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Diffusion MRI in the Neurosciences

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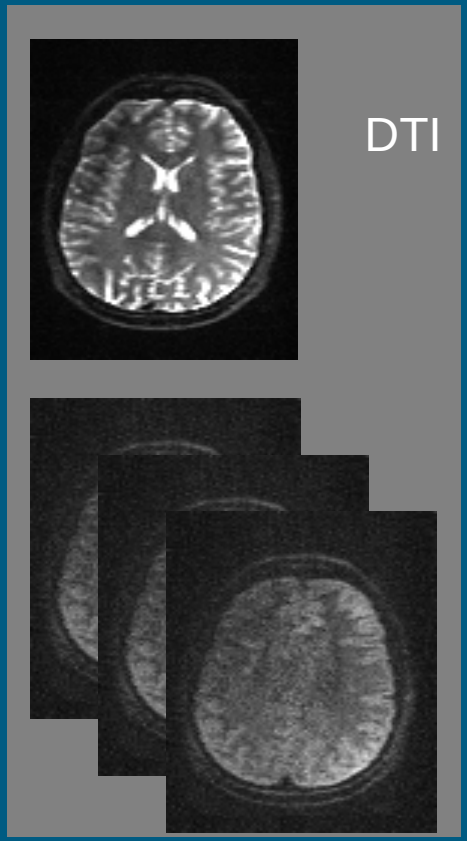
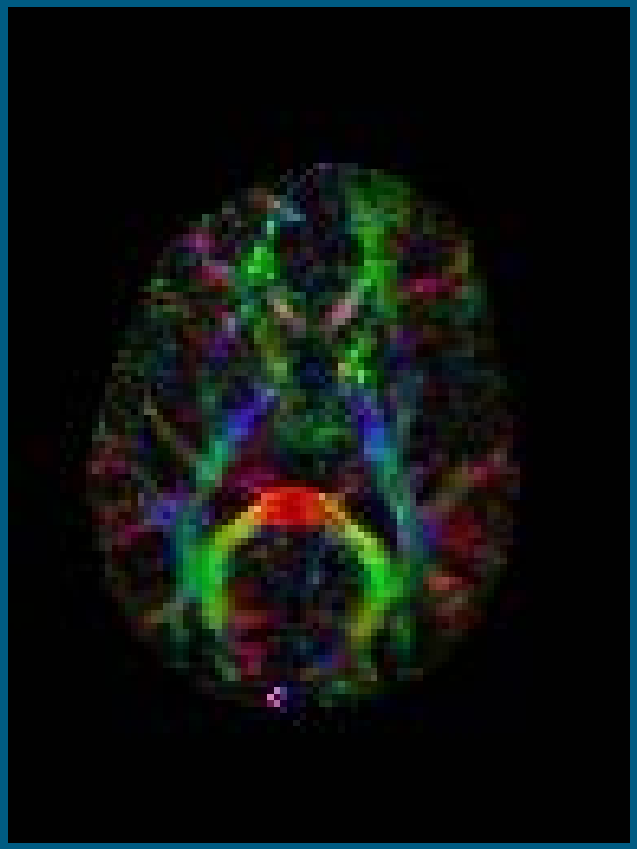
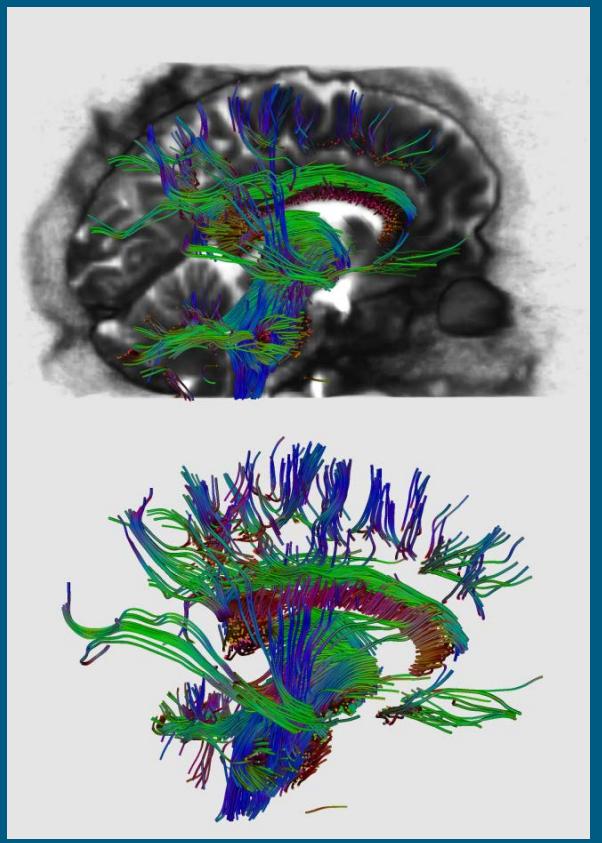






Outline

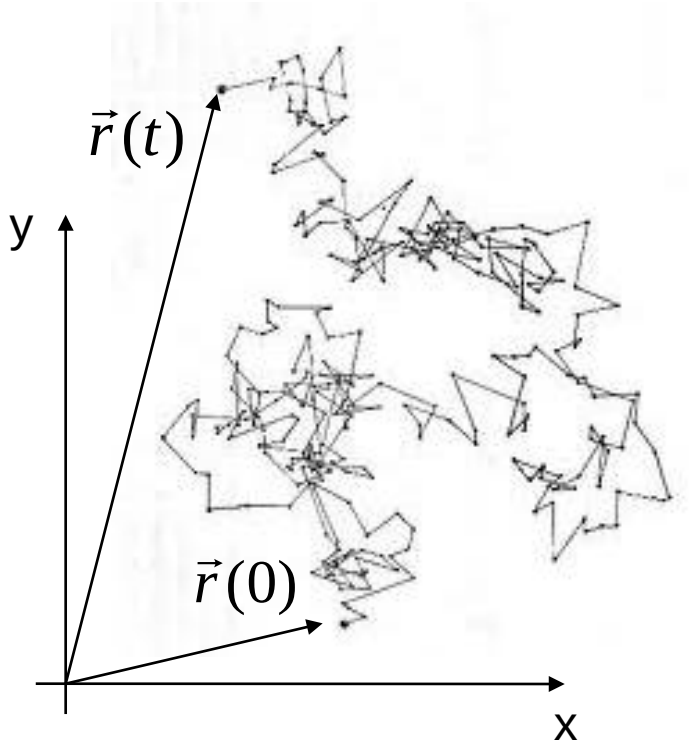
- Introduction
  - Qualitative issues of diffusion.
- Spins diffusing under a background gradient.
  - Bipolar gradient-echo sequence.
  - Stejkal-Tanner spin-echo sequence.
- Approaches to the problem
  - Microscopic approach. Quantum mechanical treatment.
    - The diffusion propagator.
    - Solution for the Stejskal-Tanner experiment.
  - Macroscopic approach. The Bloch-Torrey equation.
    - Solution for the bipolar gradient-echo.
    - Solution for the Stejkal Tanner equation.
- Diffusion in biological tissue. Hindered diffusion.
    - The ADC approach.
    - Signal attenuation.
- Anisotropic systems. The DTI approach.
  - Invariant parameters. Fractional anisotropy (FA), Mean Diffusivity (MD), etc.
- Fibre tracking.

Definition: diffusion is the thermal motion of all particles at temperatures above the absolute zero in a liquid or gas. The rate of this movement is a function of temperature, viscosity of the fluid and the size (mass) of the particles.

History …

• 1827 – Brown describes what is now known as “Brownian Motion”.

• 1905 – Einstein describes the statistical mechanics of diffusion.



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

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

Diffusion Coefficient. **Estimated from MRI signal attenuation.**

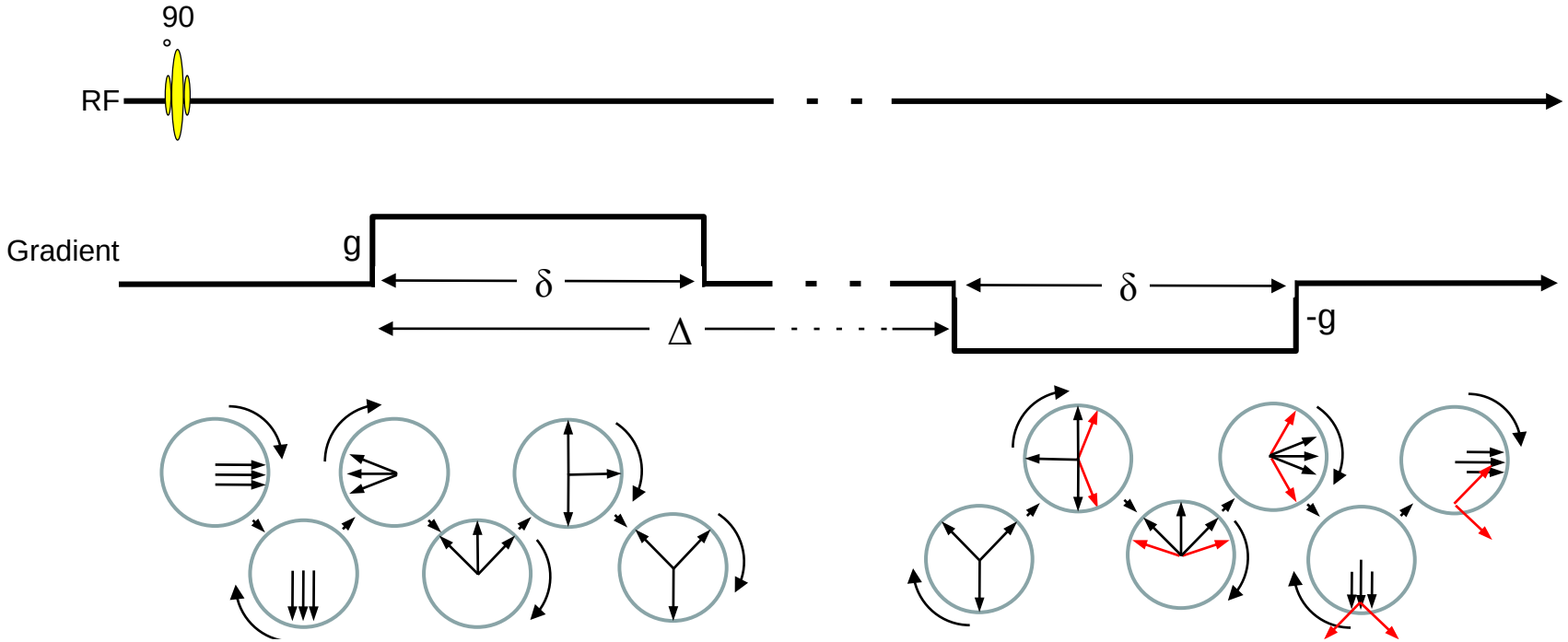
Classical representation of NMR diffusion measurements

Gradient Echo

The constant magnetic field is superimposed by an inhomogeneous field

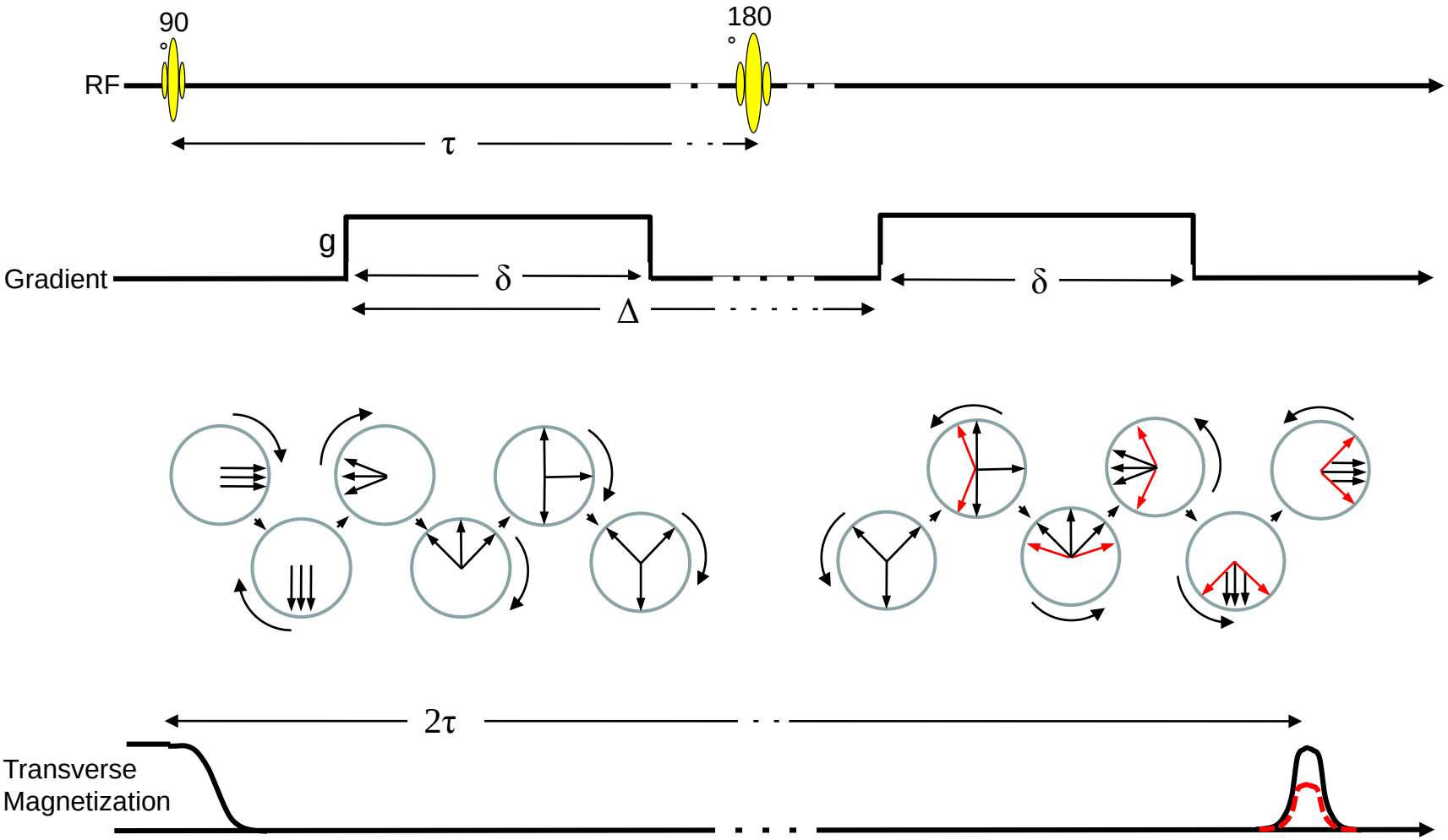
$$\Delta B_0 = \pm gz \quad \Rightarrow \quad \omega(z) \equiv \gamma(B_0 \pm gz)$$

Assuming no field inhomogeneities more than the caused by the gradient



Transverse Magnetization

Hahn spin-echo



Finally

$$\frac{M(t)}{M_0} = \iint_V p(\vec{r}_0) P(\vec{r}, \vec{r}_0, \Delta) e^{-i\gamma \vec{g}\cdot(\vec{r}-\vec{r}_0)\delta} d^3 r d^3 r_0$$

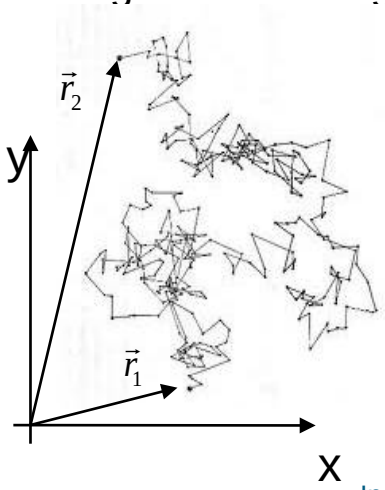
where:

$$M_0 \equiv -b\gamma\hbar \mathrm{Tr}\{I_y^2\}$$

Assuming $p(\vec{r}_0) = \frac{1}{V}$, a gradient in the *z*-direction and using the gaussian propagator, the amplitude of the signal results

$$S(T_E) = S_0 e^{-(\gamma g \delta)^2 D\Delta}$$

So one can estimate *D* by measuring changes in the signal while varying the time parameters or the gradient strength.



$$\left\langle \left| \vec{r}_2 - \vec{r}_1 \right|^2 \right\rangle = 2D\Delta$$

$$S(T_E) = S_0 e^{-\frac{1}{6}(\gamma g \delta)^2 \left\langle r^2 \right\rangle}$$

A macroscopic approach:
The Bloch-Torrey equation.

