Introduction to Diffusion-weighted Imaging

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Motivation

- Magnetic resonance imaging provides information about the spatial distribution of water.
- Diffusion-weighted MRI (DWI) provides information about the motion of water.
- DWIs are sensitive to cellular architecture and tissue integrity.
- DWI can provide quantitative measures that are directly comparable.
- Diffusion imaging can be used to identify specific white matter tracts
- Over 2000 publications combining fMRI and DWI
  - 200 since I gave this lecture last year

Outline

- What is diffusion?
- How do we measure diffusion in MRI?
- How do we extract directional information?
- What are the practical problems and limitations?
- Beyond the diffusion tensor

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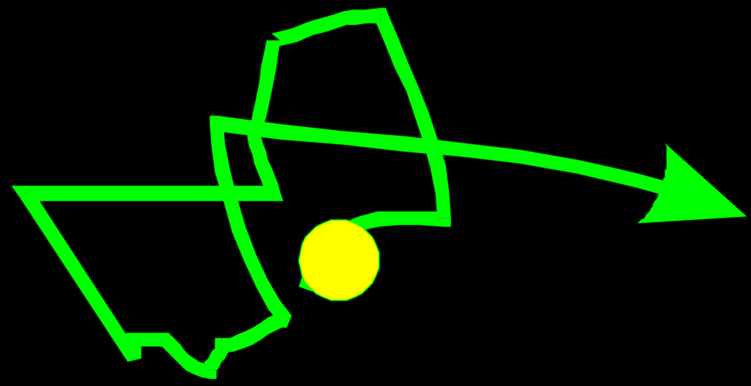
Diffusion

- Diffusion refers to the random translational (Brownian) motion of molecules that results from the thermal energy of theses molecules

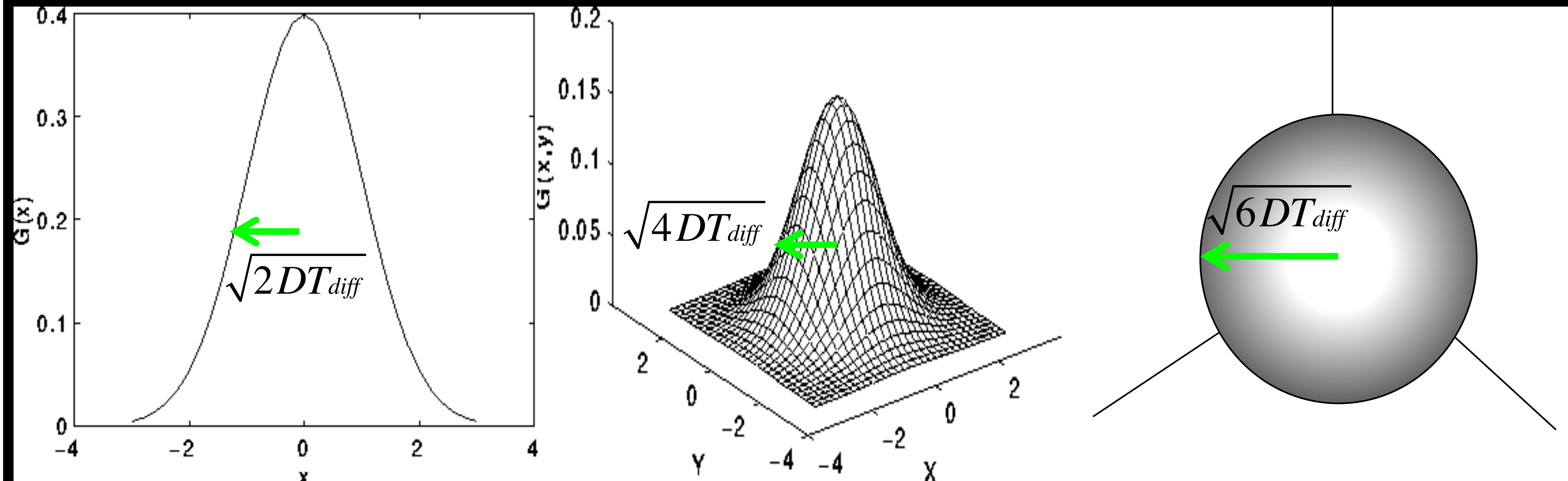


$$D = \frac{kT}{6\pi\eta R_H} \quad \text{(for sphere)}$$

Stokes-Einstein

Gaussian Distribution

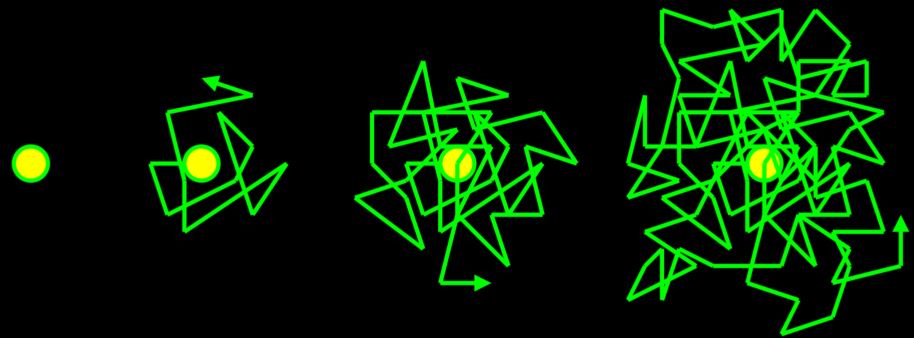
- A large number of particles that are free to diffuse have a squared displacement of a Gaussian form



1D 2D 3D

Einstein, A. Ann Physik (1905) 4: 549-590

Diffusion



$$\langle r^2 \rangle \approx 6DT_{dif}$$

<u>For H_2O at 37° C</u>

$D \approx 3.0 \times 10^{-3}\ mm^2/s$
$T_{dif} \approx 30\ ms$
$r \approx 25\ \mu m$

- If the motion of water is hindered by cell membranes, macromolecules, etc. the displacement will be less and D will appear lower.

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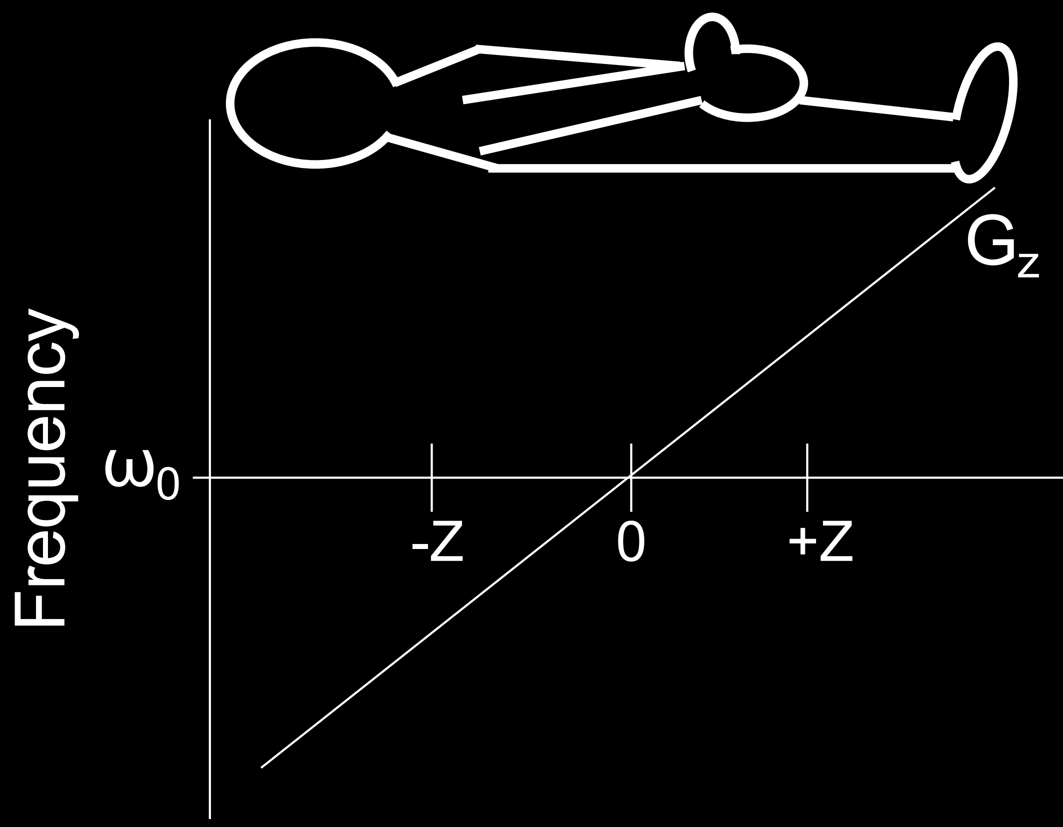
Image Intensity in MRI

- Physical property of tissue water
  - ρ proton density — Concentration of water
  - T1 relaxation time
  - T2 relaxation time
  - T2* relaxation time
  - (T1, T2, T2*) } Rotational motion, Magnetic field strength
  - D diffusion coefficient — Translational motion

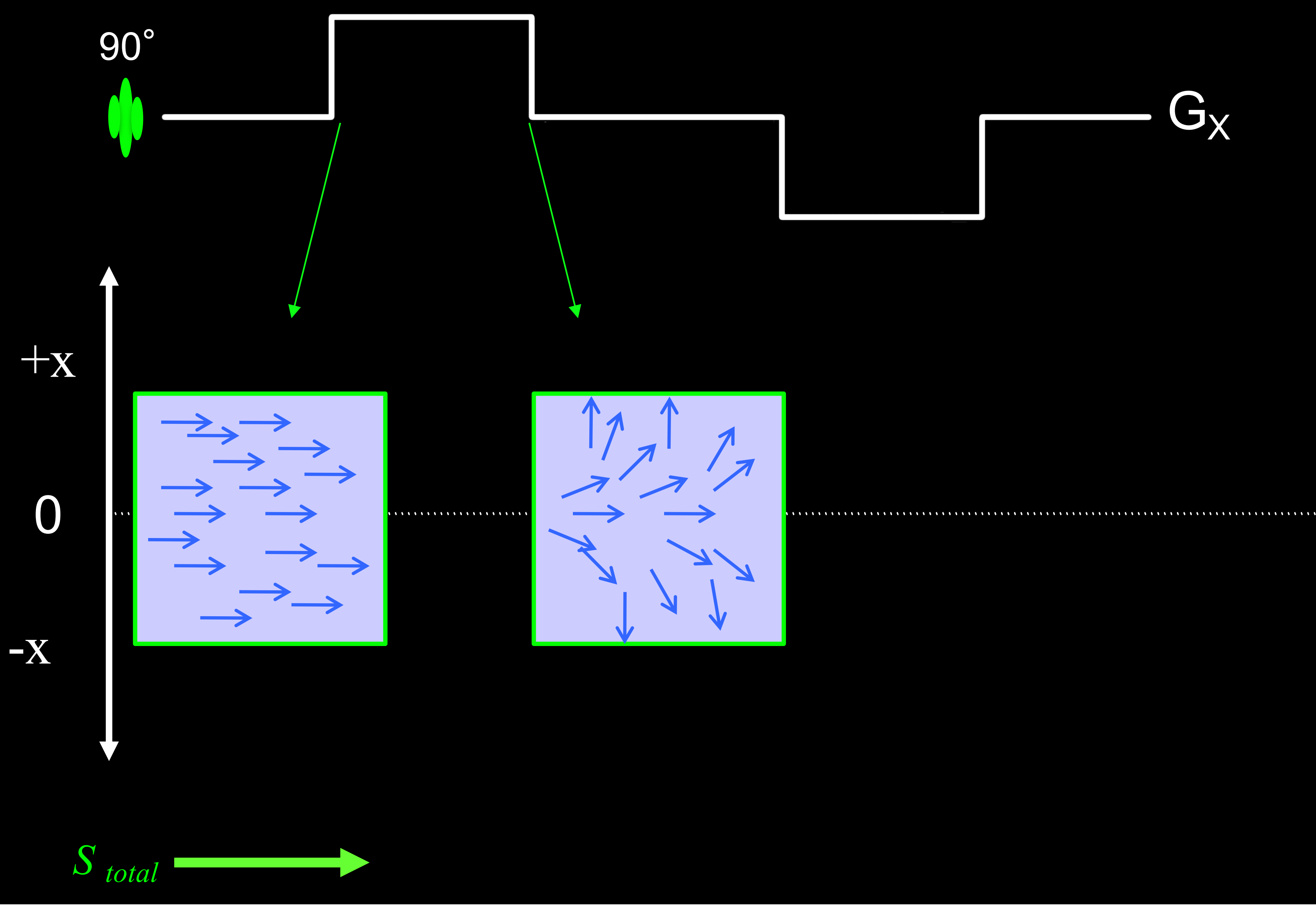
- Experimentally controlled parameters
  - Sequence — Spin-echo/gradient echo
  - TR — Time of Repetition
  - TE — Time to echo
  - b-value — diffusion-weighting factor

Gradients make the resonance frequency a function of spatial position



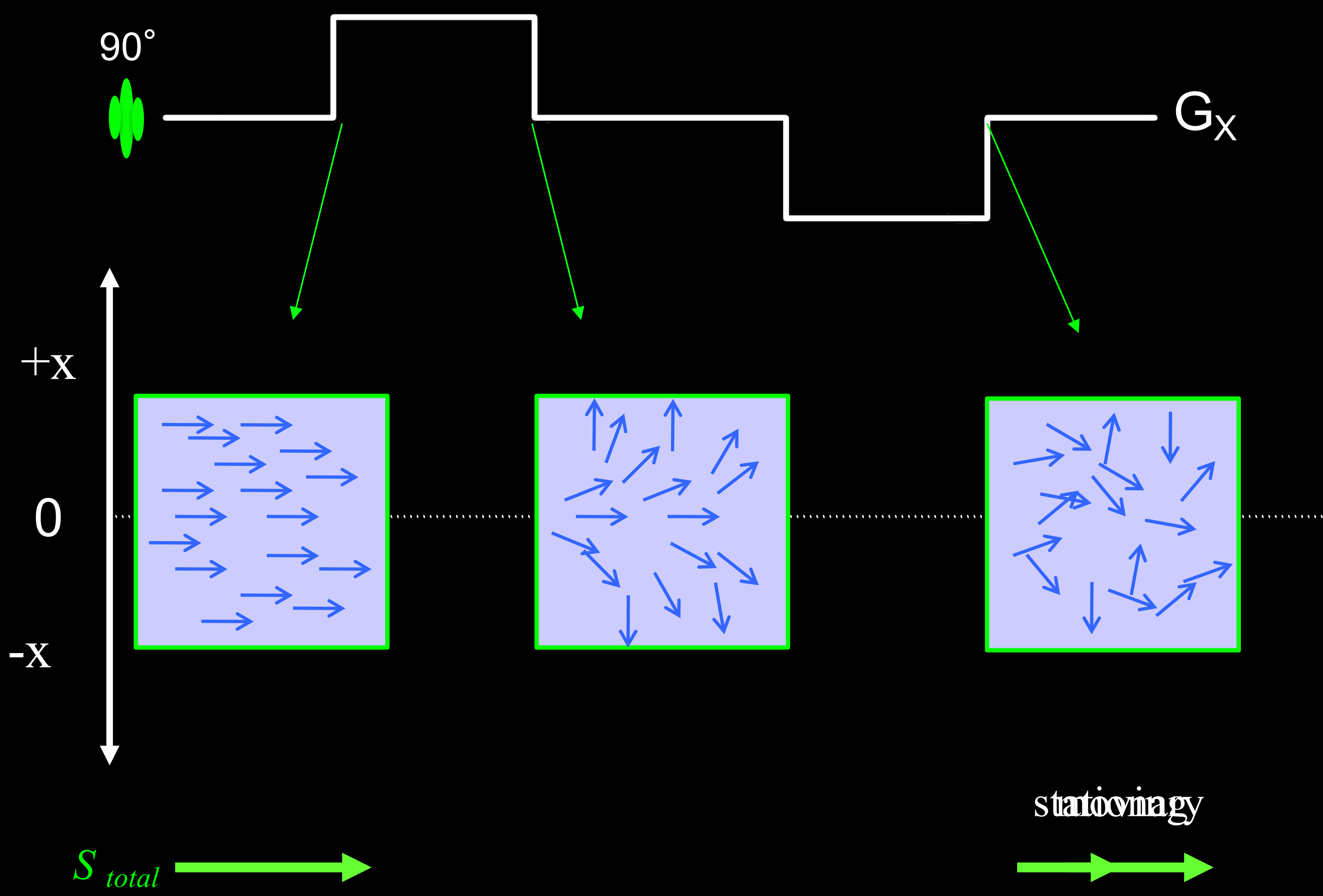
$$\omega = \gamma B = \gamma B_0 + \gamma z G_z$$

