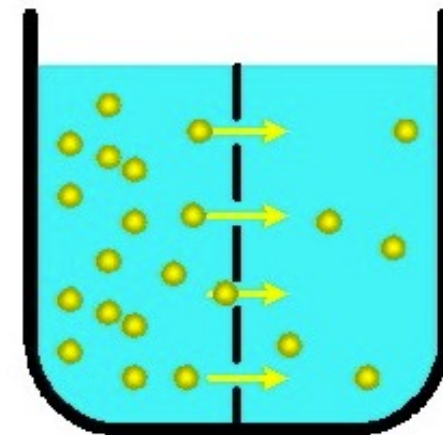


Outline

- Basics of diffusion, diffusion in tissue, measurement of diffusion using with MR
- Diffusion Parameters and Tractography
- Current Clinical Applications
- Connectomics, Advanced Diffusion Methods and Models

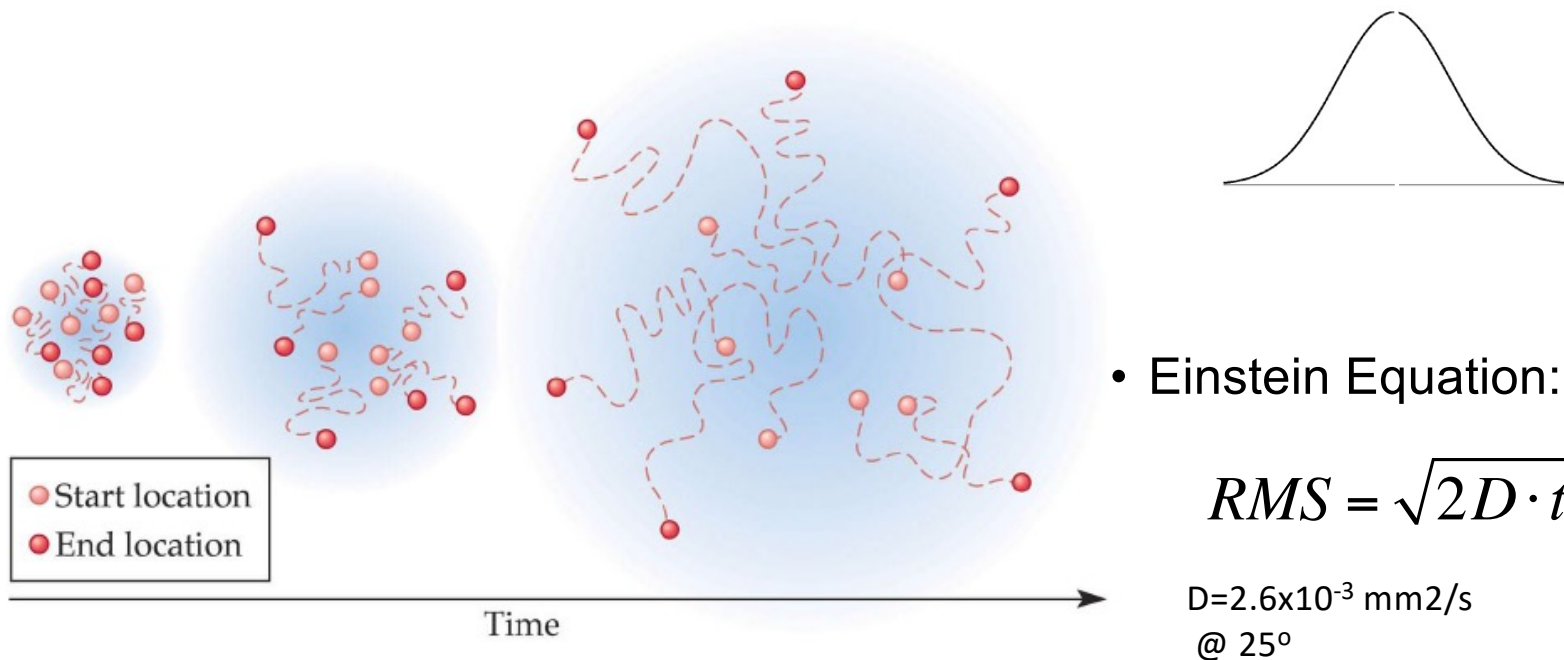
Macroscopic Diffusion



$$J = -D \cdot \nabla \cdot n(\vec{r}, t)$$

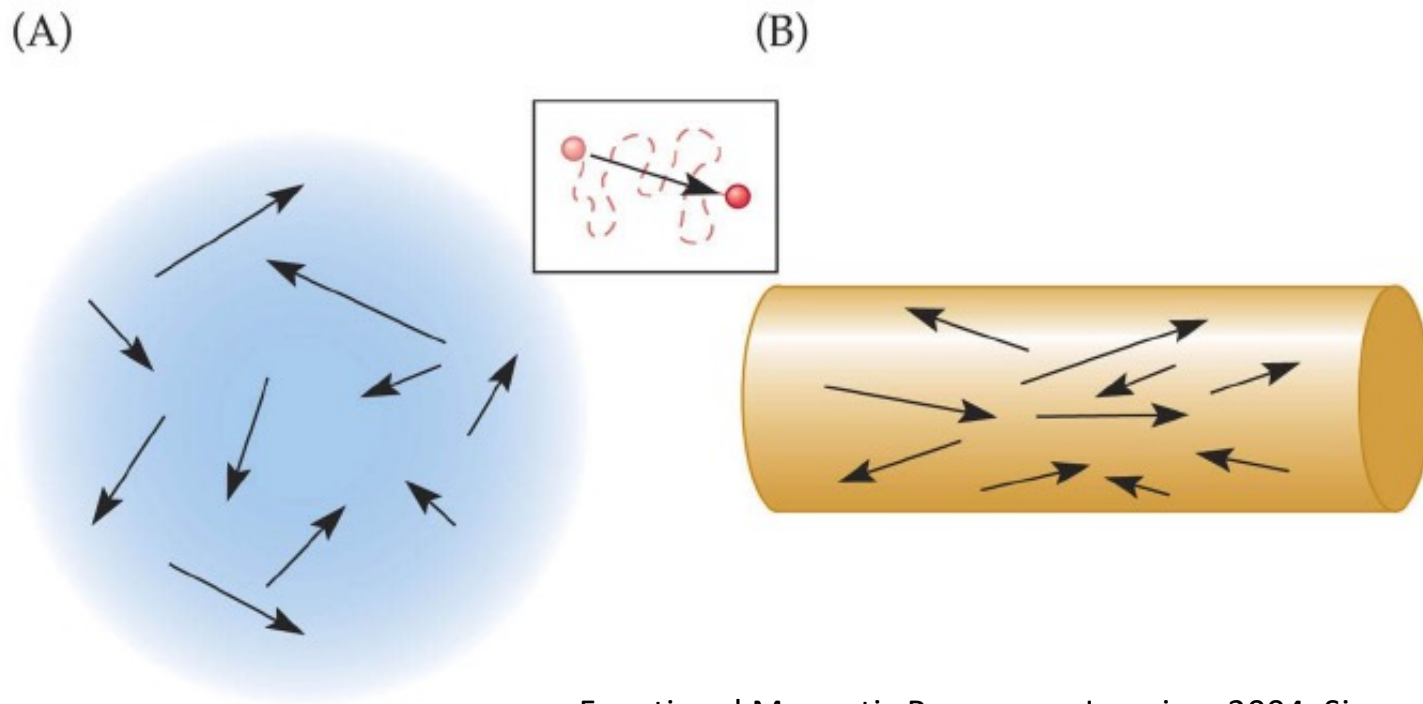
Fick's Law

Microscopic/self diffusion



Functional Magnetic Resonance Imaging. 2004. Sinauer Associates Inc

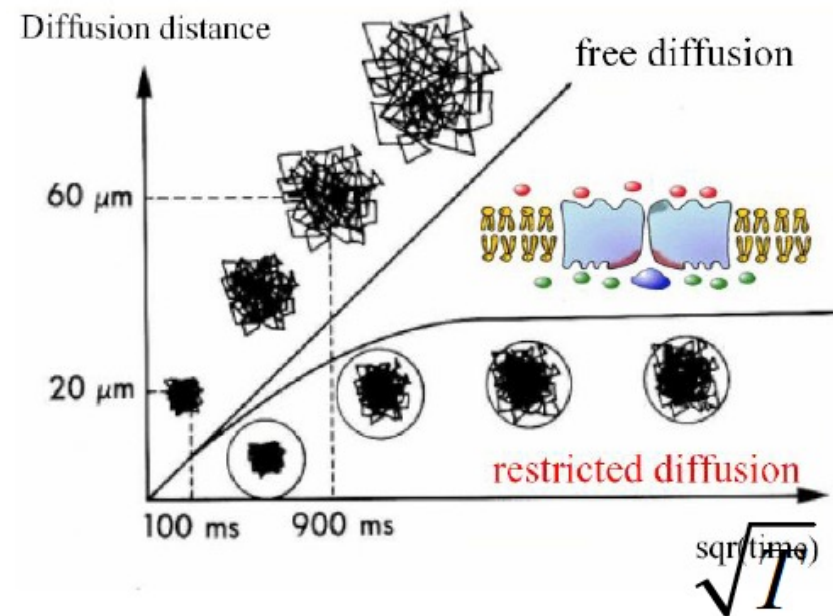
Isotropic vs Anisotropic diffusion



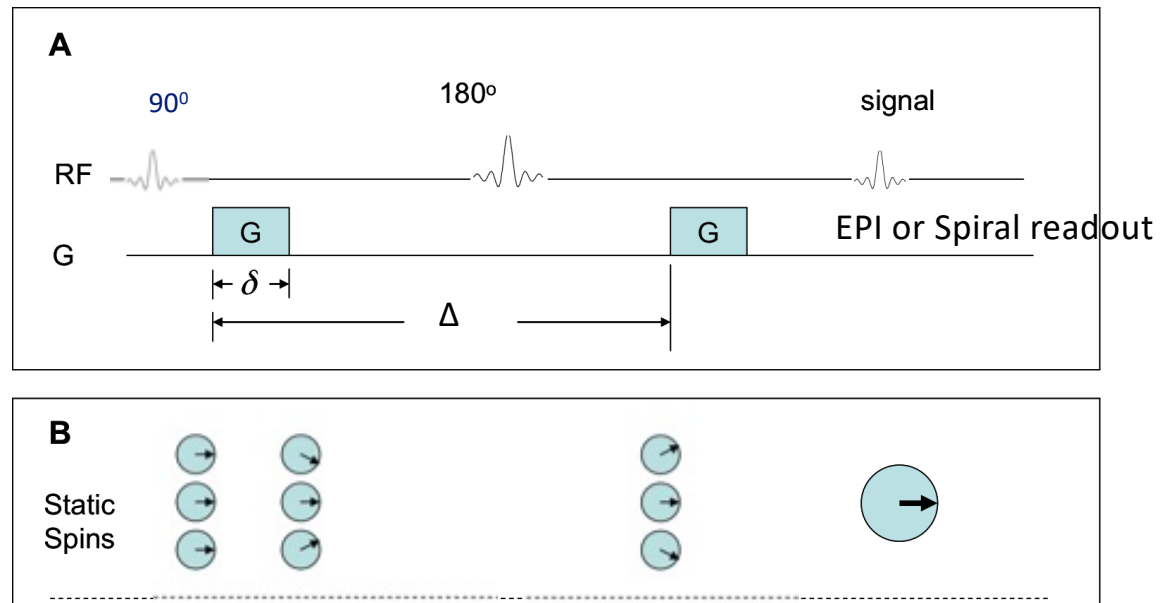
Functional Magnetic Resonance Imaging. 2004. Sinauer Associates Inc

