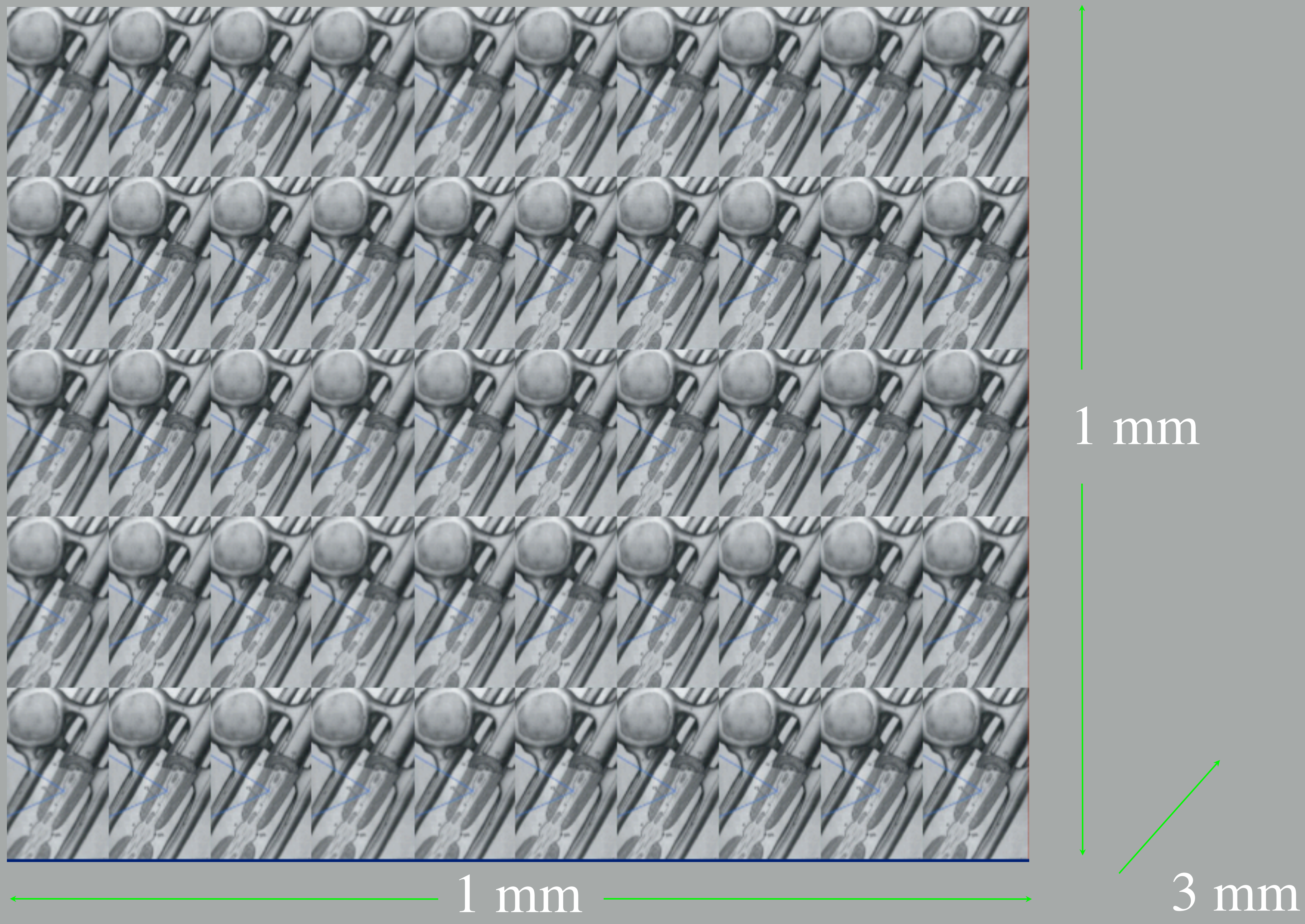
Lecture 14

Multi-fiber voxels

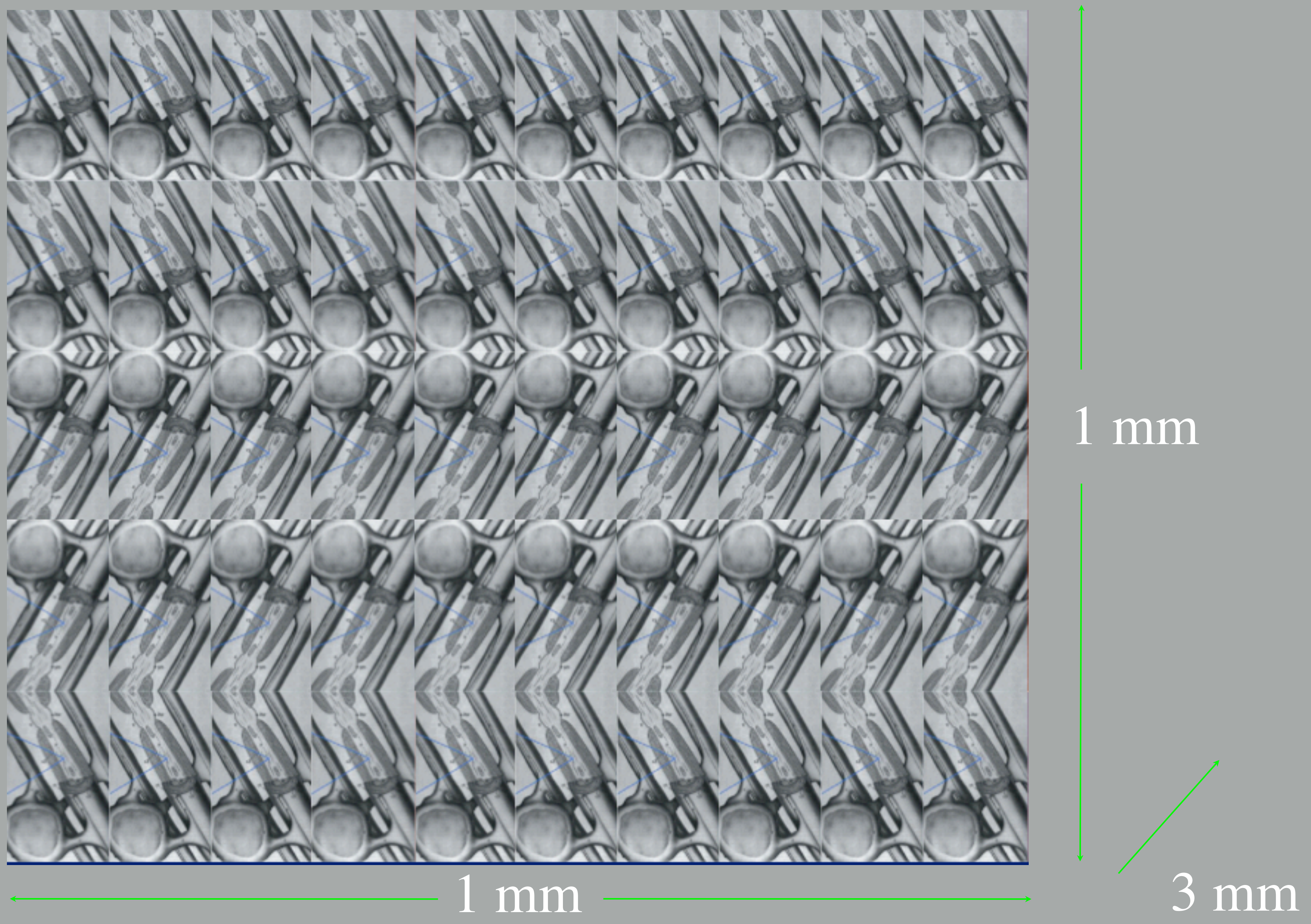
Lecture Summary

1. Failure of the standard DTI model
2. Higher order tensor modesl

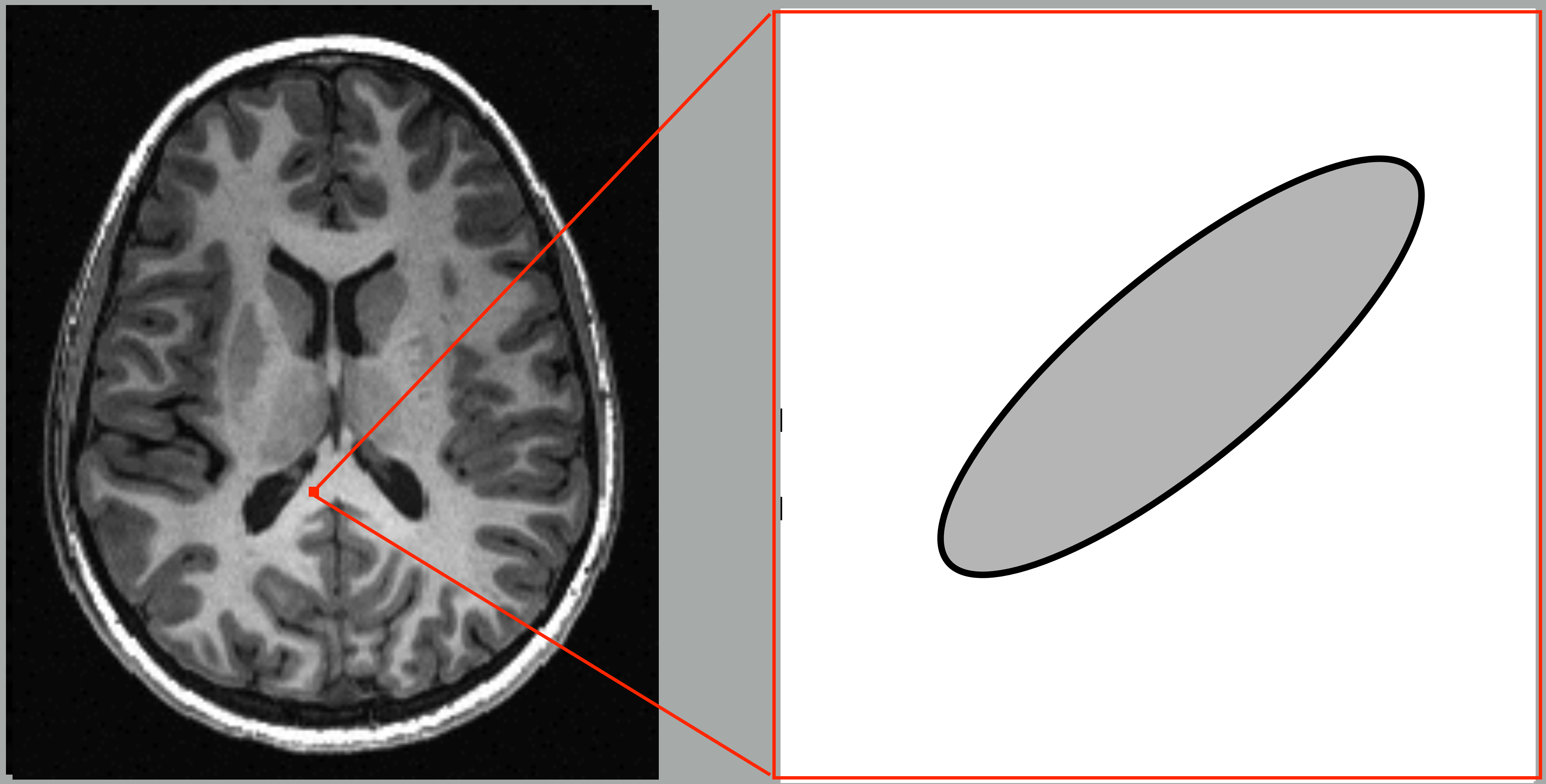
Partial voluming



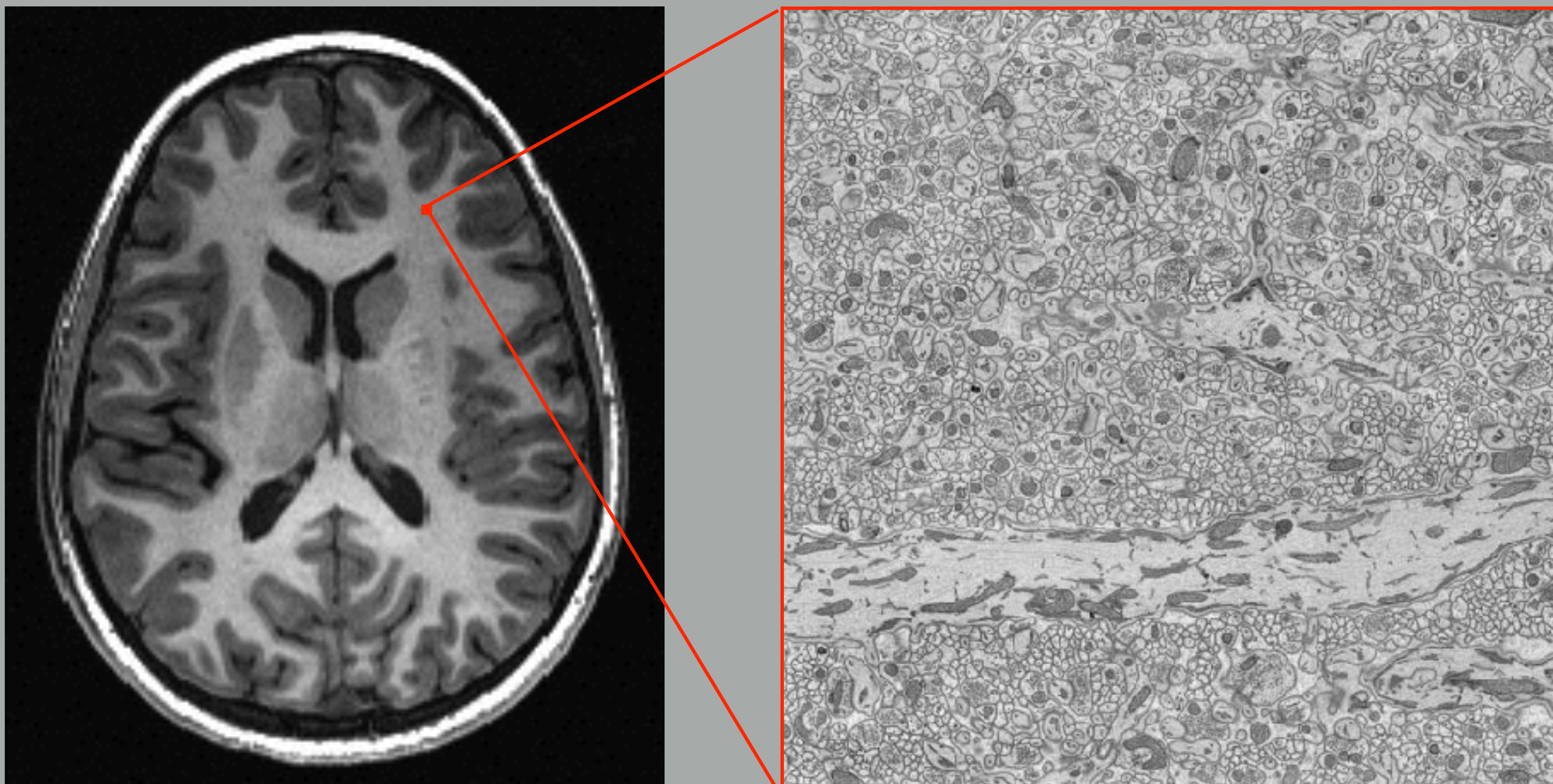
Partial voluming



What's the problem?



