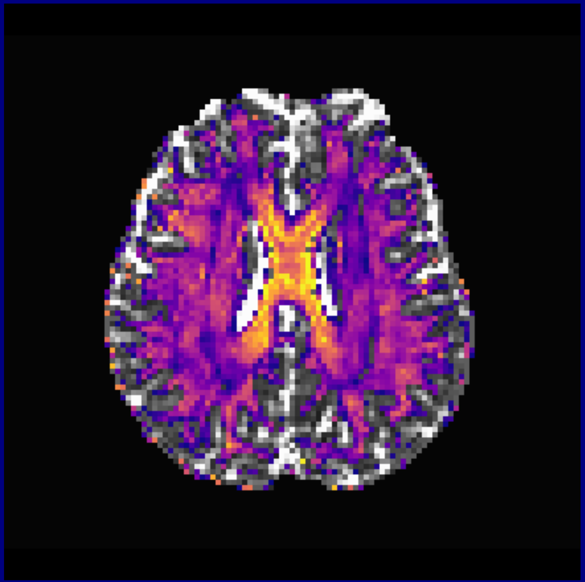
Introduction to: DWI + DTI

AFNI Bootcamp (SSCC, NIMH, NIH)



Outline

+ DWI and DTI
  - Concepts behind diffusion imaging
  - Diffusion imaging basics in brief
  - Connecting DTI parameters and geometry
  - Role of noise+distortion $\rightarrow$ DTI parameter uncertainty

What is diffusion tensor imaging?

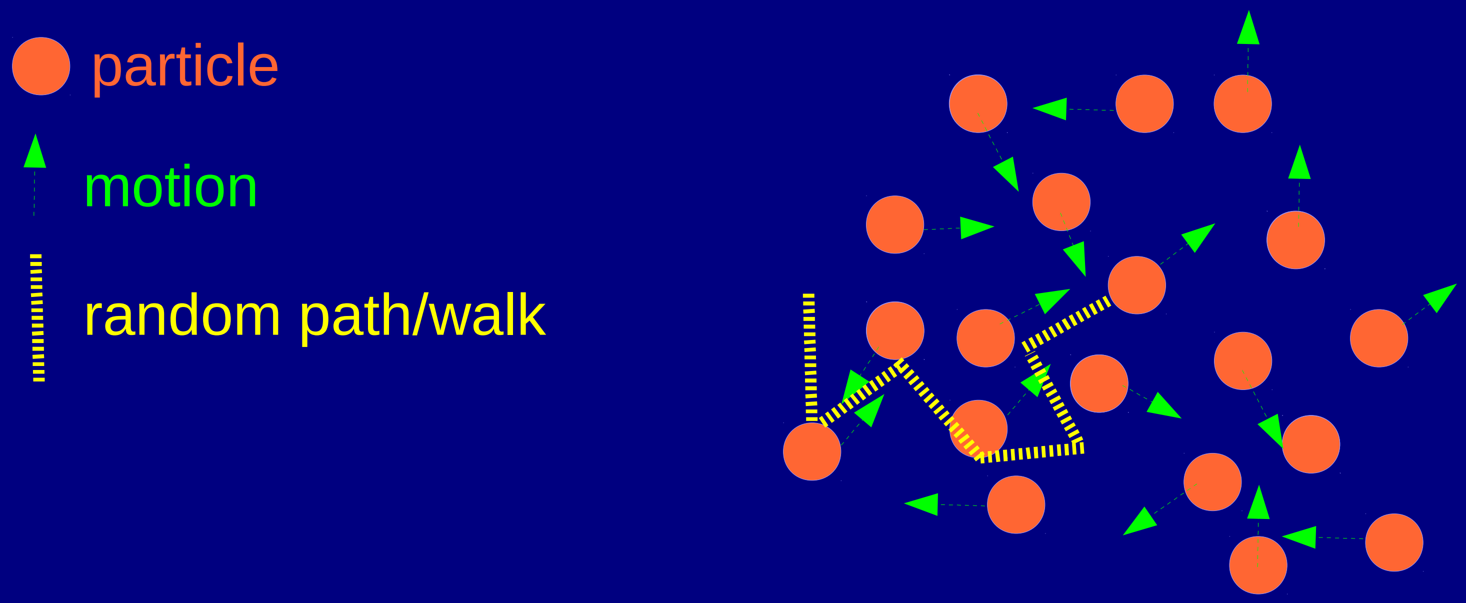
DTI is a particular kind of magnetic resonance imaging (MRI)

What is diffusion tensor imaging?

DTI is a particular kind of magnetic resonance imaging (MRI)

*D*iffusion: random motion of particles, tending to spread out

$\longrightarrow$ here, hydrogen atoms in aqueous brain tissue



What is diffusion tensor imaging?

DTI is a particular kind of magnetic resonance imaging (MRI)

*D*iffusion: random motion of particles, tending to spread out

$\longrightarrow$ here, hydrogen atoms in aqueous brain tissue

*T*ensor: a mathematical object (a matrix) to store information

$\longrightarrow$ here, quantifying particle spread in all directions

$$\mathbf{D} = \begin{pmatrix} D_{11} & D_{12} & D_{13} \\ D_{21} & D_{22} & D_{23} \\ D_{31} & D_{32} & D_{33} \end{pmatrix}$$

What is diffusion tensor imaging?

DTI is a particular kind of magnetic resonance imaging (MRI)

*D*iffusion: random motion of particles, tending to spread out

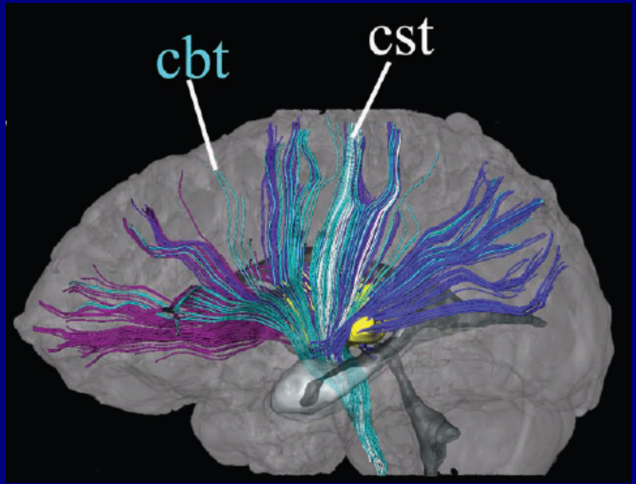
→ here, hydrogen atoms in aqueous brain tissue

*T*ensor: a mathematical object (a matrix) to store information

→ here, quantifying particle spread in all directions

*I*maging: quantifying brain properties

→ here, esp. for white matter



The DTI model:

Assumptions and relation to WM properties

Diffusion as environmental marker

Diffusion: random (Brownian) motion of particles $\rightarrow$ mixing or spreading

Ex: unstirred, steeping tea (in a large cup):

Diffusion as environmental marker

Diffusion: random (Brownian) motion of particles $\longrightarrow$ mixing or spreading

<u>Ex: unstirred, steeping tea (in a large cup):</u>

<u>Empty cup, no structure:</u>

Atoms have equal probability of movement any direction

$\longrightarrow$ spherical spread of concentration

Diffusion as environmental marker

Diffusion: random (Brownian) motion of particles → mixing or spreading

Ex: unstirred, steeping tea (in a large cup):

Empty cup, no structure:
Atoms have equal probability of movement any direction
→ spherical spread of concentration

Diffusion as environmental marker

Diffusion: random (Brownian) motion of particles $\rightarrow$ mixing or spreading

Ex: unstirred, steeping tea (in a large cup):

Empty cup, no structure:
Atoms have equal probability of movement any direction
$\rightarrow$ spherical spread of concentration

But in the presence of structures:

Diffusion as environmental marker

Diffusion: random (Brownian) motion of particles $\rightarrow$ mixing or spreading

Ex: unstirred, steeping tea (in a large cup):

Empty cup, no structure:
Atoms have equal probability of movement any direction
$\rightarrow$ spherical spread of concentration

But in the presence of structures:
Unequal probabilities of moving in different directions
$\rightarrow$ *non*spherical spread

Diffusion as environmental marker

Diffusion: random (Brownian) motion of particles → mixing or spreading

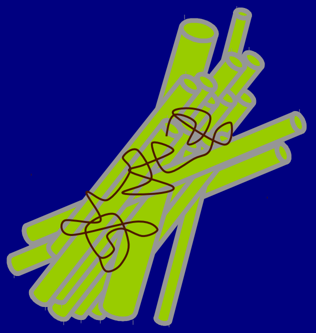
Ex: unstirred, steeping tea (in a large cup):

Empty cup, no structure:
Atoms have equal probability of movement any direction
→ spherical spread of concentration

But in the presence of structures:
Unequal probabilities of moving in different directions
→ *non*spherical spread

***→ Diffusion shape tells of* structure presence *and sp*atial orientation**

Local Structure via Diffusion MRI



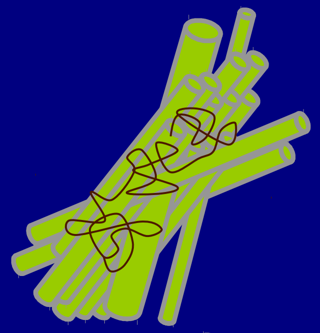
(In brief)

1) Random motion of molecules affected by local structures

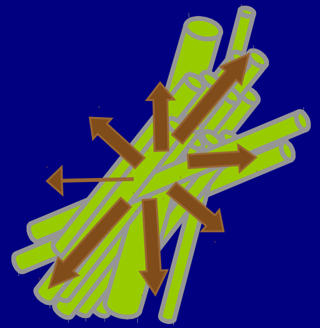
Local Structure via Diffusion MRI

(In brief)

1) Random motion of molecules affected by local structures

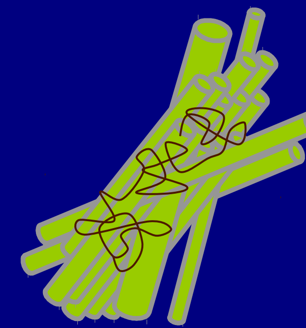


2) Statistical motion measured using diffusion weighted MRI

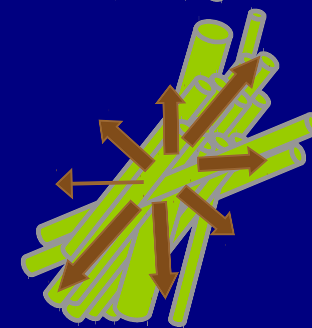


Local Structure via Diffusion MRI

(In brief)



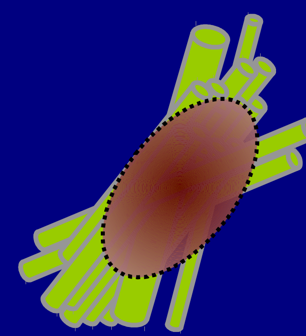
1) Random motion of molecules affected by local structures



