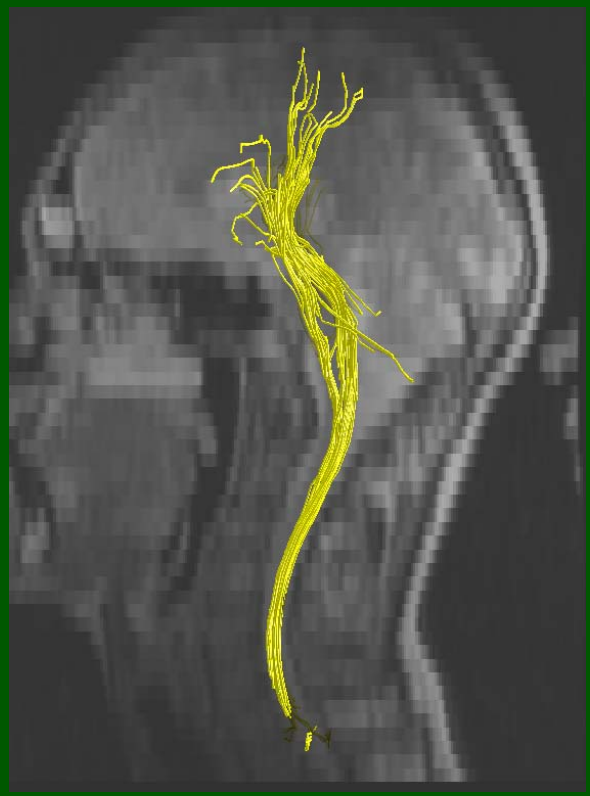
Understanding functional connectivity of the brain: Diffusion tensor magnetic resonance imaging



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WIAS, June 27, 2005

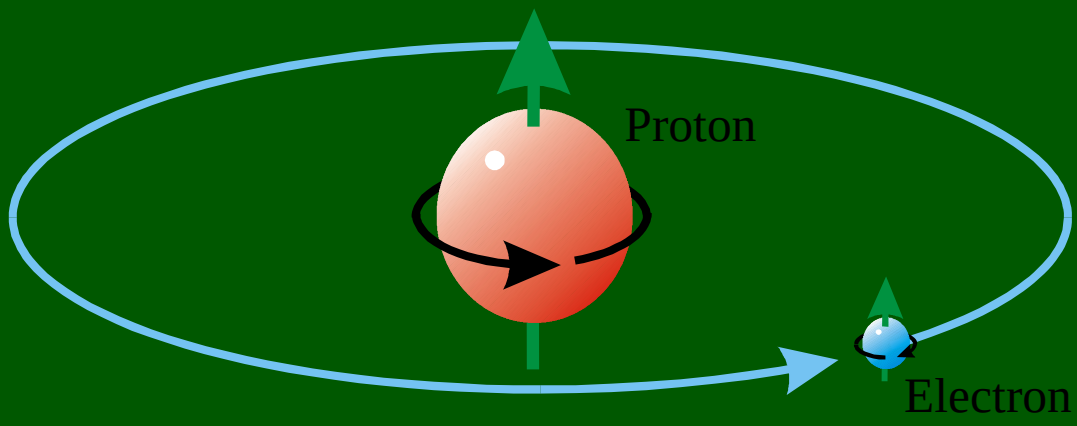
Introduction

- The MRI experiment
- Diffusion weighted/tensor imaging
- Fiber orientation mapping and fiber tracking
- Applications at Cornell Medical College
- White matter fiber tracking in inferior brain regions and cervical spinal cord
- Fiber crossings and non-Gaussian diffusion

The MRI experiment

“There is nothing that nuclear spins will not do for you, as long as you treat them as human beings"

(Erwin L. Hahn 1949)


Proton
Electron

Larmor equation

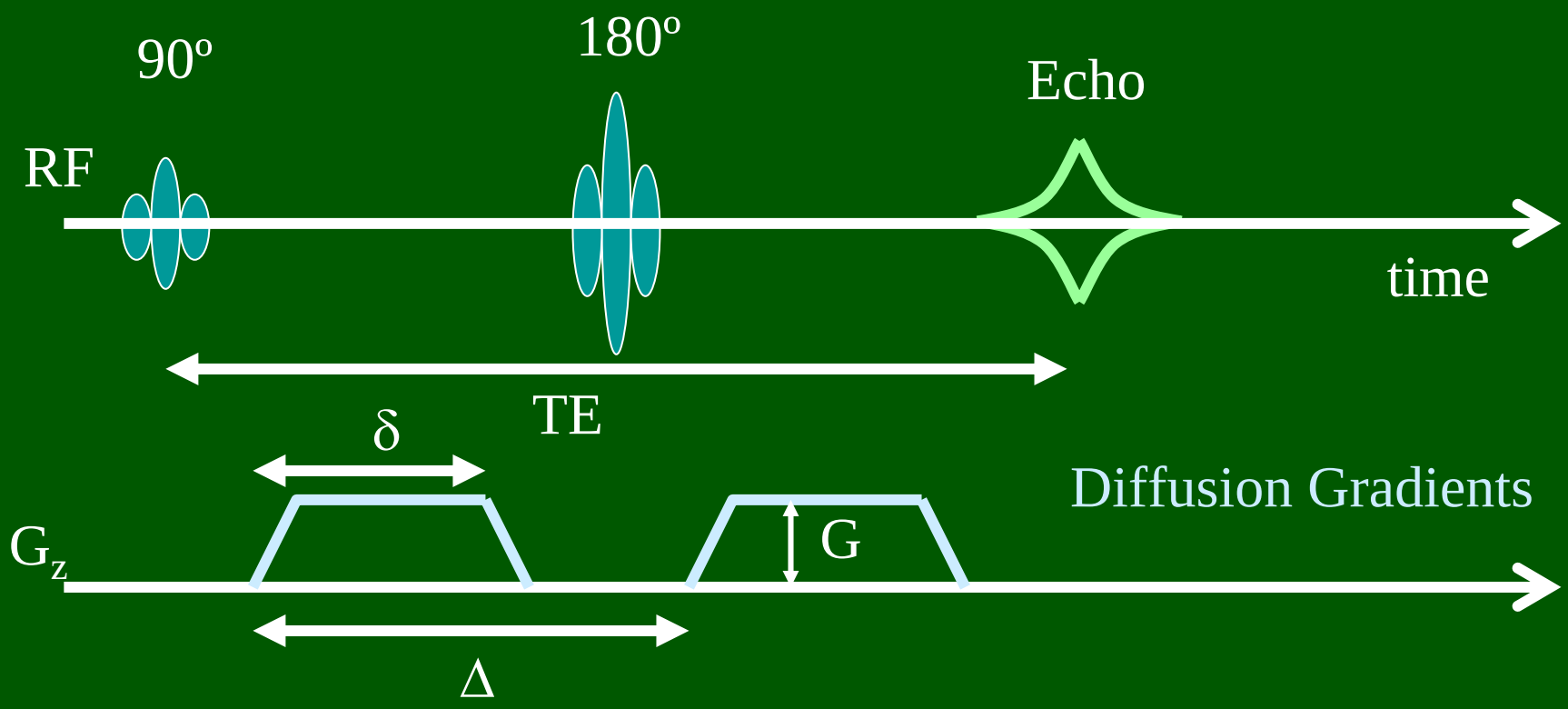
$$\omega_0 = \gamma B_0$$

Constant gradients in object:

$$\omega\,(x,y,z) = \gamma\,(B_0 + \text{grad}\ B * (x,y,z))$$

Diffusion weighted imaging (DWI)

Bipolar pulse field gradient method



R. Watts 2004

Theory

- Rigorous approach:

  Add diffusion term to Bloch equations: Bloch-Torrey equation
- More convenient approach:

  Start with probability distribution of spins and use diffusion equation

1-D approach to keep the math simple:

δ = length of diffusion gradients

Δ = duration of diffusion gradients

$P(z)$ = probability distribution

$P(z_2,z_1,\Delta)$ = propagator: probability that after a time Δ the spins are at z_2 when they were at z_1 before

Assume $\delta << \Delta$, then

First gradient: dephasing $\Phi_1 = \gamma \int_0^{\delta} Gz_1 dt = \gamma G z_1 \delta$

2nd gradient: dephasing $\Phi_2 = \gamma \int_{\Delta}^{\Delta+\delta} Gz_2 dt = \gamma G z_2 \delta$

Net dephasing $\Phi_2 - \Phi_1 = \gamma G \delta (z_2 - z_1)$

Taking into account the conditional probability (propagator) that after a time Δ the spins are at z_2 when they were at z_1 before, the signal is

$$S = S_0 \int dz_1 P(z_1) \int \exp(i\gamma\delta G(z_2 - z_1)) P(z_2, z_1, \Delta) dz_2 \qquad (*)$$

Isotropic diffusion process:

$$\partial P(z_2, z_1, t) / \partial t = D \Delta P(z_2, z_1, t) \qquad (**)$$

P is Gaussian at t=Δ:

$$P(z_2, z_1, \Delta) = (4\pi\Delta D)^{-1/2} \exp(-(z_2 - z_1)^2 / 4\Delta D)$$

[Can be checked by re-insertion into (**), homework]

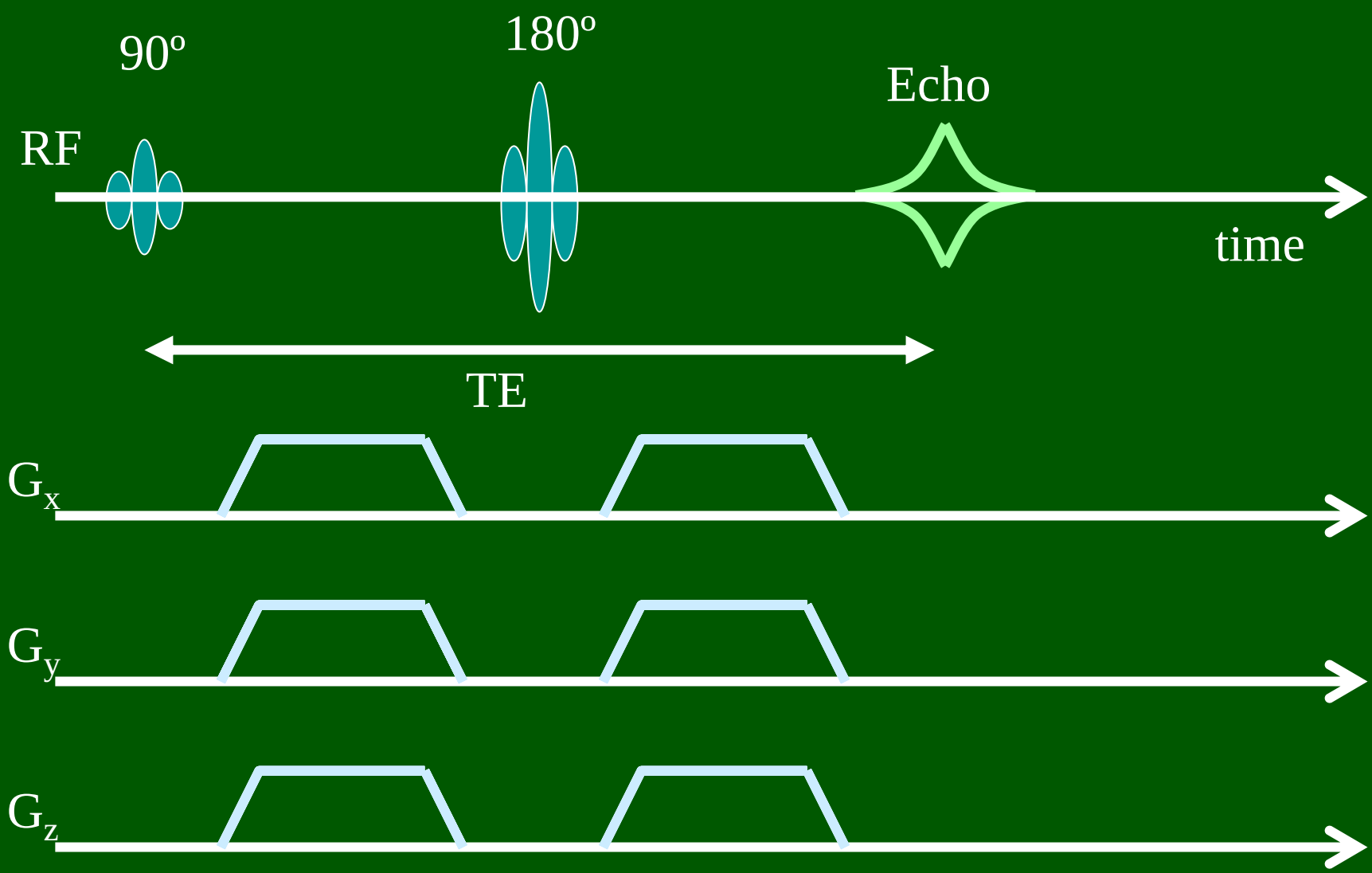
Combining this with (*), and using Einstein's law $\langle z^2 \rangle = 2Dt$, we obtain

$$S \propto \exp(-(\gamma \delta G)^2 \Delta D) = \exp(-(\gamma \delta G)^2 < z^2 > / 2)$$

