Diffusion model fitting and tractography: A primer

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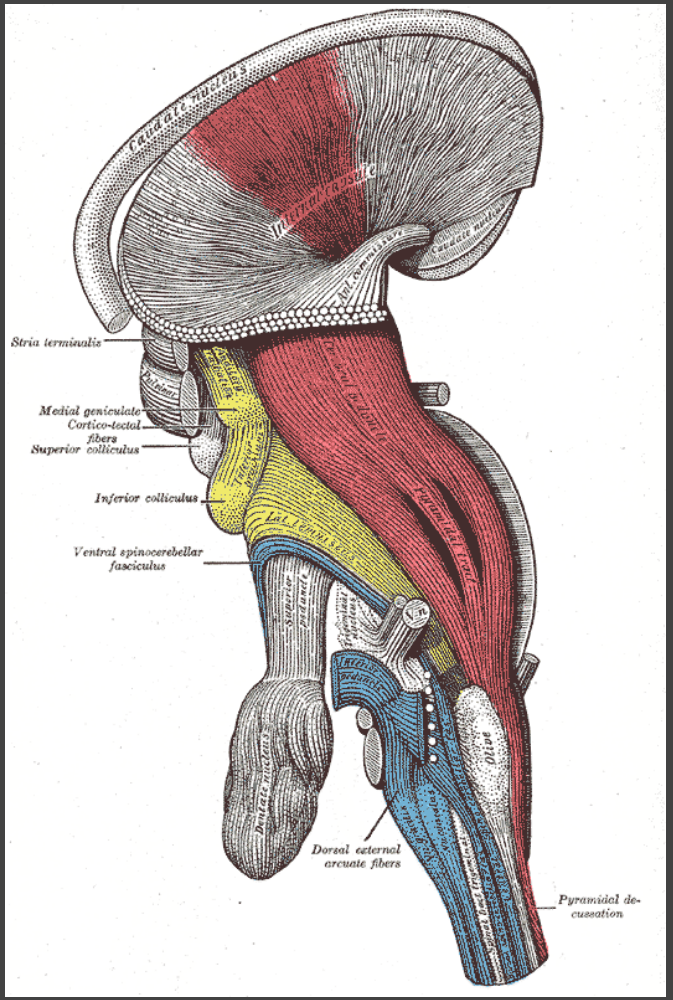
Why diffusion imaging?

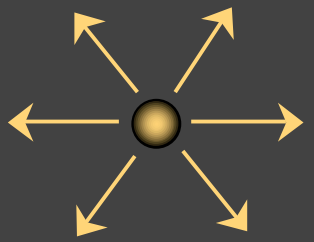
- White matter (WM) is organized in fiber bundles
- Identifying these WM pathways is important for:
  - Inferring connections b/w brain regions
  - Understanding effects of neurodegenerative diseases, stroke, aging, development …



