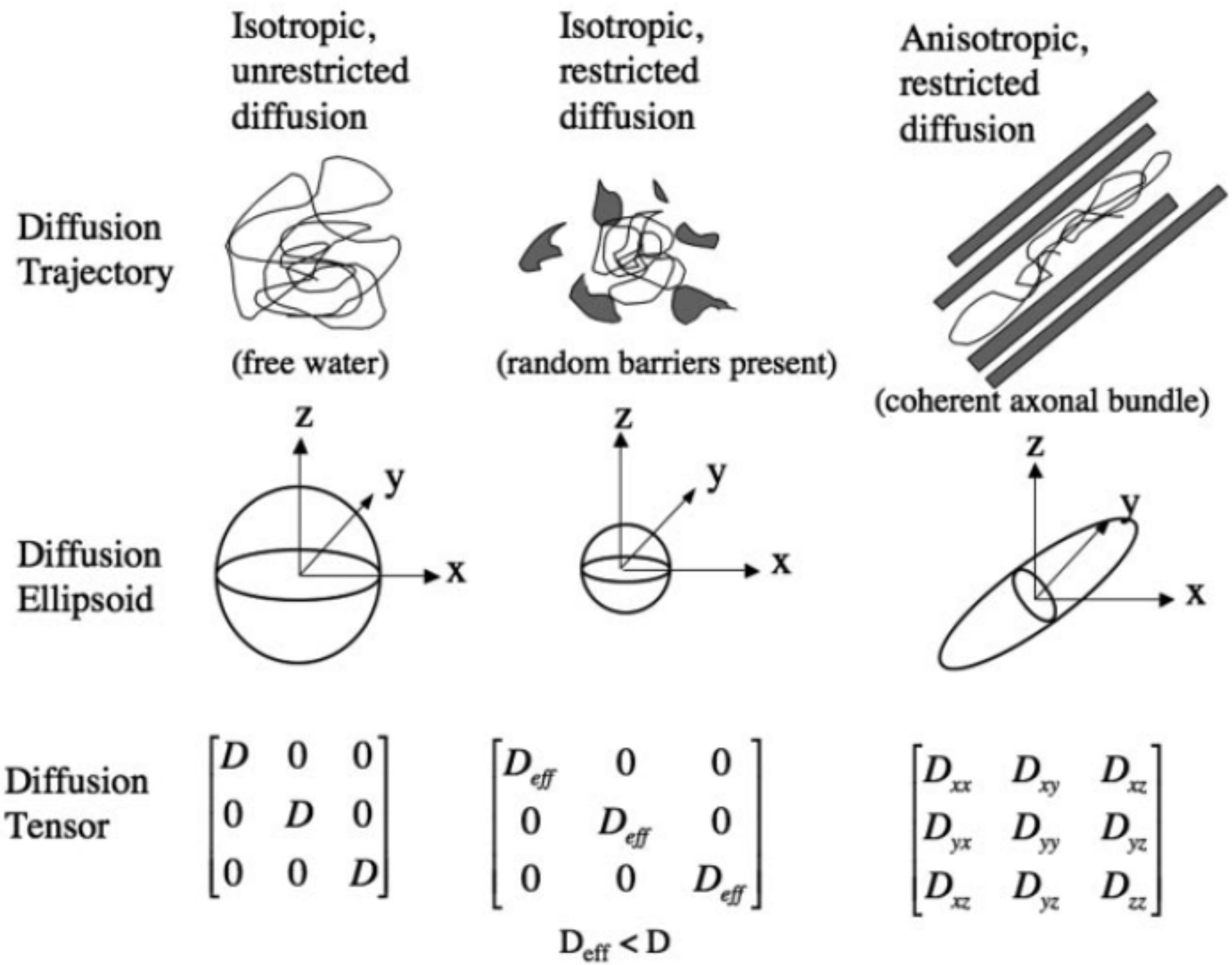
Diffusion Anisotropy

Diffusion Tensor Imaging (DTI) approach





Diffusion depends on the spatial direction along which the gradient is applied.



Isotropic, unrestricted diffusion
Isotropic, restricted diffusion
Anisotropic, restricted diffusion
Diffusion Trajectory
(free water)
(random barriers present)
(coherent axonal bundle)
Diffusion Ellipsoid
z
y
x
Diffusion Tensor
$\begin{bmatrix} D & 0 & 0 \\ 0 & D & 0 \\ 0 & 0 & D \end{bmatrix}$
$\begin{bmatrix} D_{eff} & 0 & 0 \\ 0 & D_{eff} & 0 \\ 0 & 0 & D_{eff} \end{bmatrix}$
$D_{eff} < D$
$\begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{bmatrix}$

Tensor invariants

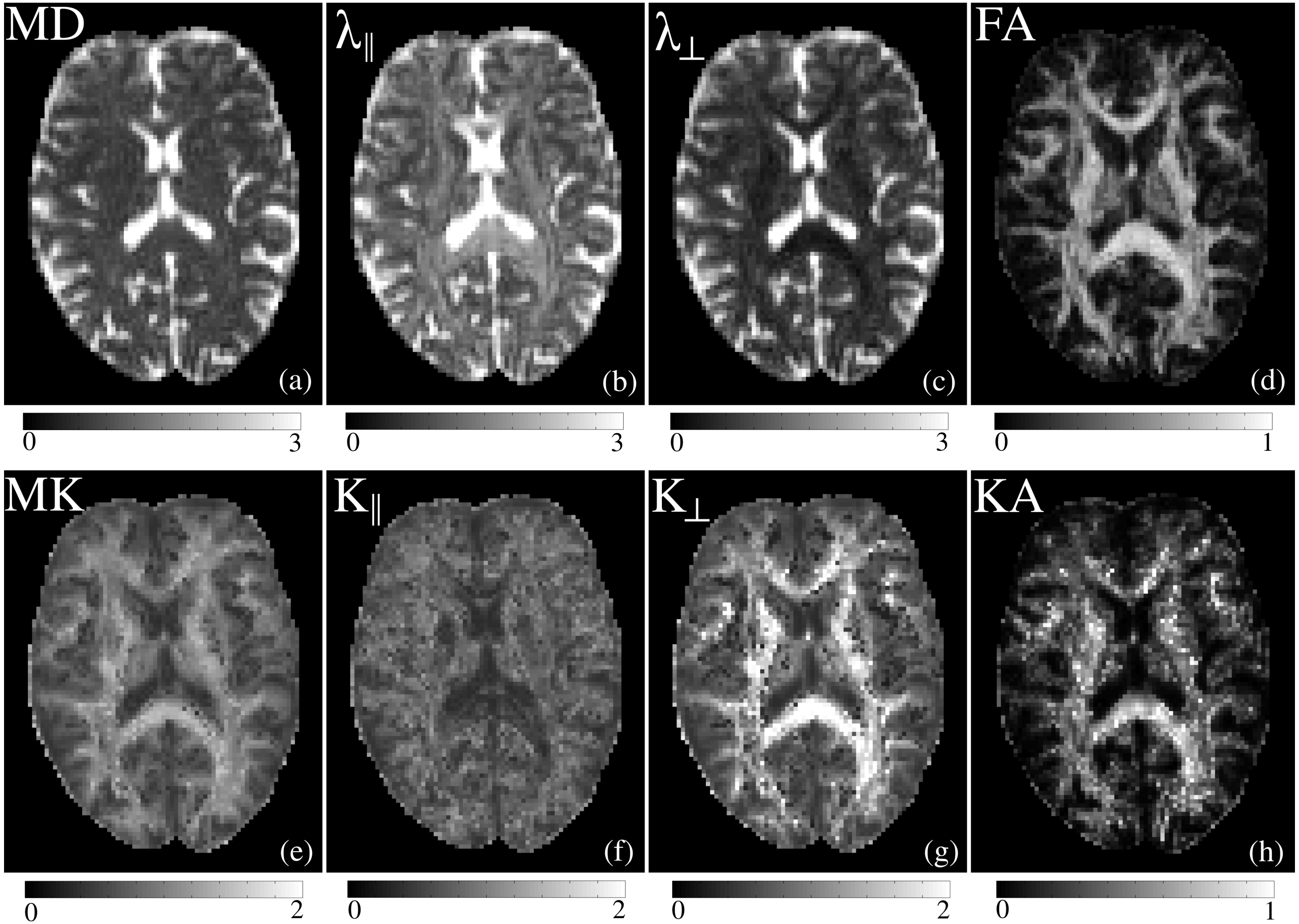
These parameters are proposed to account for physical information regardless the choice of the frame of reference.