Free Diffusion vs Restricted Diffusion

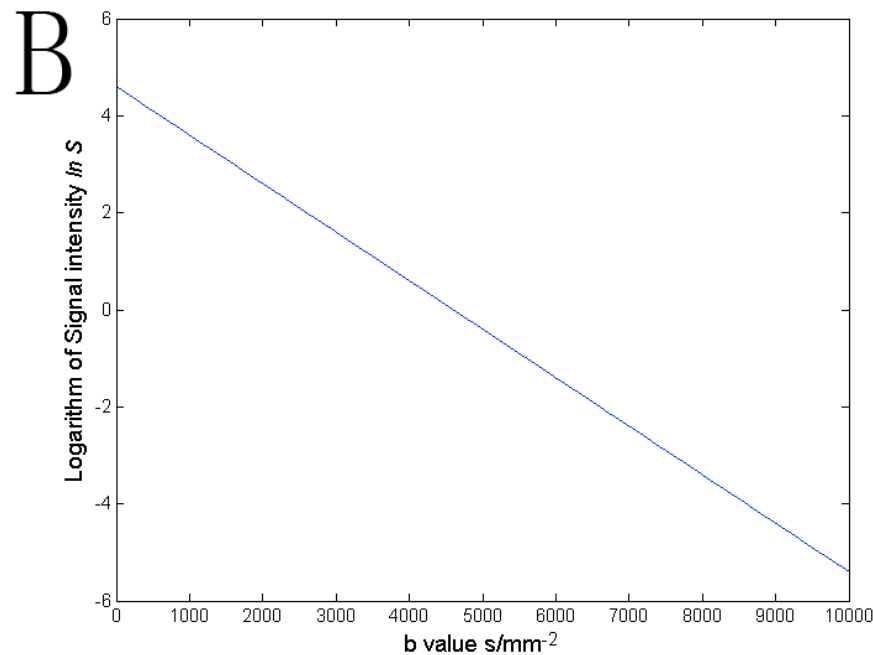
- Free or unhindered Diffusion
 - $RMS \sim \sqrt{Dt}$
 - $\sim 3\mu m^2/ms$ –Body temperature in water (CSF)
- Restricted or hindered diffusion
 - **Apparent** Diffusion Coefficient (ADC)



Stejskal-Tanner Sequence for Diffusion



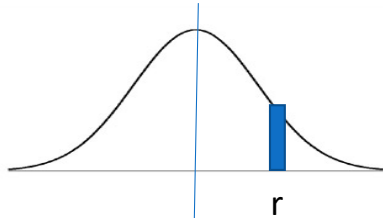
Single Direction Diffusion Signal Model



$$S = S_0 \exp(-b \cdot D)$$

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

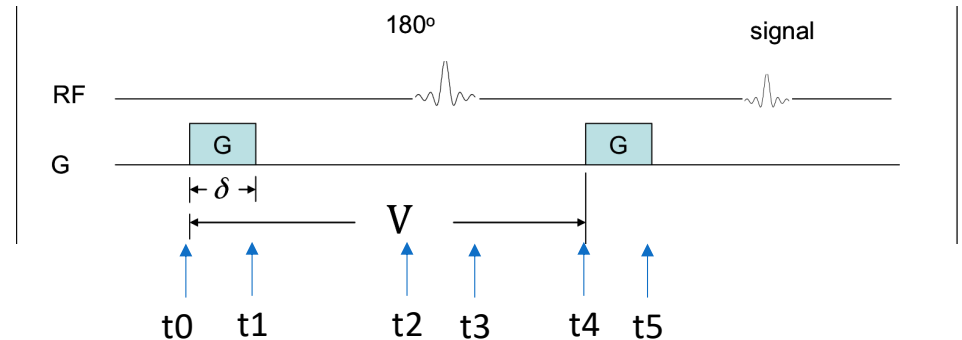
Deriving diffusion weighting equation



$$P(r) = \frac{1}{\sqrt{2\pi}\sigma} \exp\left(-\frac{r^2}{2\sigma^2}\right)$$

$$\sigma = \sqrt{2D \cdot \Delta}$$

$$\varphi(r) = \gamma G \delta r := qr$$



$$\varphi(t_0) = 0$$

$$\varphi(t_1) = \gamma B(k)t = \gamma G k \delta = \gamma G \delta k, \text{ for spin at an initial location } k$$

$$\varphi(t_2) = \varphi(t_1) = \gamma G \delta k$$

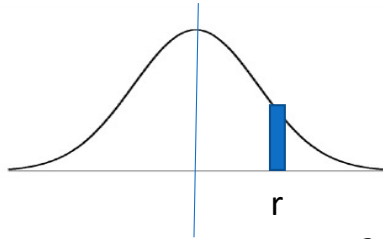
$$\varphi(t_3) = -\varphi(t_2) = -\gamma G \delta k$$

$$\varphi(t_4) = \varphi(t_3) = -\gamma G \delta k$$

$$\varphi(t_5) = \varphi(t_4) + \gamma G \delta(k+r) = \gamma G \delta r$$

Spin has moved to location $k+r$

Deriving diffusion weighting equation



$$P(r) = \frac{1}{\sqrt{2\pi}\sigma} \exp\left(-\frac{r^2}{2\sigma^2}\right)$$

$$\sigma = \sqrt{2D \cdot \Delta}$$

$$\varphi(r) = \gamma G \delta r := qr$$

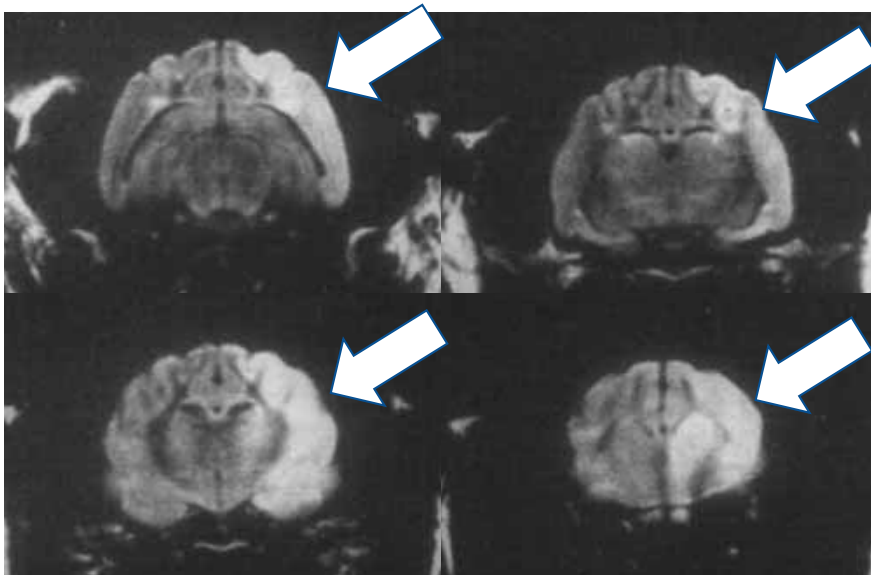
$$S = S_0 \cdot \int P(r) \cdot \exp(i\varphi(r)) dr$$

$$= \int \frac{\exp\left(-\frac{r^2}{2\sigma^2}\right)}{\sqrt{2\pi}\sigma} \exp(iqr) dr$$

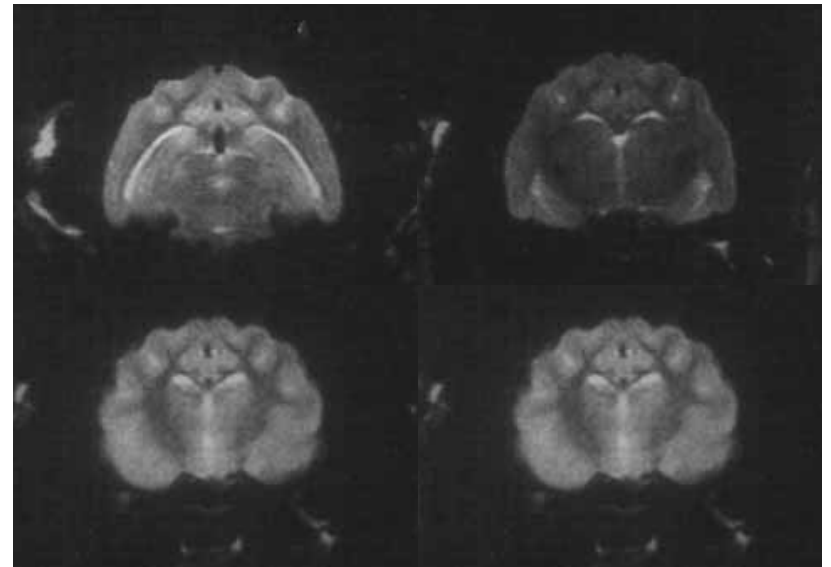
$$= \exp\left(-\frac{1}{2}\sigma^2 q^2\right) = \exp(-\gamma^2 G^2 \delta^2 \Delta D)$$

General formula:
$$b = \gamma^2 \int_0^{TE} \left(\int_0^t G(t') \cdot \text{Sign}\left(t' - \frac{TE}{2}\right) dt' \right)^2 dt$$

Early Detection of Stroke with DWI



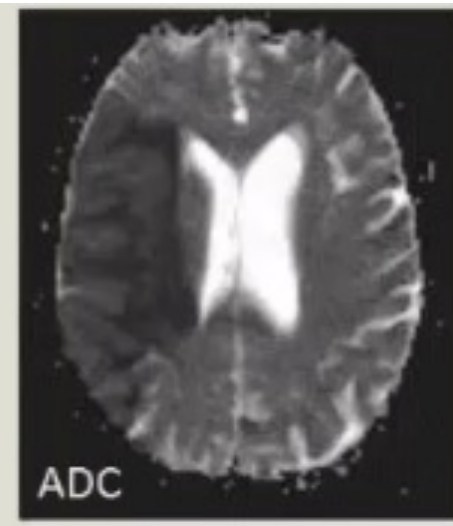
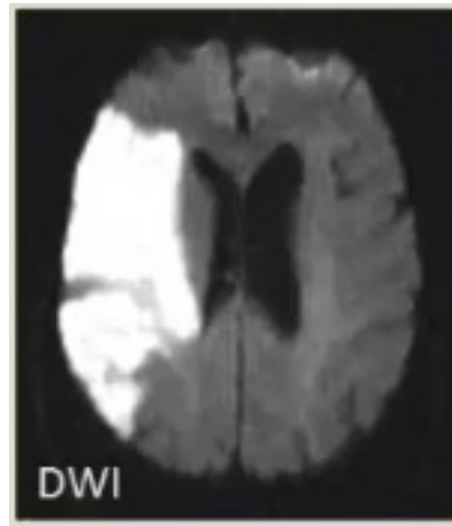
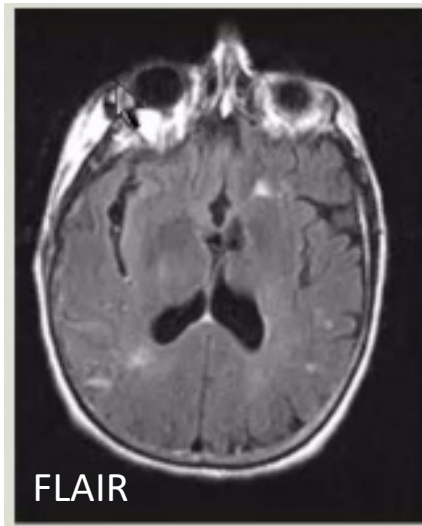
DWI taken 45mins after experimental occlusion