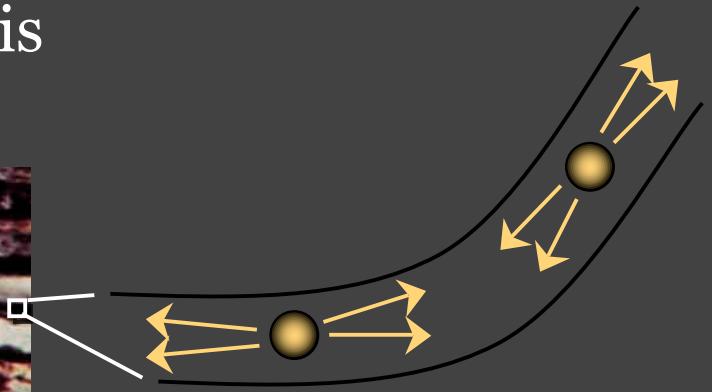
From *Gray's Anatomy: IX. Neurology*

Diffusion in brain tissue

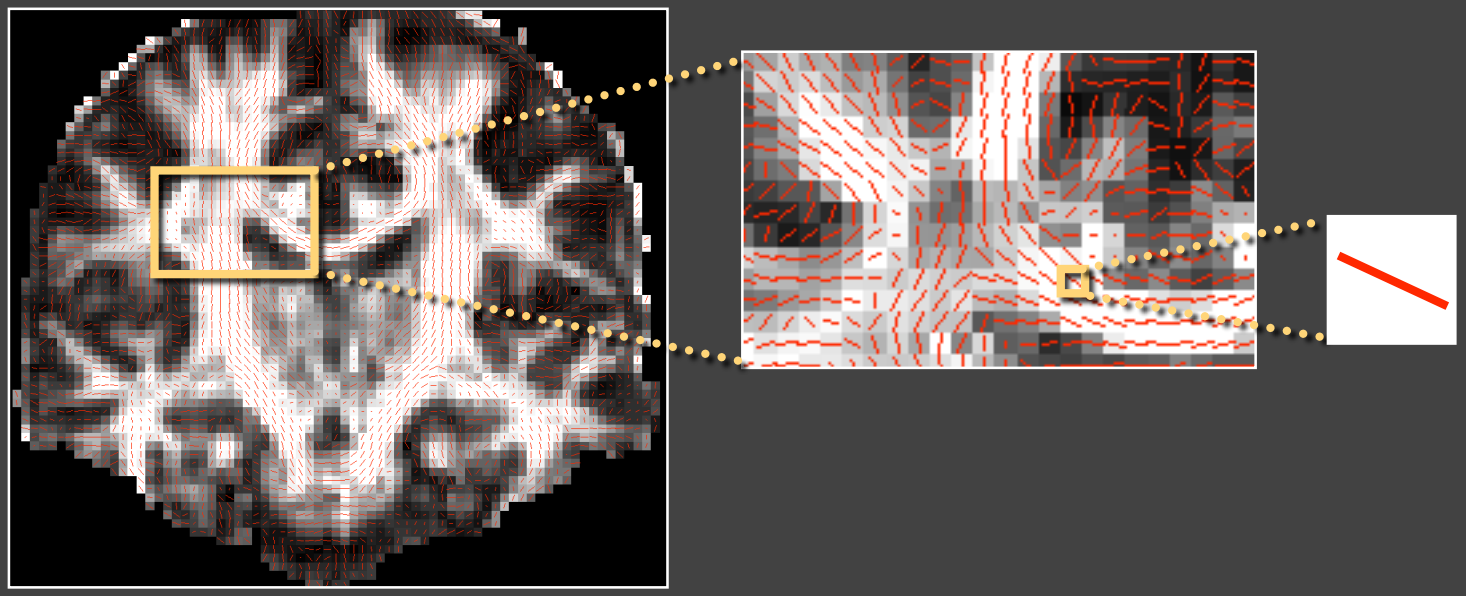
- Differentiate tissues based on the diffusion (random motion) of water molecules within them
- Gray matter: Diffusion is unrestricted ⇒ isotropic