Basic Diffusion-weighting

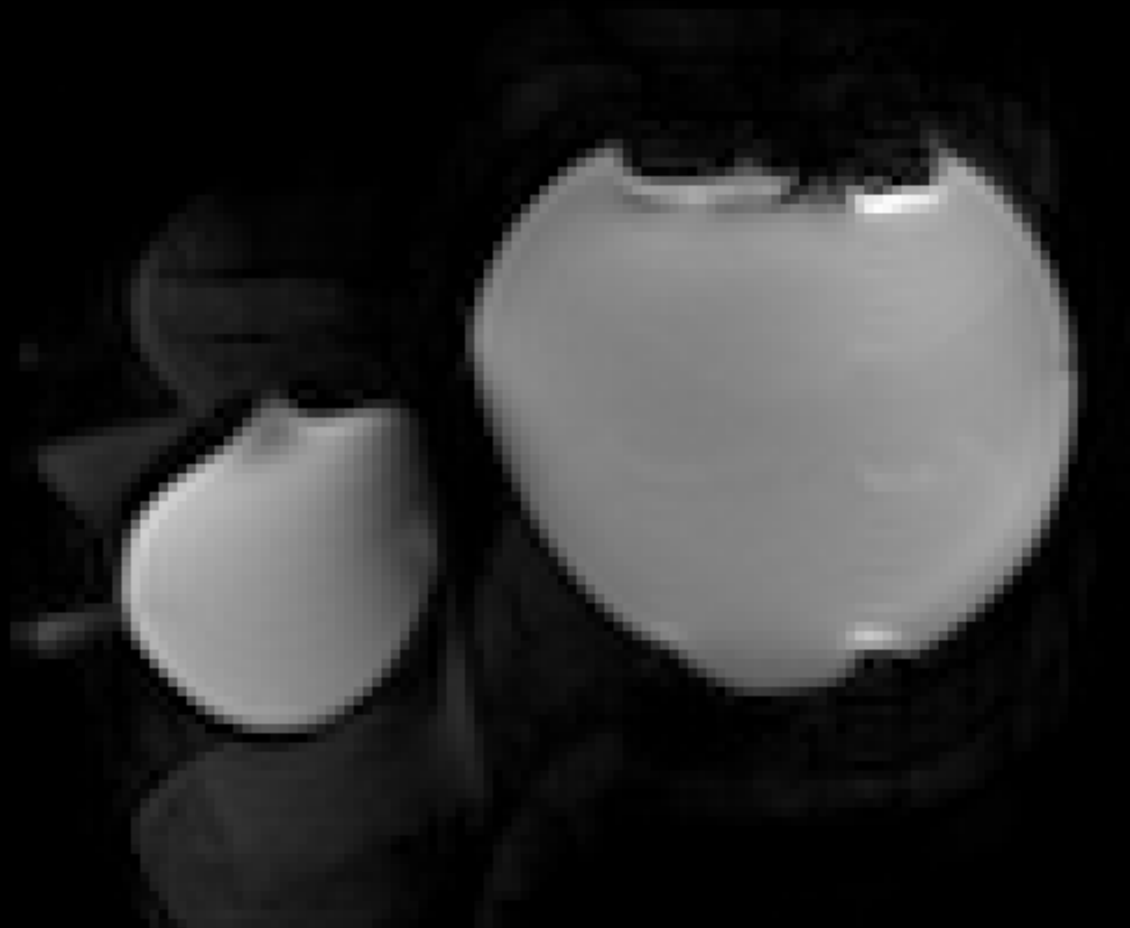


Phase Twist

Basic Diffusion-weighting

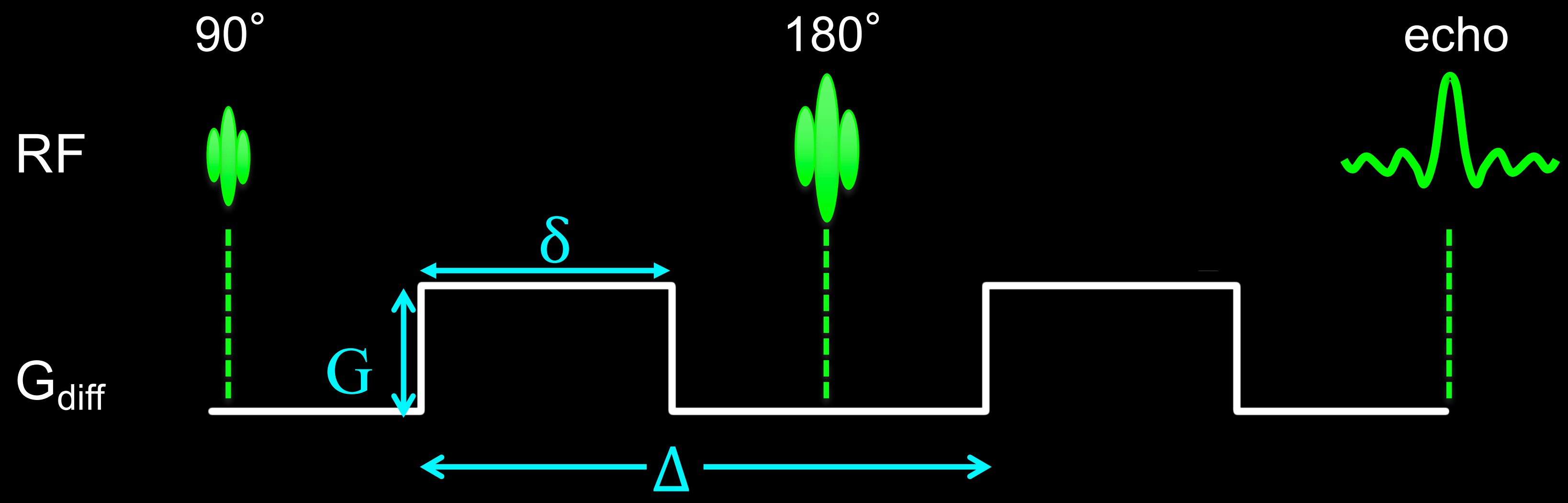


Guess the intensity



No Diffusion-weighting
Diffusion-weighted

Spin-echo Diffusion Preparation



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

Stejskal, EO and Tanner, JE. J Chem Phys (1965) 42 : 288-292

DWI

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

Non-diffusion-weighted signal intensity

B-value
sec/mm^2

Diffusion Coefficient
mm^2/sec

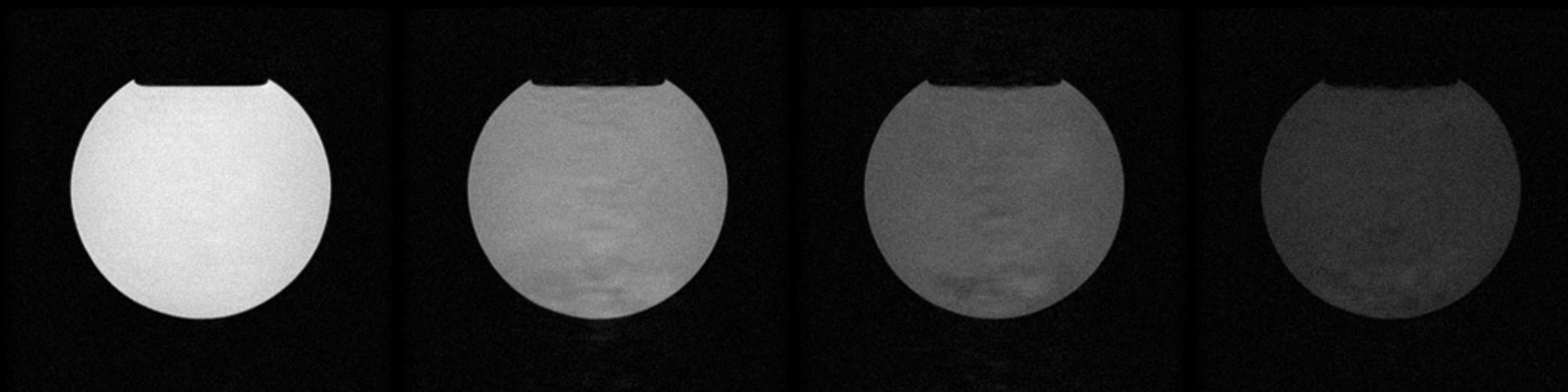
Typical DWI

- Single-shot “spin-echo” Echo Planar Imaging

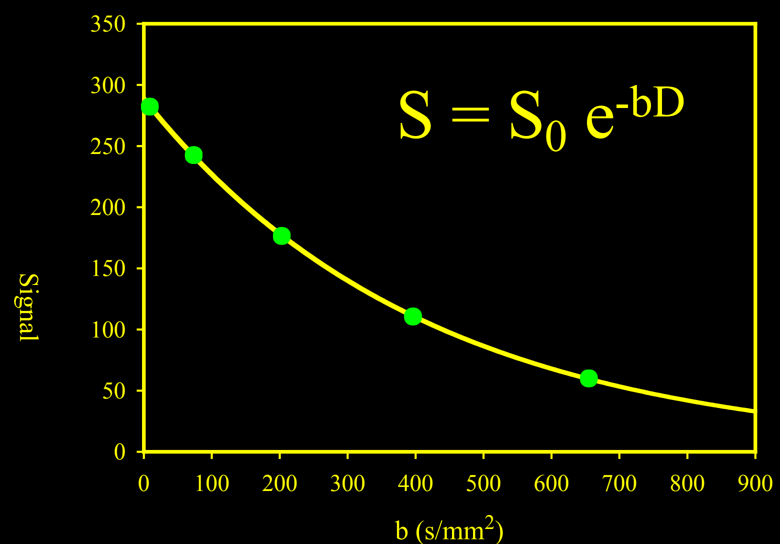
Parameter	Value	Comment
TE	50-100ms	Limited by b-value
TR	>5s	Fully relaxed
Matrix	96 x 96	2.5 x 2.5 mm
Slice Thickness	2.5 mm	Equal dimensions
B-value	~1000 s/mm^2	For brain*

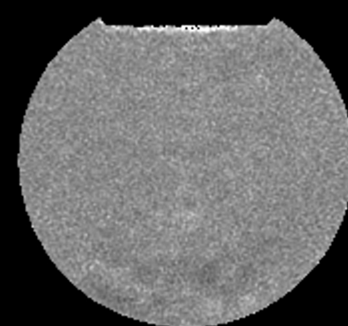
*Jones D., *et al*. Mag Res Med (1999) 42 : 515

Calculate Diffusion Parameters

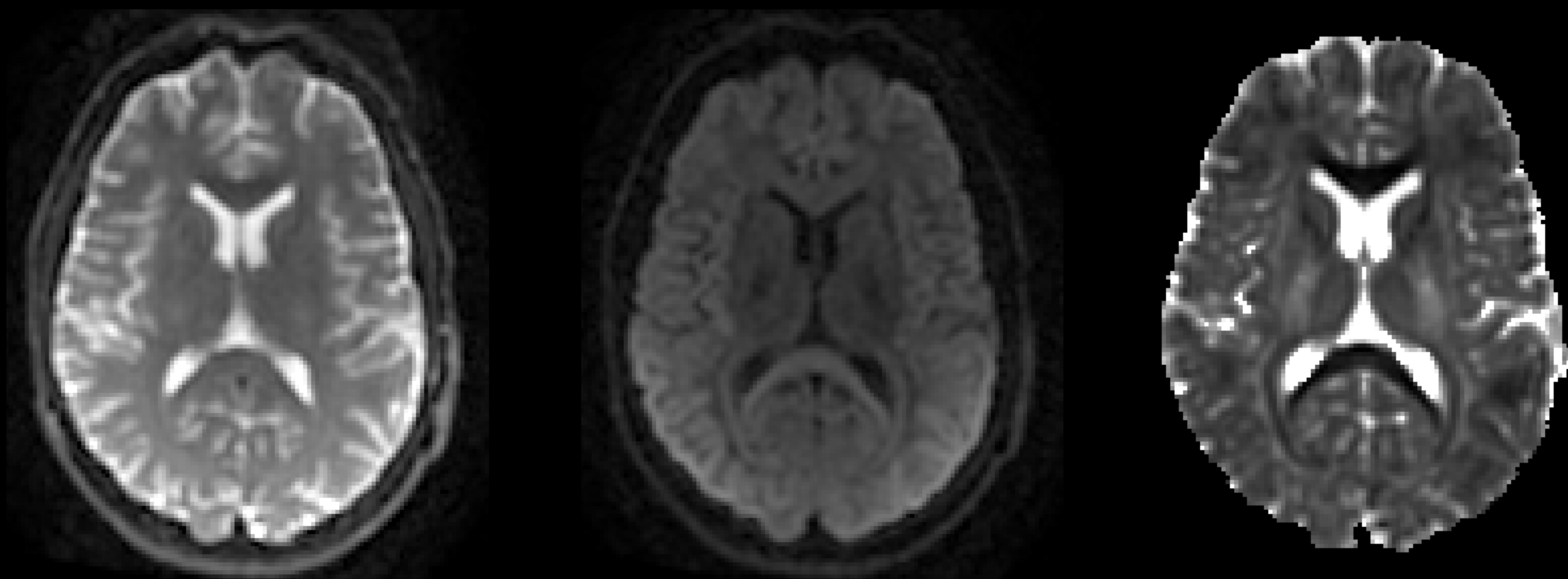


b (s/mm^2) 8 200 400 650





Diffusion map



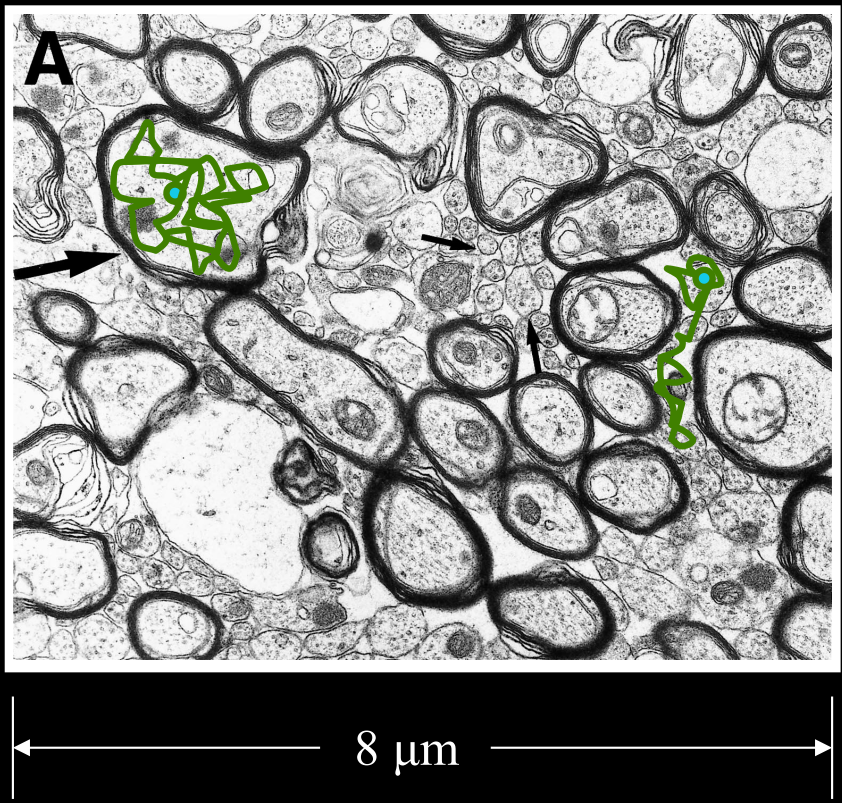
$b = 0\ s/mm^2$	$b = 1100\ s/mm^2$	Dz
I_0	Gz	$D_z = \frac{1}{-b}\ln\left(\frac{I_z}{I_0}\right)$
	$I_z = I_0 e^{-bD_z}$

Water Diffusion in Tissue

EM of mouse corpus callosum

Not Free

Cell membranes
Myelin
Organelles
Extracellular matrix

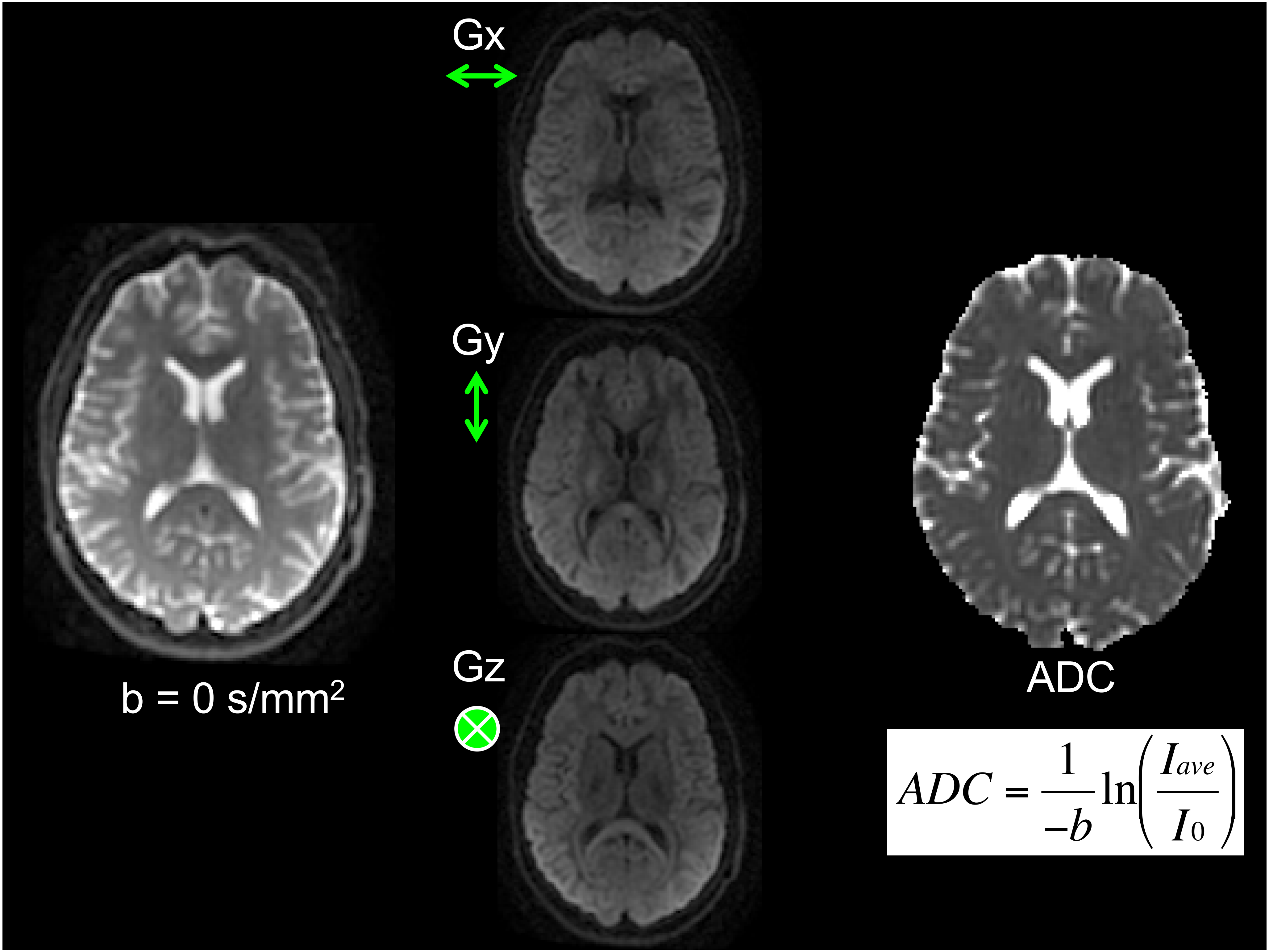


Anisotropy

D perpendicular

D parallel

$D_{perp} << D_{par}$

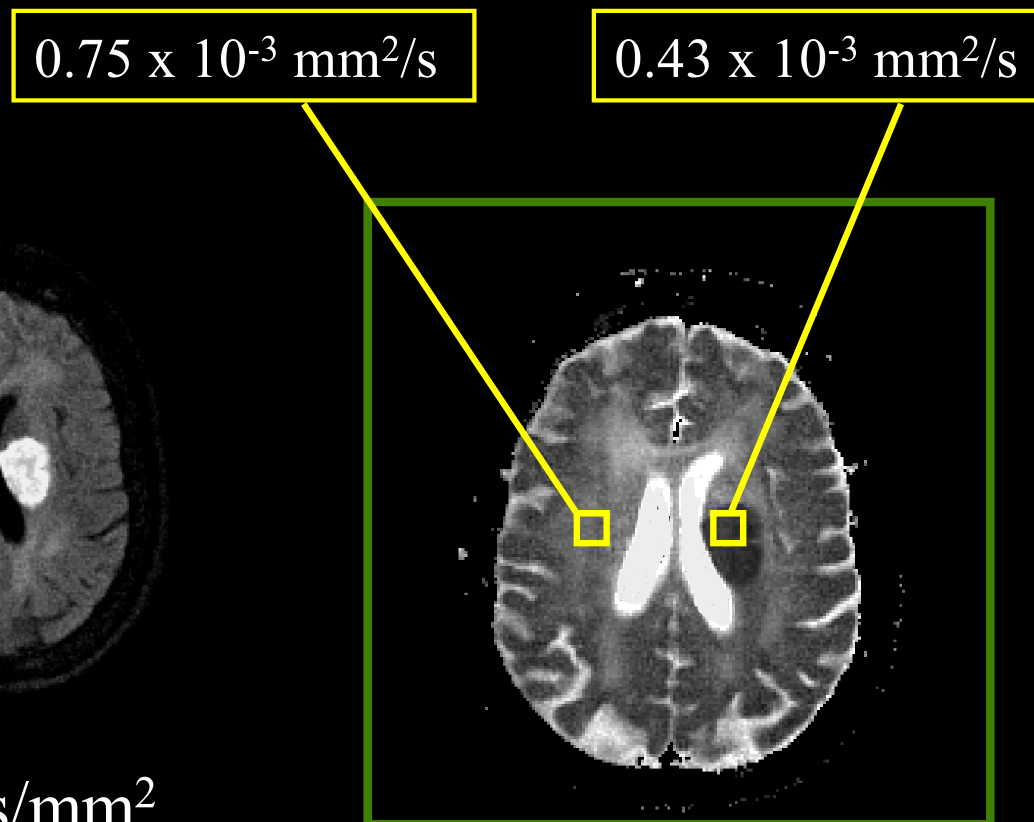


Gx
Gy
Gz
b = 0 s/mm²
ADC
$$ADC = \frac{1}{-b}\ln\left(\frac{I_{ave}}{I_0}\right)$$