T2w taken 65mins after experimental occlusion

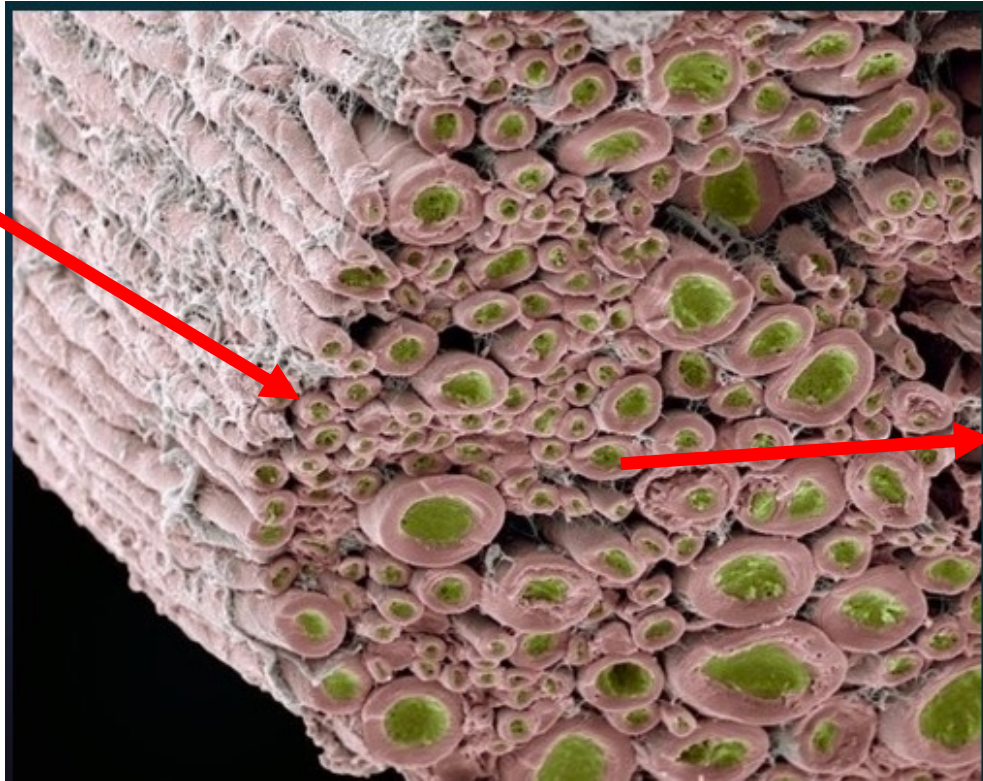
Moseley M et al. 1990. MRM

Application of DWI in Stroke



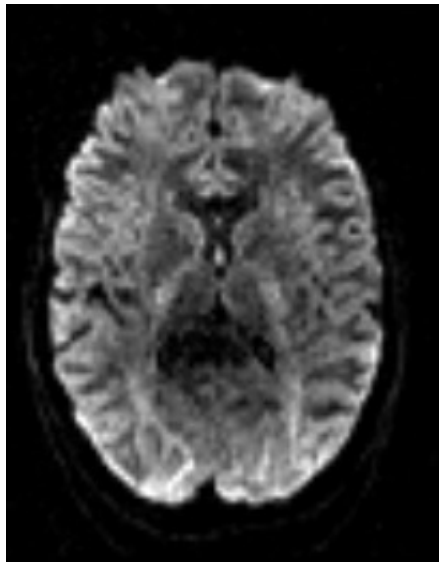
MGH

Modeling Anisotropic Diffusion

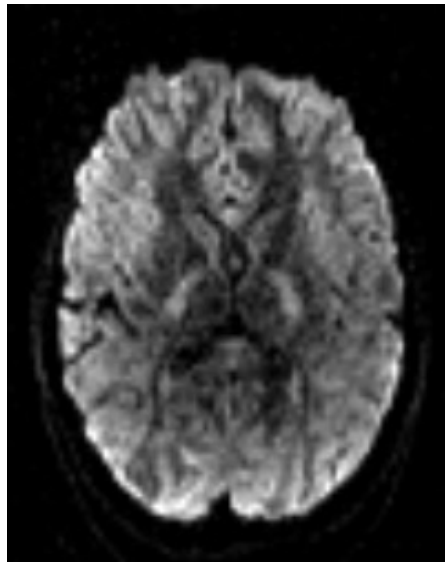


DWI

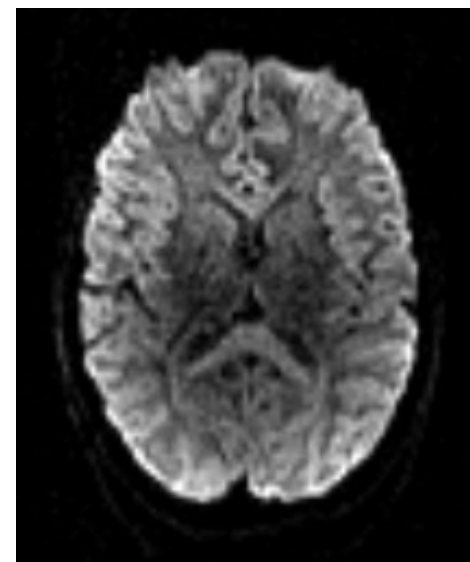
Gx



Gy



Gz

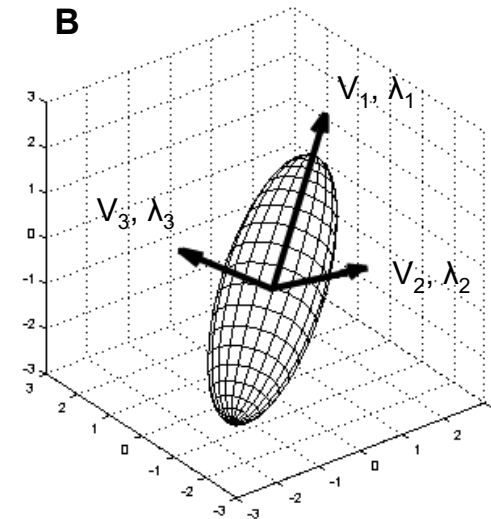


Diffusion Tensor Imaging

- Describe the diffusion process with a 3x3 Matrix (tensor)
- It is a covariance matrix of diffusion probability distribution
- Ellipsoid defines a surface of constant mean translational displacement

$$P(r) = \frac{1}{(2\pi)^{3/2}\Sigma^{1/2}} \exp\left(-\frac{1}{2}r^T\Sigma^{-1}r\right)$$

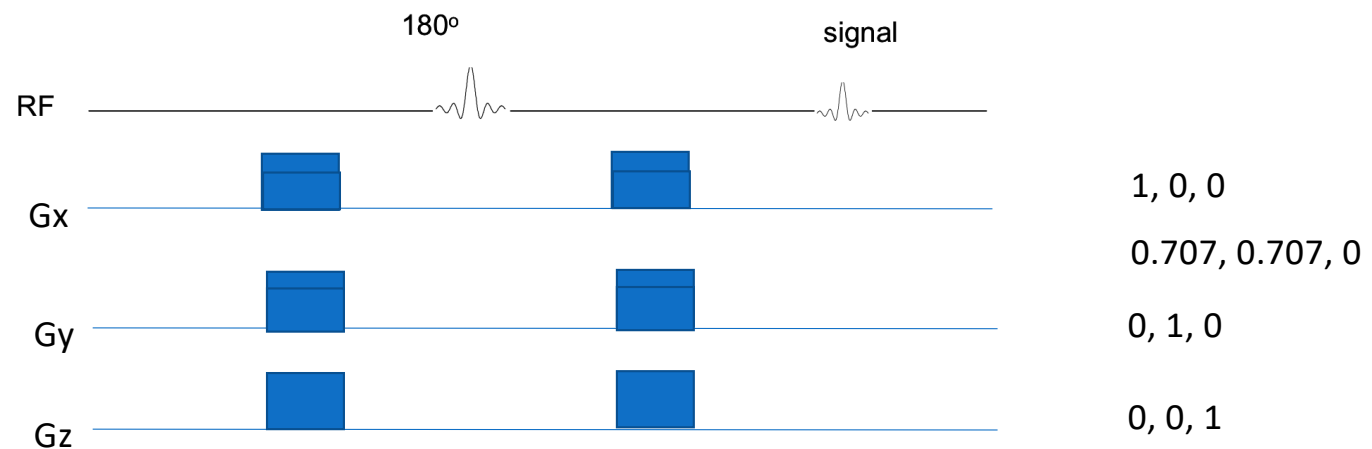
$$\Sigma = 2D_{eff} \cdot \Delta$$



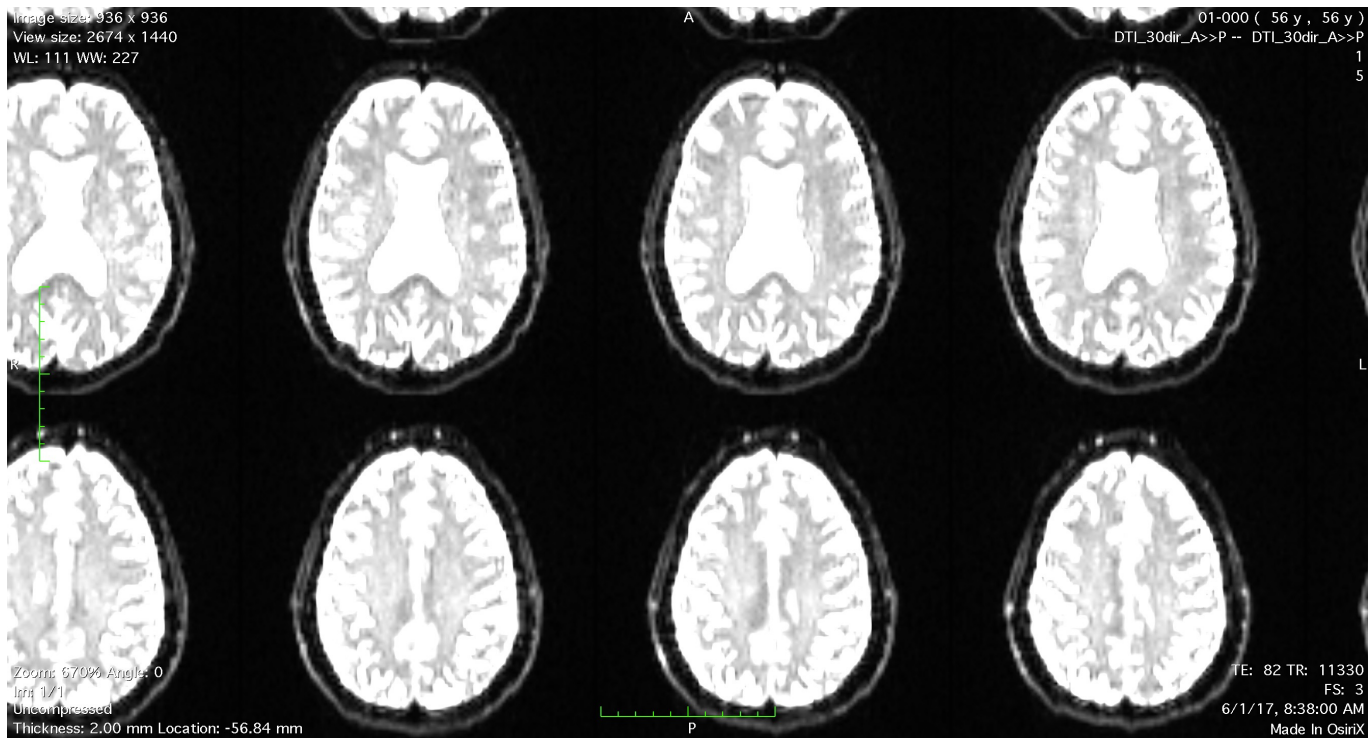
$$\mathbf{D}_{eff} = \begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{pmatrix}$$

Measuring diffusion in multiple directions

$$S(\vec{v}_i)_{i=1,\dots,n} = S_0 \cdot \exp(-b * \vec{v}_i^T \cdot D_{eff} \cdot \vec{v}_i)$$
$$\ln(S(\vec{v}_i))_{i=1,\dots,n} = \ln(S_0) - b * \vec{v}_i^T \cdot D_{eff} \cdot \vec{v}_i$$

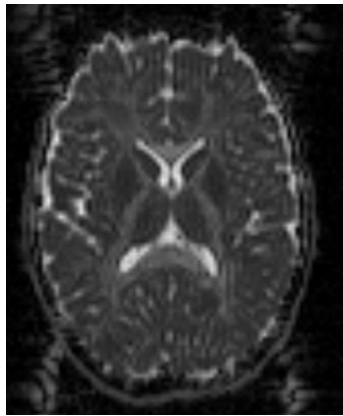


Measuring diffusion in multiple directions

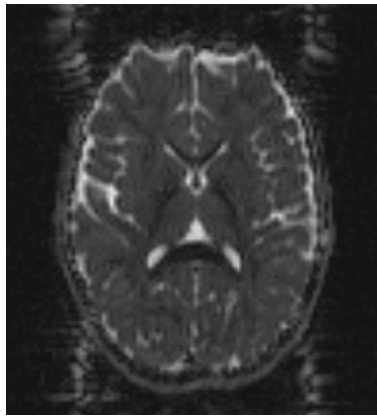


Diagonalization of the Tensor

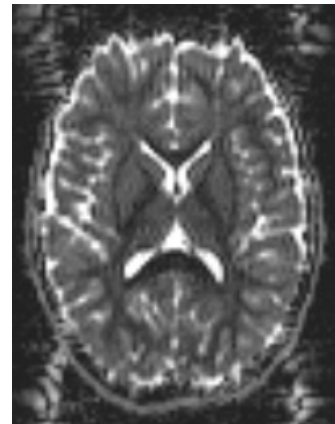
$$\mathbf{D}_{eff} = \begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{pmatrix} = [V_1, V_2, V_3] \cdot \begin{pmatrix} \lambda_1 & & \\ & \lambda_2 & \\ & & \lambda_3 \end{pmatrix} \cdot [V_1, V_2, V_3]^T$$