2) Statistical motion measured using diffusion weighted MRI

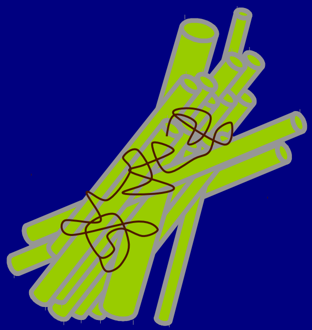
3) Bulk features of local structure approximated with various reconstruction models, mainly grouped by number of major structure directions/voxel:

- \+ one direction:
  DTI (Diffusion Tensor Imaging)

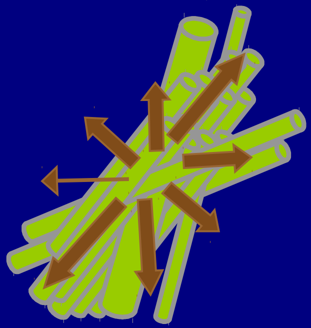


Local Structure via Diffusion MRI

(In brief)

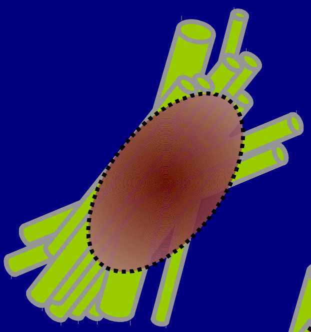


1) Random motion of molecules affected by local structures

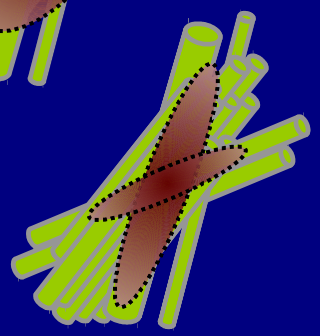


2) Statistical motion measured using diffusion weighted MRI

3) Bulk features of local structure approximated with various reconstruction models, mainly grouped by number of major structure directions/voxel:



+ one direction:
  DTI (Diffusion Tensor Imaging)



+ >=1 direction:
  HARDI (High Angular Resolution Diffusion Imaging)
  Qball, DSI, ODFs, ball-and-stick, multi-tensor, CSD, ...

Diffusion in MRI

Mathematical properties

of the matrix/tensor:

$$\mathbf{D} = \begin{pmatrix} D_{11} & D_{12} & D_{13} \\ D_{21} & D_{22} & D_{23} \\ D_{31} & D_{32} & D_{33} \end{pmatrix}$$

Having: 3 eigenvectors: $\mathbf{e}_i$

3 eigenvalues: λ_i

- Real-valued
- Positive definite ($\mathbf{r}^T\mathbf{D}\mathbf{r} > 0$)

$$\mathbf{D}\mathbf{e}_i = \lambda_i \mathbf{e}_i, \qquad \lambda_i > 0$$

- Symmetric ($D_{12} = D_{21}$, etc)

6 independent values

Diffusion in MRI

Mathematical properties of the matrix/tensor:

$$\mathbf{D} = \begin{pmatrix} D_{11} & D_{12} & D_{13} \\ D_{21} & D_{22} & D_{23} \\ D_{31} & D_{32} & D_{33} \end{pmatrix}$$

Having: 3 eigenvectors: $\mathbf{e}_i$

3 eigenvalues: λ_i

- Real-valued
- Positive definite ($\mathbf{r}^T\mathbf{D}\mathbf{r} > 0$)

  $\mathbf{D}\mathbf{e}_i = \lambda_i\,\mathbf{e}_i, \qquad \lambda_i > 0$
- Symmetric ($D_{12} = D_{21}$, etc)

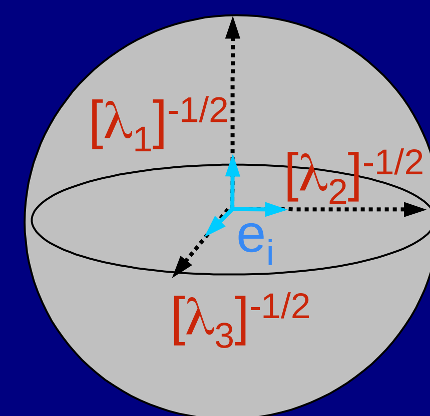
  6 independent values

Geometrically, this describes an ellipsoid surface:

$$C = D_{11}x^2 + D_{22}y^2 + D_{33}z^2 + 2(D_{12}xy + D_{13}xz + D_{23}yz)$$

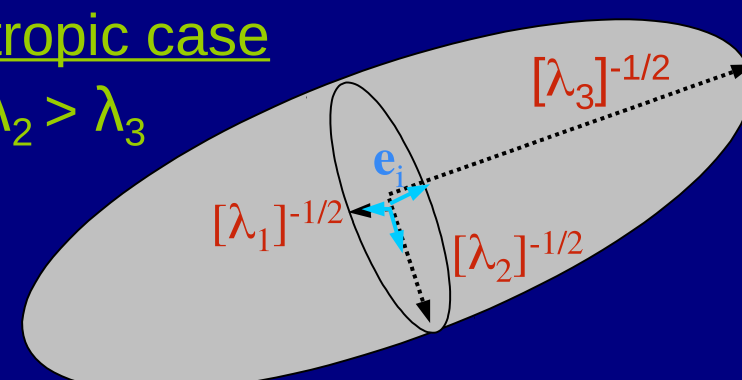
isotropic case

$\lambda_1 = \lambda_2 = \lambda_3$



anisotropic case

$\lambda_1 > \lambda_2 > \lambda_3$



DTI: ellipsoids

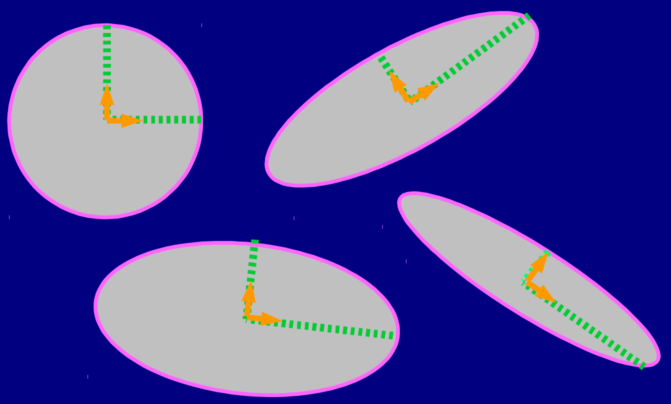
Important mathematical properties of the diffusion tensor:

+ Help to picture diffusion model:

tensor **D** → **ellipsoid surface**

eigenvectors $\mathbf{e}_i$ → orientation in space

eigenvalues λ_i → 'pointiness' + 'size'



DTI: ellipsoids

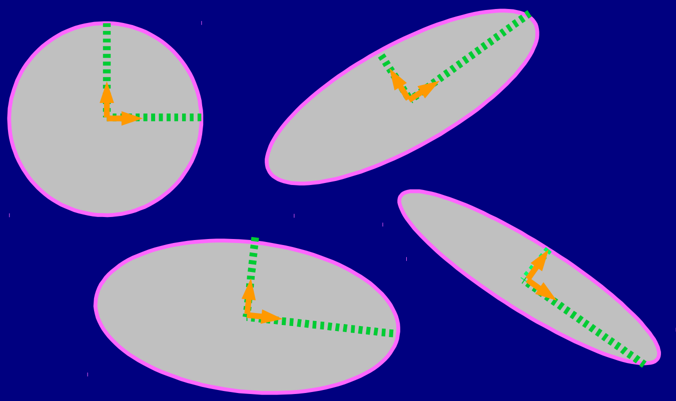
Important mathematical properties of the diffusion tensor:

+ Help to picture diffusion model:

  tensor **D** → **ellipsoid surface**

  eigenvectors $\mathbf{e}_i$ → orientation in space

  eigenvalues λ_i → 'pointiness' + 'size'



+ Determine the minimum number of

  DWIs measures needed (6 + baseline)

$$\begin{pmatrix} D_{11} & D_{12} & D_{13} \\ D_{21} & D_{22} & D_{23} \\ D_{31} & D_{32} & D_{33} \end{pmatrix}$$

DTI: ellipsoids

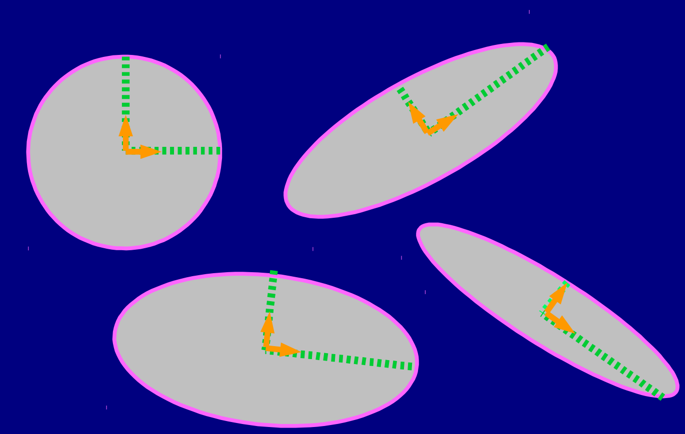
Important mathematical properties of the diffusion tensor:

+ Help to picture diffusion model:

  tensor **D** → **ellipsoid surface**

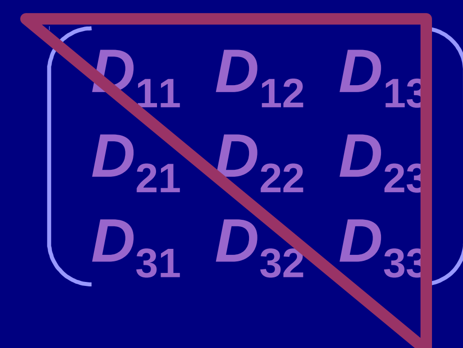
  eigenvectors $\mathbf{e}_i$ → orientation in space

  eigenvalues λ_i → 'pointiness' + 'size'



+ Determine the minimum number of

  DWIs measures needed (6 + baseline)



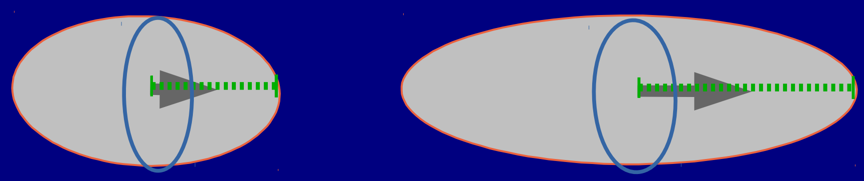
+ Determine much of the processing and

  noise minimization steps

"Big 5" DTI ellipsoid parameters

Main quantities of diffusion (motion) surface

first eigenvalue, L1
(= λ_1, parallel/axial diffusivity, AD)