Acute Stroke

b = 0 s/mm^2

720 s/mm^2



Diffusion Map

Warach S., *et al*. Ann Neurol (1995) 37:231-241

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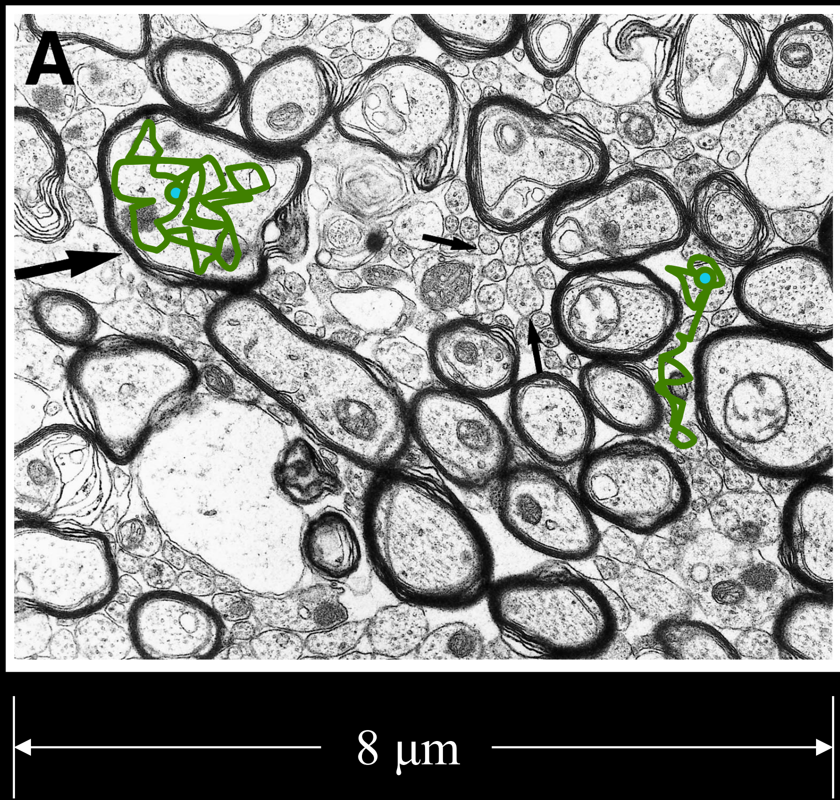


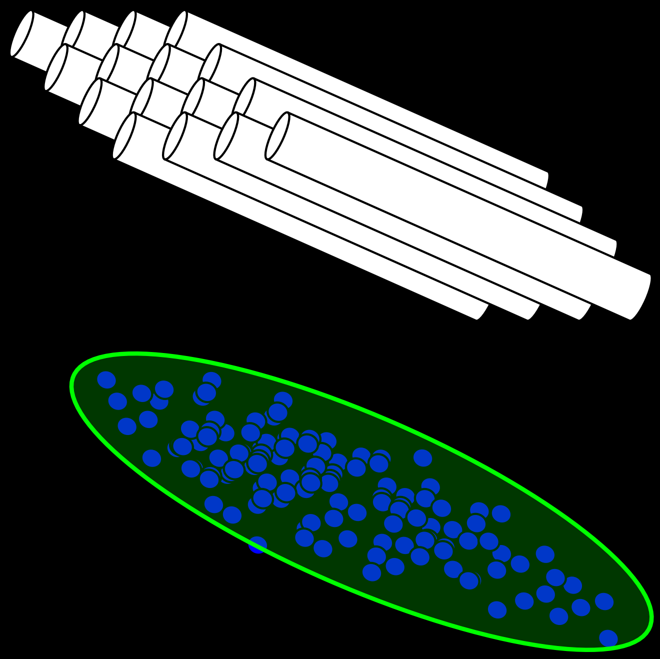
Anisotropy

$D_{perpendicular}$

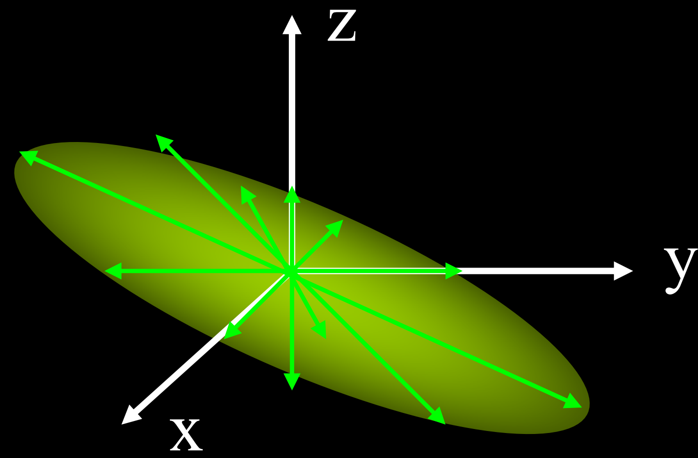
$D_{parallel}$

$D_{perp} << D_{par}$

Anisotropic Diffusion



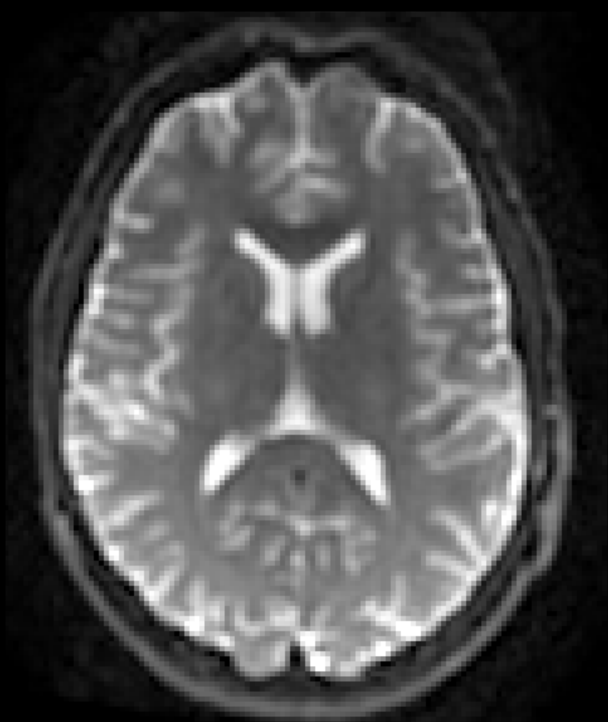
The Diffusion Tensor



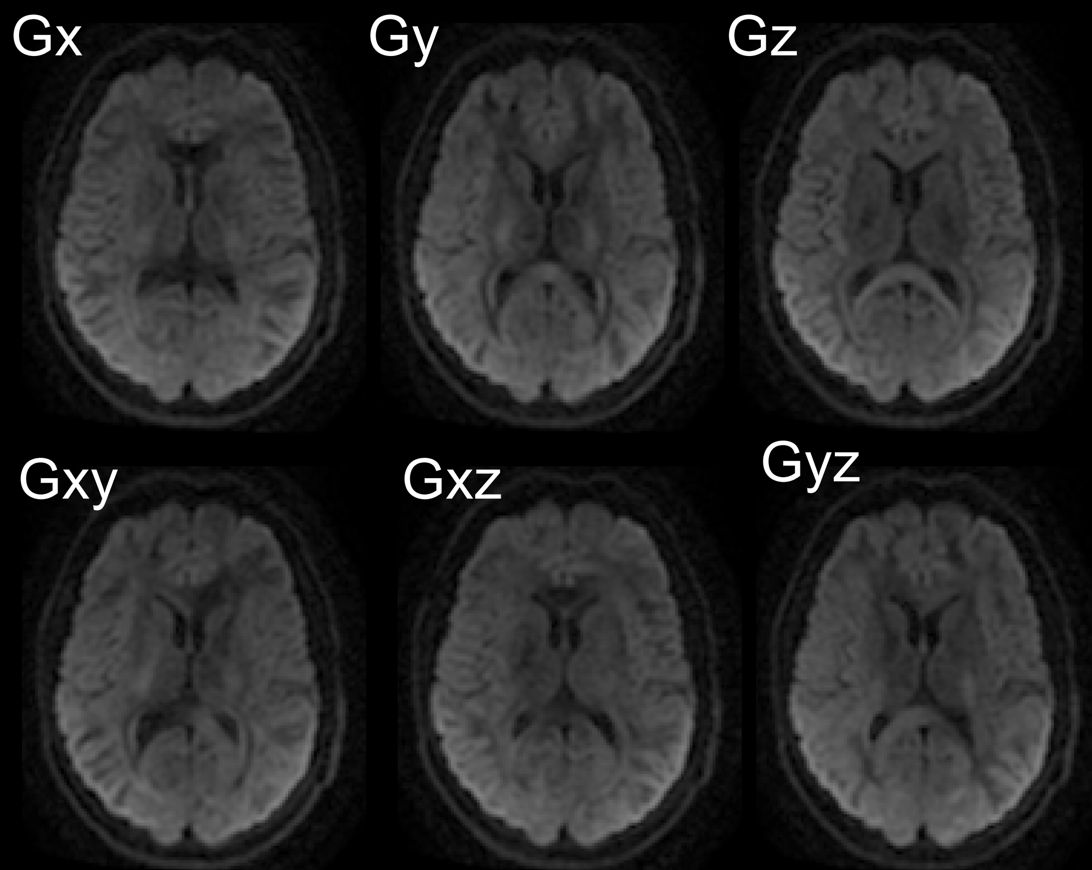
$$\underline{D} = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix}$$

Basser, P, *et. al*. J Magn Reson B (1994) 3 : 247-254

DTI

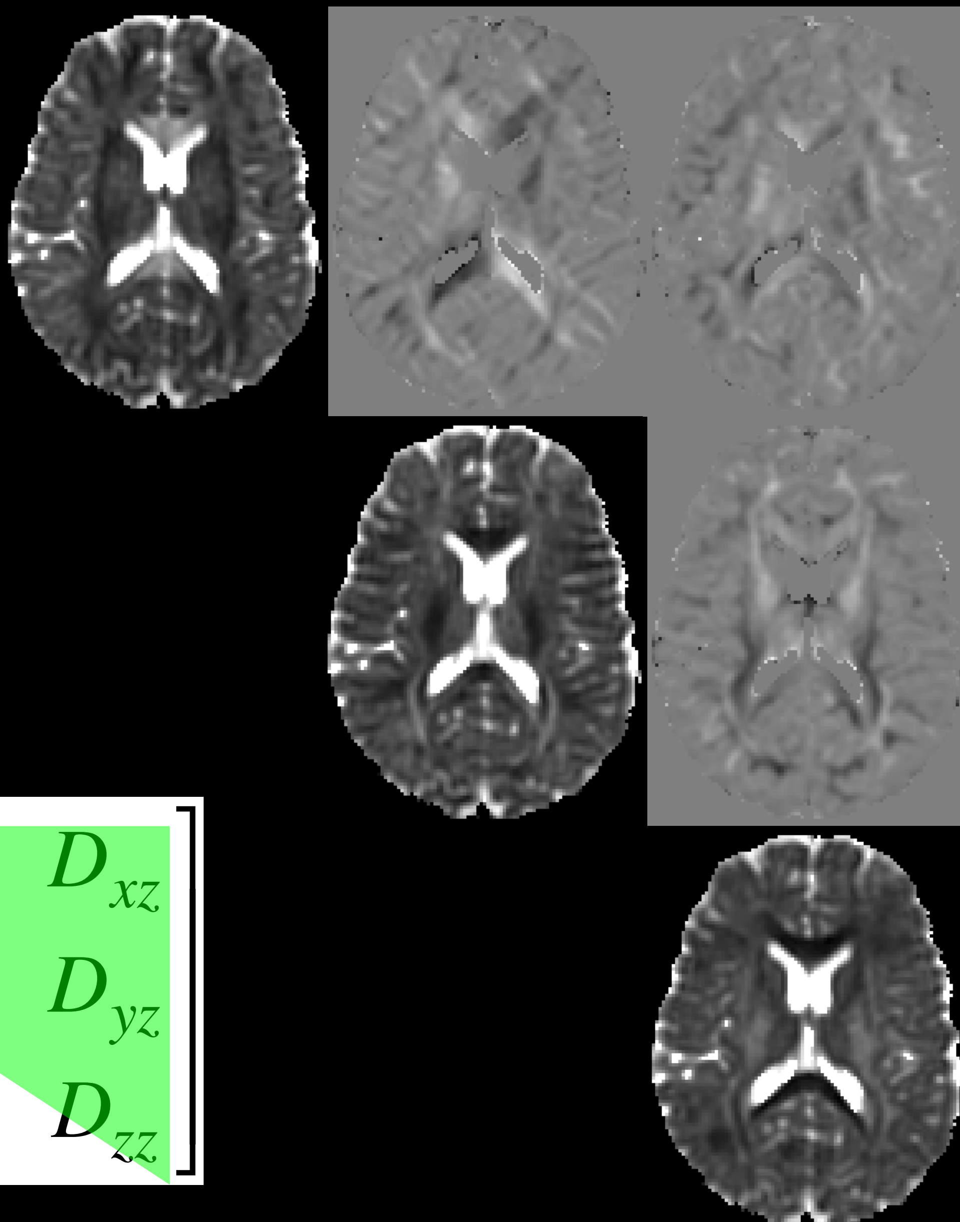


$b = 0\ s/mm^2$



$b = 1100\ s/mm^2$

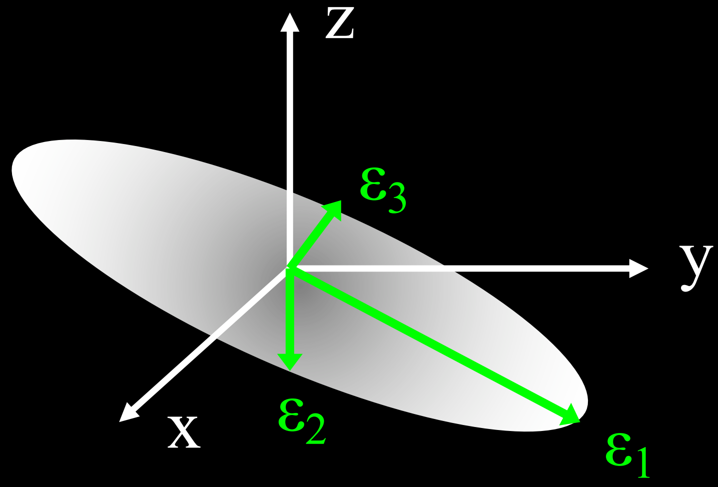
Calculate Diffusion Tensor



$$\underline{D} = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix}$$

Diagonalize DT

$$\underline{D} = \begin{bmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{bmatrix}$$

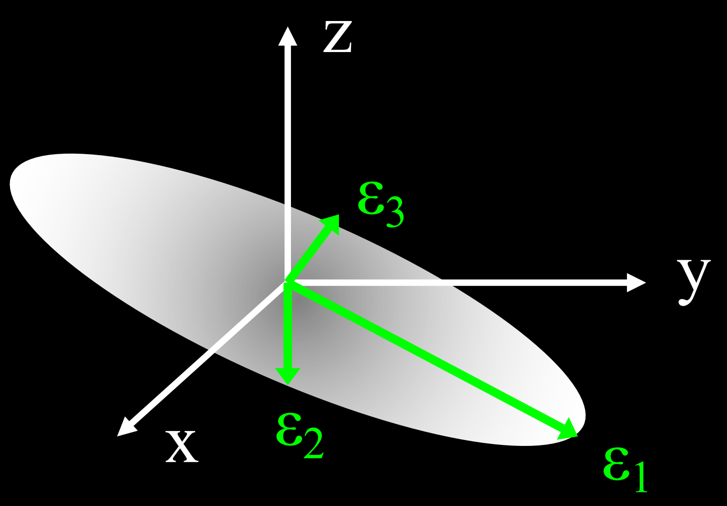


Eigenvalues

Eigenvectors

Quantitative Parameters

$$\underline{D} = \begin{bmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{bmatrix}$$



