Imaging Molecular Diffusion

Quantitative and Functional Imaging

BME 4420/7450

Fall 2022

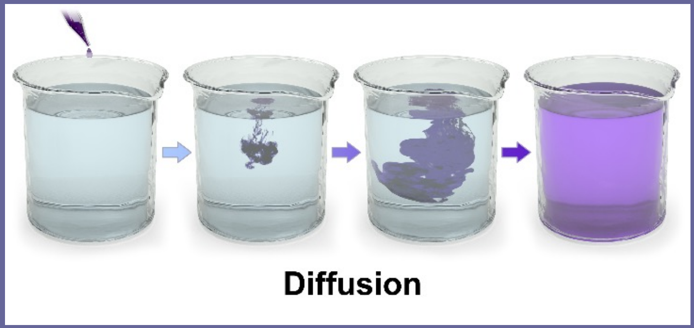
Topics

- Molecular diffusion
- How water diffusion reveals tissue microstructure
- How water diffusion is measured with MR
- Why is diffusion imaging useful in biomedicine?
- Applications

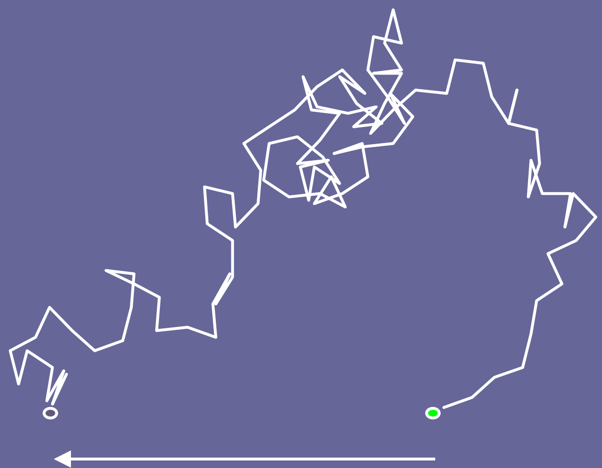
Molecular diffusion

Free diffusion of water

- Random thermal motion
- No preferred direction (isotropic)
- Modeled as a random walk
- Net displacement:
  $\langle r^2 \rangle = 2DT$
- D = 2.5 microns^2/msec



en.wikipedia.org



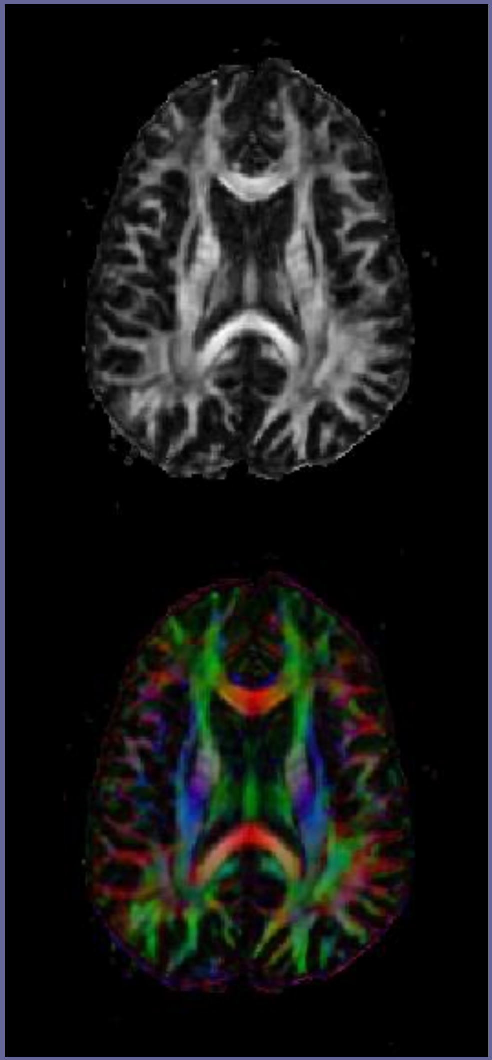
Water diffusion reflects tissue microstructure

- Diffusion of water in tissue
  - Constrained by cell membranes
  - Preferred direction of membranes -> preferred direction of water diffusion
- Largest displacements
  - Parallel to axons in brain
- Variation of displacements over orientations reflects
  - Membrane density
  - Membrane permeability
  - Fiber coherence (angular deviation)

Beaulieu, *NMR Biomed*, 2002

Diffusion Anisotropy reveals fiber bundle orientation

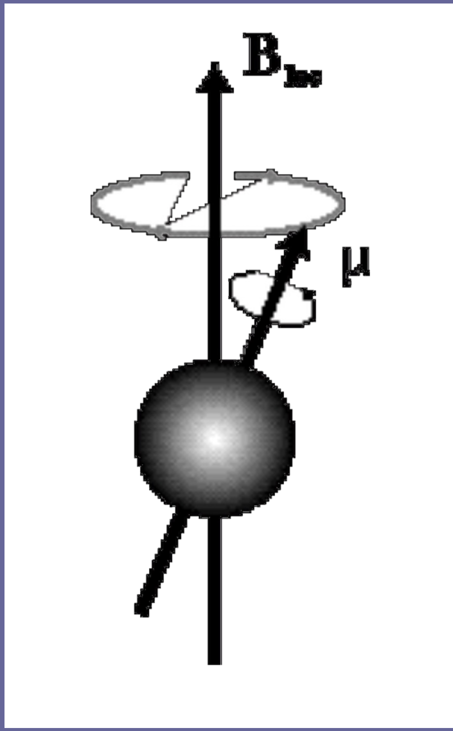
- Anisotropy maps
  - Bright in coherent white matter
  - Darker
    - Where fibers diverge
    - In gray matter
  - Fractional Anisotropy (FA): $0 \leq FA \leq 1$
- Orientation information
  - Color code FA by fiber direction
    - Red = Right/Left
    - Green = Anterior/Posterior
    - Blue = Superior/Inferior
- Reveals structure within white matter



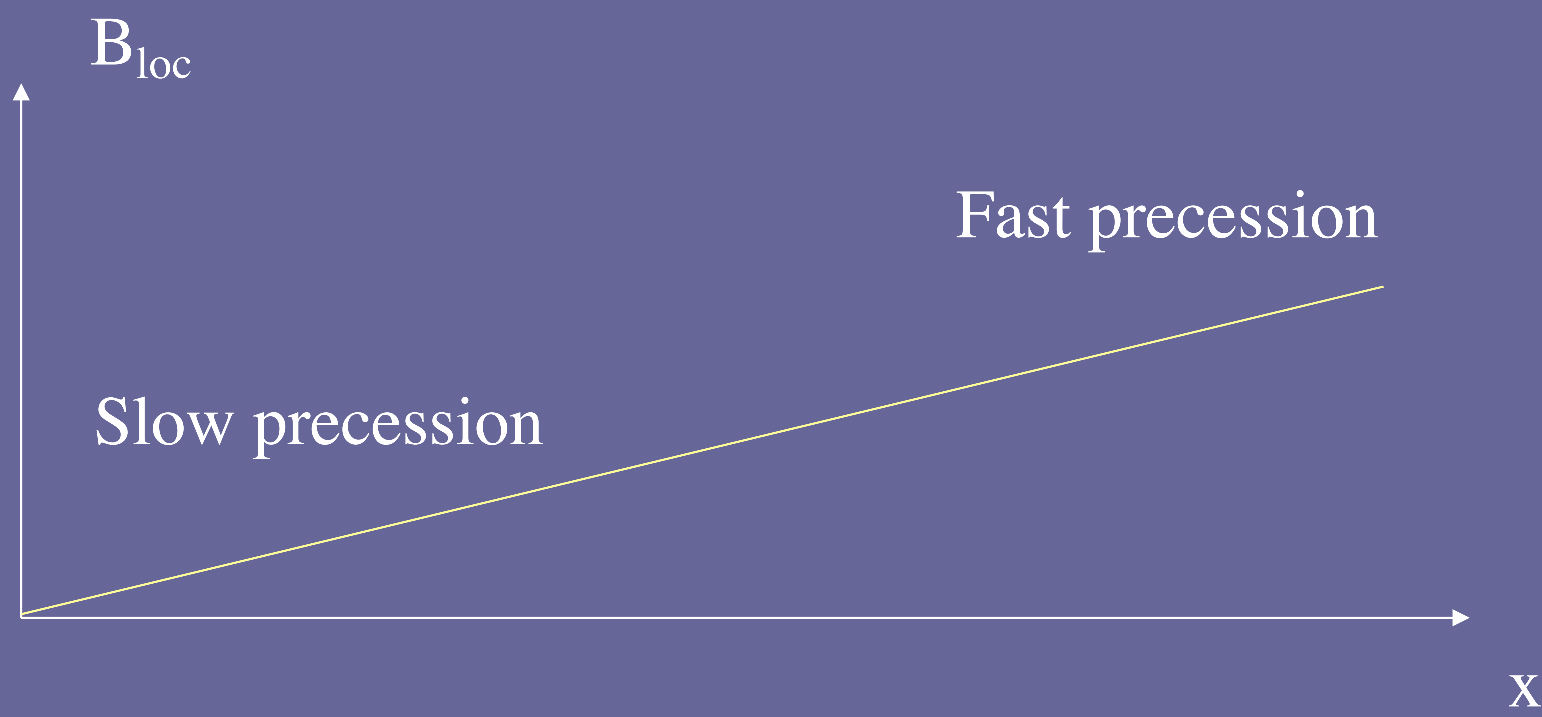
Measuring water diffusion with MRI

Spin precession reveals diffusion

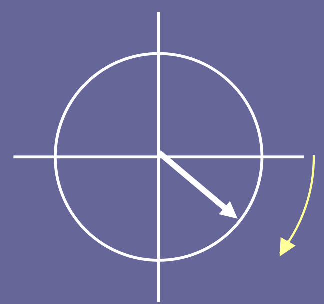
- Spins precess around a magnetic field, B_{loc}
- Rate of precession is proportional to B_{loc}
- Use the precession frequency to determine spin position
- Use <u>changes</u> in frequency to determine <u>changes</u> in position