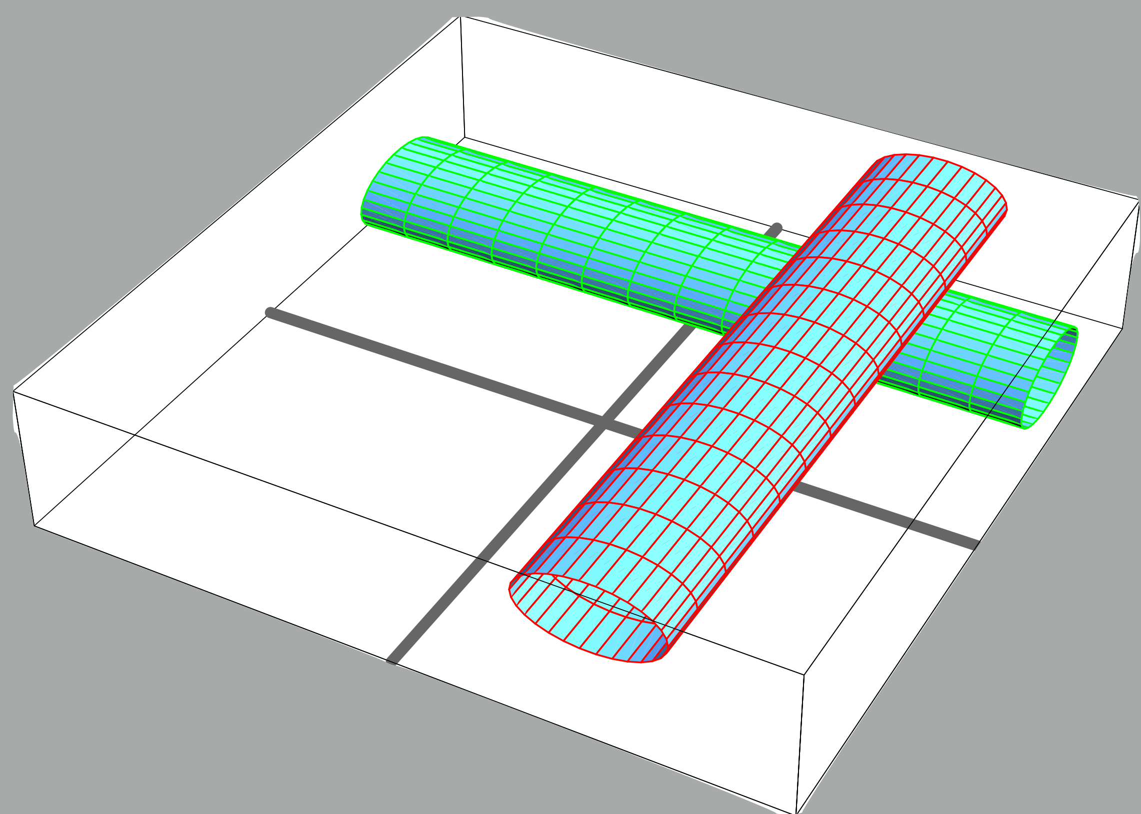
But we know Neural Tissues aren't that simple

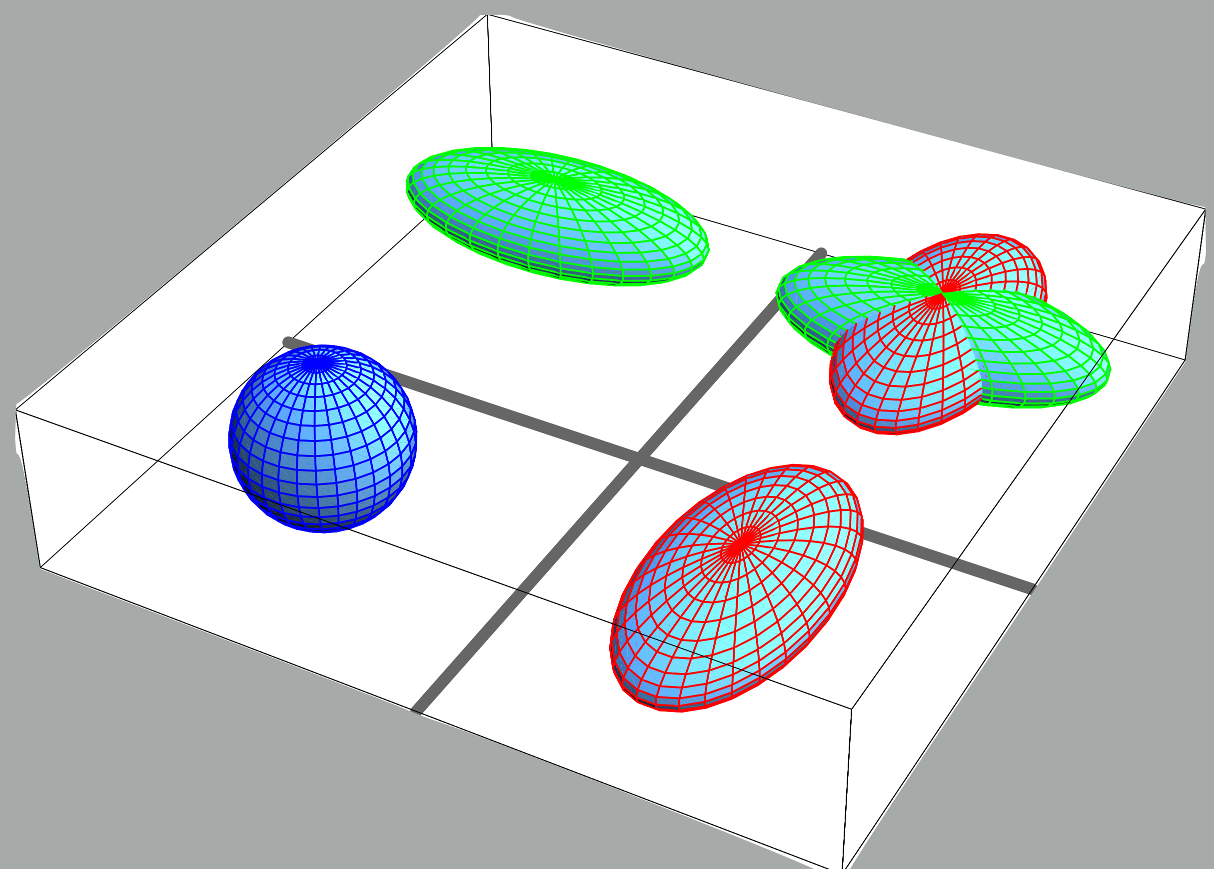


Rat WM electron microscopic image
Courtesy, M. Ellisman, UCSD

Failure of the standard model

A simple partial-volume model



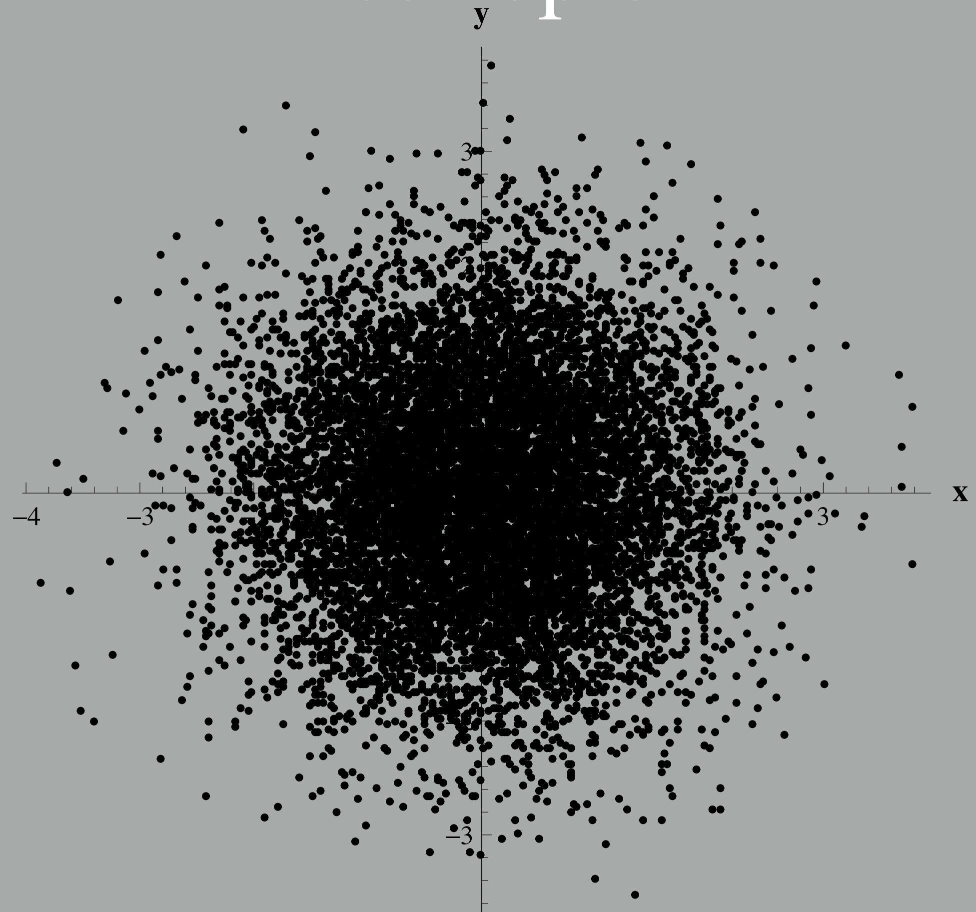


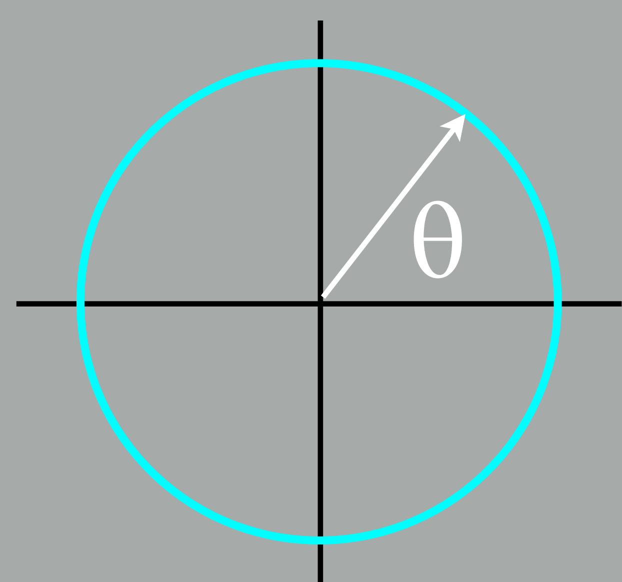
Two crossing fibers

resulting distributions

Ambiguities in the standard model

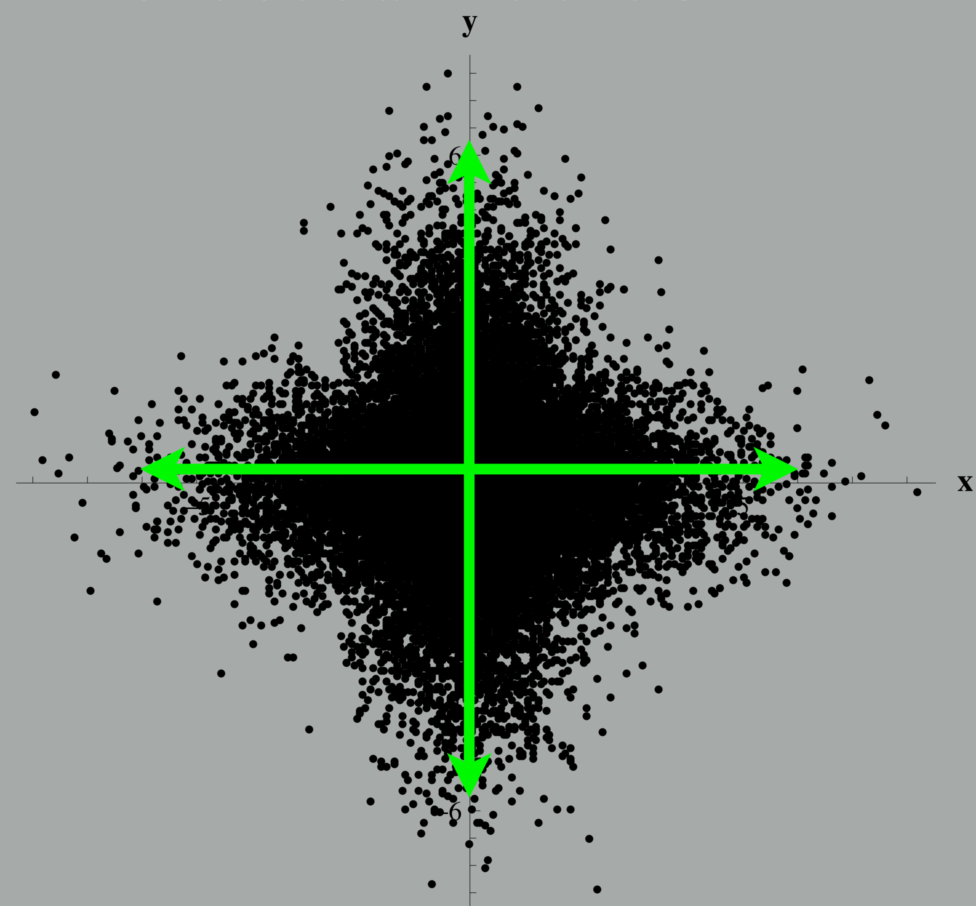
isotropic

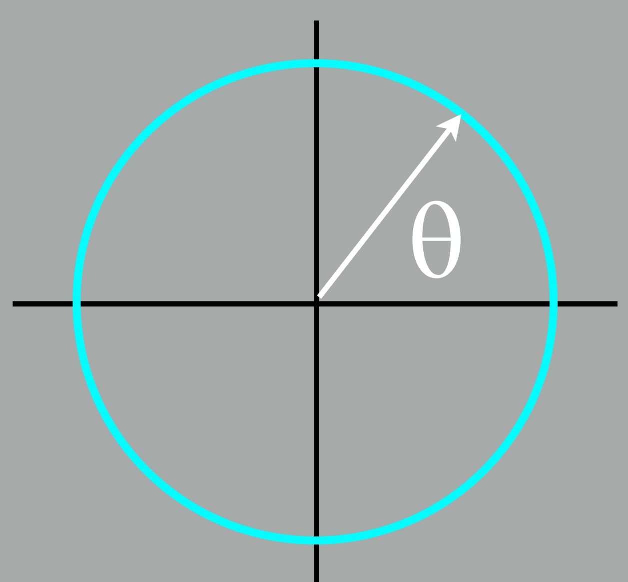




D(θ)

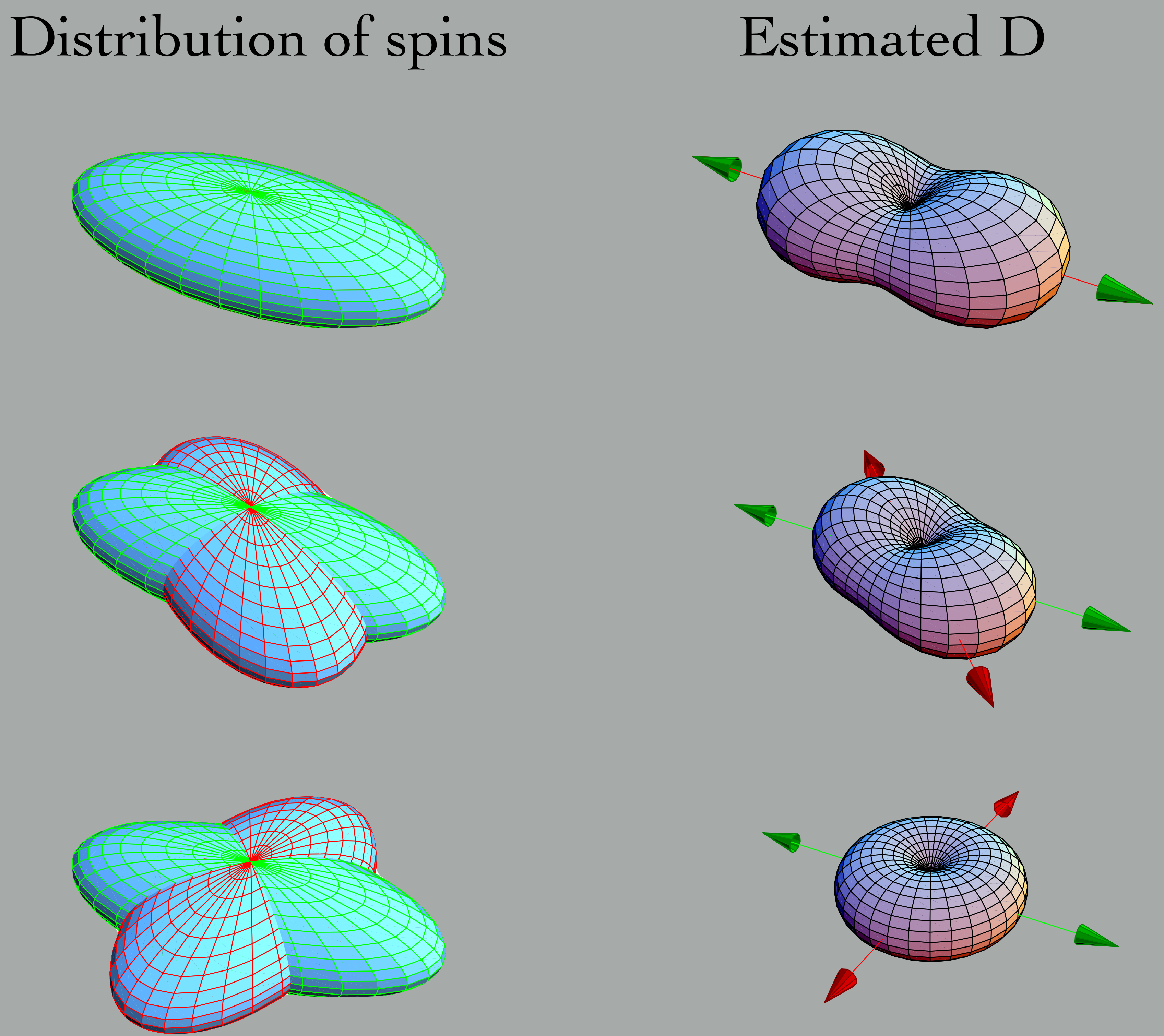
crossed fibers 90°





D(θ)