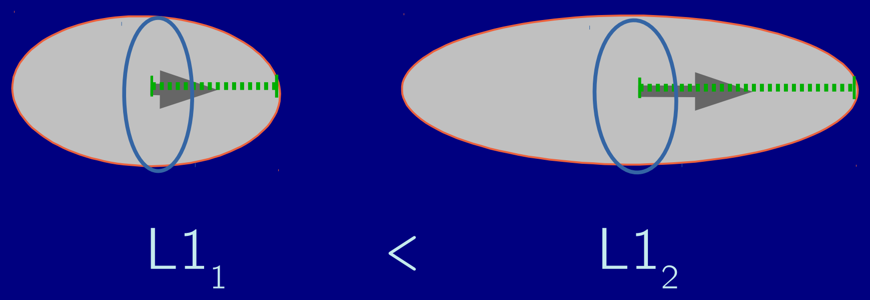


$L1_1 < L1_2$

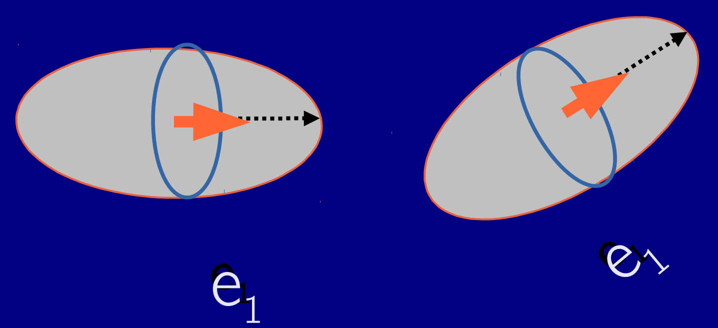
"Big 5" DTI ellipsoid parameters

Main quantities of diffusion (motion) surface

first eigenvalue, L1
(= λ_1, parallel/axial diffusivity, AD)



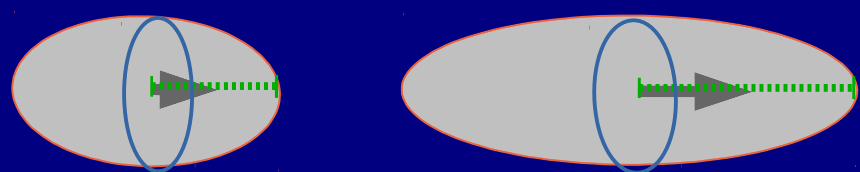
first eigenvector, e_1
(DT orientation in space)



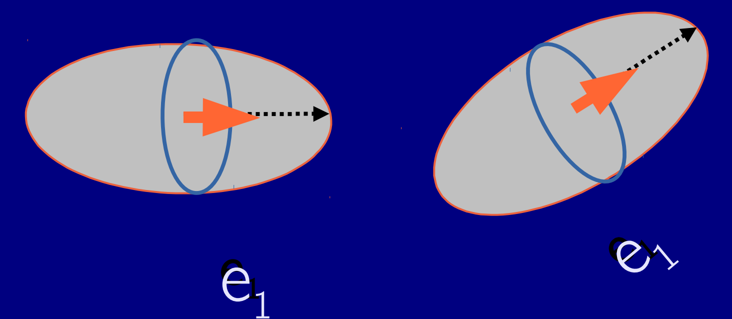
“Big 5” DTI ellipsoid parameters

Main quantities of diffusion (motion) surface

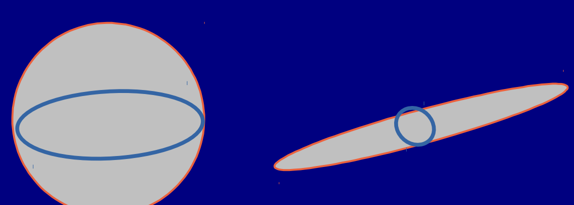
first eigenvalue, L1
(= λ_1, parallel/axial diffusivity, AD)



first eigenvector, e_1
(DT orientation in space)



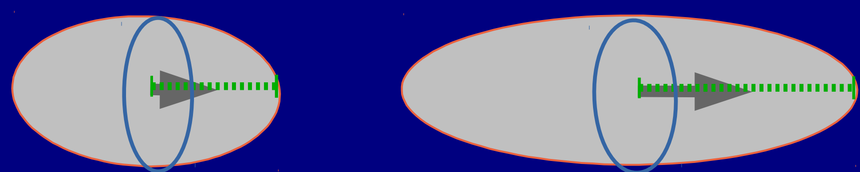
Fractional anisotropy, FA
(stdev of eigenvalues)



“Big 5” DTI ellipsoid parameters

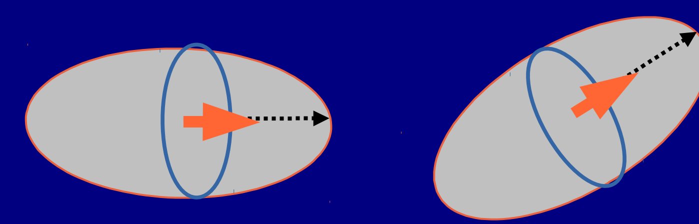
Main quantities of diffusion (motion) surface

first eigenvalue, L1
(= λ_1, parallel/axial diffusivity, AD)



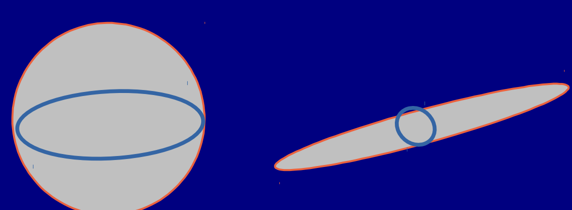
$L1_1$ < $L1_2$

first eigenvector, e_1
(DT orientation in space)



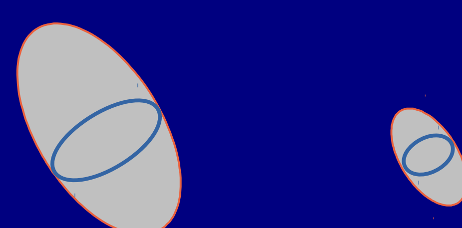
e_1 e_1

Fractional anisotropy, FA
(stdev of eigenvalues)



FA≈0 FA≈1

Mean diffusivity, MD
(mean of eigenvalues)

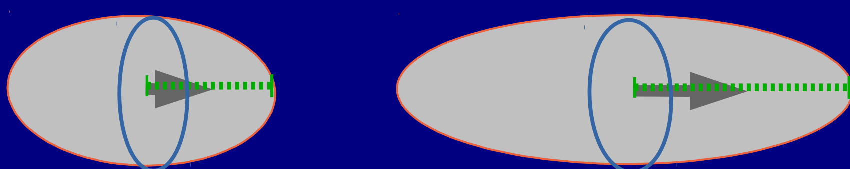


MD_1 > MD_2

"Big 5" DTI ellipsoid parameters

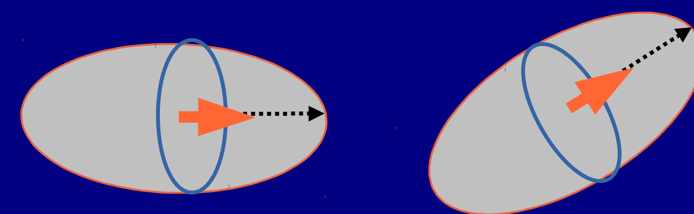
Main quantities of diffusion (motion) surface

first eigenvalue, L1
(= λ_1, parallel/axial diffusivity, AD)



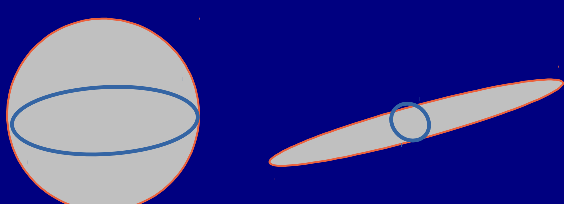
$L1_1$ < $L1_2$

first eigenvector, e_1
(DT orientation in space)



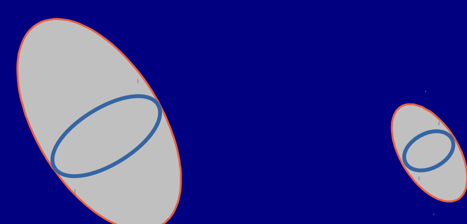
e_1 e_1

Fractional anisotropy, FA
(stdev of eigenvalues)



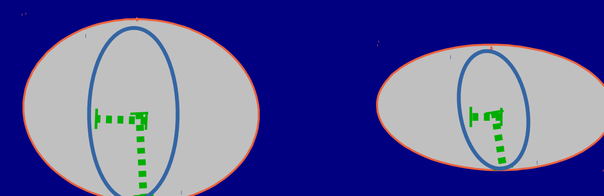
FA≈0 FA≈1

Mean diffusivity, MD
(mean of eigenvalues)



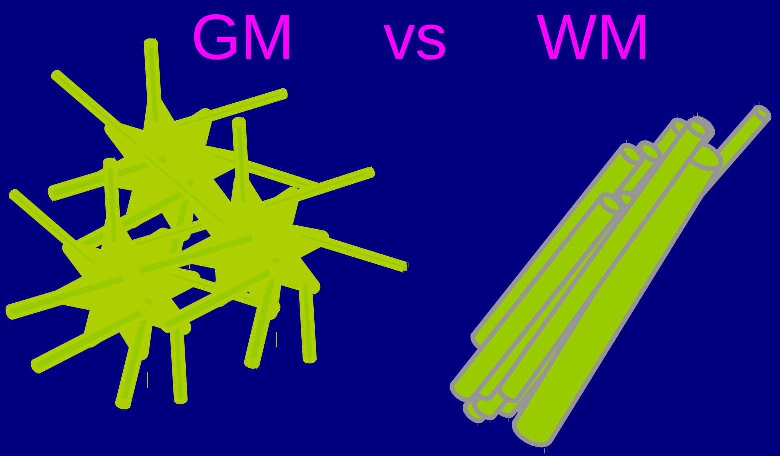
MD_1 > MD_2

Radial diffusivity, RD
(= $(\lambda_2+\lambda_3)/2$)