H.C. Torrey showed in 1956 how the Bloch equations would change for an ensemble of spins diffusing in the presence of a magnetic field gradient.

The Bloch-Torrey equation for the evolution of the distribution of magnetization ***m*** in the presence of a magnetic field $\boldsymbol{B}_z$ is,

Larmor precession $\omega \equiv \gamma B_0$ Longitudinal relaxation

$$\frac{\partial \vec{m}(\vec{r},t)}{\partial t} = \gamma \vec{m}(\vec{r},t) \times \vec{B}_0 - \frac{m_x \hat{e}_x + m_y \hat{e}_y}{T_2} - \frac{m_z - m_0}{T_1}\hat{e}_z + \vec{\nabla}^T \vec{\vec{D}} \vec{\nabla} \vec{m}(\vec{r},t)$$

Transversal relaxation Diffusion term

$$\begin{cases} B_z(\vec{r},t) = B_0 + \vec{g}(t)\cdot\vec{r} \\ \vec{g}(t) = \dfrac{\partial B_z}{\partial x}\hat{e}_x + \dfrac{\partial B_z}{\partial y}\hat{e}_y + \dfrac{\partial B_z}{\partial z}\hat{e}_z \end{cases}$$

Solution for an infinite system.

Defining m_+ as the circular component of the transverse spatial magnetization distribution

$$m_+(\vec{r},t) = m_x(\vec{r},t) + i m_y(\vec{r},t)$$

$$\frac{\partial m_+}{\partial t} = -i\gamma m_+ B_z - \frac{m_+}{T_2} + \vec{\nabla}^T \overleftrightarrow{D} \vec{\nabla} m_+$$

$m_+(\vec{r},0) = p_0(\vec{r})$

(Initial condition)

In the absence of diffusion, m_+ is exponentially damped with relaxation time T_2.

Proposing the next solution $m_+(\vec{r},t) = \psi(\vec{r},t) e^{-i\omega_0 t - t/T_2}$ (going to the rotating frame)

One gets the next differential equation

$$\frac{\partial \psi}{\partial t} = -i\gamma(\vec{g}\cdot\vec{r})\psi + \vec{\nabla}^T \overleftrightarrow{D} \vec{\nabla} \psi$$

The general solution is $$\psi(\vec{r},t) = A(t)e^{-i\gamma\vec{r}\cdot\int_0^t \vec{g}(t')dt'}$$

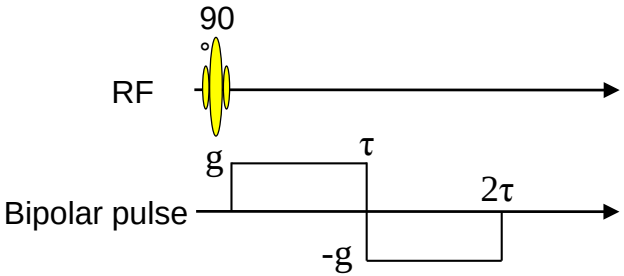
Assuming D = constant, $$\frac{d\ln A(t)}{dt} = -\gamma^2 D\int_0^t \vec{g}(t')dt'\cdot\int_0^t \vec{g}(t')dt'$$

$$\frac{A(t)}{A_0} = \exp\left(-\gamma^2 D\int_0^t dt''\left[\left(\int_0^{t''}\vec{g}(t')dt'\right)\cdot\left(\int_0^{t''}\vec{g}(t')dt'\right)\right]\right)$$

Relative signal amplitude.

Gradient

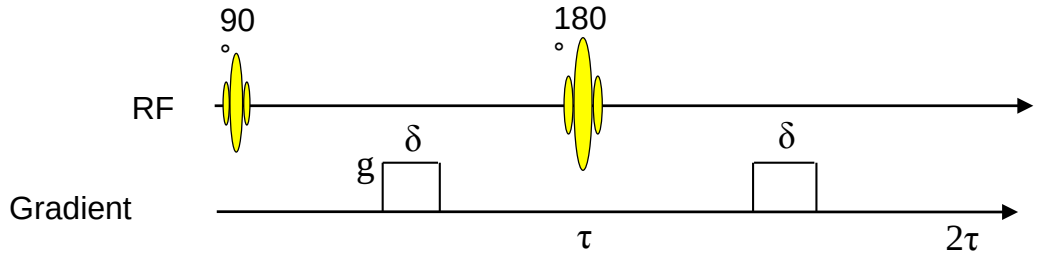
Solution for a Gradient Echo bipolar pulse.



$$\int_0^{t''} \vec{g}(t')dt' = \begin{cases} gt'' \\ -g(t''-2\tau) \end{cases}$$

$$\frac{A(t)}{A_0} = \exp\left(-\frac{2}{3}\gamma^2 D g^2 \Delta^3\right)$$

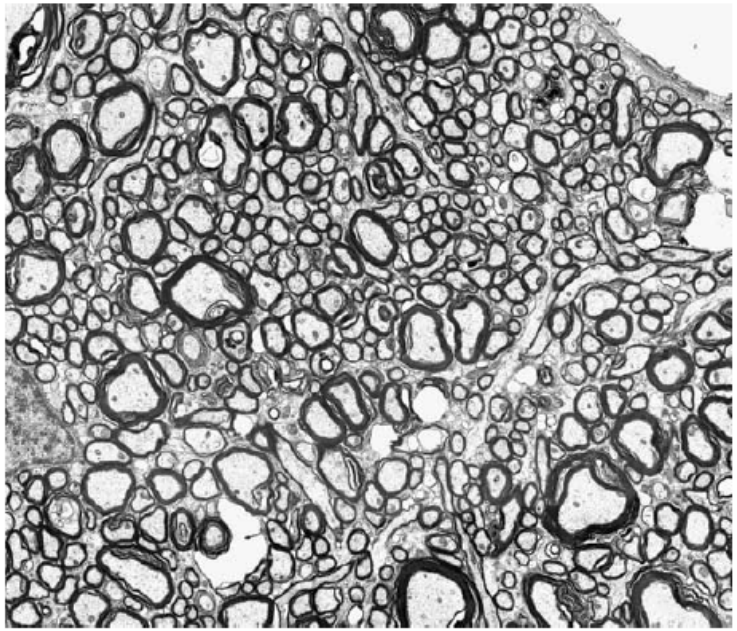
Solution for the Stejkal-Tanner pulse sequence.



$$\frac{A(t)}{A_0} = \exp\left(-\gamma^2 g^2 \delta^2 \left(\Delta - \frac{\delta}{3}\right) D\right) \equiv \exp(-bD)$$

Diffusion in biological tissue.
Apparent Diffusion Coefficient (ADC) approach.

- ADC is a phenomenological parameter that incorporates integrative information on the tissue microstructure.
- It is insensitive to microstructure details.
- It is a very important biomarker for identifying pathologies.



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

For a given gradient direction, the signal attenuation at the echo time can be written as

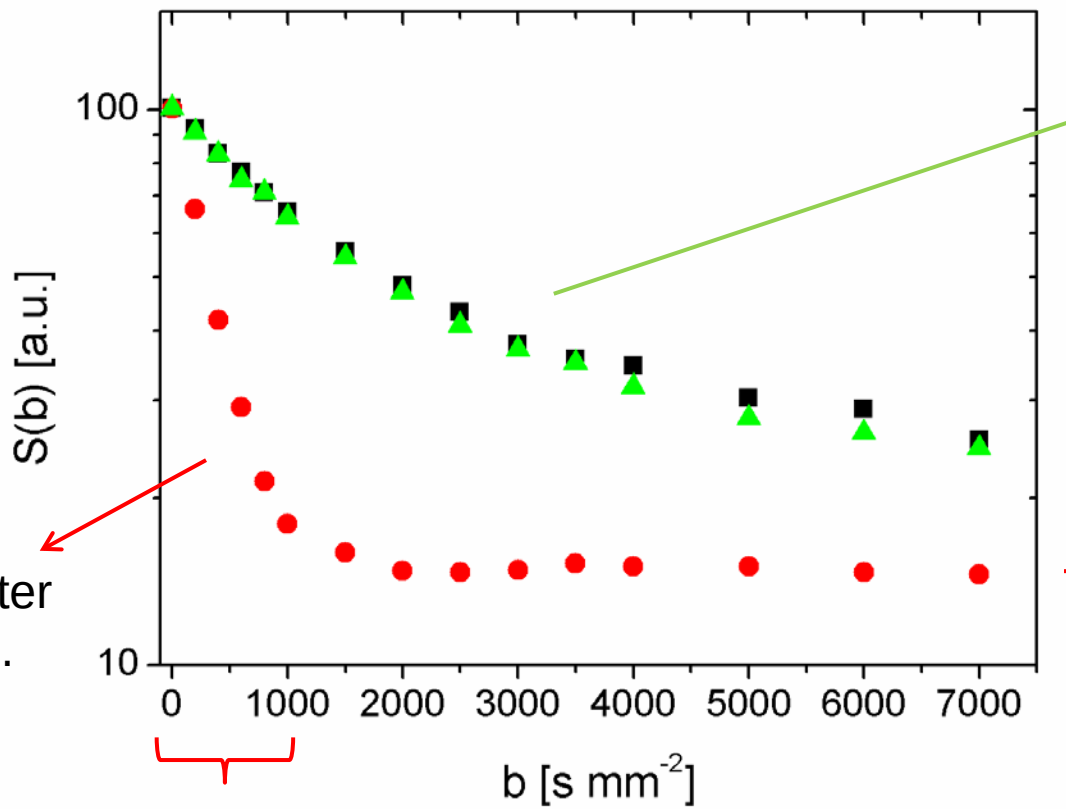
$$S(b) = S_0 e^{-b \cdot ADC}$$

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

Then one needs to measure S_0, the non-diffusion-weighted value (no gradients), and the signal for at least a non-zero *b*-value.

The usual range for the *b*-values is (0-1000) s/mm^2. For grater *b*-values, the attenuation is not longer monoexponential.

Typical diffusion signal attenuations.



Diffusion is restricted, i.e. the initial slope is smaller than in the free-diffusion case.

Free water diffusion.

Background noise.

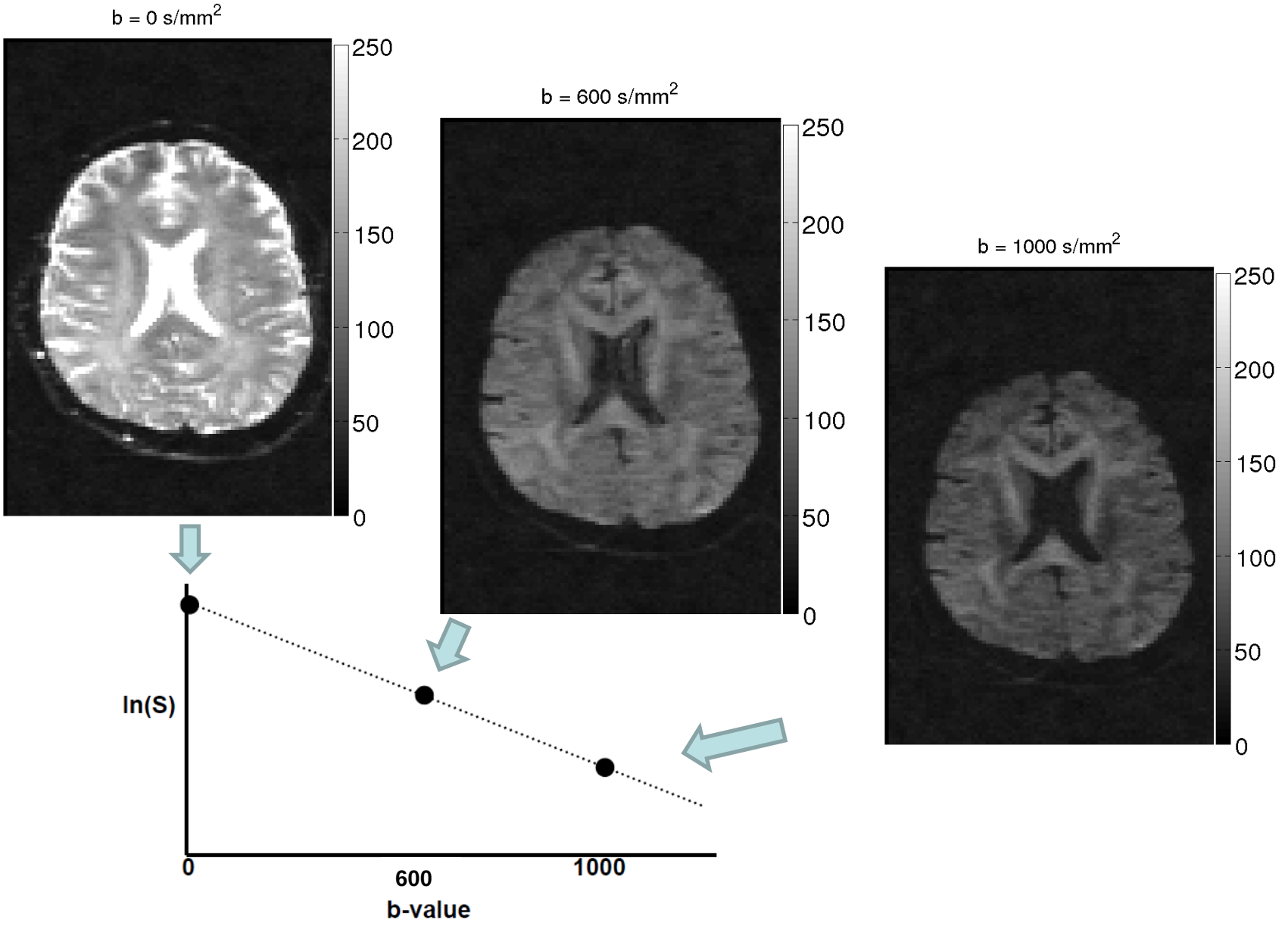
Valid range for the ADC approach.