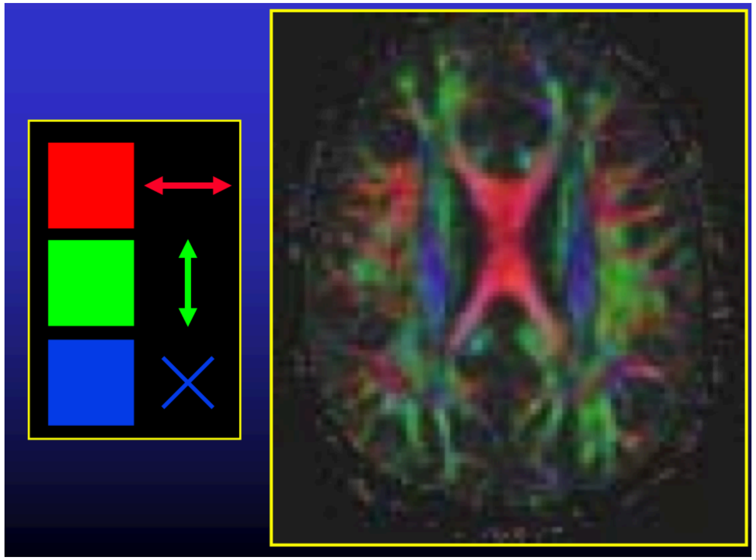
Mean Diffusivity
$$MD = \frac{1}{3}(\lambda_1 + \lambda_2 + \lambda_3)$$

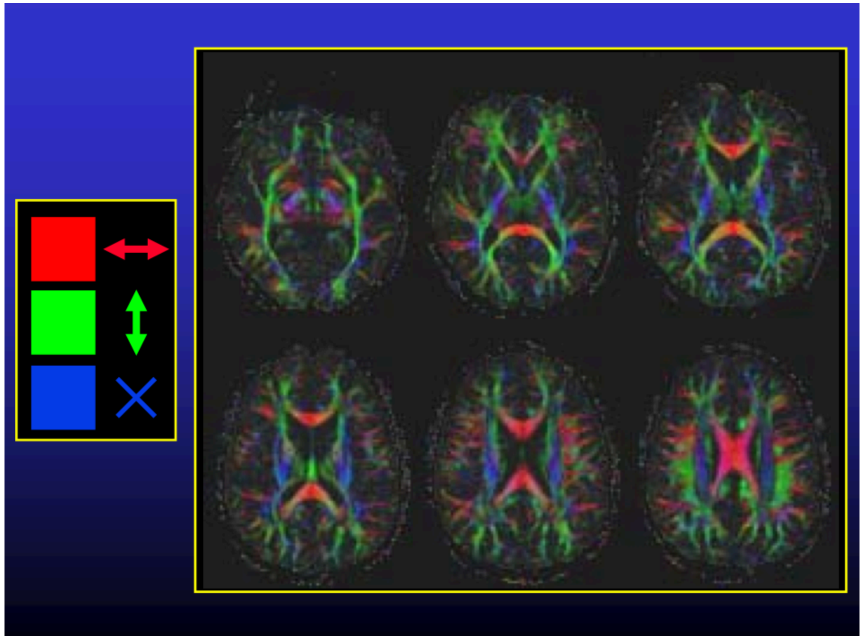
Fractional Anisotropy
$$FA = \sqrt{\frac{3}{2}}\sqrt{\frac{(MD-\lambda_1)^2 + (MD-\lambda_2)^2 + (MD-\lambda_3)^2}{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}}$$

Isotropic system
FA= 0

$0 \geq FA \geq 1$

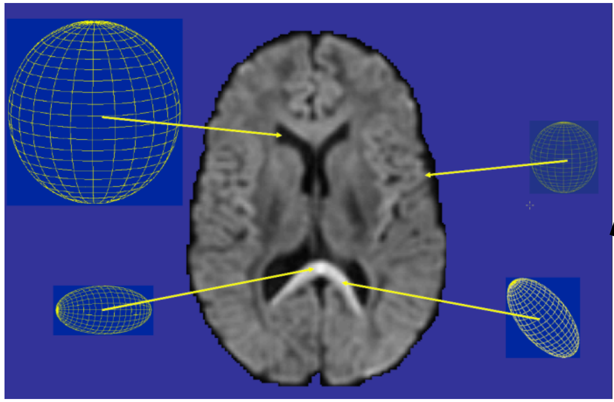

MD
(a)
0
3
λ∥
(b)
0
3
λ⊥
(c)
0
3
FA
(d)
0
1
MK
(e)
0
2
K∥
(f)
0
2
K⊥
(g)
0
2
KA
(h)
0
1

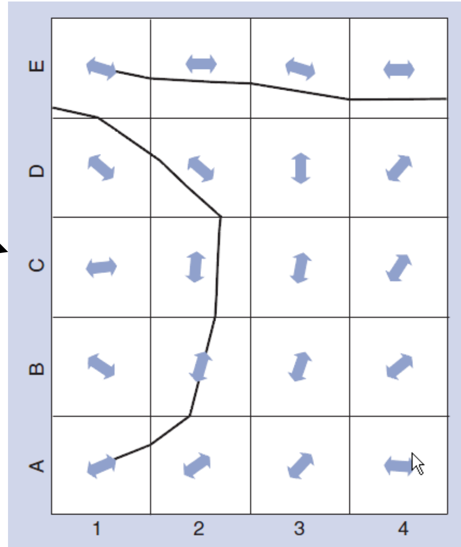


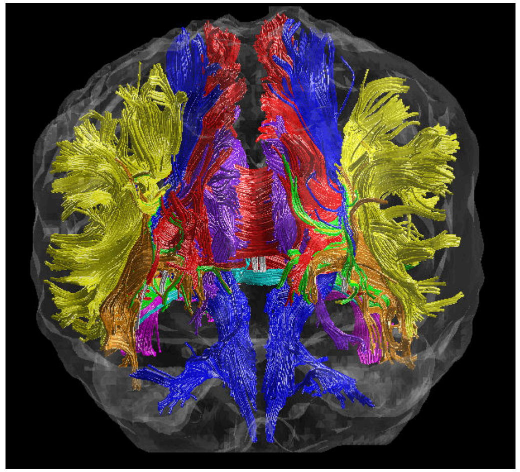


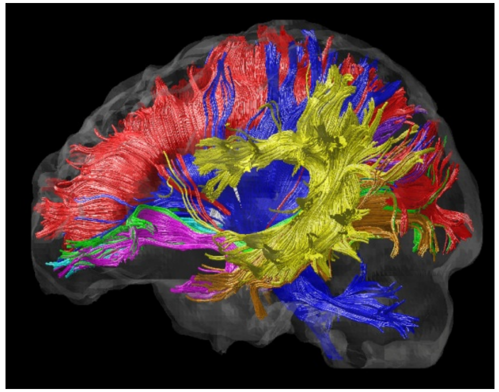
Anisotropy enables “fibre tracking”

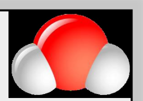
different gradient directions





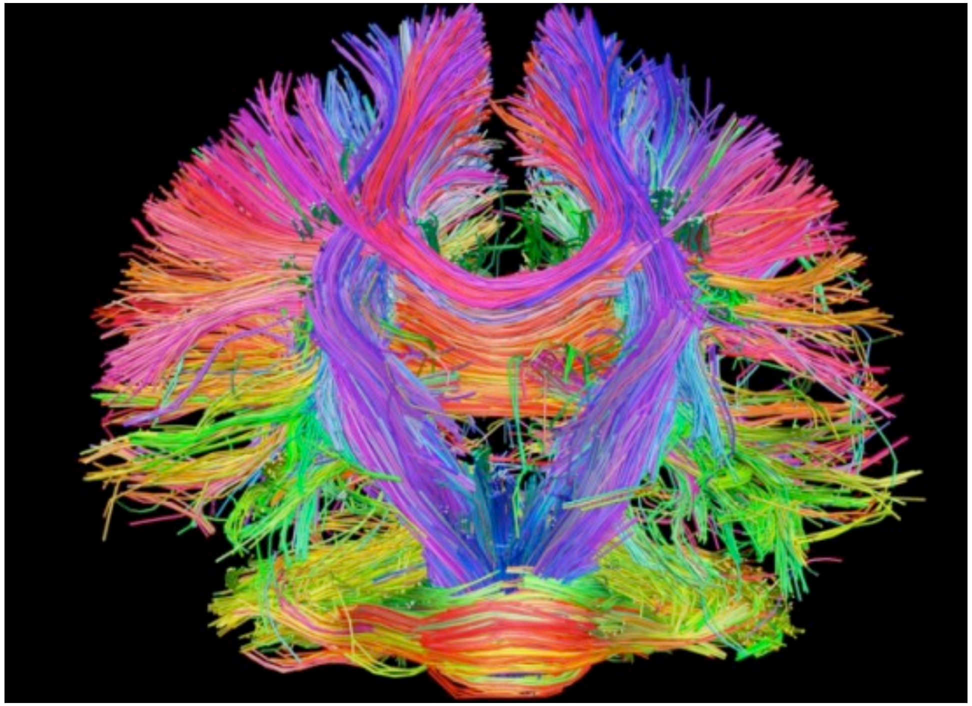


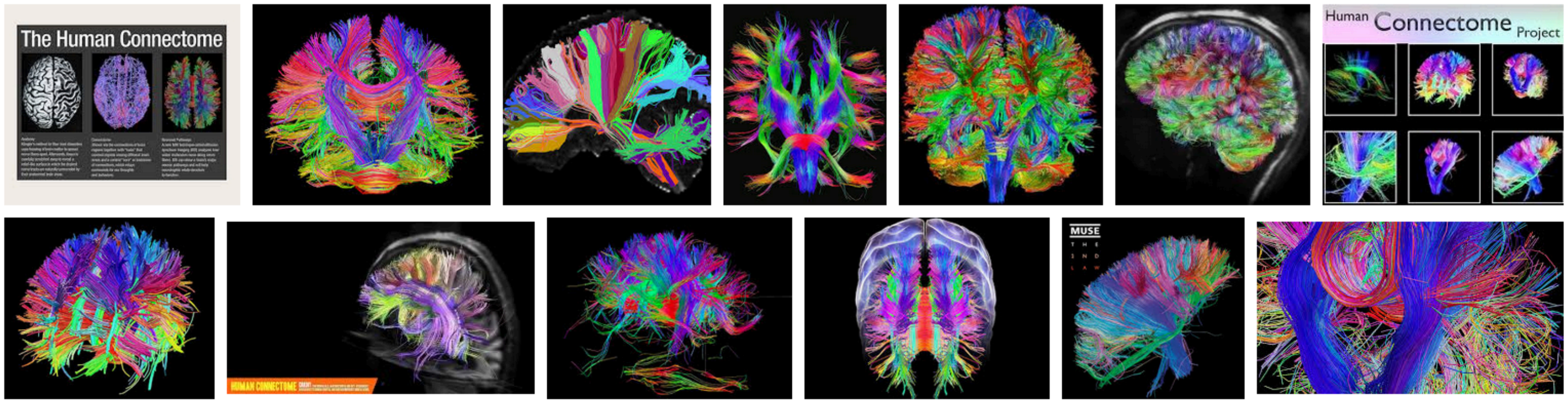




Many challenges for theoretical and experimental physicists in developing new improved methods and algorithms