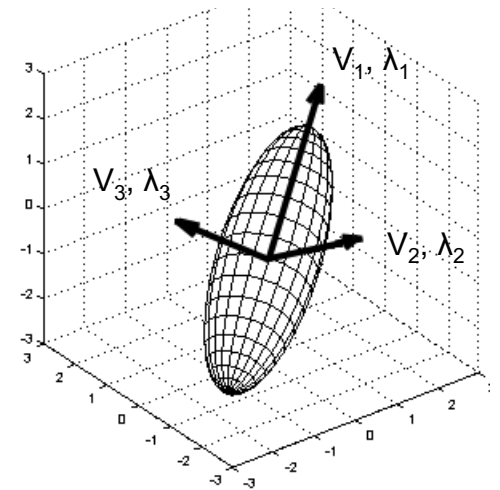
λ_1



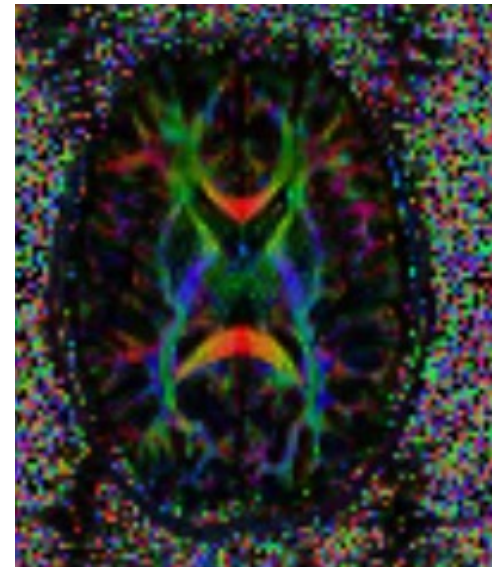
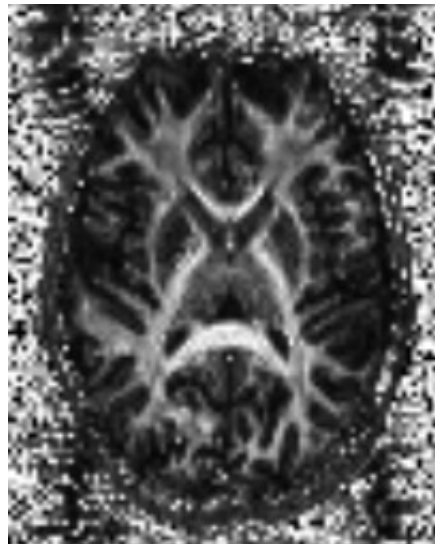
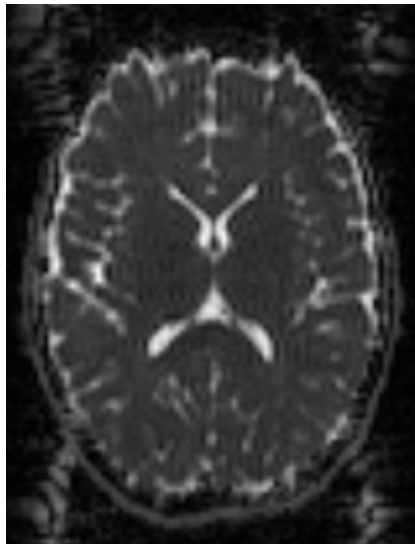
λ_2



λ_3



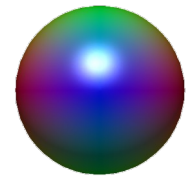
Commonly Used Metrics and Demo



$$MD = \frac{\lambda_1 + \lambda_2 + \lambda_3}{3}$$

$$FA = \frac{\sqrt{\frac{3}{2} \cdot \frac{(\lambda_1 - MD)^2 + (\lambda_2 - MD)^2 + (\lambda_3 - MD)^2}{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}}}{1}$$

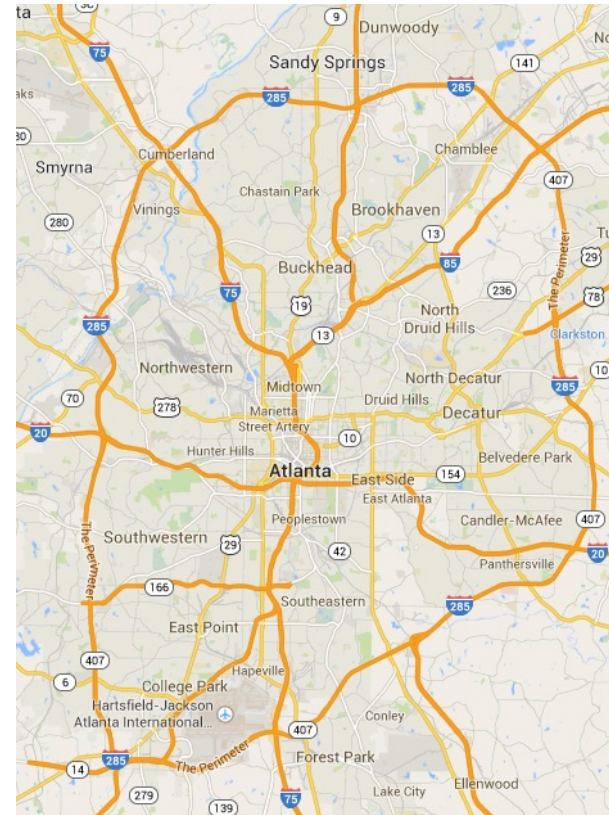
Color FA



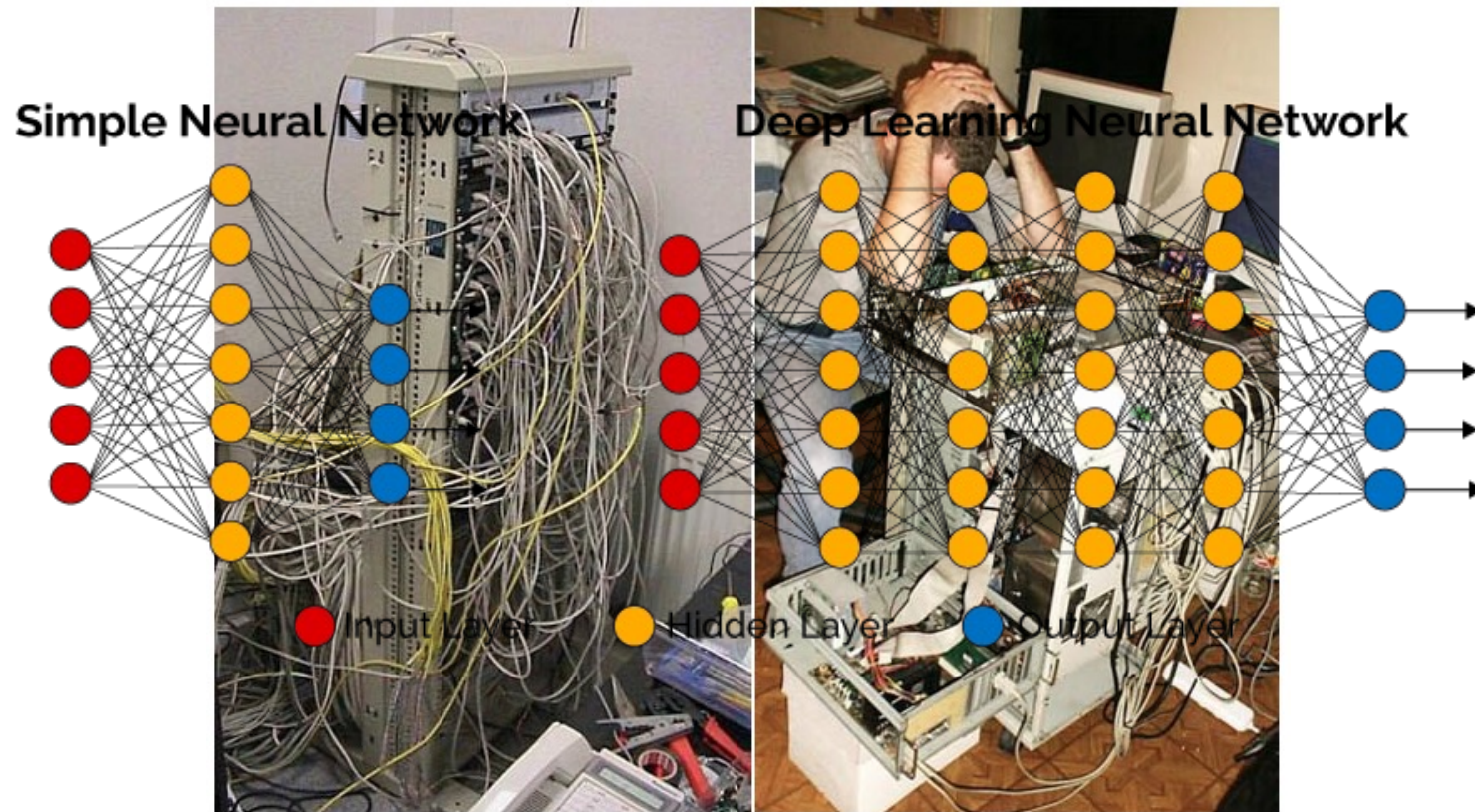
Demo codes

- <https://randomprogram.net/software/Slides/DTI-processing-codes.zip>

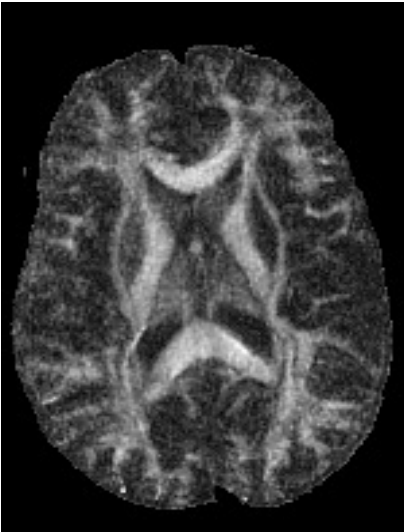
Wiring of the Brain



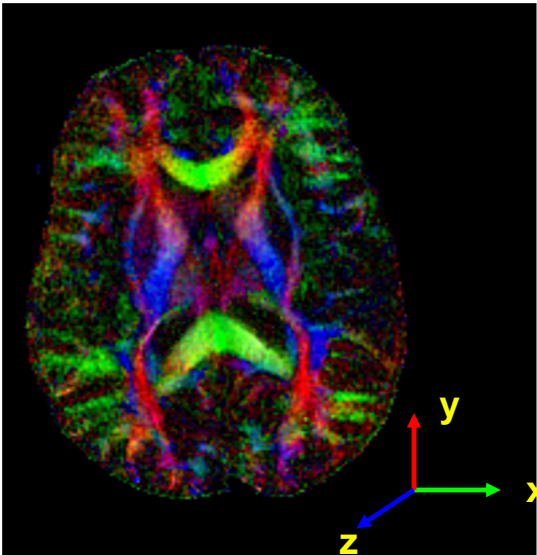
It's all about how things are wired



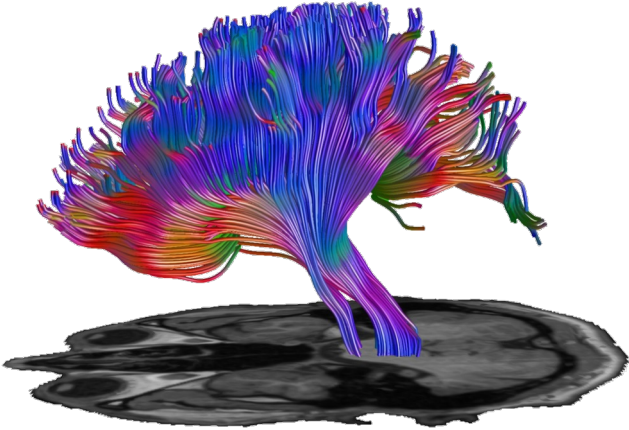
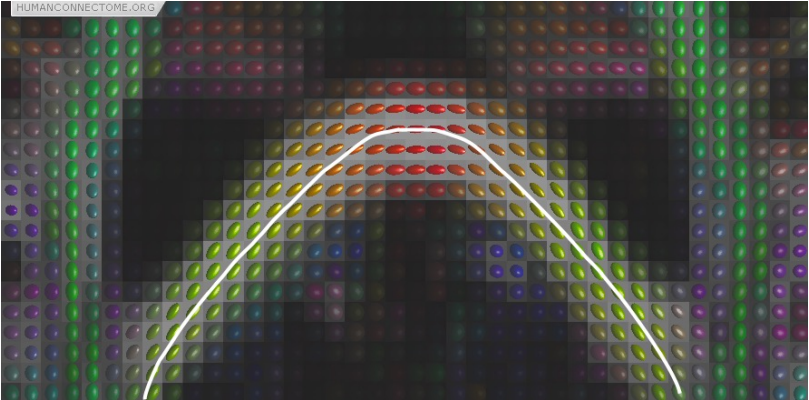
How Do We Show DTI: Tractography!