- White matter: Diffusion is restricted ⇒ anisotropic



How to describe diffusion

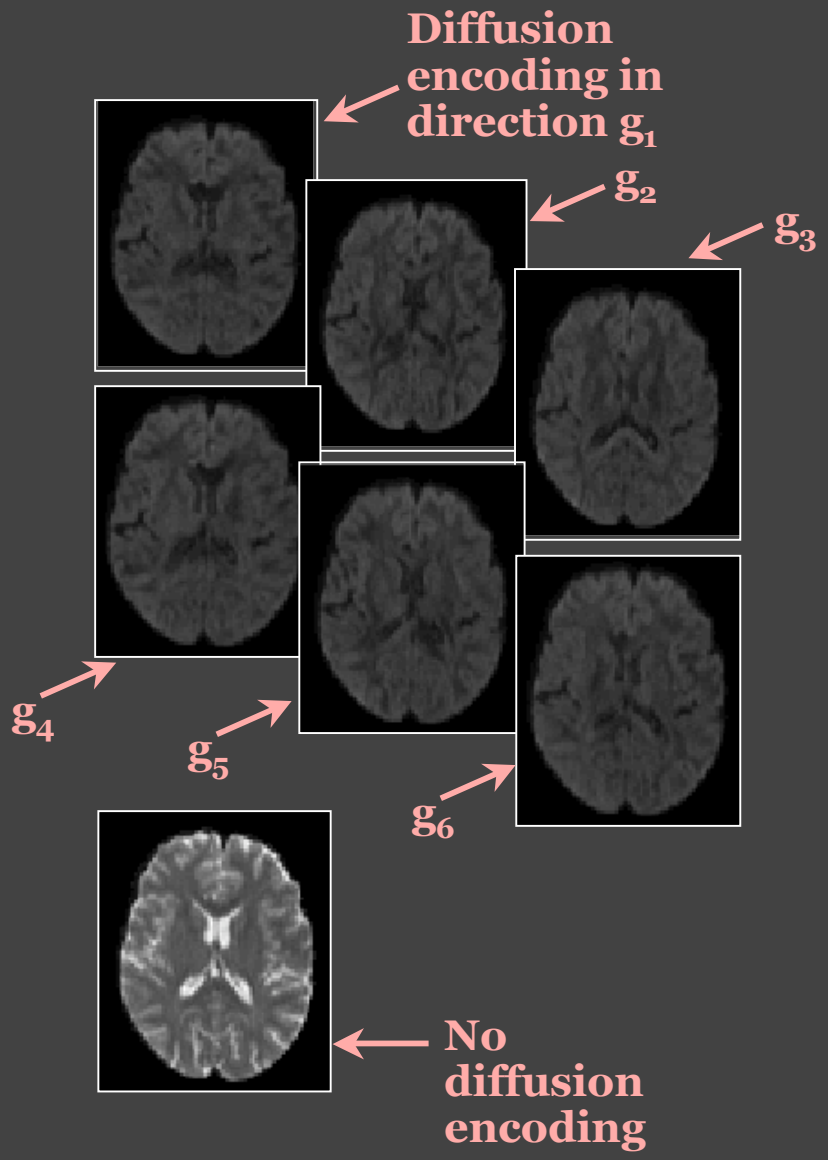


At every voxel we want to know:

- Is this in white matter?
- If yes, what pathway(s) is it part of?
  - What is the orientation of diffusion?
  - What is the magnitude of diffusion?

Diffusion MRI

- Magnetic resonance imaging can provide "diffusion encoding"
- Magnetic field strength is varied by gradients in different directions
- Image intensity is attenuated depending on water diffusion in each direction
- Compare with baseline images to infer on diffusion process

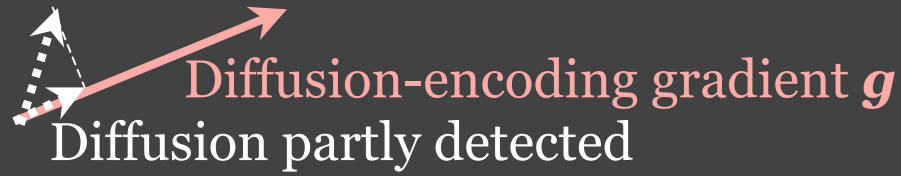


Need to know: Gradient directions

- True diffusion direction || Applied gradient direction
  ⇒ Maximum attenuation

- True diffusion direction ⊥ Applied gradient direction
  ⇒ No attenuation

- To capture all diffusion directions well, gradient directions should cover 3D space uniformly



How many gradient directions?

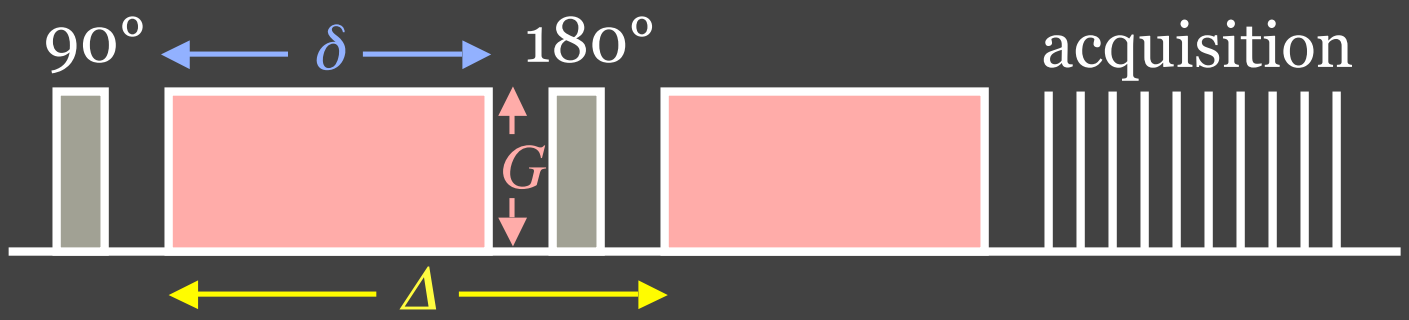
- Acquiring data with more gradient directions leads to:
  - + More reliable estimation of diffusion measures
  - – Increased imaging time ⇒ Subject discomfort, more susceptible to artifacts due to motion, respiration, etc.
- Diffusion tensor imaging (DTI):
  - – Six directions is the minimum
  - – Usually a few 10's of directions
- Diffusion spectrum imaging (DSI):
  - – Usually a few 100's of directions