From image gallery
www.neuroimaging.tau.ac.il

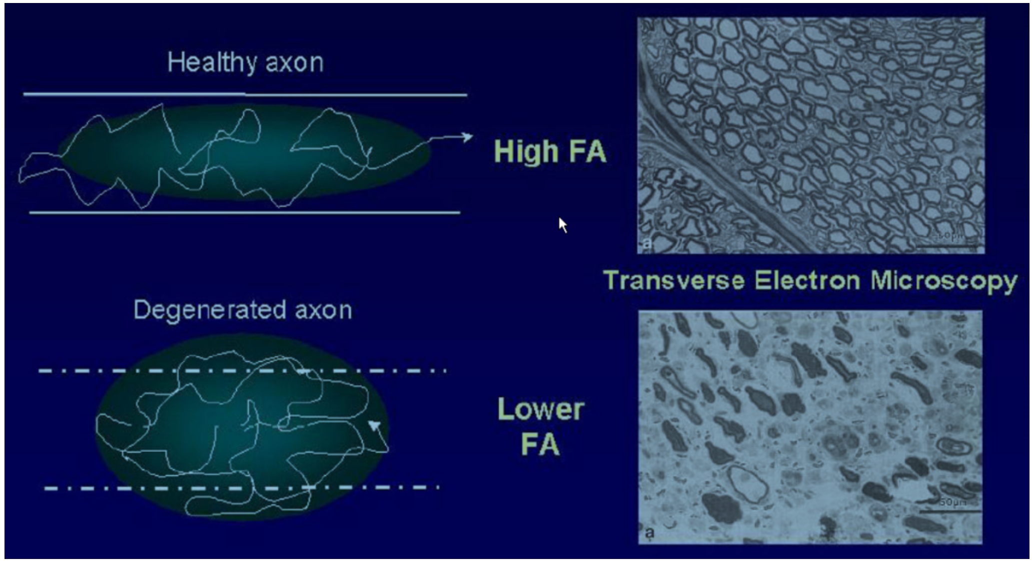


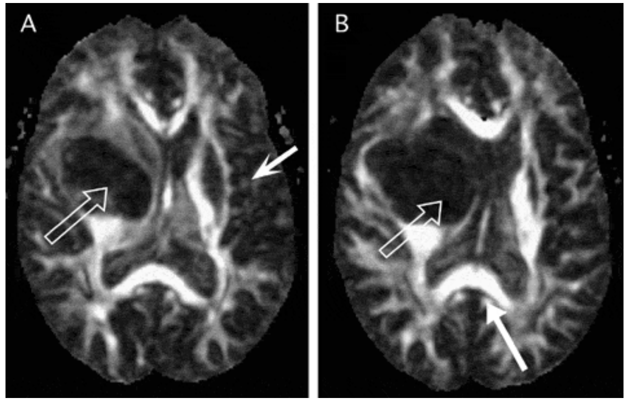

The Human Connectome
Human Connectome Project
HUMAN CONNECTOME
MUSE

Diffusion MRI applications

- Normal brain development and aging
- Congenital anomalies and diseases of white matter
- Traumatic brain injury
- Encephalopathies – toxic, metabolic, infectious
- Demyelinating and neurodegenerative diseases
- Ischemia and stroke
- Neoplasm, preoperative planning
- Epilepsy
- Dementia, schizophrenia, depression
- Developmental disorders – autism

Pathological tissue and diffusion





www.currentprotocols.com/protocol/mia0604

unique opportunities in diagnostics:

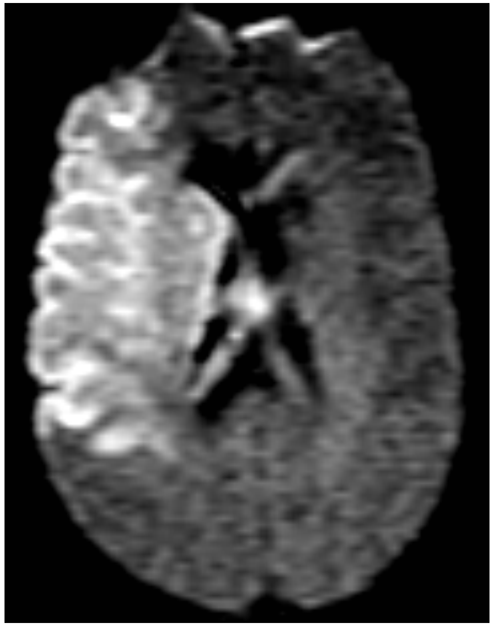
tumors, stroke, neurodegenerative diseases, injuries, etc.…

Example: Detection of Acute Stroke

"**Diffusion Weighted Imaging (DWI**) has proven to be the most effective means of detecting early strokes" **Lehigh Magnetic Imaging Center**

Conventional T_2 WI

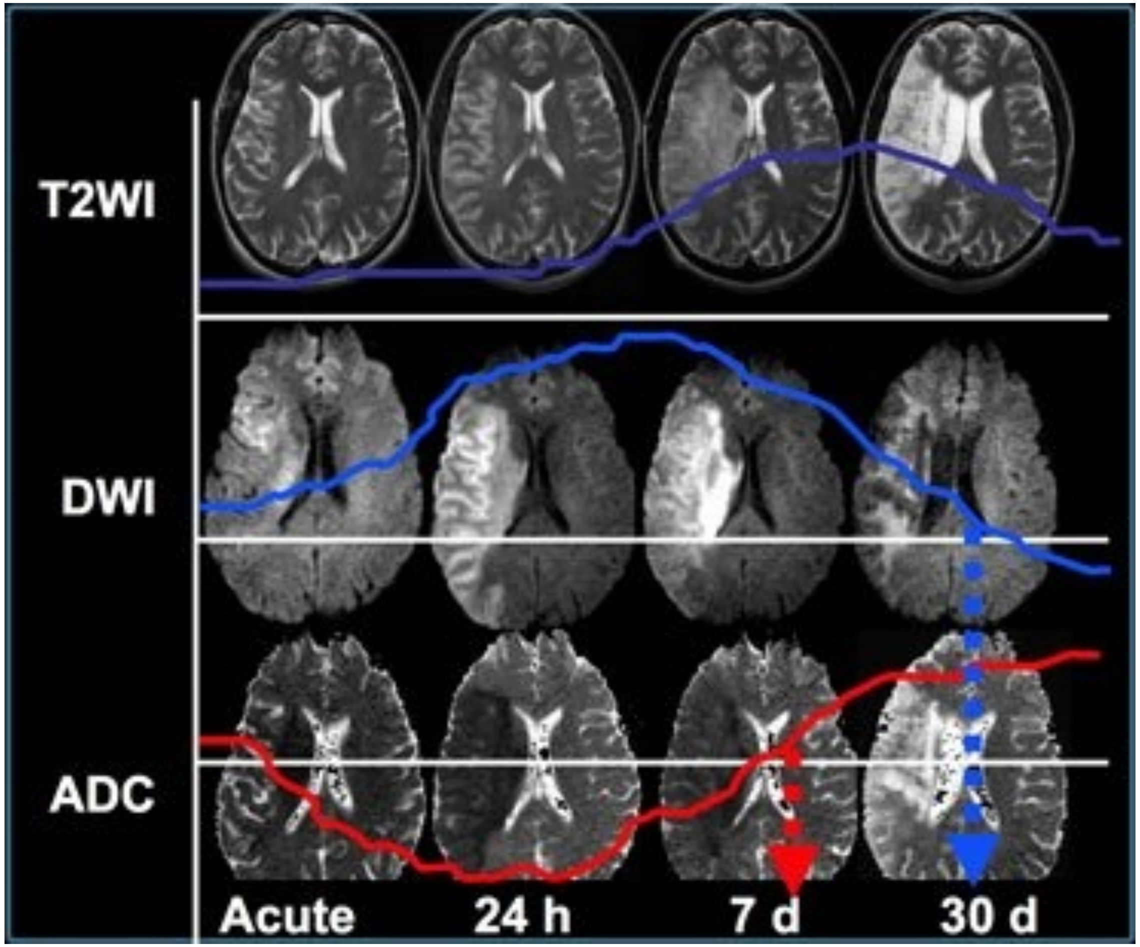
DW-EPI



Sodium ion pumps fail - water goes in cells and can not diffuse – DW image gets bright (note – much later cells burst and stroke area gets very dark)

Early detection of stroke

DWIs permit earlier detection of stroke than other methods such as T2I (T2 weighted image).



http://www.radiologyassistant.nl/en/483910a4b6f14

Possible origin of diffusion contrast in stroke

IC water fraction increases
(cells swell)