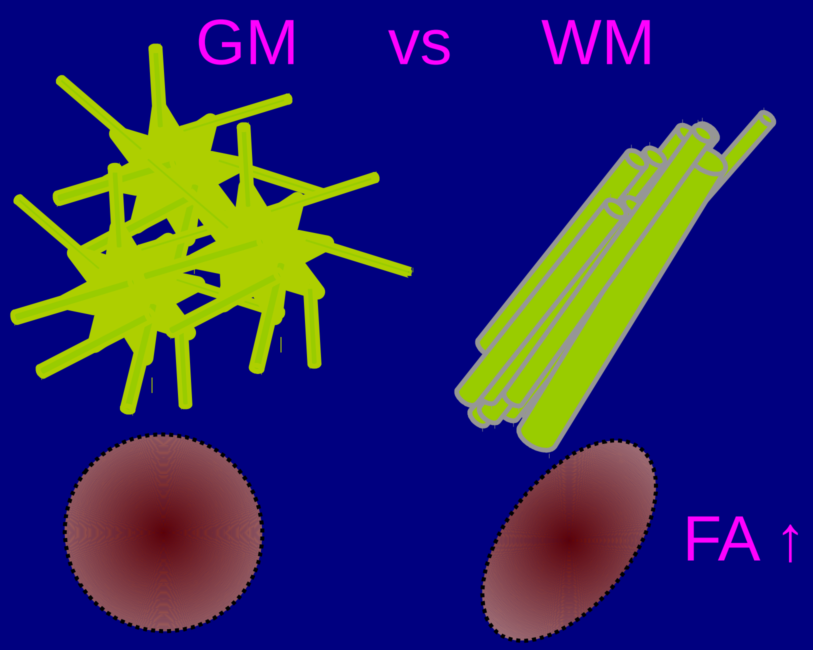


RD_1 > RD_2

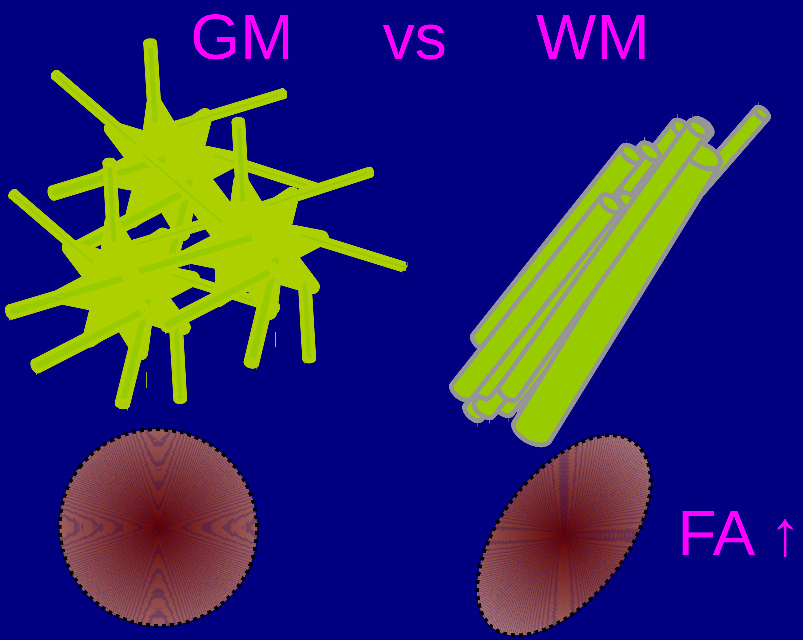
Cartoon examples: white matter ↔ FA



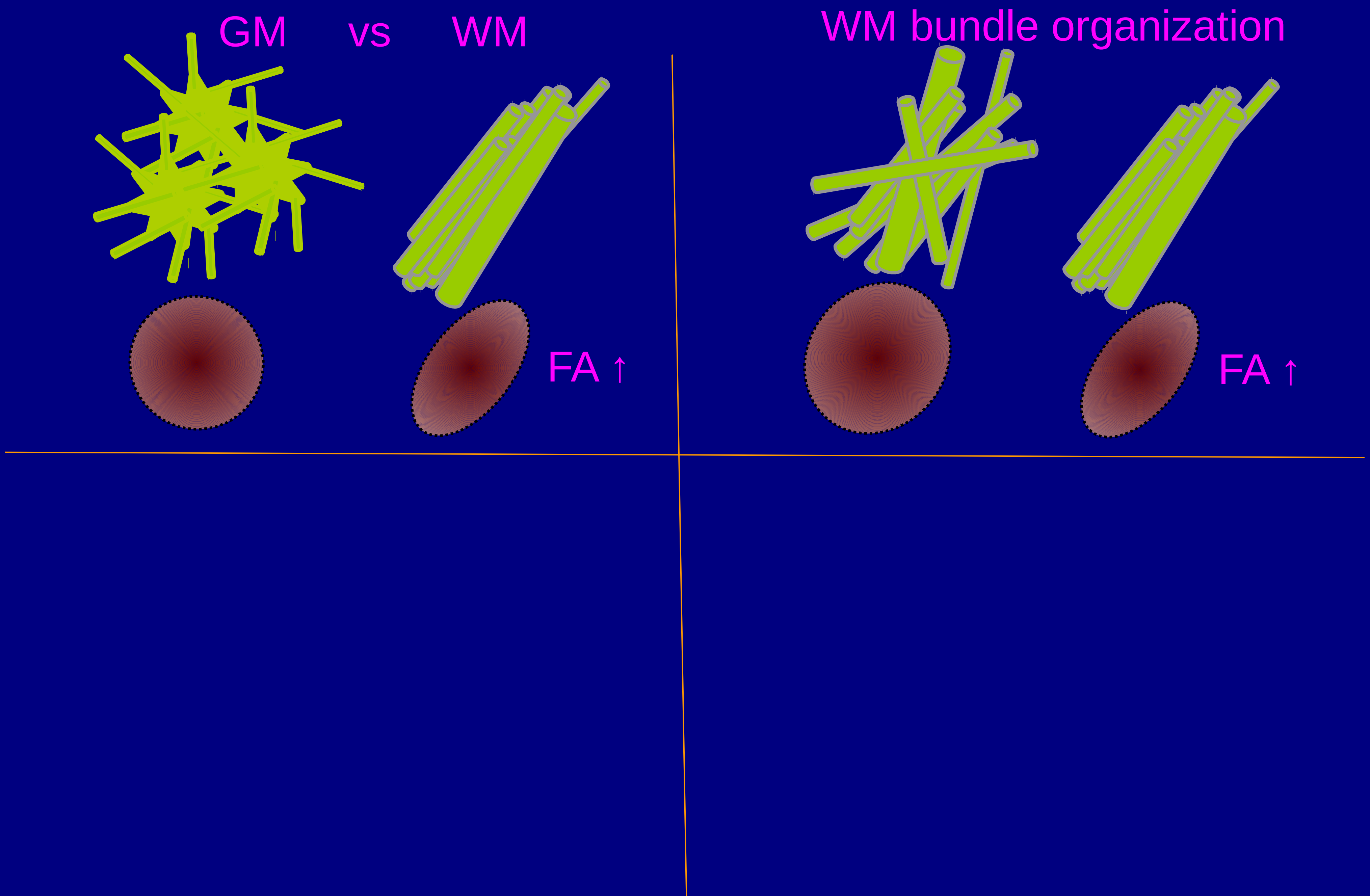
Cartoon examples: white matter ↔ FA



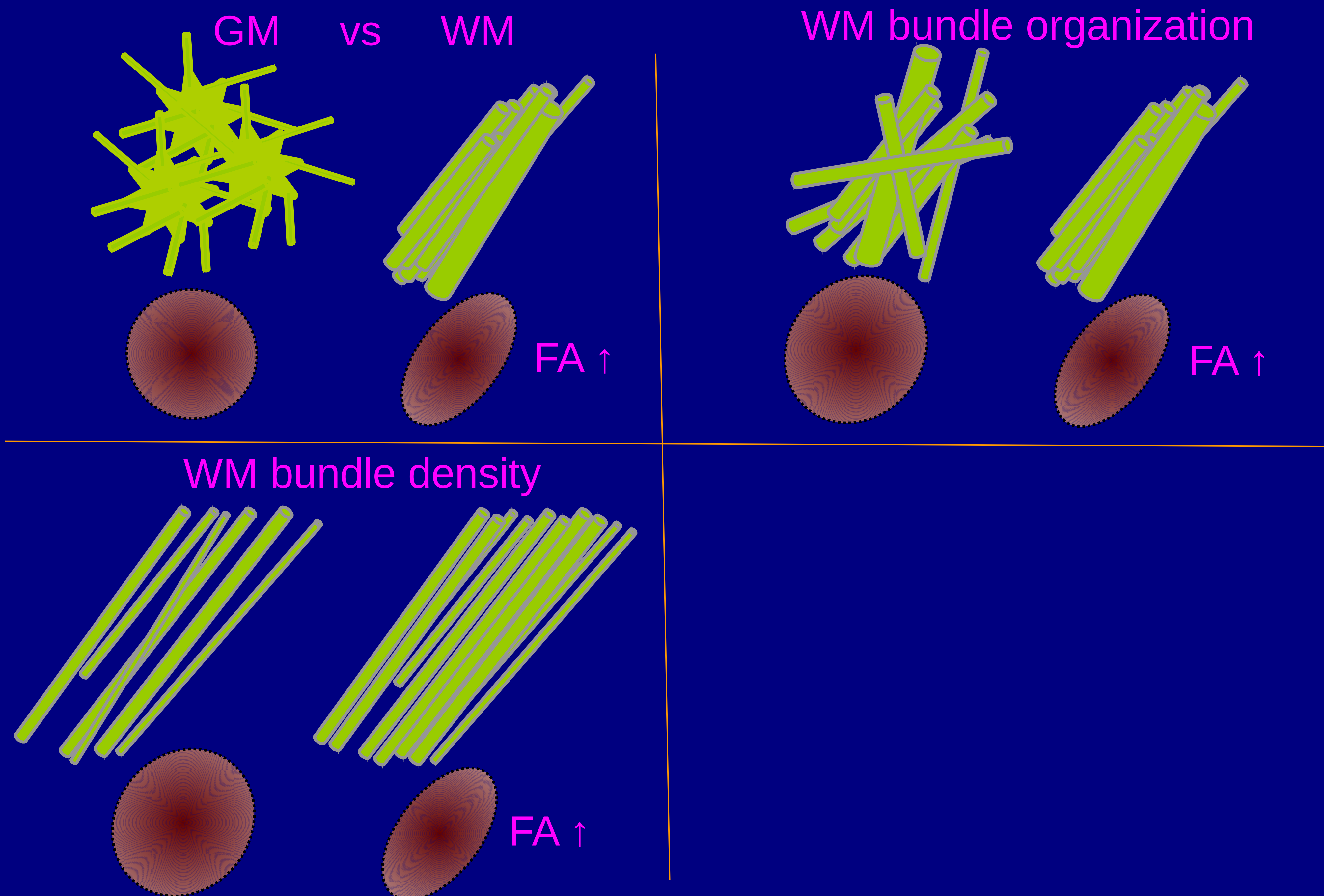
Cartoon examples: white matter ↔ FA



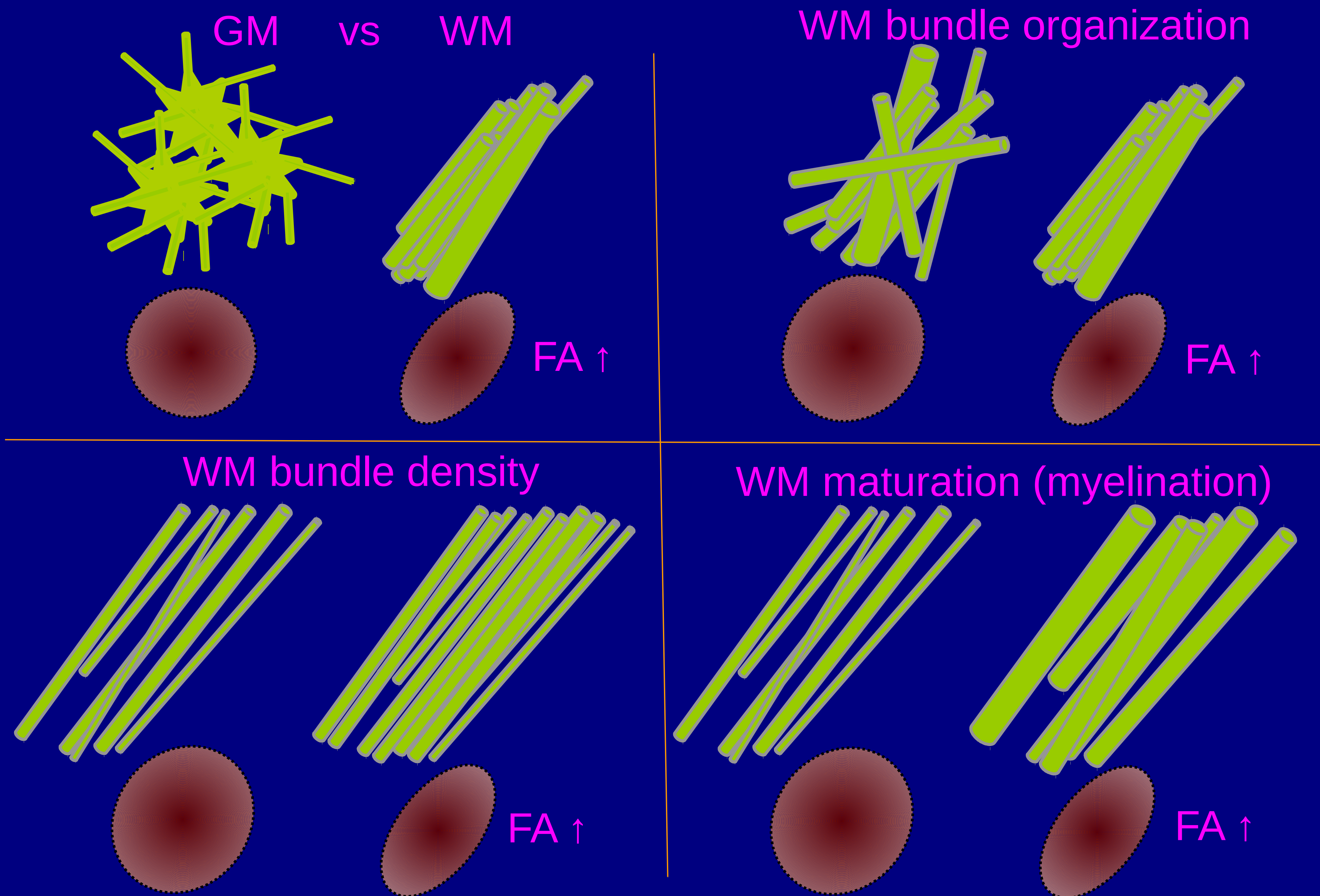
Cartoon examples: white matter ↔ FA



Cartoon examples: white matter ↔ FA



Cartoon examples: white matter ↔ FA



Interpreting DTI parameters

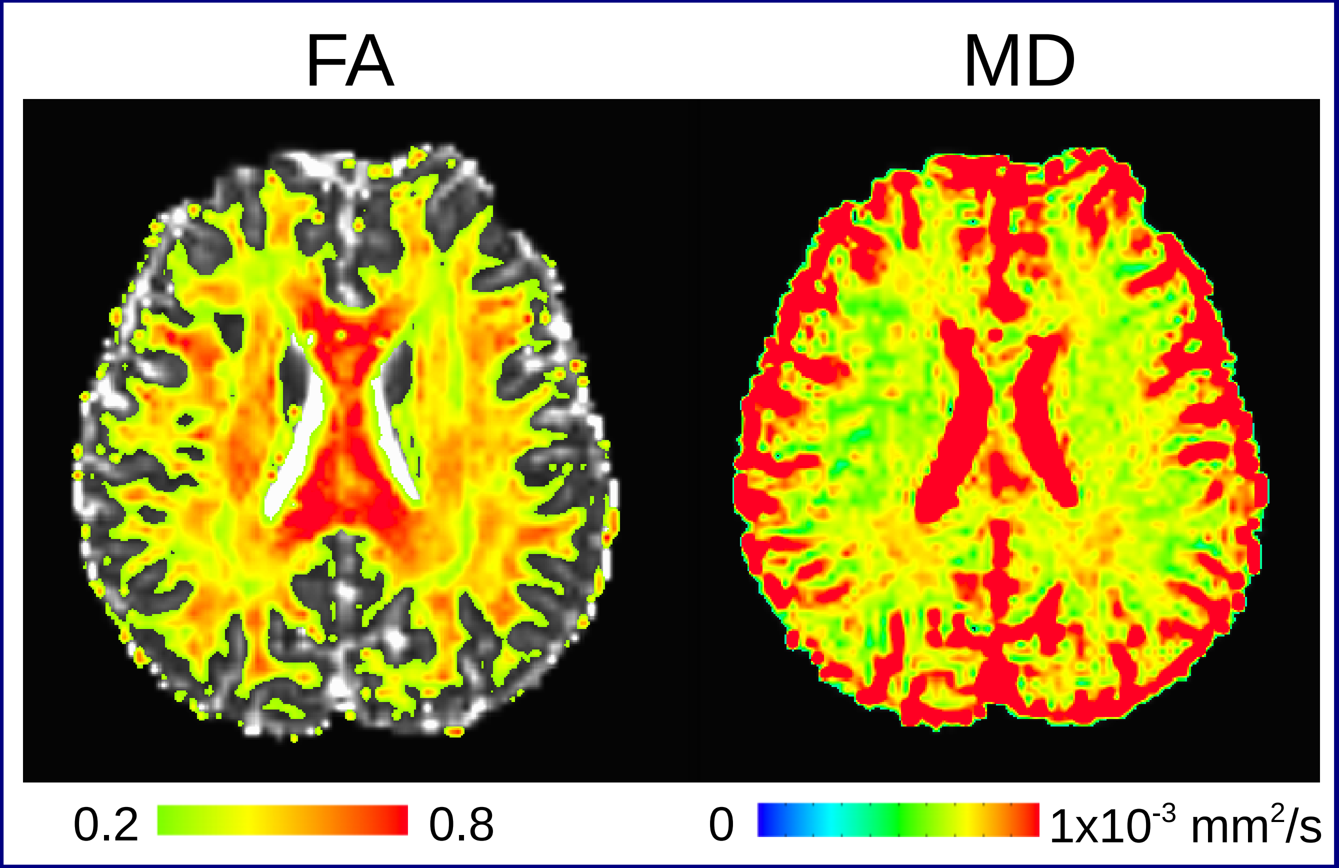
General literature:

FA: measure of fiber bundle coherence and myelination

- in adults, FA>0.2 is proxy for WM

MD, L1, RD: local density of structure

e_1: orientation of major bundles



Interpreting DTI parameters

General literature:

FA: measure of fiber bundle coherence and myelination

- in adults, FA>0.2 is proxy for WM

MD, L1, RD: local density of structure