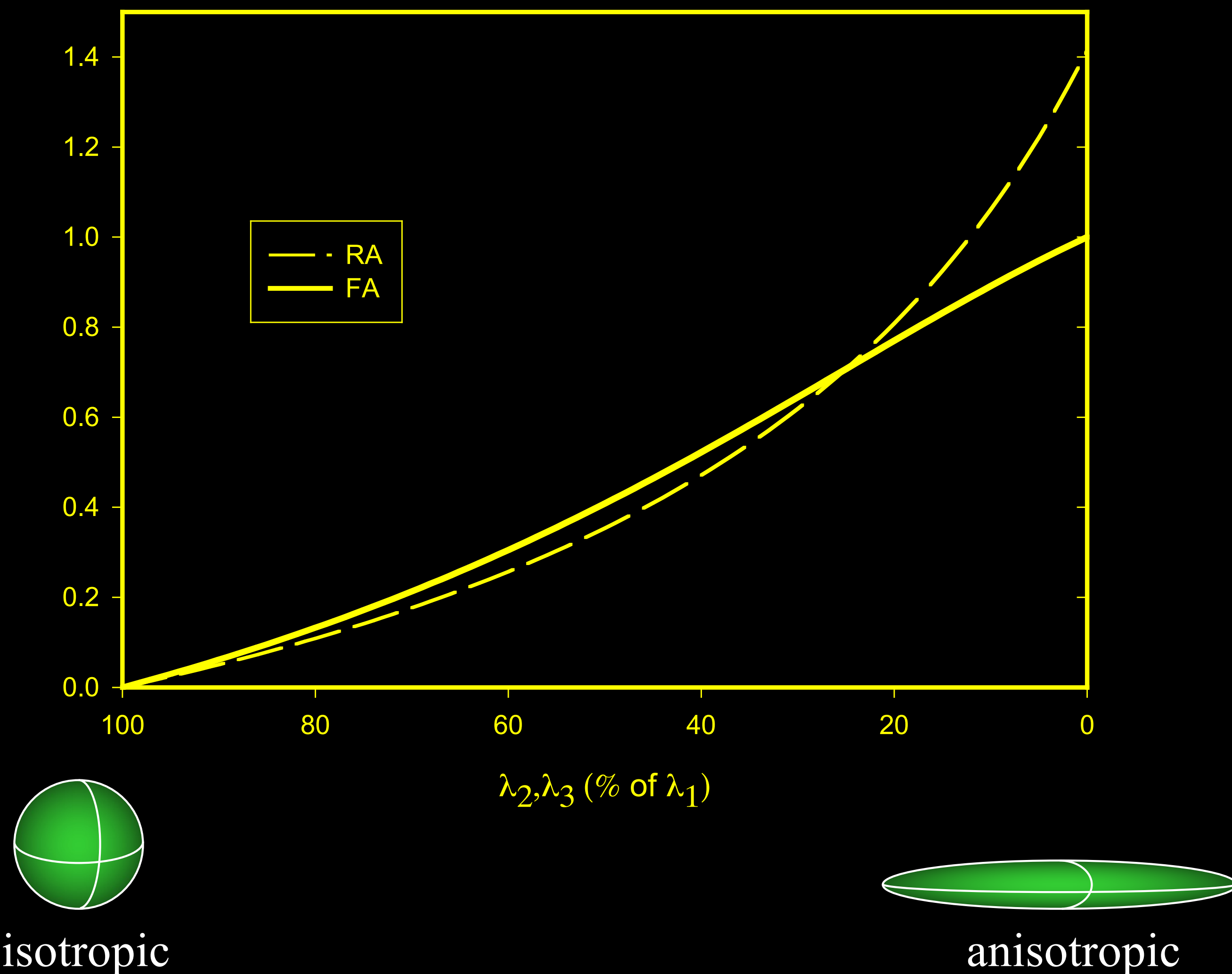
Average Diffusivity

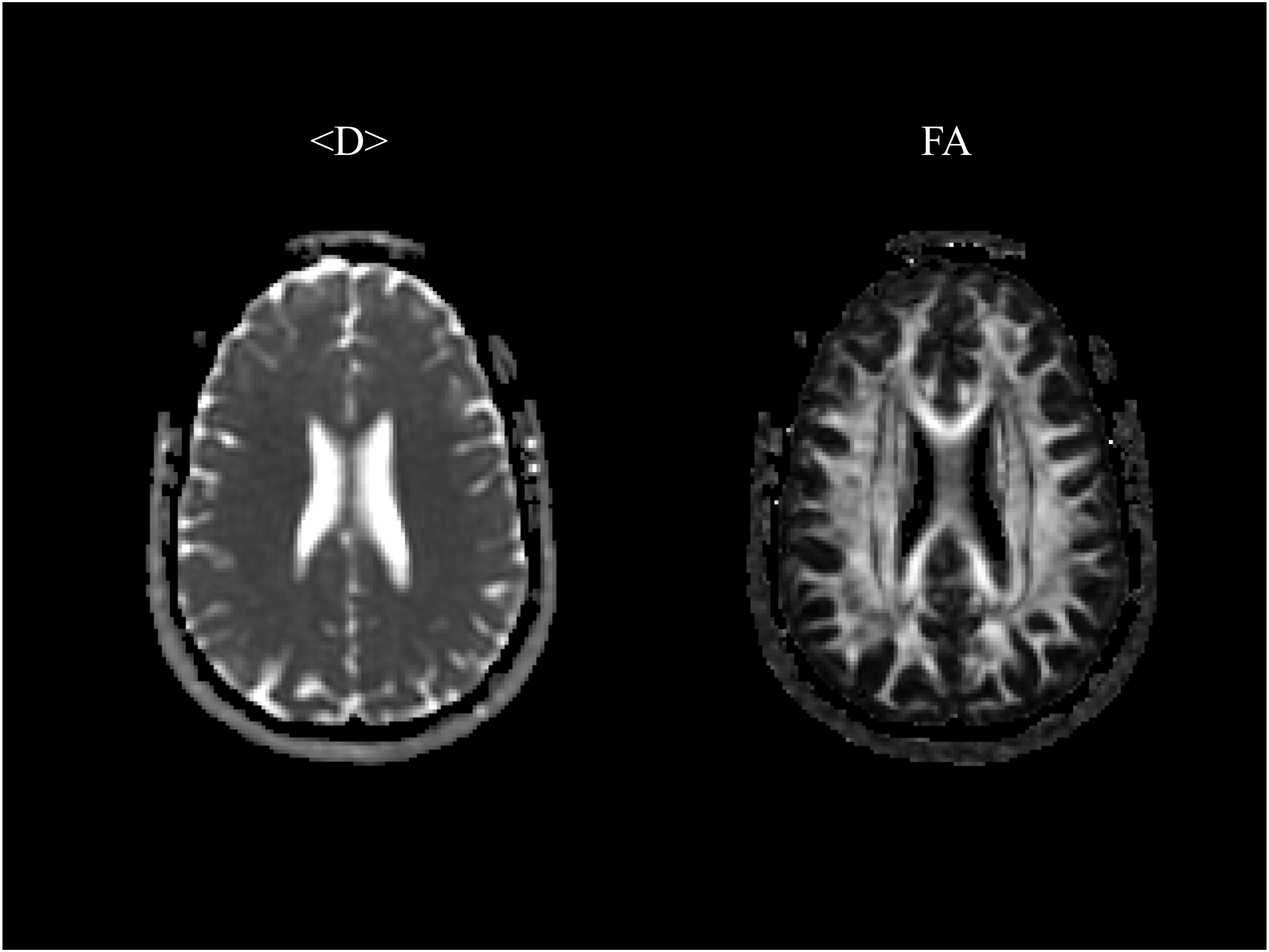
$$\langle D \rangle = \frac{\lambda_1 + \lambda_2 + \lambda_3}{3}$$

Fractional Anisotropy

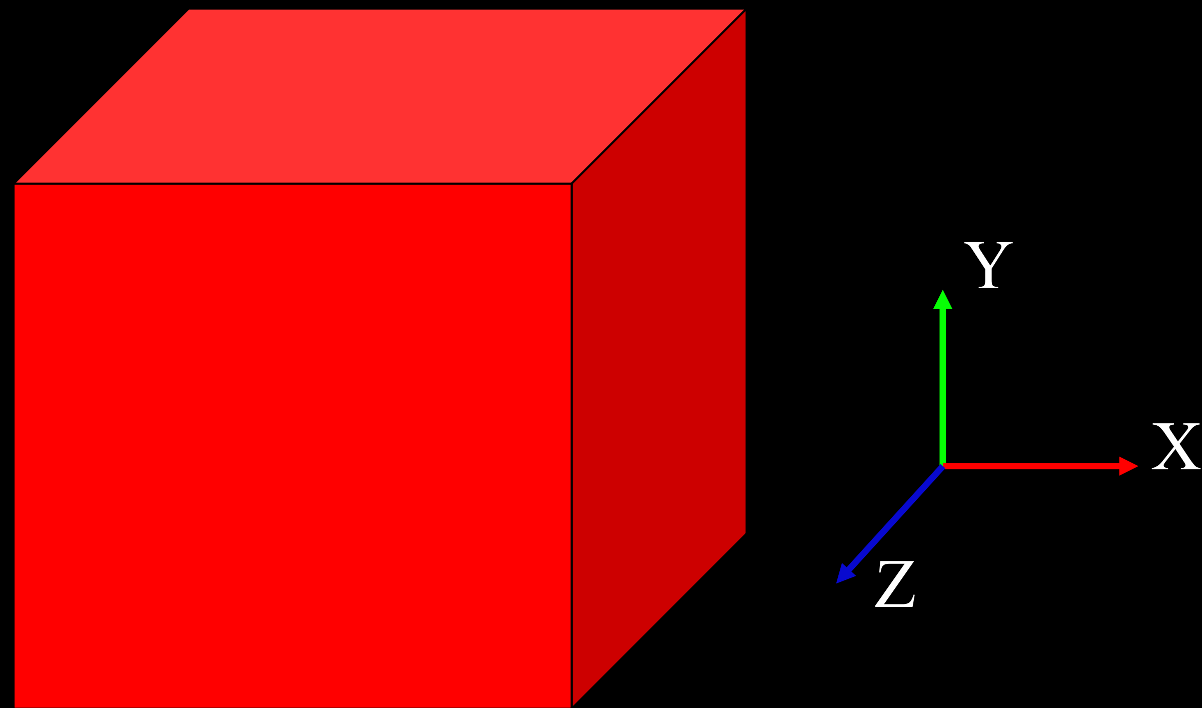
$$FA = \frac{\sqrt{3\left(\lambda_1 - \langle\lambda\rangle\right)^2 + \left(\lambda_2 - \langle\lambda\rangle\right)^2 + \left(\lambda_3 - \langle\lambda\rangle\right)^2}}{\sqrt{2\left(\lambda_1^2 + \lambda_2^2 + \lambda_3^2\right)}}$$

$$0 \leq \mathbf{FA} \leq 1$$


RA
FA
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
100
80
60
40
20
0
λ2,λ3 (% of λ1)
isotropic
anisotropic


<D>
FA

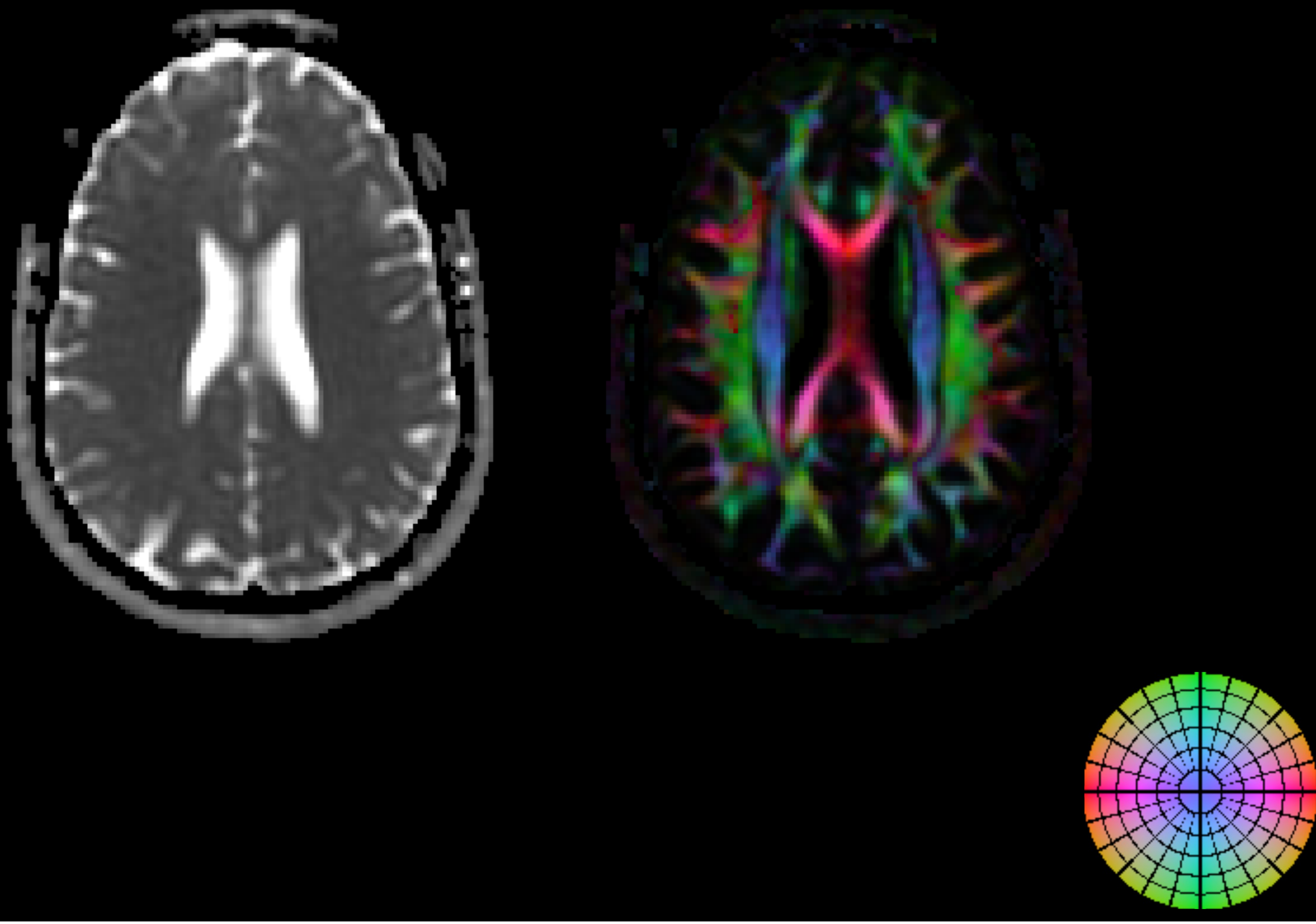
Directional Encoding for DTI

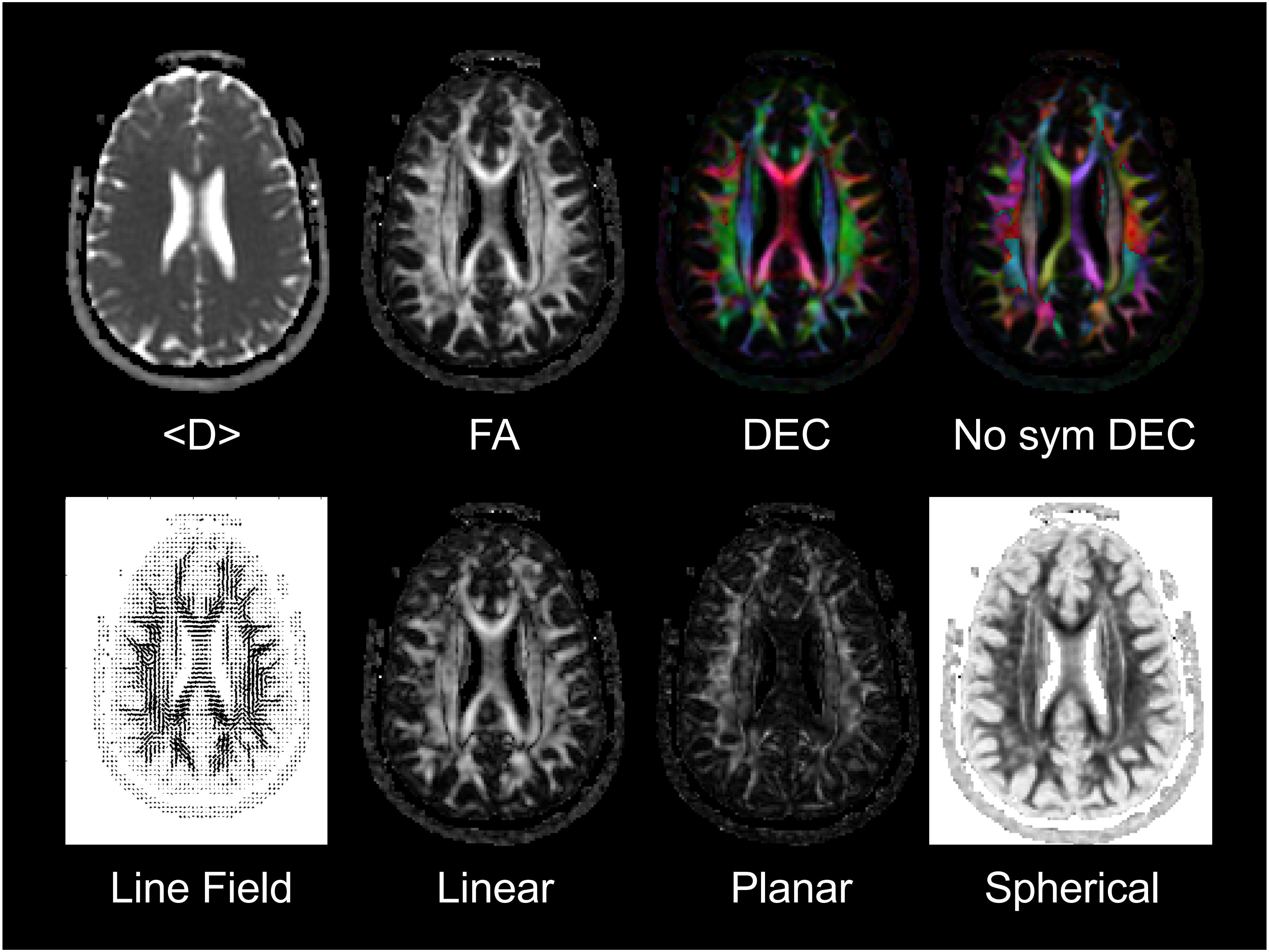


$$\underline{D} = \begin{bmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{bmatrix}$$

Pajevic S. and Pierpaoli C., Magn Reson Med (1999) 43 : 526-540

<D> Directional Encoded Color Map

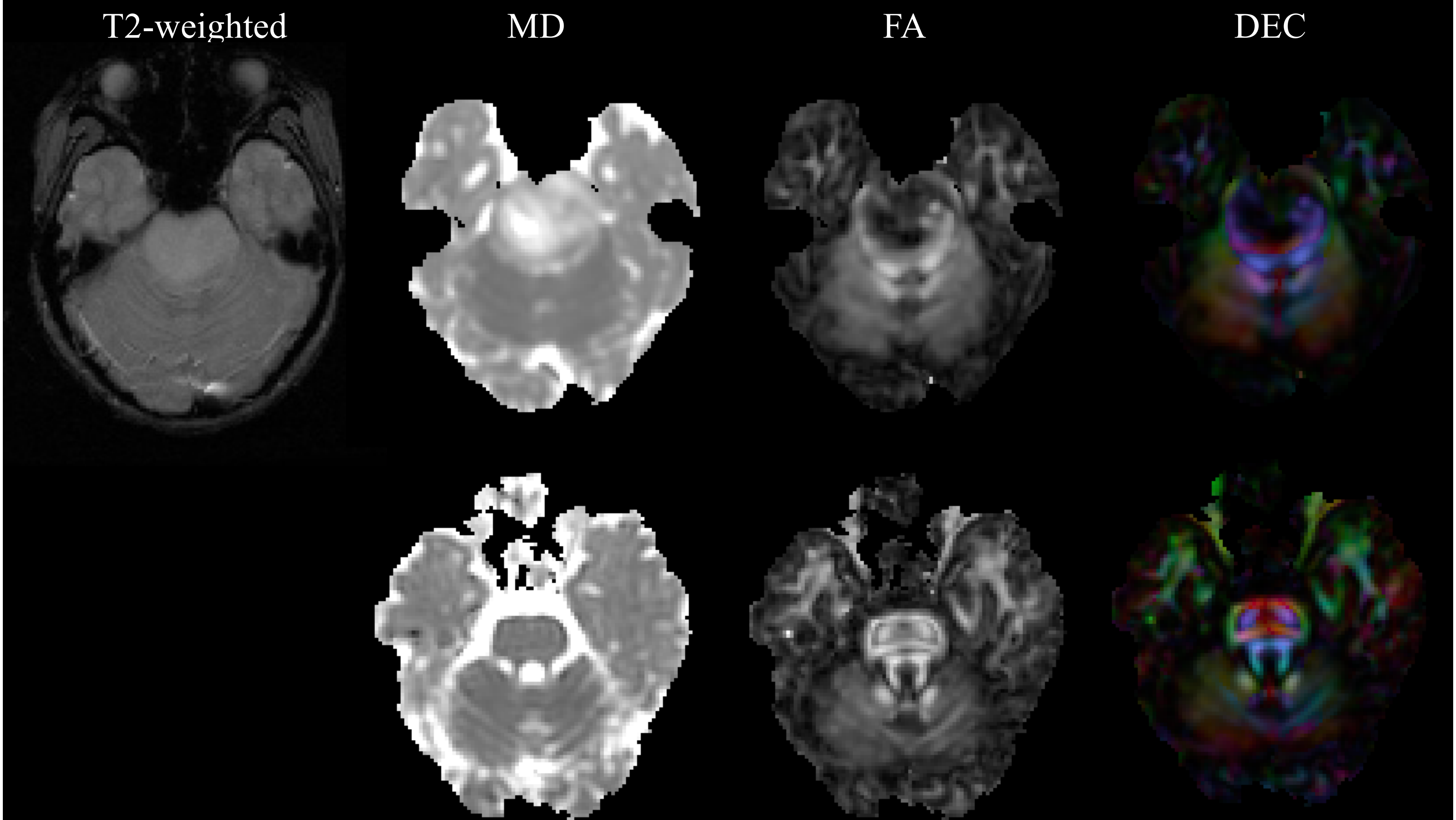



<D>
FA
DEC
No sym DEC
Line Field
Linear
Planar
Spherical

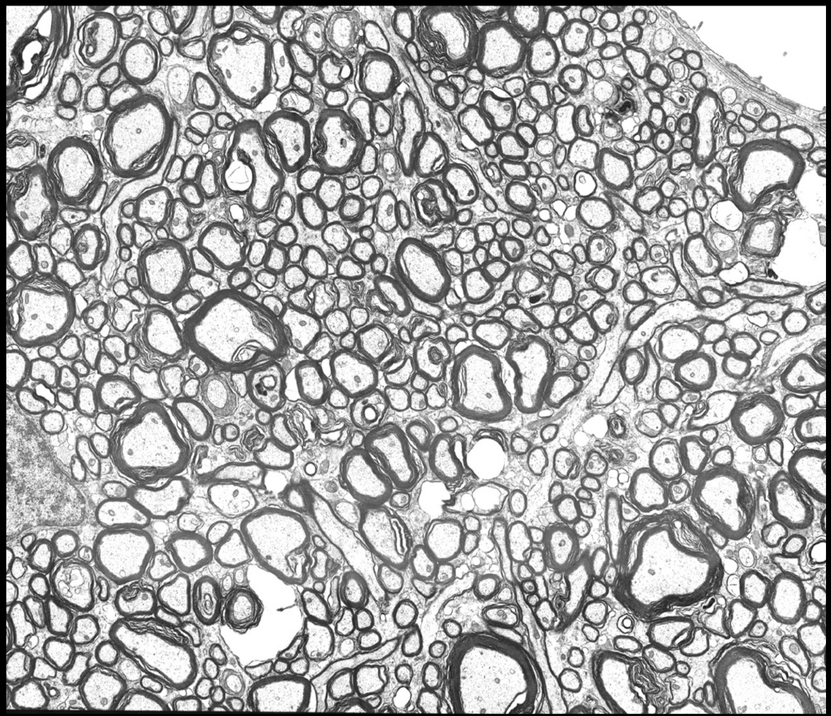
Applications of DTI

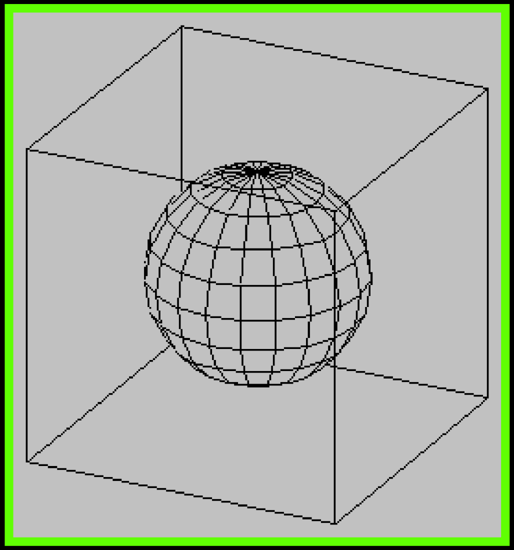
- Cerebral Ischemia (Stroke)
- Brain Cancer and Effects of Radiotherapy
- Multiple Sclerosis
- Epilepsy
- Metabolic Disorders
- Normal Brain Maturation and Aging
- Traumatic Brain Injury
- Alzheimer's Disease
- Amyotrophic Lateral Sclerosis
- Niemann-Pick type C Disease
- Dementias
- Connectivity