↓

Tortuosity of the ECS increases

↓

ADC decreses

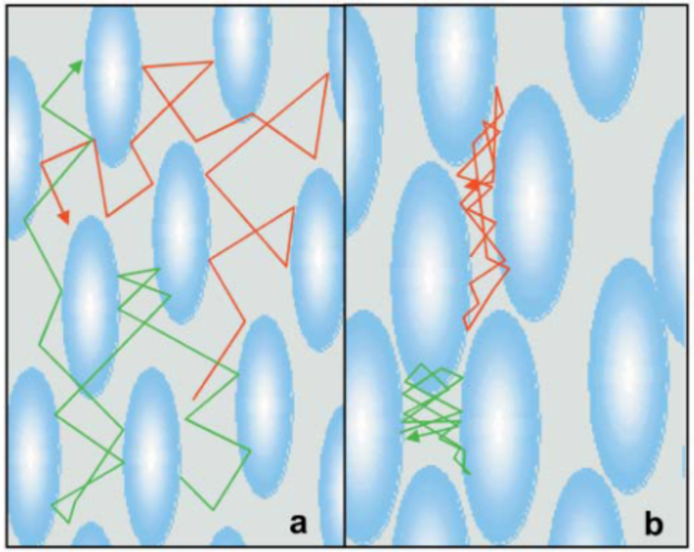
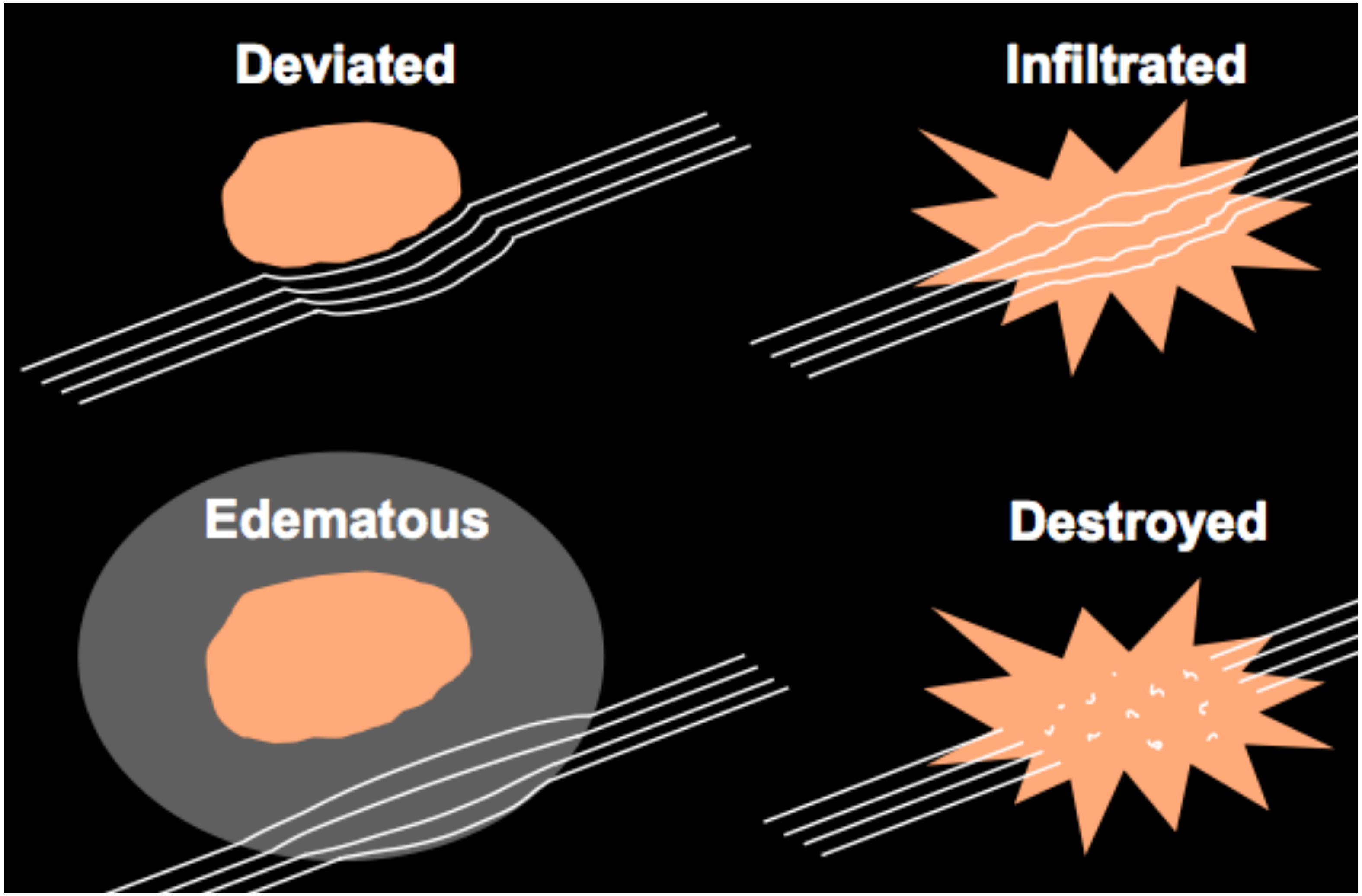


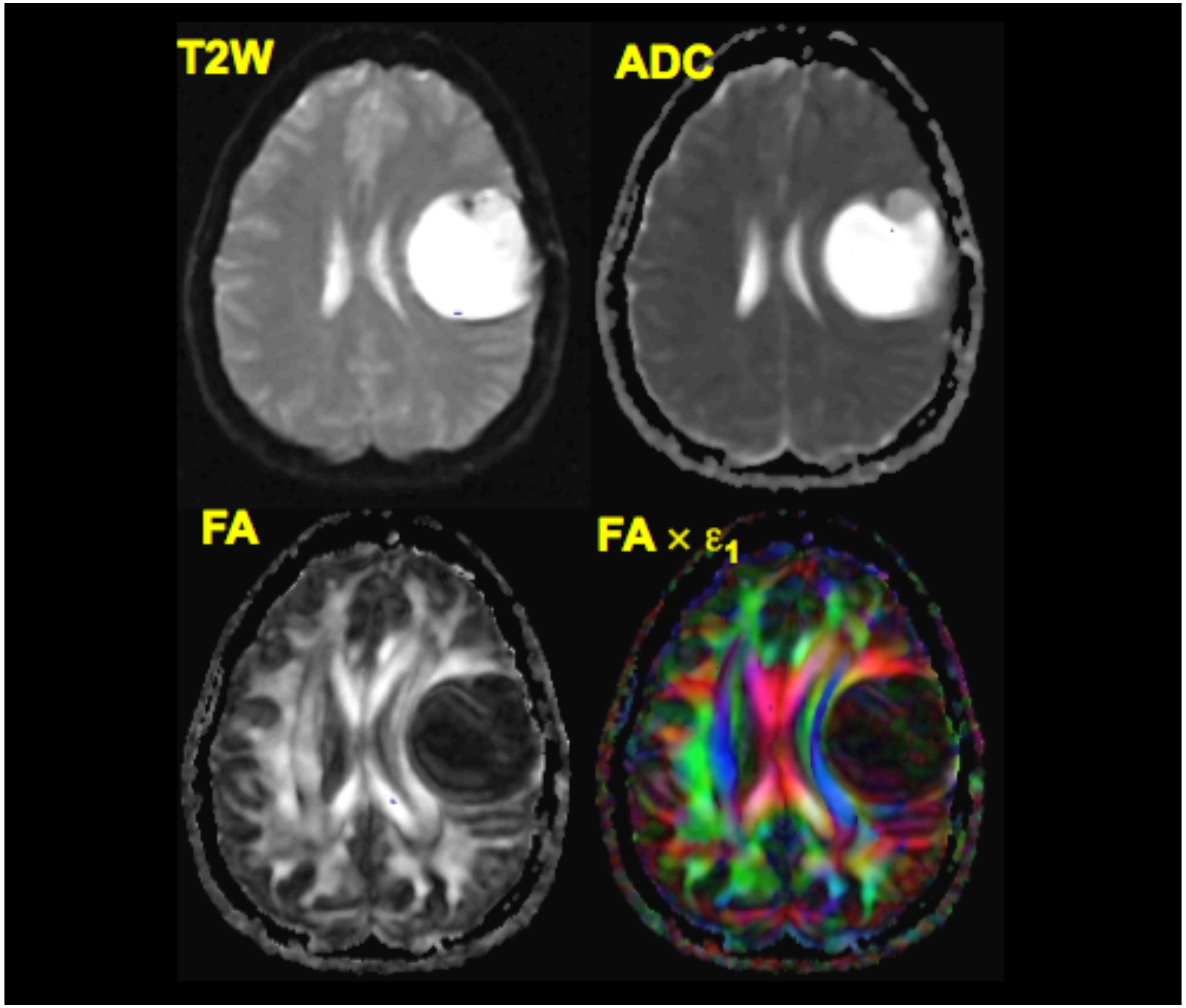
Fig. 9. Diagram of the cellular structure in (a) normal brain tissue and (b) in the early stage of cerebral ischemia. In the early stage of cerebral ischemia, there is a net increase in intracellular water leading to an increase in tortuosity of the extracellular space. Due to this effect, diffusion water molecules hit the cell membrane more often, leading to an ADC decrease.