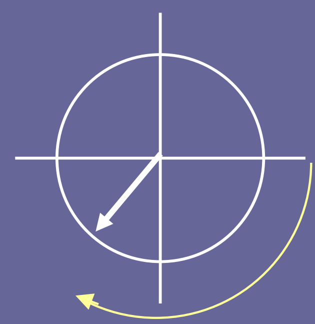


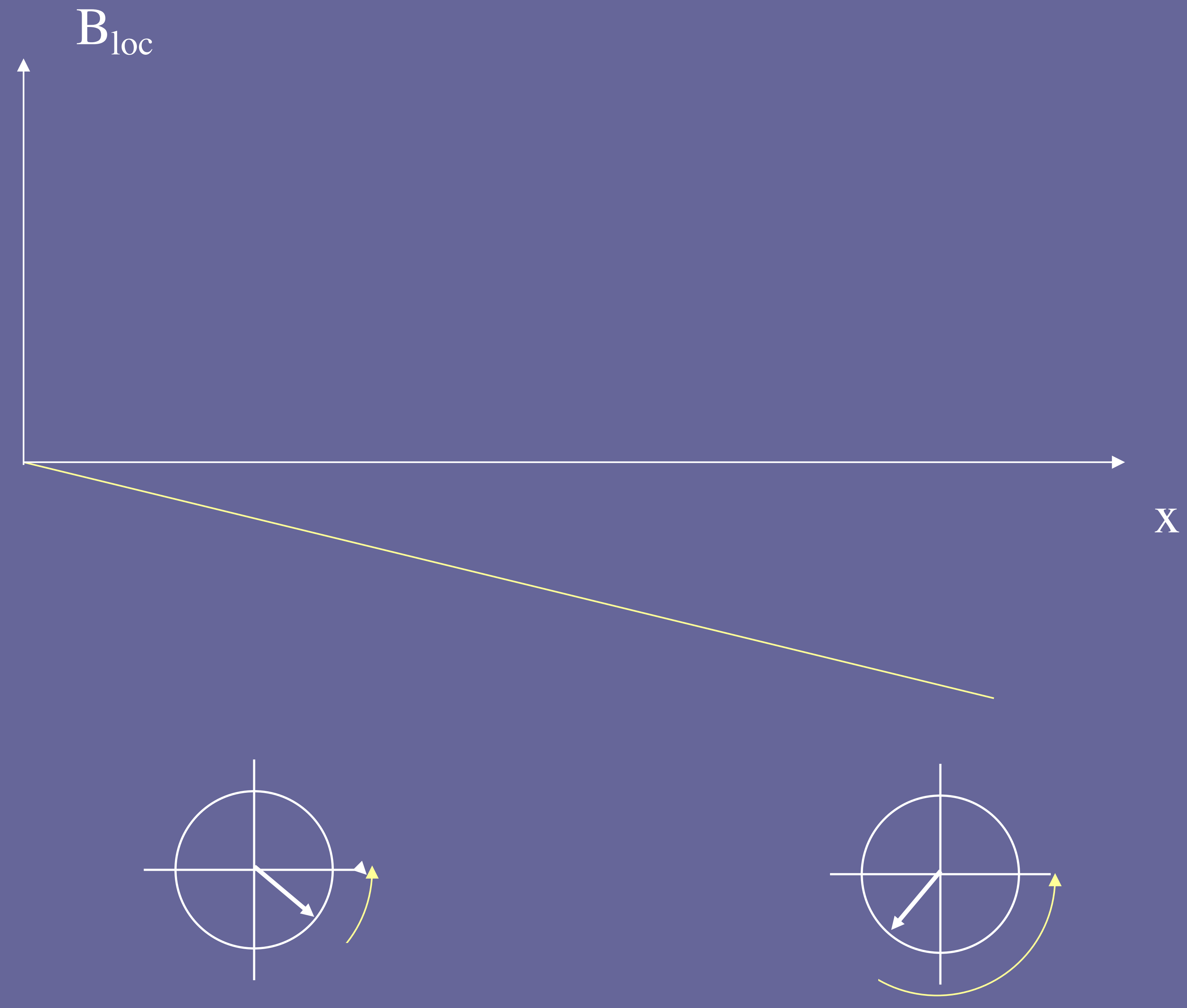
Effect of a field gradient



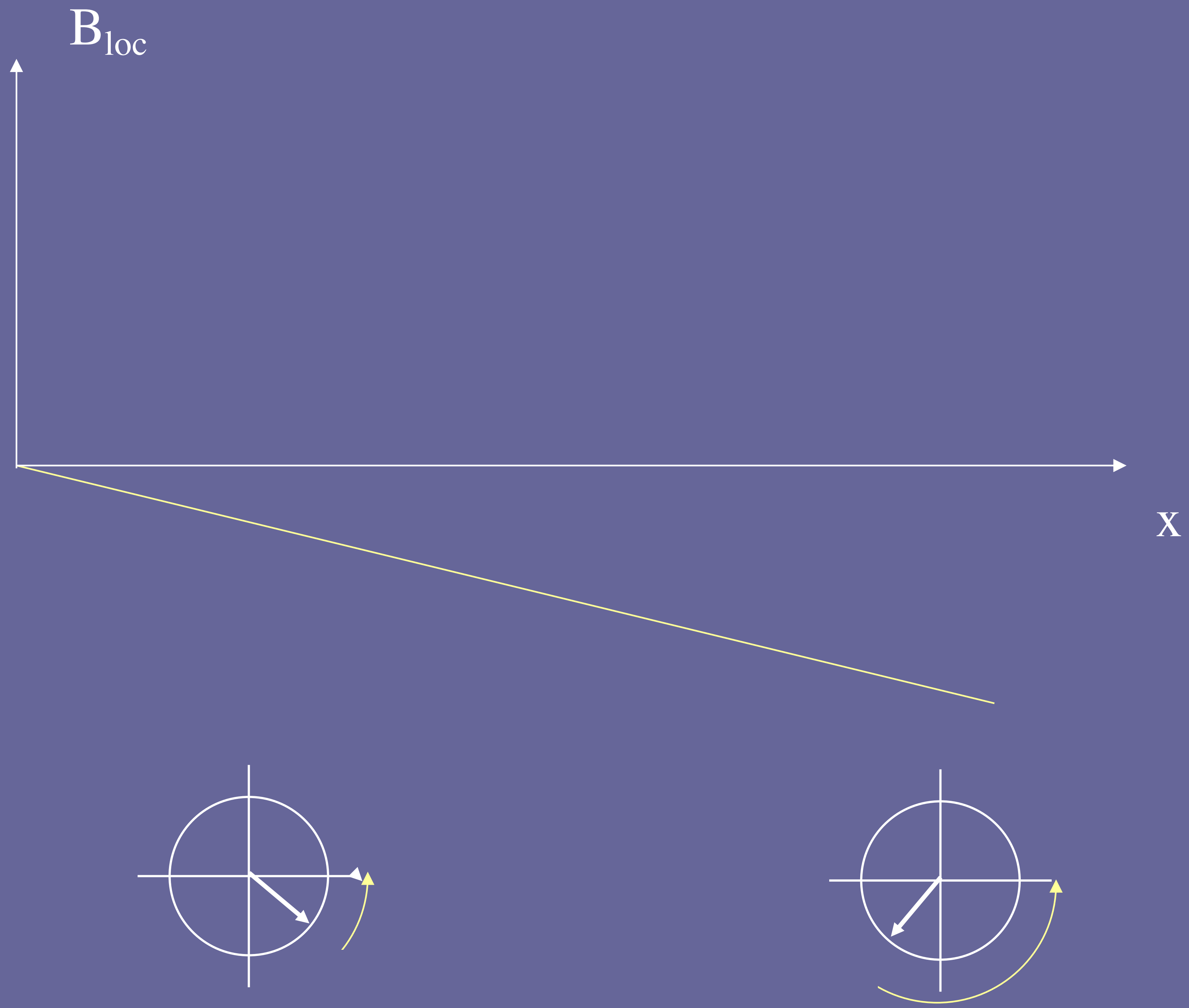
$$\omega = \gamma B_{loc}$$





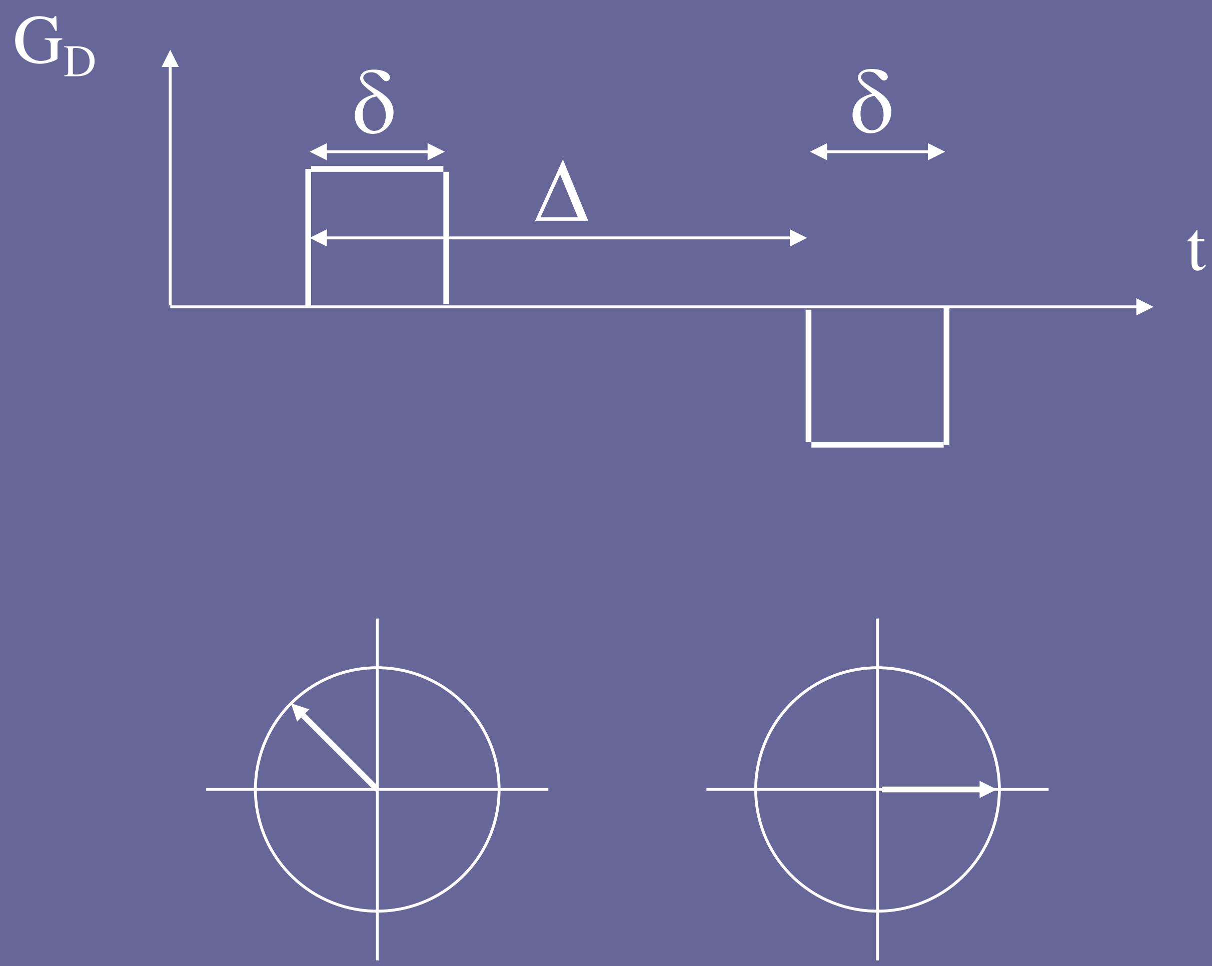


B_{loc}
x