$$\ln \frac{S(b)}{S_0} = -b \cdot ADC$$

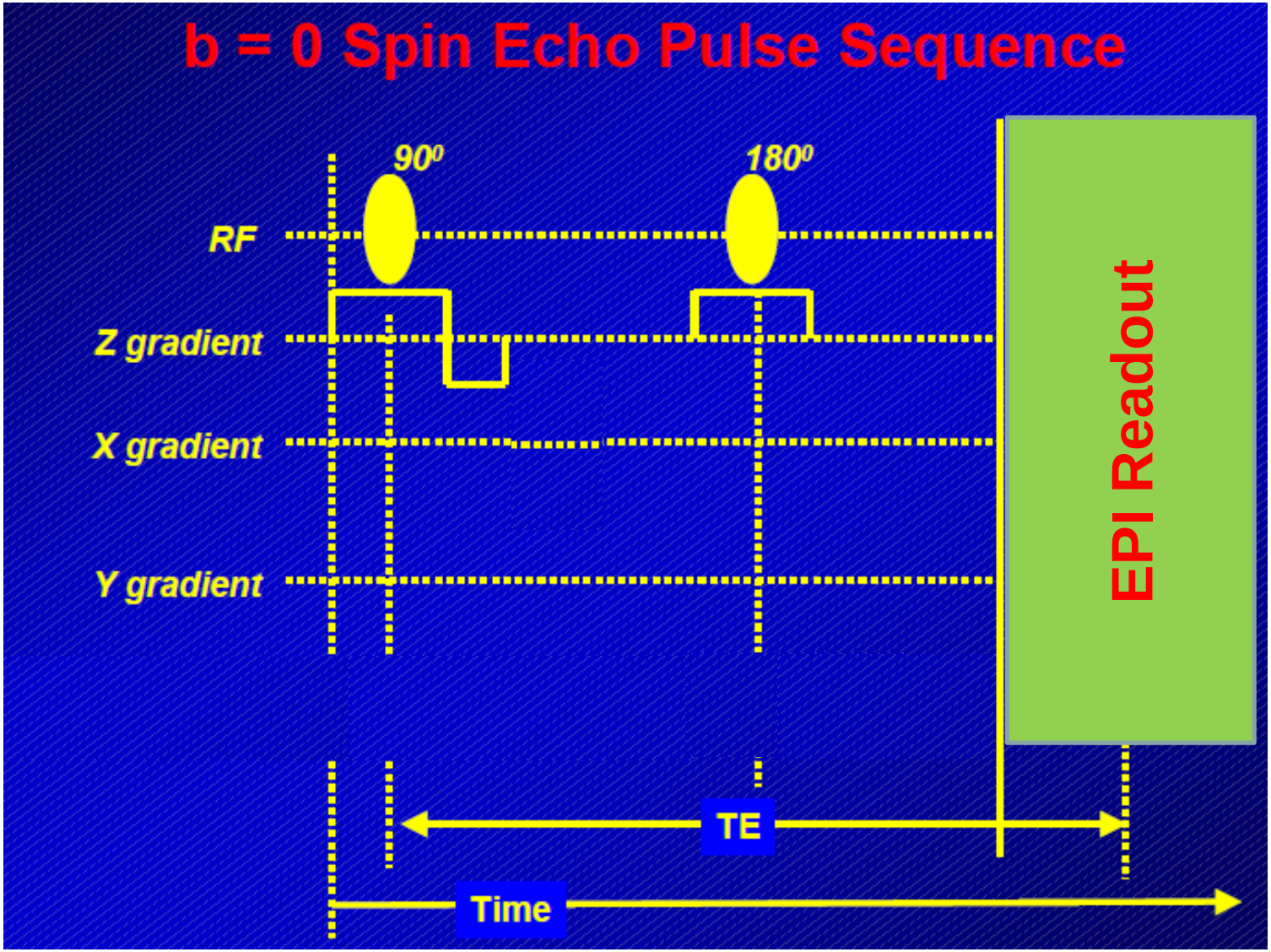
The ADC is given by the slope of the signal attenuation in a logarithmic scale.

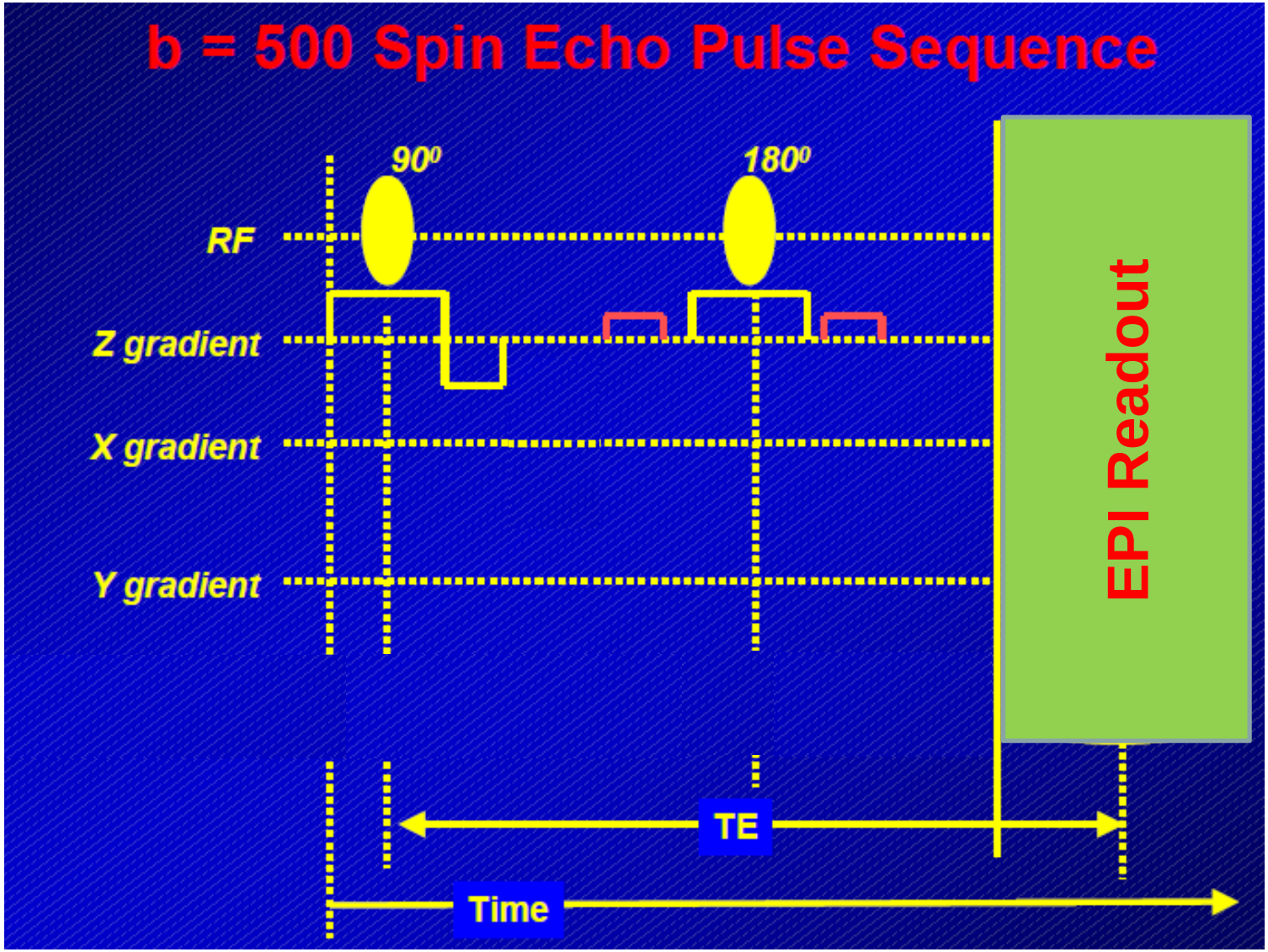
ADC = 2.3*10^{-3} mm^2/s for free water at 24° C.

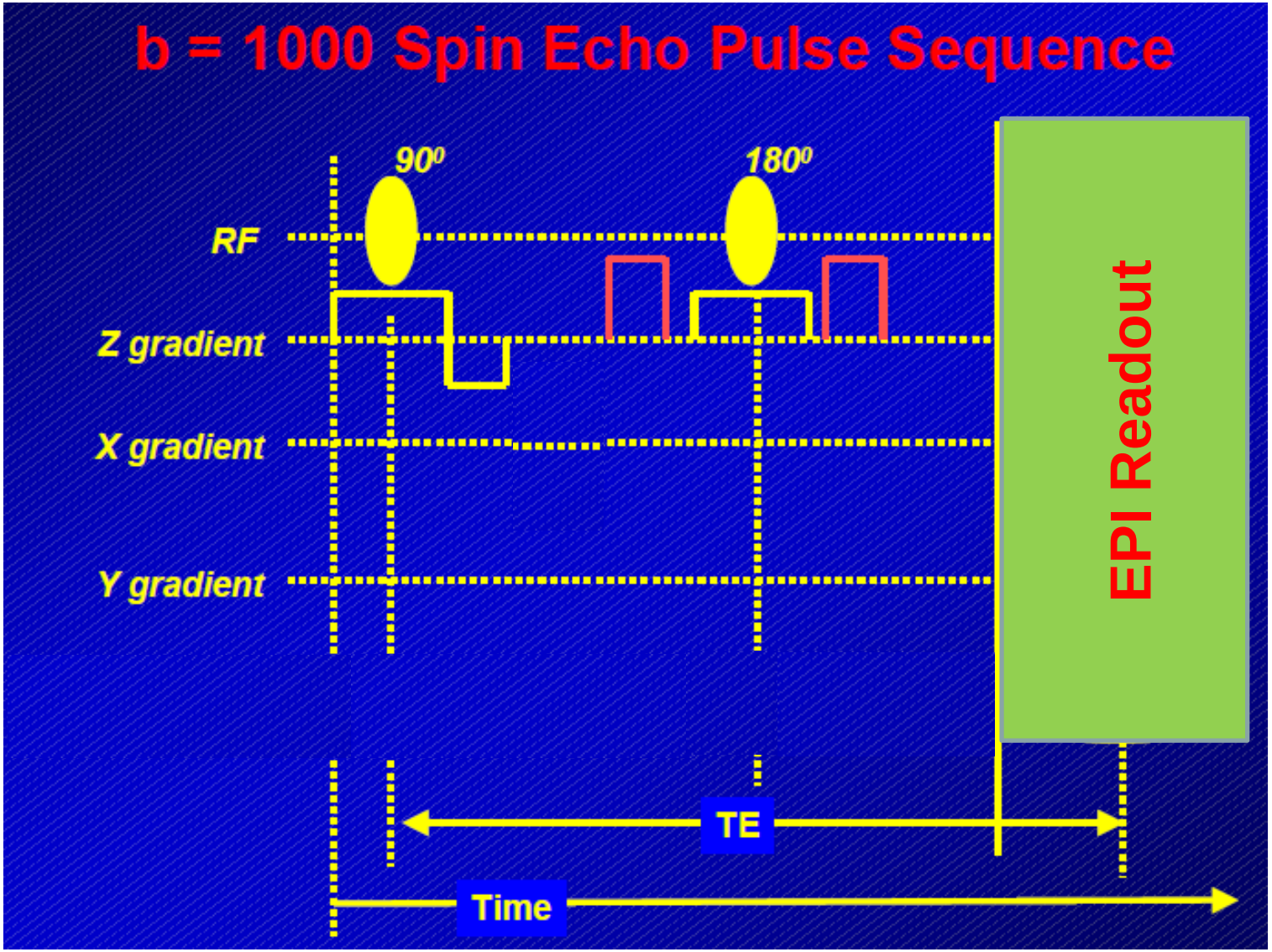
Diffusion weighted imaging (DWI) in the human brain.



DWI signal acquisition. Gradient along *z*-direction case.