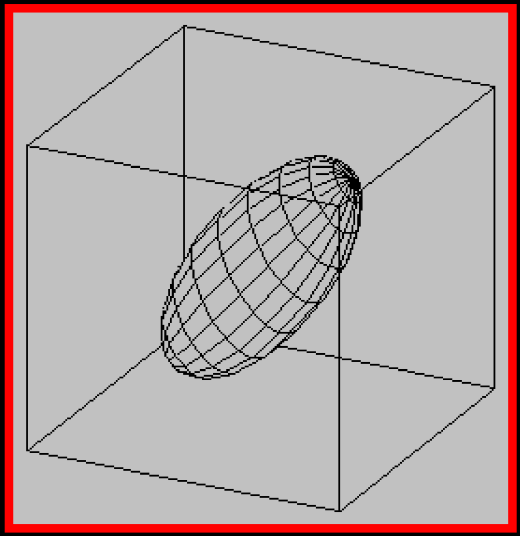
Pediatric DIPG



Guess the ellipsoid







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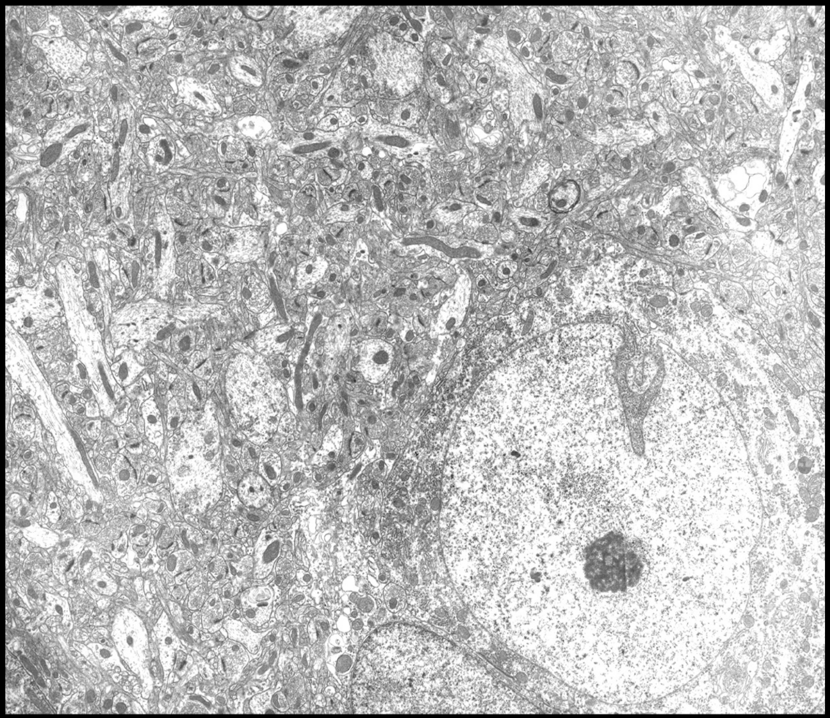

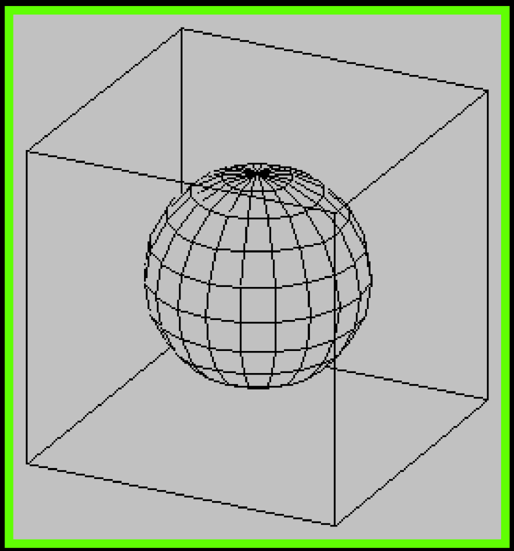

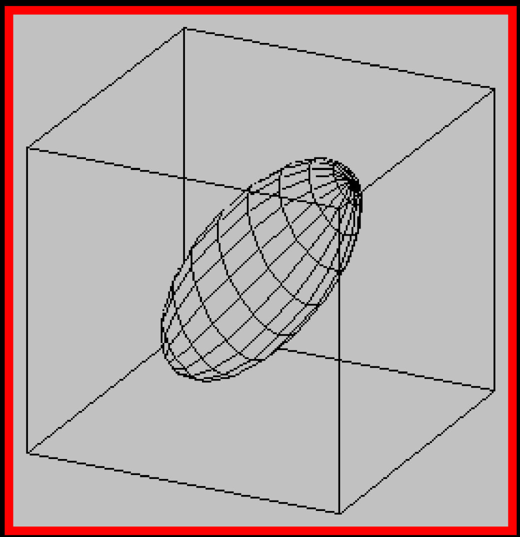

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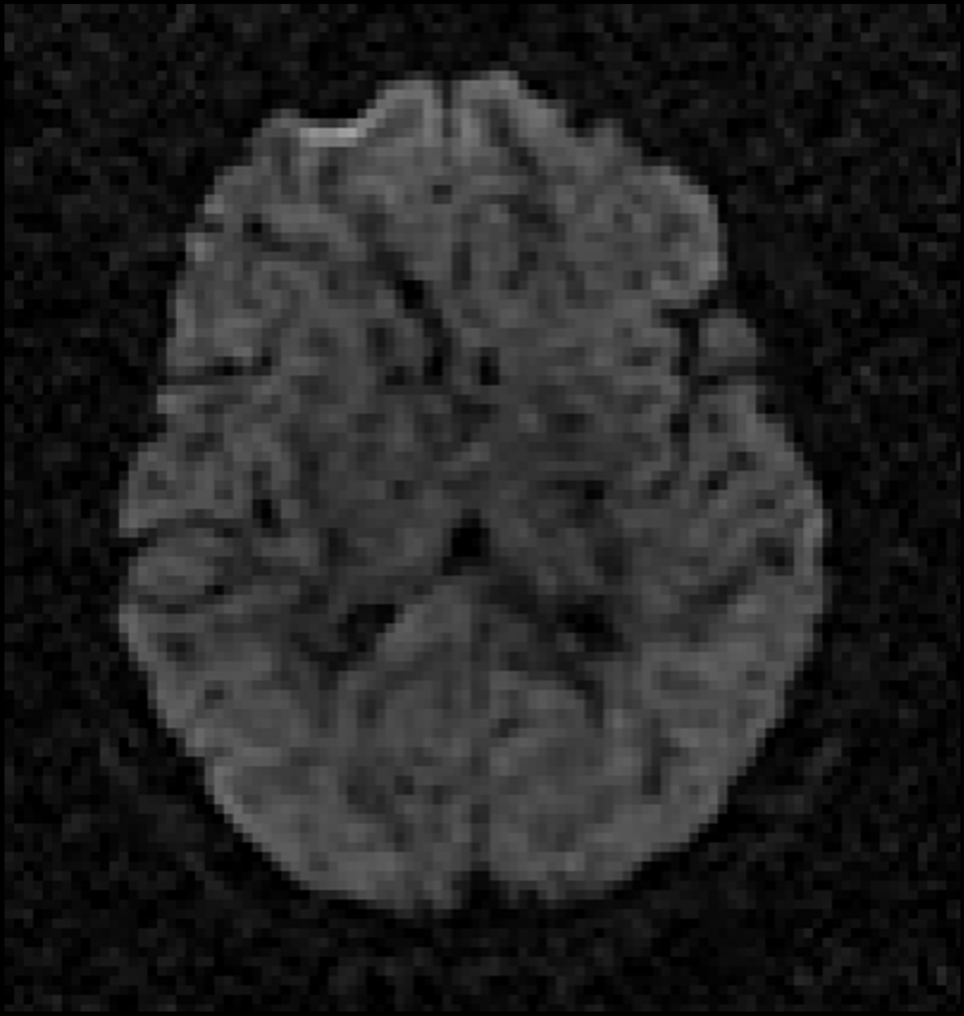
Typical DW SSEPI



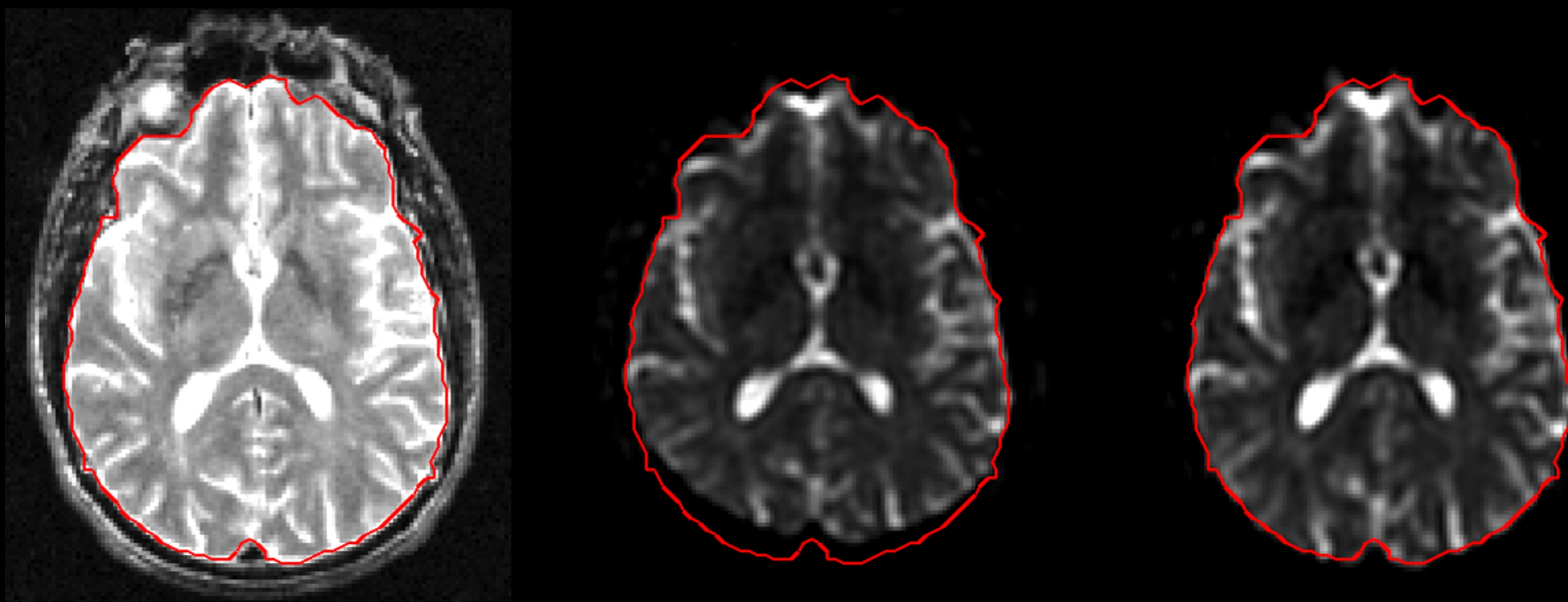
PRO

- Time Efficient
- Insensitive to Bulk motion

CON

- Low Resolution
- Distortions - Field inhomogeneities
- Distortions - Diffusion weighting