$\mathbf{e}_1$: orientation of major bundles

Cautionary notes:

- Degeneracies of structural interpretations
- Changes in myelination may have small effects on FA
- WM bundle diameter << voxel size
  - don't know location/multiplicity of underlying structures
- More to diffusion than structure-- e.g., fluid properties
- Noise, distortions, etc. in measures

Acquiring DTI data:

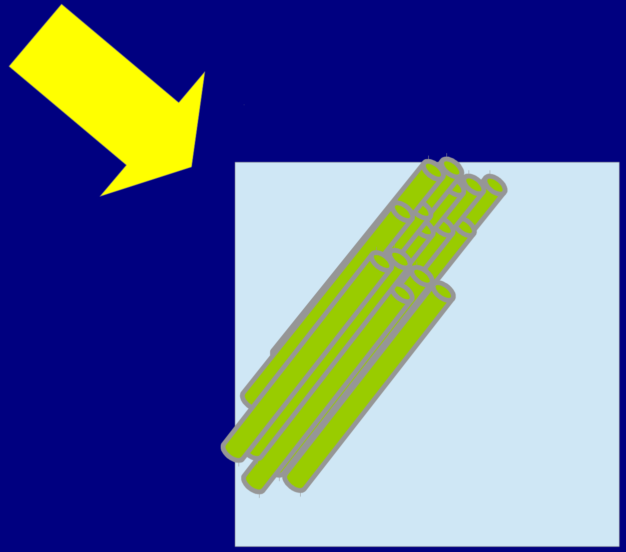
diffusion weighted gradients in MRI

Diffusion weighted imaging

For a given voxel, observe relative diffusion along a given 3D spatial orientation (gradient)

DW gradient

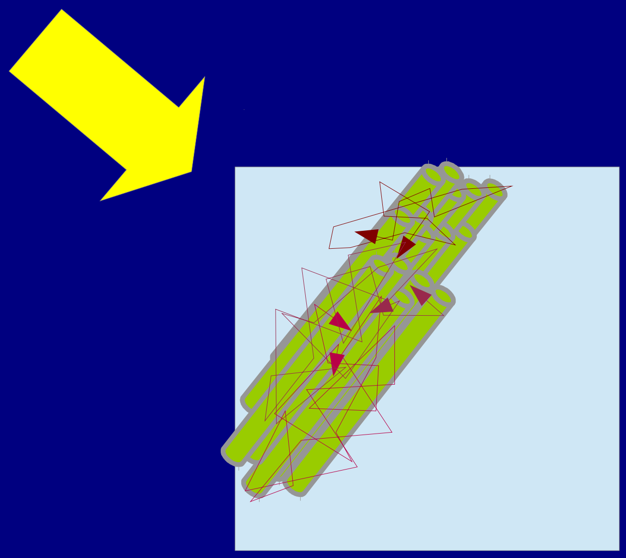
$\mathbf{g}_\mathrm{i} = (g_x, g_y, g_z)$



Diffusion weighted imaging

For a given voxel, observe relative diffusion along a given 3D spatial orientation (gradient)

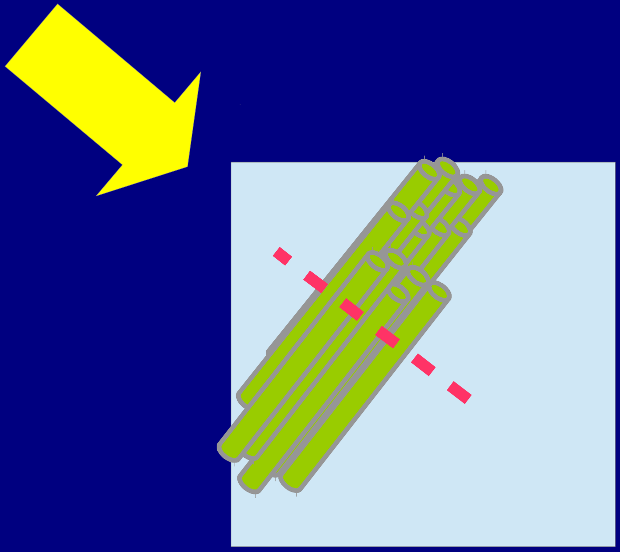
DW gradient
$\mathbf{g}_{\mathbf{i}} = (g_x, g_y, g_z)$