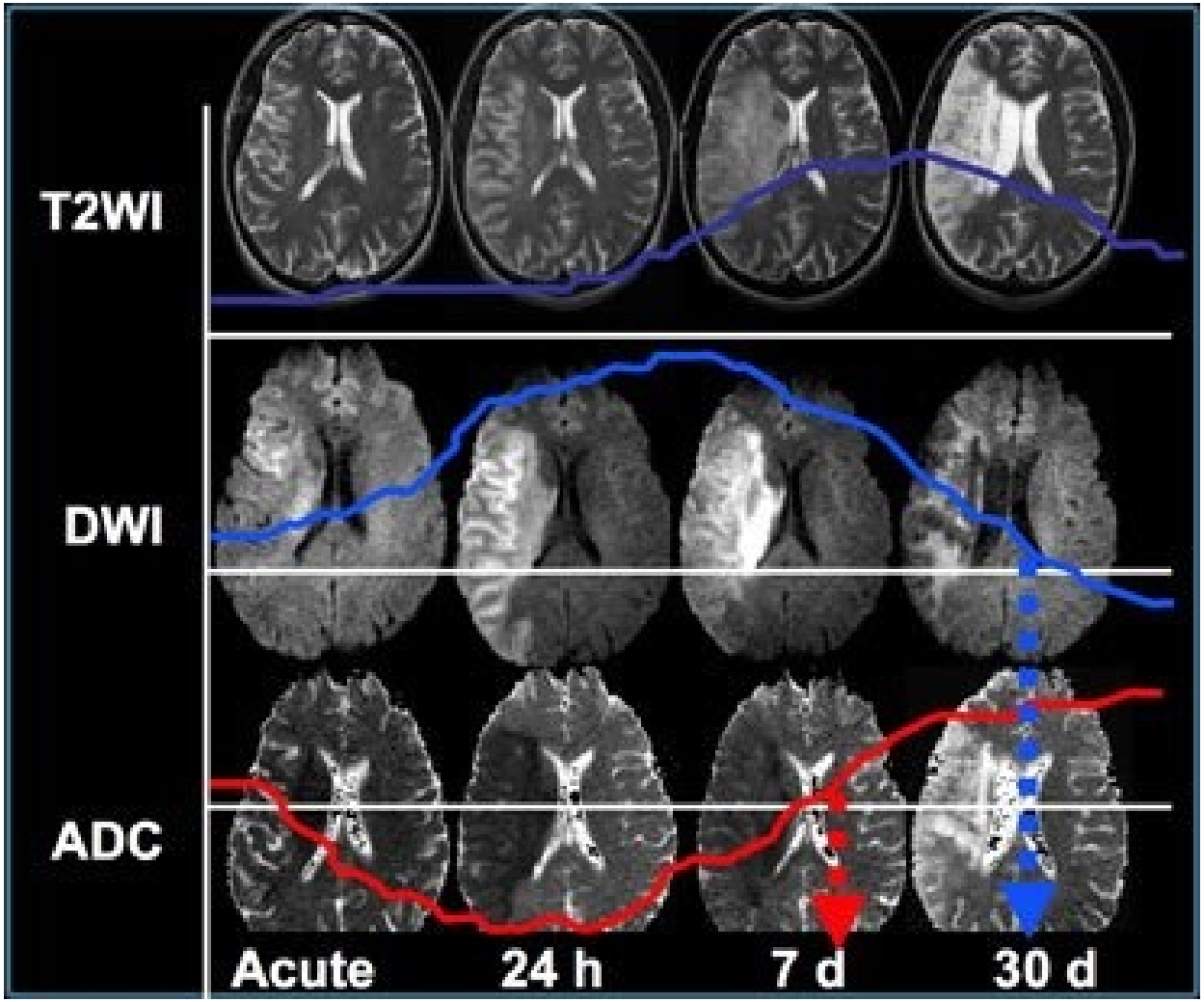



b = 500 Spin Echo Pulse Sequence
90⁰
180⁰
RF
Z gradient
X gradient
Y gradient
EPI Readout
TE
Time


b = 1000 Spin Echo Pulse Sequence
90⁰
180⁰
RF
Z gradient
X gradient
Y gradient
EPI Readout
TE
Time

An application of DWI. Early detection of stroke.

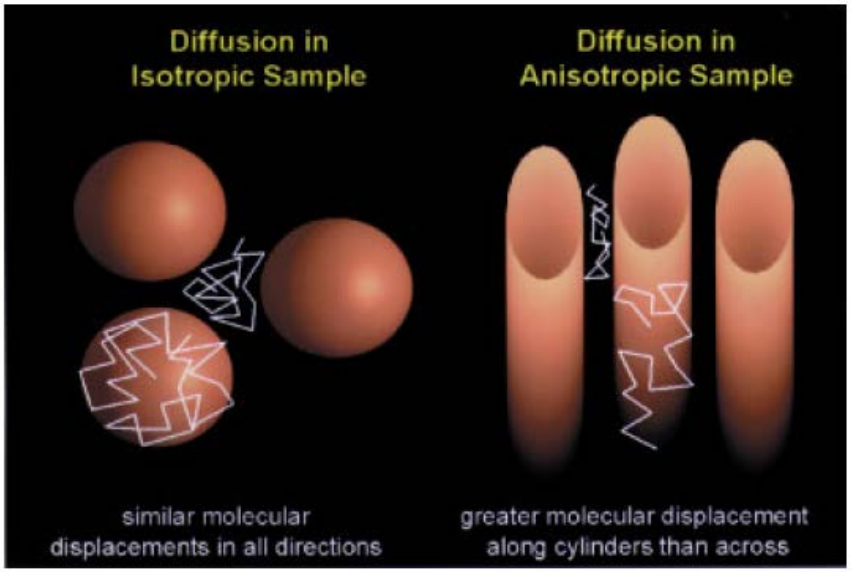
DWIs permit earlier detection of stroke than other methods such as T2WI (T2 weighted image).

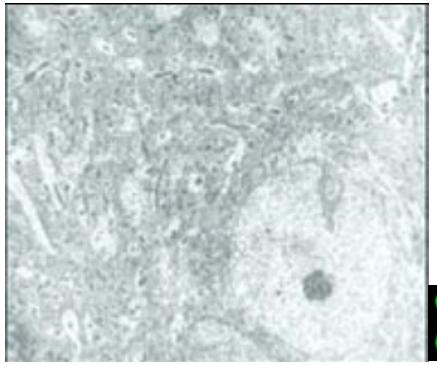


http://www.radiologyassistant.nl/en/483910a4b6f14

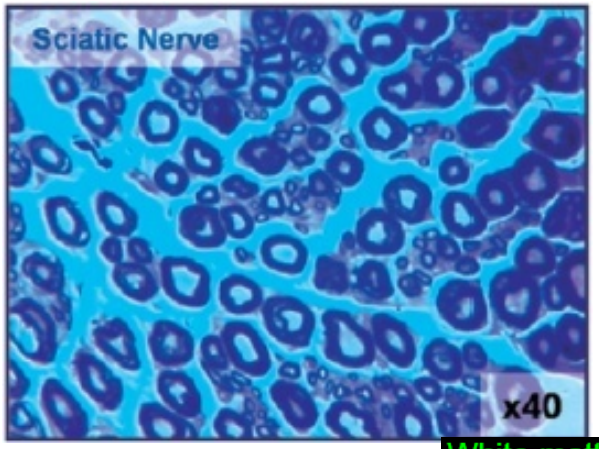
Diffusion Anisotropy.
Diffusion Tensor Imaging (DTI) approach.

There are some cases in which diffusion depends on the spatial direction along which the gradient is applied.

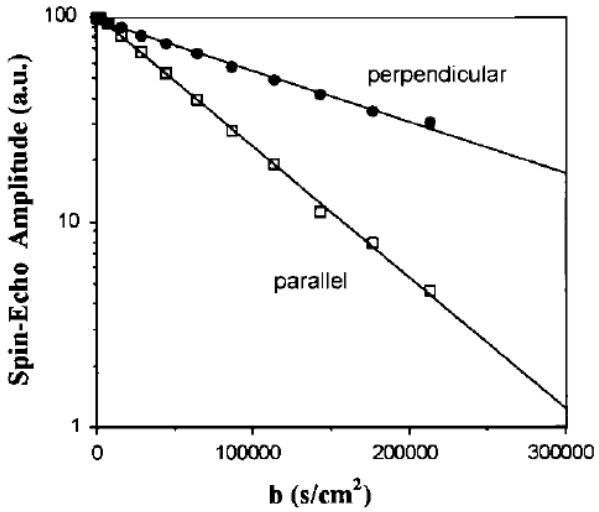




Gray matter
(Cortex)



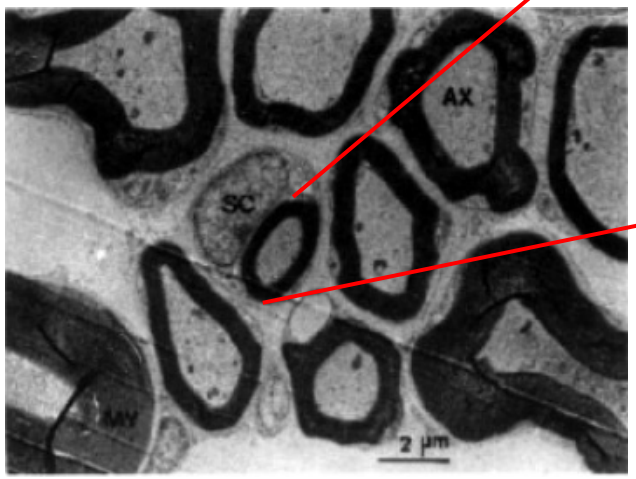
White matter
(Corpus callosum)

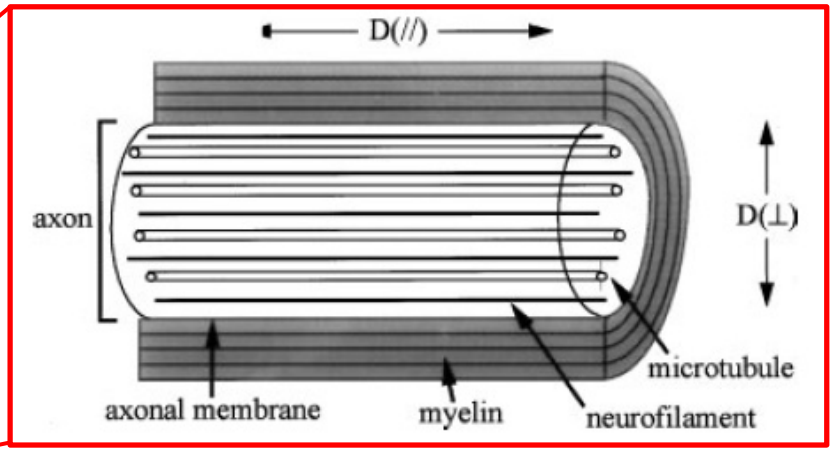


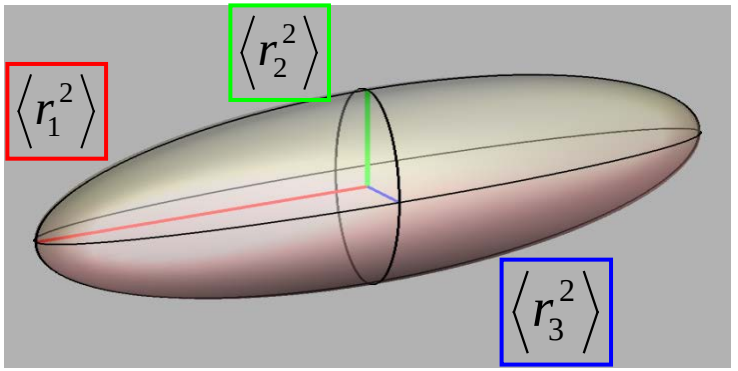
The presence of elongated cells, such as axons and dendrites, affects the trajectory of diffusion molecules, making diffusion along the main directions less obstructed than in a direction perpendicular to the main axes.

According to Einstein's relation, the mean square displacement in a given direction "*i*", and a diffusion time t_d, will be:

$$\left\langle r_i^2 \right\rangle = 2D_i t_d$$







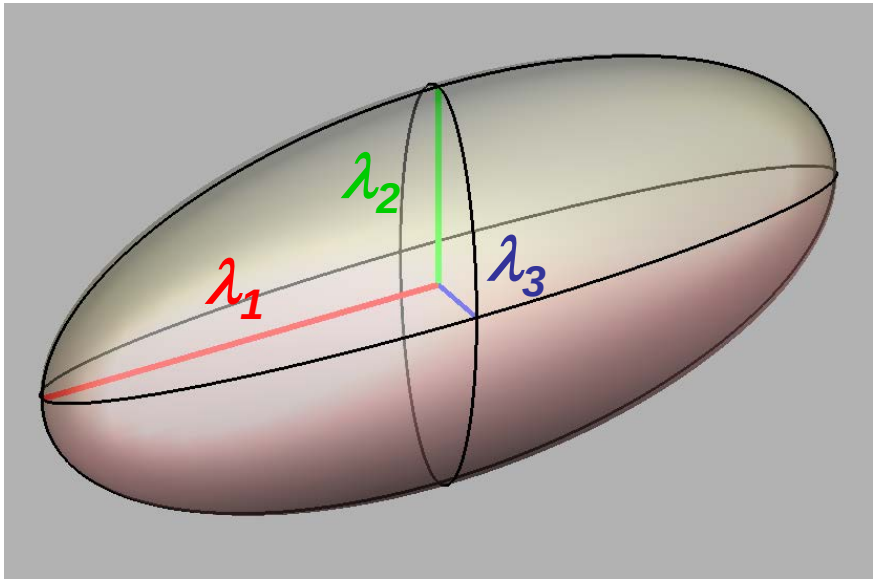
Formally, anisotropic diffusion is characterized by a diffusion tensor D_{ij} and the signal attenuation can be written as:

Signal attenuation.

$$S(\mathbf{b}) = S_0 e^{-\sum_{i,j} b_{ij} D_{ij}}$$

b-matrix (matrix of *b*-values).

$$b_{ij} = \gamma^2 \int_0^T \left[\int_0^t g_i(t')dt' \int_0^t g_j(t')dt' \right] dt$$



$$\overleftrightarrow{D} = \begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{pmatrix}$$

General coordinate frame.

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

Principal axes frame.

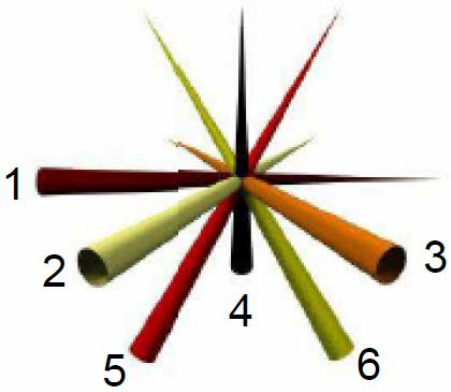
Since ***D*** is a second-order symmetric positive definite tensor, one needs to know the ADC for at least 6 non-collinear directions.

From the experiment to the diffusion tensor.