CON: Distortions from field inhomogeneities

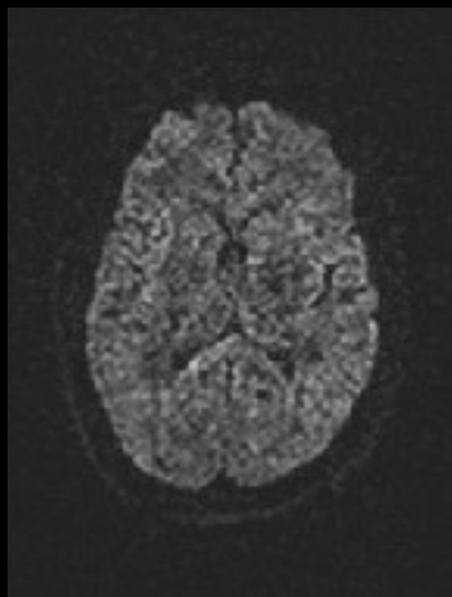


T2-weighted FSE

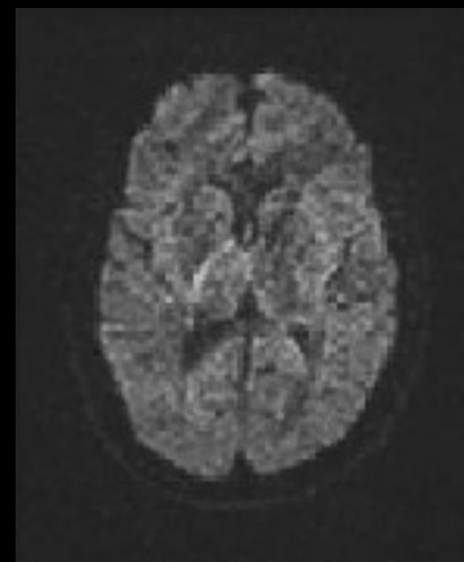
Non-diffusion-weighted SSEPI

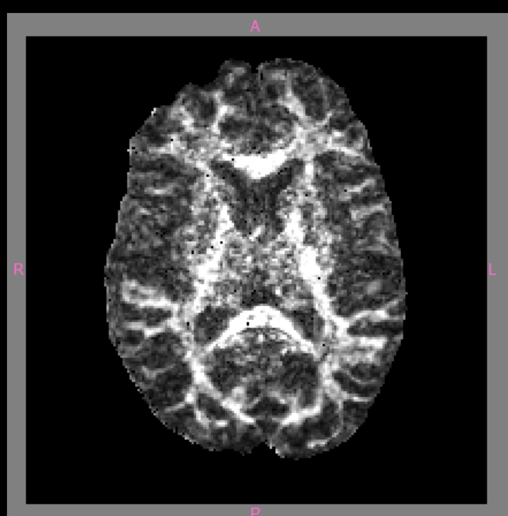
SSEPI corrected

CON: Distortions from DW

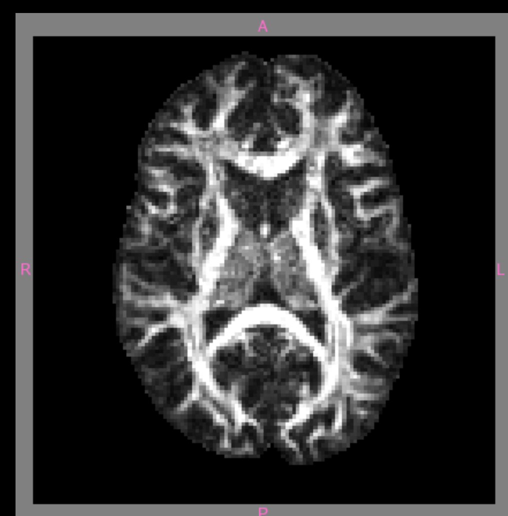


DW
SSEPI
volumes





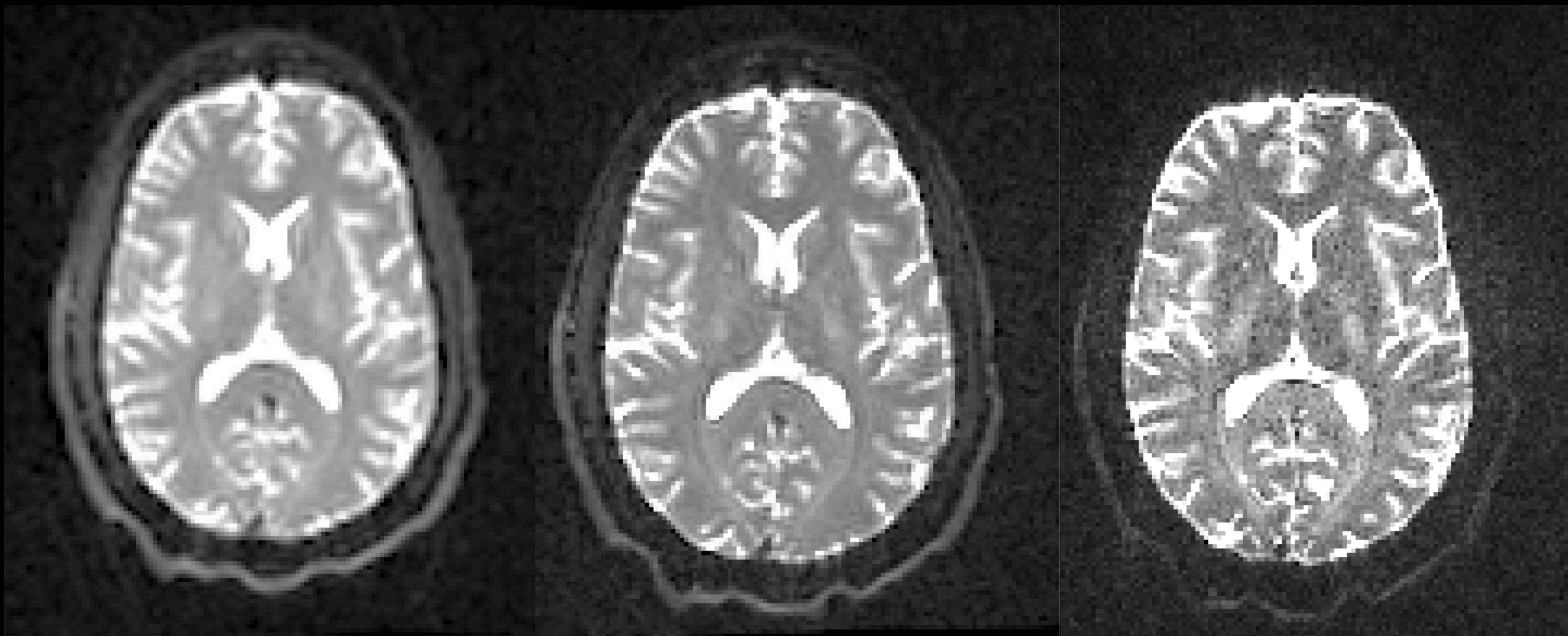
FA maps



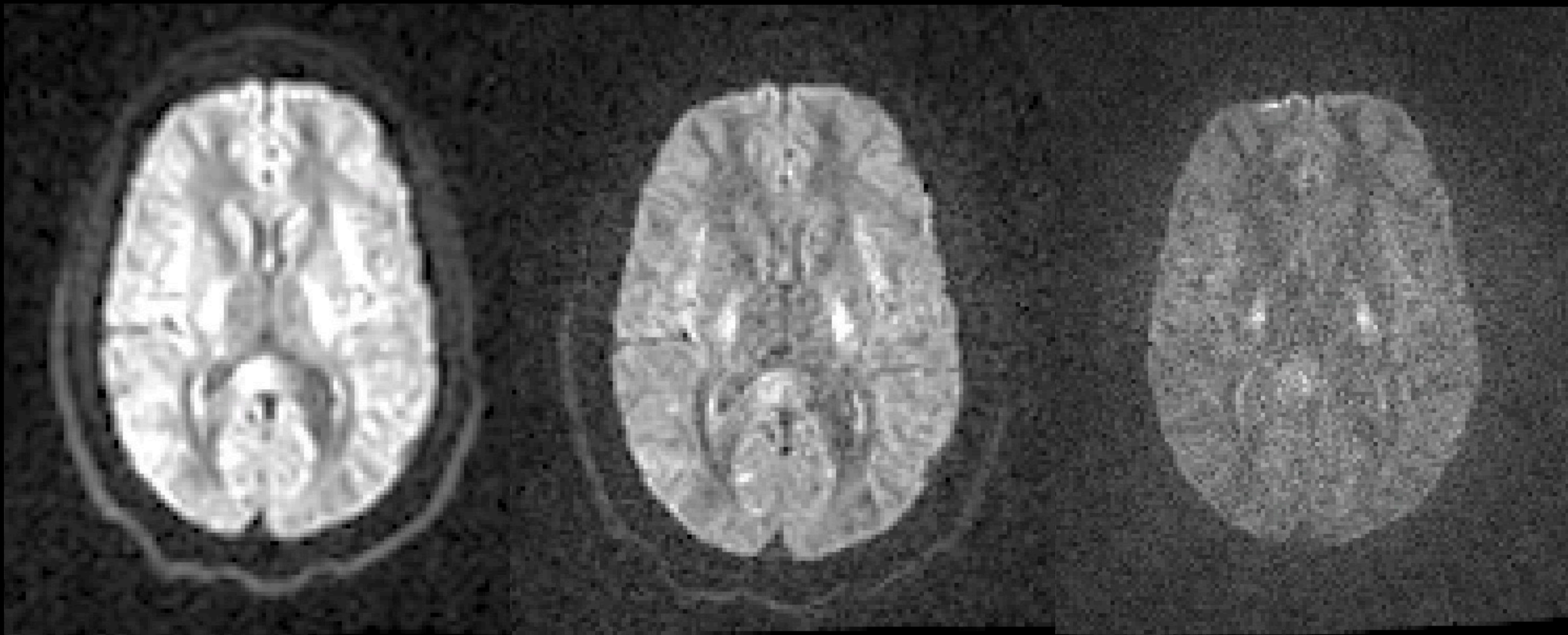
Other Common Problems in DTI

- Low SNR
- Incomplete Fat Suppression
- Bulk movement
- Cardiac pulsation

Low SNR



Low SNR

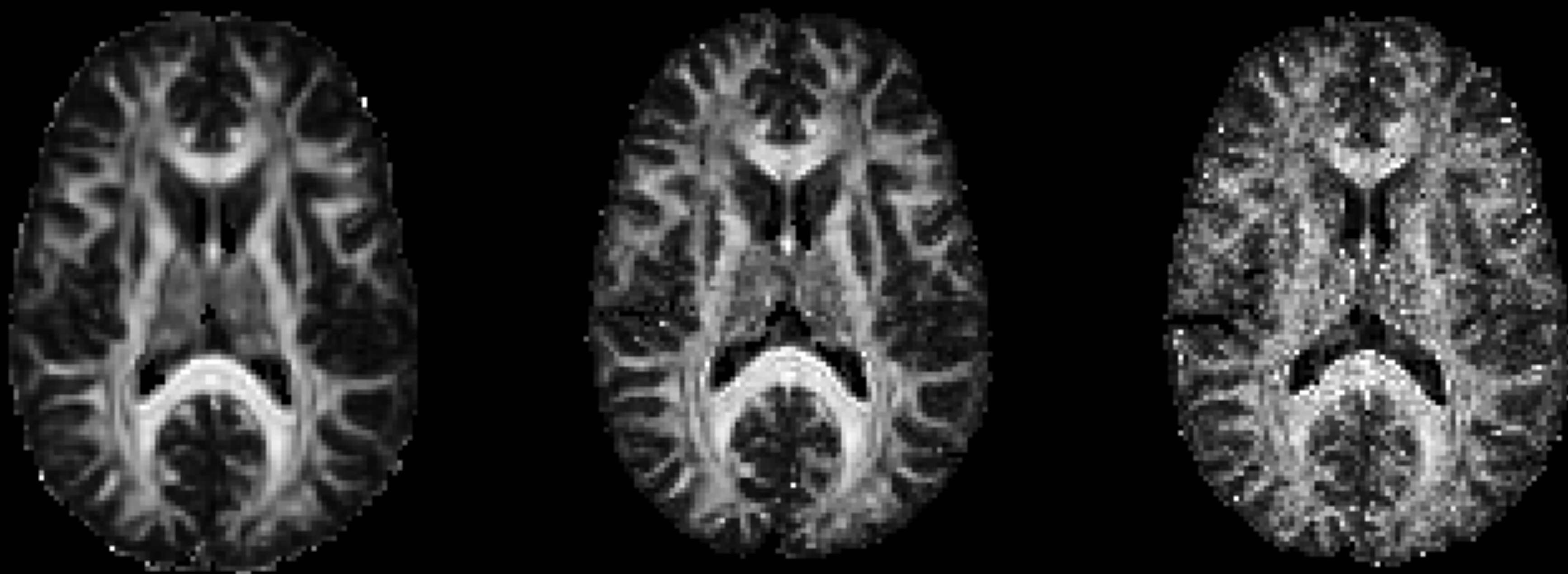


2.5 mm iso
15.625 mm^3

1.7mm iso
4.913 mm^3

1.3mm iso
2.197 mm^3

Low SNR

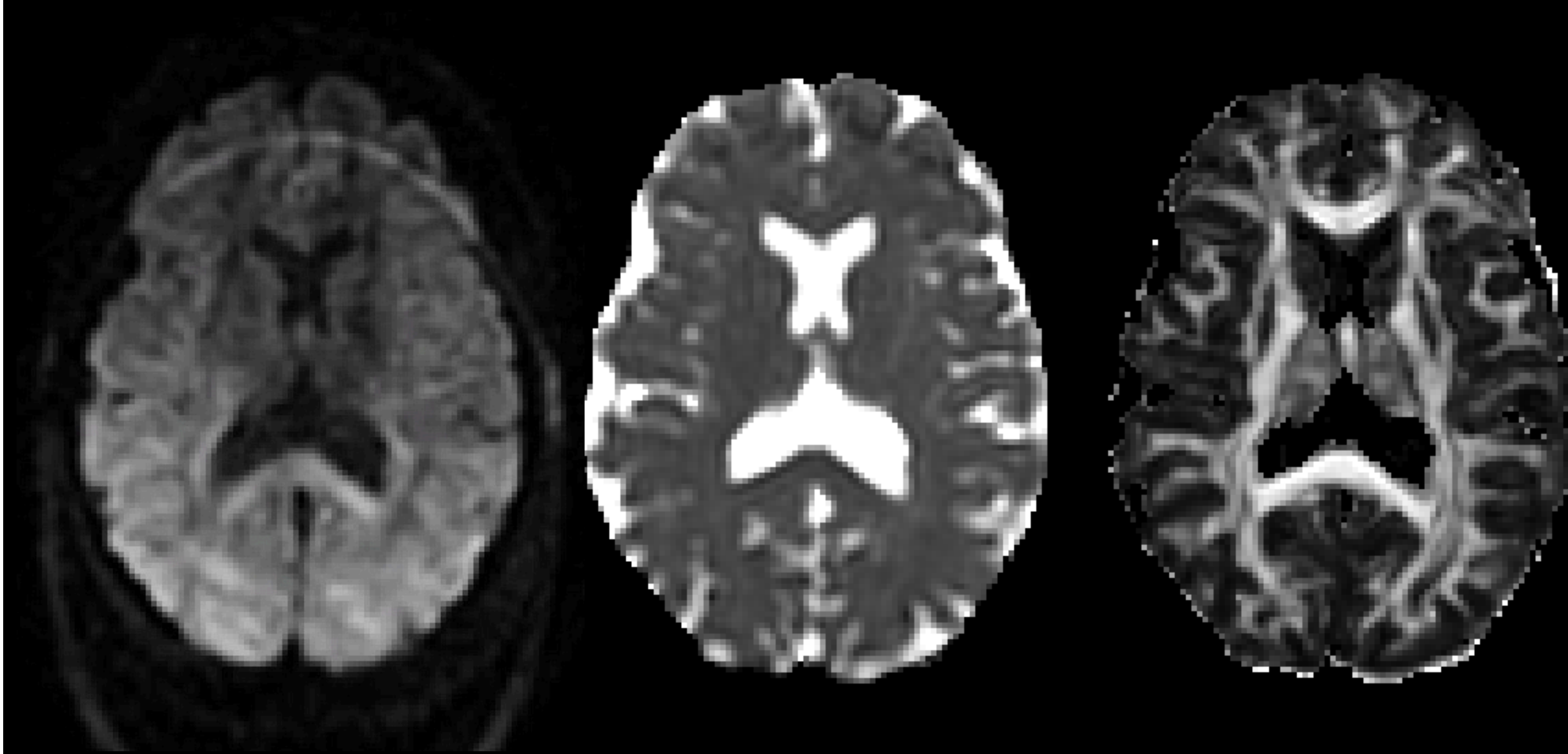


2.5 mm iso
15.625 mm^3

1.7mm iso
4.913 mm^3

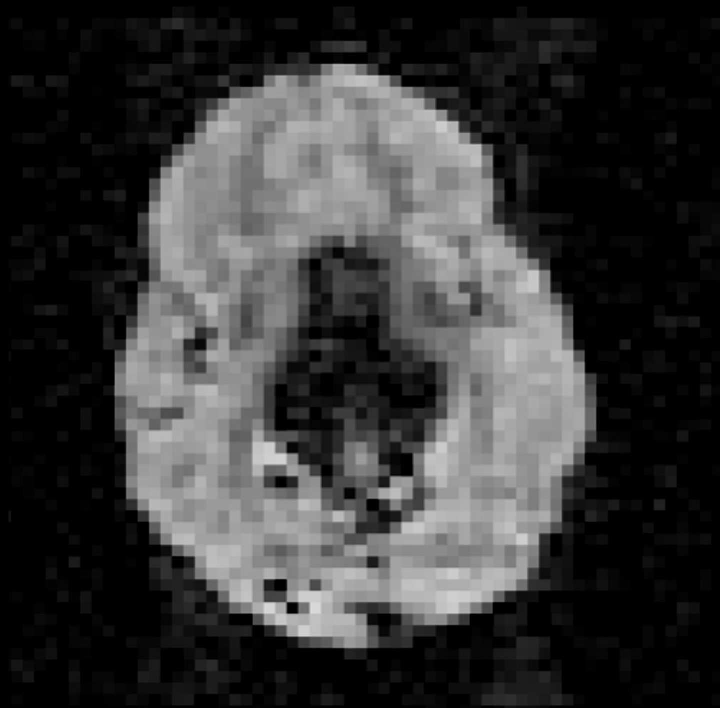
1.3mm iso
2.197 mm^3

Incomplete Fat Suppression



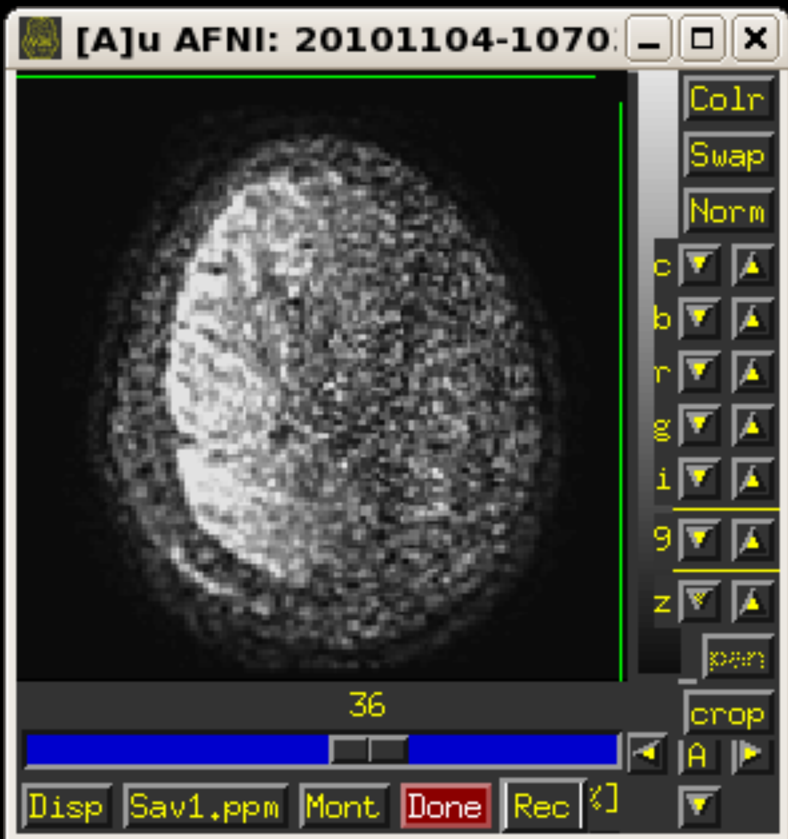
b=1100 s/mm^2 MD FA

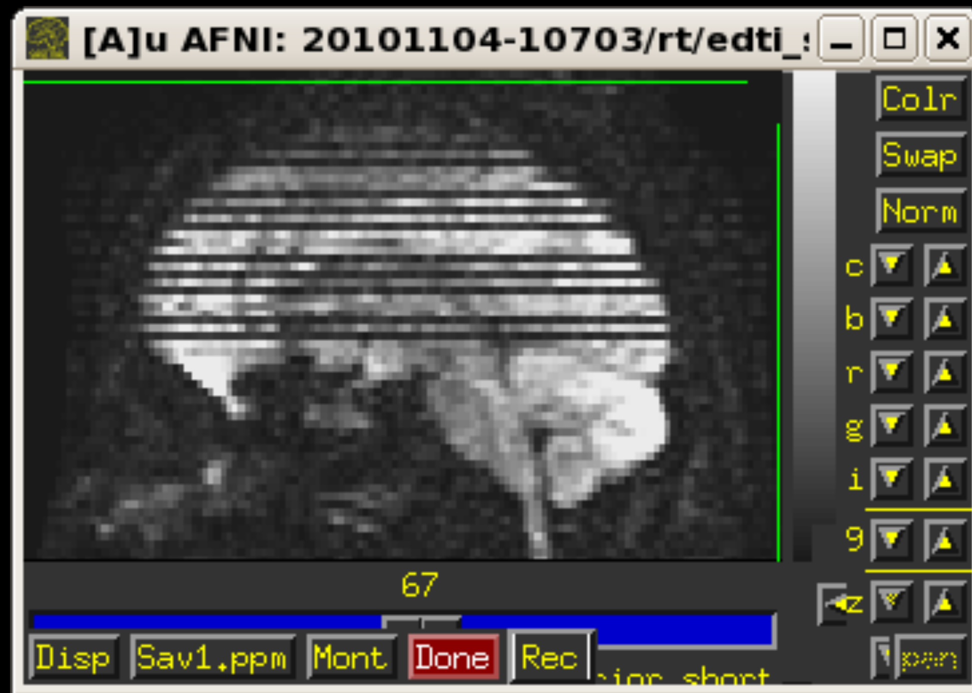
Cardiac Pulsation



Diffusion weighting in Z

Bulk Movement