Need to know: b-value

- The b-value depends on pulse sequence parameters:

$$b = \gamma^2 G^2 \delta^2 (\Delta - \delta/3)$$

  - γ the gyromagnetic ratio
  - G the strength of the diffusion-encoding gradient
  - δ the duration of each diffusion-encoding pulse
  - Δ the interval b/w diffusion-encoding pulses



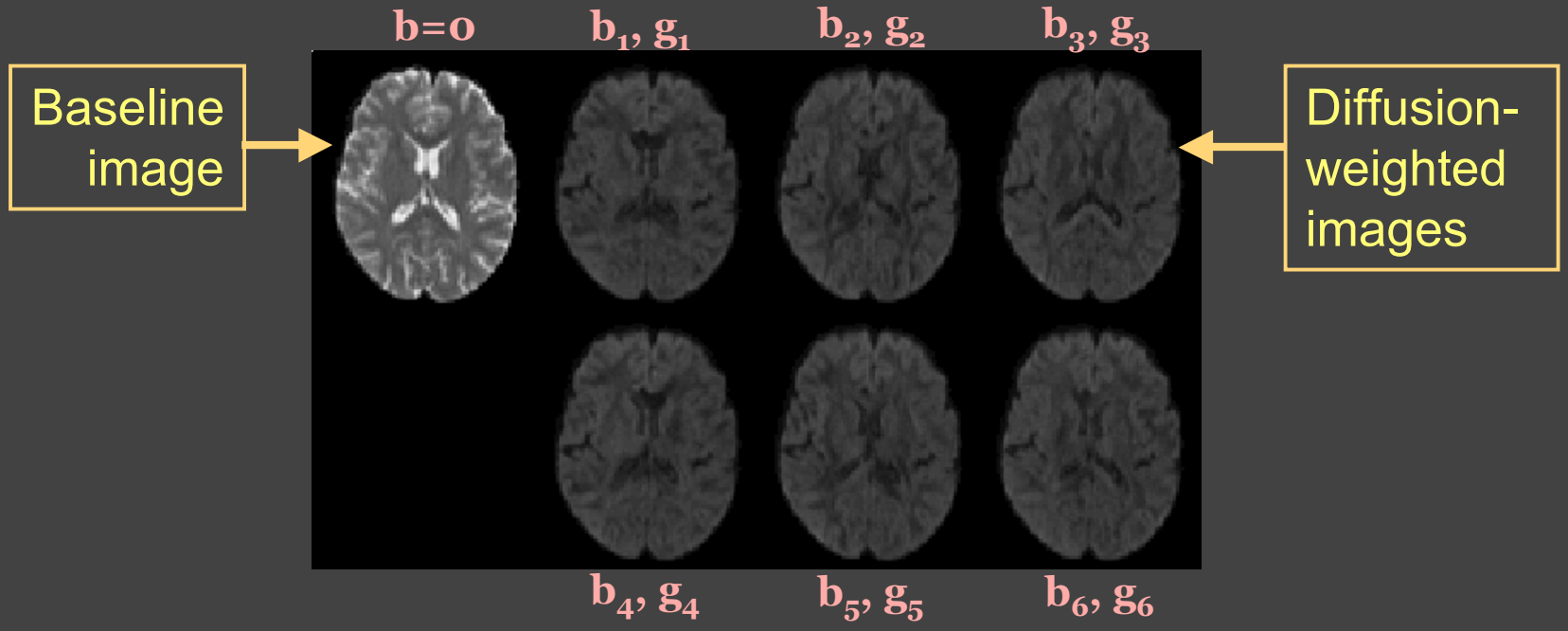
How high b-value?