DTI "FA" map

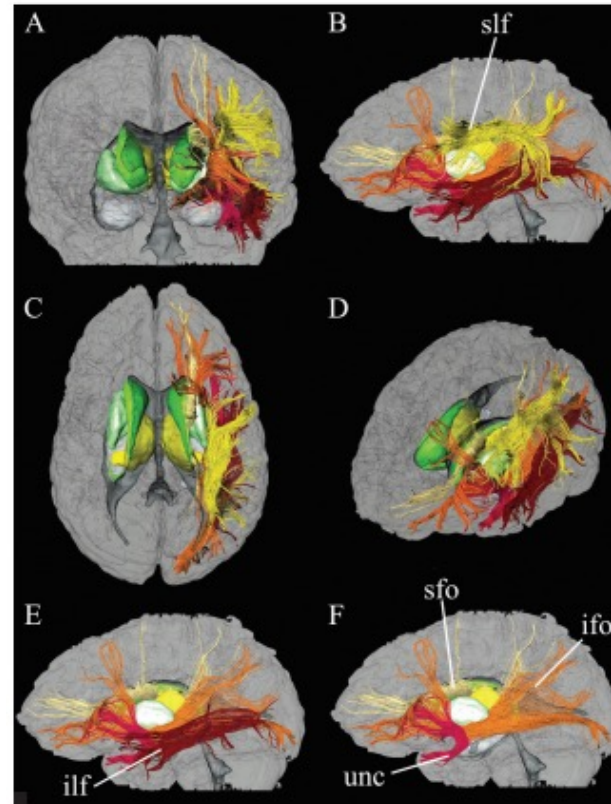
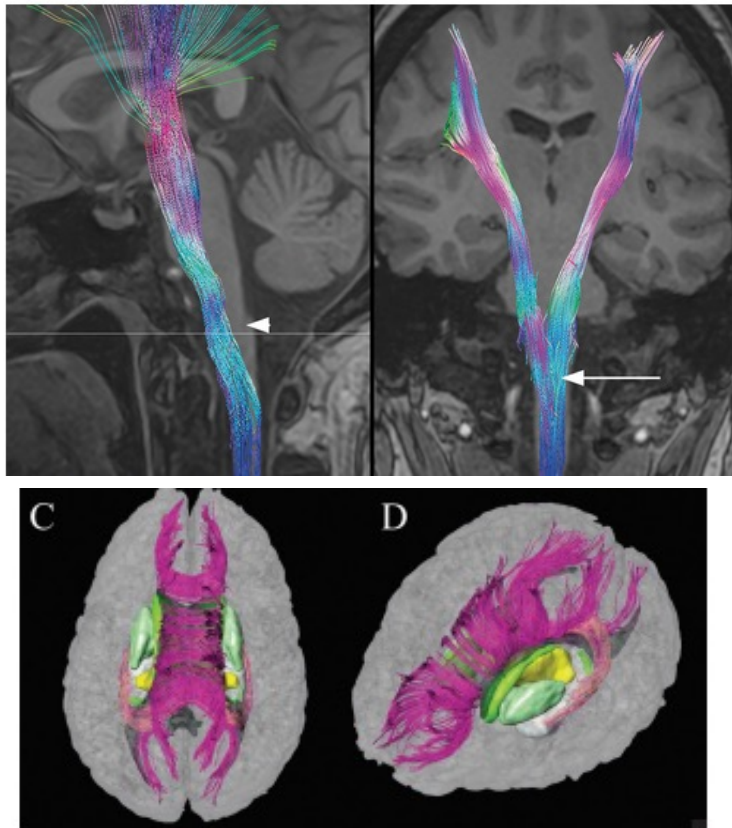


Color "FA" map



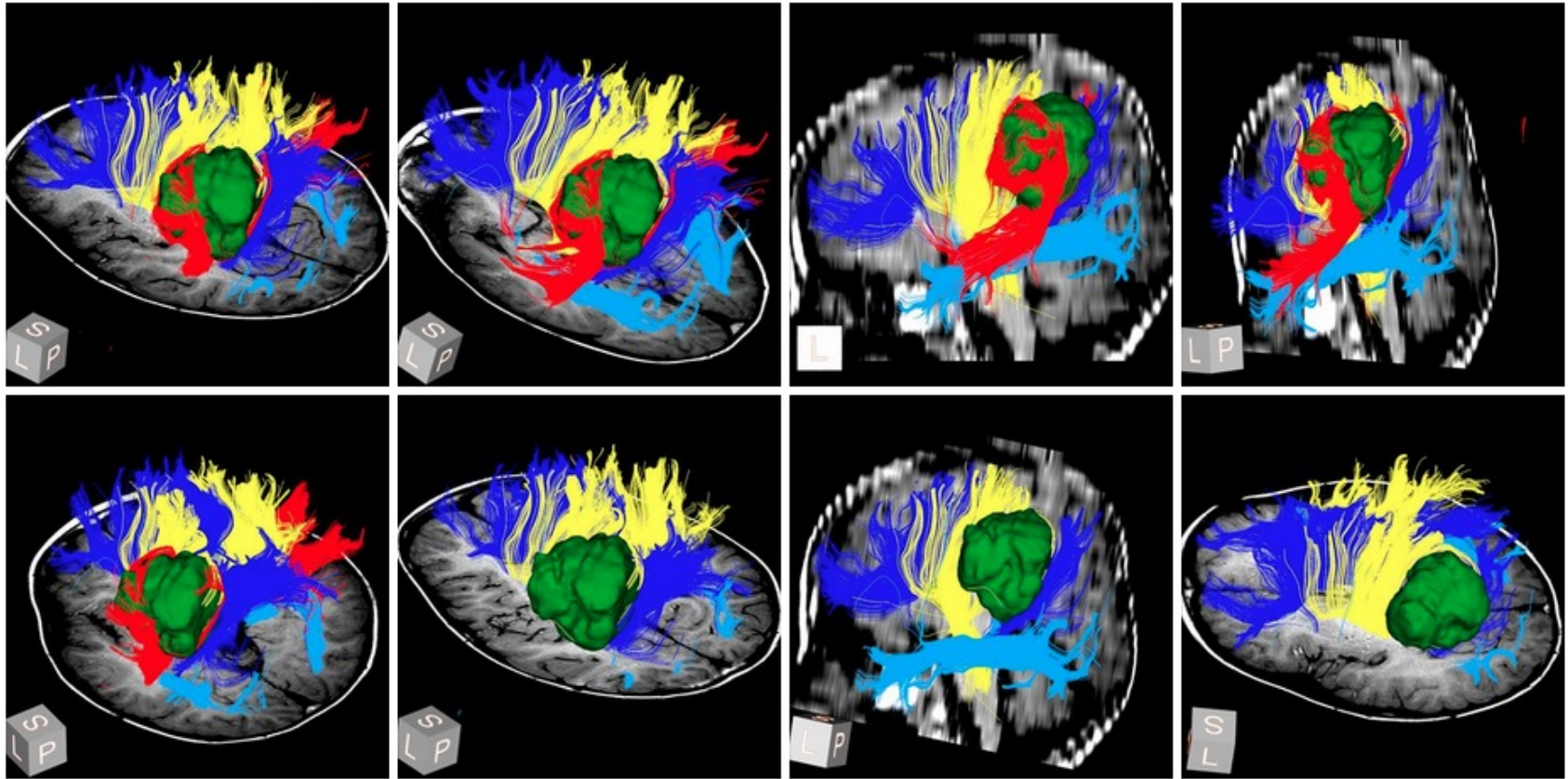
Fiber
Tractography

Major Fiber Systems in the Brain

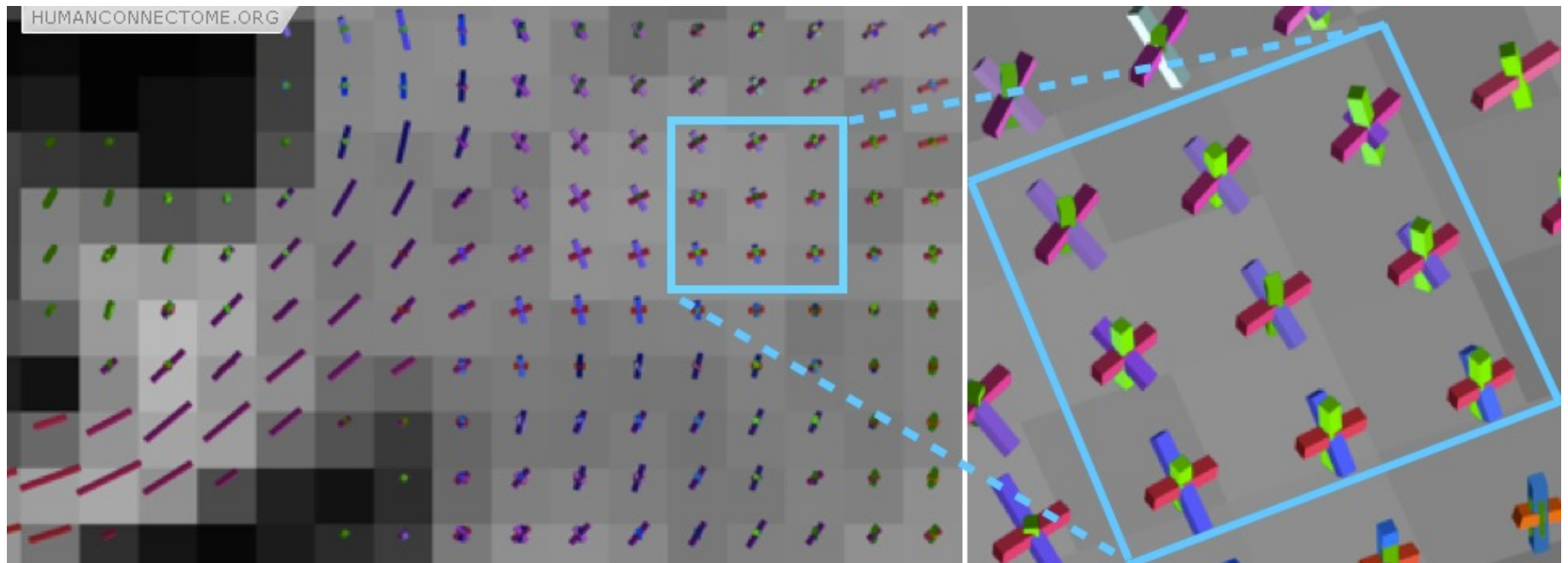


Wakana S. et al. 2003. Radiology

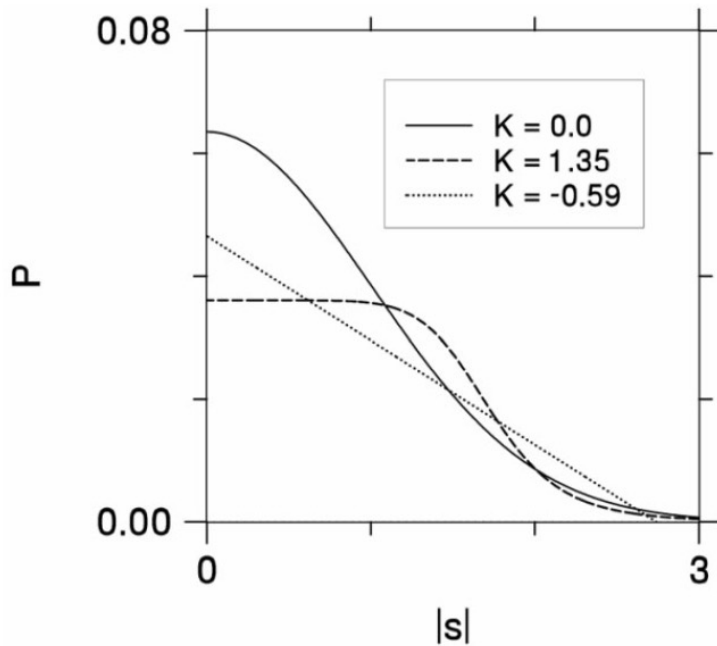
Tractography in Surgery Planning



Crossing Fiber Issue



Pushing to higher order: Diffusion Kurtosis Imaging



$$\ln [S(b)] = \ln [S(0)] - bD_{\text{app}} + \frac{1}{6} b^2 D_{\text{app}}^2 K_{\text{app}} + O(b^3),$$