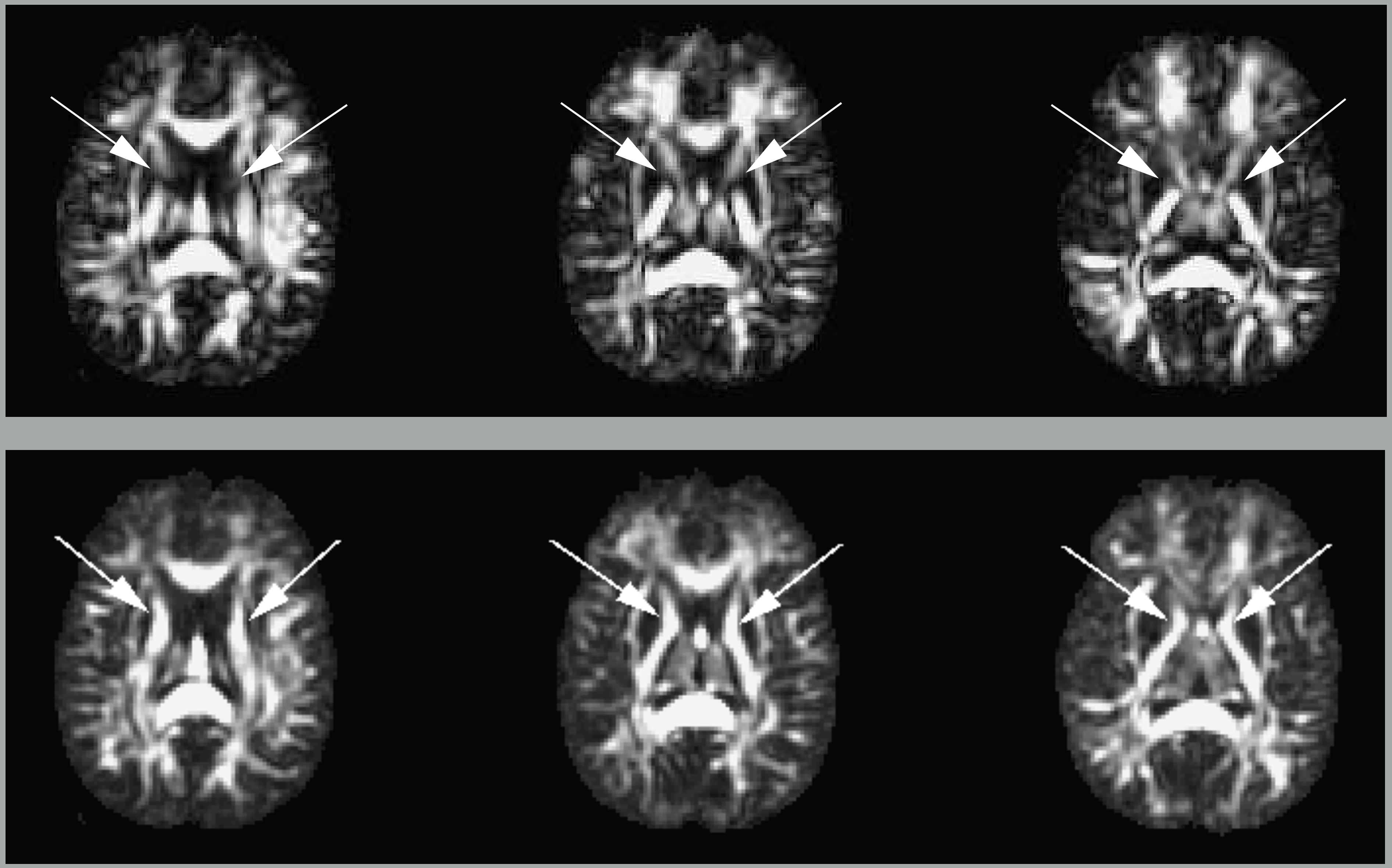
Failure of the standard model



Ambiguities in the Standard DTI Model

FA

Variance of Measurements

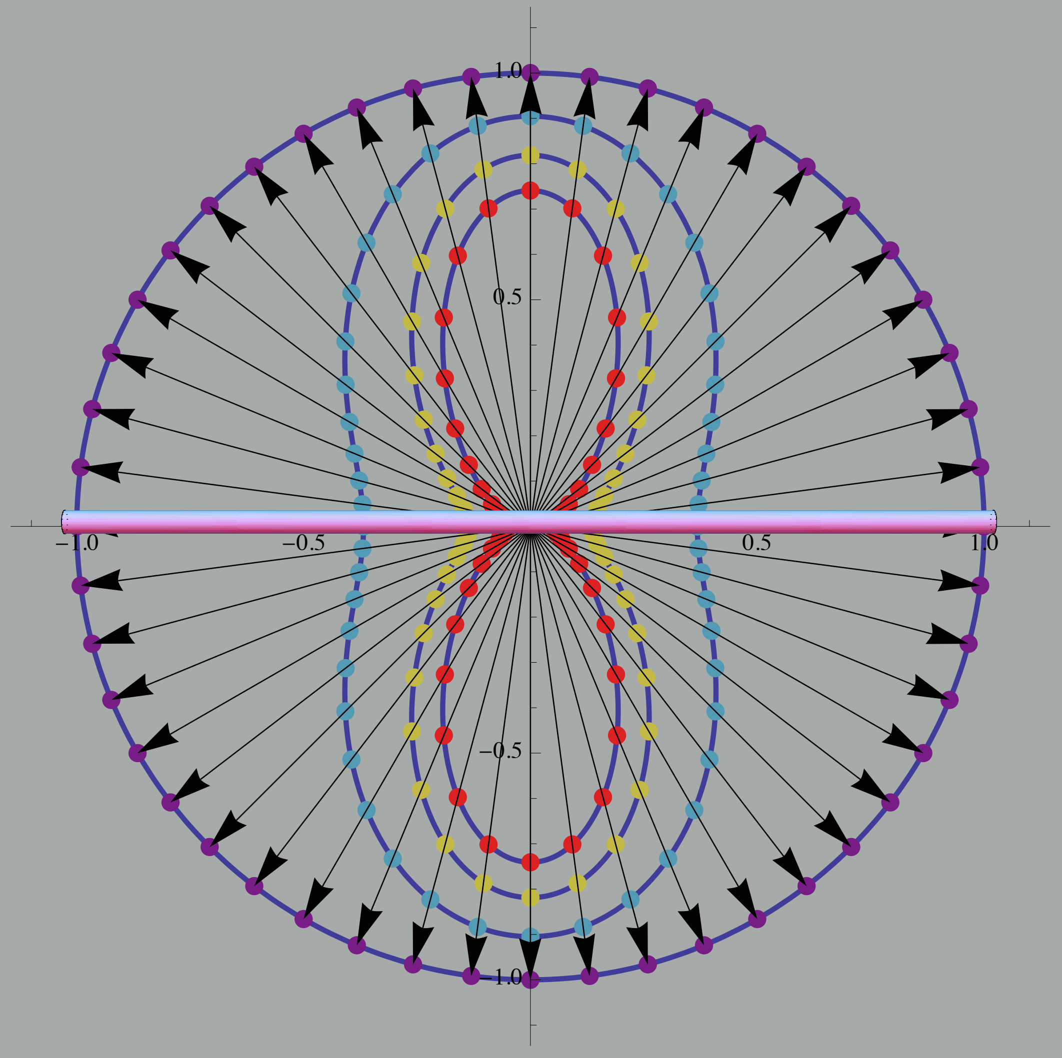


Frank, et. al. MRM 2001

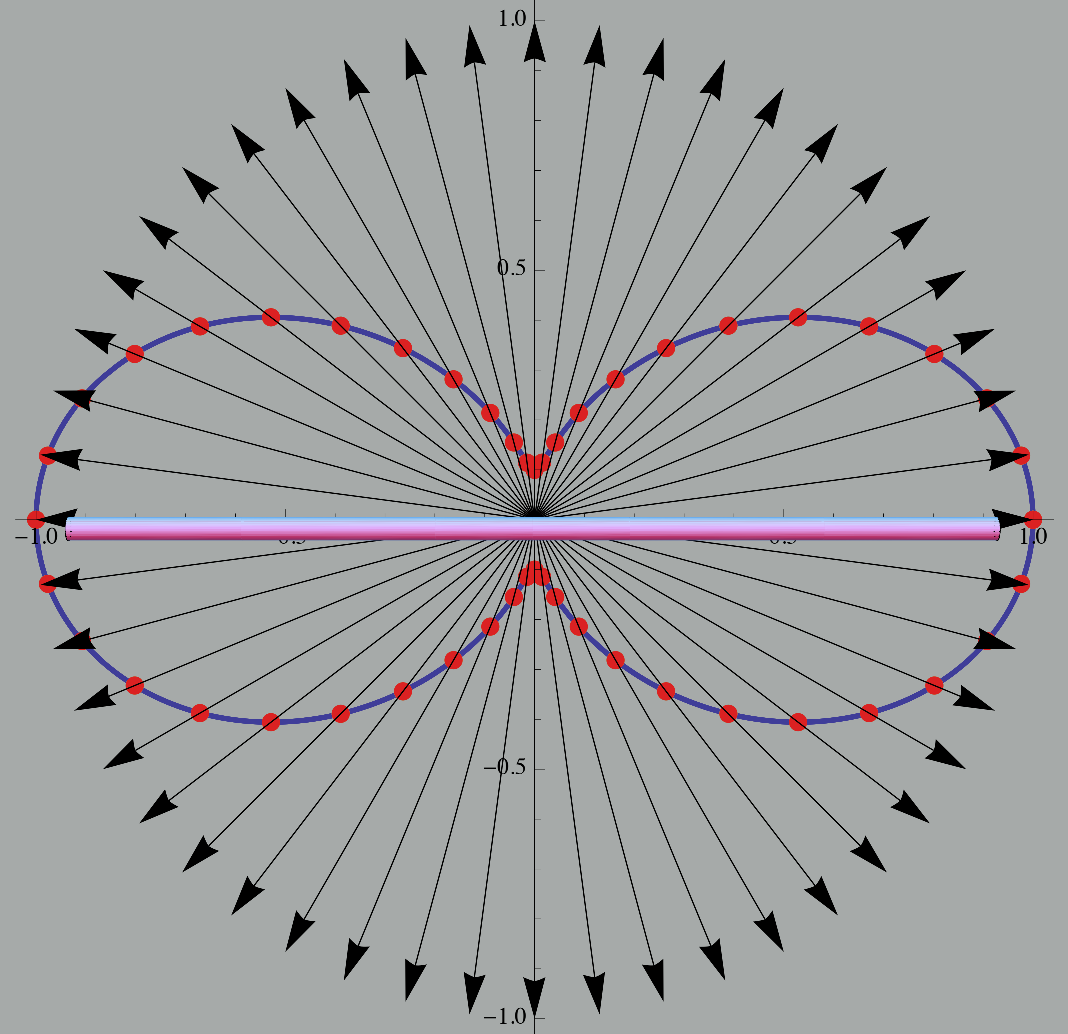
High Angular Resolution DTI (HARDI)

b = 0, 500, 1000, 1500

$d\theta = 0$



signal



D_{app}

Structure of lobes relative to fiber orientation is “non-intuitive”!

Two fiber model

$$S = fe^{-bD(\theta)} + (1-f)e^{-bD(\theta+d\theta)}$$

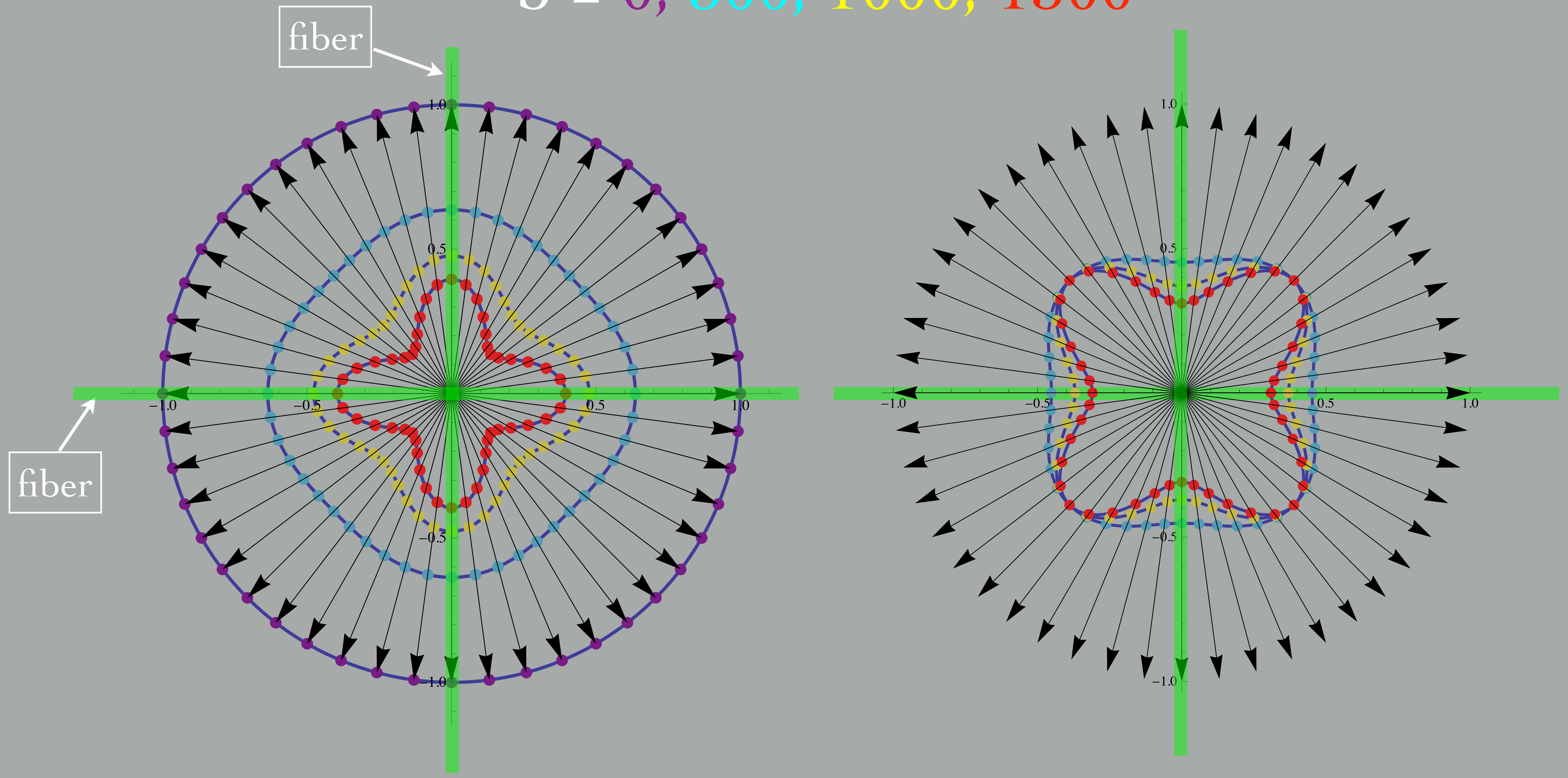
$D(\theta)$ = diffusion profile for single fiber as a function of angle θ in the plane

$d\theta$ = angle between fibers

f = volume fraction

High Angular Resolution DTI (HARDI)

b = 0, 500, 1000, 1500



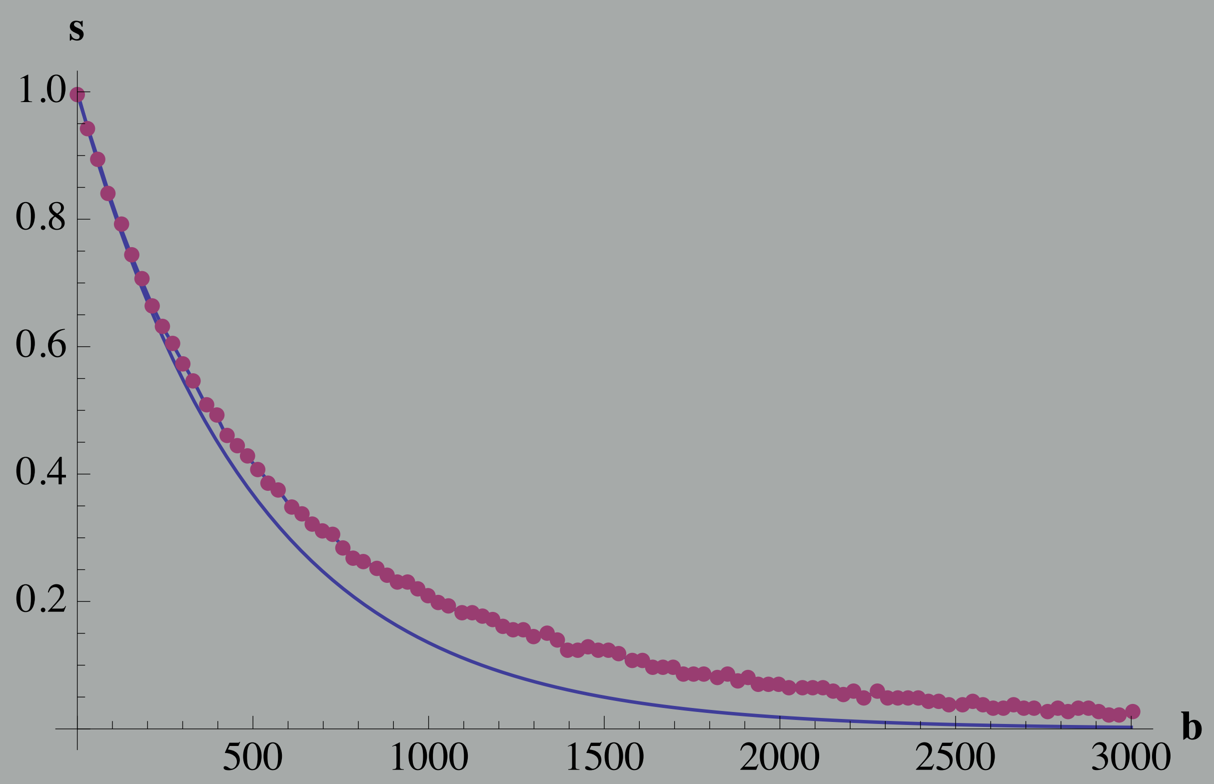
signal

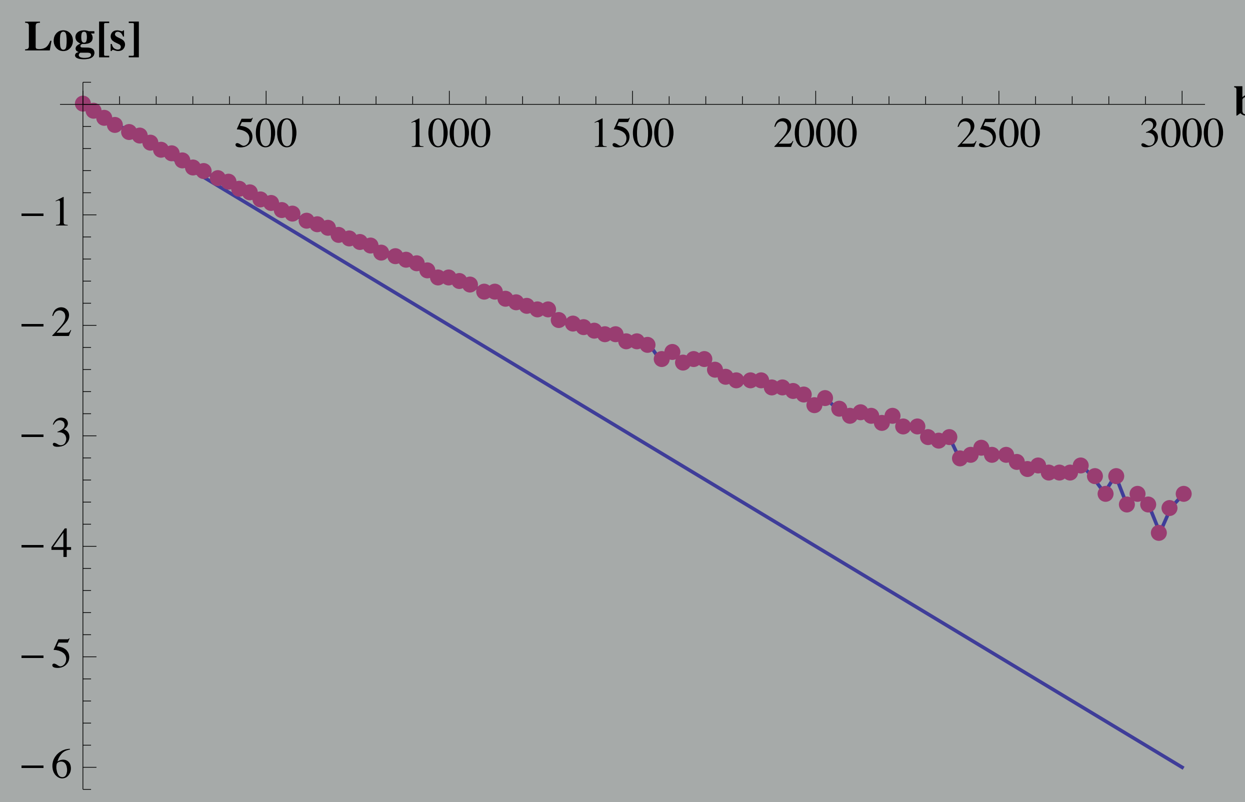
$D_{app}(\theta)$

Structure of lobes relative to fiber orientation is “non-intuitive”!