[requires integration in the complex domain, not trivial, refer to integral table]

- We only consider lumped parameter model
  $S = S_0 \exp(-bD)$,
  where b is the b-value, fixed in experiment by
- Stejskal-Tanner equation: $b = (g\gamma\delta)^2(\Delta - \delta/3)$
- Example:
  b = 1000 s/mm^2,
  D = 0.003 mm^2/s in water at 37^o C:
  Signal drops about 95% as compared with the
  b = 0 (T2-weighted) image

Diffusion tensor imaging



R. Watts 2004

Anisotropic attenuation

- Remember: One dimensional lumped parameter model: $S = S_0 \, exp \, (-bD)$
- Now: Directionality dependence

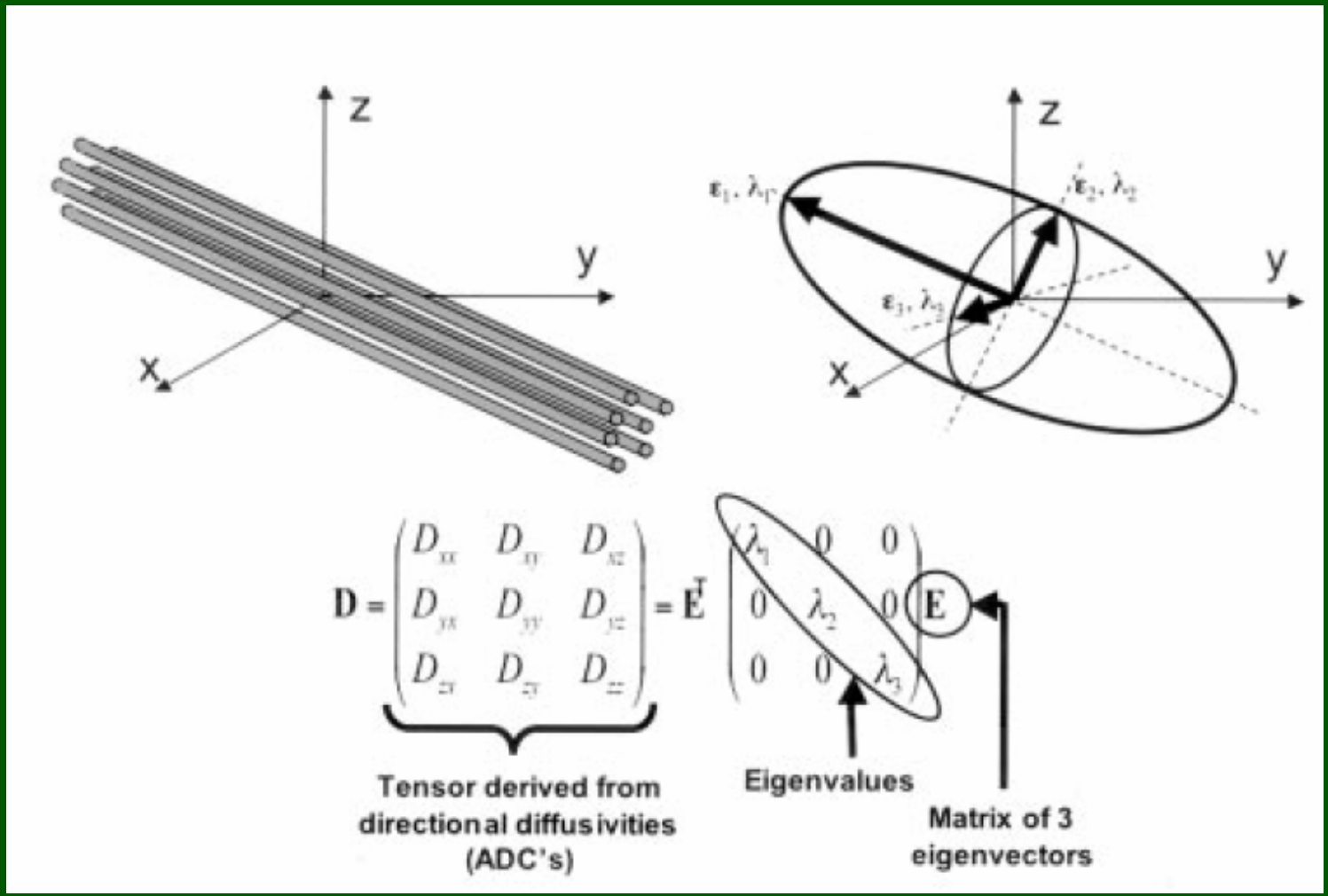
  $S = S_0 \, exp \, (- \, b \, \mathbf{g}^t \, D \, \mathbf{g})$,

  where **g** is a vector containing the diffusion gradient direction,

  and *D* is the diffusion ***tensor***

S_0 S_1 S_2 S_3 S_4 S_5 S_6
$\mathbf{g}_0 = \begin{pmatrix} 0 \\ 0 \\ 0 \end{pmatrix}$ $\mathbf{g}_1 = \begin{pmatrix} 1 \\ 1 \\ 0 \end{pmatrix}$ $\mathbf{g}_2 = \begin{pmatrix} 0 \\ 1 \\ 1 \end{pmatrix}$ $\mathbf{g}_3 = \begin{pmatrix} 1 \\ 0 \\ 1 \end{pmatrix}$ $\mathbf{g}_4 = \begin{pmatrix} 0 \\ 1 \\ -1 \end{pmatrix}$ $\mathbf{g}_5 = \begin{pmatrix} 1 \\ -1 \\ 0 \end{pmatrix}$ $\mathbf{g}_6 = \begin{pmatrix} -1 \\ 0 \\ 1 \end{pmatrix}$

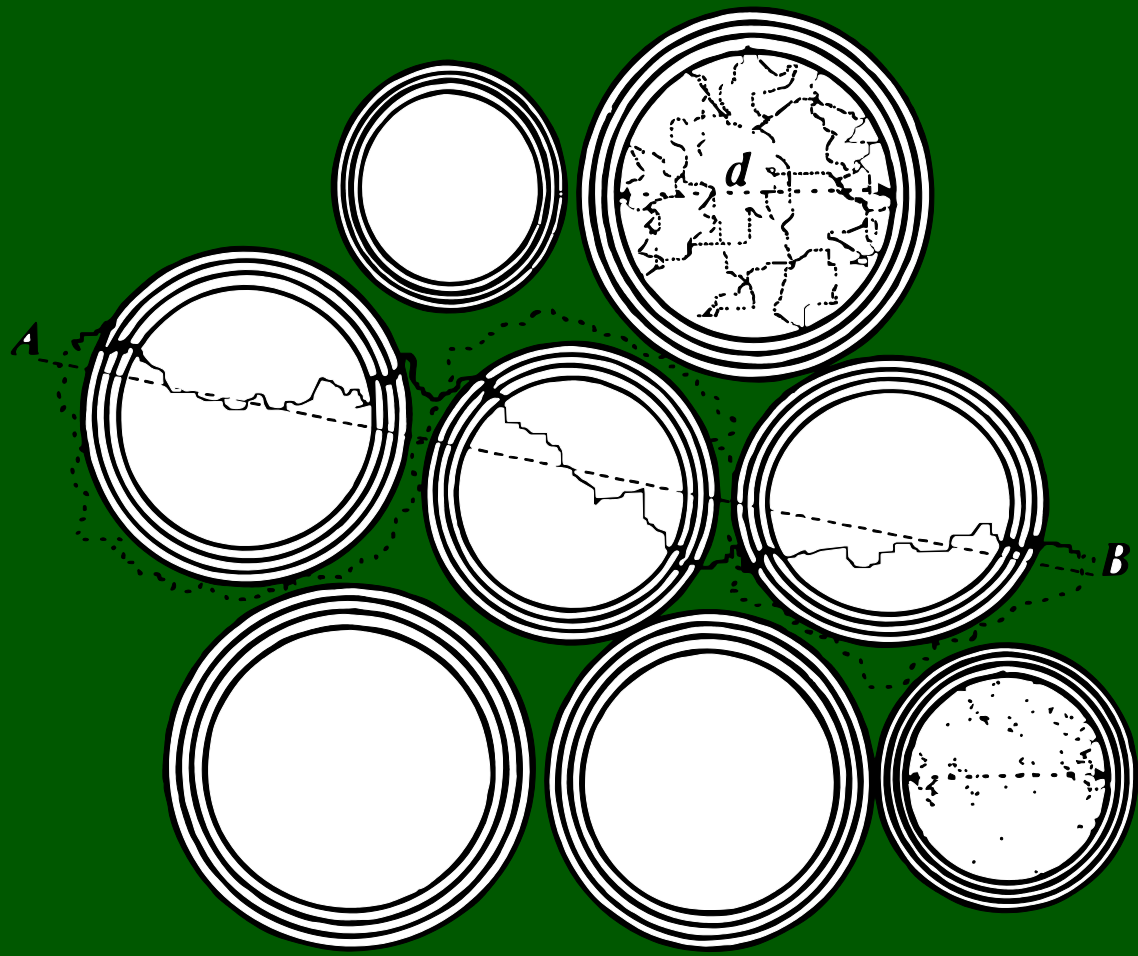
The diffusion tensor



Jellison 2004

What is measured?

Restricted, permeable barrier, hindered diffusion?



D. Le Bihan 1995

How many measurements?

- One needs to measure the symmetric diffusion tensor and a *b=0* weighted image
- 6+1=7 measurements
- It has been shown that more = better: 6 icosahedral directions are not rotationally invariant (precision matrix contains 15 indep. parameters and depends on tensor itself)

Fiber orientation mapping

Some invariants (not depending on angle of coordinate system):

Mean diffusivity = $tr(D)/3 = (D_{xx}+D_{yy}+D_{zz})/3$

Fractional anisotropy =

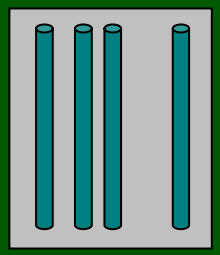
$[\ 3\{(\lambda_1-\Lambda)^2+(\lambda_2-\Lambda)^2+(\lambda_3-\Lambda)^2\} / \{2(\lambda_1^2+\lambda_2^2+\lambda_3^2)\}\ ]^{1/2}$

with $\Lambda=(\lambda_1+\lambda_2+\lambda_3)/3$

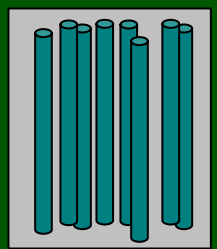
Interpreting Diffusivity and FA

Diffusivity and FA help determine the **number**, **size** and **myelination** of fibers, whereas only FA gives information about **directionality**.