One has to measure a non-weighted signal value S_0 (b = 0 s/mm^2) and N diffusion-weighted signals S_k (k = 1..N ≥ 6). Then, one has to solve the next system of equations

$$\ln \frac{S_k}{S_0} = -\sum_{i,j} b_{ij}^k D_{ij}$$

- For N = 6, the solution is exact.
- For N ≥ 6, the system is overdetermined: tensor estimation is more robust

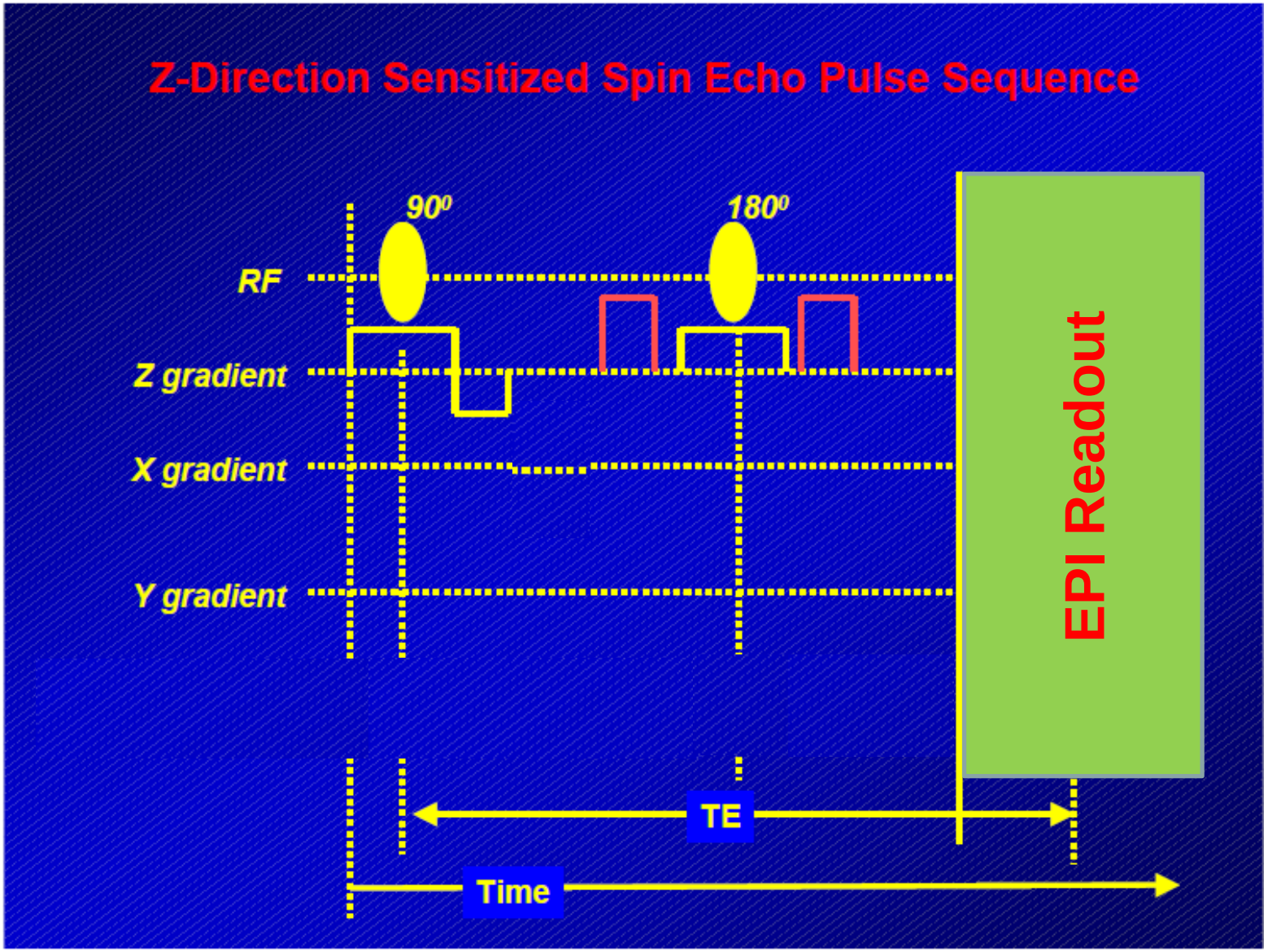


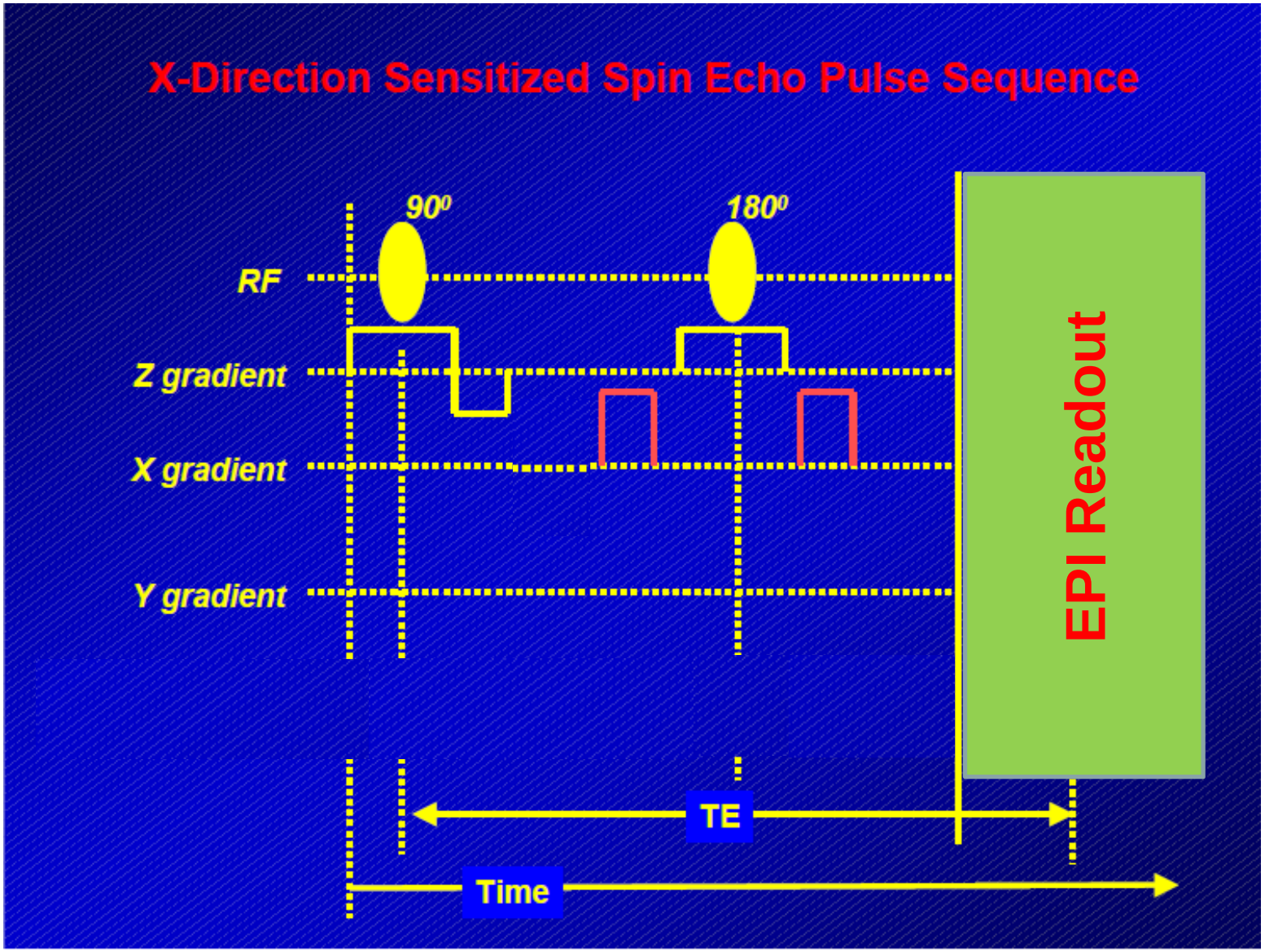
6 directions

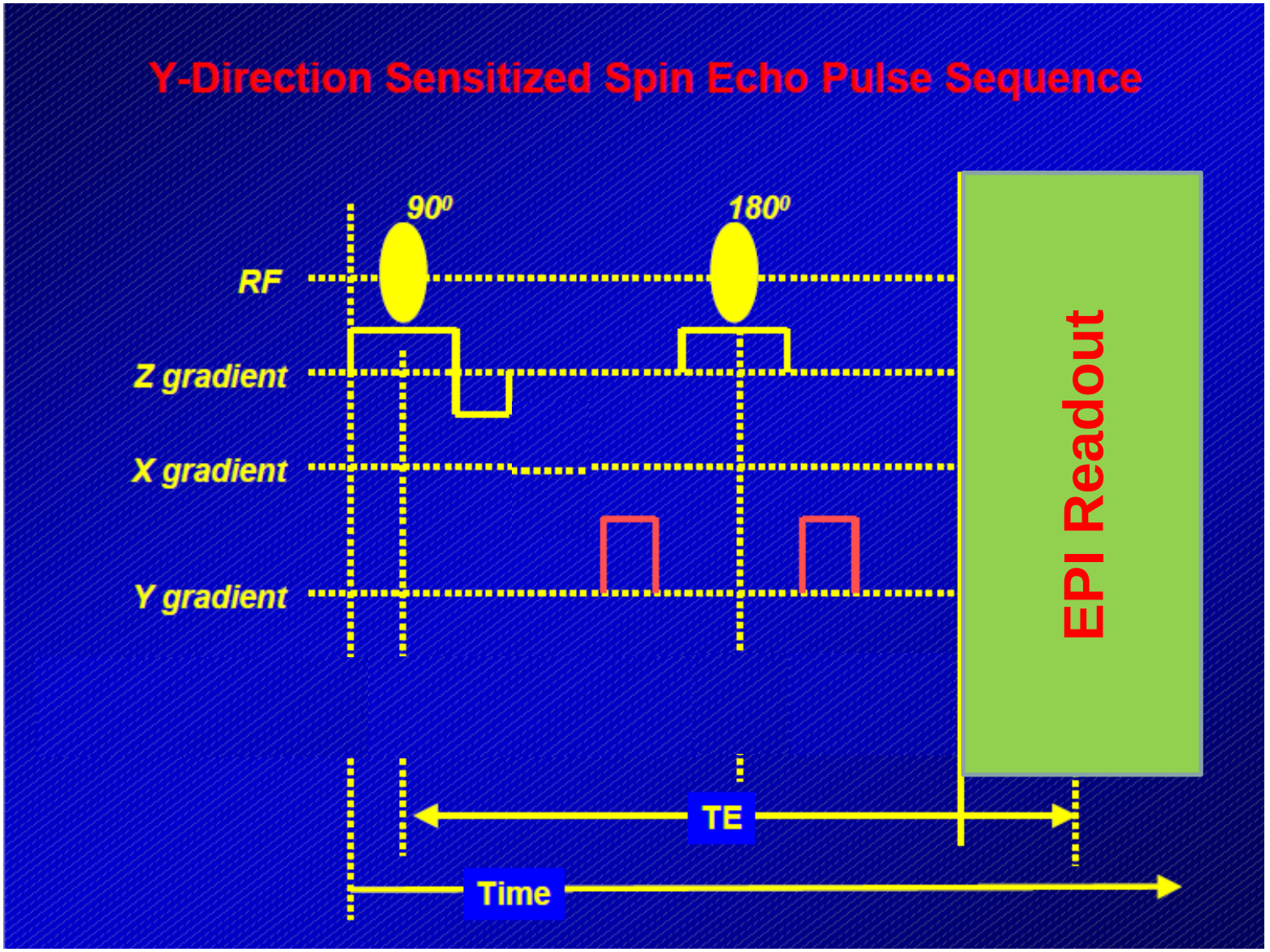
12 directions

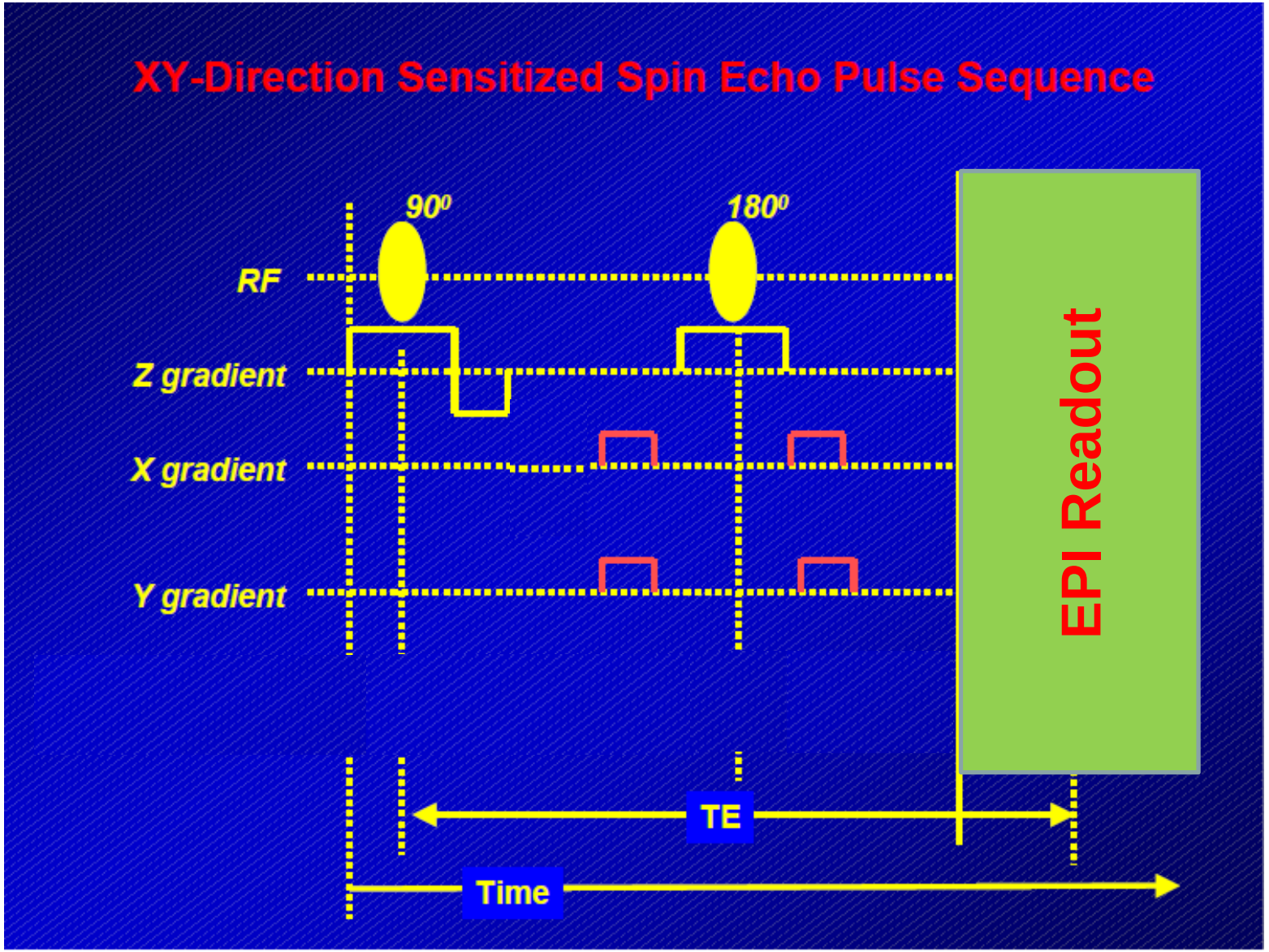
30 directions

The number of gradient directions available for clinical applications ranges from 6 up to 256.


Z-Direction Sensitized Spin Echo Pulse Sequence
90⁰
180⁰
RF
Z gradient
X gradient
Y gradient
EPI Readout
TE
Time


X-Direction Sensitized Spin Echo Pulse Sequence
90⁰
180⁰
RF
Z gradient
X gradient
Y gradient
EPI Readout
TE
Time


Y-Direction Sensitized Spin Echo Pulse Sequence
90⁰
180⁰
RF
Z gradient
X gradient
Y gradient
EPI Readout
TE
Time


XY-Direction Sensitized Spin Echo Pulse Sequence
90⁰
180⁰
RF
Z gradient
X gradient
Y gradient
EPI Readout
TE
Time

Tensor invariants.