Failure of the standard model

Not only angular issues, but b-value dependencies as well!

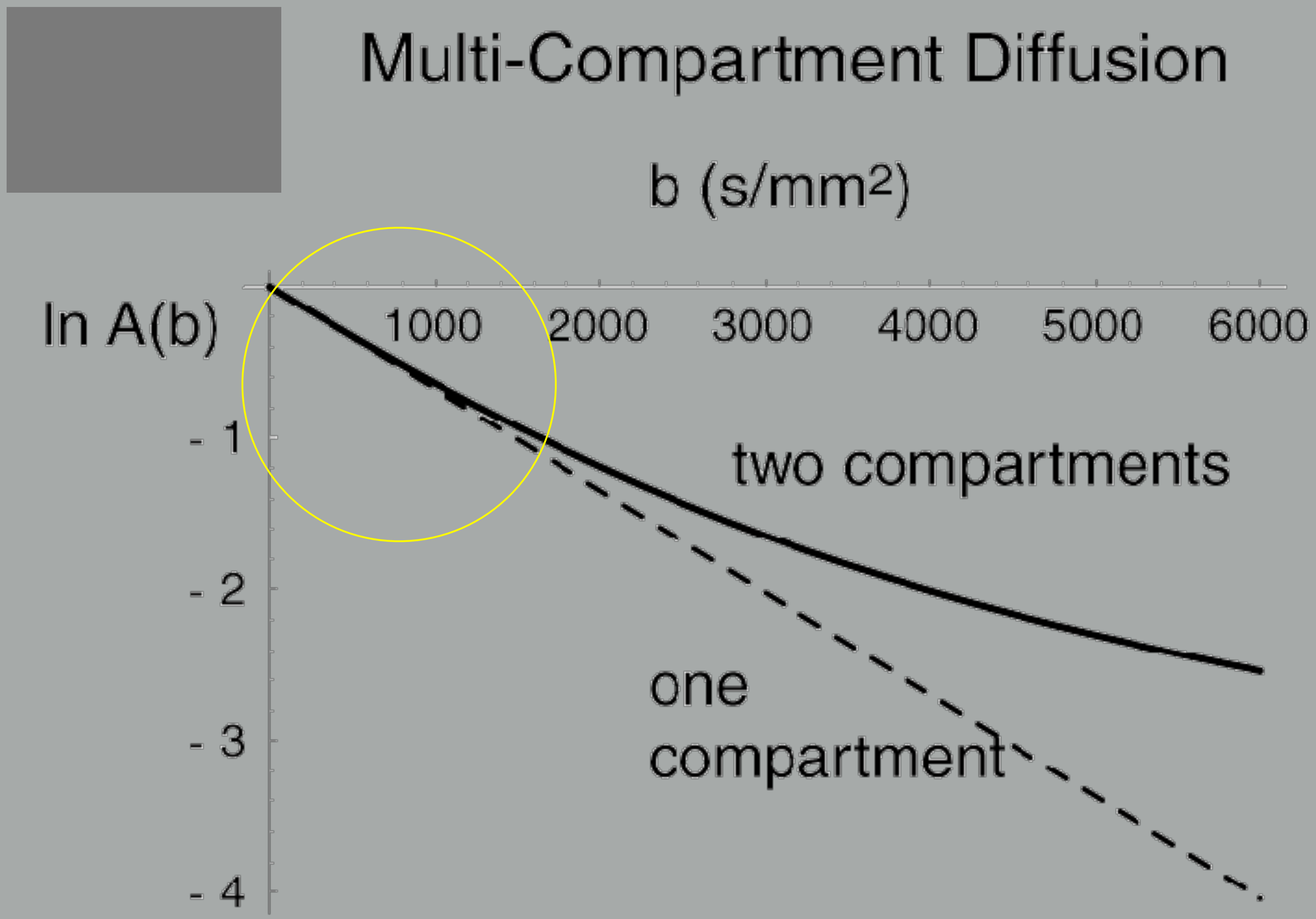




$$\frac{S(b)}{S(0)} = f e^{-bD_1} + (1-f)e^{-bD_2}$$

simple two diffusion coefficient model

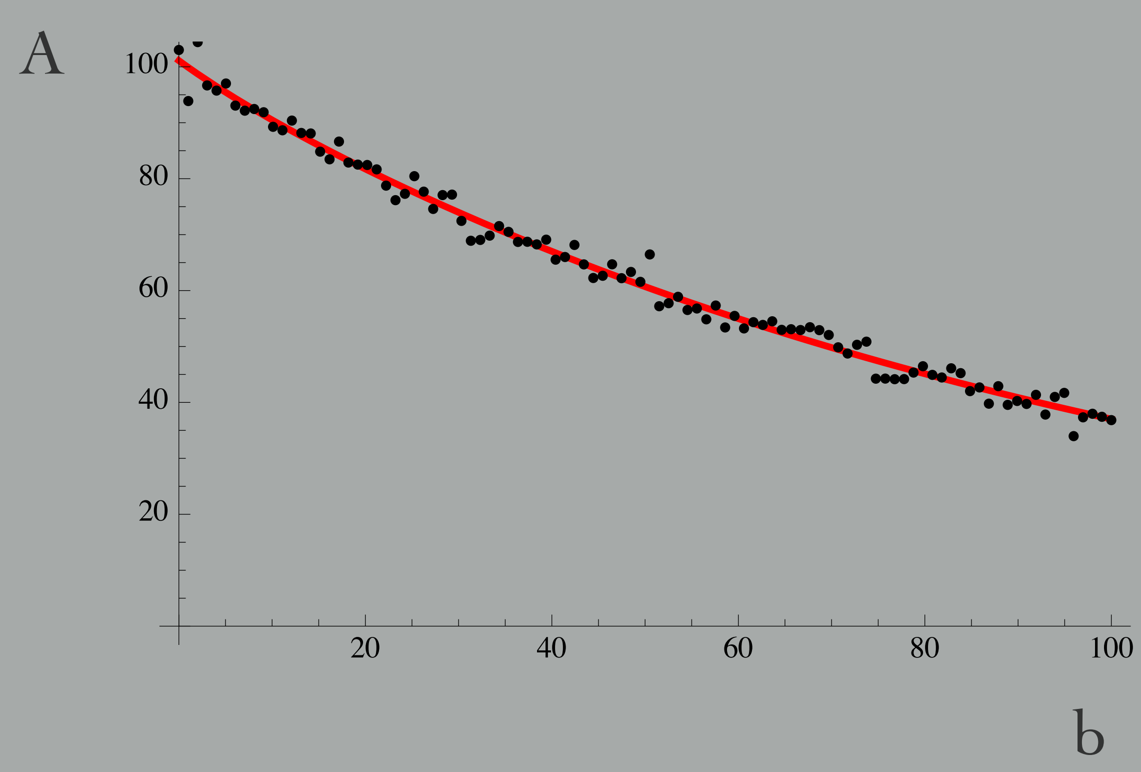
Ambiguities in the Standard DTI Model



Mono-exponential

SNR=50

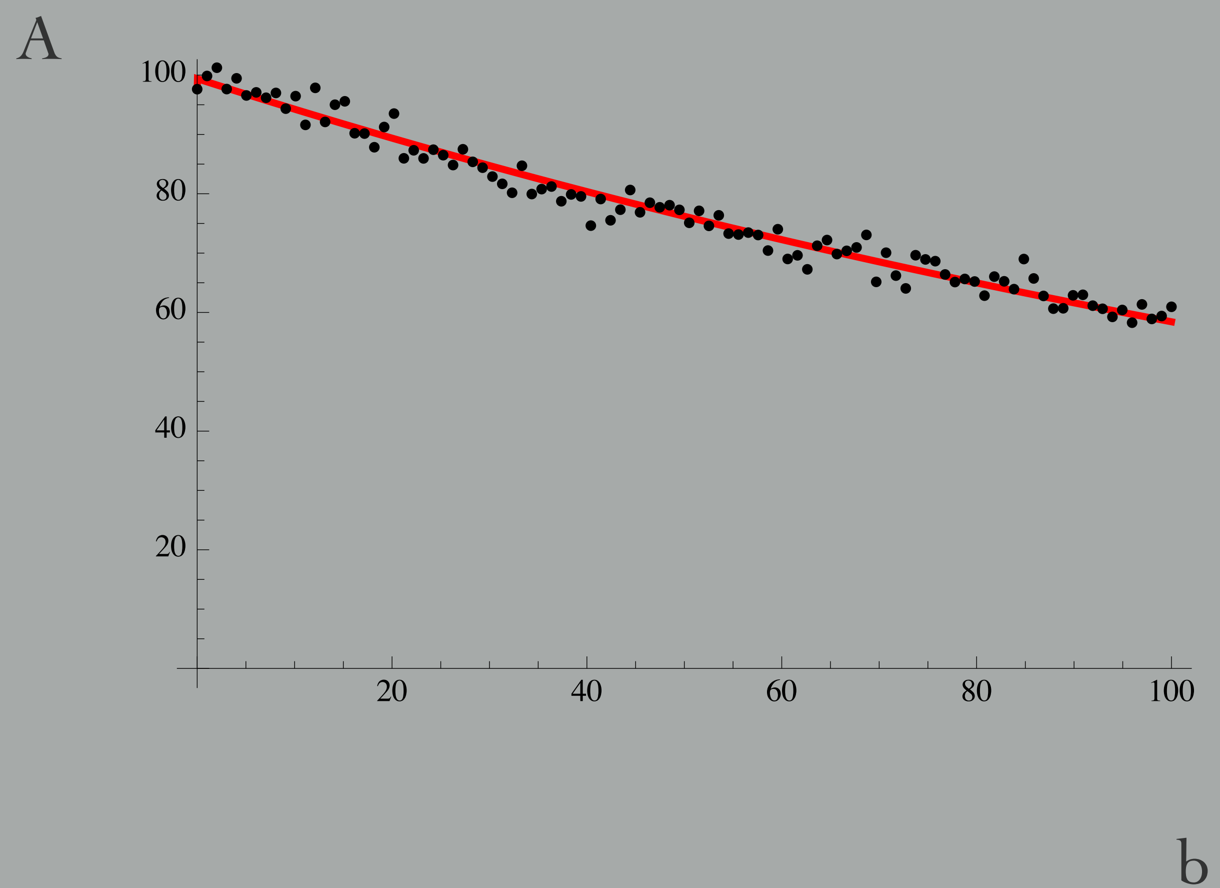
$$b = 100, \{D_1, D_2\} = \{.01, .01\} \quad f = .5$$



But bi-exponential decay can look mono-exponential

SNR=50

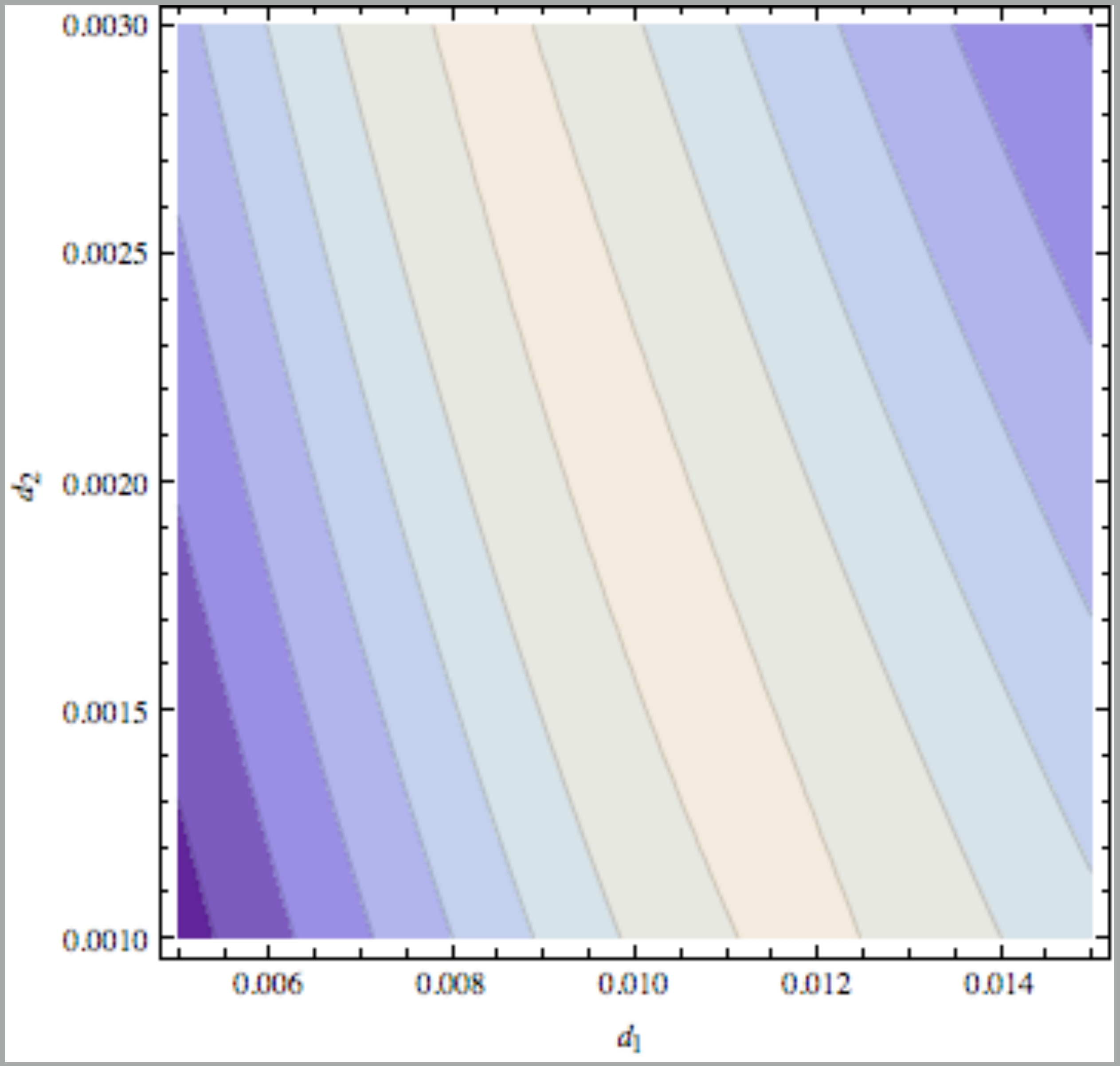
$$b = 100, \{D_1, D_2\} = \{.01, .002\} \quad f = .5$$