Number of fibers

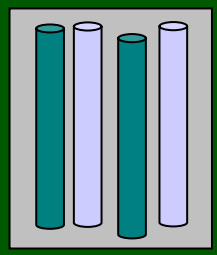


High Diffusivity
Low FA

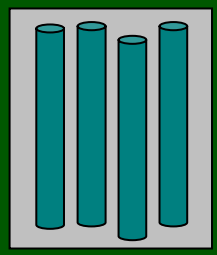


High FA
Low Diffusivity

Myelination of fibers

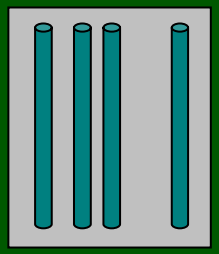


High Diffusivity
Low FA

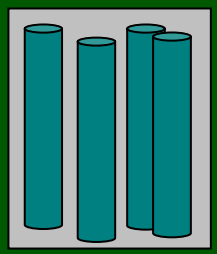


High FA
Low Diffusivity

Size of fibers

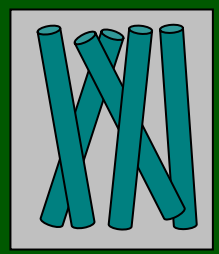


High Diffusivity
Low FA

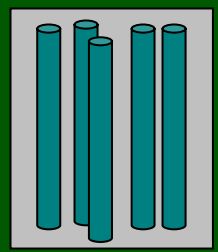


High FA
Low Diffusivity

Directionality of Fibers

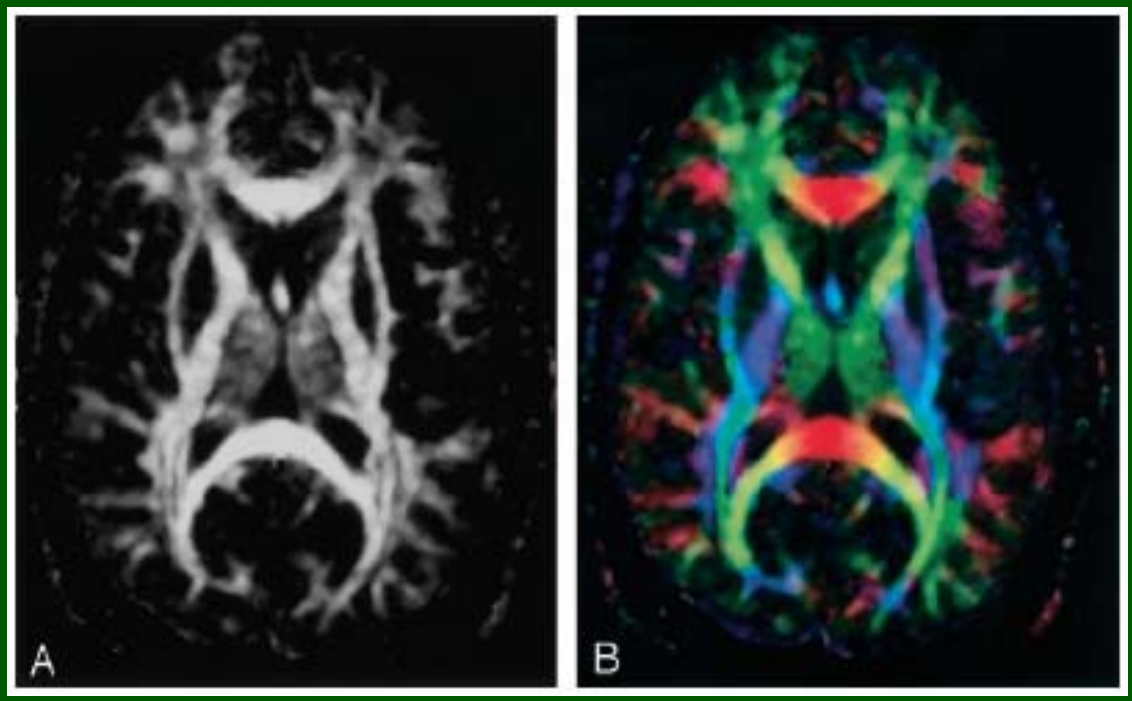


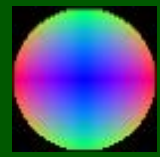
Low FA
Same Diffusivity



High FA
Same Diffusivity

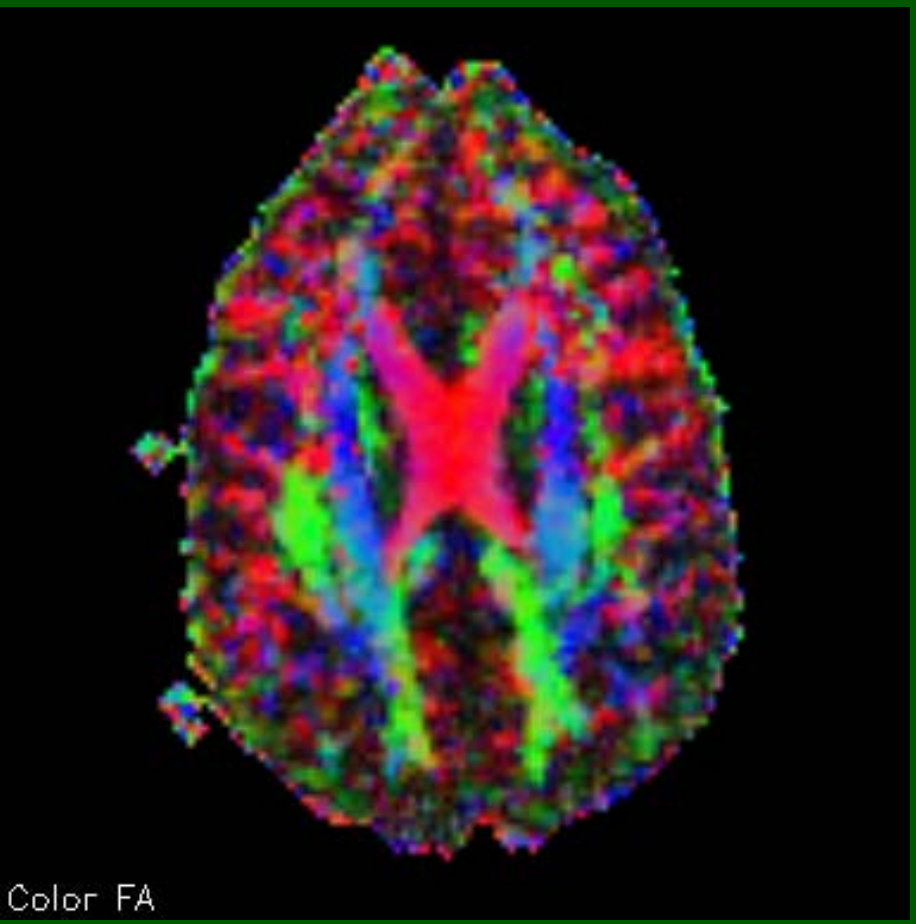
S. Maier and M. Kubicki
http://www.na-mic.org/

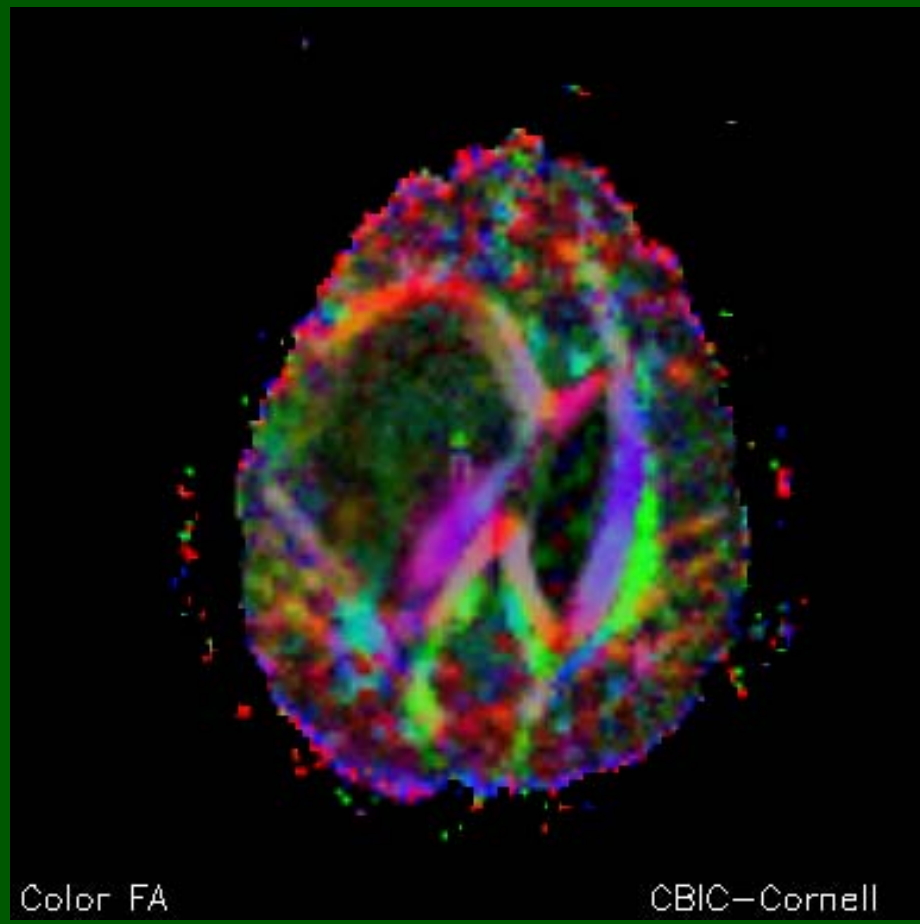




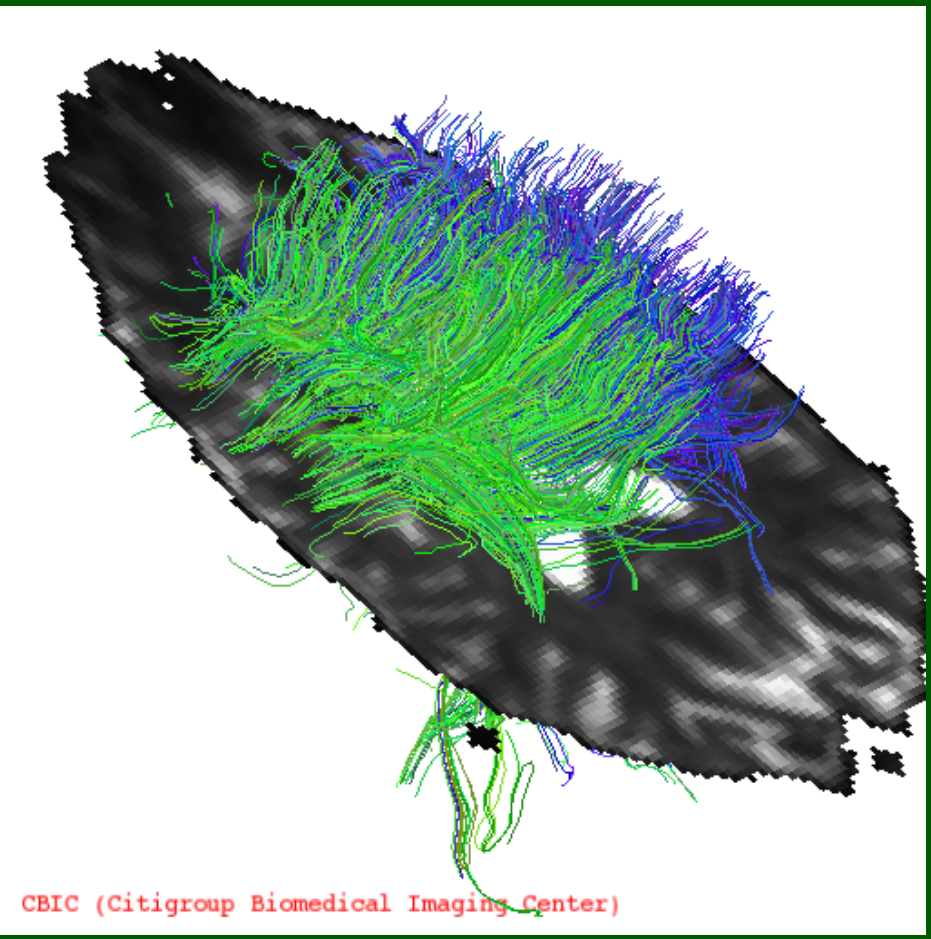
Jellison 2004

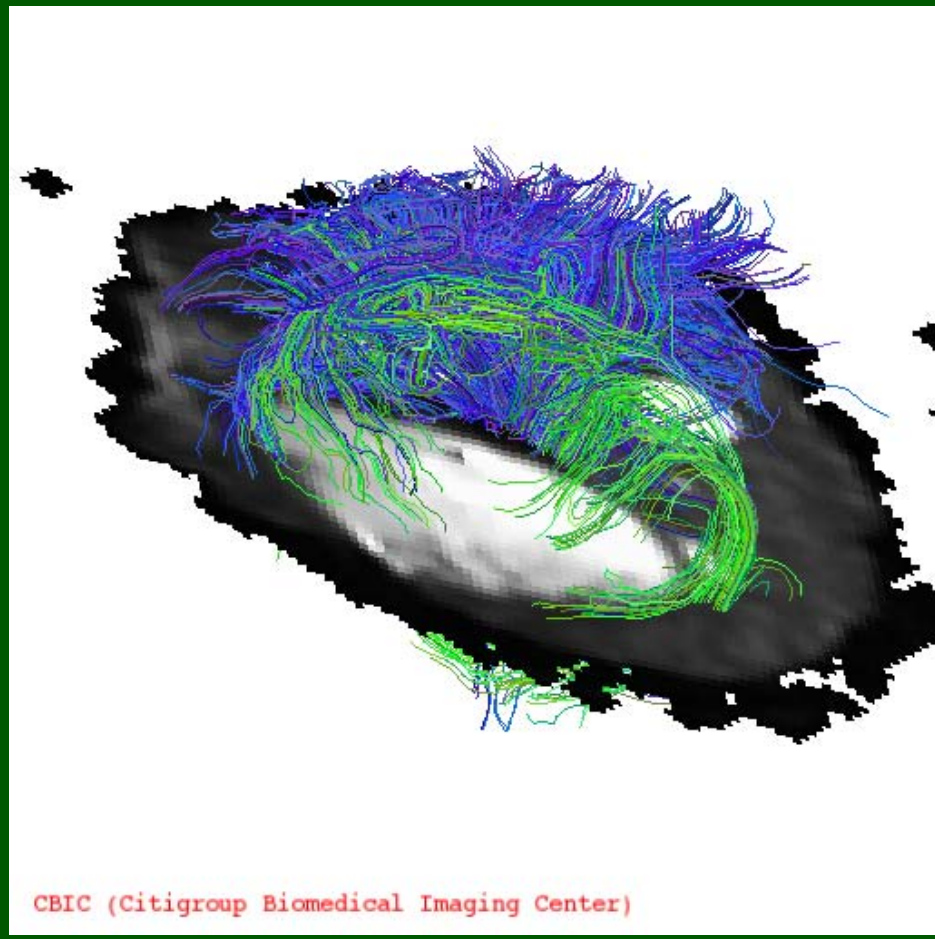
Directionality maps of normal brain and brain with tumor