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

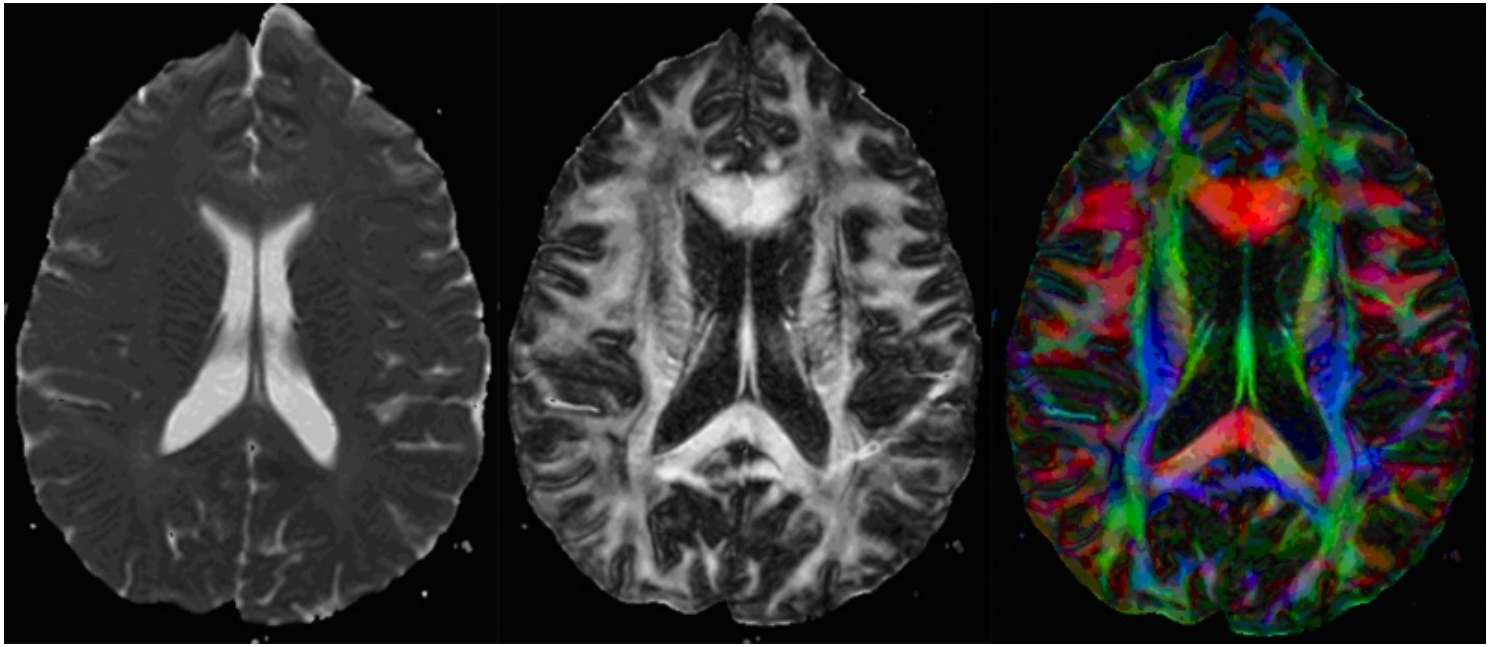
$$\vec{\vec{D}} = \begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{pmatrix} \Rightarrow \text{Diagonalization} \Rightarrow \begin{cases} \lambda_i & \text{eigenvalues.} \\ \vec{v}_i & \text{eigenvectors.} \end{cases}$$

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 $\Rightarrow$ $0 \geq FA \geq 1$ $\Leftarrow$ Diffusion allowed in only one direction.

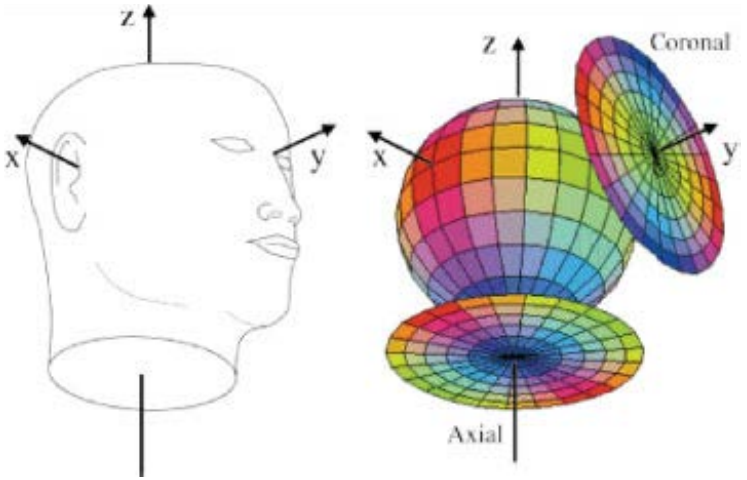
MD FA Colour-encoded FA



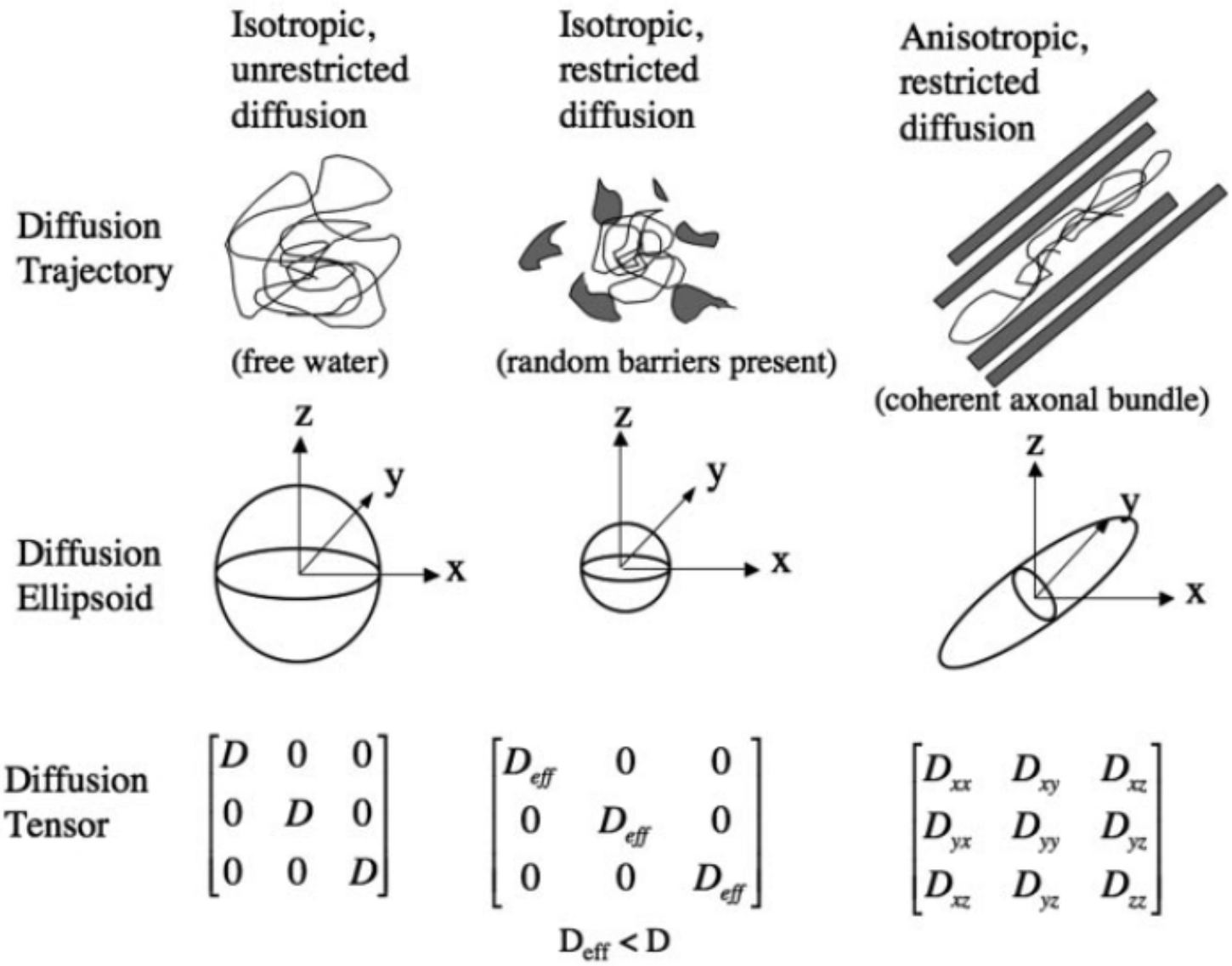
Colour-encoded FA

$\vec{v}_3$ Eigenvector associated to the main eigenvalue, modulated by FA

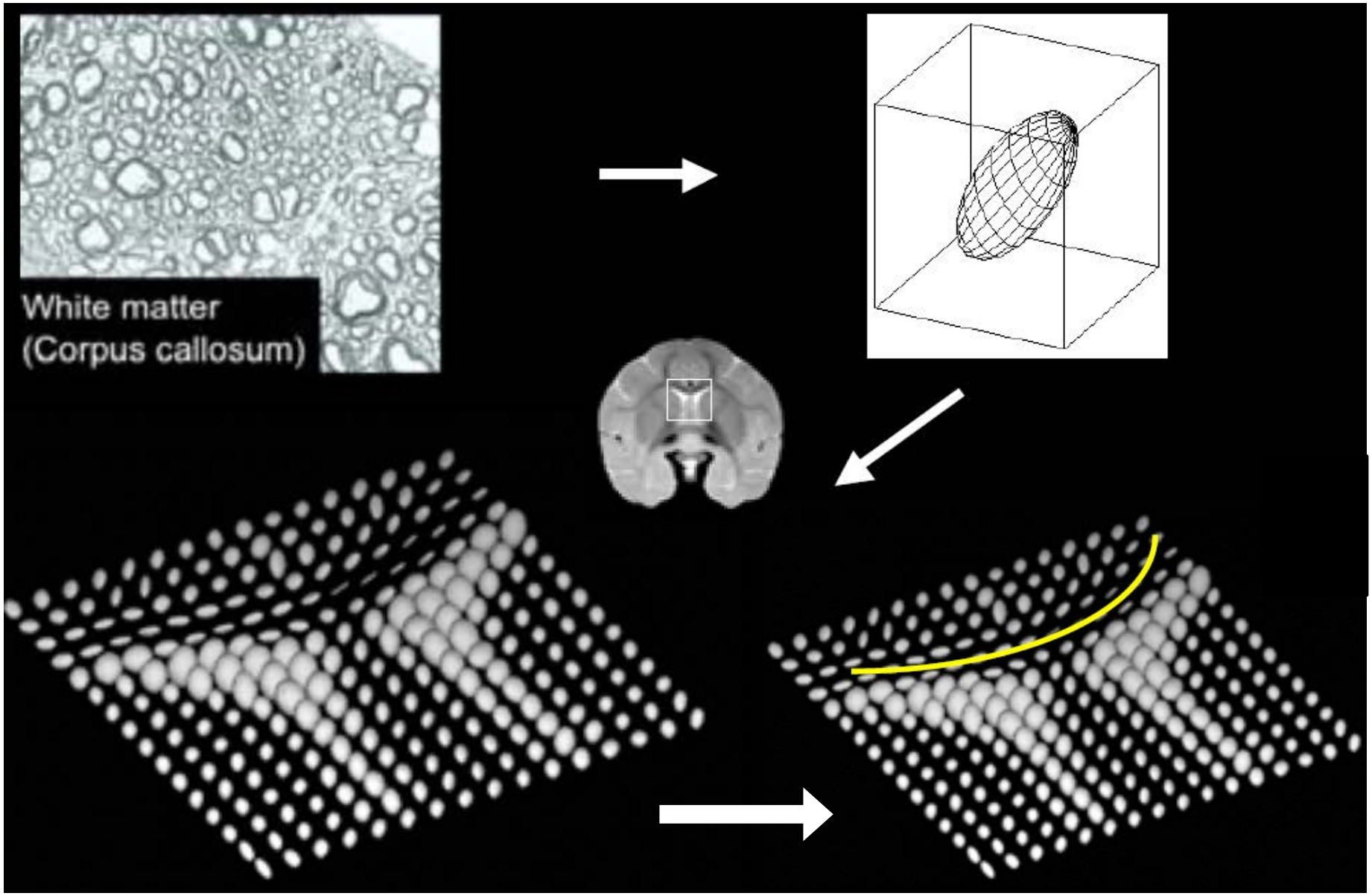
- red = left-right.
- green = anterior-posterior.
- blue = top-bottom.