S. Heiland, 2003

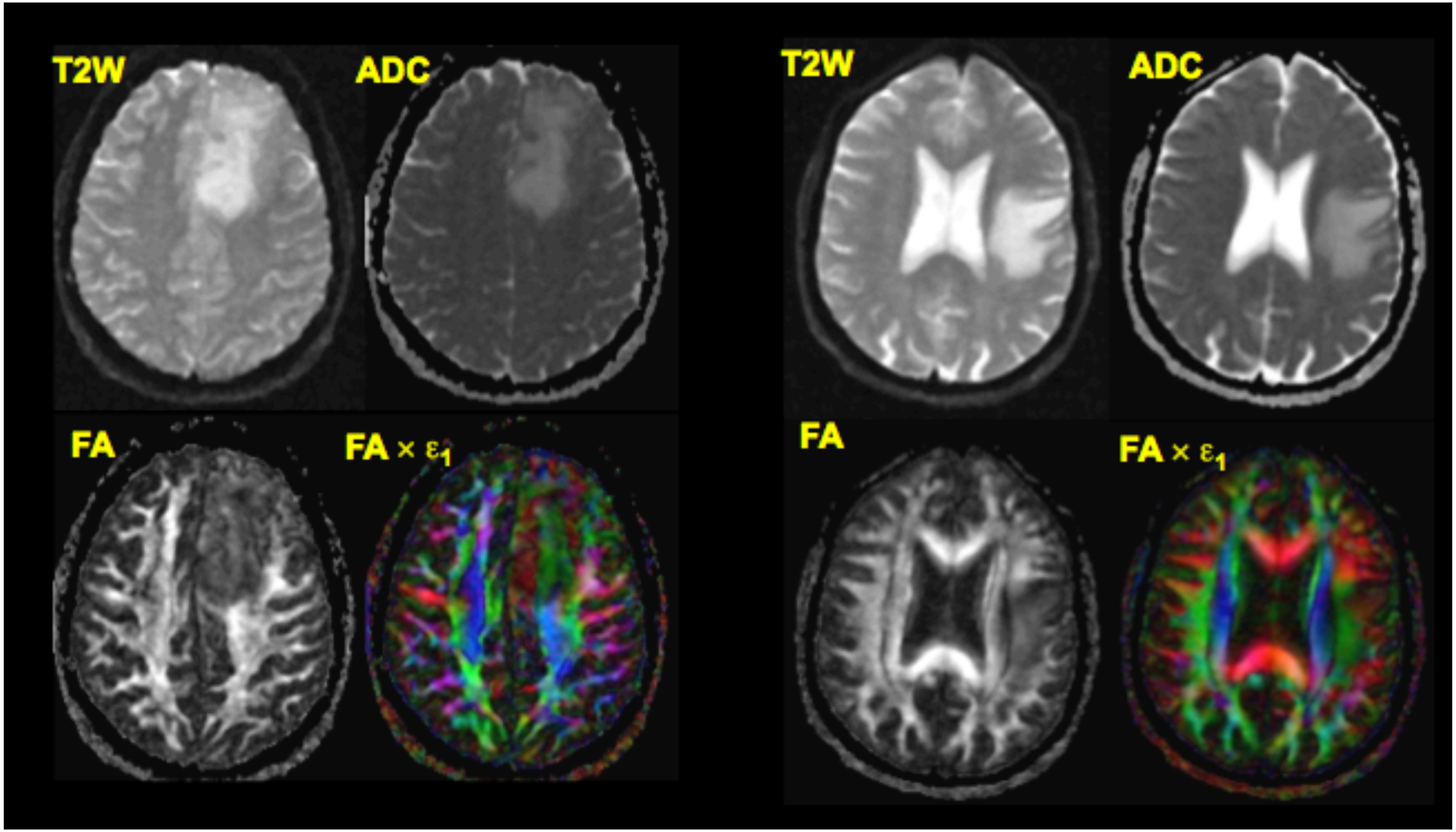
DTI in Cerebral Neoplasms



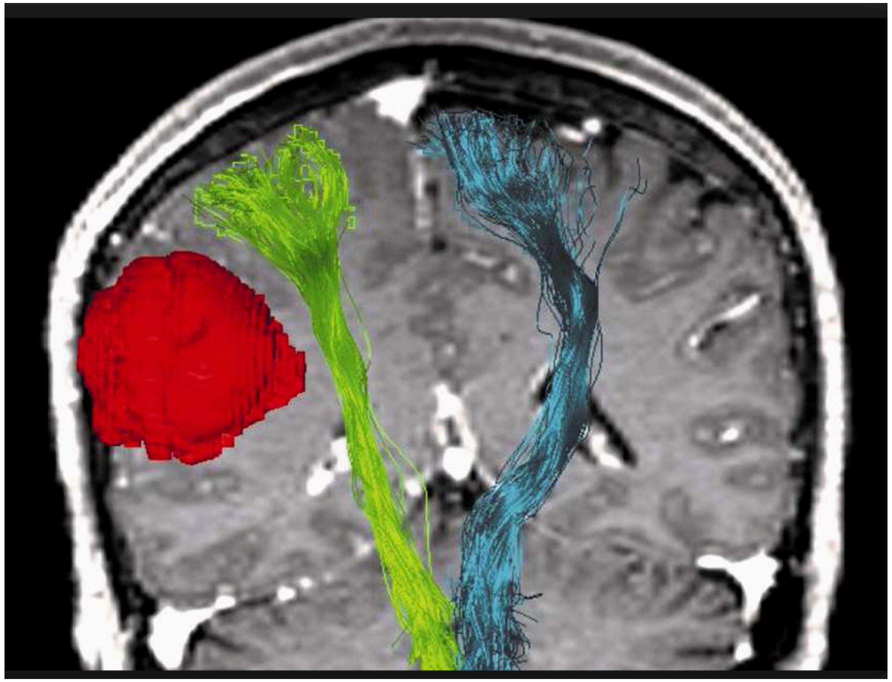
Tract Displacement

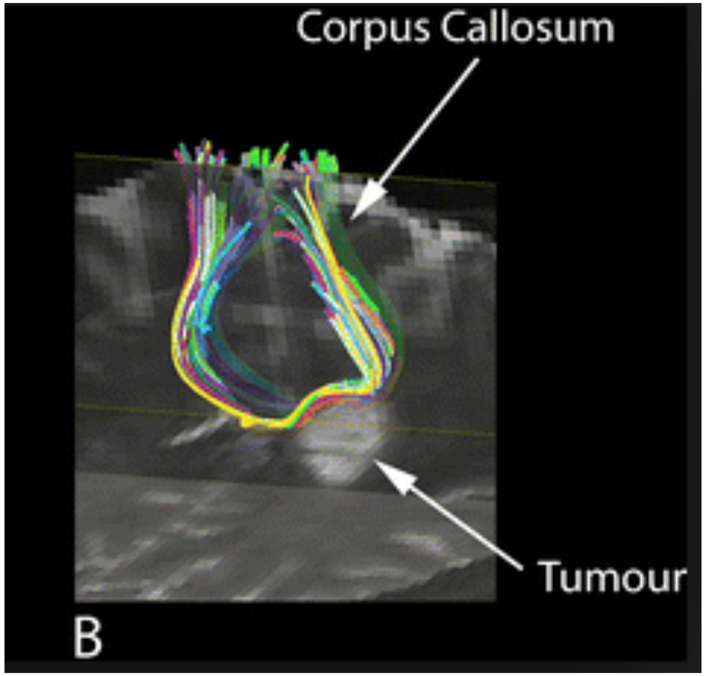


Tract Infiltration, oedema

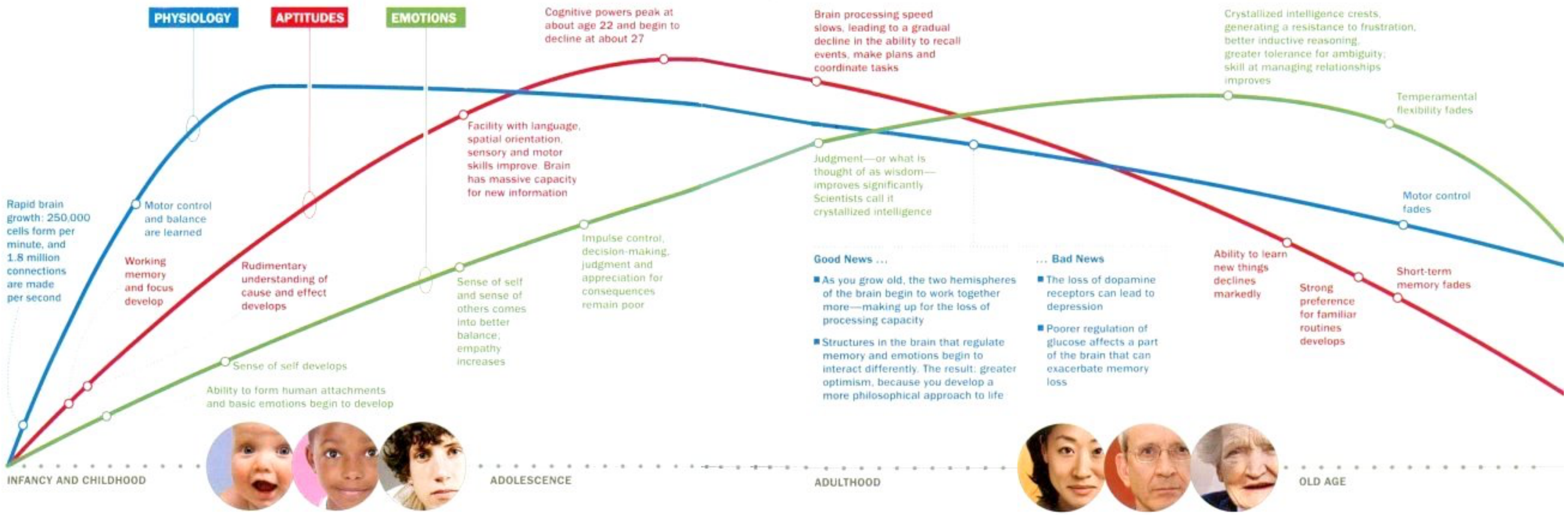


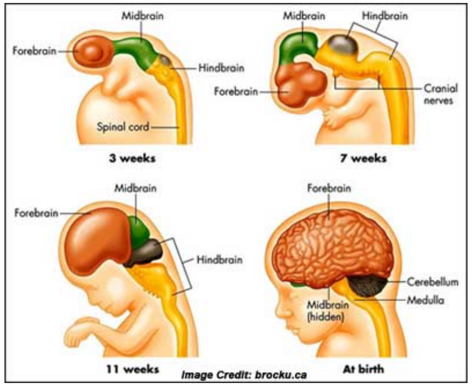
DTI in neurosurgery

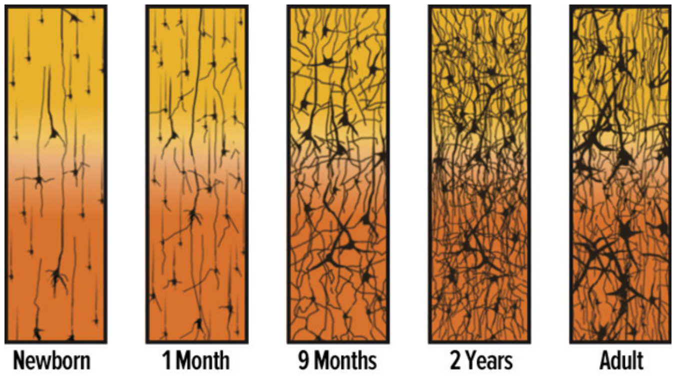


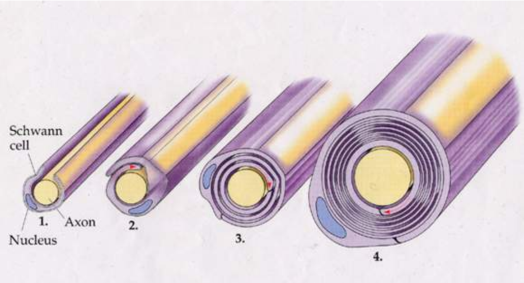


Brain Development and Ageing – Lifelong Changes

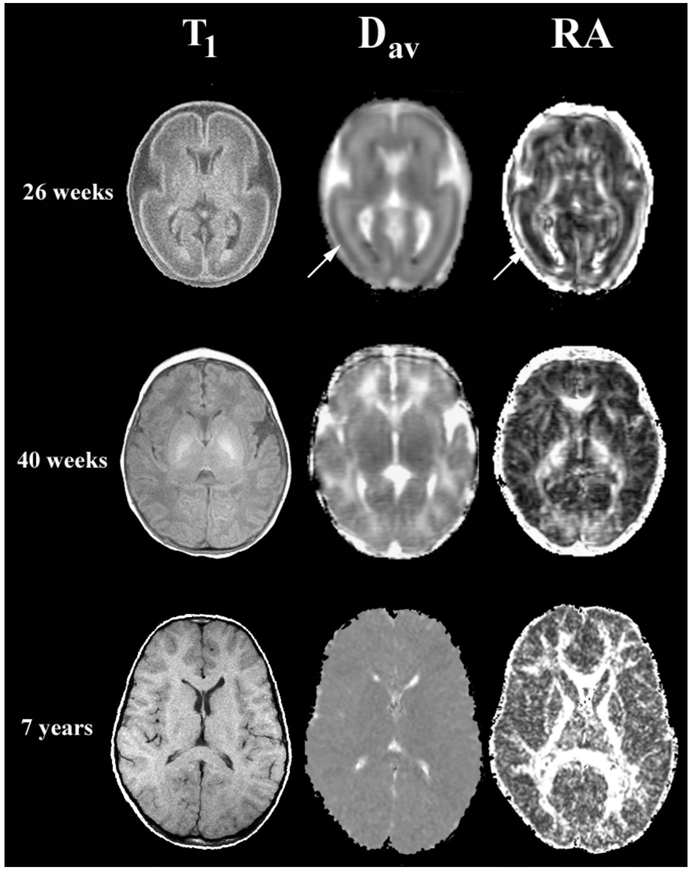


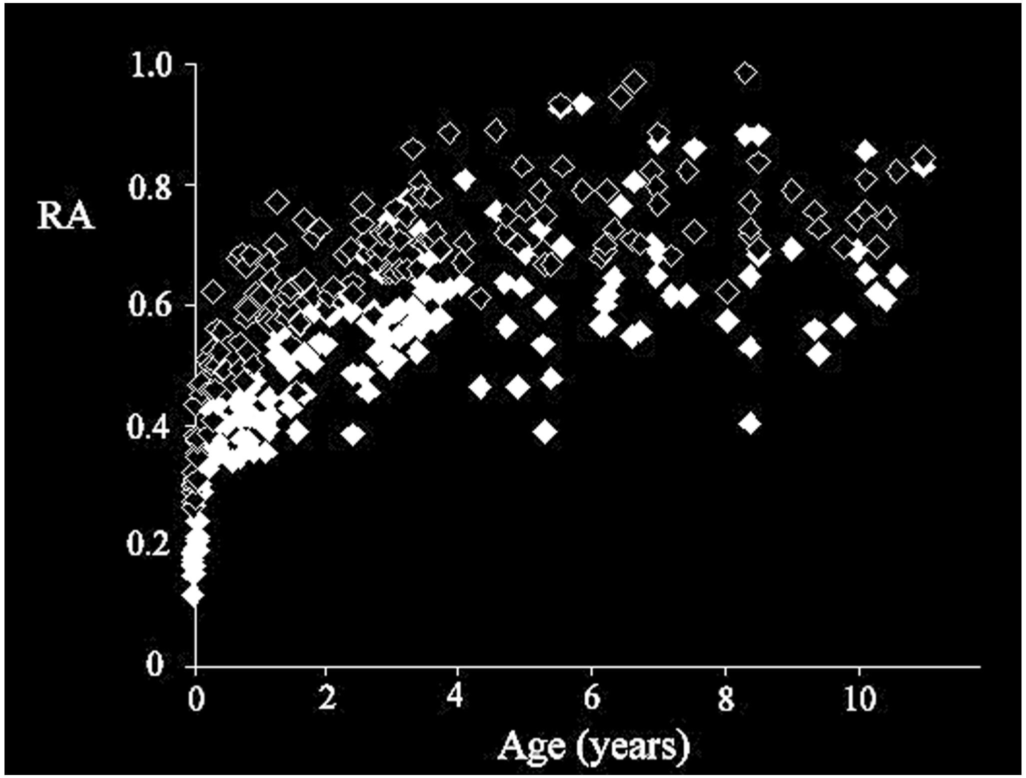






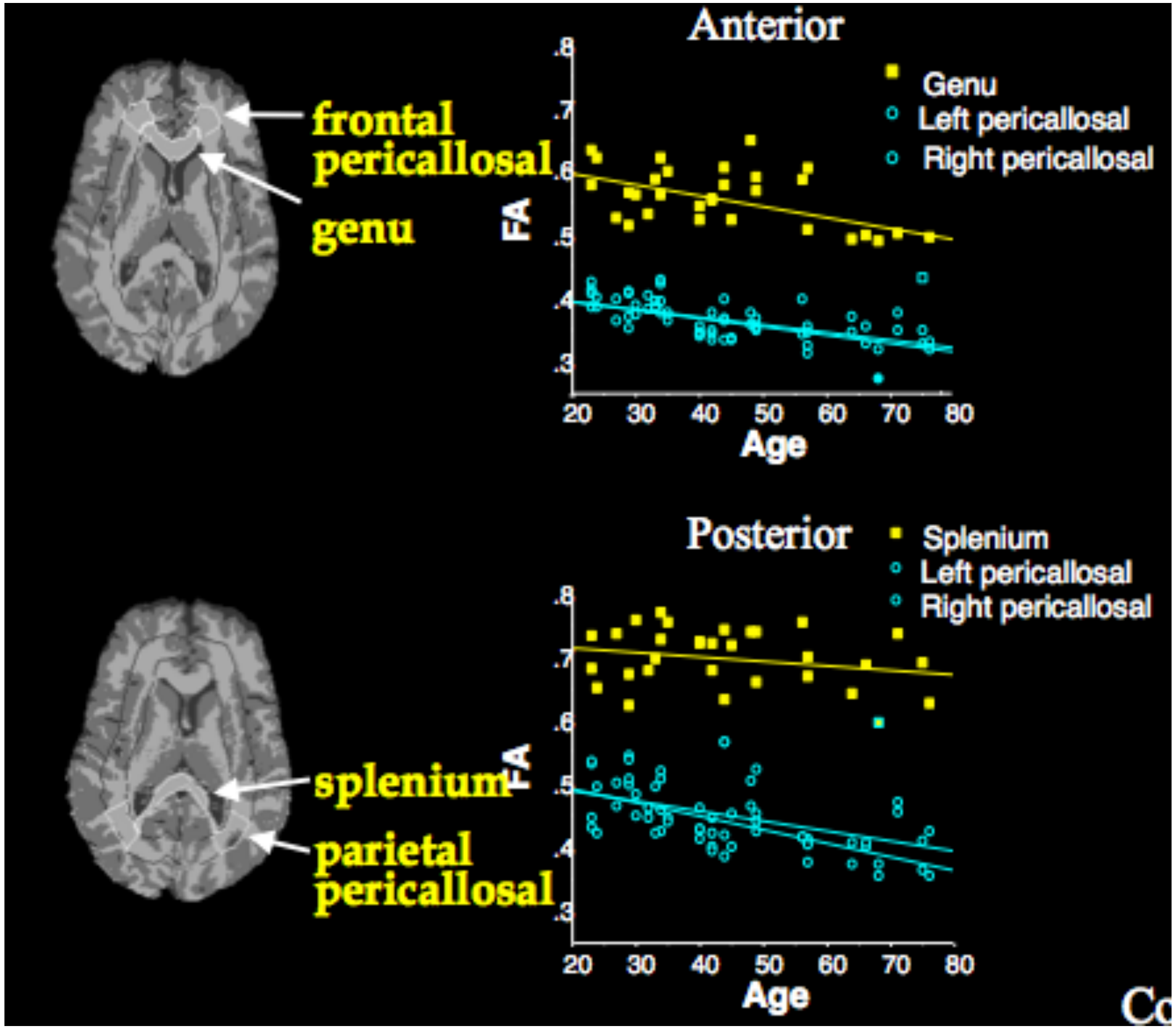
Normal Brain Development