White matter fiber tractography


CBIC (Citigroup Biomedical Imaging Center)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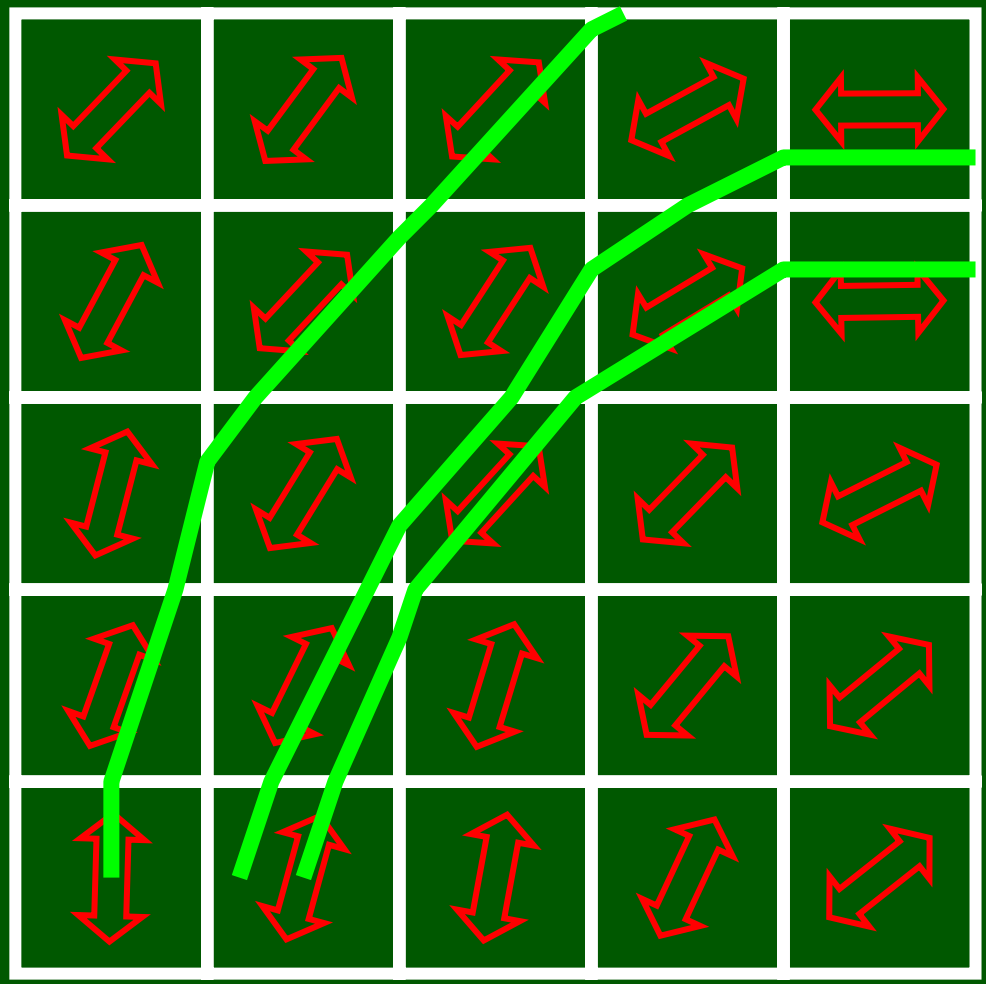
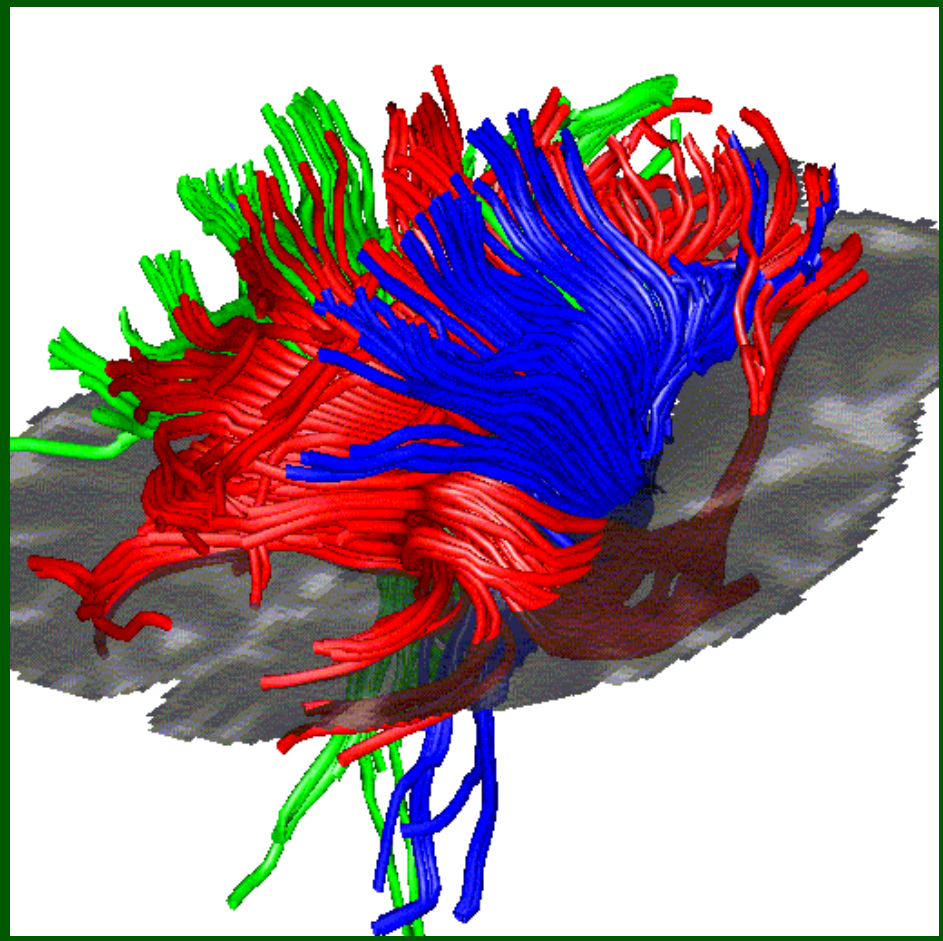


Direction of greatest diffusion

R. Watts 2004,
Mori et al, 1999



R. Watts 2004

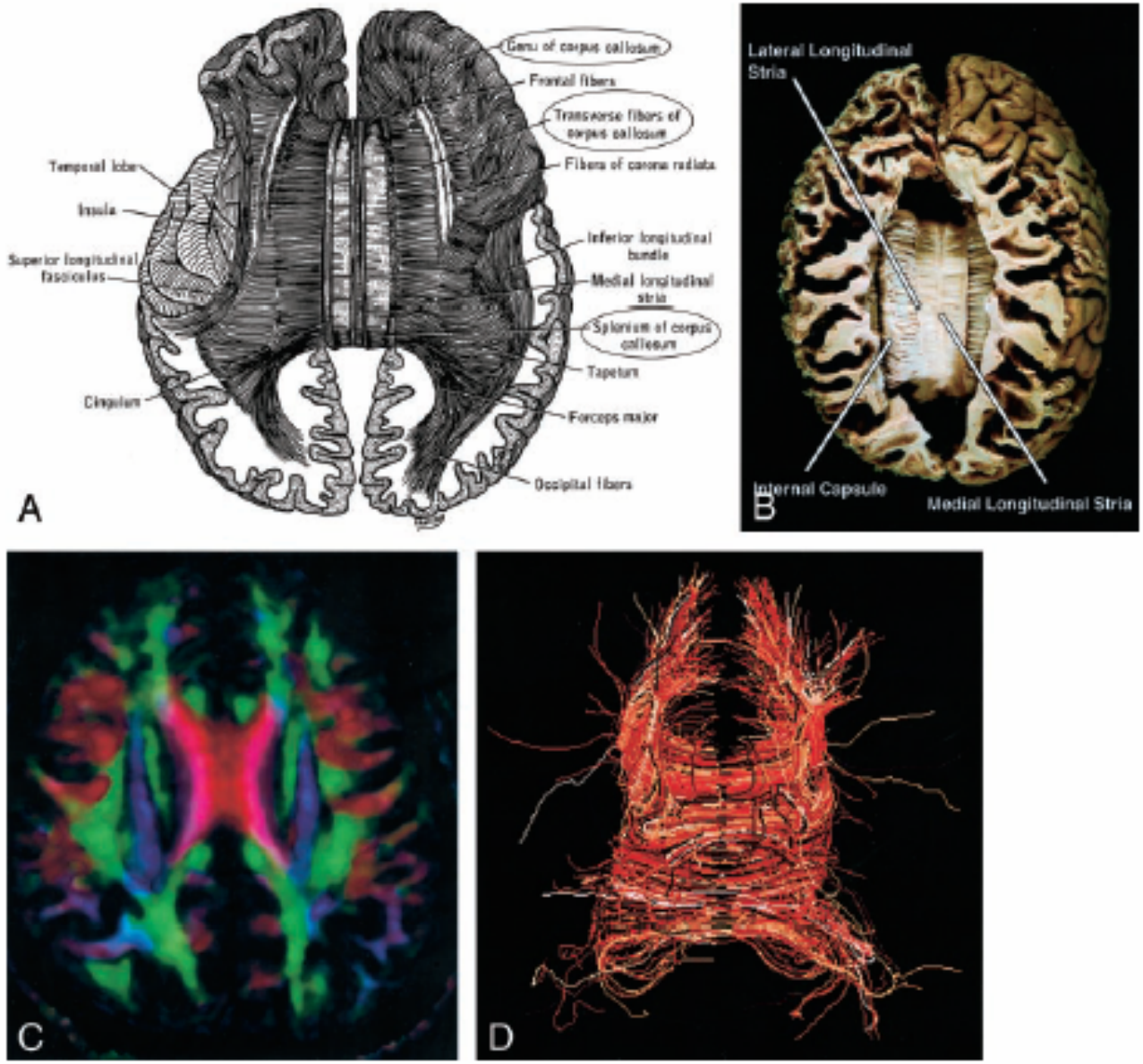
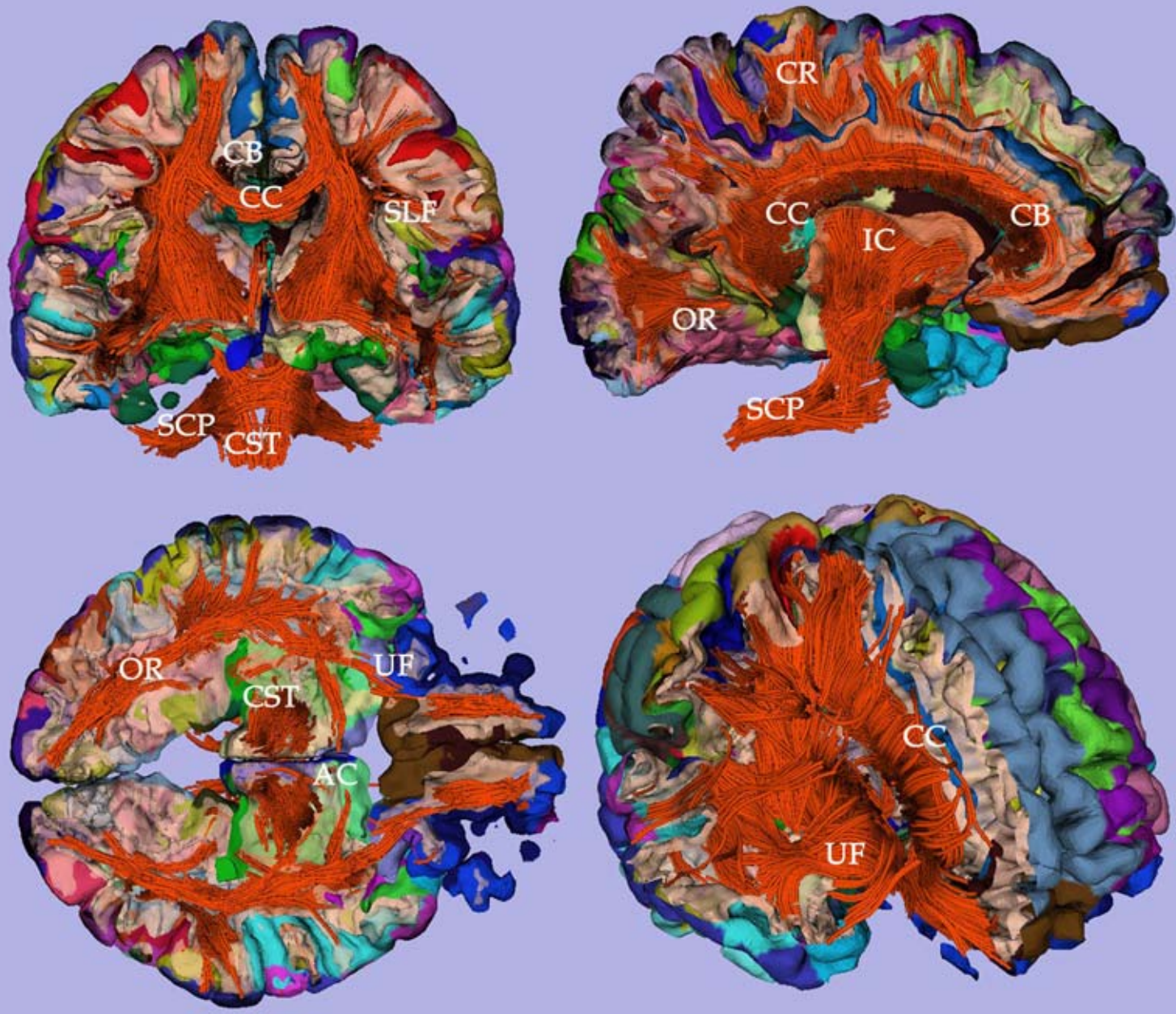