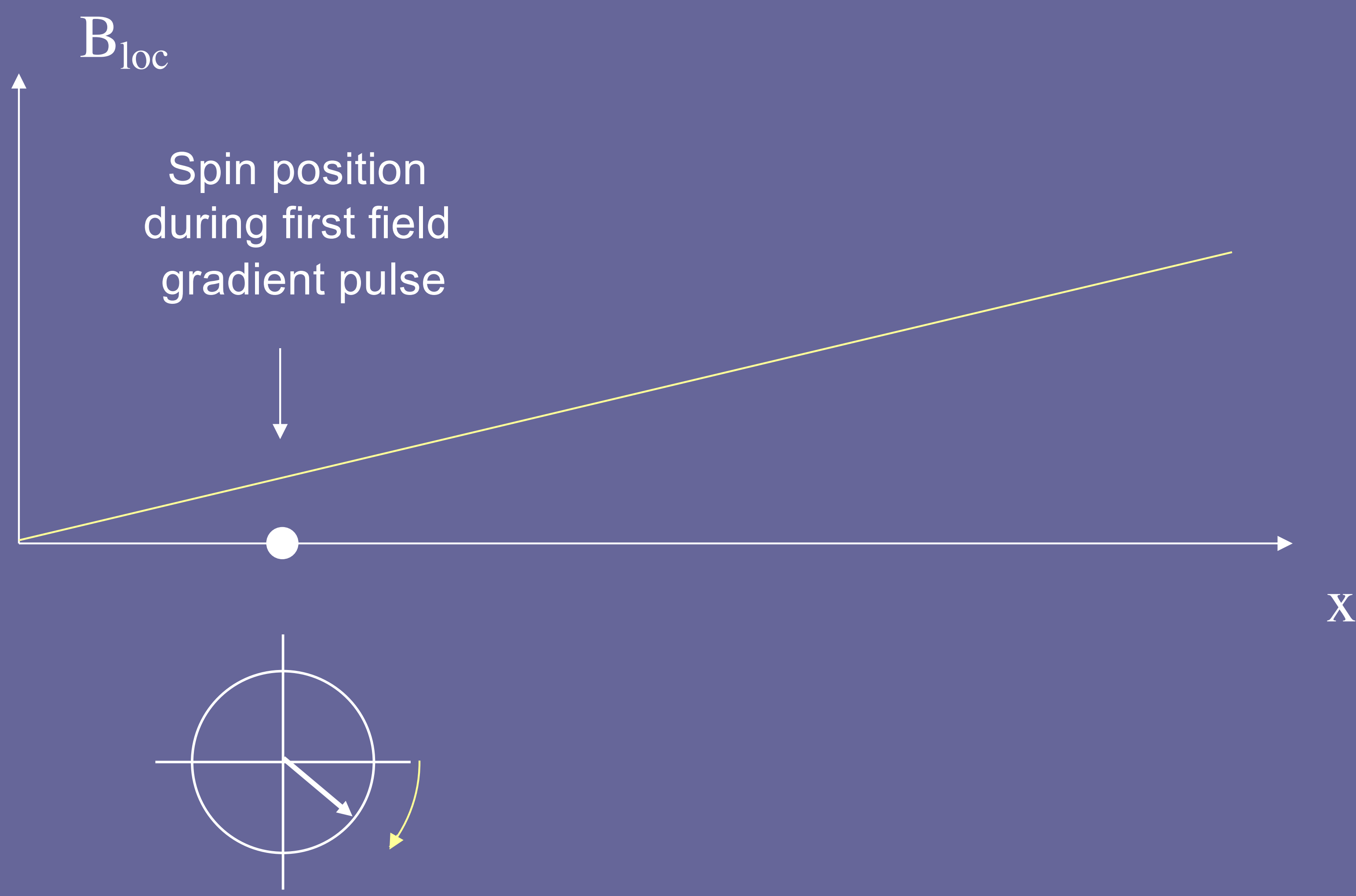


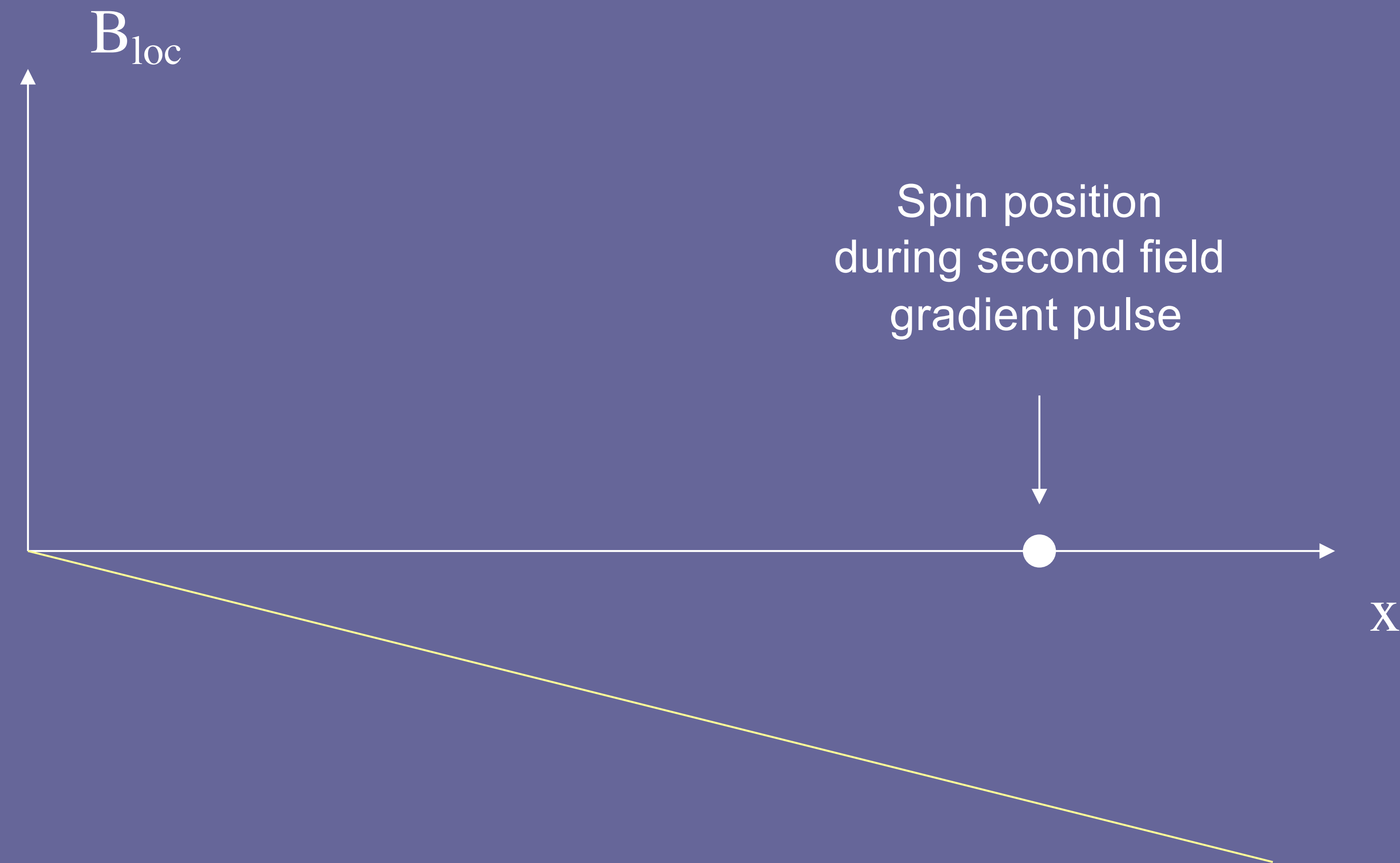
Stationary spins are rephased by reversing the field gradient

Gradient pulse sequence

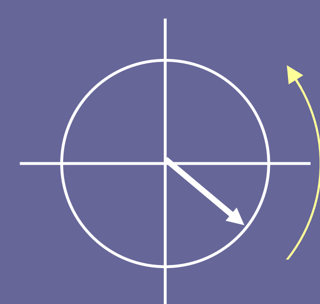


What about a moving spin?