- Increasing the b-value leads to:
  - + Increased contrast b/w areas of higher and lower diffusivity
  - – Decreased signal-to-noise ratio ⇒ Less reliable estimation of diffusion measures
- DTI: b ~ 1000 sec/mm²
- DSI: b ~ 10,000 sec/mm²
- Data can be acquired at multiple b-values for trade-off
- Repeat acquisition and average to increase signal-to-noise ratio

Looking at the data

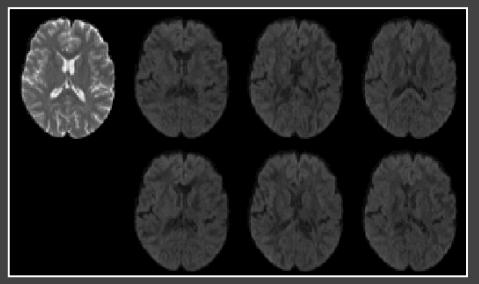
A diffusion data set consists of:

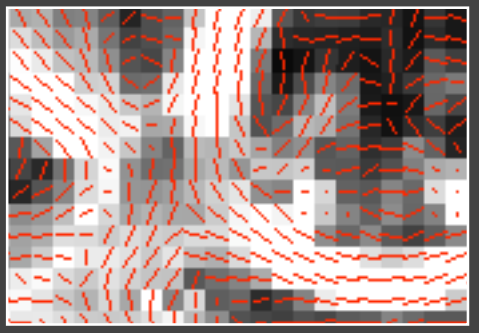
- A set of non-diffusion-weighted a.k.a "baseline" a.k.a. "low-b" images (b-value = 0)
- A set of diffusion-weighted images acquired with different gradient directions g_1, g_2, … and b-value >0
- The diffusion-weighted images have lower intensity values

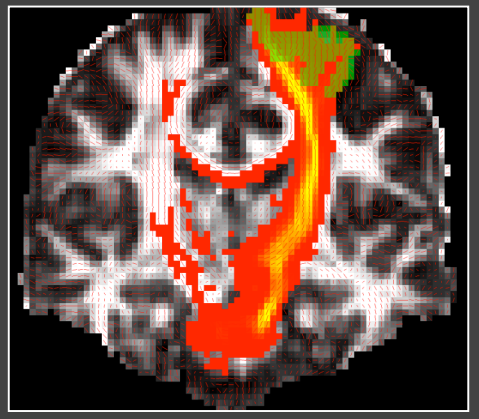


Data analysis steps

- Pre-process images
  - FSL: eddy_correct, rotate_bvecs
- Fit a diffusion model at every voxel
  - DTK: DSI, Q-ball, or DTI
  - FSL: Ball-and-stick (bedpost) or DTI (dtifit)
- Reconstruct pathways
  - DTK: Deterministic tractography using DSI, Q-ball, or DTI model
  - FSL: Probabilistic tractography (probtrack) using ball-and-stick model