Posterior probability of bi-exponential decay

SNR=50

$$b = 100, \{D_1, D_2\} = \{.01, .002\} \quad f = .5$$

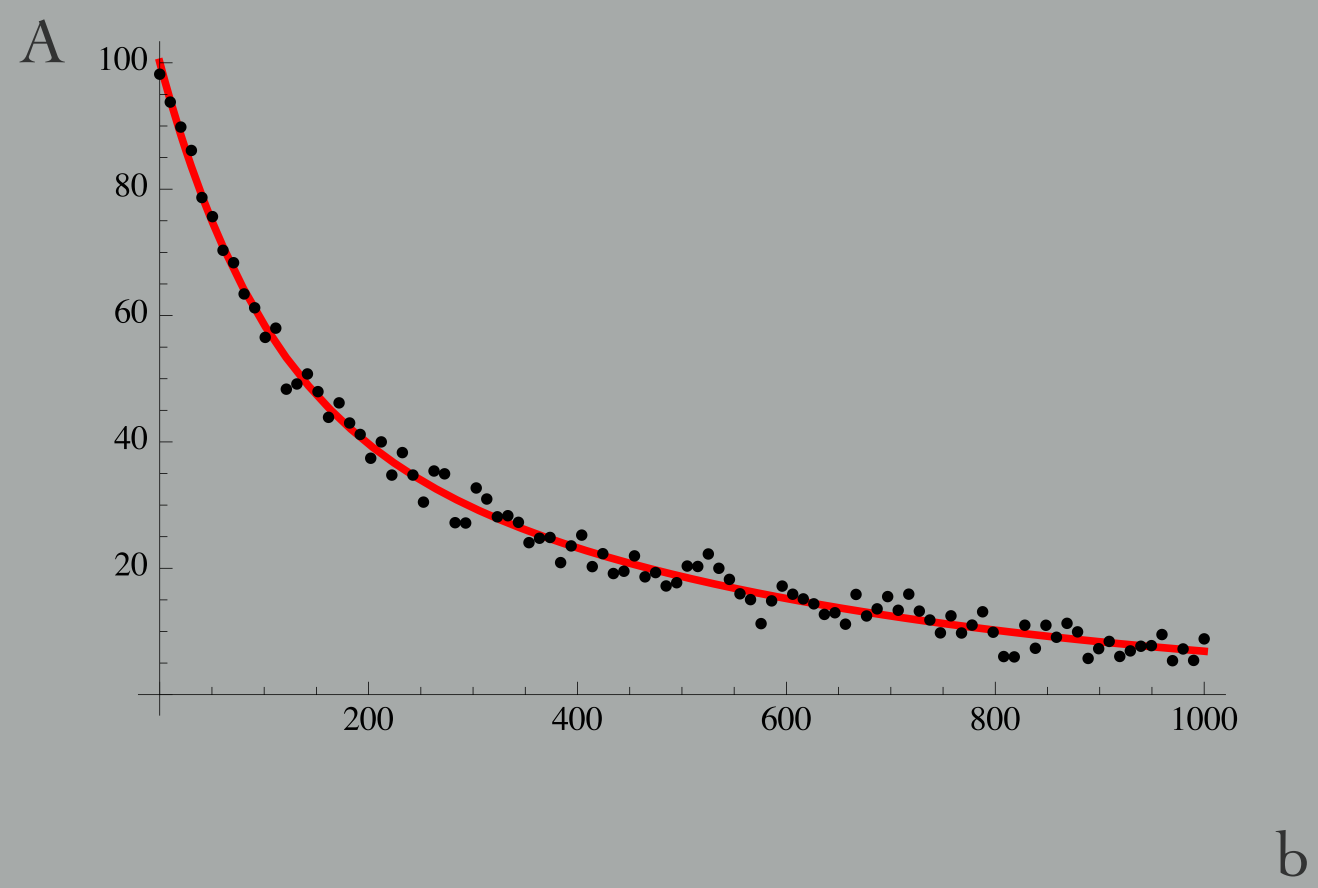


$$p(D_1, D_2 | s, b)$$

Bi-exponential decay

SNR=50

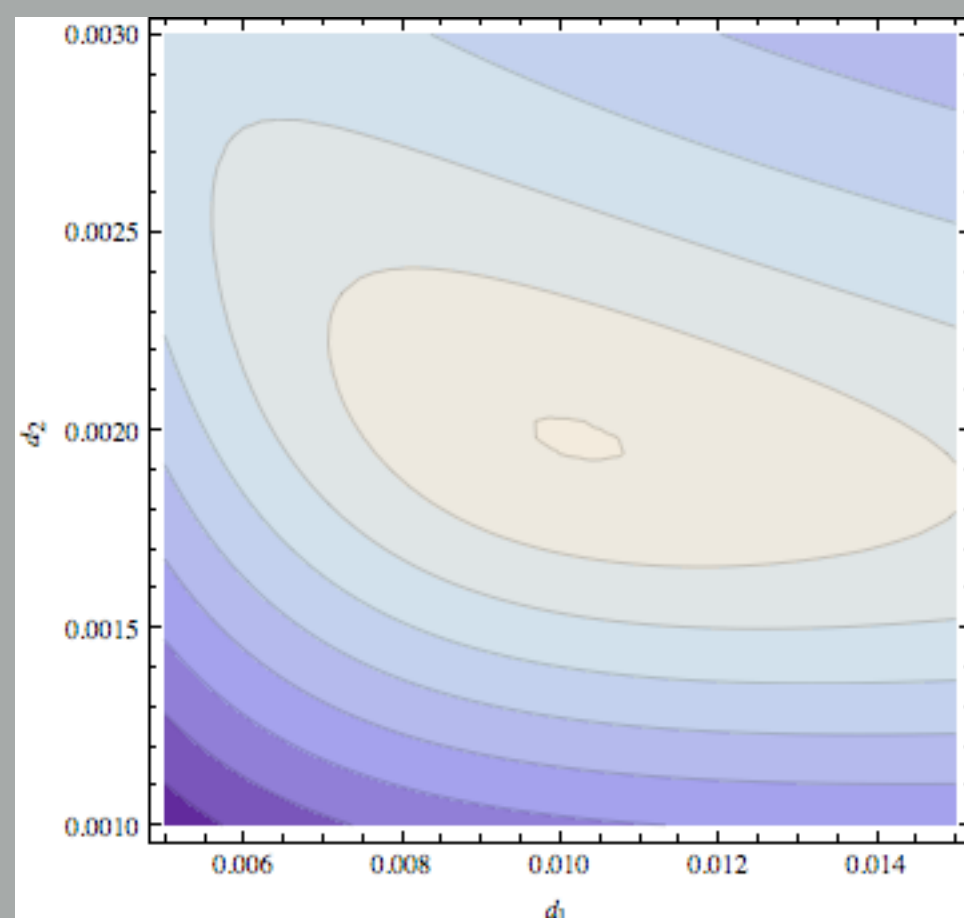
$$b = 1000, \{D_1, D_2\} = \{.01, .002\} \qquad f = .5$$



Posterior probability of bi-exponential decay

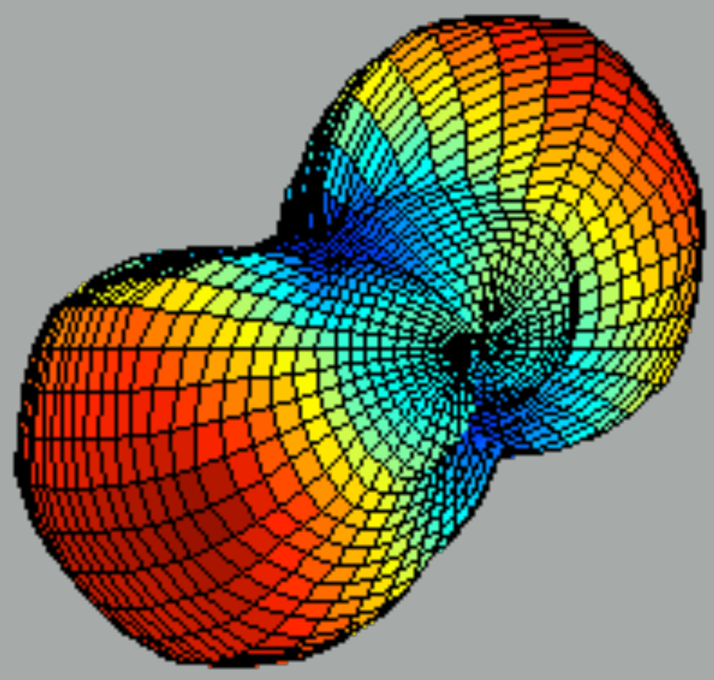
SNR=50

$$b = 1000, \{D_1, D_2\} = \{.01, .002\} \qquad f = .5$$

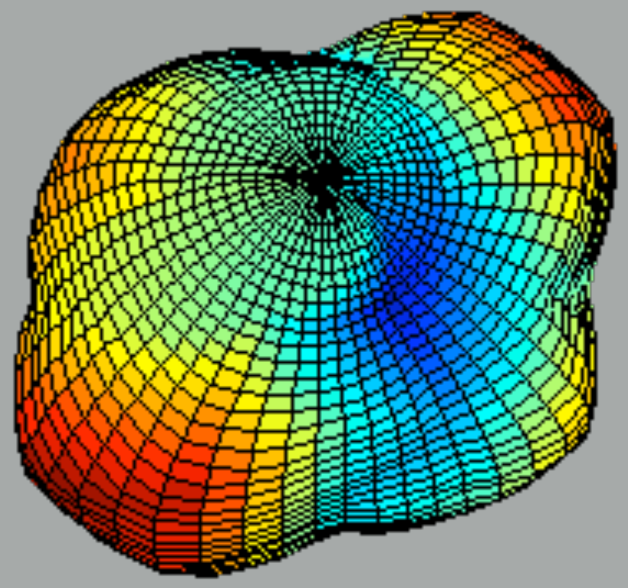


$$p(D_1, D_2 | s, b)$$

Diffusion data in normal human brain



Corpus Callosum



Corona Radiata

The Diffusion Signal

Signal and Distribution are
Fourier Transform pairs

$$\mathfrak{s}(q,\tau) = \int P(\bar{r},\tau)e^{-iq\cdot\bar{r}}d\bar{r}$$

$$\mathfrak{s}(q,\tau) \equiv \frac{s(q,\tau)}{s(0)}$$

$$P(\bar{r},\tau) = \int \mathfrak{s}(q,\tau)e^{iq\cdot\bar{r}}dq$$

Representations of waves

Which coordinate system is most appropriate?

What is the symmetry of the problem?

Representations of waves

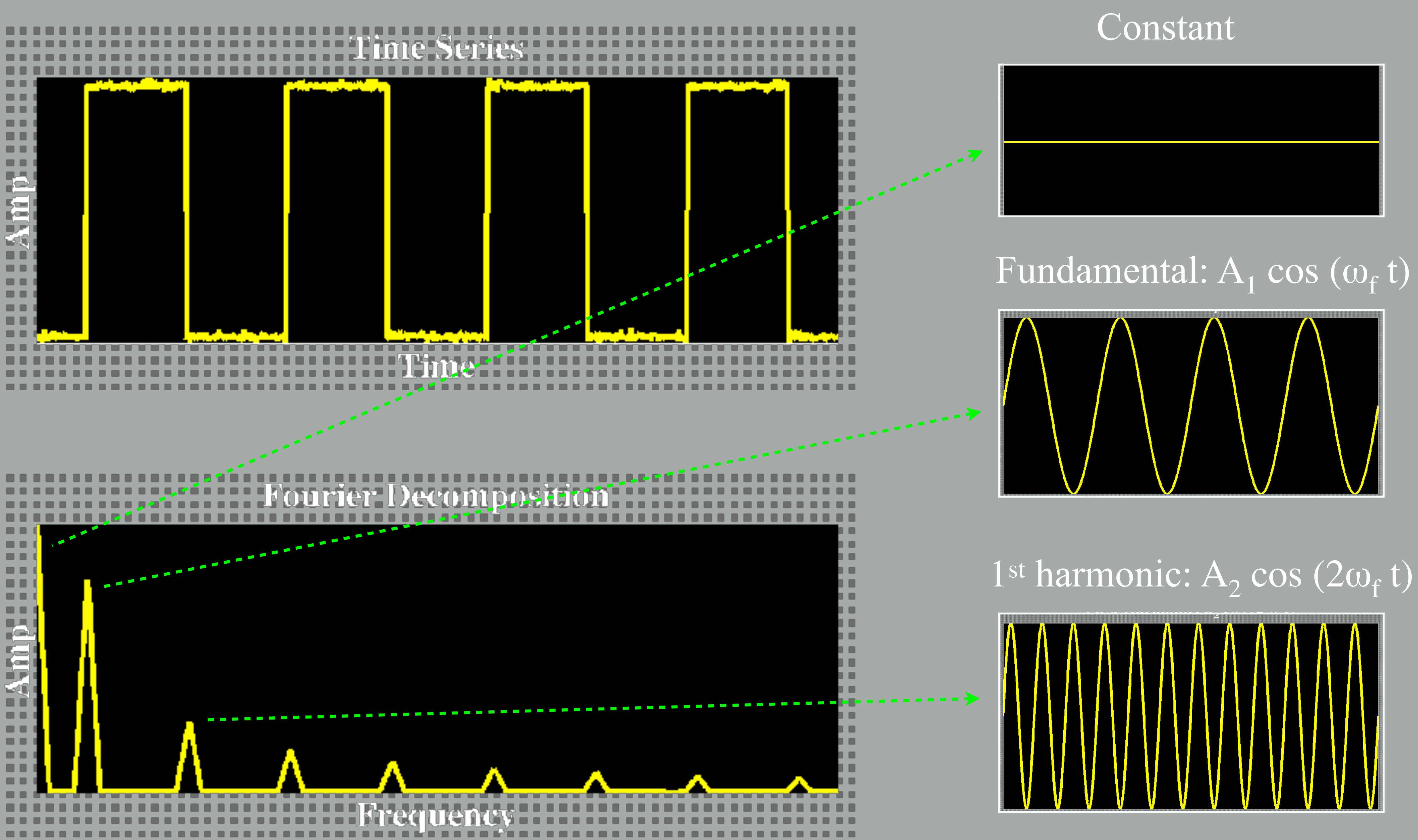
Cartesian symmetry

Fourier basis functions

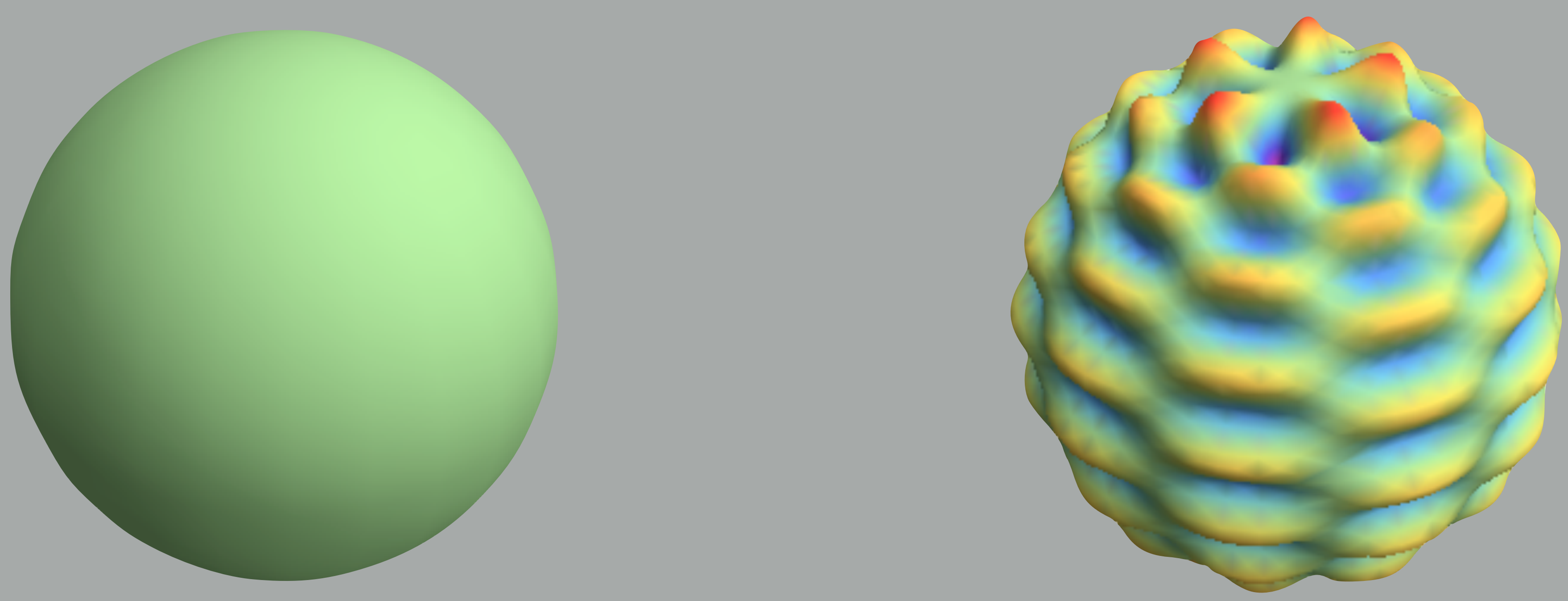
Radial symmetry

Which basis functions?

A familiar harmonic decomposition



Representation of spherical functions



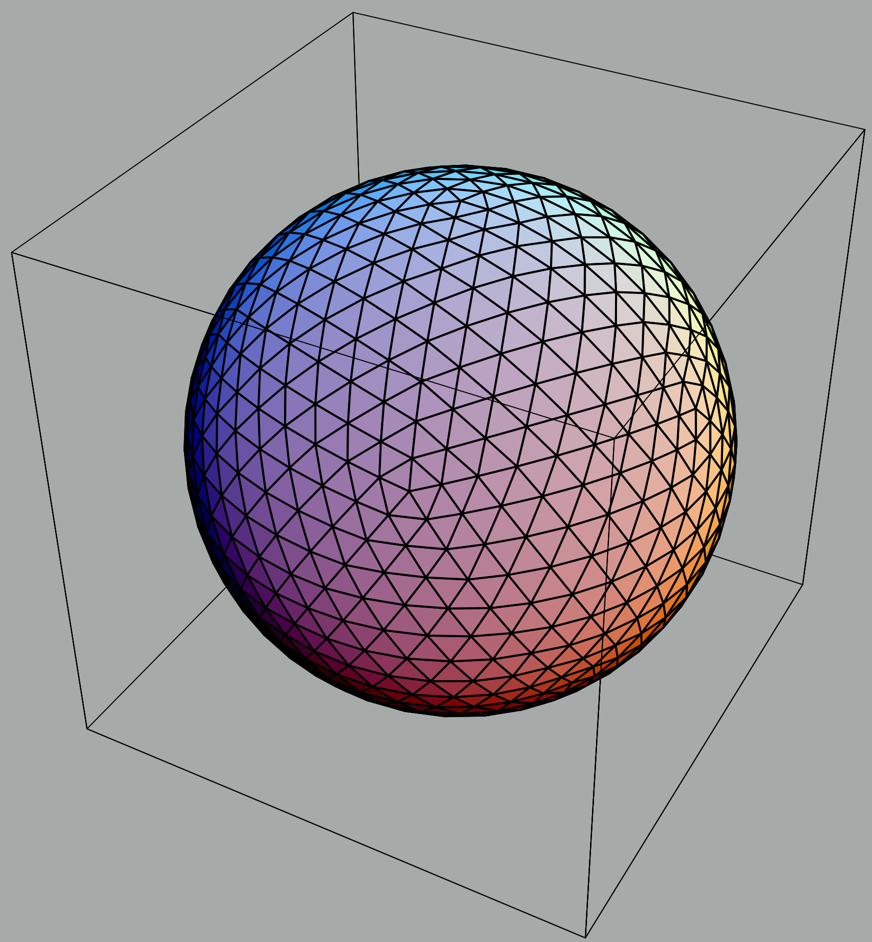
The Diffusion Signal

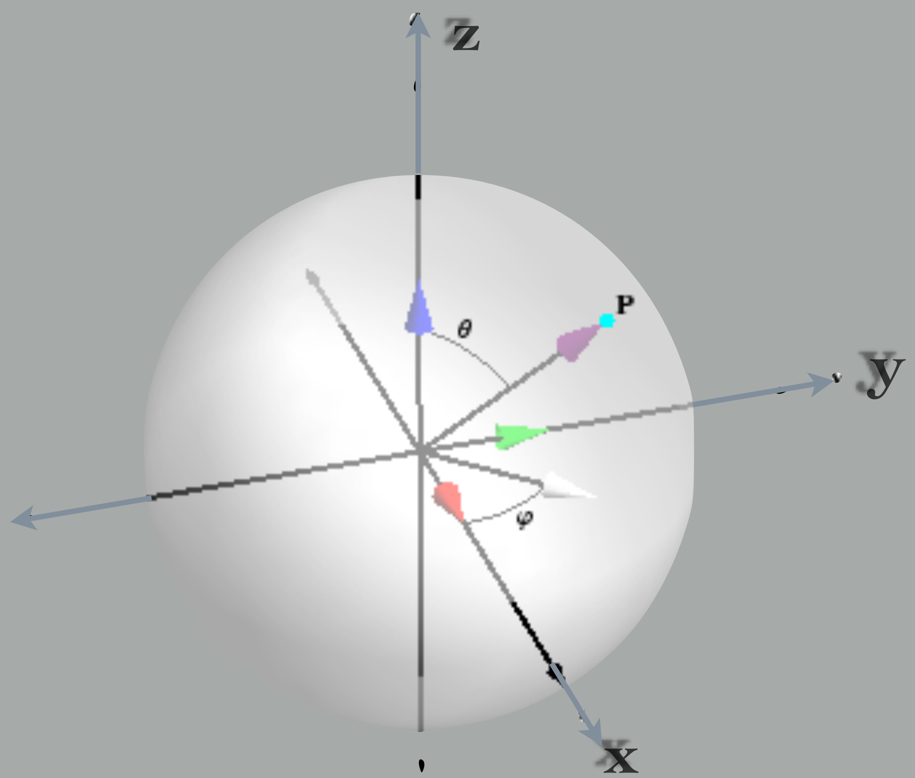
One could sample all of q-space,
but for efficiency, we sample a shell,
so we have data on a spherical surface

$$P(\bar{r}, \tau) = \int \mathfrak{s}(q, \tau) e^{iq \cdot \bar{r}} dq$$

Not enough q data to do this integral!