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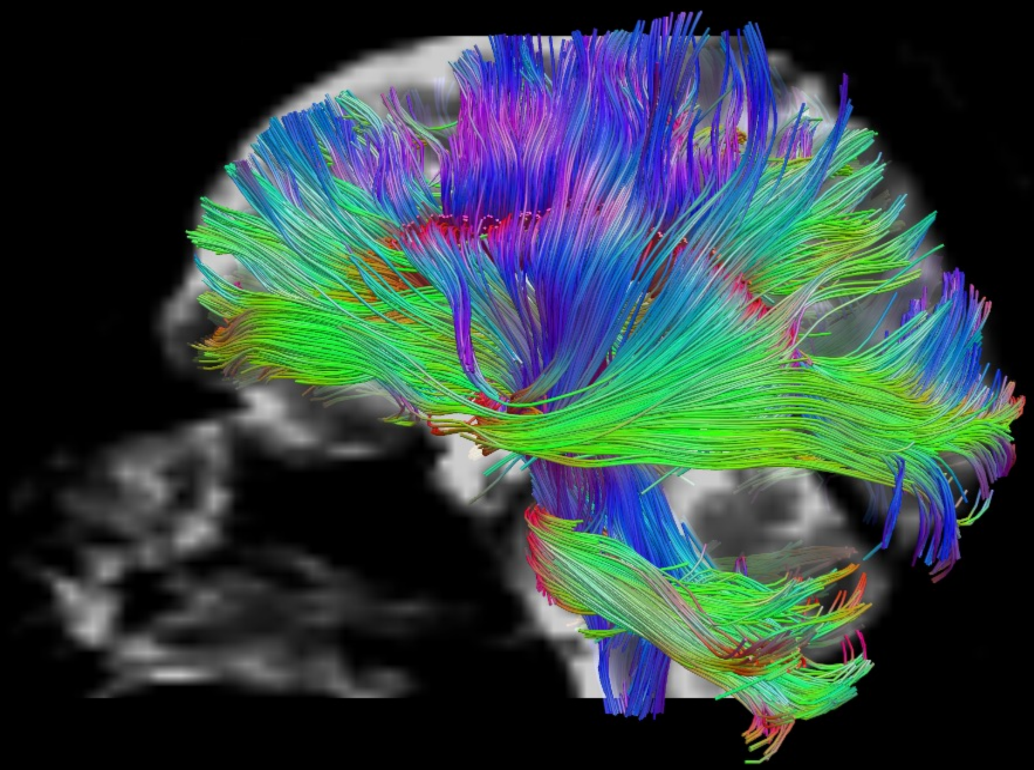
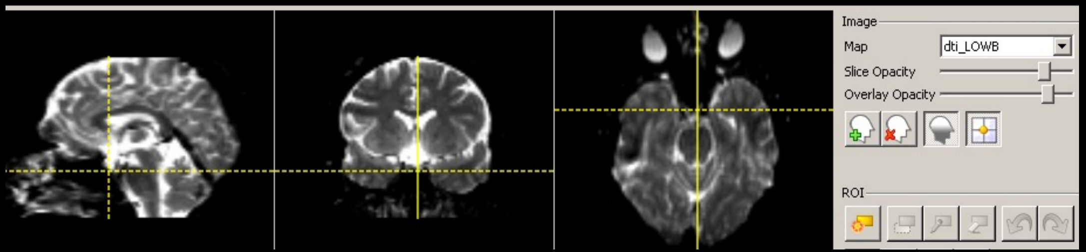
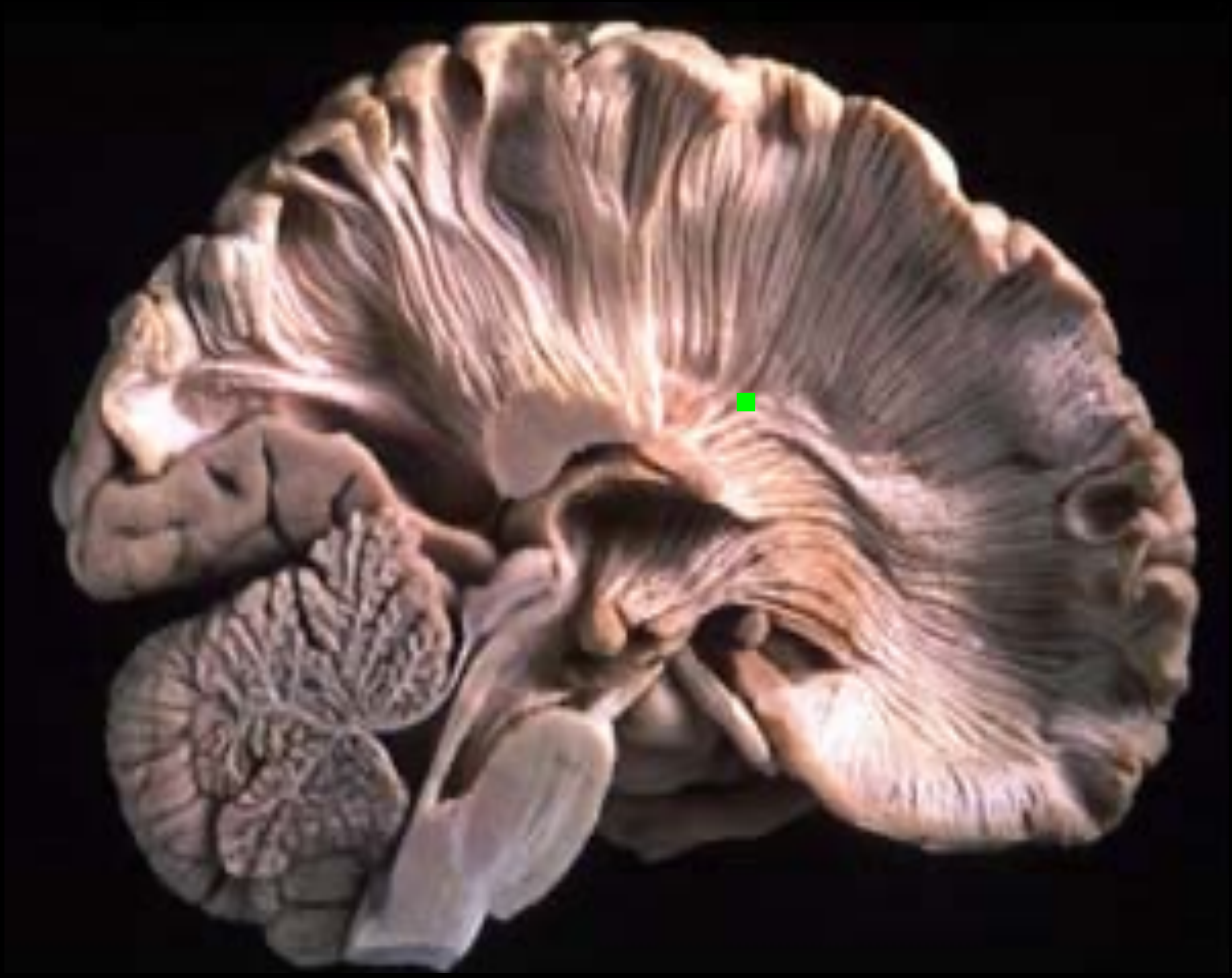
What isTractography?

The use of orientation information from diffusion imaging to reconstruct estimates of white matter pathways in the brain.





Limitation to DTI comes from partial volume effects



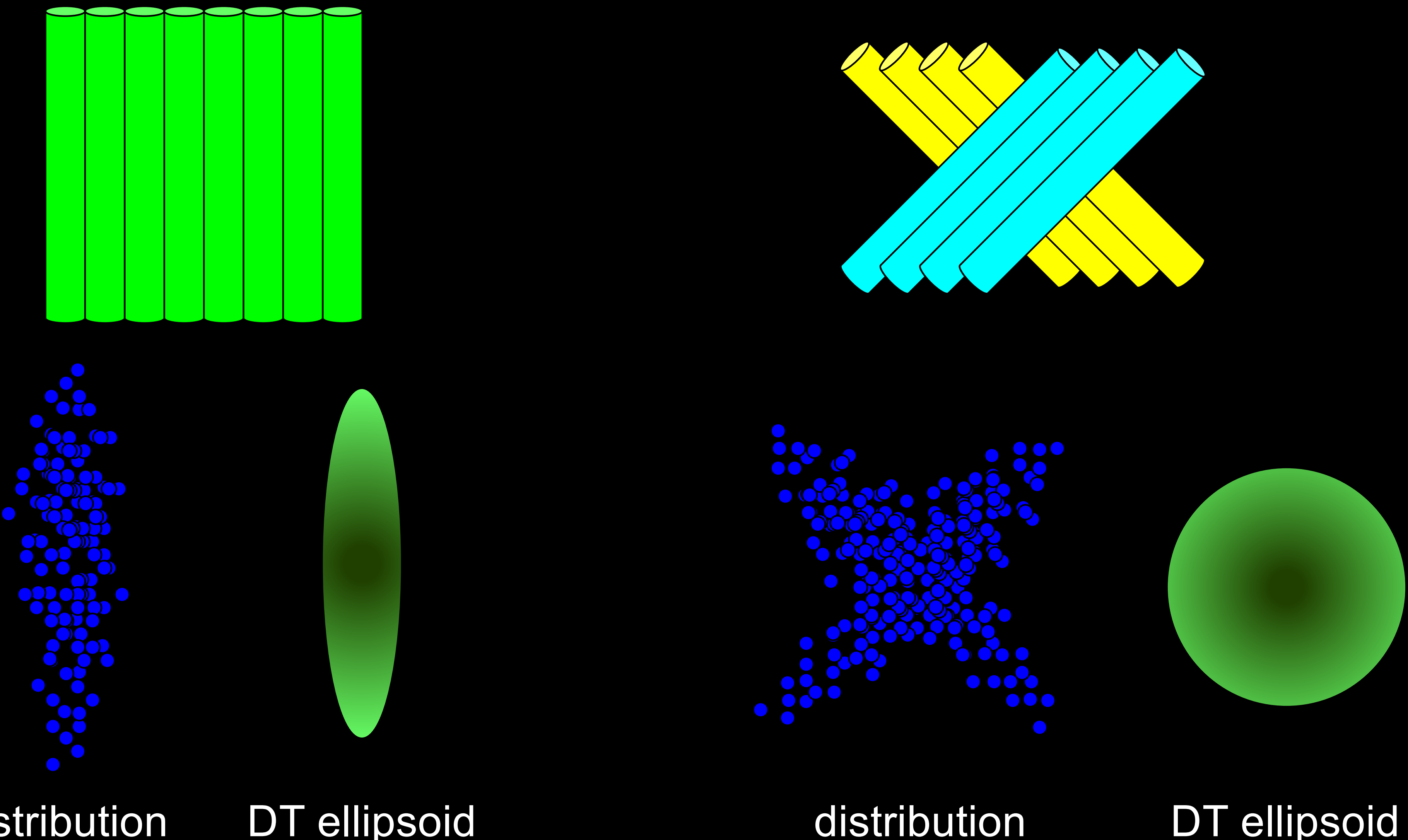
Typical resolution

for SSEPI DTI

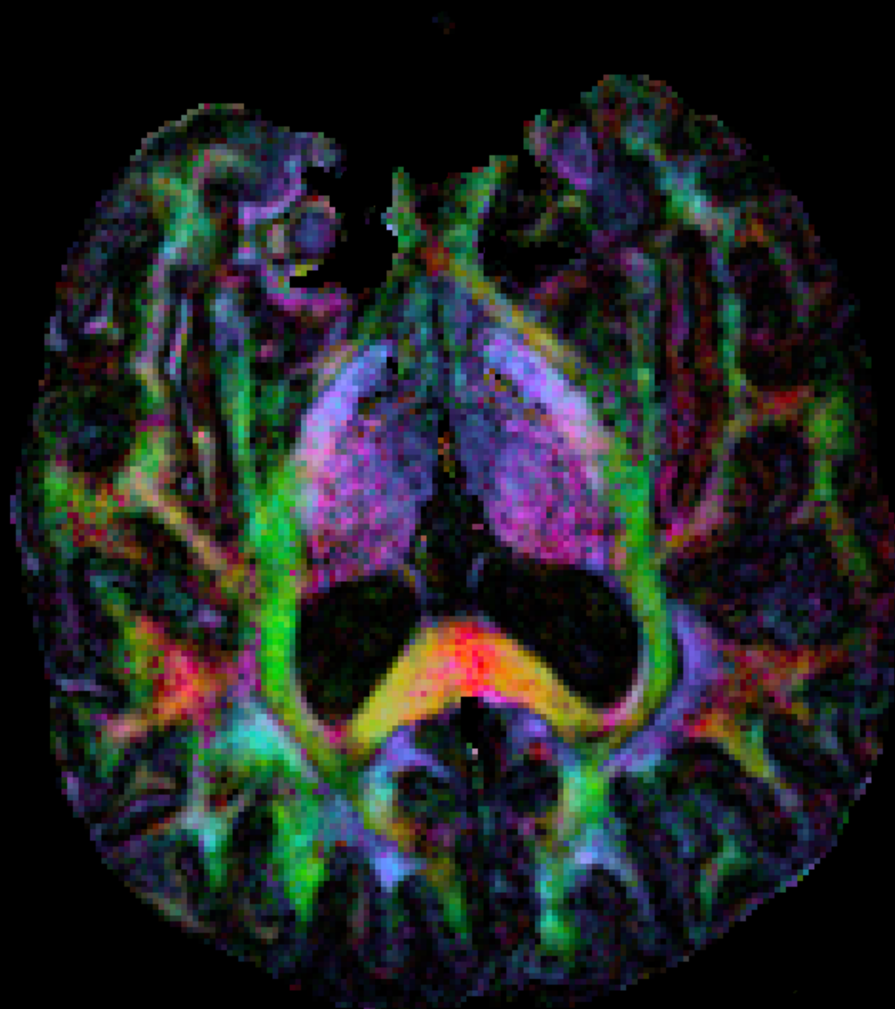
2.5 x 2.5 x 2.5 mm

Cortical projection systems of left cerebral hemisphere

Partial Volume Effect



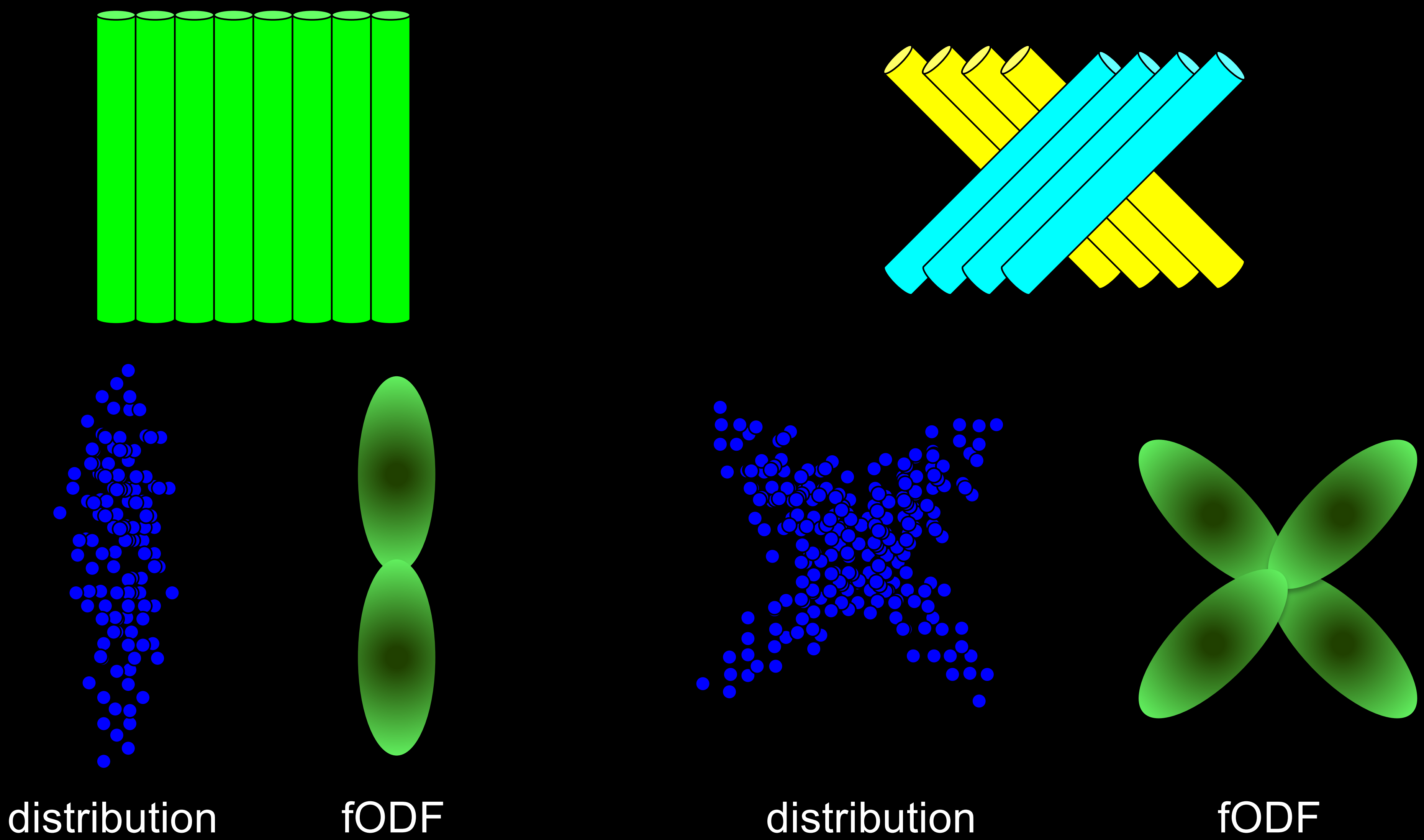
Sub-millimeter DTI

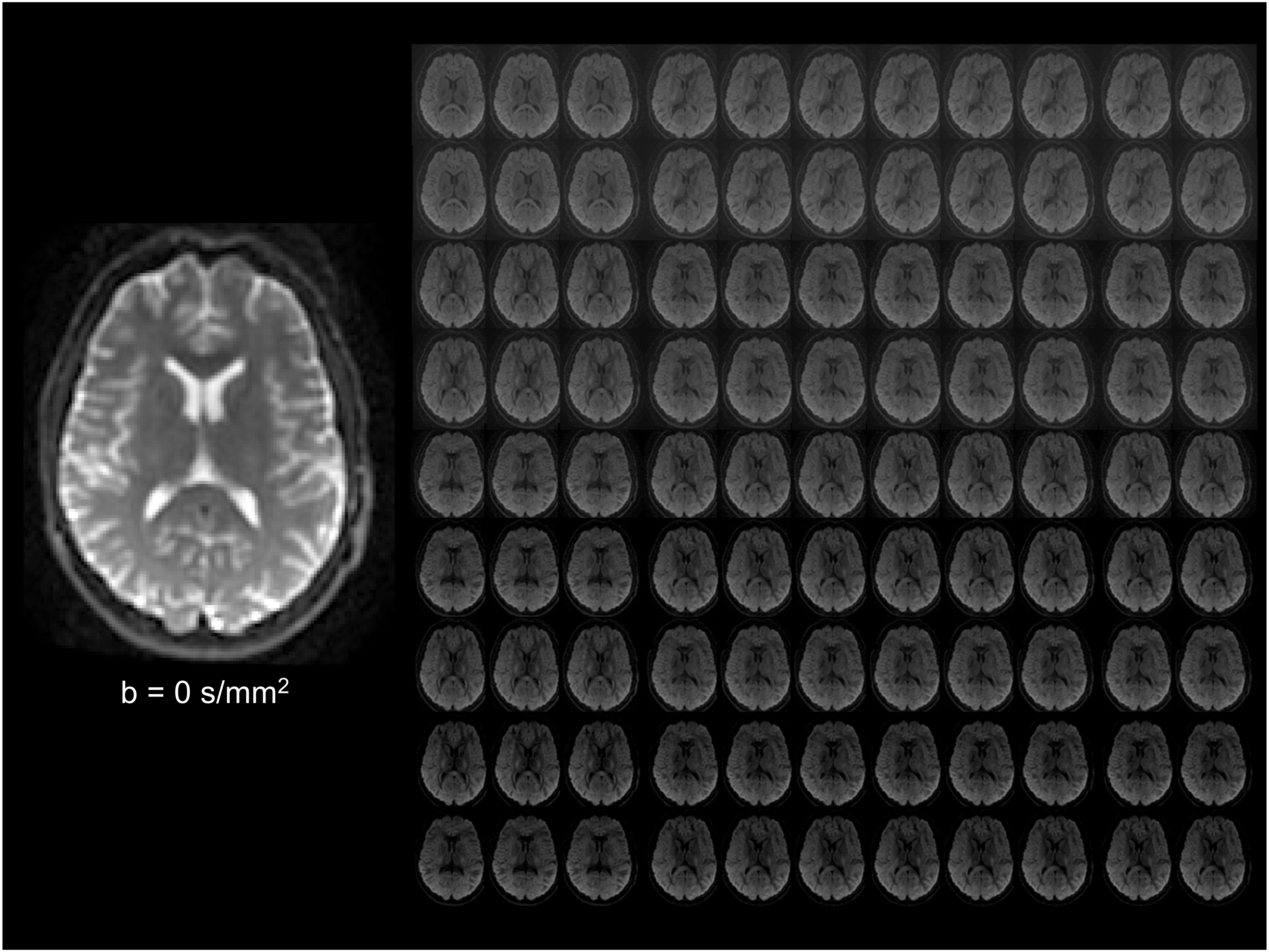


Beyond Standard DTI

- High Angular Resolution Diffusion Imaging (HARDI)
  - Multi-tensor models
  - Non-parametric algorithums
    - DSI, Qball, SD, PAS

Non-parametric Algorithms




b = 0 s/mm²

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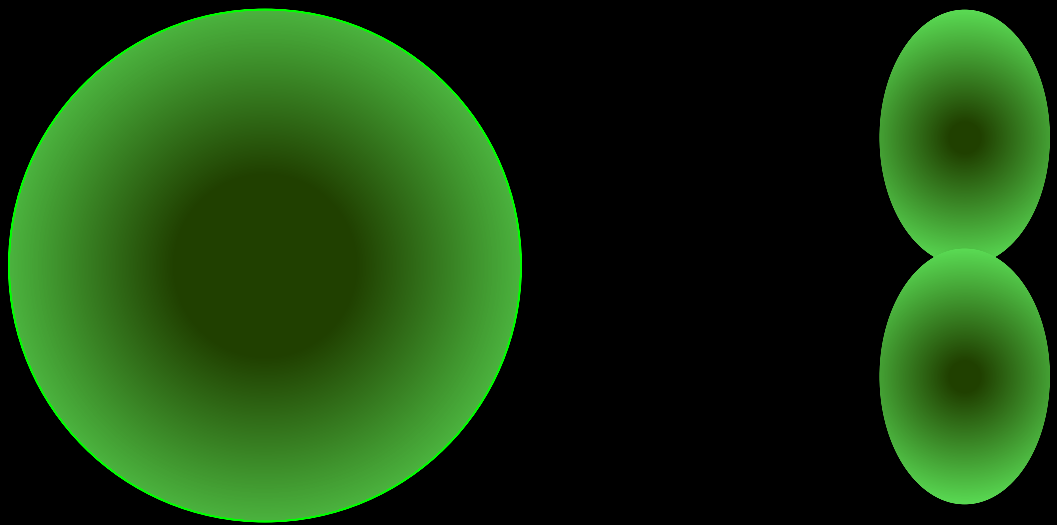
THANK YOU