Diffusion weighted imaging

For a given voxel, observe relative diffusion along a given 3D spatial orientation (gradient)

DW gradient
$\mathbf{g}_i = (g_x, g_y, g_z)$



MR signal is attenuated by diffusion throughout the voxel in that direction:

$$S_i = S_0 \, e^{-b \, \mathbf{g}_i^T \mathbf{D} \, \mathbf{g}_i}$$

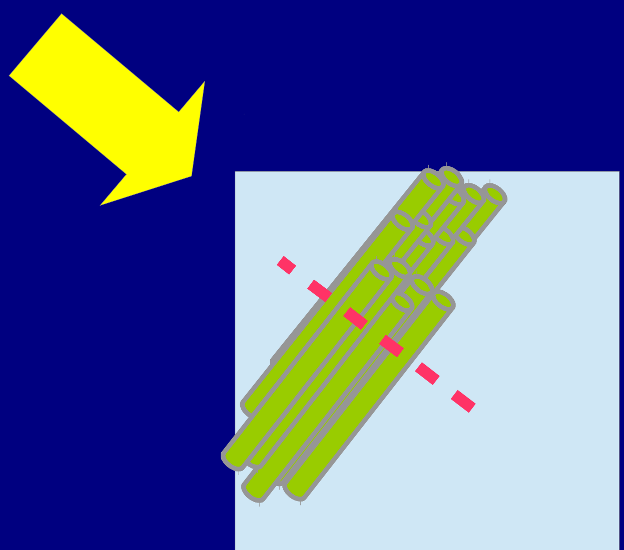
→ ellipsoid equation of diffusion surface:
$C = \mathbf{r}^T \mathbf{D}^{-1} \mathbf{r}.$

Diffusion weighted imaging

For a given voxel, observe relative diffusion along a given 3D spatial orientation (gradient)

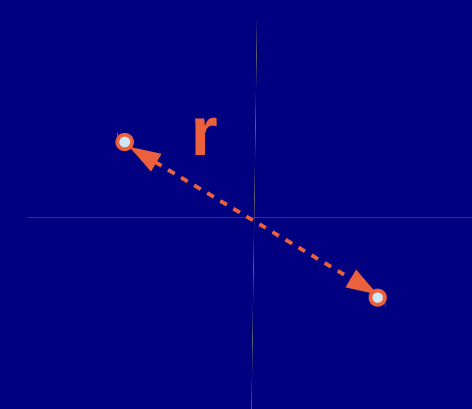
DW gradient

$\mathbf{g}_\mathbf{i} = (g_x, g_y, g_z)$



diffusion motion ellipsoid:

$C_2 = \mathbf{r}^T \mathbf{D}^{-1} \mathbf{r}.$

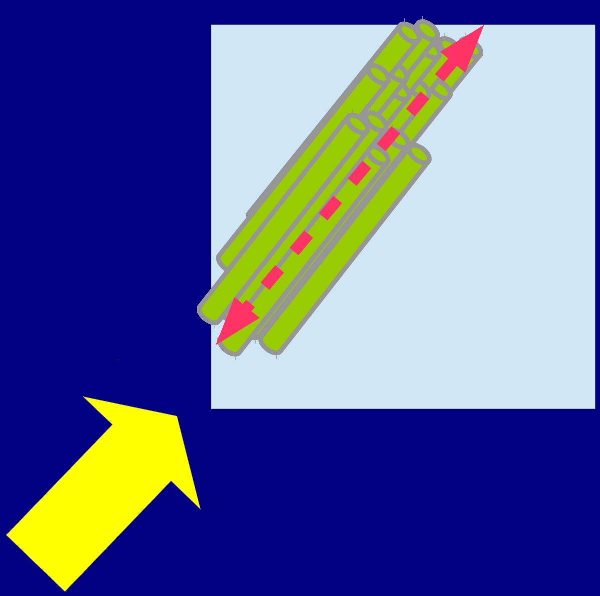


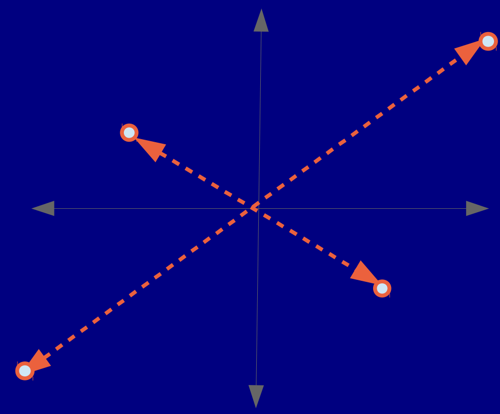
Diffusion weighted imaging

For a given voxel, observe relative diffusion along a given 3D spatial orientation (gradient)

DW gradient
$\mathbf{g}_\mathbf{i} = (g_x, g_y, g_z)$

diffusion motion ellipsoid:
$C_2 = \mathbf{r}^T \mathbf{D}^{-1} \mathbf{r}.$





Diffusion weighted imaging

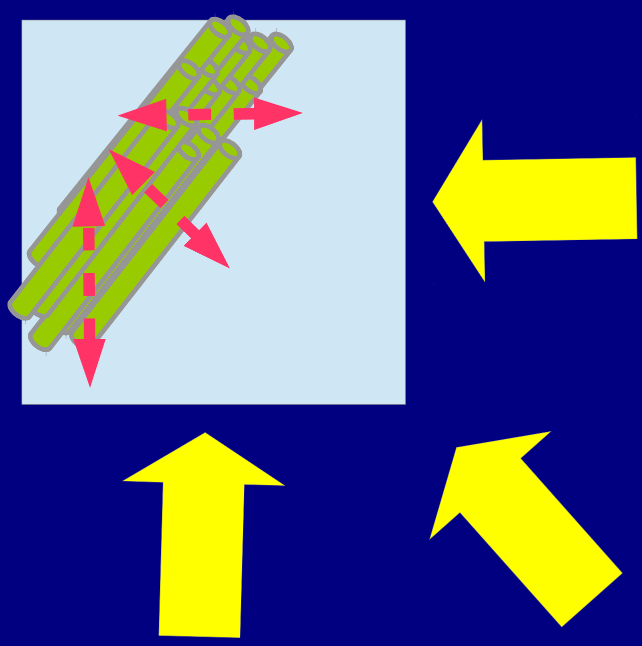
For a given voxel, observe relative diffusion along a given 3D spatial orientation (gradient)

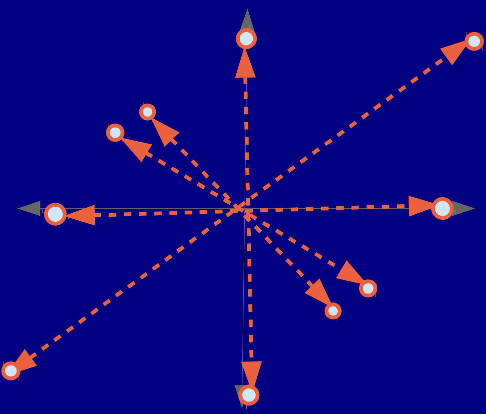
DW gradient

$\mathbf{g}_\mathbf{i} = (g_x, g_y, g_z)$

diffusion motion ellipsoid:

$C_2 = \mathbf{r}^T \mathbf{D}^{-1} \mathbf{r}.$





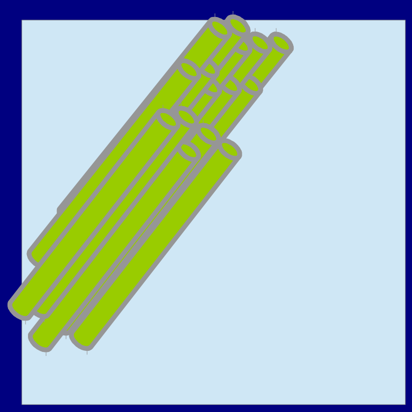
Diffusion weighted imaging

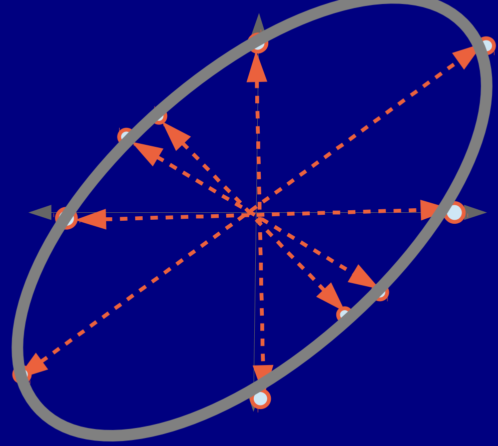
For a given voxel, observe relative diffusion along a given 3D spatial orientation (gradient)

DW gradient
$\mathbf{g}_i = (g_x, g_y, g_z)$

diffusion motion ellipsoid:

$C_2 = \mathbf{r}^T \mathbf{D}^{-1} \mathbf{r}.$

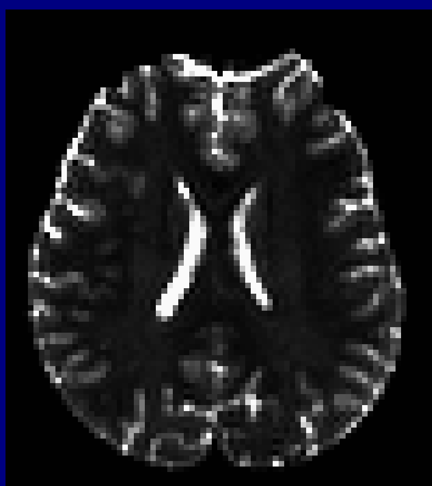




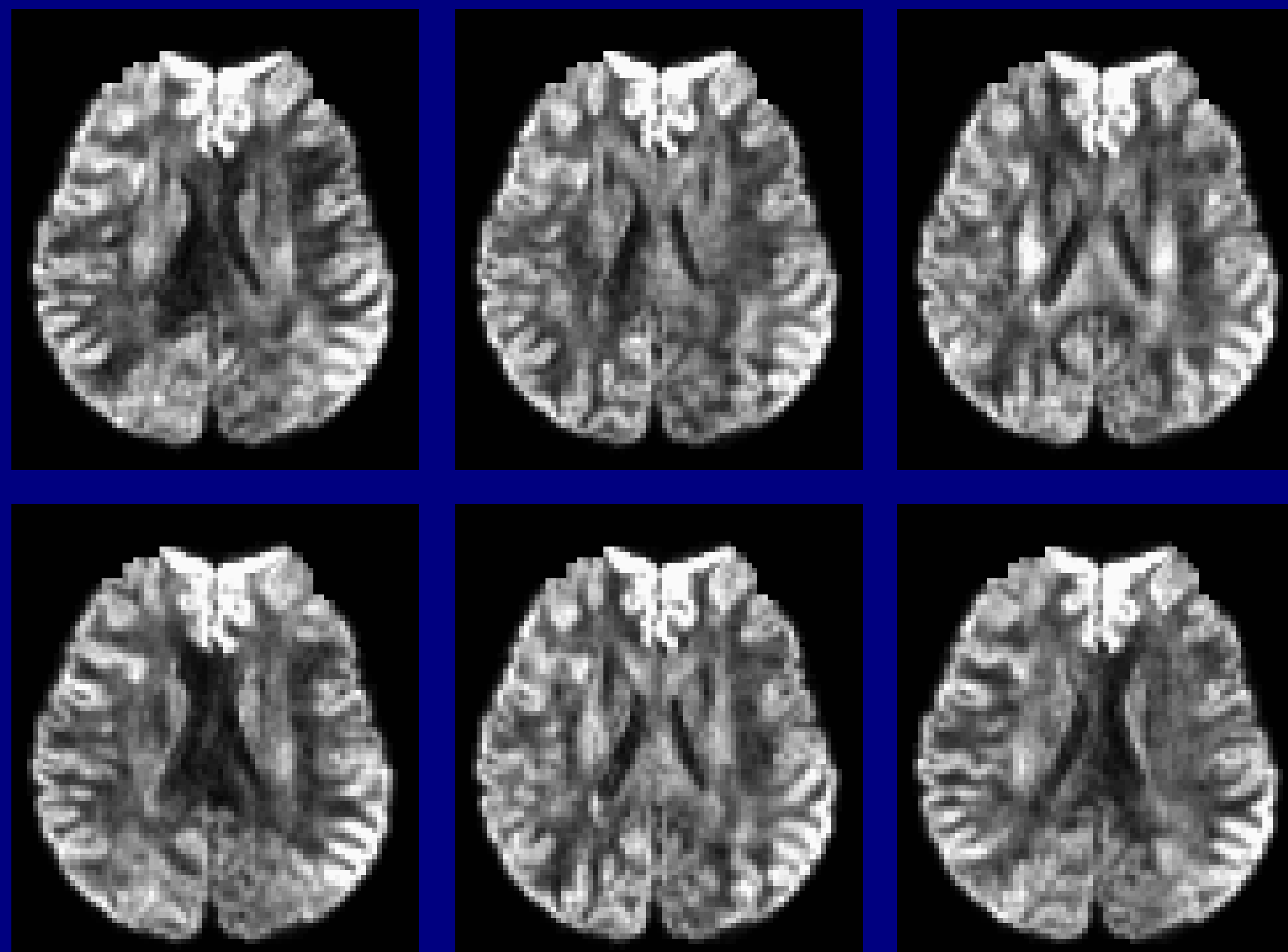
Individual points → Fit ellipsoid surface
Individual signals → Solve for **D**

Sidenote: what DWIs look like

Unweighted reference $b=0\ s/mm^2$

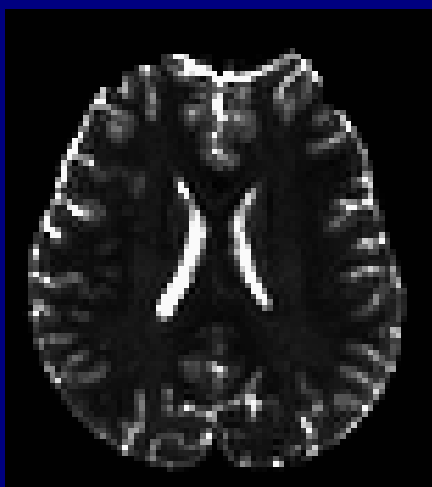


Diffusion weighted images (example: $b=1000\ s/mm^2$)

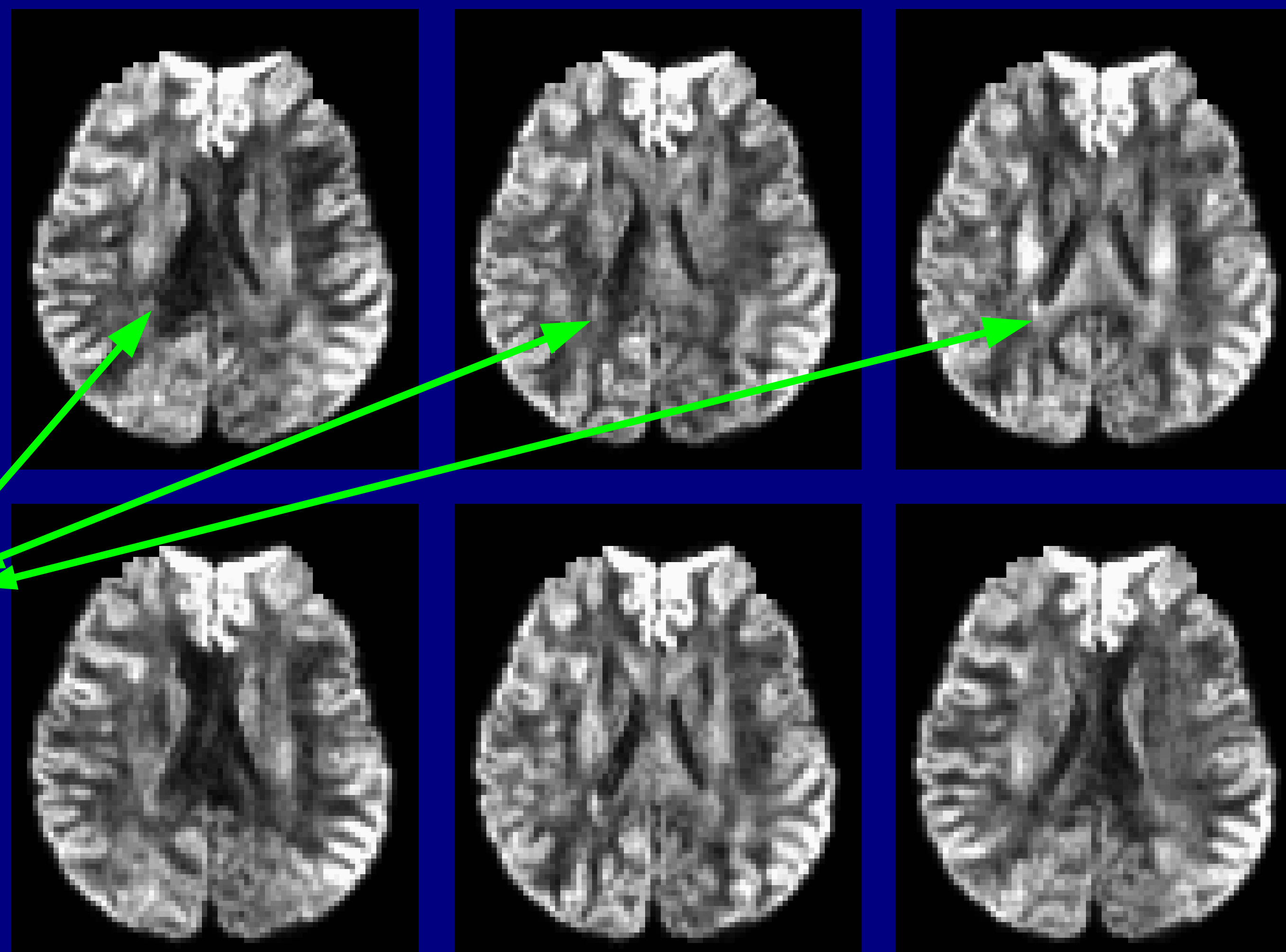


Sidenote: what DWIs look like

Unweighted reference
$b=0\ s/mm^2$



Diffusion weighted images
(example: $b=1000\ s/mm^2$)



(Each DWI has a different brightness pattern: viewing structures from different angles.)

Noise in DW signals

MRI signals have additive noise

$$S_i = S_0 \, e^{-b \, \mathbf{g}_i^T \mathbf{D} \, \mathbf{g}_i} + \varepsilon,$$

where ε is (Rician) noise.

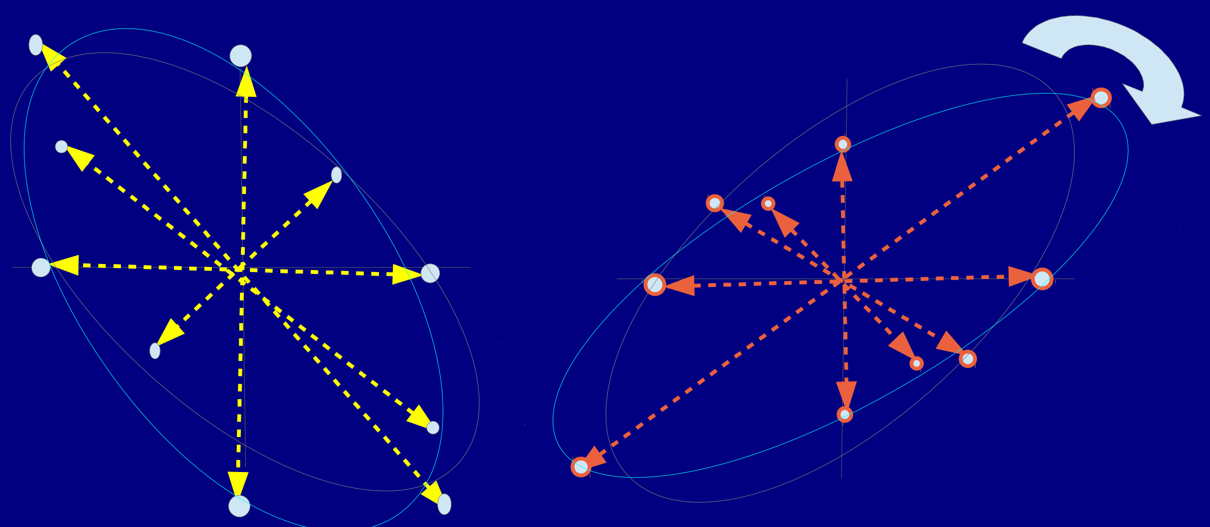
Noise in DW signals

MRI signals have additive noise

$$S_i = S_0\, e^{-b\, \mathbf{g}_i^T \mathbf{D}\, \mathbf{g}_i} + \varepsilon,$$

where ε is (Rician) noise.