FIG 14. Corpus callosum, axial view.

A–D, Illustration (*A*), gross dissection (*B*), directional map (*C*), and tractogram (*D*). The largest WM fiber bundle, the corpus callosum connects corresponding areas of cortex between the hemispheres. Close to the midline, its fibers are primarily left-right oriented, resulting in its red appearance on this DTI map. However, callosal fibers fan out more laterally and intermingle with projection and association tracts, resulting in more complex color patterns.

Jellison 2004



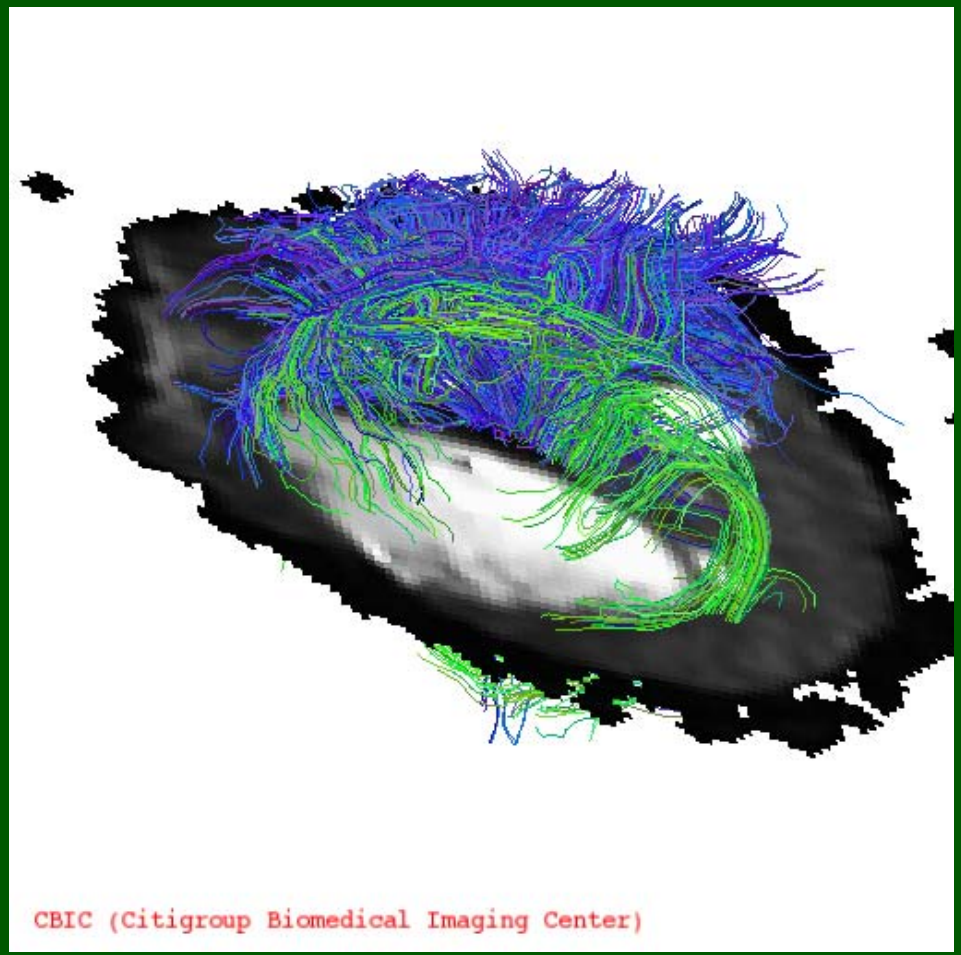
Hae-Jeong Park, Ph.D., 2003

Applications at WMC

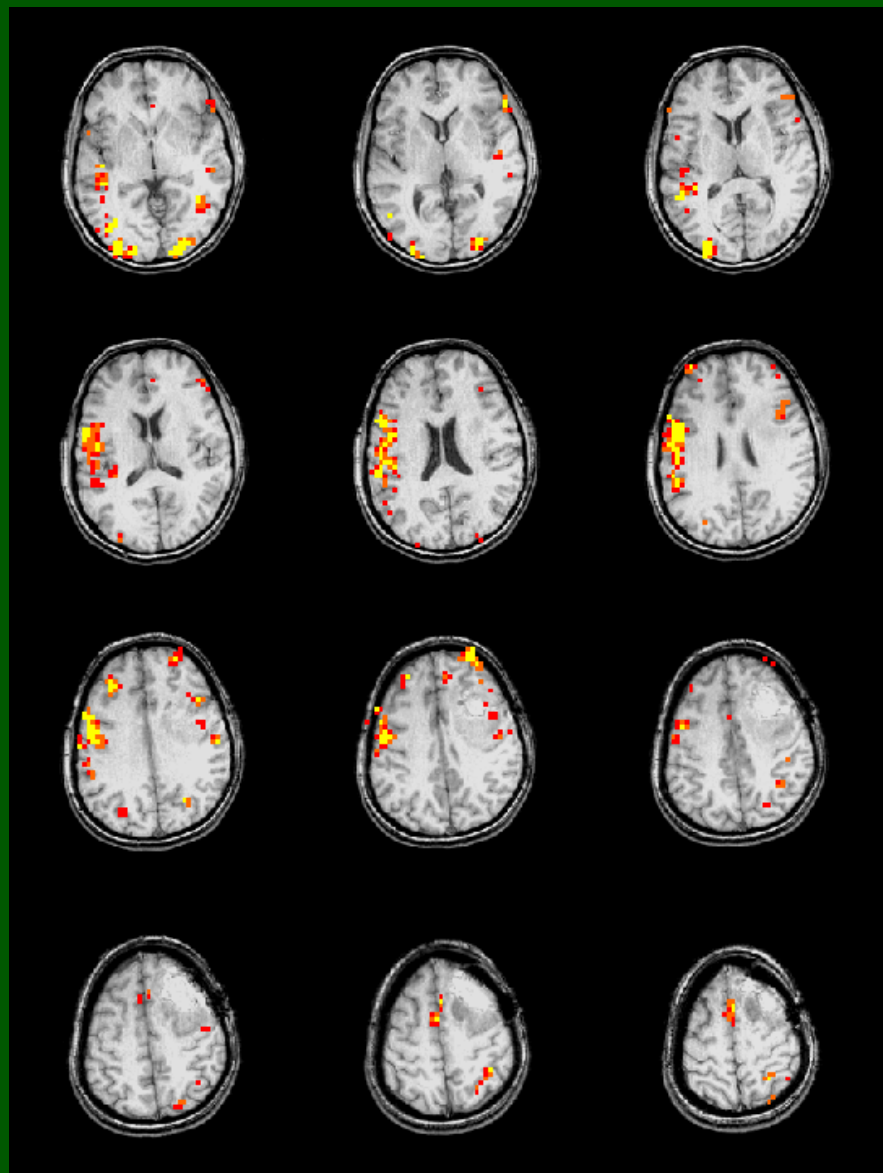
- Presurgical planning in epilepsy/tumor patients (Neurosurgery / Radiology)
- Quantification of white matter lesions in traumatic brain injury (Brain Trauma Foundation / Sackler Institute for Developmental Psychobiology)
- Case studies with the Department of Neurology and Neuroscience

Presurgical planning

Neurosurgery/Radiology at NYPH (tumor & epileptic surgery) and CBIC

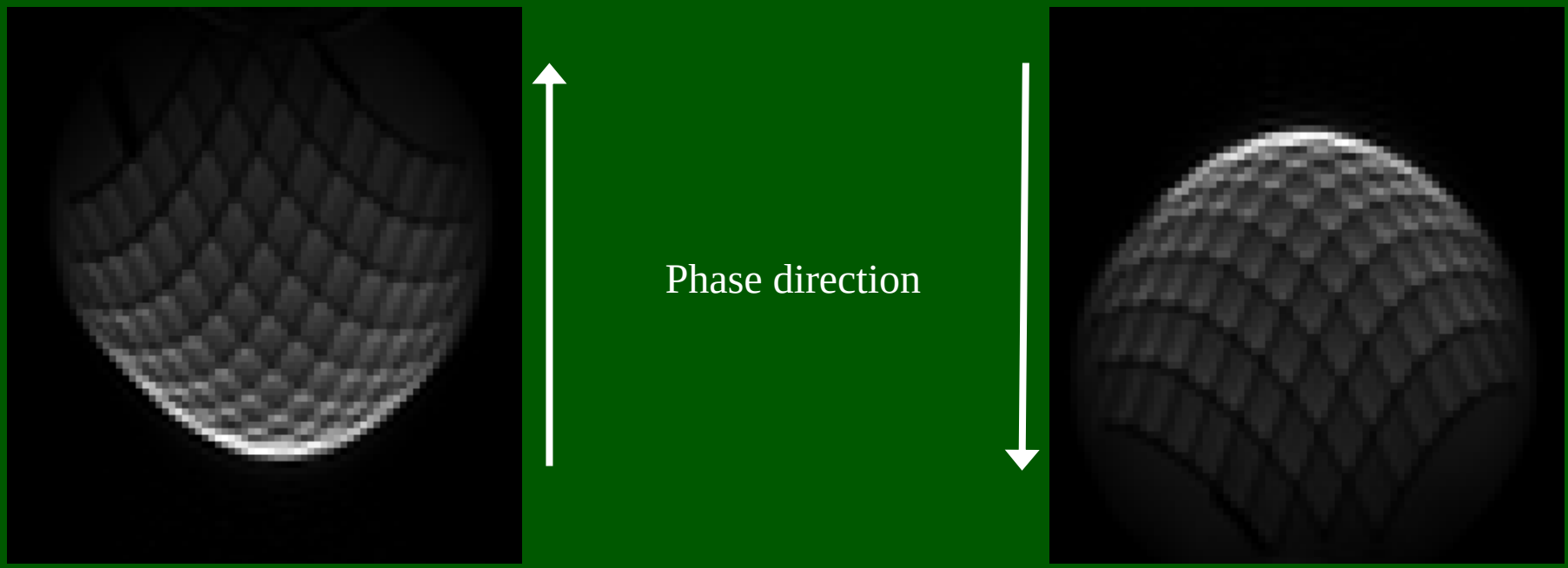


Patient with tumor infiltrating brain tissue,
block design rhyming paradigm,
ca 100 repetitions a 2s, 0.63<R<0.73, overlaid
onto anatomical image