Spherical Coordinates





Representations of planar functions

Fourier decomposition:

$$f(\omega, t) = \sum_j a_j e^{-i\omega_j t}$$

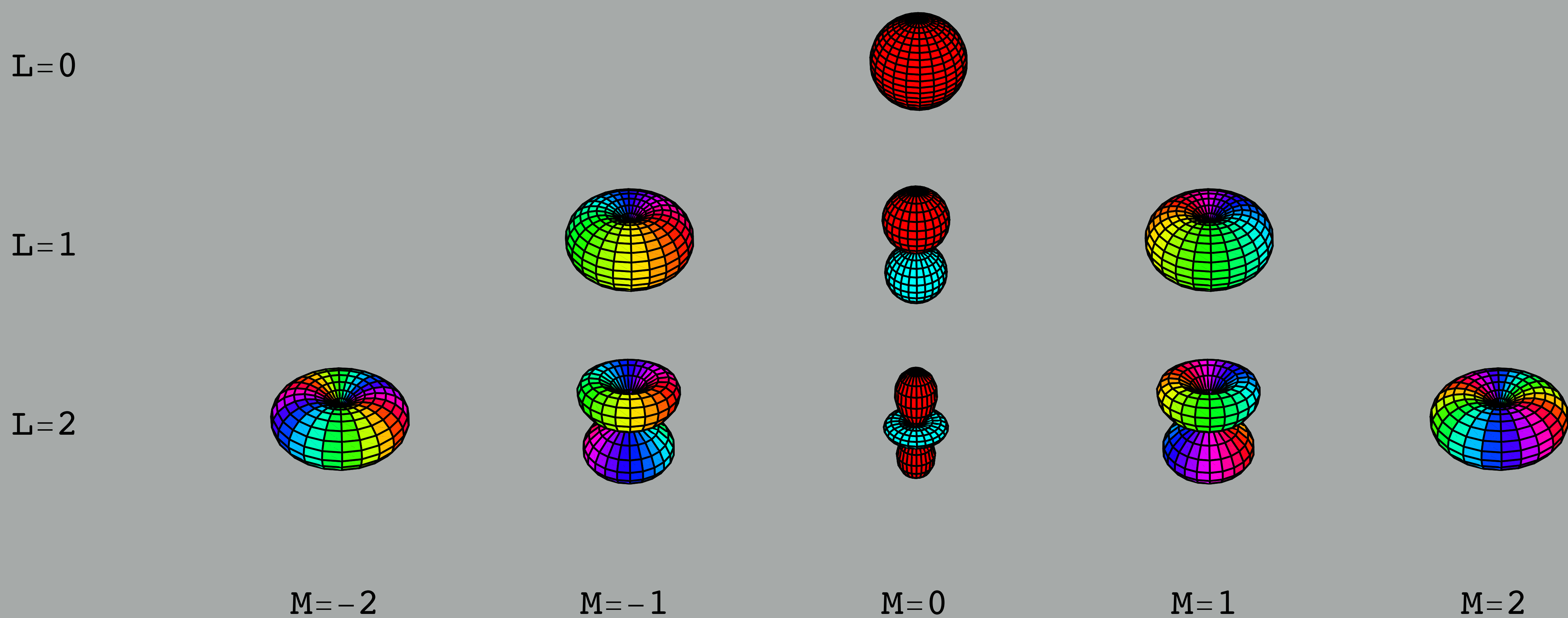
Representations of spherical functions

$$f(\theta, \phi) = \sum_{l=0}^{\infty} \sum_{m=-l}^{l} a_{lm} Y_{lm}(\theta, \phi)$$

$$Y_{lm}(\theta, \phi) = \text{spherical harmonics}$$

$$a_{lm} = \text{spherical harmonic coefficients}$$

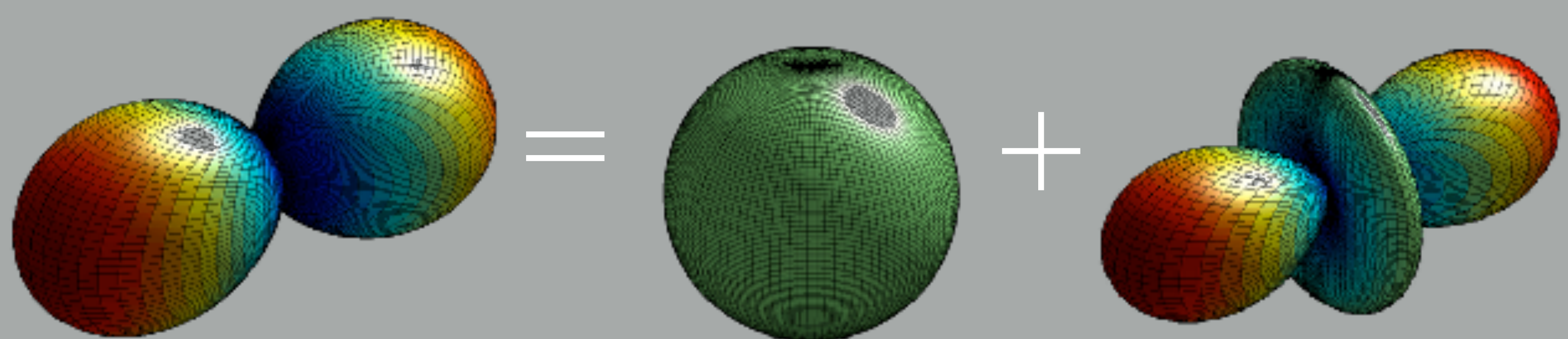
Spherical Harmonics



color represents phase

Harmonic Decomposition

Single Fiber



L=0 L=2

Orthonormal Functions

The spherical harmonics are *orthonormal*
They are orthogonal (perpendicular) and normalized

$$\int d\Omega \, Y^*_{lm}(\Omega) Y_{l'm'}(\Omega) = \delta_{ll'} \delta_{mm'}$$

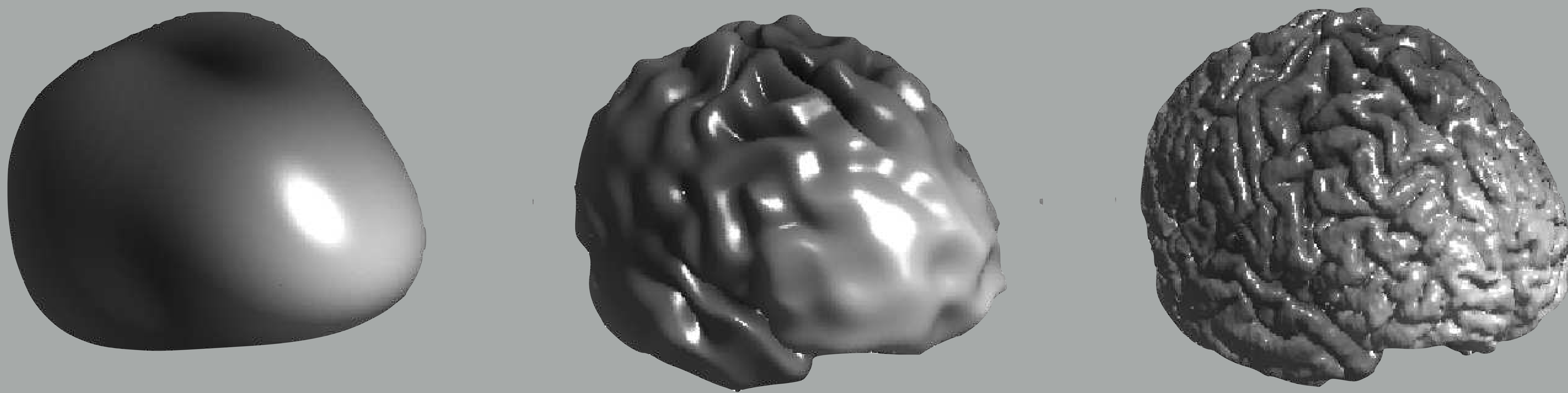
$$\Omega = (\theta, \phi)$$

Orthonormal Functions

This allows us to easily calculate the coefficients, given

$$a_{lm} = \int d\Omega \, f(\Omega) Y^*_{lm}(\Omega)$$

Representation of Shapes



$l_{max} = 5$ $\quad$ $l_{max} = 25$ $\quad$ $l_{max} = 75$

Cortical surface description in terms of spherical harmonics of maximum degree l_{max}

Representations of spherical functions

the signal

$$S(\theta, \phi) = \sum_{l=0}^{\infty} \sum_{m=-l}^{l} s_{lm} Y_{lm}(\theta, \phi)$$

the angular distribution of fibers

$$P(\vartheta, \varphi) = \sum_{l=0}^{\infty} \sum_{m=-l}^{l} p_{lm} Y_{lm}(\vartheta, \varphi)$$

Representations of spherical functions

the signal coefficients

$$s_{lm} = \int_0^{2\pi} \int_0^{\pi} Y_{lm}^*(\theta, \phi) S(\theta, \phi) \sin\theta \, d\theta \, d\phi$$

the PDF coefficients

$$p_{lm} = \int_0^{2\pi} \int_0^{\pi} Y_{lm}^*(\theta, \phi) P(\theta, \phi) \sin\theta \, d\theta \, d\phi$$

Orientation Distribution Function (ODF)

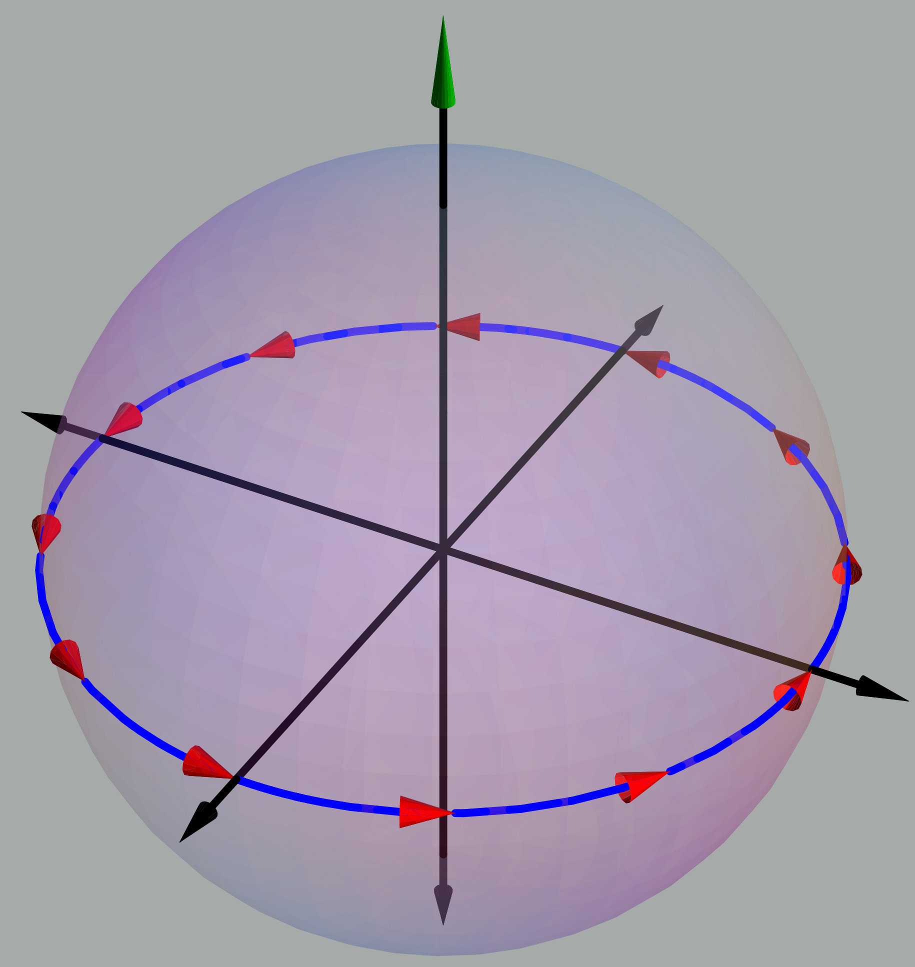
Funk-Radon Transform

$$\mathrm{ODF}_q(\theta, \phi) = \int_{C_{\theta,\phi}} S(\theta, \phi) \sin\theta \, d\theta d\phi$$

Tuch, et. al. MRM 2001

Orientation Distribution Function (ODF)

Funk-Radon Transform



Tuch, et. al.

Orientation Distribution Function (ODF)

$$\mathrm{ODF}_q(\theta, \phi) = \sum_{l=0}^{\infty} \sum_{m=-l}^{l} o_{lm} Y_{lm}(\theta, \phi)$$

Anderson, et. al. MRM 2001

Orientation Distribution Function (ODF)

where

SHD of signal

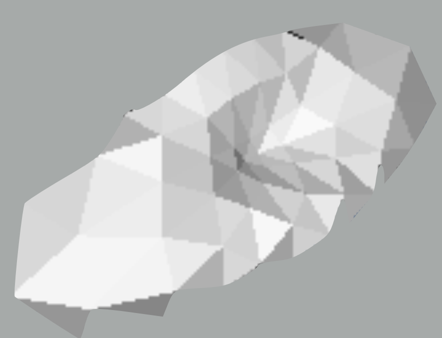
$$o_{lm} = \frac{2\pi|\boldsymbol{q}|}{s_o}\xi(l)s_{lm}\eta_l$$

$$\xi(l) = (-1)^{l/2}\frac{(l+1)!!}{(l+1)l!!} \qquad \eta_l = \begin{cases} 1 & \text{even } l \\ 0 & \text{odd } l \end{cases}$$

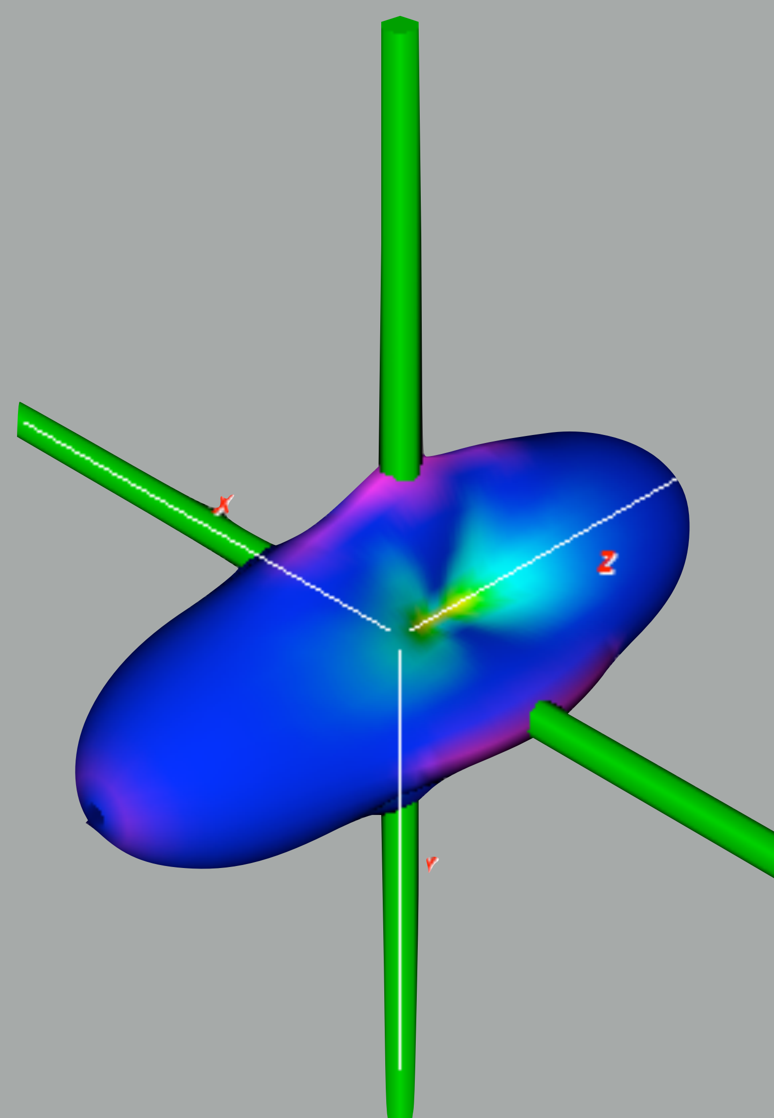
$$l!! = \begin{cases} l\cdot(l-2)\cdot(l-4)\cdot\ldots 4\cdot 2) & l \text{ even} \\ l\cdot(l-2)\cdot(l-4)\cdot\ldots 3\cdot 1) & l \text{ odd} \end{cases}$$