→ Leads to errors in surface fit, equivalent to *rotations* and *rescalings* of ellipsoids:



'Un-noisy' vs perturbed/noisy fit

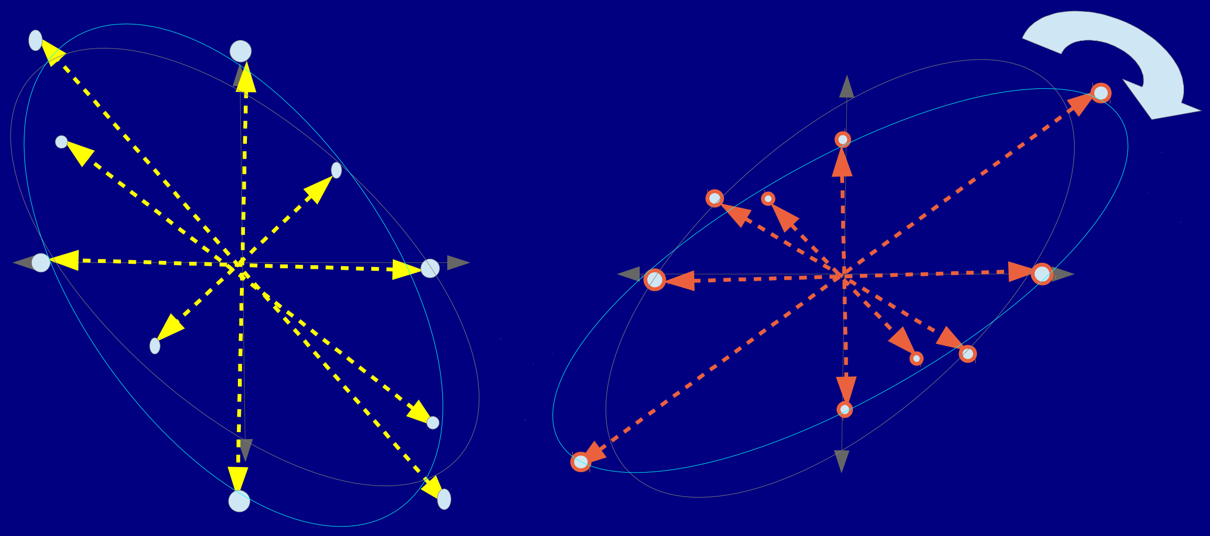
Noise in DW signals

MRI signals have additive noise

$$S_i = S_0\, e^{-b\, \mathbf{g}_i^T \mathbf{D}\, \mathbf{g}_i} + \varepsilon,$$

where ε is (Rician) noise.

→ Leads to errors in surface fit, equivalent to *rotations* and *rescalings* of ellipsoids:



'Un-noisy' vs perturbed/noisy fit

<u>Leads to standard:</u>

+ 30 DWs (~12 clinical)
+ repetitions of b=0
+ DW *b* chosen by:
  MD * *b* ≈ 0.84
+ nonlinear tensor fitting

Distortions in DWI volumes

There are also **serious** sources of distortion when acquiring DWIs:

+ Subject motion
  due to movement during/between volume acq. -> signal loss/overlap

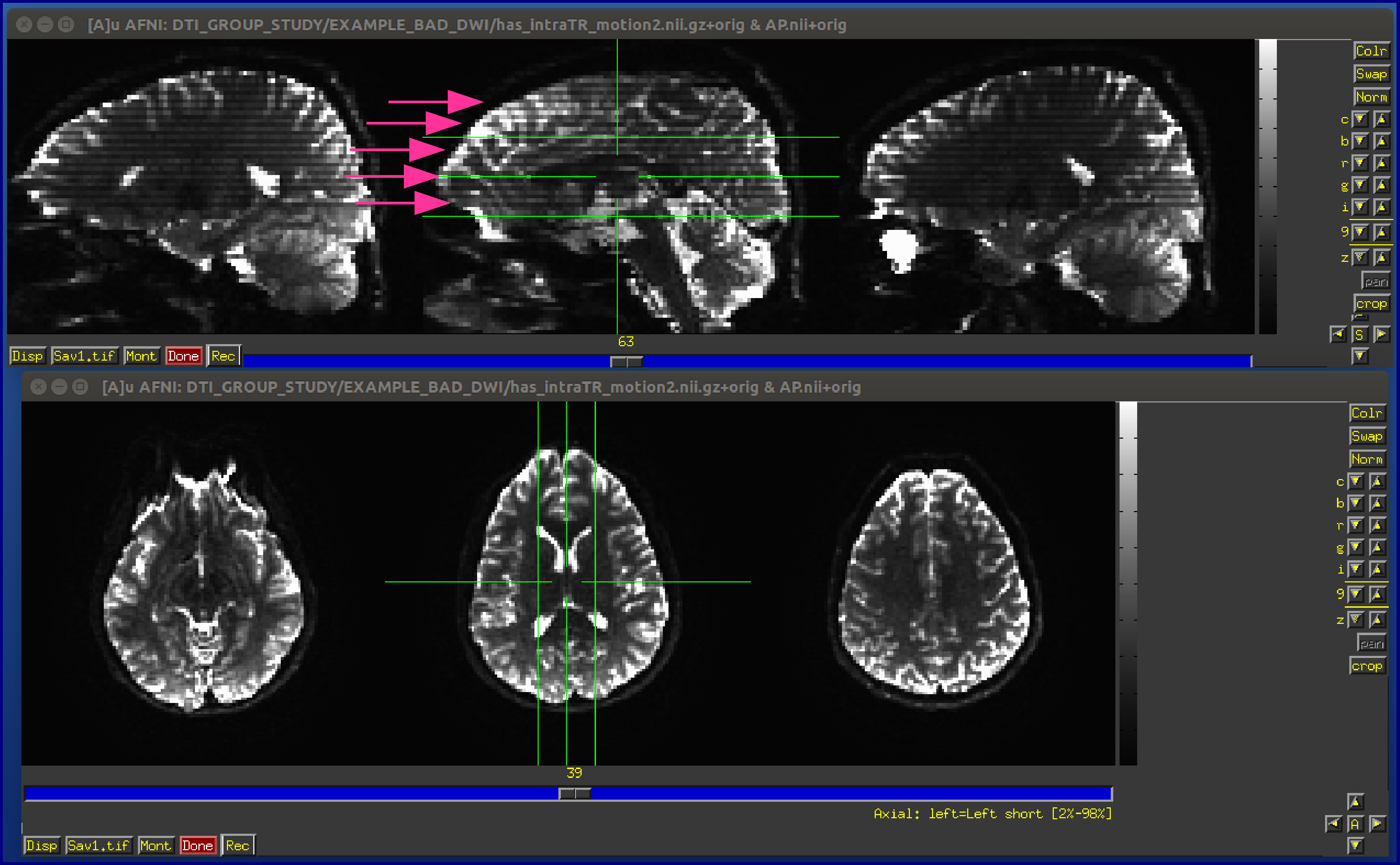
+ Eddy current distortion
  due to rapid switching of gradients -> nonlinear/geometric distortions

+ EPI distortion
  due to B0 inhomogeneity -> geometric distortions along phase encoding dir, signal pileup or attenuation

---> And effects combine! Need careful acquisition (sometimes perhaps even **re**acquisitions) and post-processing.

Distortions in DWI volumes

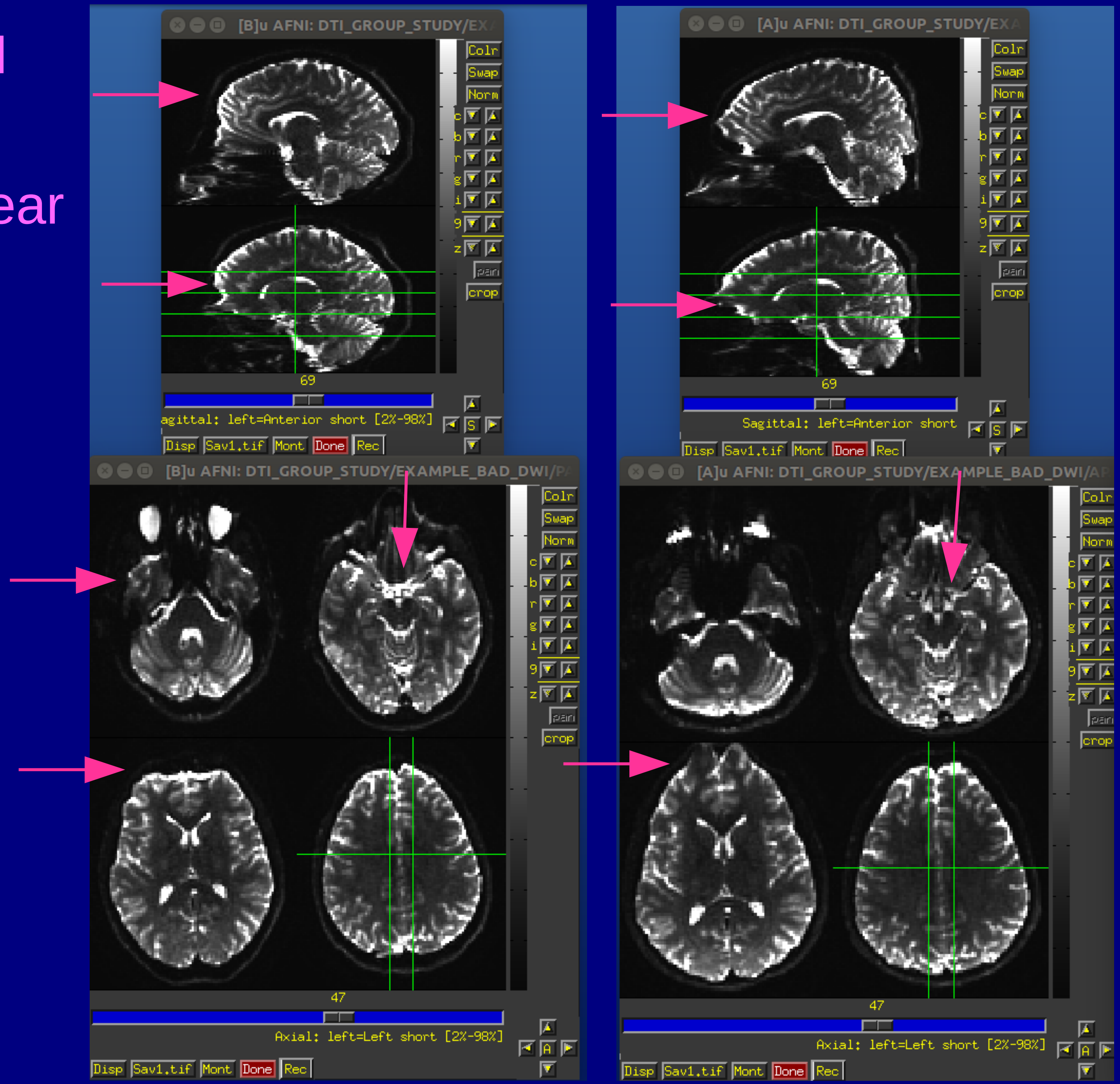
From subj motion: interleaved brightness distortions



Distortions in DWI volumes

From eddy and EPI distortions:

+ geometric/nonlinear warping
+ signal pileup and attenuation



SUMMARY

+ Diffusion-based MRI uses application of magnetic field gradients to probe the relative diffusivity of molecules along different directions.
+ DTI combines that information into a simple shape family, spheroids, to summarize the diffusivity.
+ From the DT, several useful properties are described in terms of scalar (e.g., FA, MD, L1) and vector (e.g., V1) parameters.
+ Many “standard” interpretations of DTI parameters exist (i.e., higher FA = “better” WM), but we must be cautious.
+ Distortions and noise affect all DTI estimates, and we must consider the consequences of these in all analyses.