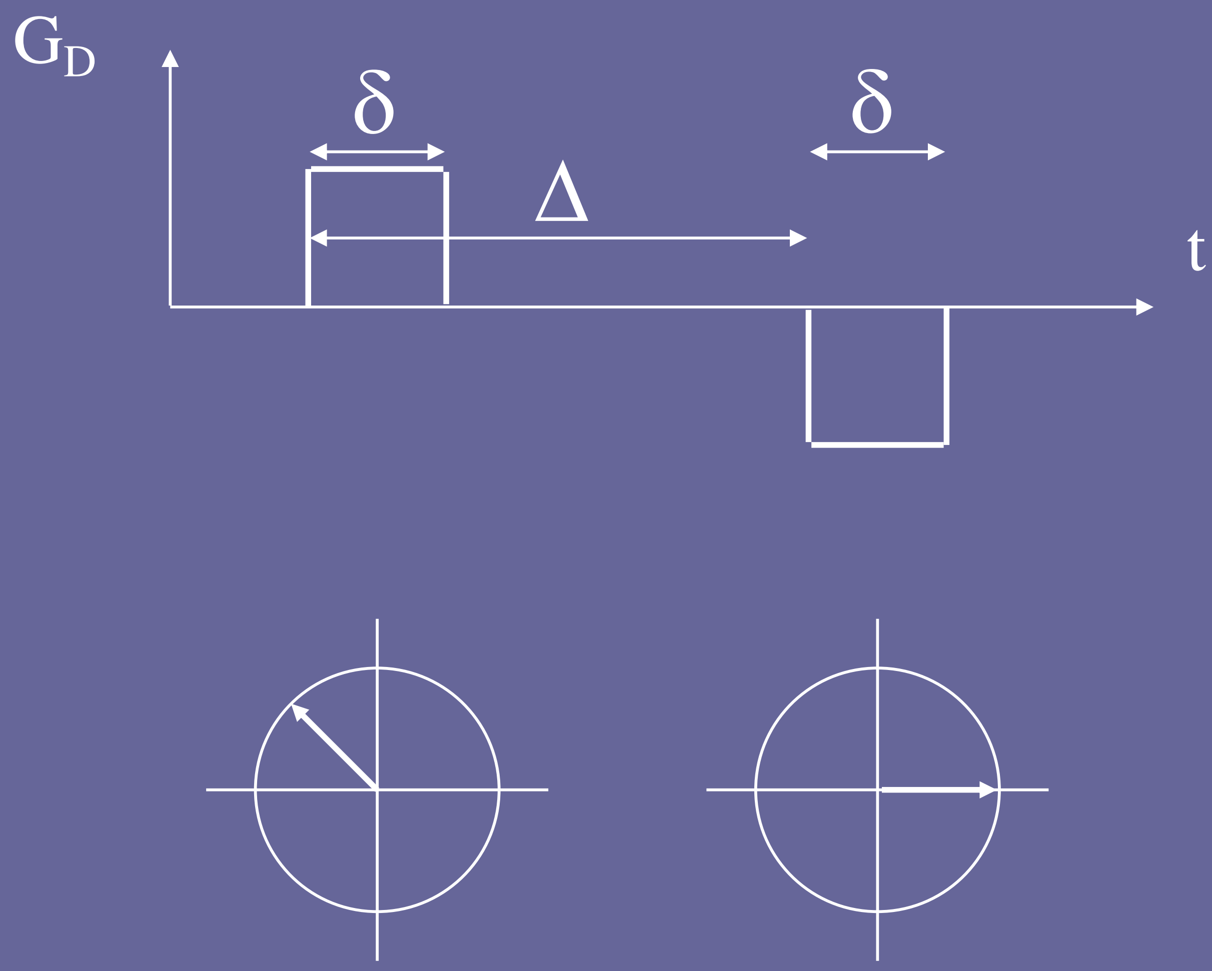


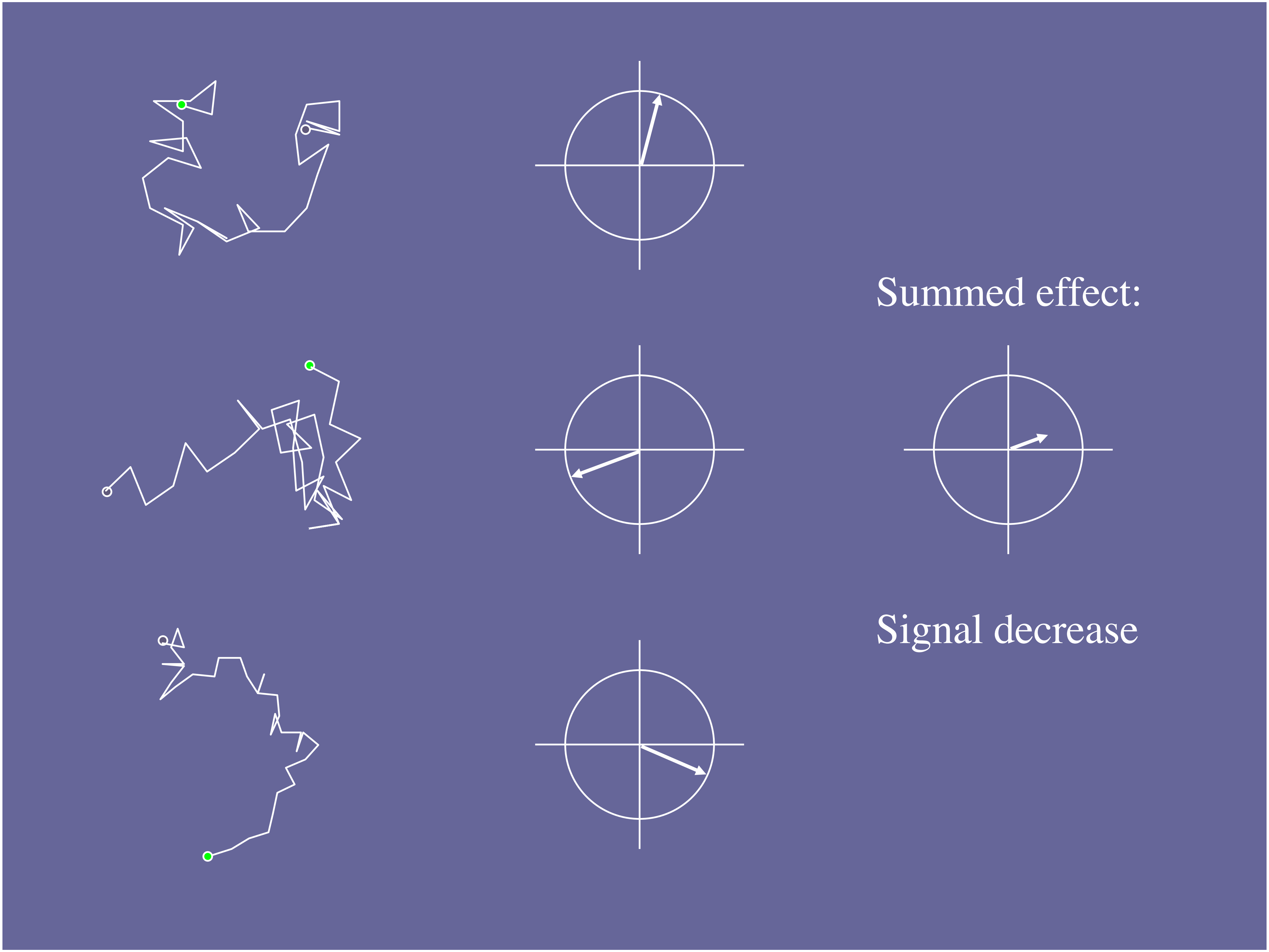


=>Residual phase is proportional to displacement



Displacement encoding



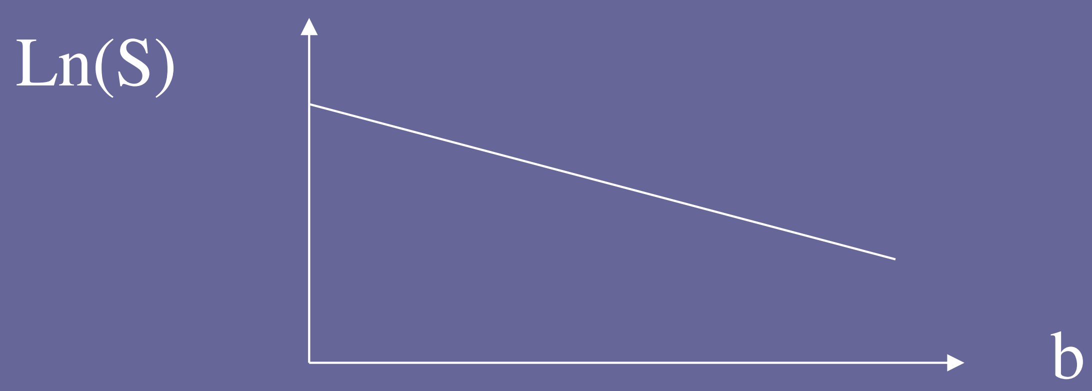

Summed effect:
Signal decrease

Diffusion attenuates signal

- Signal depends on spin displacements

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

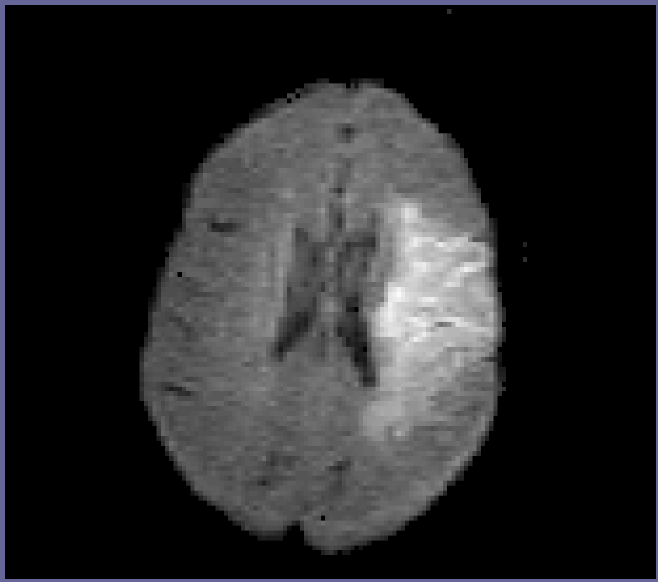
$$D = \frac{\langle r^2 \rangle}{2T}$$



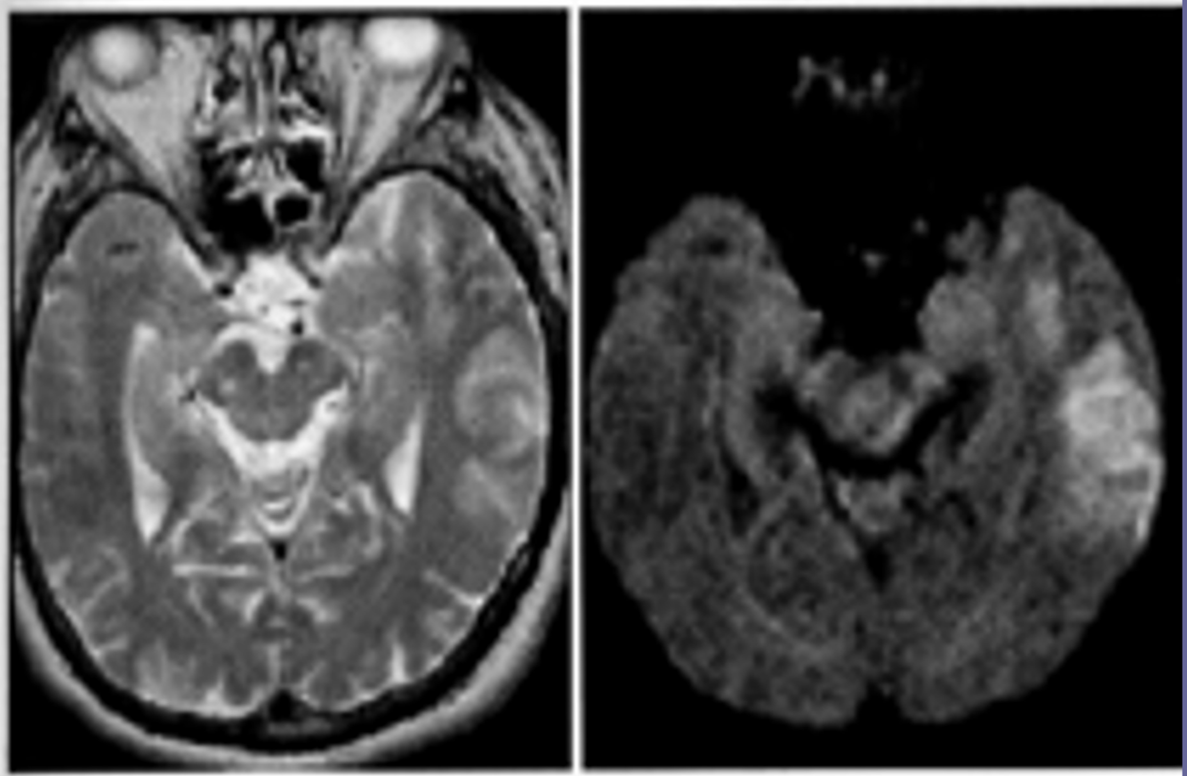
Why is diffusion imaging useful in biomedicine?

Water diffusion reflects changes in tissue microstructure

- Diffusion weighted imaging
- Diffusion in stroke
  - Decreases within ~1 min
  - Diffusion drops by ~40%



Acute stroke does not affect T_2

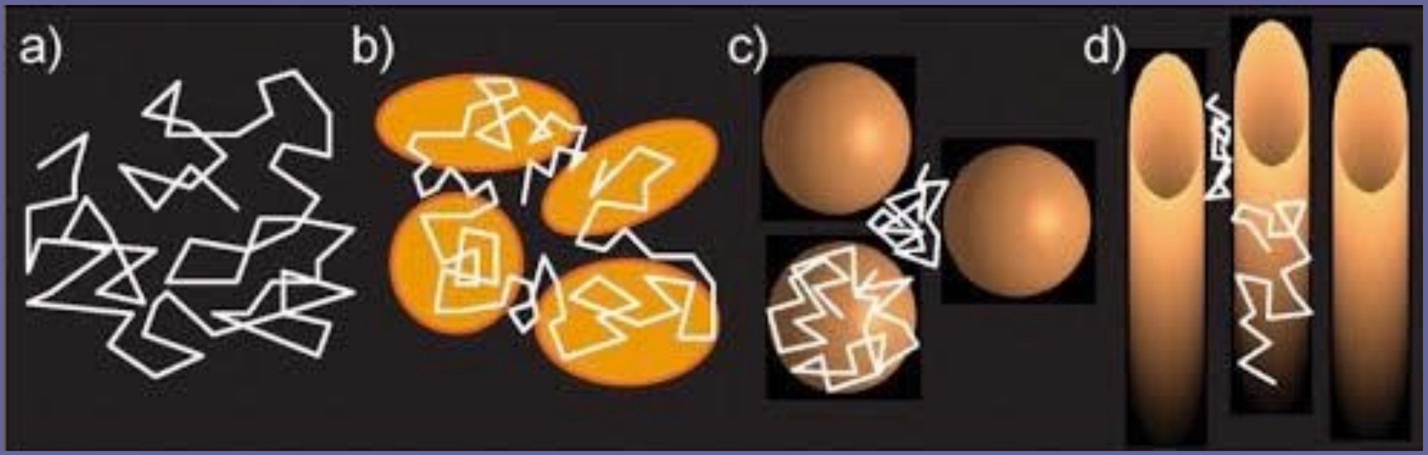


T2 FSE

Isotropic DWI

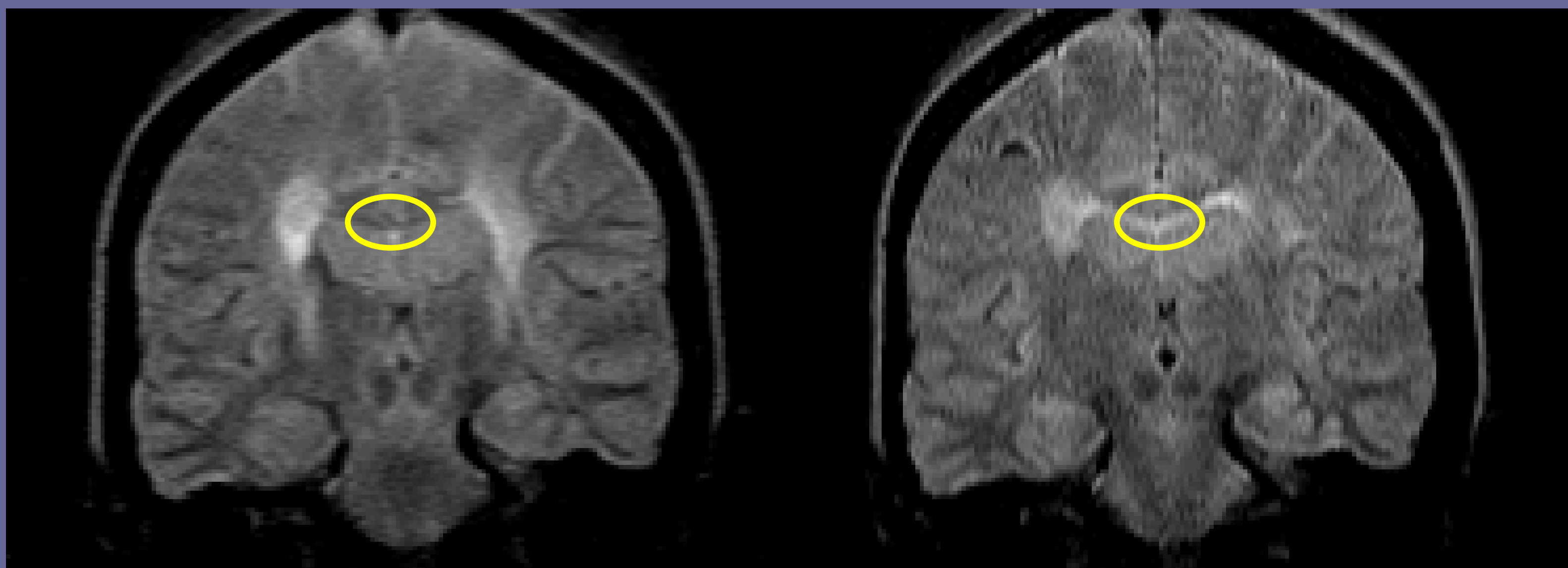
Diffusion reflects tissue microstructure

- Dominated by diffusion barriers (e.g., cell membranes)
- Water diffusion reflects the geometry of cell membranes in tissues



Jones (2011)

In-class exercise: what orientation do axons have in the ROI?