J. Neil, Washington Univ., St. Louis

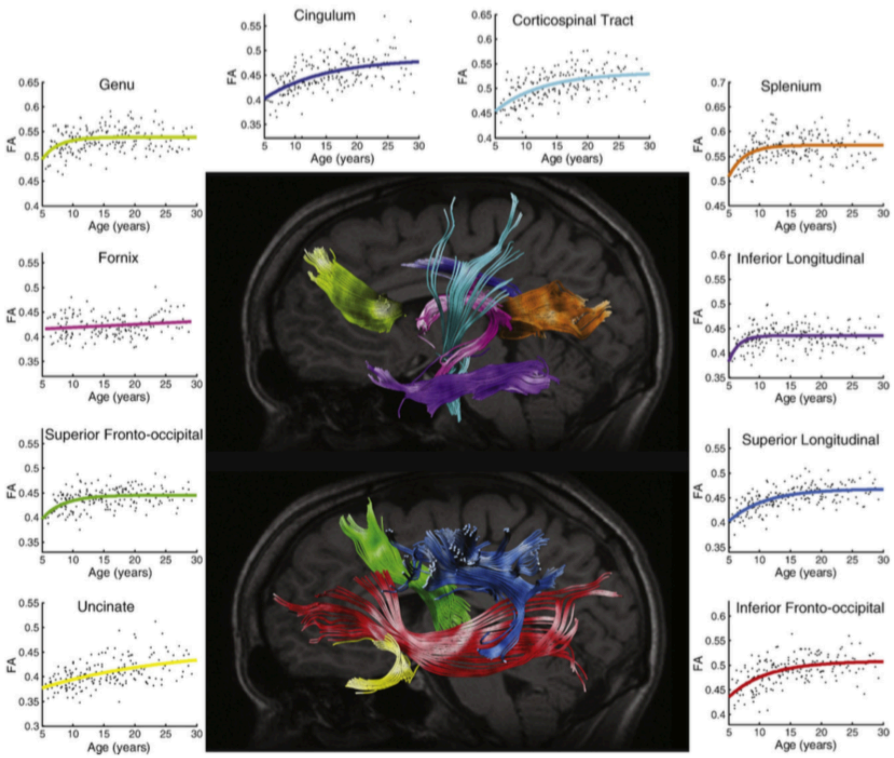
Healthy Brain Ageing



Pfefferbaum, MRM 2010

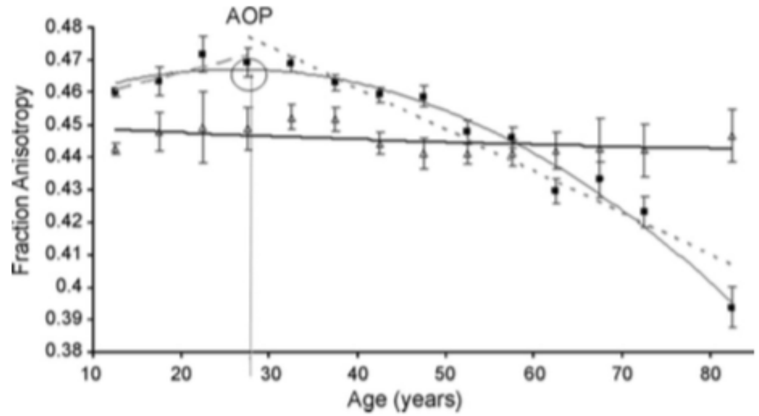
JÜLICH
FORSCHUNGSZENTRUM

DTI: Lifespan trajectories + heterochronicity of different fibres/regions



C. Lebel et al., NeuroImage (2008)

202 subjects aged 5-30 years; 10 fibres; hierarchical pattern of maturation in which areas with frontal-temporal connections develop more slowly than others.



FA values for Corona Radiata ( ) and Cortical-Spinal tract (△)

P. Kochunov et al., Neurobiology of Aging, 2010.