Summary so far …

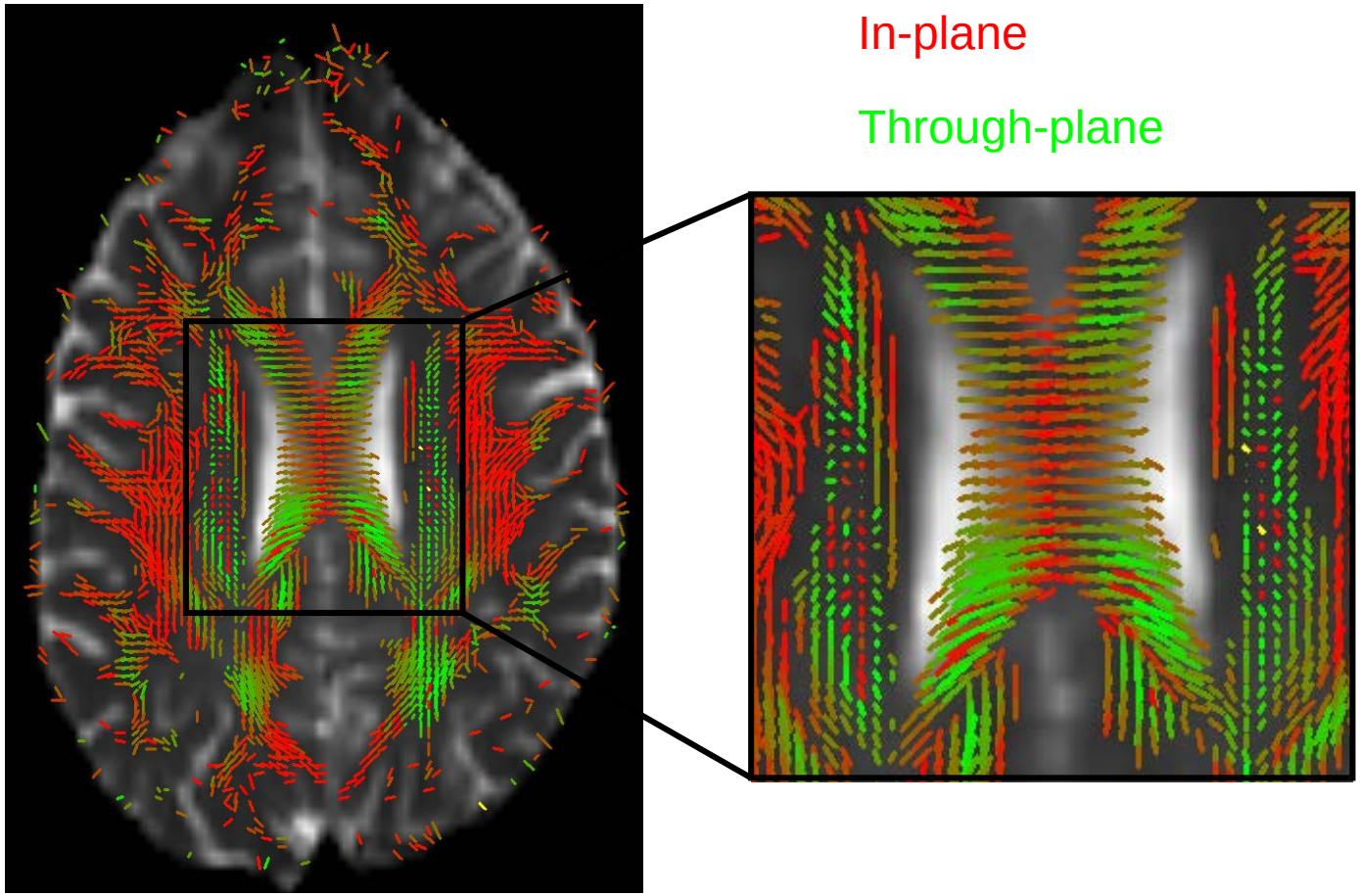


Fibre Tracking

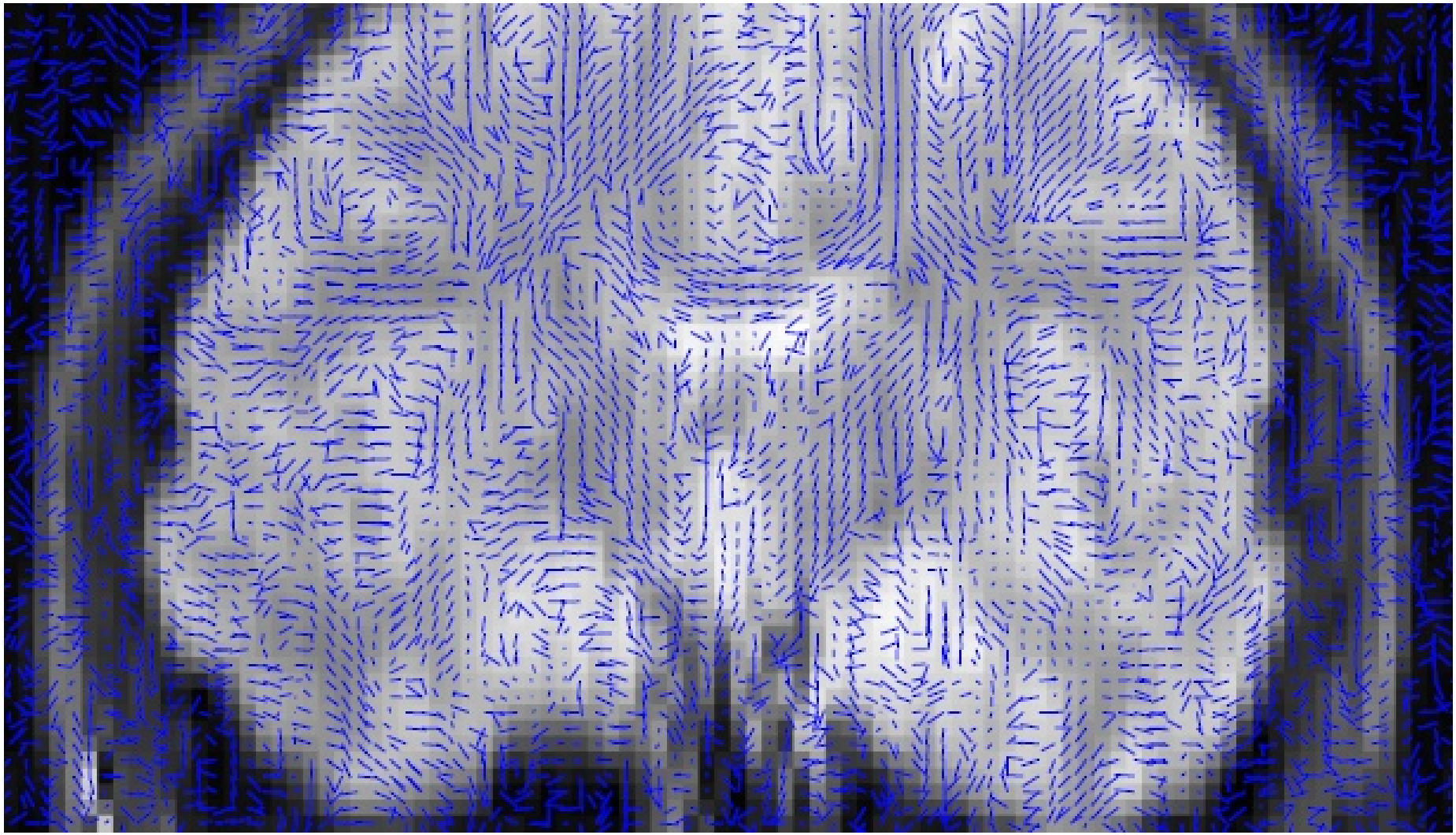


- Assuming that the largest principal axis of the diffusion tensor aligns with the predominant fibre orientation.

- Construct a vector field



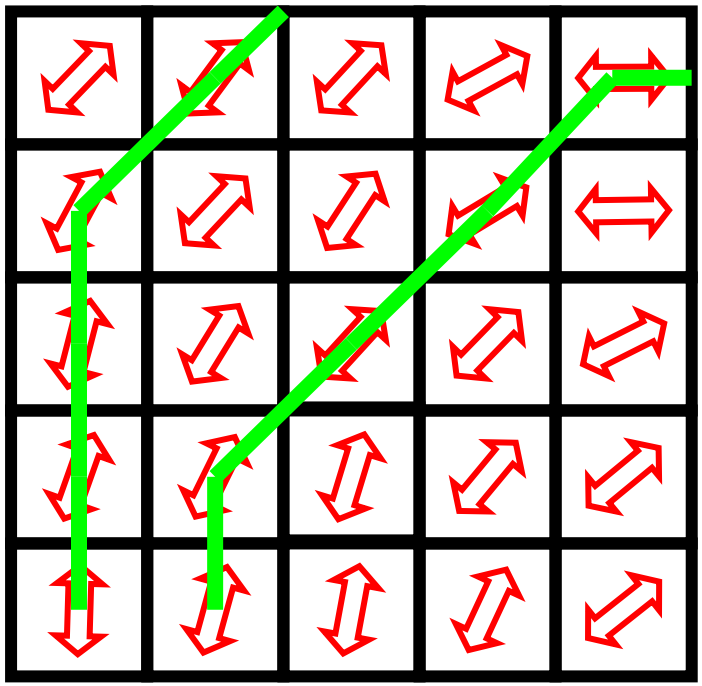
Another vector field map

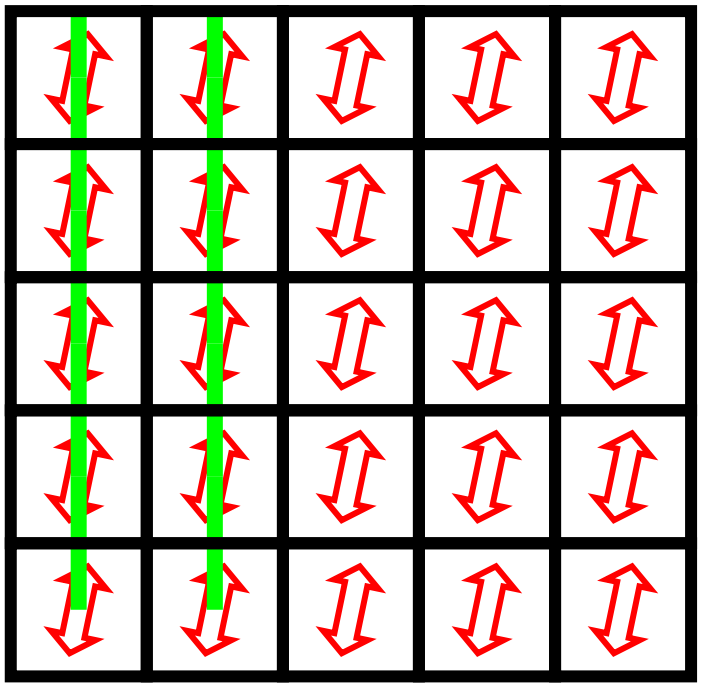


Discrete vector field

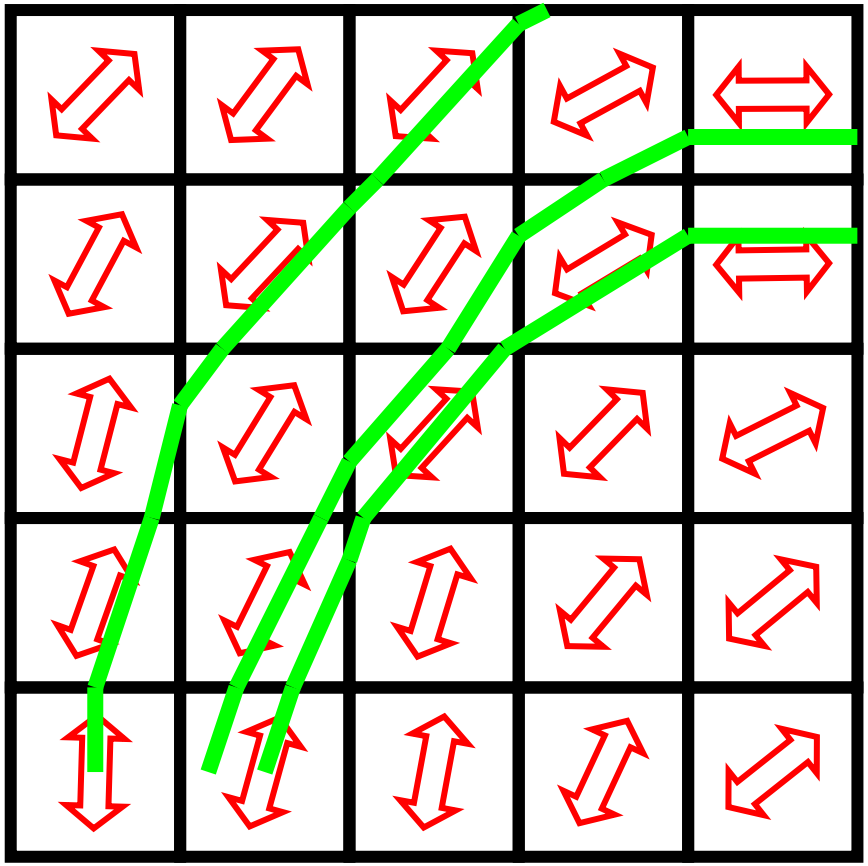
- Connect voxels on the basis of discrete vector fields (local principal eigenvector orientation)

- FA threshold (0.25-0.35). Helps to exclude gray matter and to segment white matter tracts that are separated by gray matter.