Fiber tracking in inferior brain regions and cervical spine

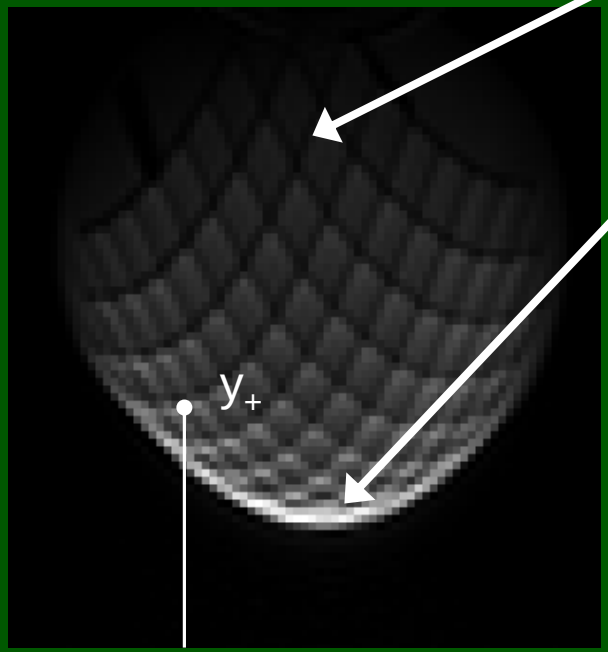
Geometric distortions

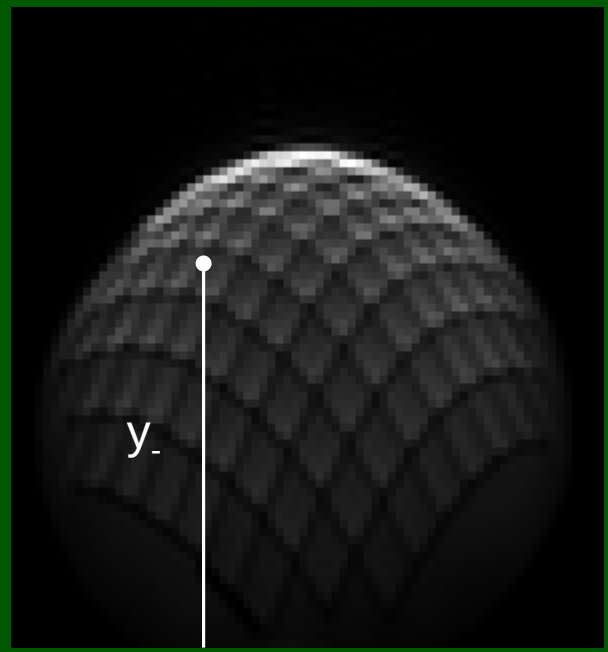


$y_+ = y + \Delta y$

$y_- = y - \Delta y$

Intensity distortions

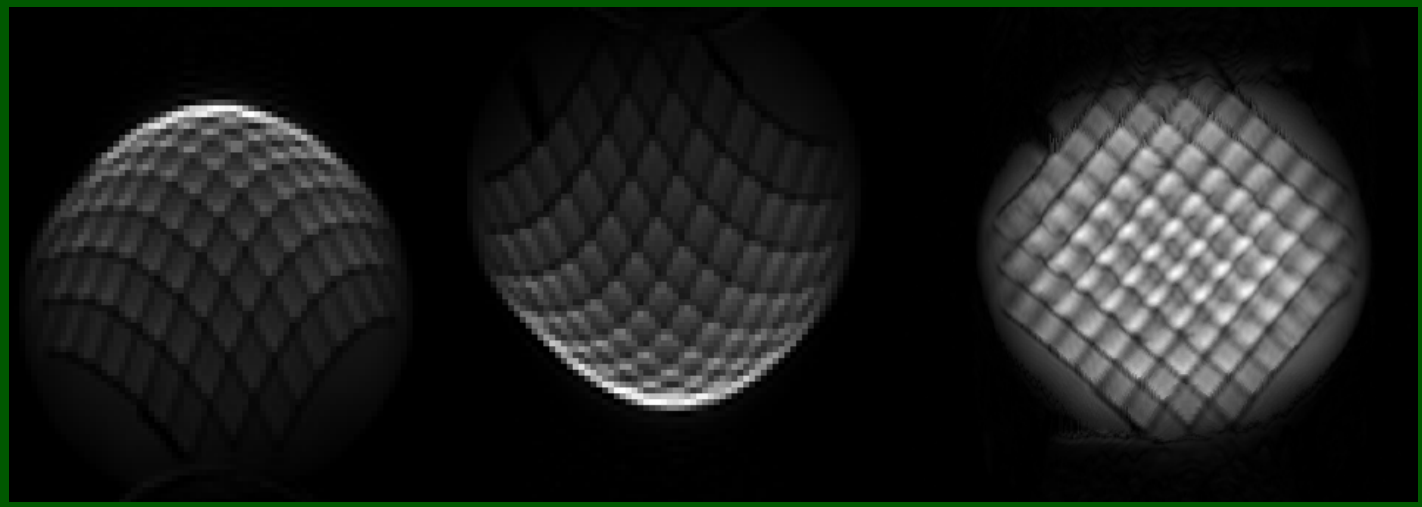




$$\int_0^{y_+} I_+(y_+)\,dy_+ = \int_0^{y_-} I_-(y_-)\,dy_-$$

Correction:
Acquire both gradient directions and merge images

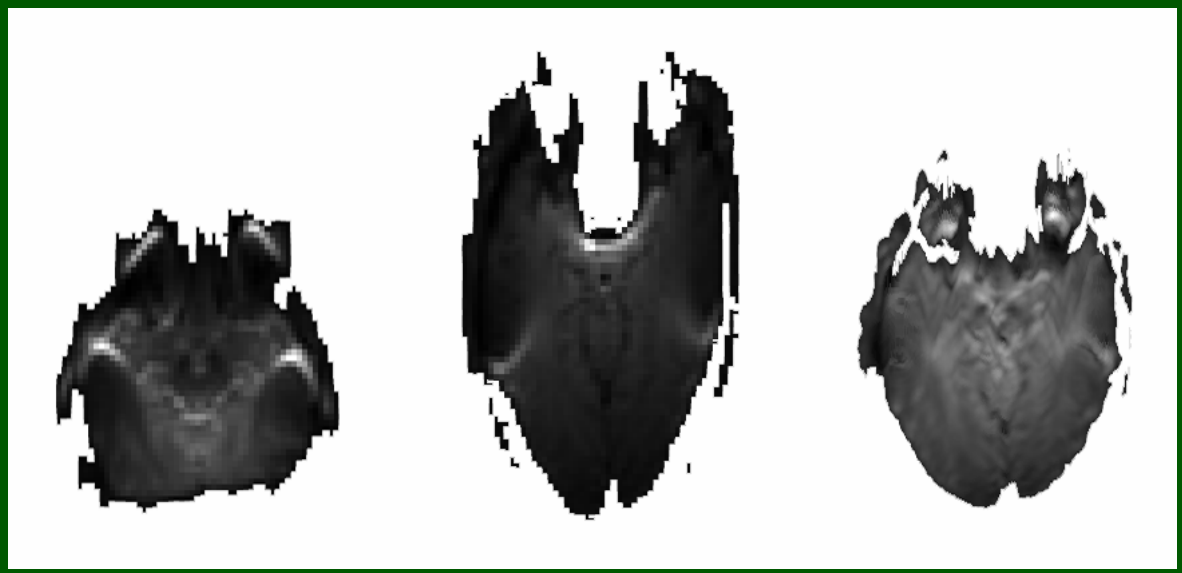
Geometry: $y = (y_+ + y_-)/2$ *Intensity:* $I = 2I_+ I_- /(I_+ + I_-)$

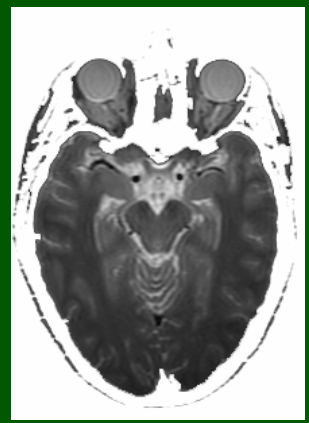


Chang, Fitzpatrick, IEEE Trans. Med. Imaging 11, 319 (1992)
Bowtell et al., Proc. of the 2nd Meeting of the Soc. of Magn. Res. 411 (1994)
Andersson, Skare, Ashburner, Neuroimage 20, 870 (2003)
Morgan et al., JMRI 19, 499 (2004)

Geometric distortions

I_+ I_- Corrected Anatomical reference

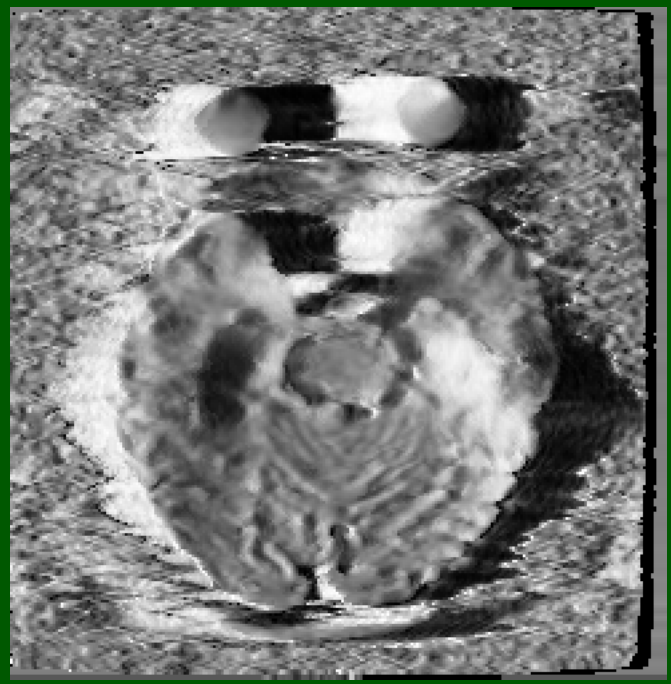




(All images scaled to individual full intensity range)