Diffusion weighting

$S = S_0 e^{-bD_{xx}}$

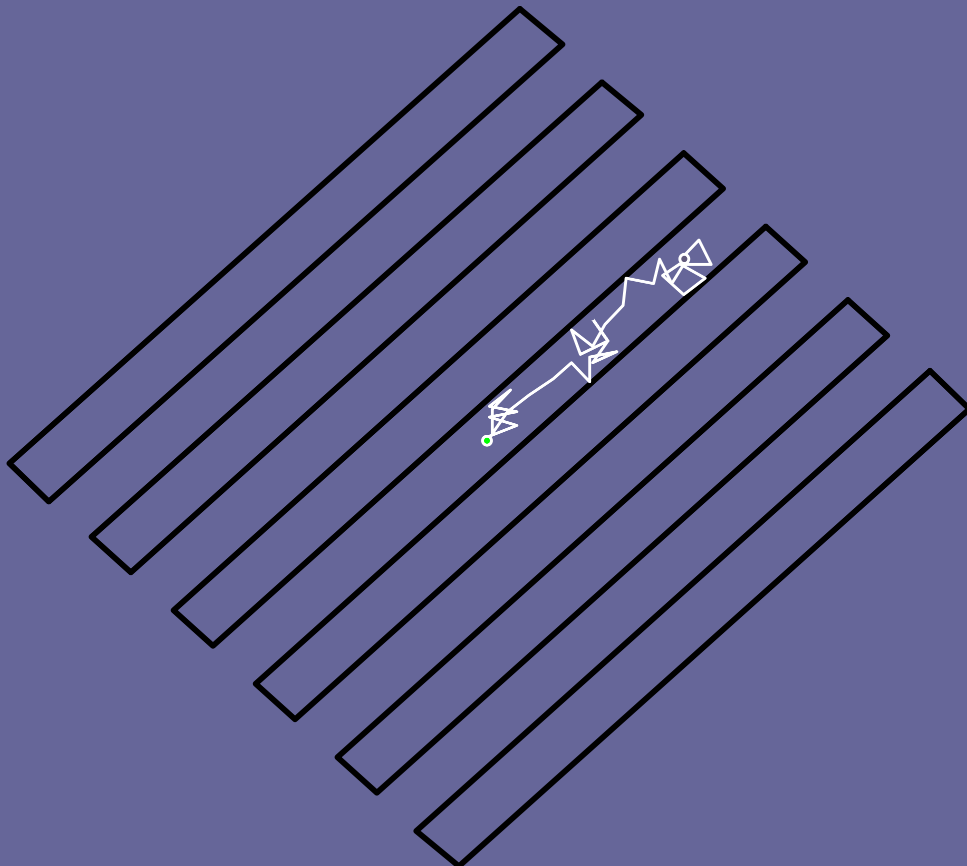
$S = S_0 e^{-bD_{yy}}$

Describe anisotropic diffusion with a diffusion tensor

- Describes diffusion in 3 dimensions:

$$D_{ij} = \frac{\langle r_i r_j \rangle}{2T}$$

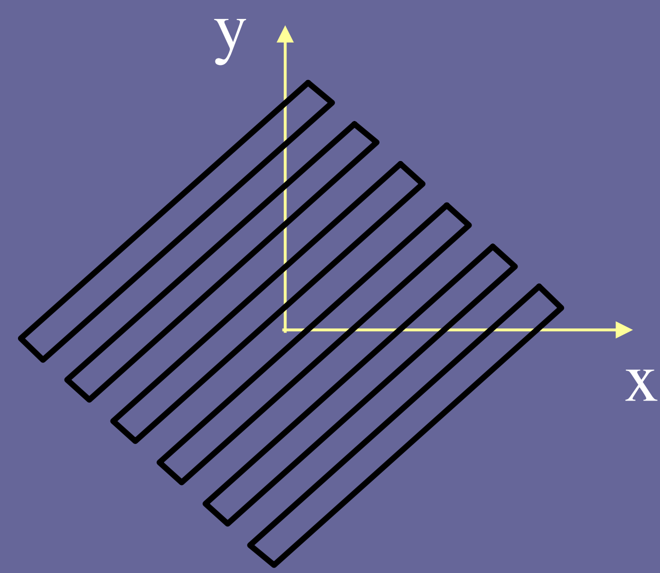
- 3x3 matrix



Matrix diagonalization

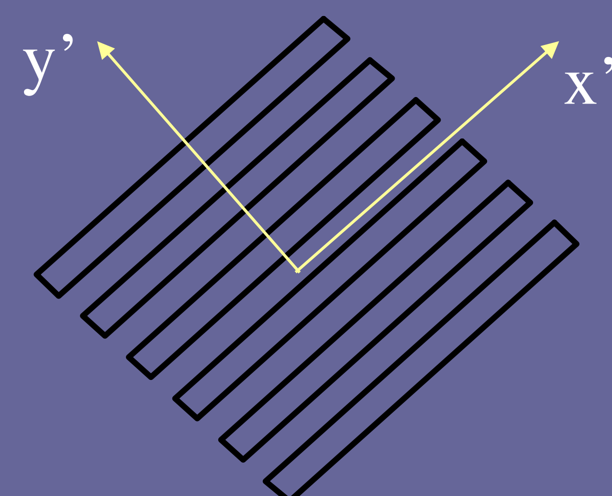
- Transform from

$$\begin{pmatrix} D_{xx} & D_{xy} \\ D_{yx} & D_{yy} \end{pmatrix} = \frac{1}{2T} \begin{pmatrix} \langle x^2 \rangle & \langle xy \rangle \\ \langle yx \rangle & \langle y^2 \rangle \end{pmatrix}$$



- To the form

$$\begin{pmatrix} D_{x'x'} & 0 \\ 0 & D_{y'y'} \end{pmatrix} = \frac{1}{2T} \begin{pmatrix} \langle (x')^2 \rangle & \langle x'y' \rangle \\ \langle y'x' \rangle & \langle (y')^2 \rangle \end{pmatrix}$$



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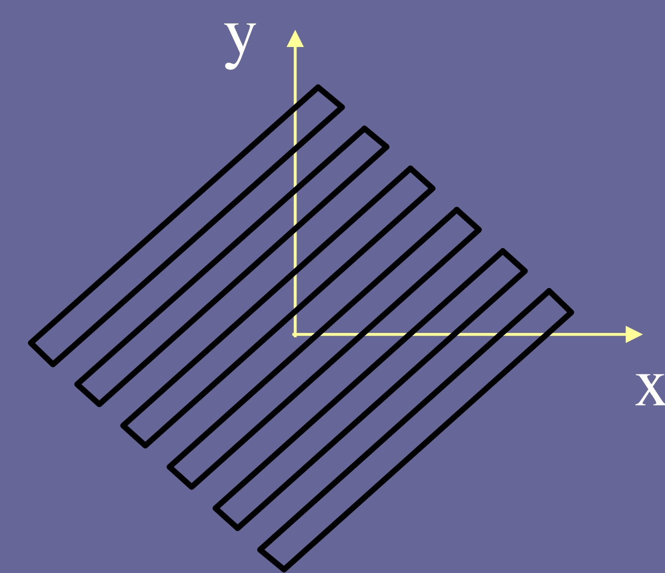
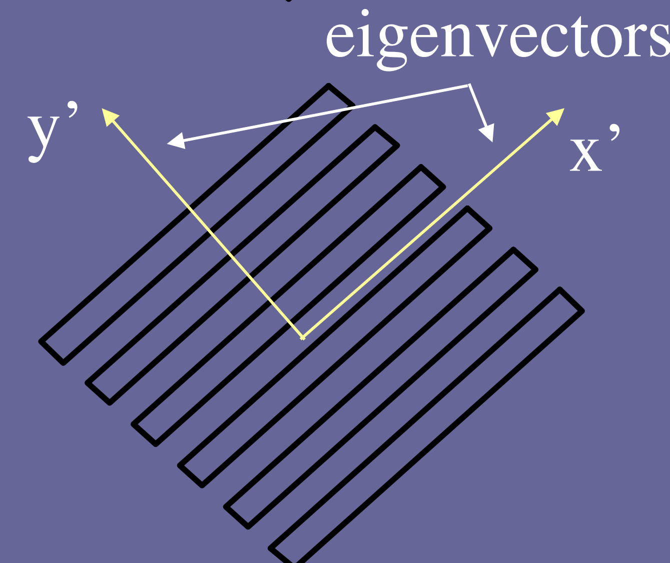


- To the form

$$\begin{pmatrix} D_{x'x'} & 0 \\ 0 & D_{y'y'} \end{pmatrix} = \frac{1}{2T}\begin{pmatrix} \langle (x')^2 \rangle & \langle x'y' \rangle \\ \langle y'x' \rangle & \langle (y')^2 \rangle \end{pmatrix}$$

eigenvalues



Measuring D

- For isotropic diffusion

$$S = S_0 \cdot e^{-bD}$$

- For anisotropic diffusion

$$S = S_0 \cdot e^{-\sum_{i,j=1}^{3} b_{ij} D_{ij}}$$

where

$$b_{ij} = \gamma^2 \delta^2 G^2 (\Delta - \delta/3) n_i n_j$$
$$= b\, n_i n_j$$

and $\hat{n}$ is a unit vector in the direction of the gradient.

Measuring *D*

- Estimate the tensor

$$\begin{pmatrix} D_{xx} & D_{xy} \\ D_{yx} & D_{yy} \end{pmatrix}$$

using

$$ln(S/S_0) = -b \sum_{i,j} n_i n_j D_{ij}$$

- Requires diffusion weighting in three directions:

$$\vec{G}||\hat{x}: \quad ln(S/S_0) = -bD_{xx}$$

$$\vec{G}||\hat{y}: \quad ln(S/S_0) = -bD_{yy}$$

$$\vec{G}||\hat{x}+\hat{y}: \quad ln(S/S_0) = -b\left(\frac{1}{2}D_{xx} + D_{xy} + \frac{1}{2}D_{yy}\right)$$

Measuring *D*

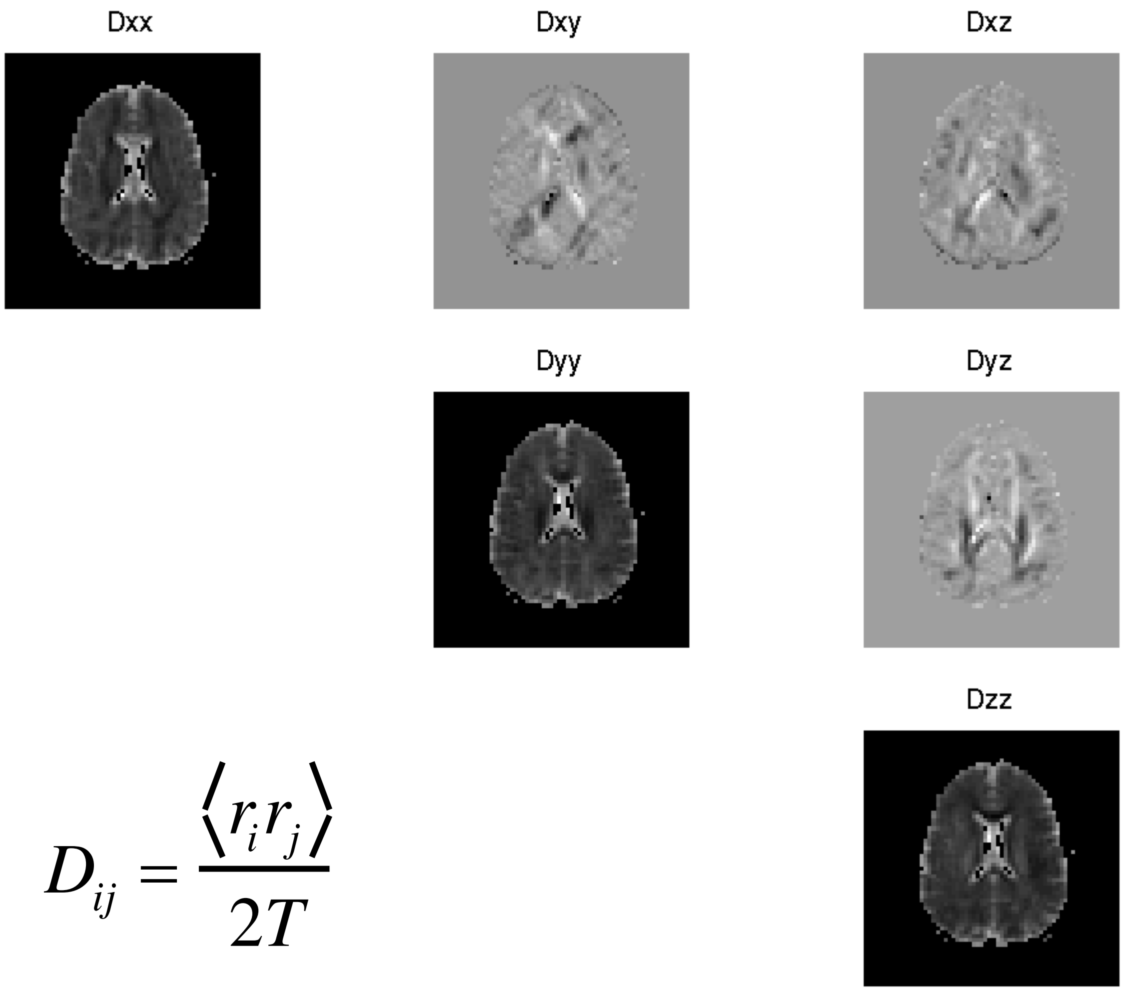
- D is a symmetric matrix
- 3 unknowns in 2 dimensions:

$$\tilde{D} = \begin{pmatrix} D_{xx} & D_{xy} \\ D_{xy} & D_{yy} \end{pmatrix}$$

- 6 unknowns in 3 dimensions:

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

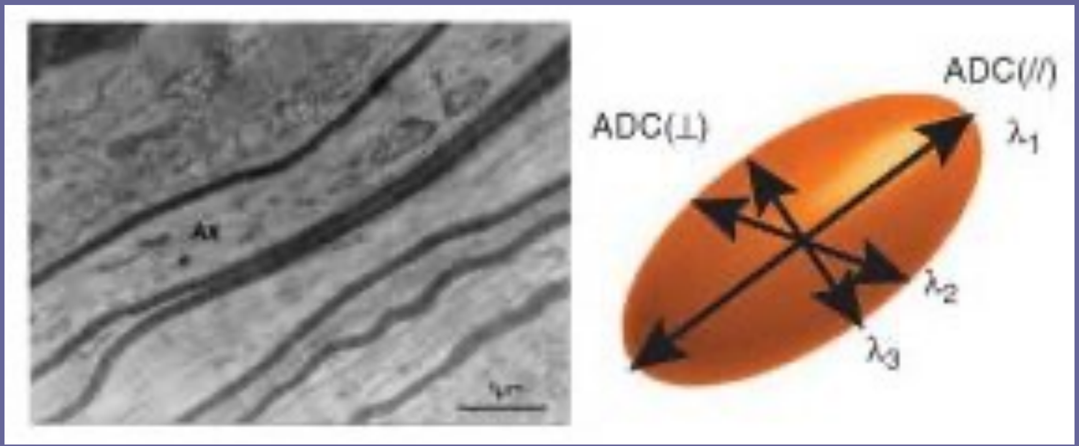
Tensor components



$$D_{ij} = \frac{\langle r_i r_j \rangle}{2T}$$

Interpreting the diffusion tensor

- Orientation: largest diffusivity is parallel to axons (single fiber)
- Anisotropy: cell membranes have a preferred orientation

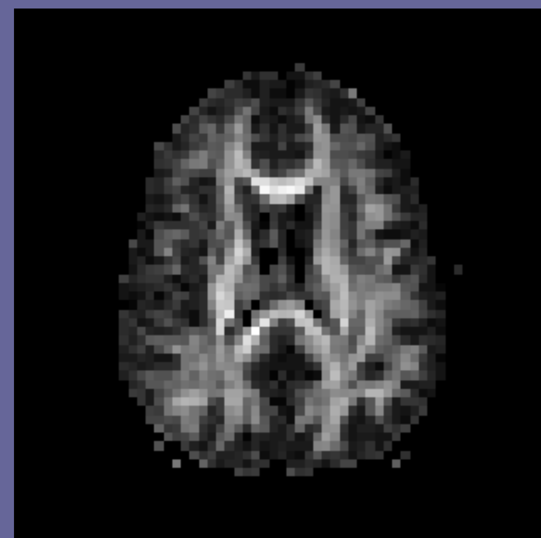


Jones (2011)

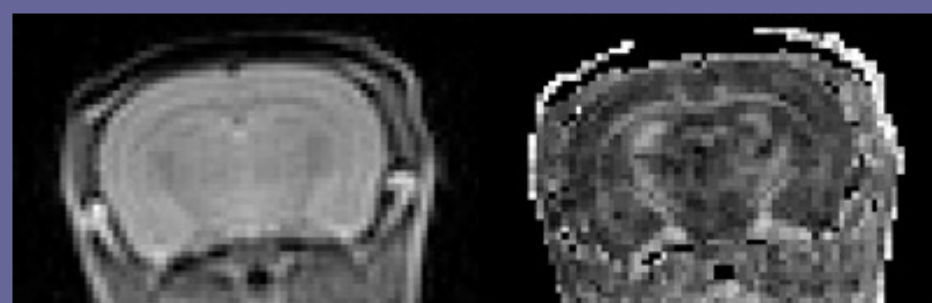
Applications of diffusion imaging

Anisotropy reflects axon 'integrity'

- Altered in
  - Traumatic brain injury
  - Schizophrenia
  - Alcoholism
  - Multiple sclerosis
  - Dyslexia
  - Premature birth
  - Old age

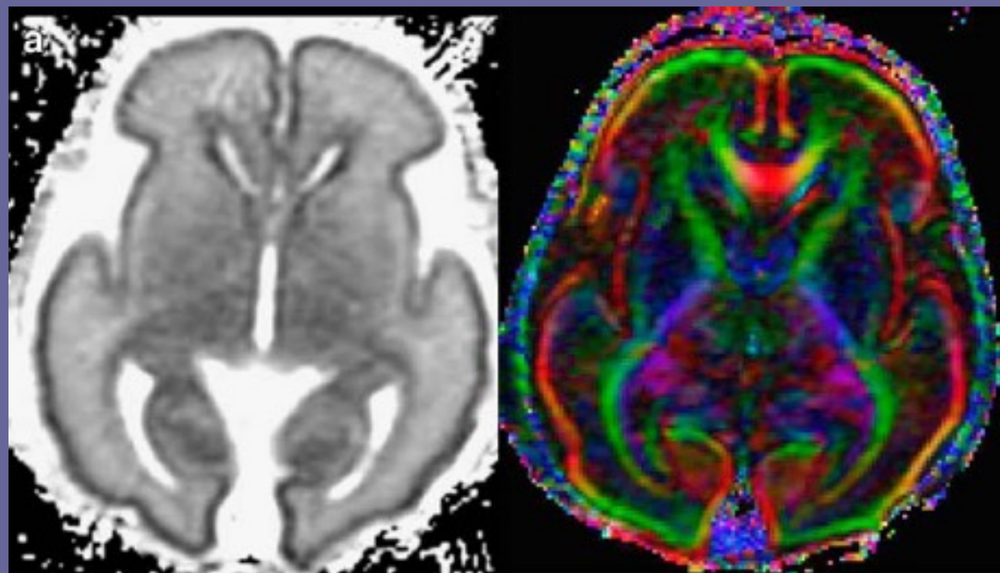


Human

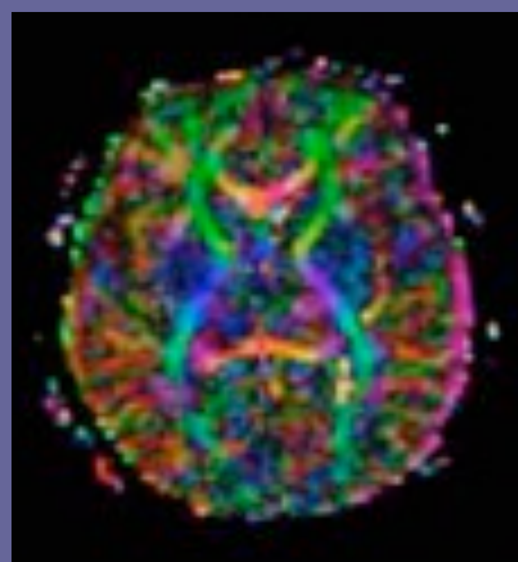


Mouse

Anisotropic diffusion changes during development



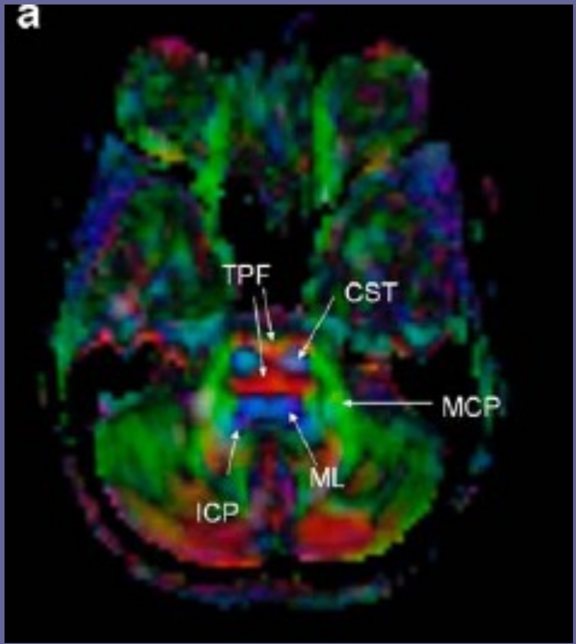
Preterm newborn
(26 wk PCA)

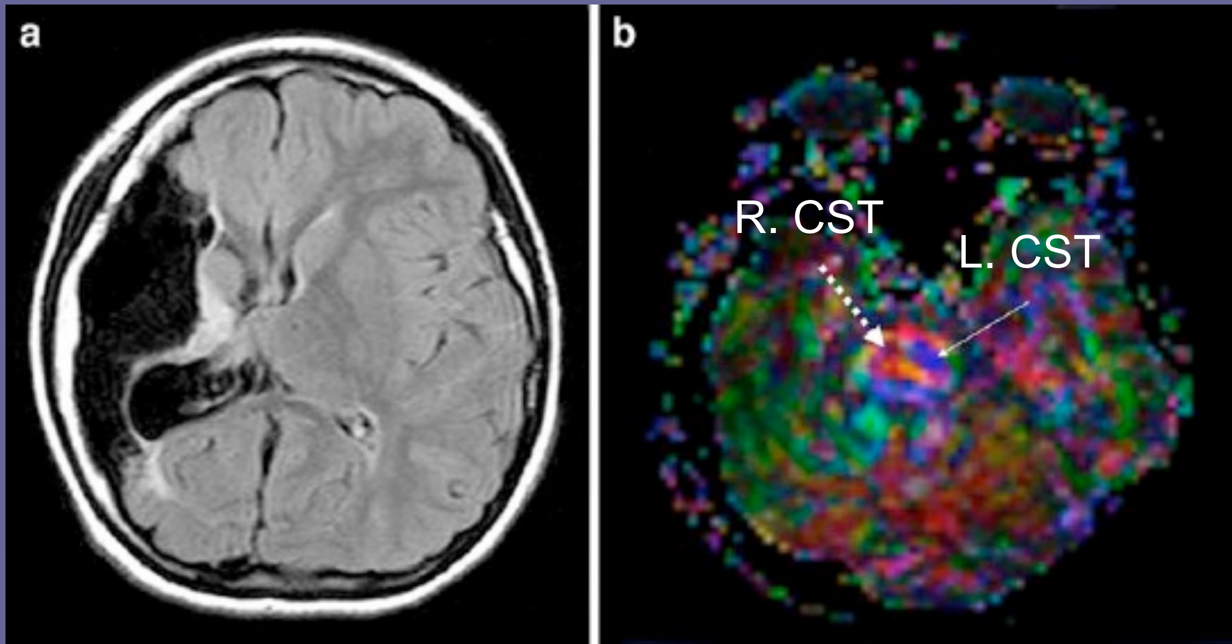


5 month old

Rollins, Pedr Radiol (2007)

White matter changes remote to injury





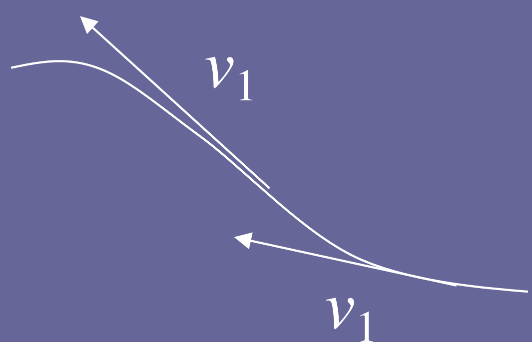
Rollins, Pedr Radiol (2007)