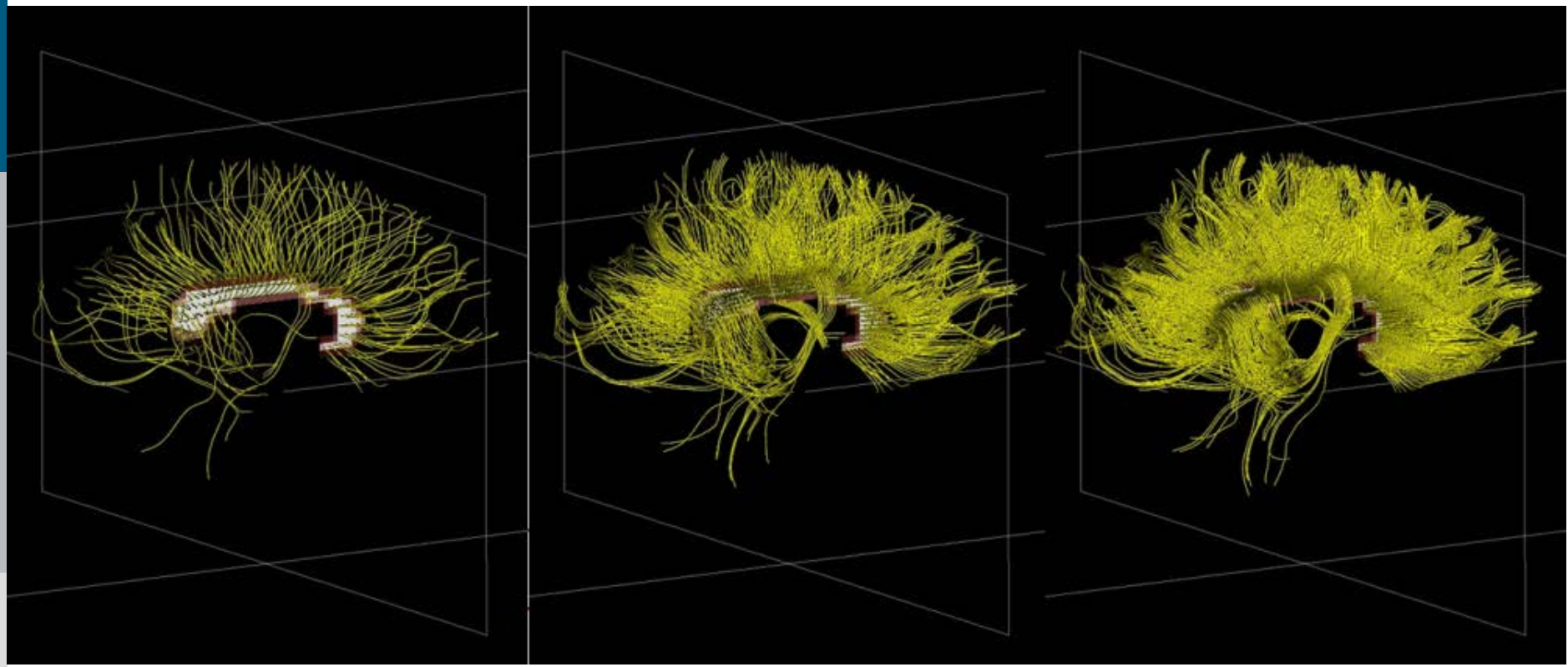


Continuous vector field



Corpus callosum tracking

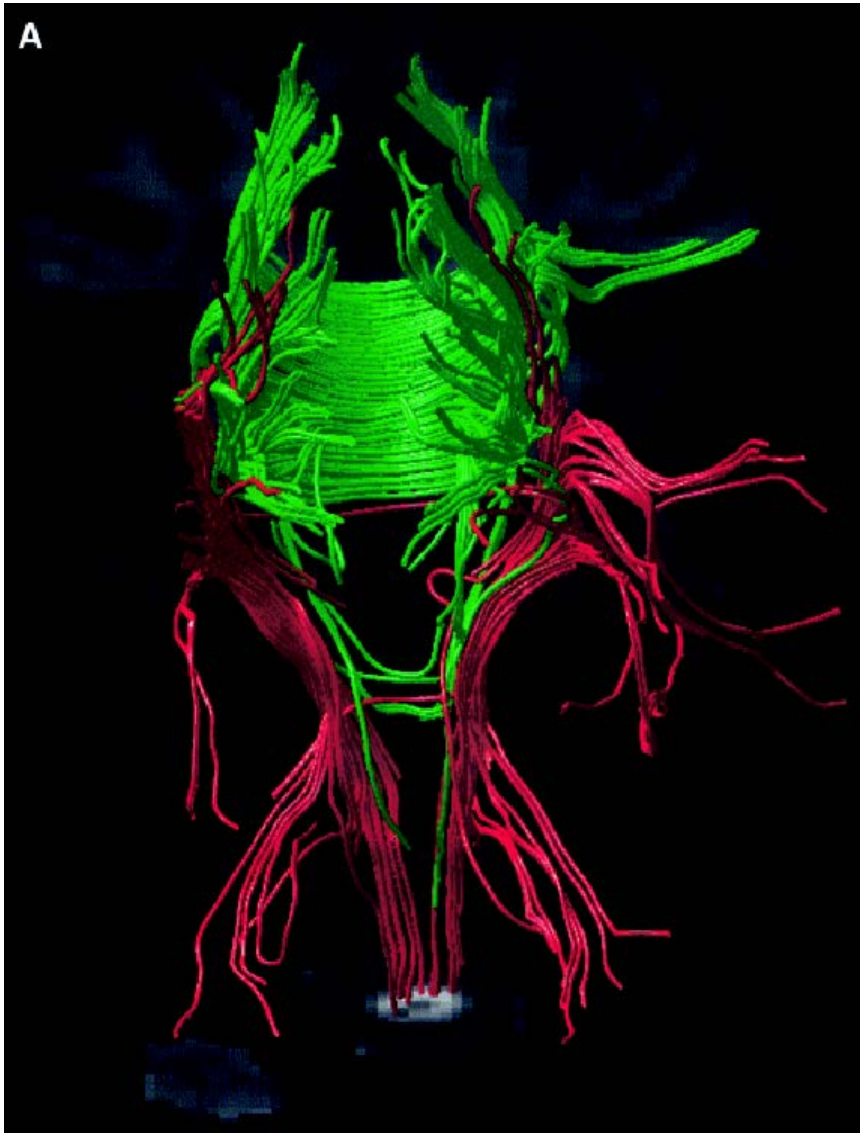
Choose to seed the tracking using a single point, a region of interest or a volume.

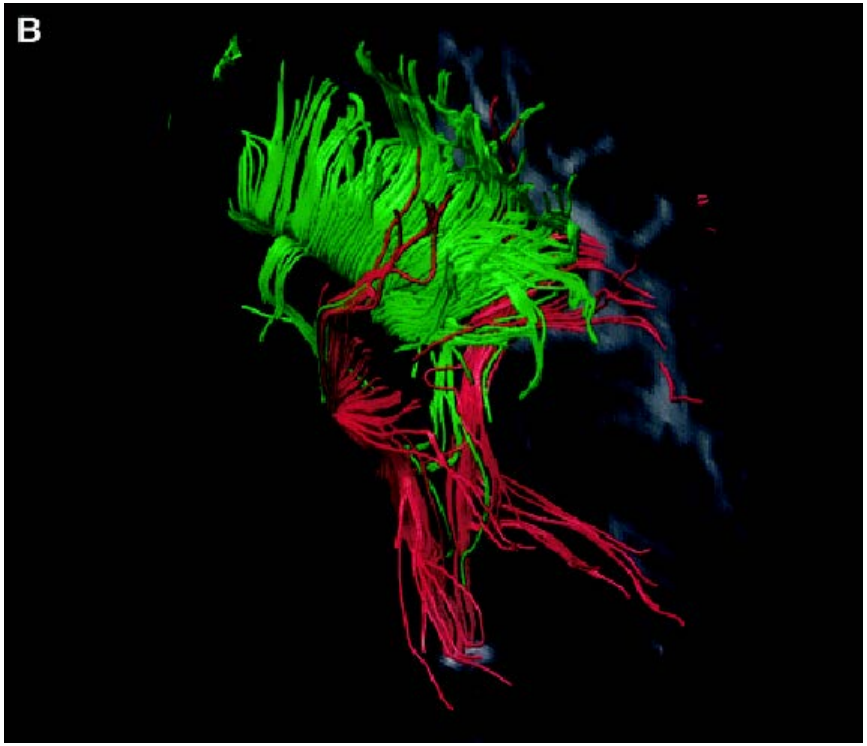


Fibre tracking by seeding a region of region of interest in the corpus callosum with increasing fibre densities.

http://www.bioimagesuite.org/doc/node24.html#SECTION06310000000000000000

Pretty Pictures…



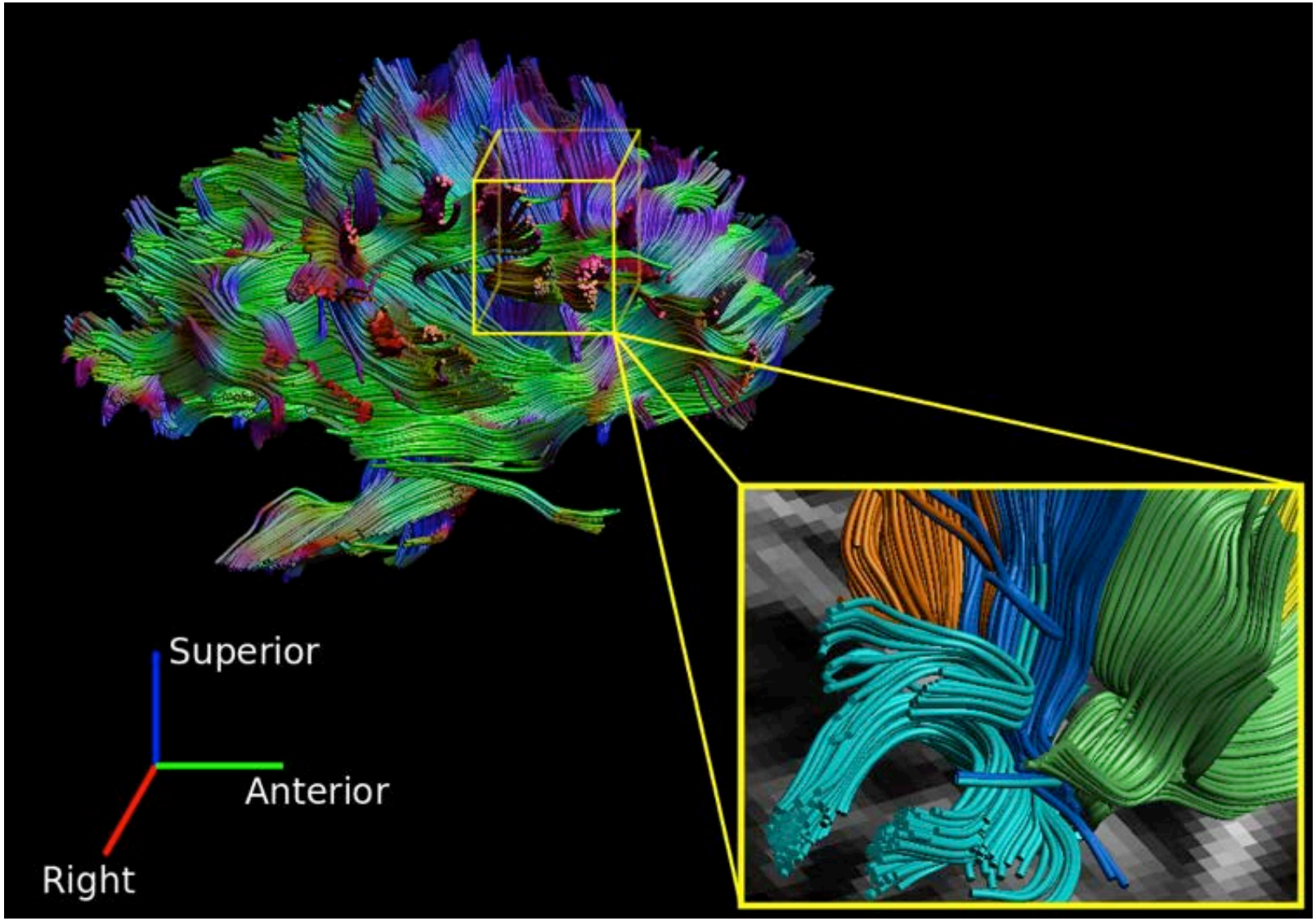


Isotropic resolution diffusion tensor imaging with whole brain acquisition in a clinically acceptable time

–D.K. Jones, S.C.R. Williams, D. Gasston, M.A. Horsfield, A. Simmons, R. Howard

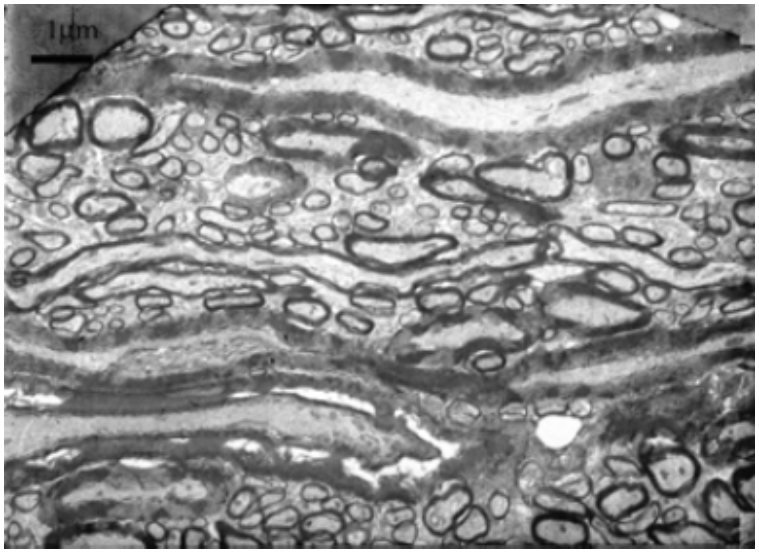
–Human Brain Mapping 15, 216-230 (2002)

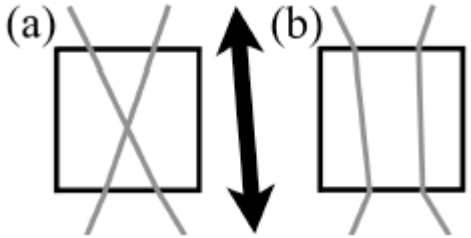
Pretty Pictures…

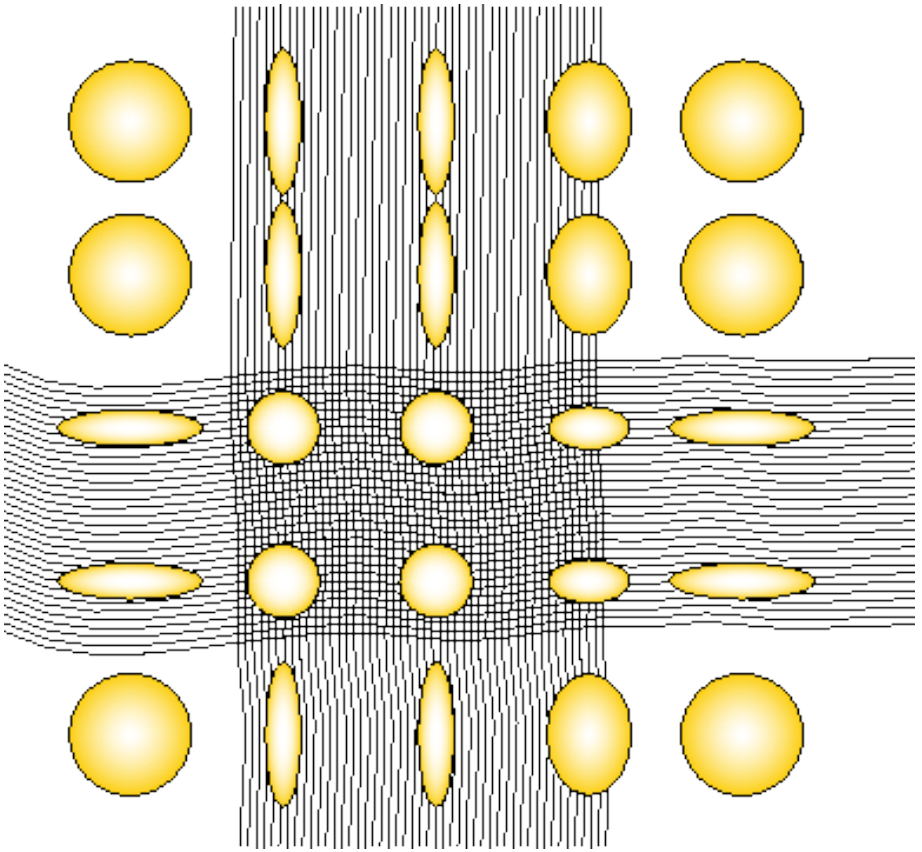


Limits of DTI.
The problem of multiple fibres populations.

An inherent problem of DTI is the impossibility to recognize crossing fibres.







Suggested notes

- H. C. Torrey, “Bloch Equations with Diffusion Terms”, Physical Review, vol. 104, 563 (1956).
- A. Abragam, “Principles of Nuclear Magnetism”. Oxford Univ. Press. London and New York (1961).
- J. Kärger, H. Pfeifer and W. Heink, ”Principles and Application of Self-Diffusion Measurements by Nuclear Magnetic Resonance”. Advances in Magnetic Resonance, vol. 12 (1988).
- D. A. Yablonskiy and A. L. Sukstanskii, “Theoretical models of the diffusion weighted MR signal”. NMR in Biomedicine, vol. 23, 661 (2010).