- 831 subjects aged 11-90 years;
- 9 fibres;
- Age of peak: 23.1–39.4 years
- Rate of decline correlates with rates of maturation

Advanced

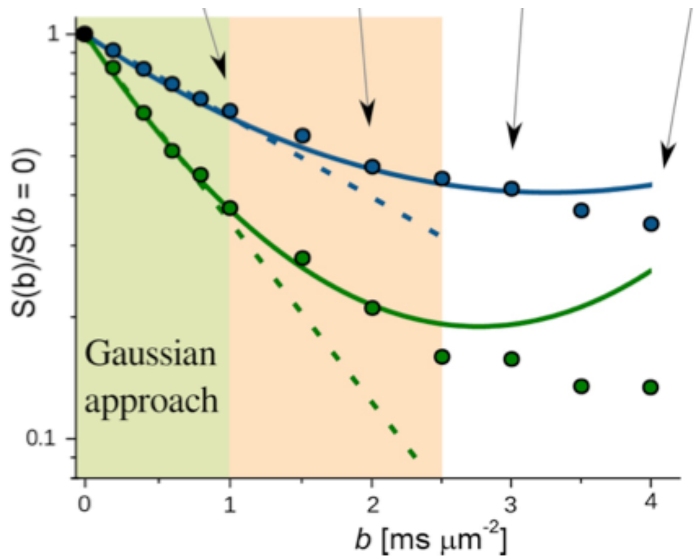
Diffusion Kurtosis Imaging (DKI)

kurtosis

$$\ln \frac{S(b)}{S_0} = -bD_K + \frac{1}{6}\left(bD_K\right)^2 K + \vartheta\left(b^3\right)$$

Monoexponential

Non-exponential

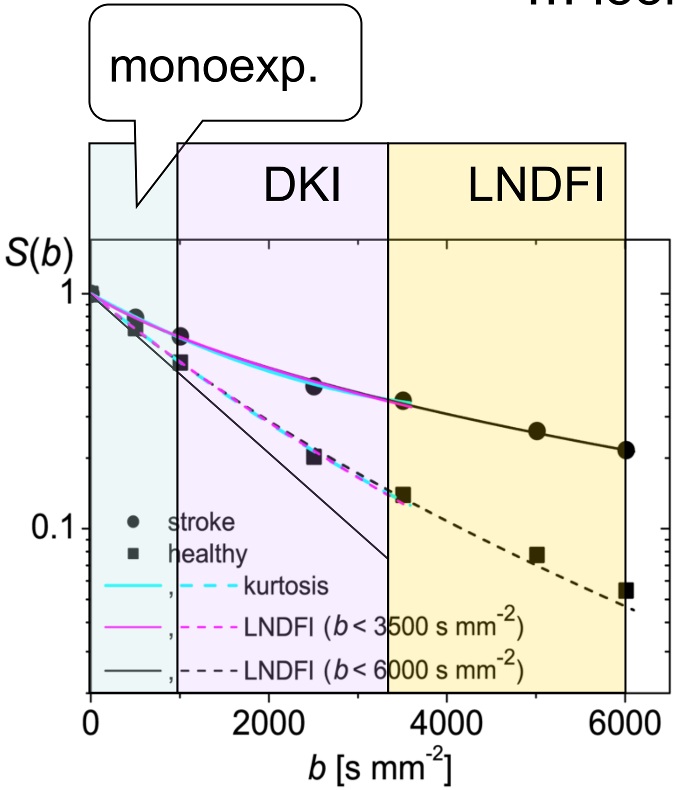


- extension of DTI, requires more acquisition time
- provides a new biomarker: (mean) diffusional kurtosis, MK
- richer information on complexity of microstructure
- Applications (stroke, neurodegenerative pathologies)