Jensen JH. et al. 2005. MRM

Mean Diffusivity vs Kurtosis

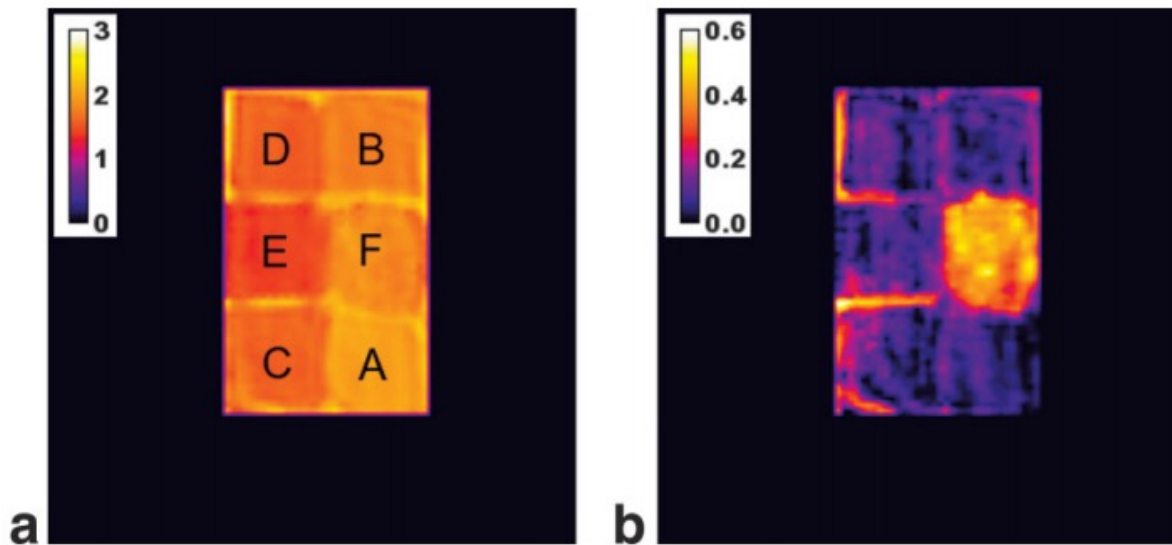
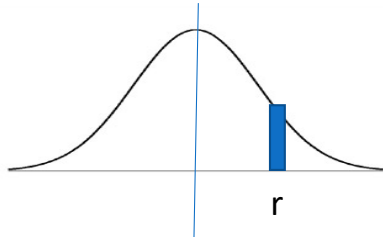


FIG. 5. Parametric maps of the apparent diffusion coefficient (left) and the apparent diffusional kurtosis (right) for the phantom in the slice direction. The scale bar for the diffusion coefficient is in units of $\mu\text{m}^2/\text{ms}$. Bottles a through e contain sucrose solutions with sucrose concentrations ranging from 5 to 25%. Bottle f contains pureed asparagus. The average kurtosis map clearly reveals the higher degree of structure in asparagus bottle, which is not evident in the diffusion coefficient map.

Jensen JH. et al. 2005. MRM

Deriving diffusion weighting equation



$$P(r) = \frac{1}{\sqrt{2\pi}\sigma} \exp\left(-\frac{r^2}{2\sigma^2}\right)$$

$$\sigma = \sqrt{2D \cdot \Delta}$$

$$\varphi(r) = \gamma G \delta r := qr$$

$$S = S_0 \cdot \int P(r) \cdot \exp(i\varphi(r)) dr$$

$$= \int \frac{\exp\left(-\frac{r^2}{2\sigma^2}\right)}{\sqrt{2\pi}\sigma} \exp(iqr) dr$$

$$= \int \frac{\exp\left(-\frac{r^2}{2\sigma^2} + iqr\right)}{\sqrt{2\pi}\sigma} dr$$

$$= \int \frac{\exp\left(-\frac{(r - iq\sigma^2)^2}{2\sigma^2} - \frac{q^2\sigma^4}{2\sigma^2}\right)}{\sqrt{2\pi}\sigma} dr$$

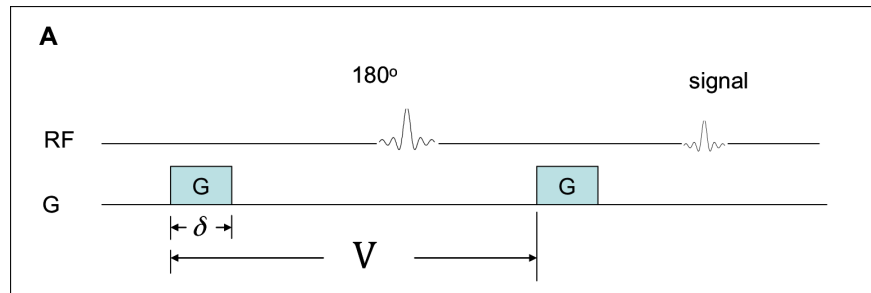
$$= \exp\left(-\frac{q^2\sigma^2}{2}\right) \int \frac{\exp\left(-\frac{(r - iq\sigma^2)^2}{2\sigma^2}\right)}{\sqrt{2\pi}\sigma} dr$$

$$= \exp\left(-\frac{q^2\sigma^2}{2}\right) \int_{-\infty+iq\sigma^2}^{+\infty+iq\sigma^2} \frac{\exp\left(-\frac{r^2}{2\sigma^2}\right)}{\sqrt{2\pi}\sigma} dr$$

$$= \exp(-\gamma^2 G^2 \delta^2 \Delta D)$$

$$b = \gamma^2 \int_0^{TE} \left(\int_0^t G(t') \cdot \text{Sign}\left(t' - \frac{TE}{2}\right) dt' \right)^2 dt$$

Q-Space Imaging: 1-D



$$q = \gamma G \delta$$

$$S(q) = \int \exp(iqx) \cdot p(x) dx$$

Diffusion Propagator p

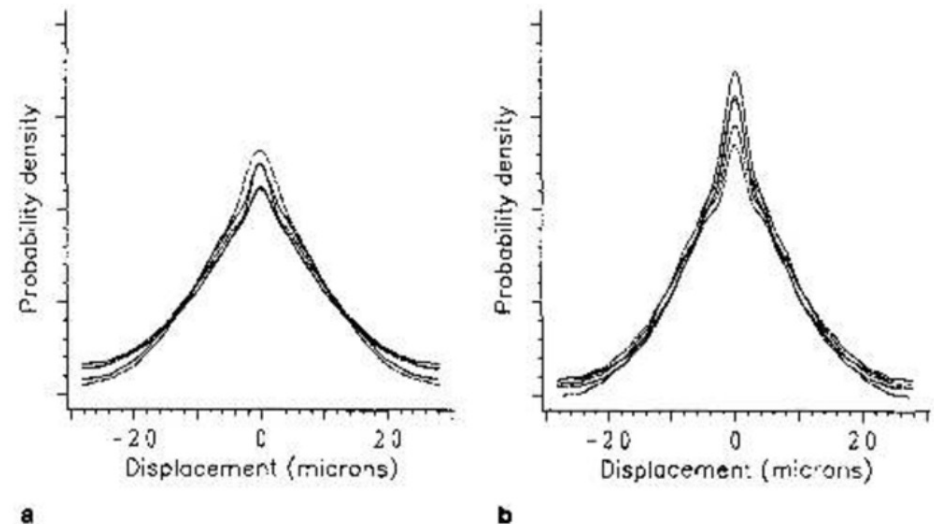
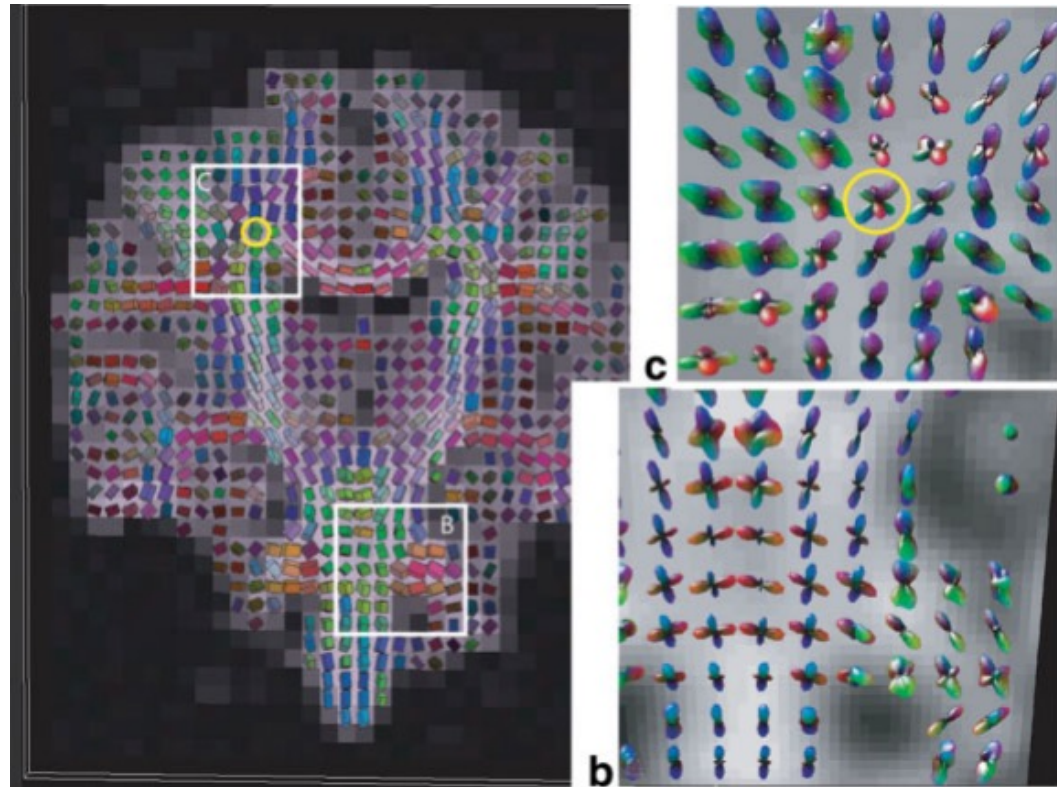
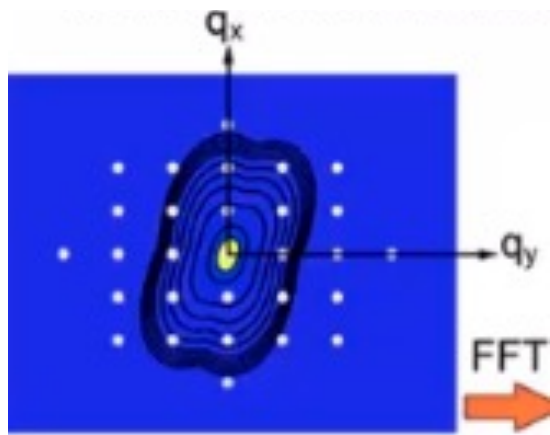


Fig. 2. Brain water displacement profiles. The profiles obtained from five normal animals are shown Fig. 2a, and those acquired 1 h *postmortem* in Fig. 2b. The diffusion period was 101 ms in duration.