Shift for distortion correction

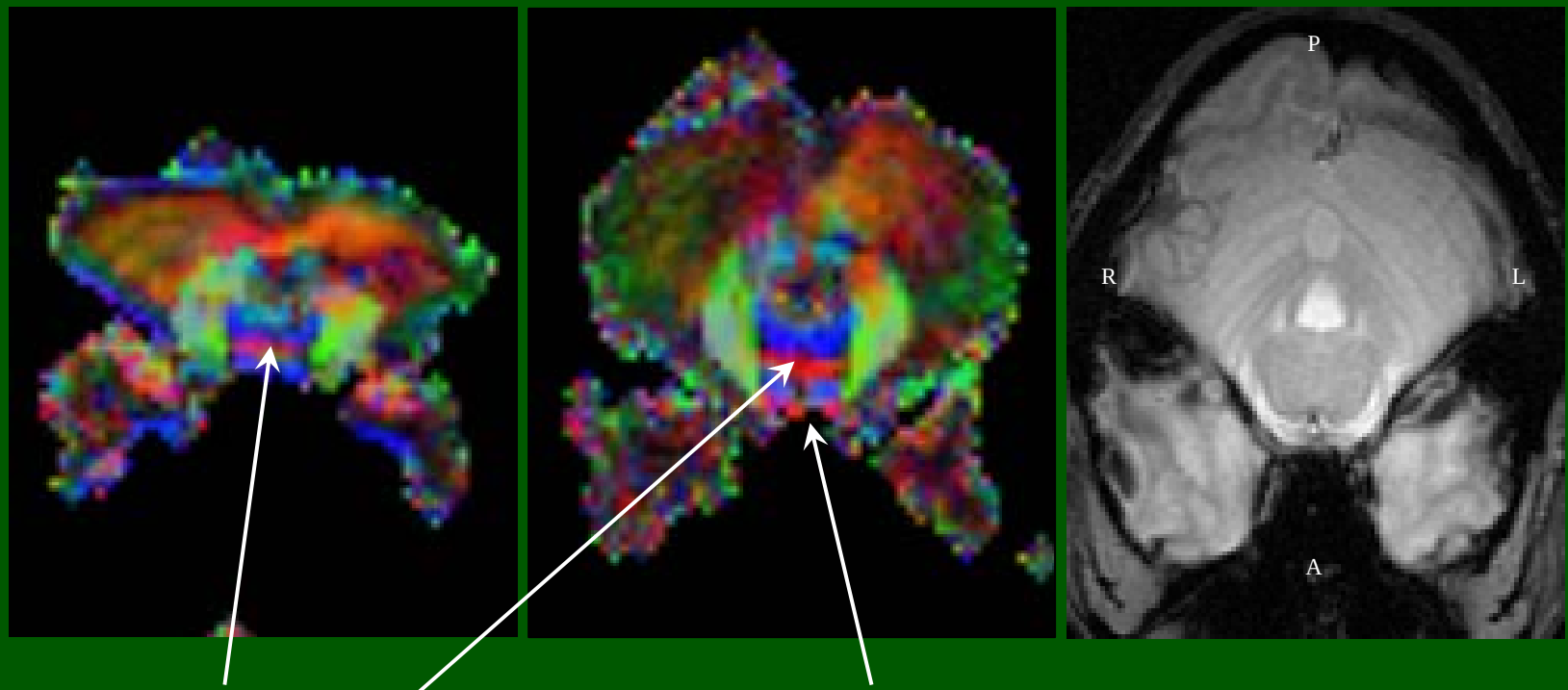
Factor for intensity correction

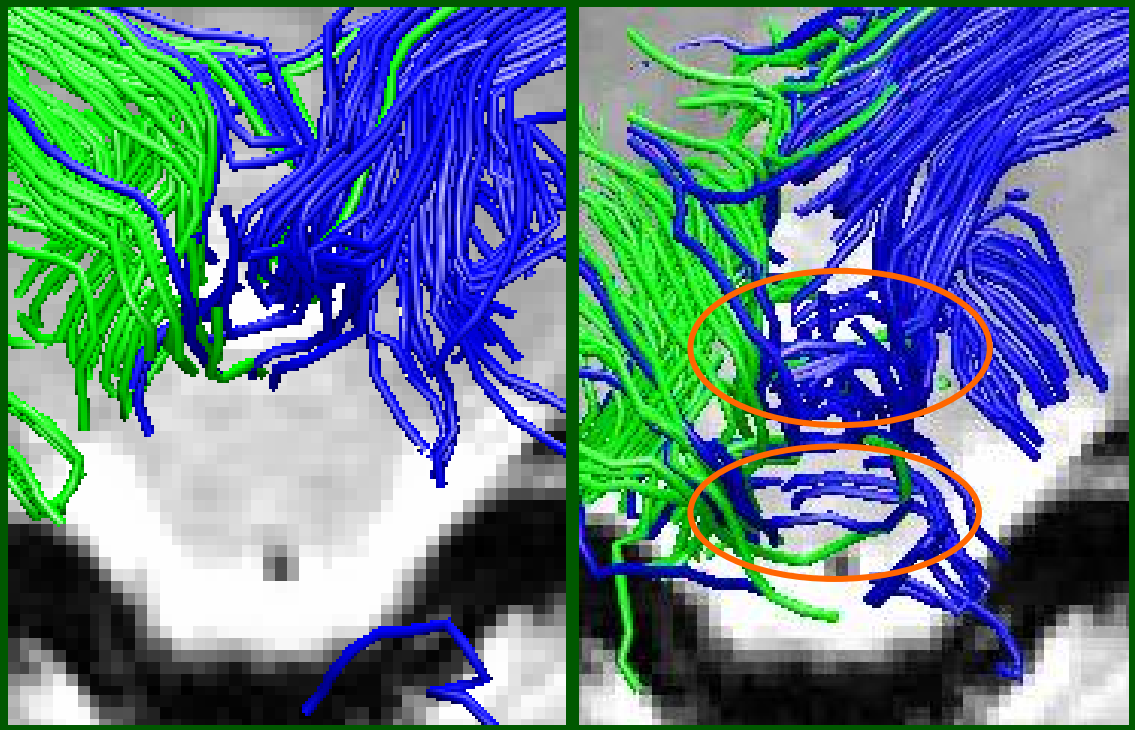


Phase direction

DTI with reversed gradients

Example: Cerebellum



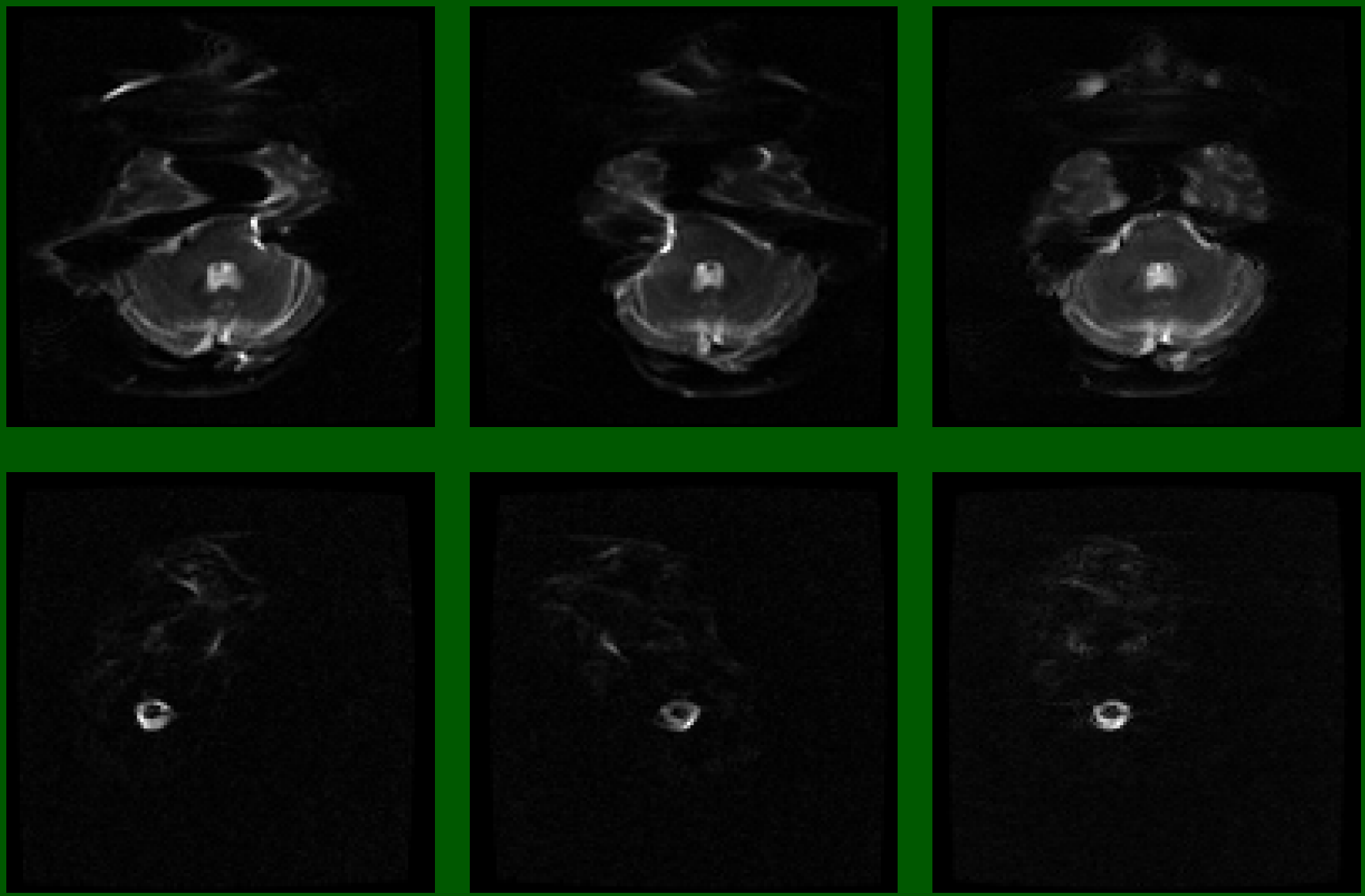


pontine
crossing tract

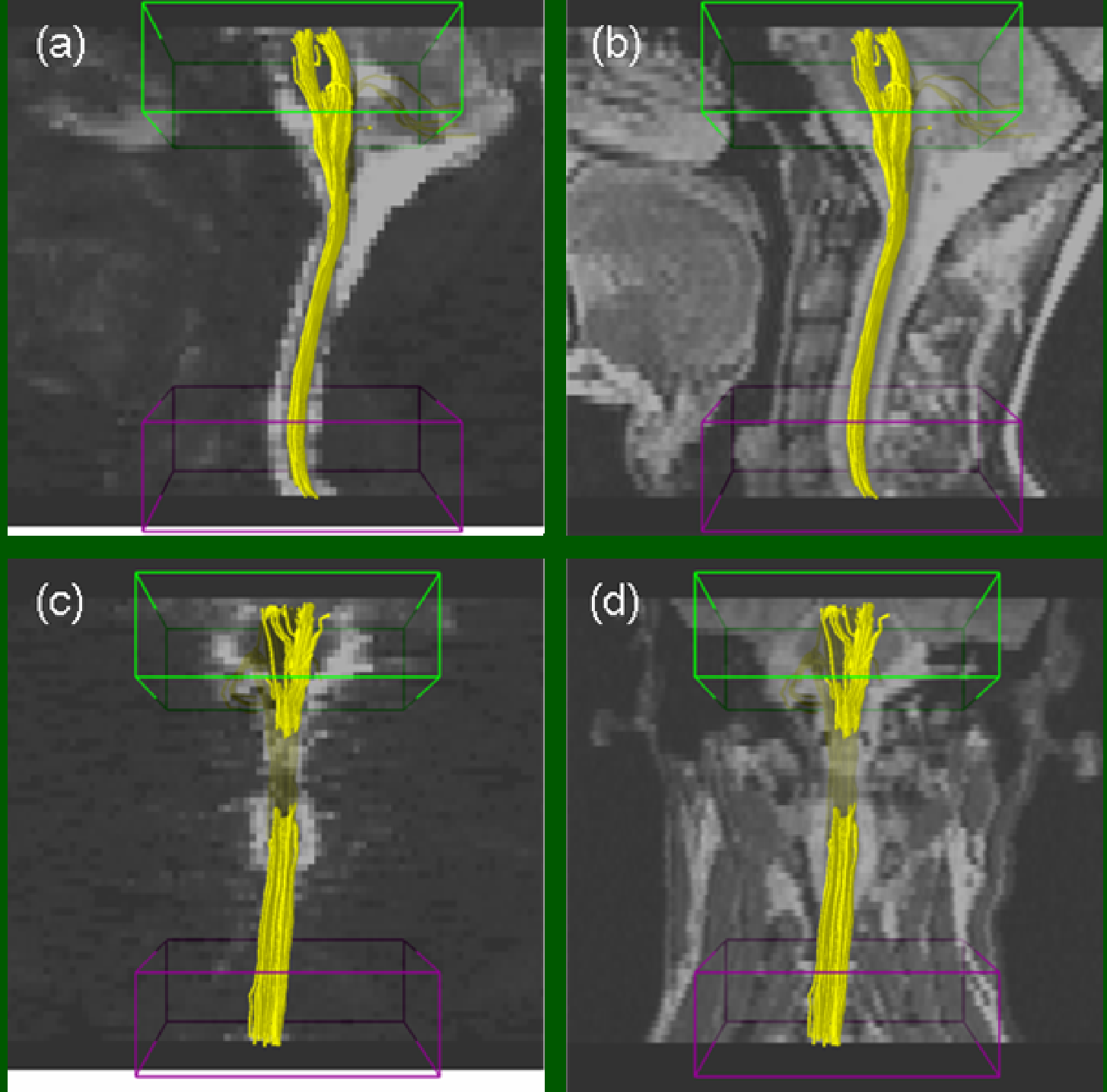
middle cerebellar
peduncle

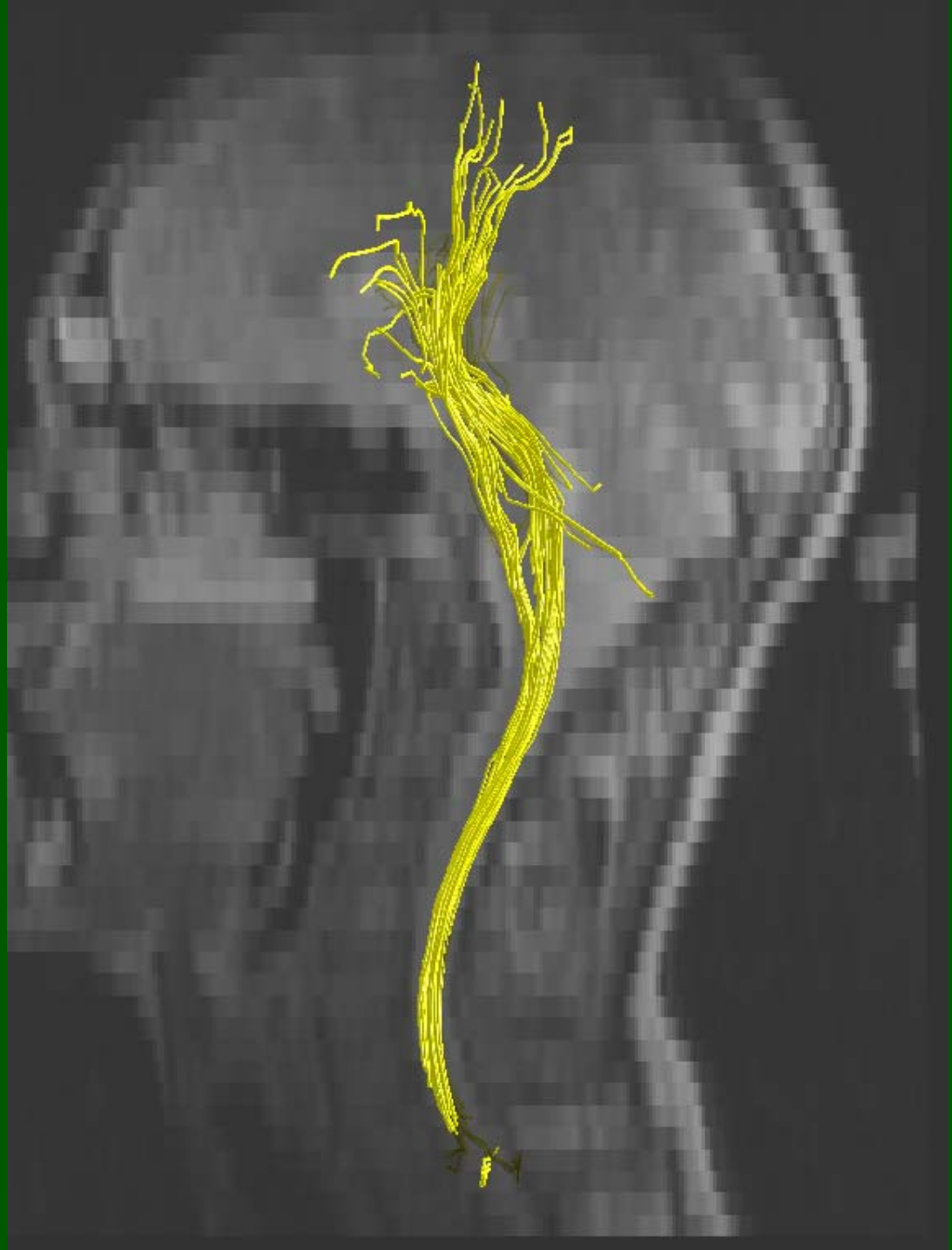
Application to inferior brain regions and spinal cord

I_+ I_- Corrected



4 channel phased array torso coil


(a)
(b)
(c)
(d)



Fiber crossings and non-Gaussian diffusion

q-space imaging

Resolves intravoxel orientational heterogeneity
(crossing / branching / kissing fibers)

- Remember:

$$S = S_0 \int dz_1 P(z_1) \int \exp(i\gamma\delta G(z_2 - z_1)) P(z_2, z_1, \Delta) dz_2$$

- Define $q = \gamma\delta G$ and $z = z_2 - z_1$ to get

$$S(q, \Delta) = S_0 \int \exp(iqz) P(z, \Delta) dz$$

- Therefore, the signal *S* is again the Fourier-transform of a density *P*
- By inversion, one can measure *P.*
- This requires lots of *q*-values, i.e., one needs to vary timing δ or gradient strength *G*.

Q-ball imaging

- Drastically reduced scan time
- HARDI-sequence (High angular resolution diffusion imaging)
- Spherically sampled data
- Postprocessing (Funk Radon transform)

The orientation distribution function (ODF)

$P(\mathrm{r}) = F[S(\mathrm{q})]$ (**r** and **q** are reciprocal vectors)

ODF: $\psi(\mathrm{u}) = \frac{1}{Z} \int_0^\infty P(r\mathrm{u})dr$

Q-Ball imaging: Sample only on a sphere, not on 3D volume:

Funk-Radon transform
= extension of planar Radon transform to the sphere
= transform from sphere to sphere
= line integral along equator of sphere, for each vector on sphere

w = unit direction vector
f(**w**) = scalar function on sphere
u = direction of interest