Anderson, et. al. MRM 2001

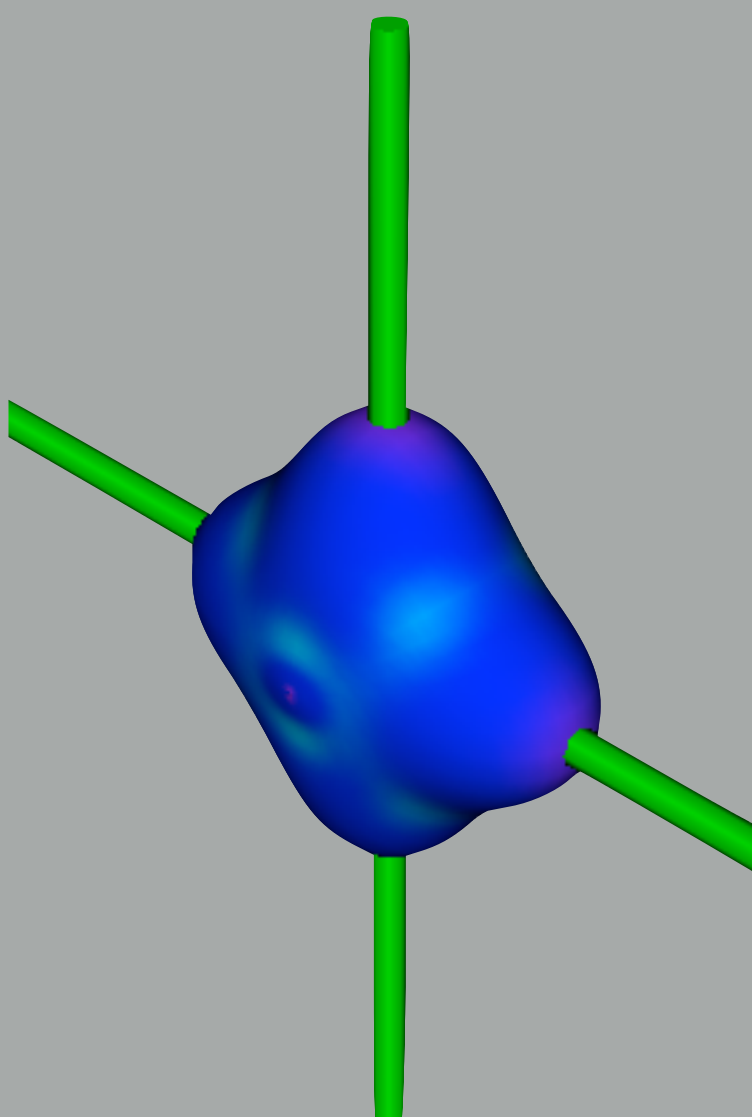
Signal SHD



signal

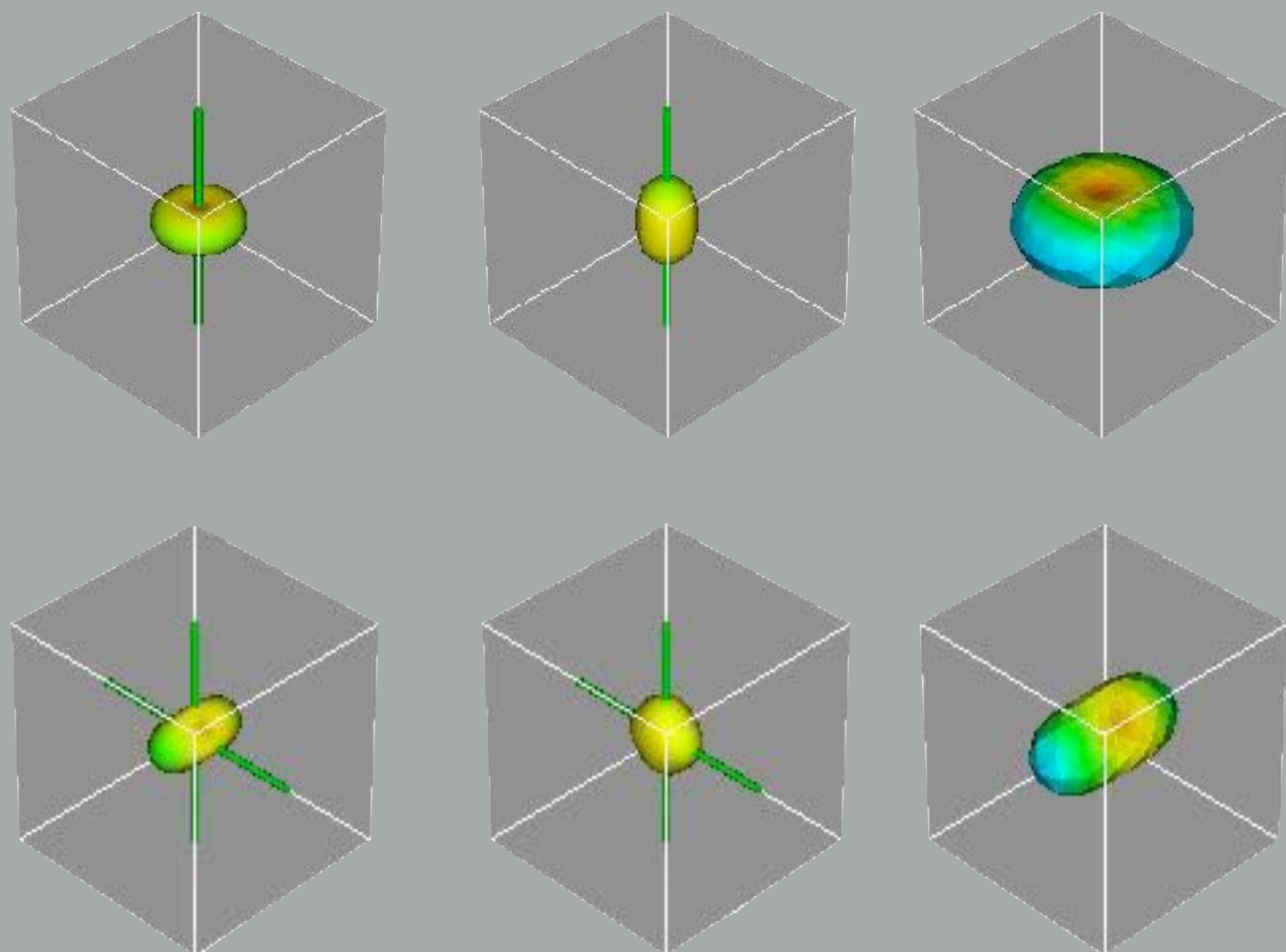


SHD of signal



ODF

Signal SHD

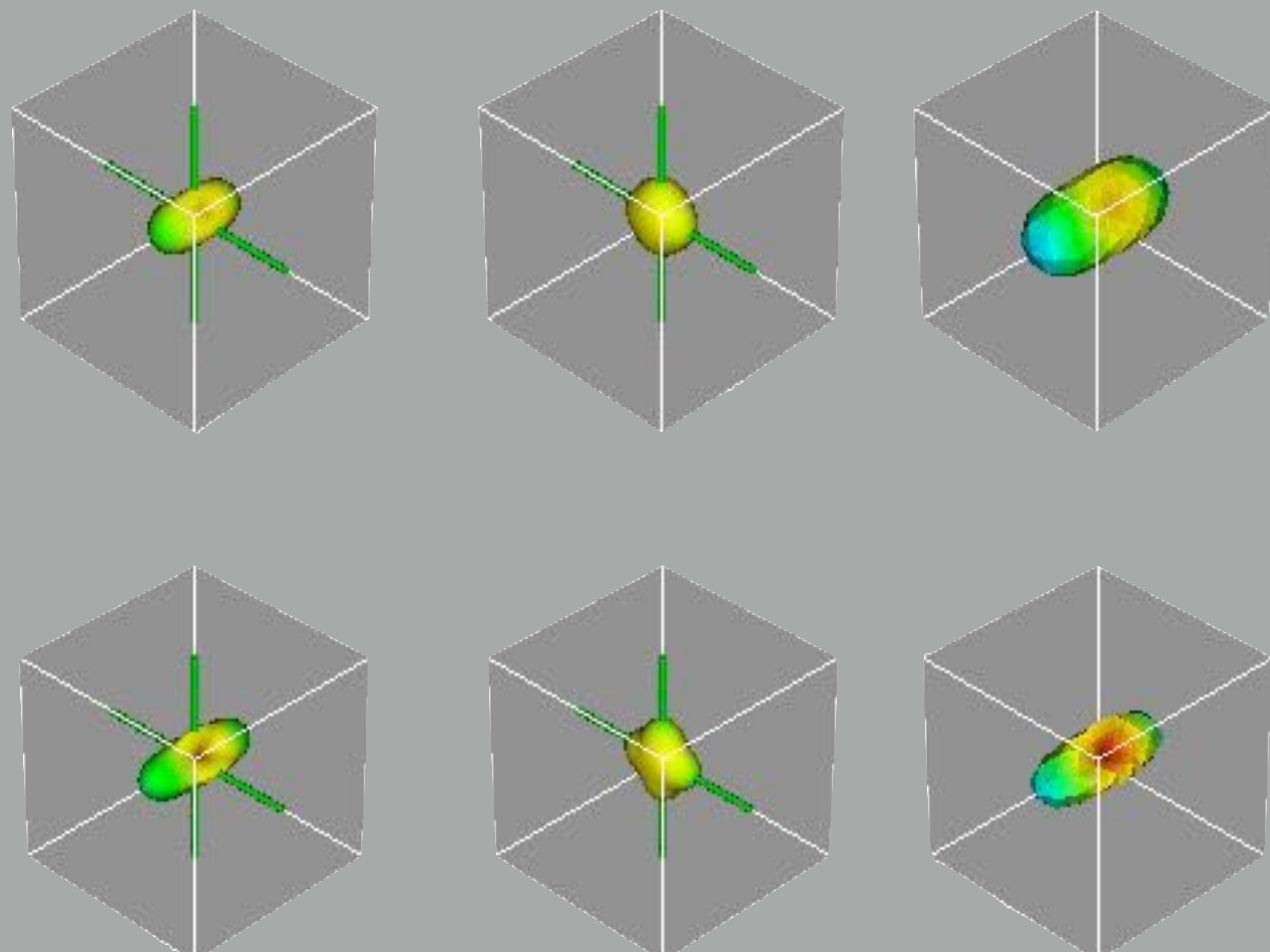


b=1500 mm^2/s

b=1500 mm^2/s

SHD of signal | ODF | signal

Signal SHD

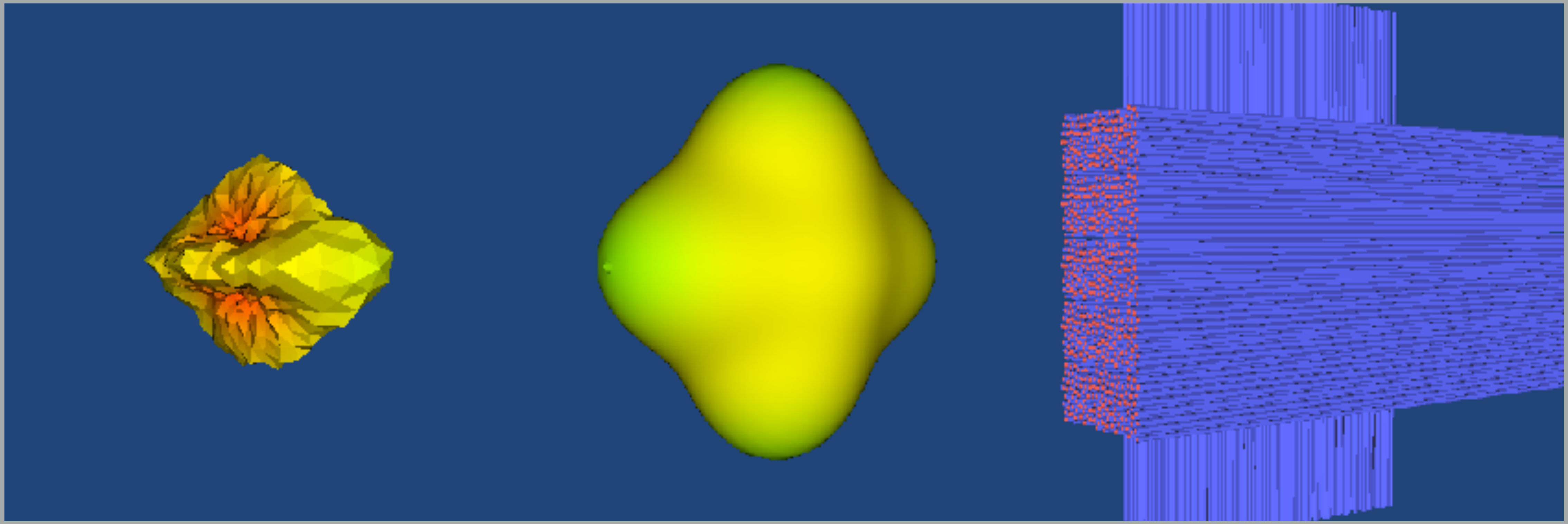


$b=1500\ mm^2/s$

$b=3000\ mm^2/s$

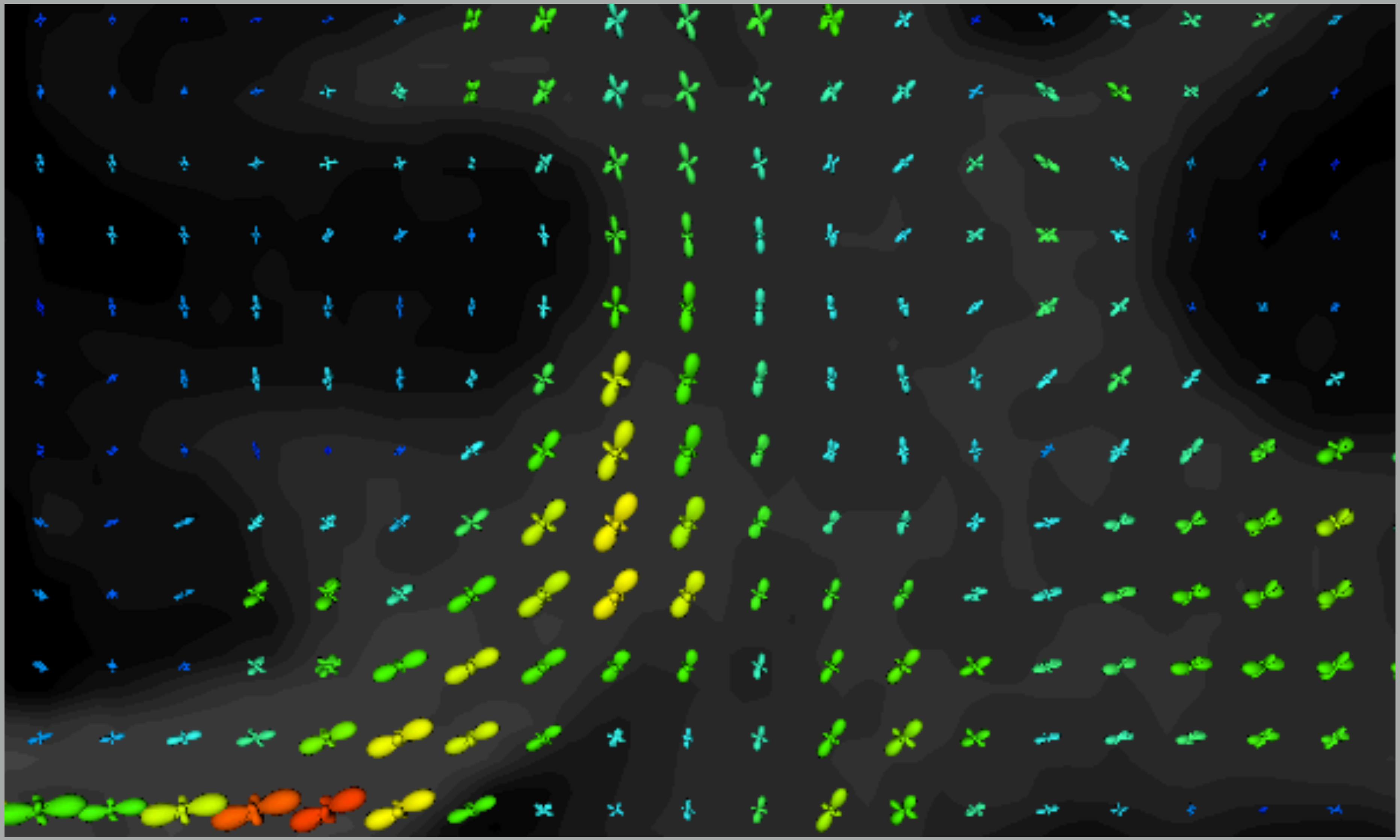
SHD of signal ODF signal

Signal SHD

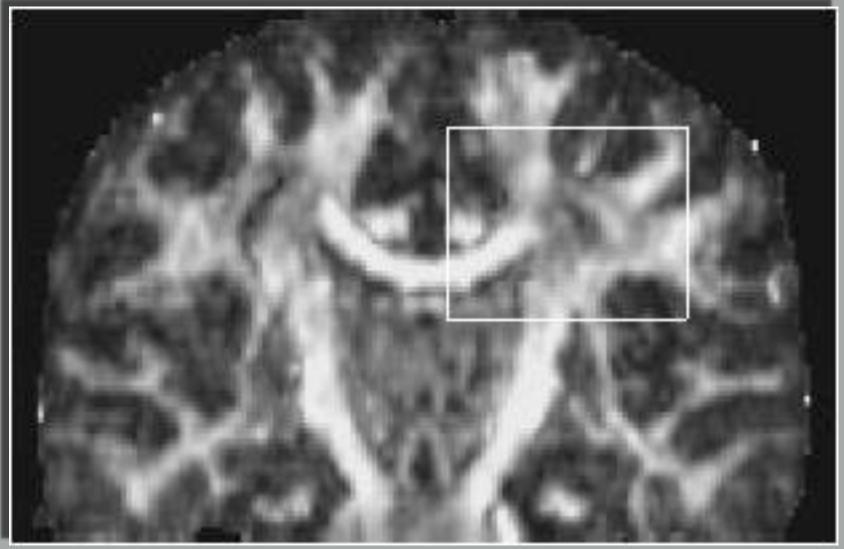


signal ODF fiber model

ODF in normal human



anisotropic components of ODF

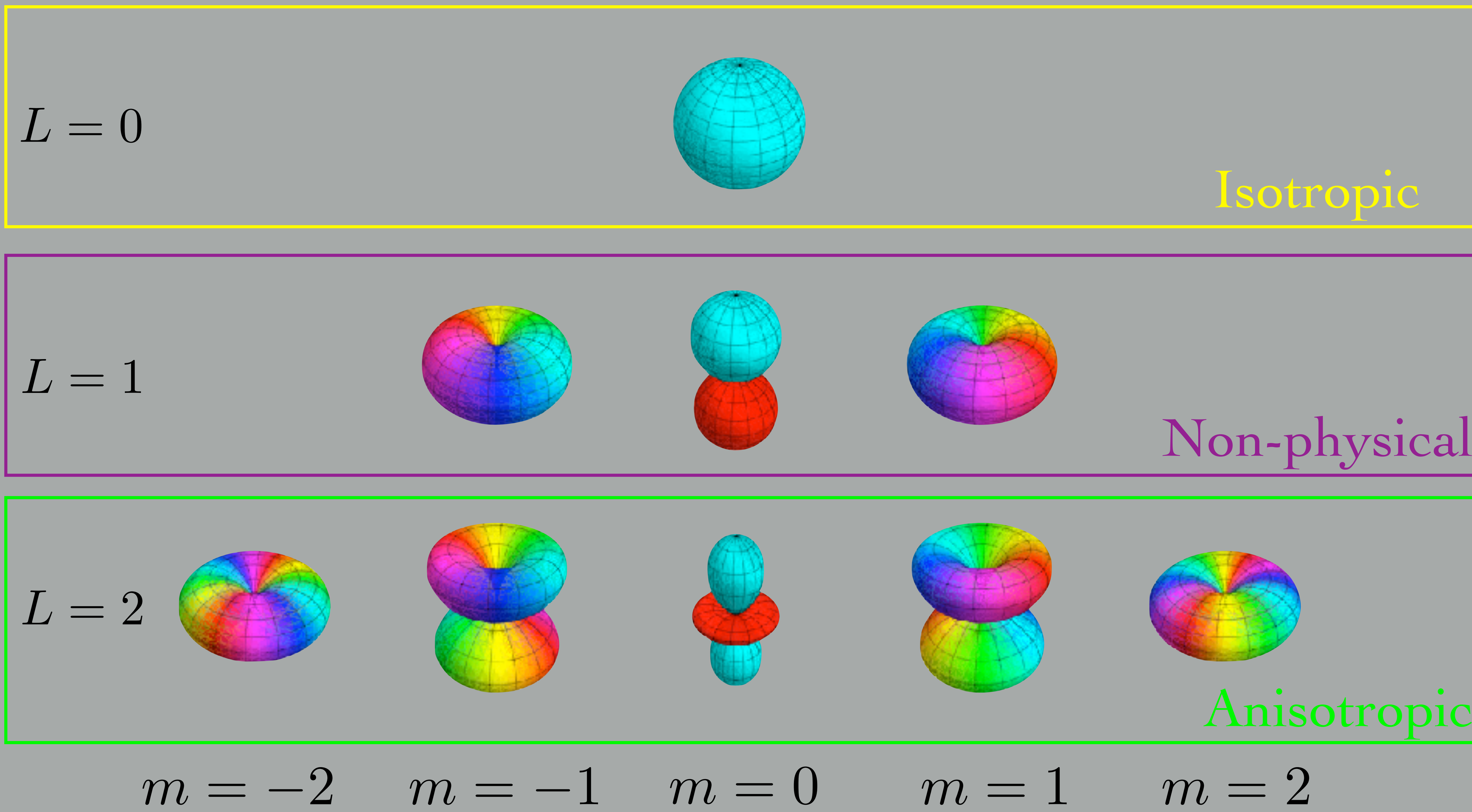


Diffusion Anisotropy in standard DTI model

Fractional Anisotropy

$$\boxed{FA = \sqrt{\frac{3}{2}\frac{\overline{(\delta\lambda)^2}}{\overline{\lambda^2}}}}$$

Spherical Harmonics