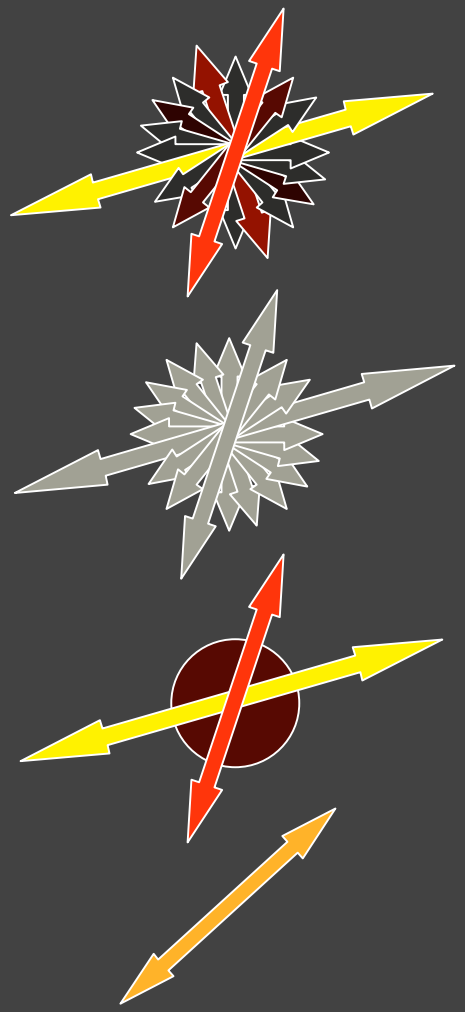






DTK: www.trackvis.org, FSL: www.fmrib.ox.ac.uk/fsl

Models of diffusion

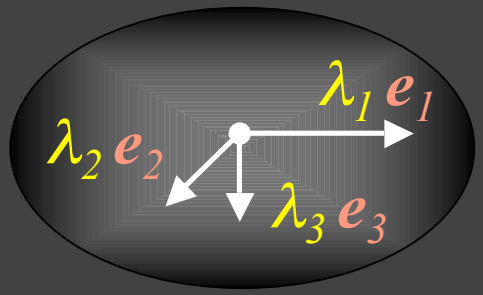


Model	Software
Diffusion spectrum: Full distribution of orientation and magnitude	DTK (DSI option)
Orientation distribution function (ODF): No magnitude info	DTK (Q-ball option)
Ball-and-stick: Orientation and magnitude for up to N anisotropic compartments (default N=2)	FSL (bedpost)
Tensor: Single orientation and magnitude	DTK (DTI option) FSL (dtifit)

A bit more about the tensor

- A tensor can be thought of as an ellipsoid

- It can be defined fully by:
  - 3 eigenvectors e_1, e_2, e_3 (orientations of ellipsoid axes)
  - 3 eigenvalues λ_1, λ_2, λ_3 (lengths of ellipsoid axes)

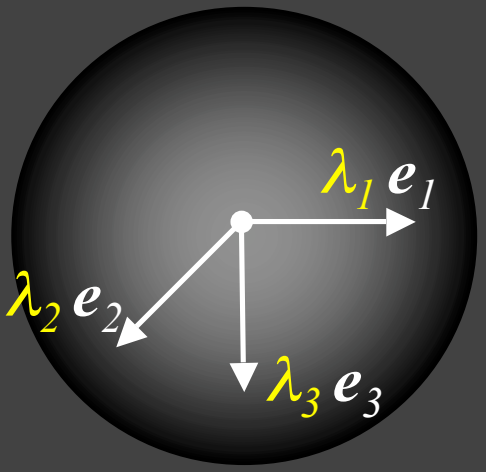


Tensor: Physical interpretation

- Eigenvectors express diffusion direction
- Eigenvalues express diffusion magnitude

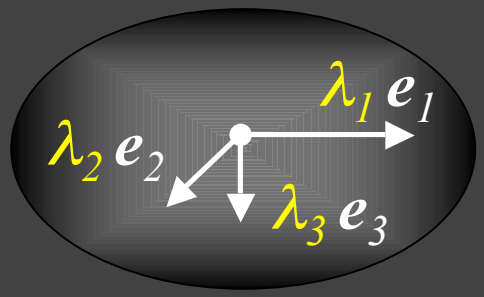
Isotropic diffusion:

$\lambda_1 \approx \lambda_2 \approx \lambda_3$

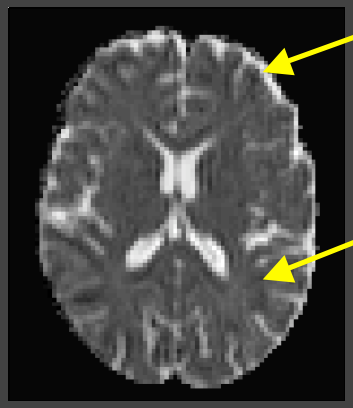


Anisotropic diffusion:

$\lambda_1 >> \lambda_2 \approx \lambda_3$

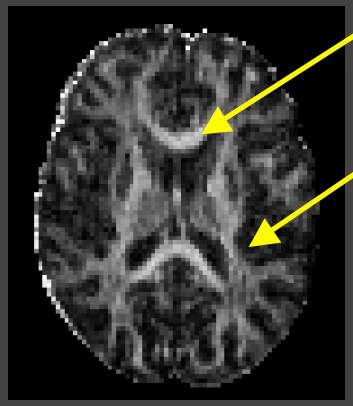


Tensor: Summary measures



- Mean diffusivity (MD): Mean of the 3 eigenvalues

$$MD(j) = [\lambda_1(j)+\lambda_2(j)+\lambda_3(j)]/3$$



- Fractional anisotropy (FA): Variance of the 3 eigenvalues, normalized so that $0 \leq (FA) \leq 1$

$$FA(j)^2 = \frac{3}{2} \frac{[\lambda_1(j)-MD(j)]^2 + [\lambda_2(j)-MD(j)]^2 + [\lambda_3(j)-MD(j)]^2}{\lambda_1(j)^2 + \lambda_2(j)^2 + \lambda_3(j)^2}$$