$$G[f(\mathrm{w})](\mathrm{u}) = \int f(\mathrm{w})\delta(\mathrm{w'u})d\mathrm{w}$$

Extended FRT: Maps from 3D Cartesian space to sphere

x = unit direction vector
r = particular radius at which FRT is evaluated
f(**x**) = scalar function in 3D Cartesian space

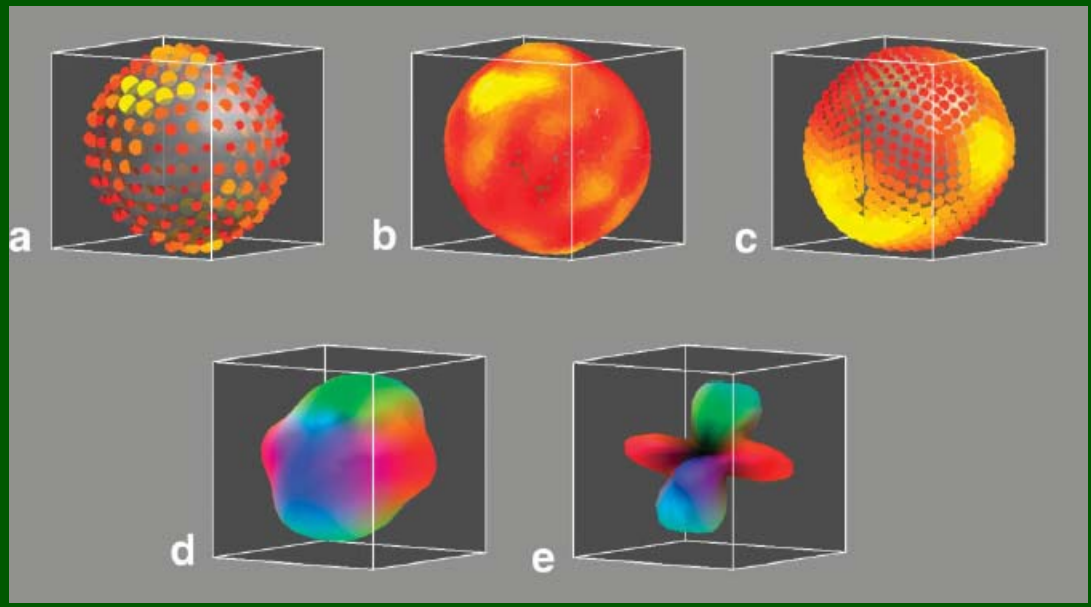
$$G_r = G[f(\mathrm{w})](\mathrm{u}, r) = \int f(\mathrm{x})\delta(\mathrm{x'u})\delta(|\mathrm{x}| - r)d\mathrm{x}$$

Theorem (D. S. Tuch):
The extended FRT of the diffusion signal gives a strong approximation to the ODF, i.e.,

$$\psi(\mathrm{u}) \approx \frac{1}{Z}\, G_r[S(\mathrm{q})]$$ (**u** and **q** are reciprocal vectors)

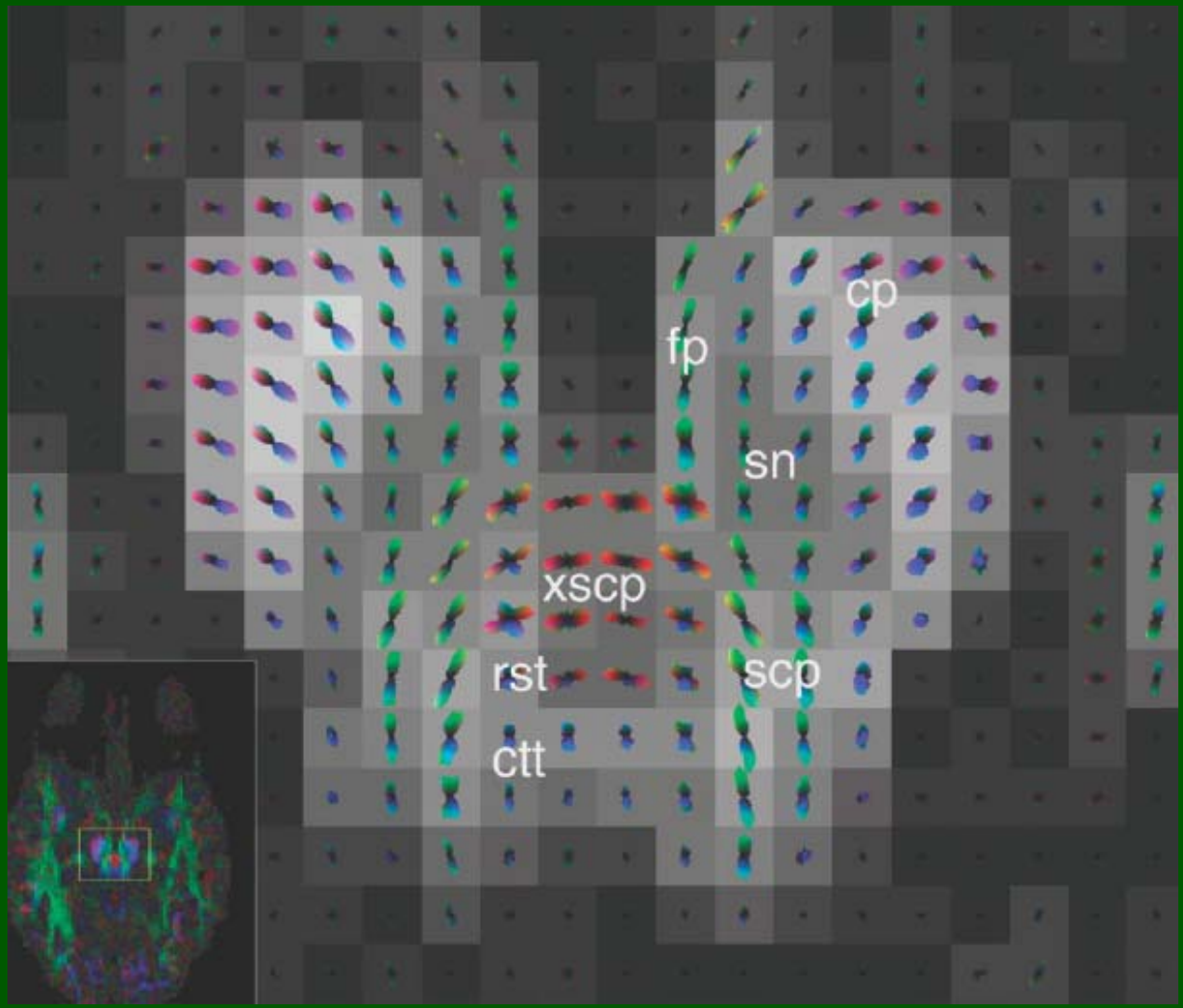
The sum of the diffusion signal over an equator approximately gives the diffusion probability in the direction normal to the plane of the equator.

Central element:
The diffusion orientation distribution function (ODF)



(a) Diffusion signal sampled on fivefold tessellated icosahedron (*m* 252).
The signal intensity is indicated by the size and color (white yellow red) of the dots on the sphere.
(**b**) Regridding of diffusion signal onto set of equators around vertices of fivefold tessellated dodecahedron.
(**c**) Diffusion ODF calculated using FRT.
(**d**) Color-coded spherical polar plot rendering of ODF.
(**e**) Min–max normalized ODF. (D. S. Tuch 2004)

ODF map of caudal midbrain



cp, cerebral peduncle;
ctt, central tegmental tract;
fp, frontopontine tract;
rst, reticulospinal tract;
scp, superior cerebellar peduncle;
sn, substantia nigra;
xscp, crossing of the superior cerebellar peduncle.

Tuch 2004

Mathematical/statistical problems

- How to reduce # of measurements?
- How to smooth tensor fields? (bias-variance optimum?)
- Can one learn more about tissue properties than fiber directions from ODF?
- Global fiber tracking algorithms?
- Do proper bootstrapping?