Normal brainstem anatomy

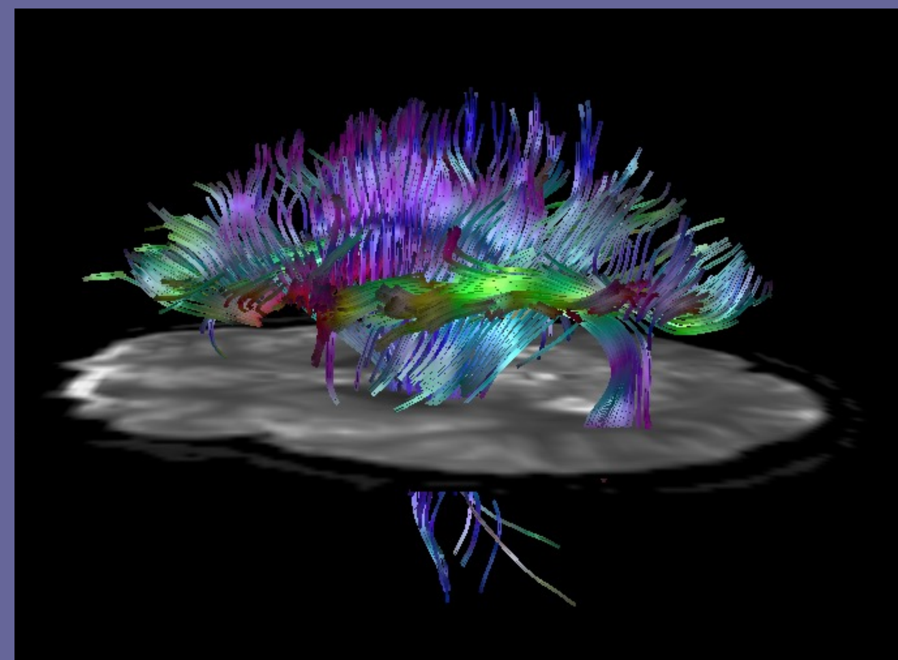
11 yo with perinatal infarct and cortical spinal tract (CST) changes

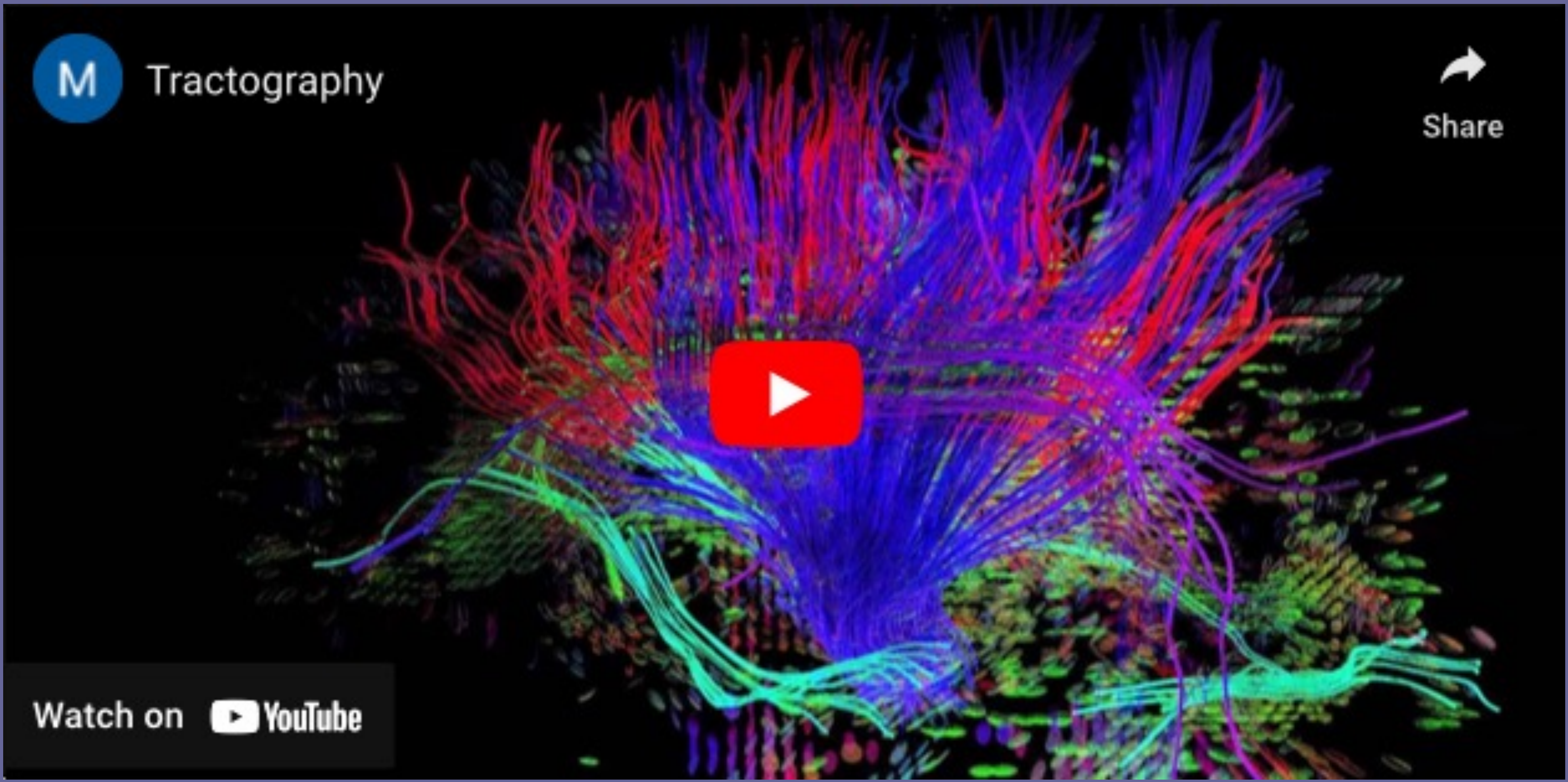
Fiber tracking

- Fiber paths calculated from fast diffusion direction



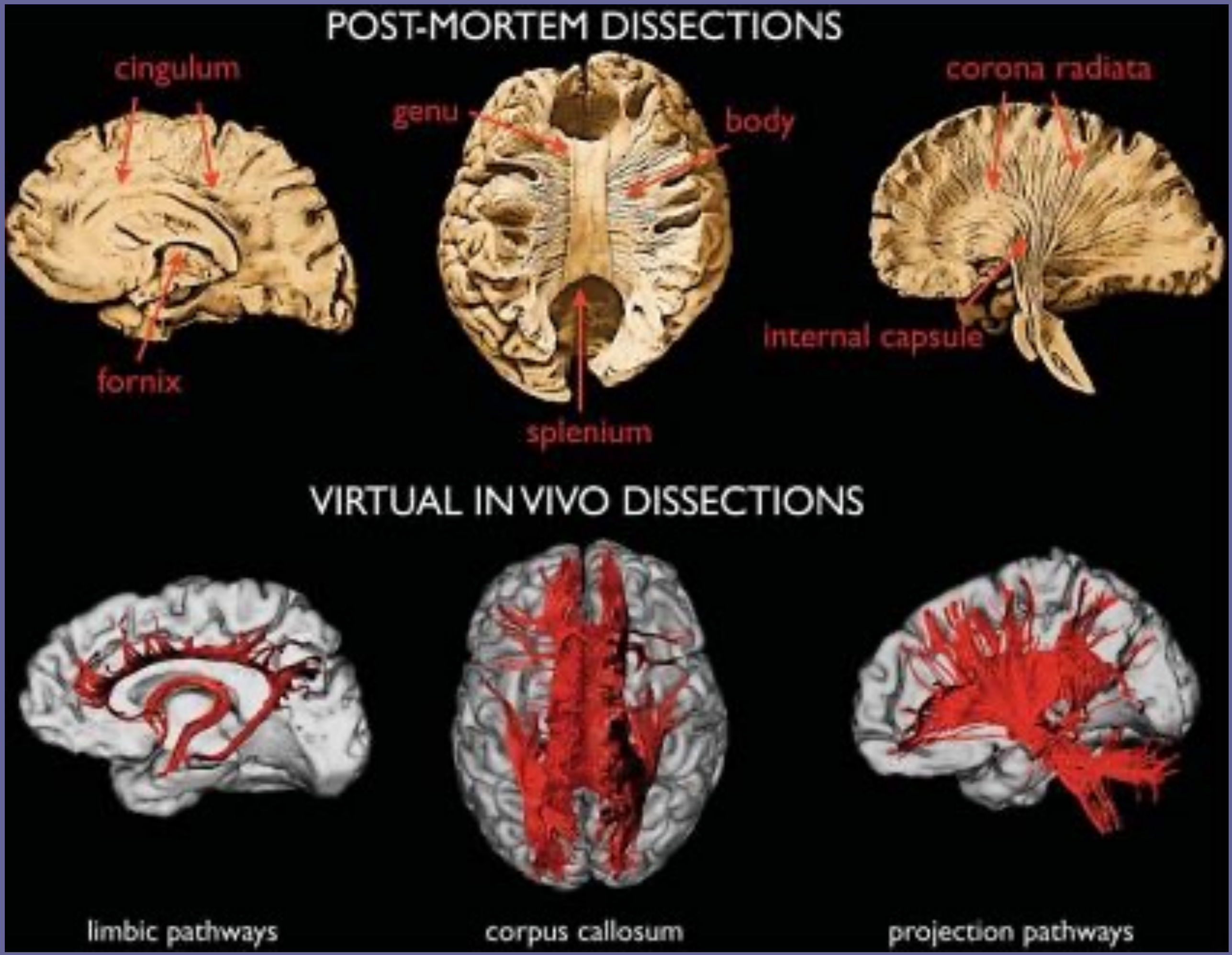
- Integrate starting from user-defined seed points