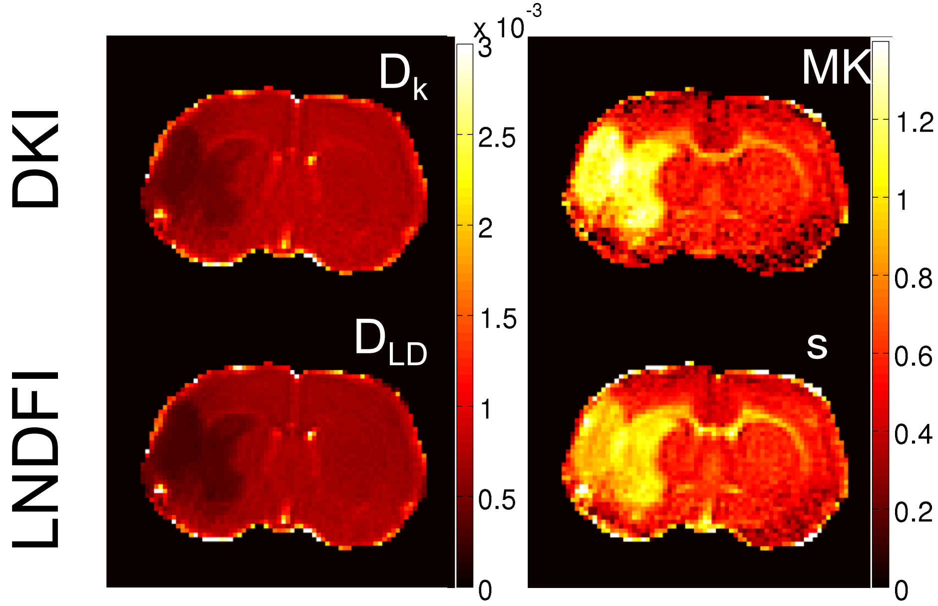
JH Jensen et al., MRM, 2005

Deviations from the Gaussian model

… looking for novel biomarkers



Rat brains

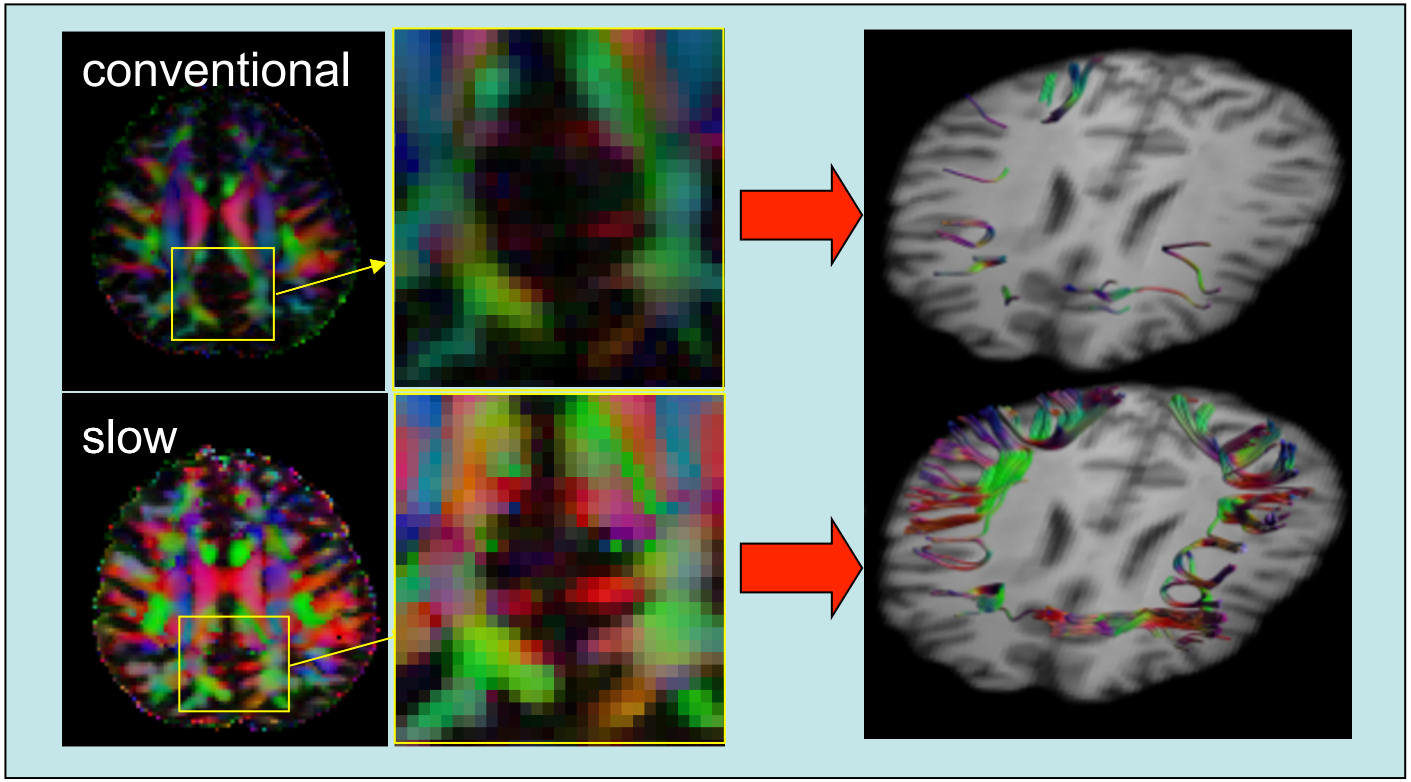


strongly enhanced contrast
in the damaged tissue!!

Neurospin, CEA, 7T Bruker;

BEDTA: benefits for fibre tracking

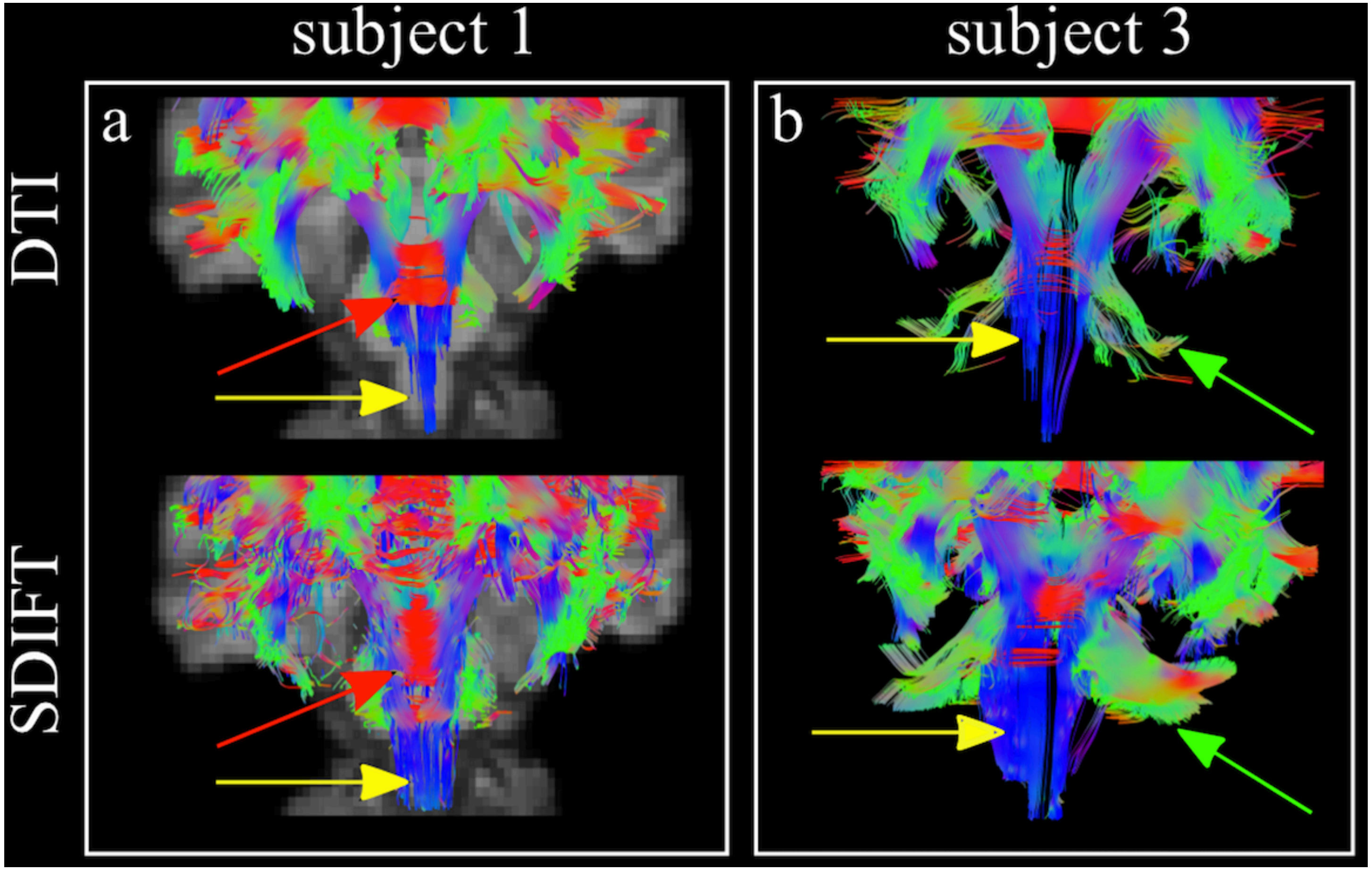
Pre-cortical fibres



more WM structures and more fibre tracks are visualised!

Grinberg F., et al., Neuroimage, 2011

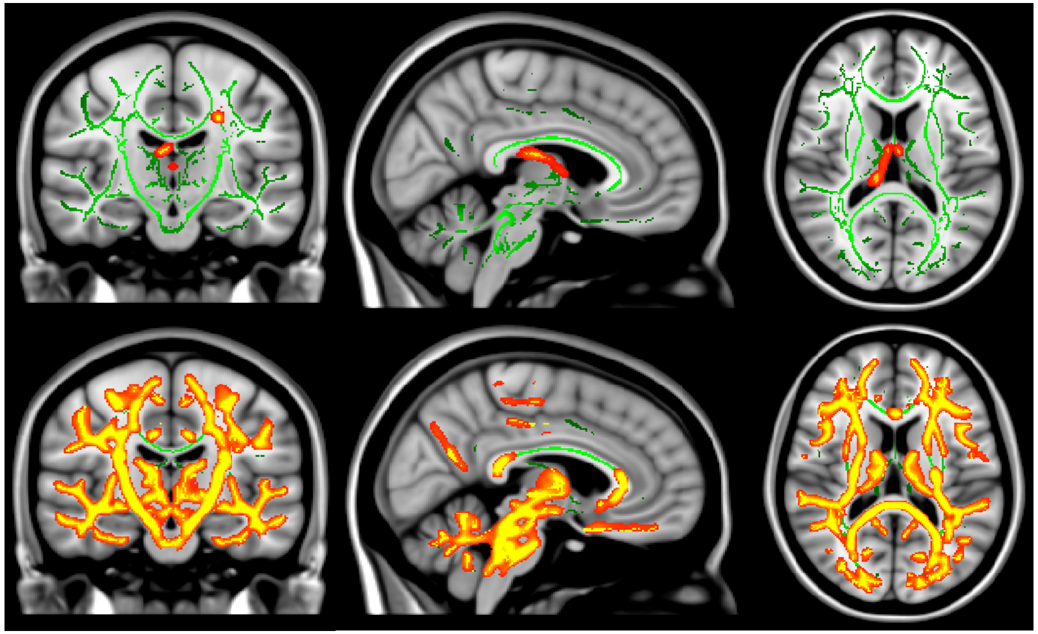
Fibre tracks –
Dr. I. Maximov, E. Farrher


subject 1
subject 3
a
b
DTI
SDIFT

Children versus adults

FA

MK



MNI152 Coordinates: X = 5; Y = -17; Z = 14;

END

… thank you for attention!