Diffusion Profile

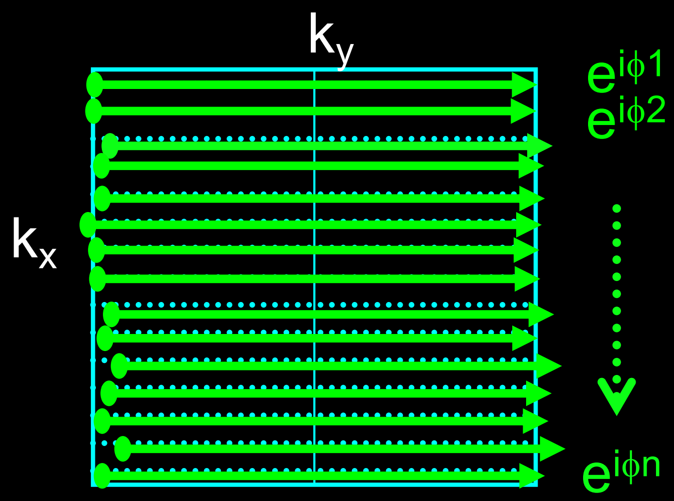


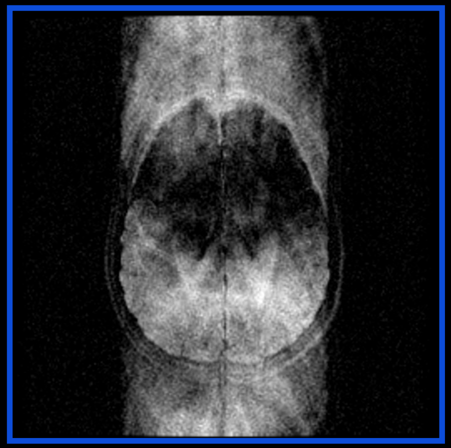
Isotropic

Anisotropic

Inherent Motion in Living Systems

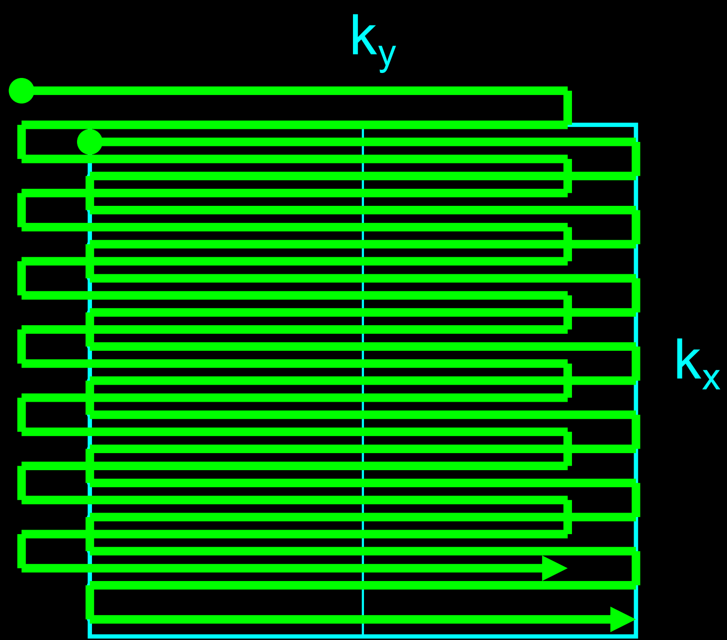
Diffusion-Weighted
MRI





$$S_n(t) = F[\, k_x(t)+\Delta k_{xn},\, k_{yn}+\Delta k_{yn}]\, e^{i\phi_n}$$

PRO: insensitive to bulk motion



$$S(t) = F[\, k_x(t)+\Delta k_x,\ k_y+\Delta k_y]\ e^{i\phi}$$

DWI

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

Non-diffusion-weighted signal intensity

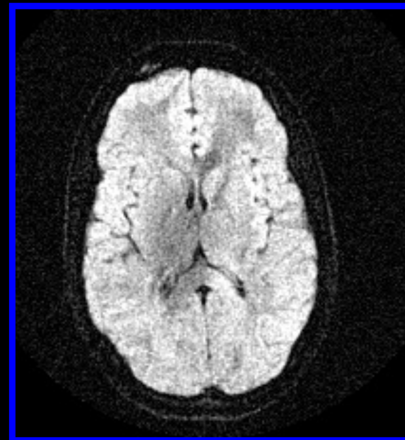
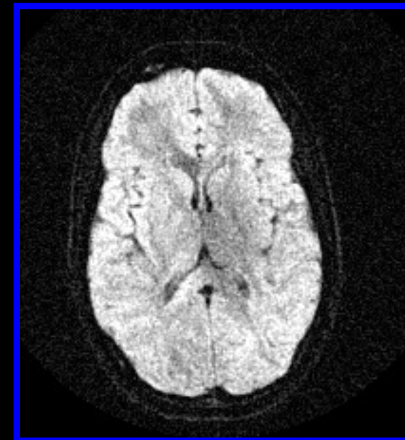
B-value
sec/mm^2

Diffusion Coefficient
mm^2/sec

Take two measures of signal and solve for D.

$$D = \frac{1}{-b} \ln\left(\frac{S}{S_0}\right)$$

Average (Trace) Image

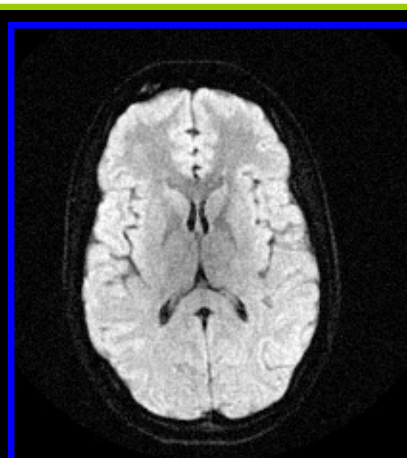




$$I_{xx} = I_0 e^{-bD_{xx}}$$

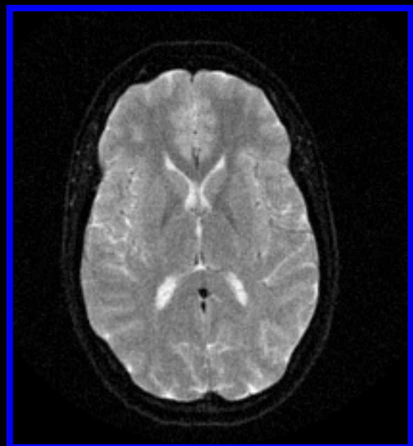
$$I_{yy} = I_0 e^{-bD_{yy}}$$

$$I_{zz} = I_0 e^{-bD_{zz}}$$

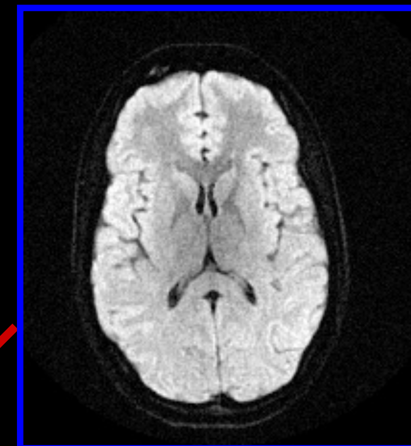
$$I_{Ave} = \sqrt[3]{I_{xx} \times I_{yy} \times I_{zz}}$$



Calculated the ADC

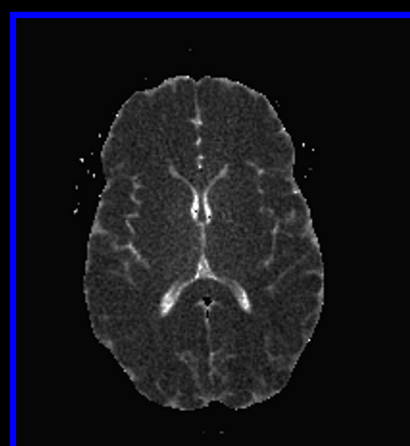


b-value = 0

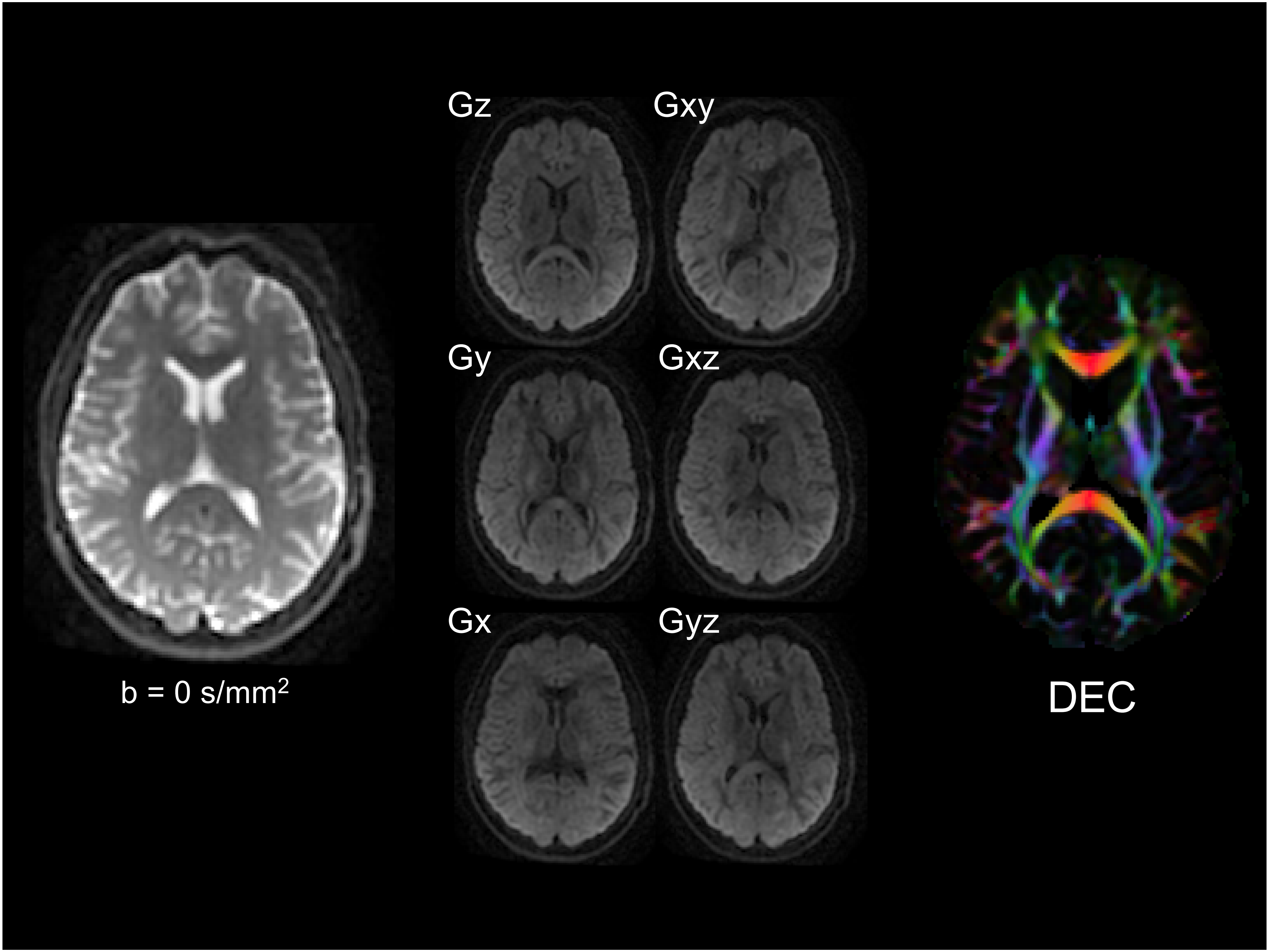


I_{ave}

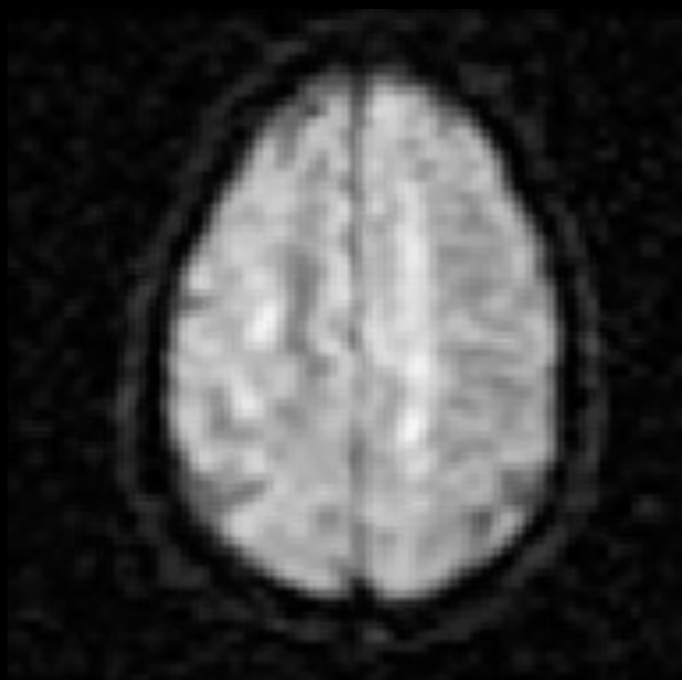
$$ADC = -\frac{1}{b}\ln\left(\frac{I_{Ave}}{I_0}\right)$$



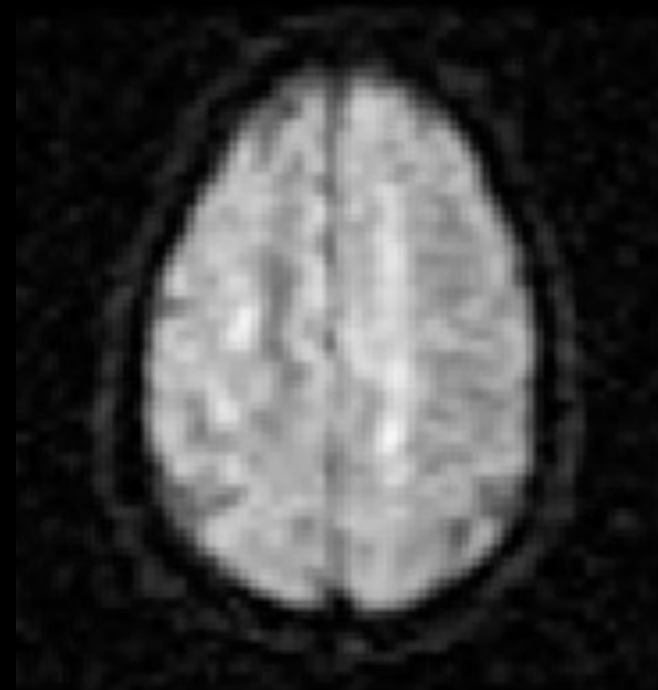
ADC map (mm^2/sec)


Gz
Gxy
Gy
Gxz
Gx
Gyz
b = 0 s/mm2
DEC

Not all processing software is created equal!



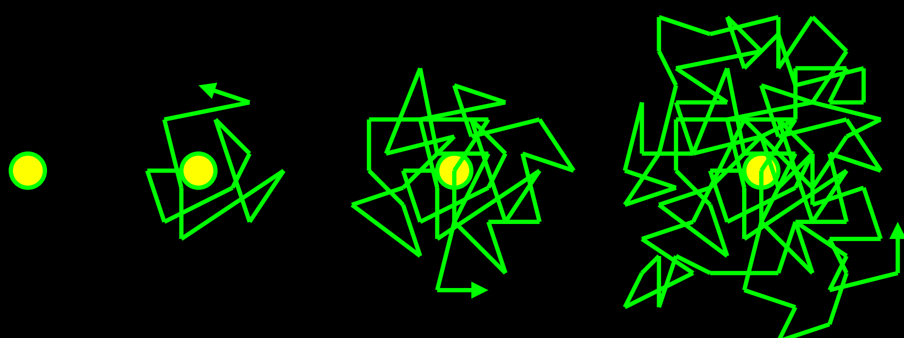
Competitor



TORTOISE

Diffusion-Weighted MRI (DWI)

- Sensitizes MRI image intensity to small, thermally induced random motion of water molecules
- The motion of water within tissue is extremely sensitive to the microscopic architecture and integrity of the tissue



$$\langle r^2 \rangle \approx 6DT_{dif}$$

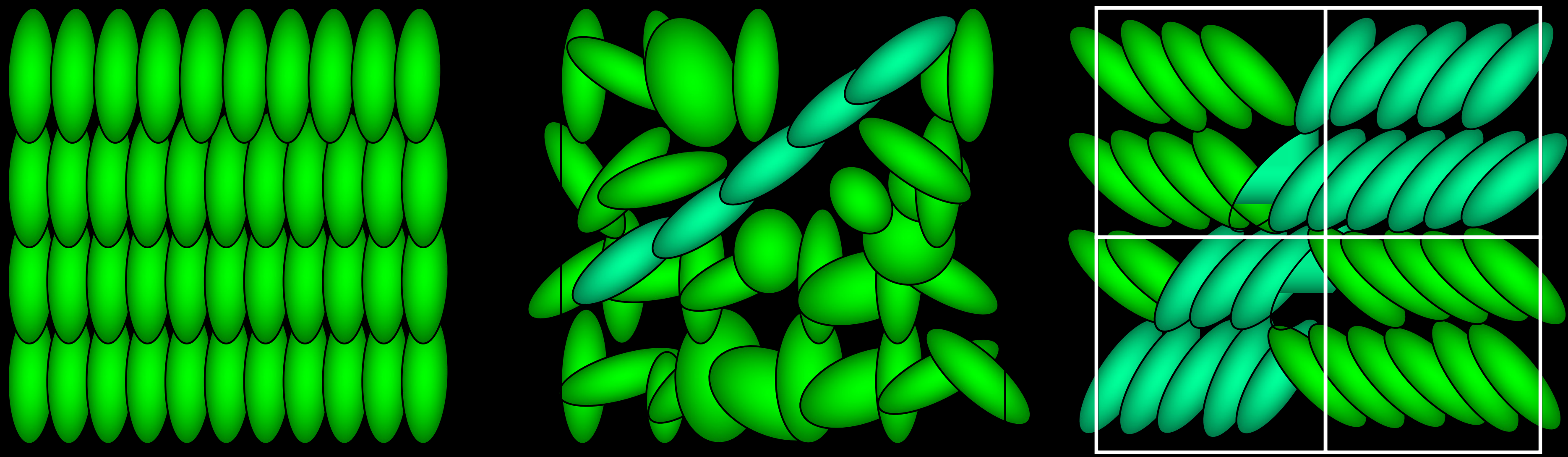
$D \approx 3.0\text{x}10^{-3}\ mm^2/s$

$T_{dif} \approx 30\ ms$

$r \approx 25\ \mu m$

Einstein, A. Ann Physik (1905) 4: 549-590

Limitation to DTI : Spatial resolution



Identical anisotropy maintained throughout the entire voxel

Anisotropy a small fraction of the voxel. Not experimentally observed

Complete anisotropy, but variable orientation. Experimentally isotropic.