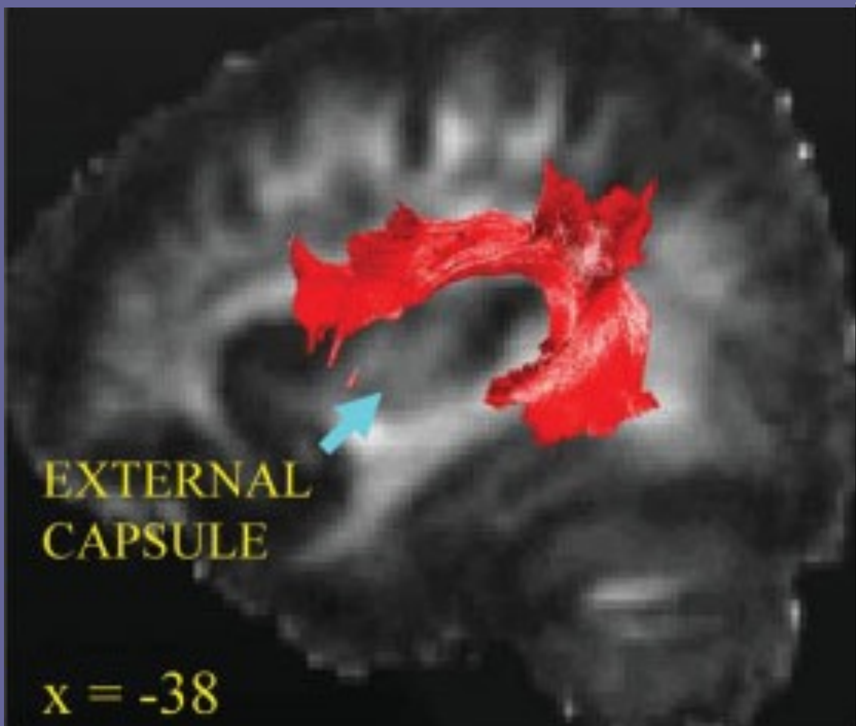
https://youtu.be/wy8KEUmyasA

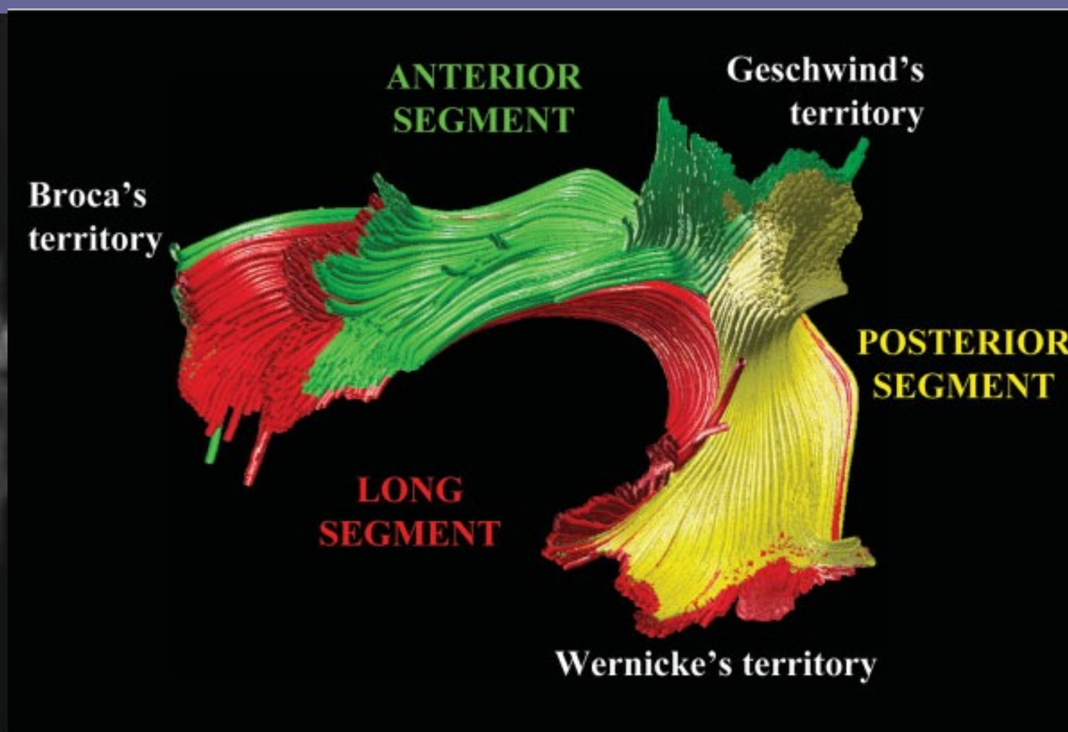
Tractography for white matter segmentation



Jones (2011)

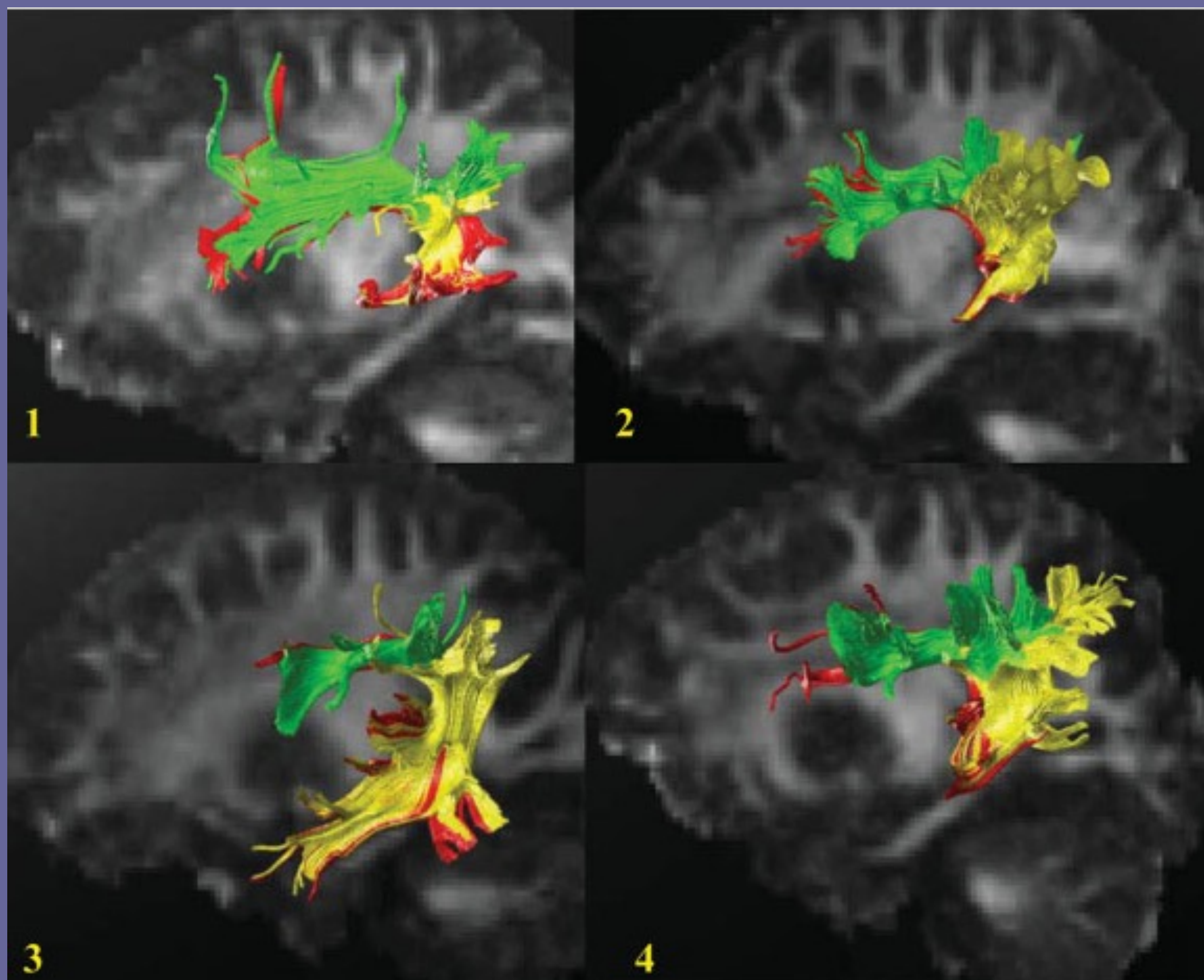
Arcuate fasciculus





Catani et al (2005)

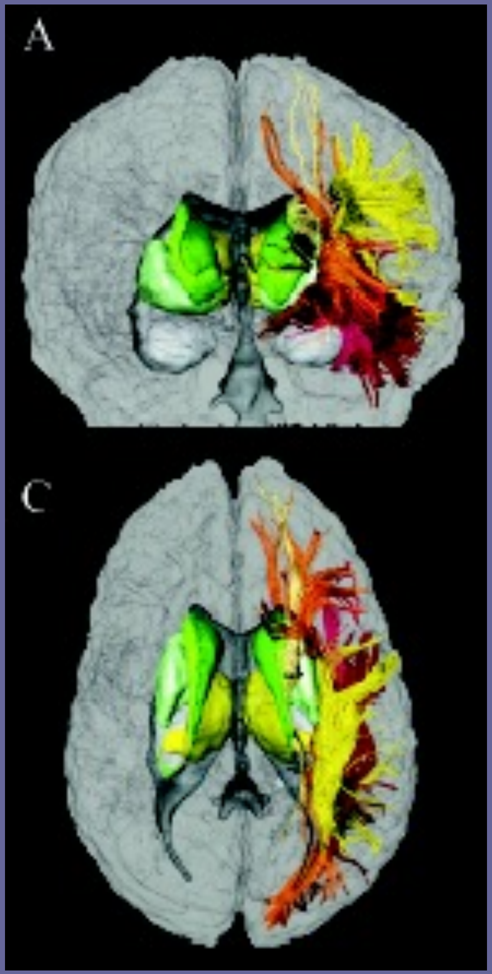
Individual variability



Catani et al (2005)

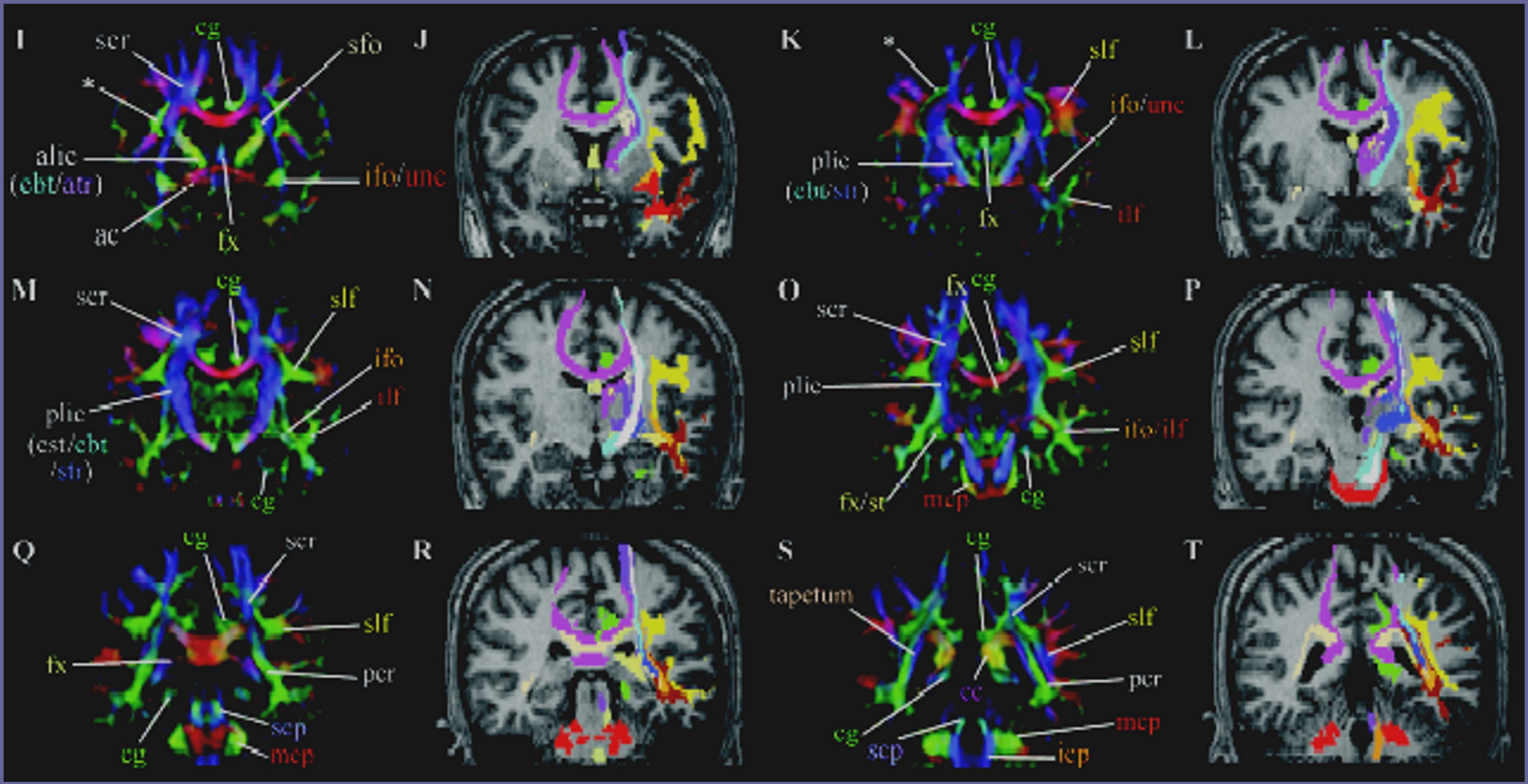
Information from MR fiber tracking

- What regions are connected? (fiber tracking)
- Extent of connections? (volume of fiber bundles)
- Are the connections intact? (axial, radial diffusivities)



Wakana, Radiology (2004)

Fiber segmentation



Wakana, Radiology (2004)

Summary

- Diffusion tensor imaging reveals tissue microstructure
  - Anisotropy of cell membranes
- Reflects microstructural changes in disease
  - Brain, but also
  - Cardiac/skeletal muscle
  - Kidney
- Makes non-invasive fiber tracking possible
- Segments the white matter
- Provides a basis for network models of the brain

Sources

- Catani M, Jones DK, ffytche DH, *Perisylvian Language Networks of the Human Brain*. Ann Neurol 57: 8 (2005).
- Conturo TE et al., *Tracking neuronal fiber pathways in the living human brain*. Proc Natl Acad Sci USA (1999).
- *Diffusion MRI: Theory, Methods, and Applications*, DK Jones, ed. (Oxford, 2011)
- https://doctorlib.info/anatomy/neuroanatomy-illustrated-colour-text/13.html
- Wakana S, et al. *Fiber tract-based atlas of human white matter anatomy*. Radiology (2004).