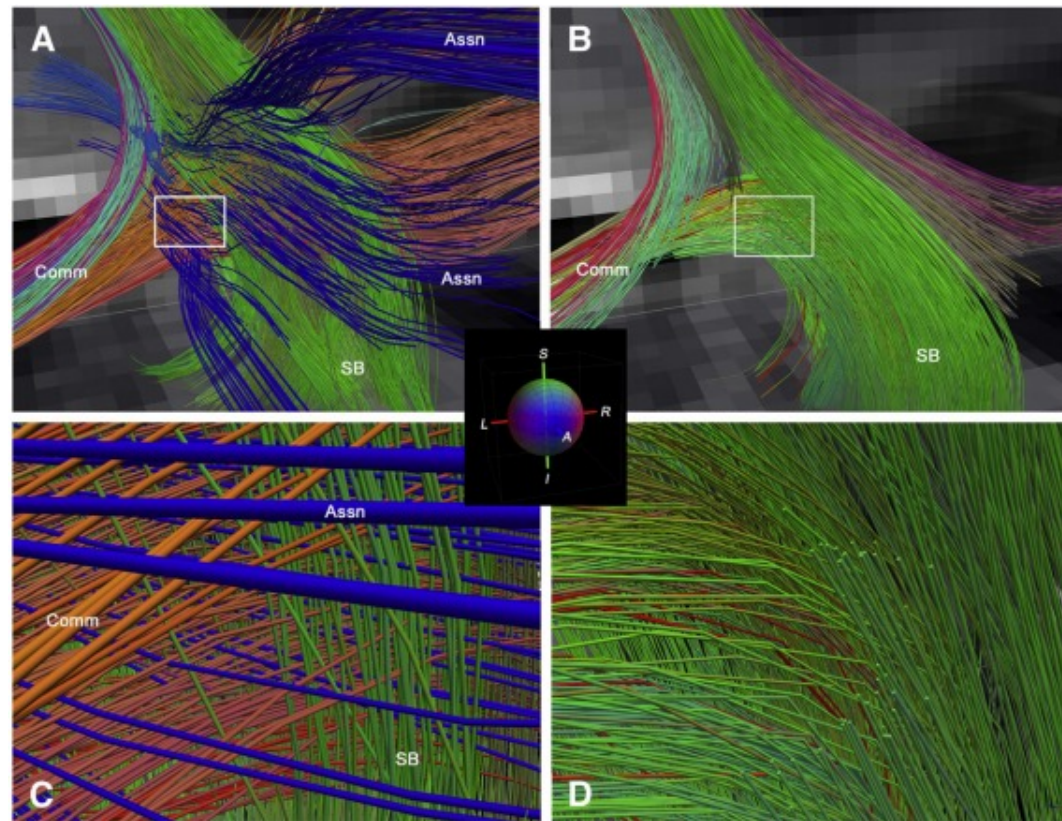
King M. 1994. MRM

Diffusion Spectrum Imaging



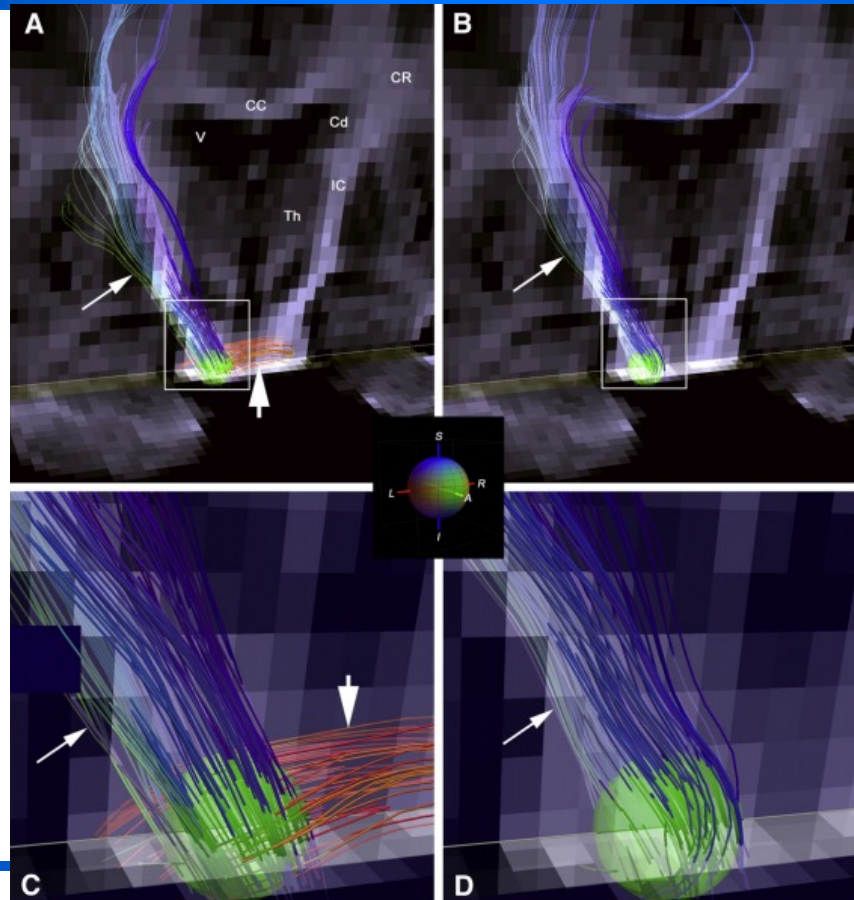
Wedeen V. 2005. Neuroimage

Diffusion Spectrum Imaging



Wedeen V. 2008. Neuroimage

Diffusion Spectrum Imaging



Other Advanced Methods

- Q-Ball Imaging
- Multi-Tensor Model
- High Order Tensor
- ...

Tuch D. 2004. MRM

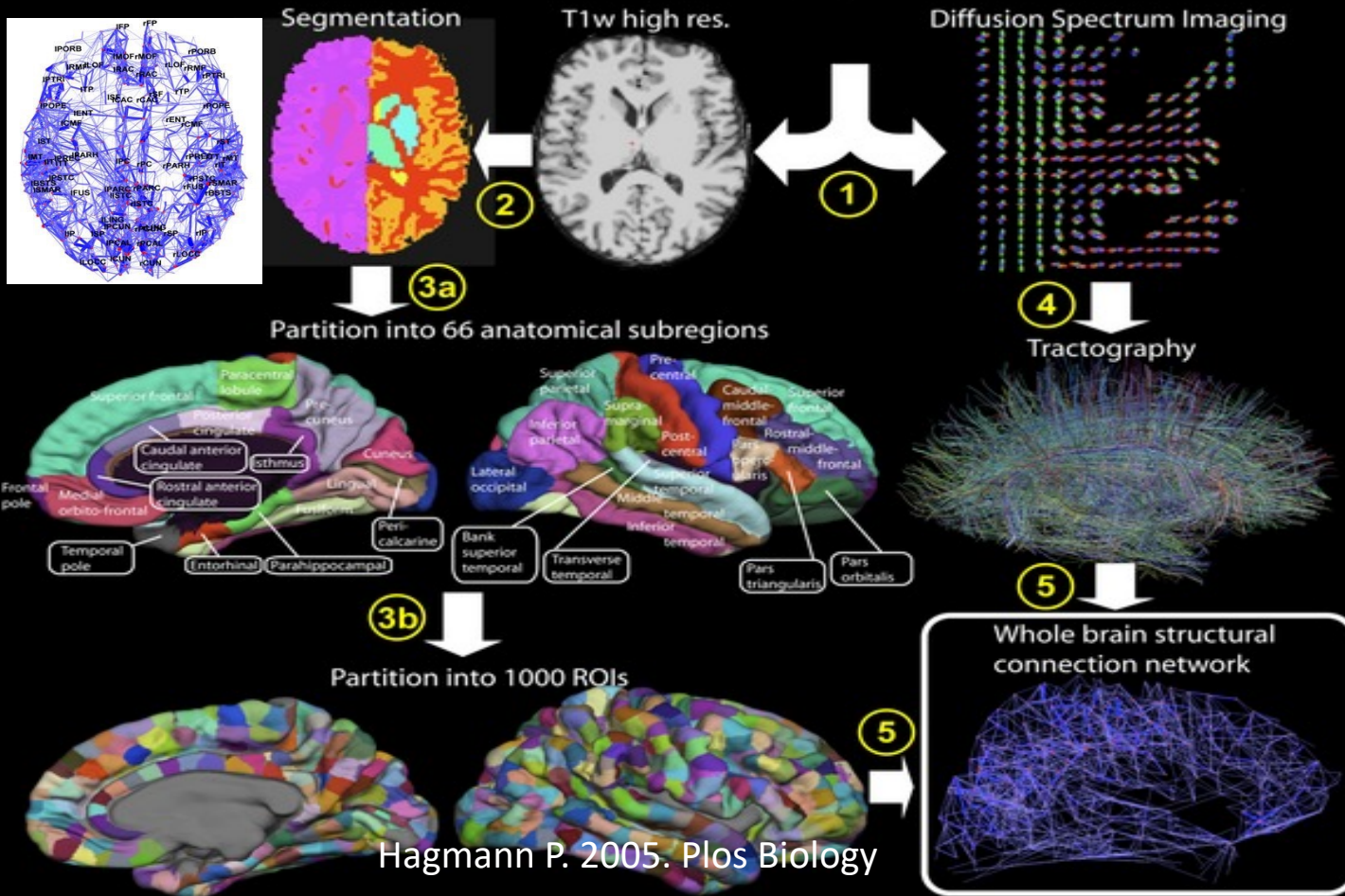
Liu C. 2010. MRM

Schultz T. 2010.

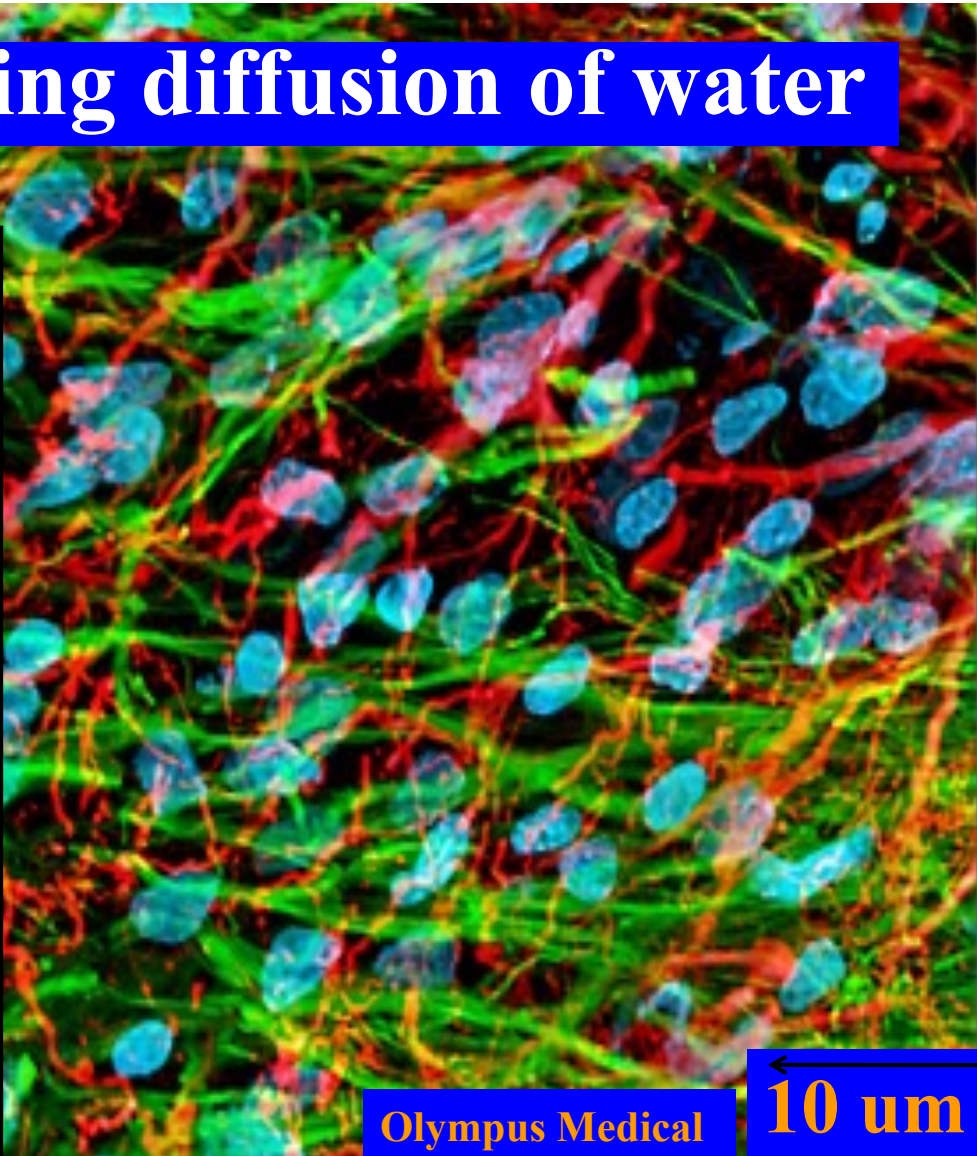
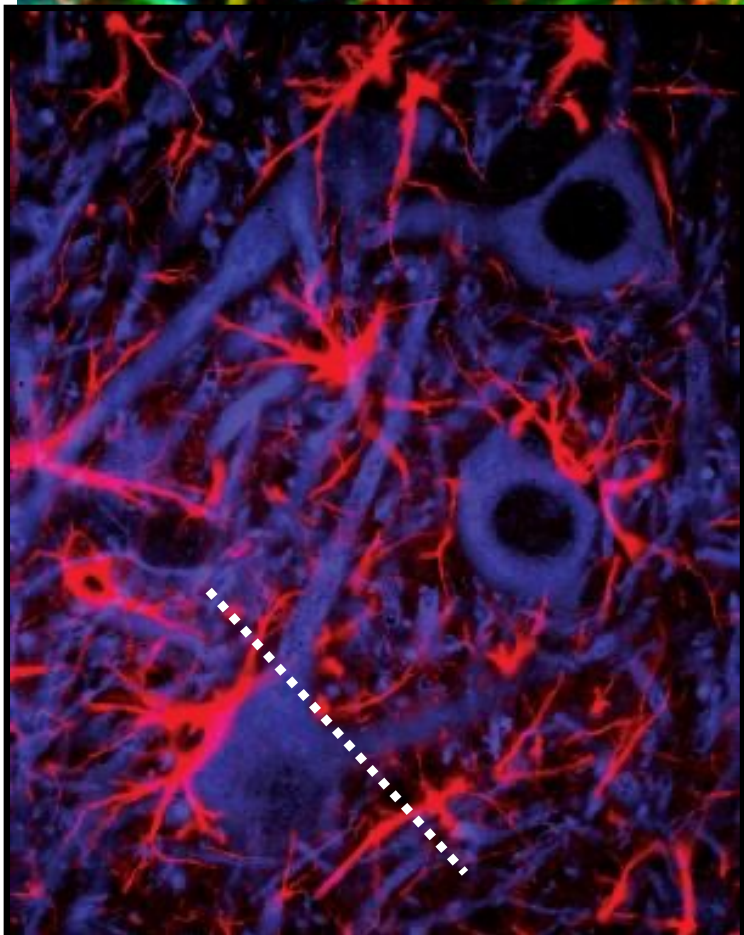
Med Image Comput Comput Assist Interv.