Tensor: More summary measures

- Axial diffusivity: Greatest eigenvalue

  $AD(j) = \lambda_1(j)$

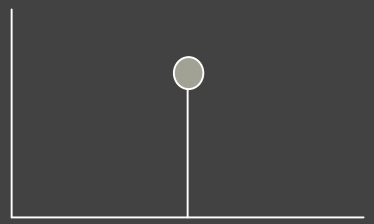
- Radial diffusivity: Average of 2 lesser eigenvalues

  $RD(j) = [\lambda_2(j) + \lambda_3(j)]/2$

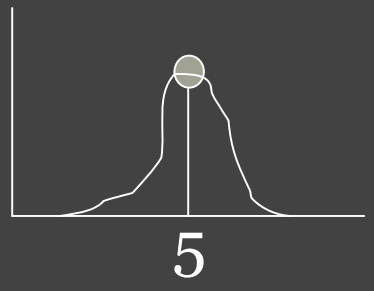
- Inter-voxel coherence: Average angle b/w the major eigenvector at some voxel and the major eigenvector at the voxels around it

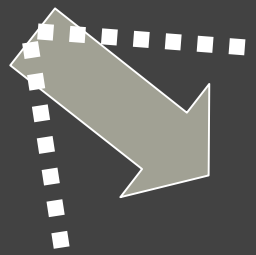
Deterministic vs. probabilistic

- Deterministic methods give you an estimate of model parameters



- Probabilistic methods give you the uncertainty (probability distribution) of the estimate

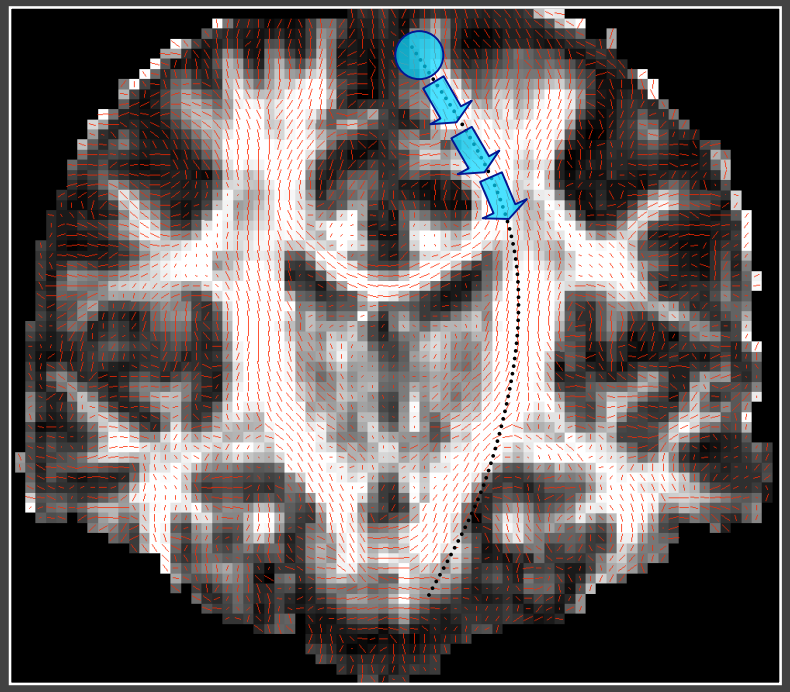




Tractography

Deterministic:

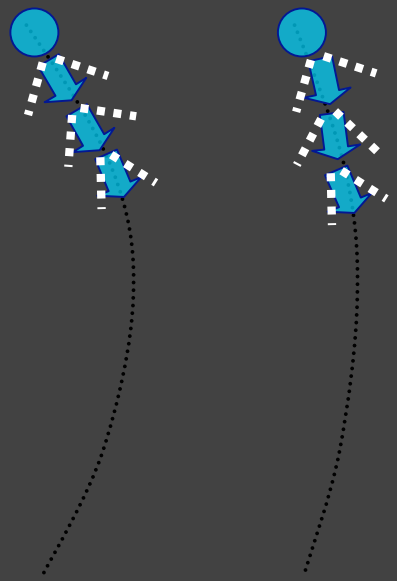
One streamline per seed voxel



Probabilistic:

Multiple streamline samples per seed voxel (drawn from probability distribution)

Sample 1 Sample 2 ...



Tractography outputs

Deterministic:

One streamline per seed voxel

Probabilistic:

A probability distribution

(sum of all streamline samples from all seed voxels)