The Connectome

MRI Acquisition



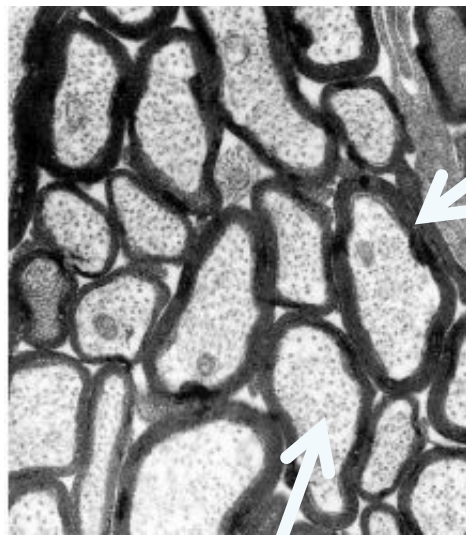
What's effecting diffusion of water



Olympus Medical

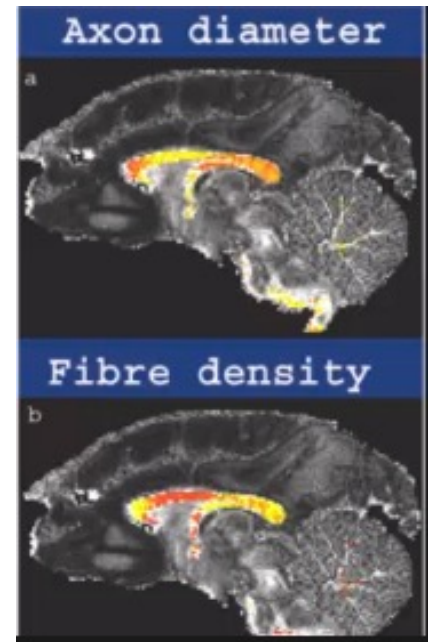
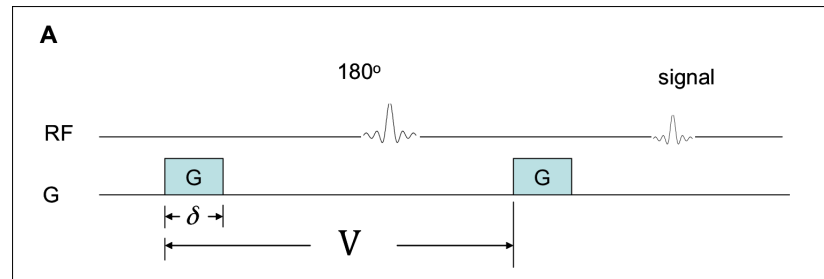
10 um

Microstructure Imaging with Diffusion



Axon

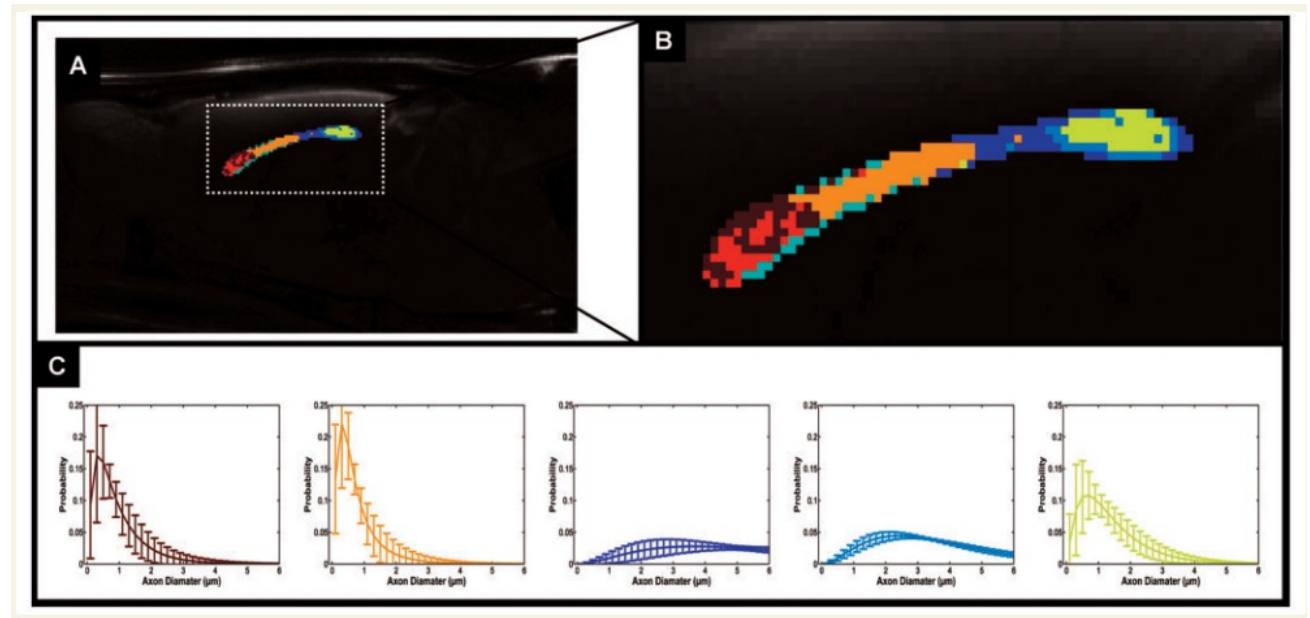
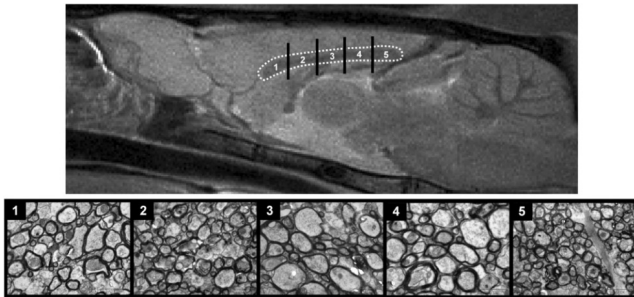
Myelin



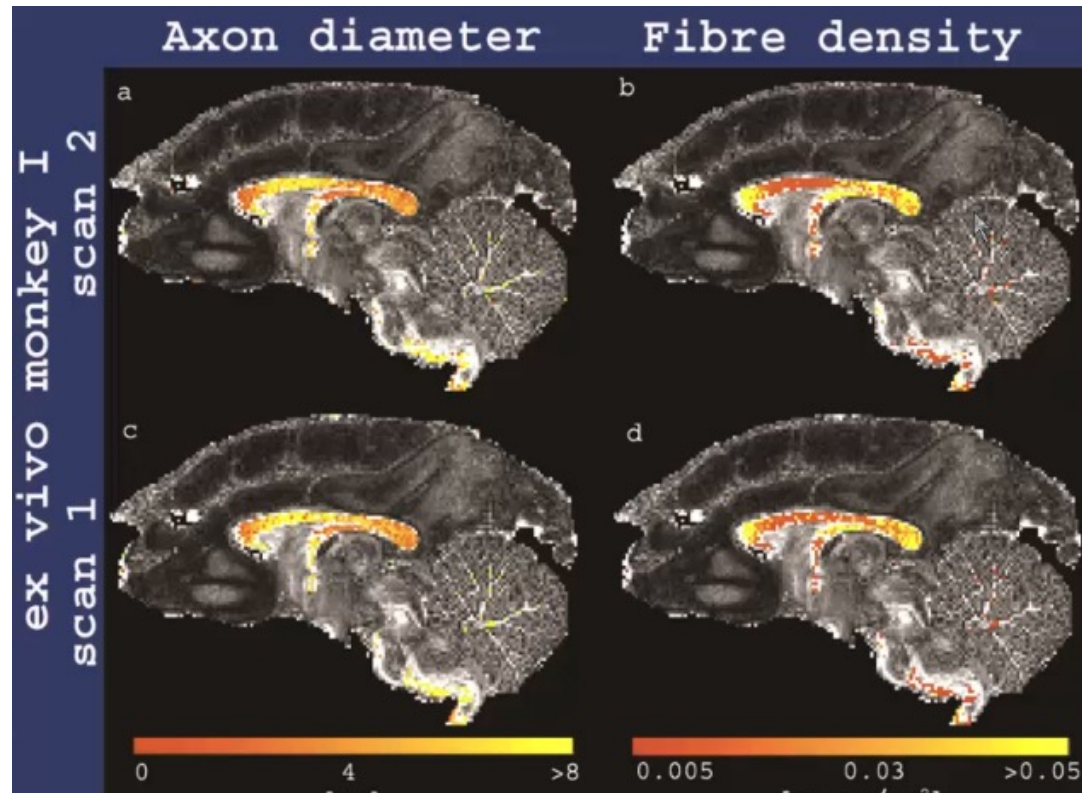
Alexander Neuroimage 2010

AxCalib (Barazany Brain 2009)

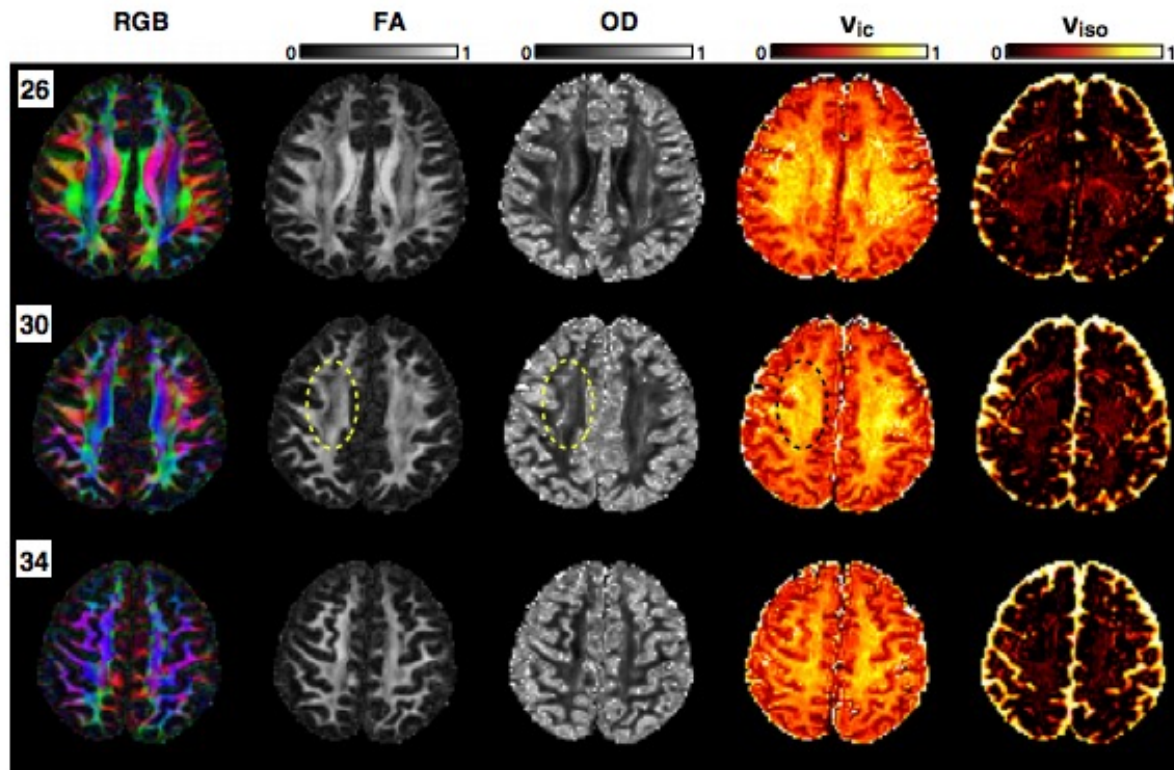
$\delta=3.2\text{ms}$
 $\Delta=\{11,20,30,60,100\}\text{ms}$



ActiveAx Alexander Neuroimage 2010



NODDI:



Zhang H. et al. 2012 NeuroImage

Other important topics not covered

- Multi-shot diffusion MRI sequence
- Eddy-current induced distortion
- Double-refocused spin echo for reducing eddy-current distortion
- Other diffusion sensitizing approach
 - Stimulated echo-based diffusion weighting

Thank You

- dqiu3@emory.edu