Laplace Series

$$
\begin{aligned}
f(\theta,\phi) &= \sum_{l=0}^{\infty}\sum_{m=-l}^{-l} a_{lm}Y_{lm}(\theta,\phi) \\
&= a_{00}Y_{00}(\theta,\phi) + \sum_{l=2}^{\infty}\sum_{m=-l}^{-l} a_{lm}Y_{lm}(\theta,\phi) \\
&= \underbrace{\frac{a_{00}}{\sqrt{4\pi}}}_{\text{isotropic}} + \underbrace{\sum_{l=2}^{\infty}\sum_{m=-l}^{-l} a_{lm}Y_{lm}(\theta,\phi)}_{\text{anisotropic}}
\end{aligned}
$$

l even

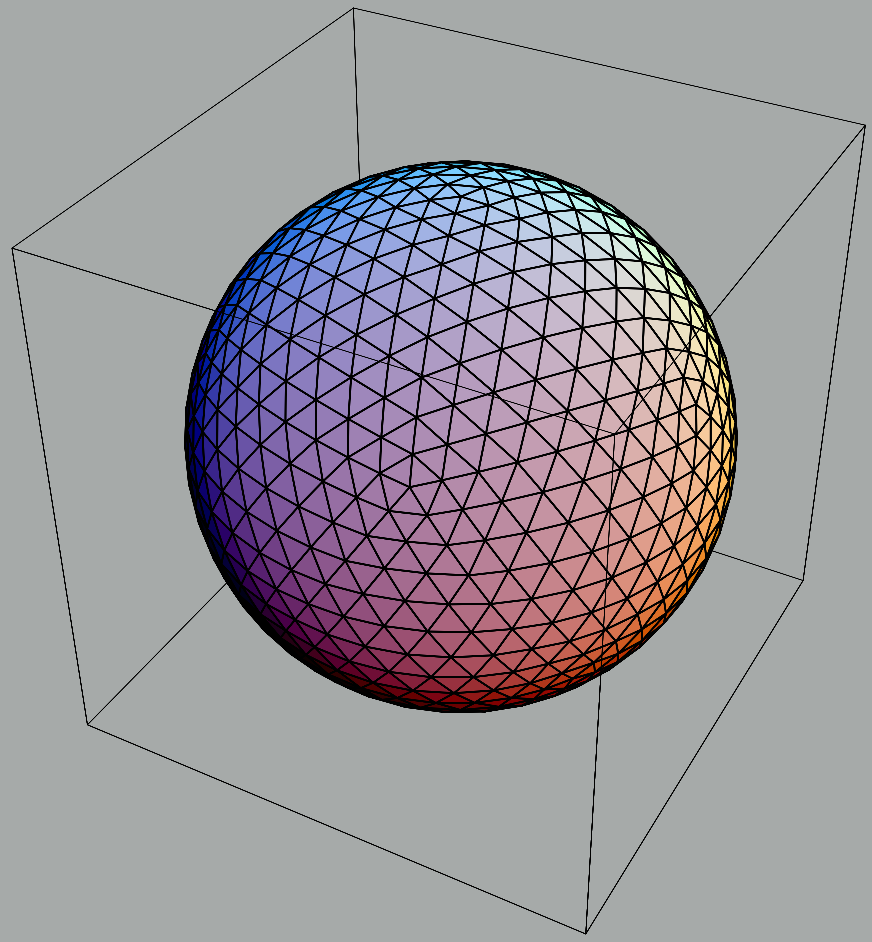
Generalized Diffusion Anisotropy

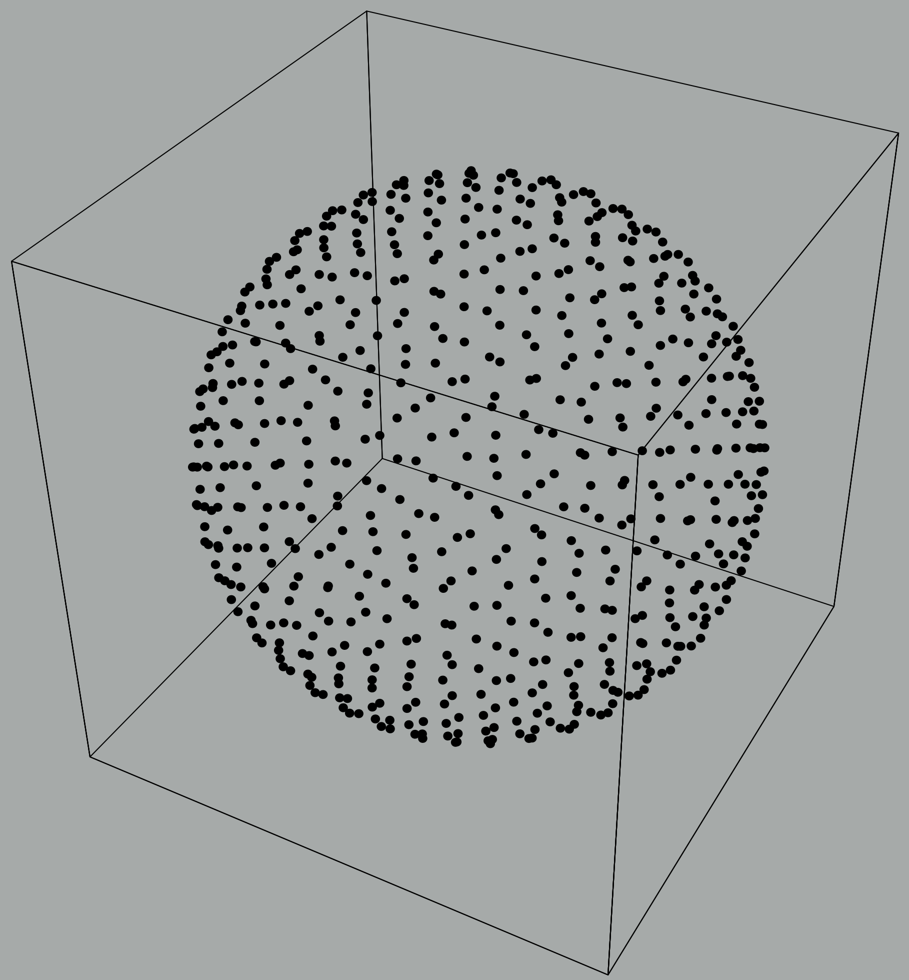
anisotropic component

$$f(\theta, \phi) - \frac{a_{00}}{\sqrt{4\pi}} = \sum_{l=2}^{\infty} \sum_{m=-l}^{-l} a_{lm} Y_{lm}(\theta, \phi)$$

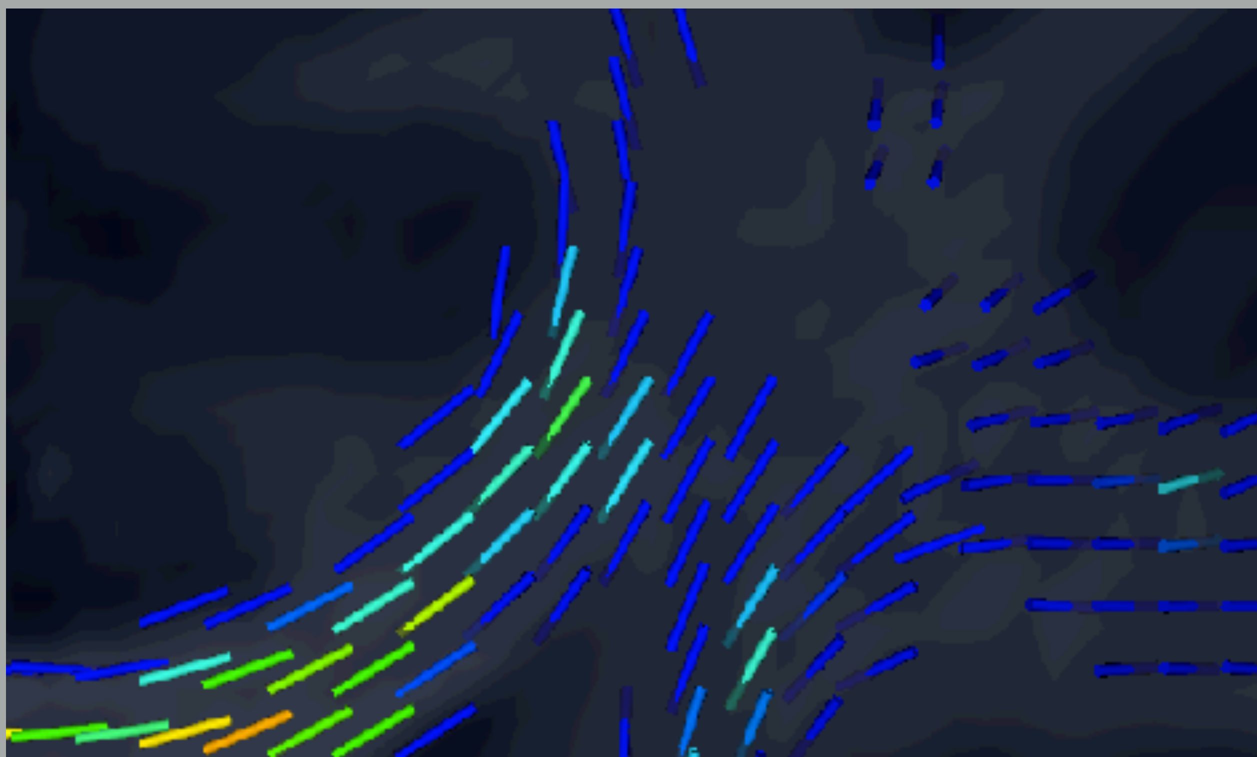
l even

High Angular Resolution Sampling

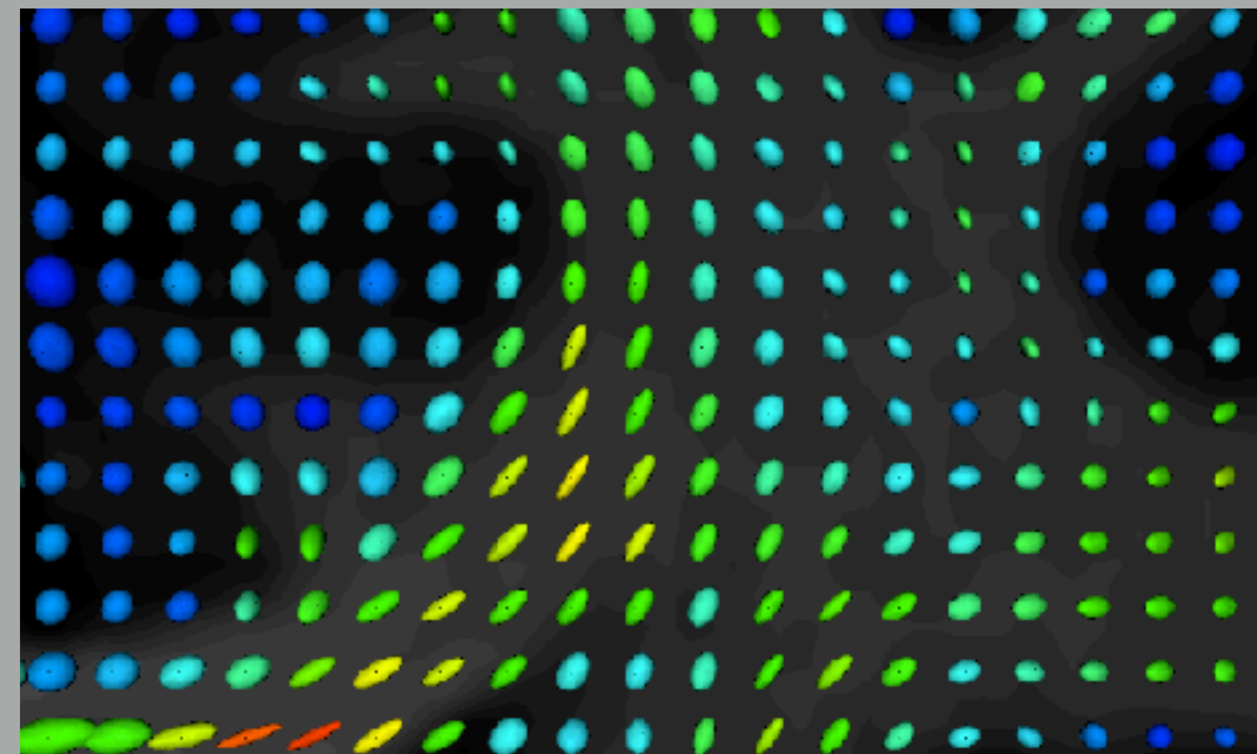




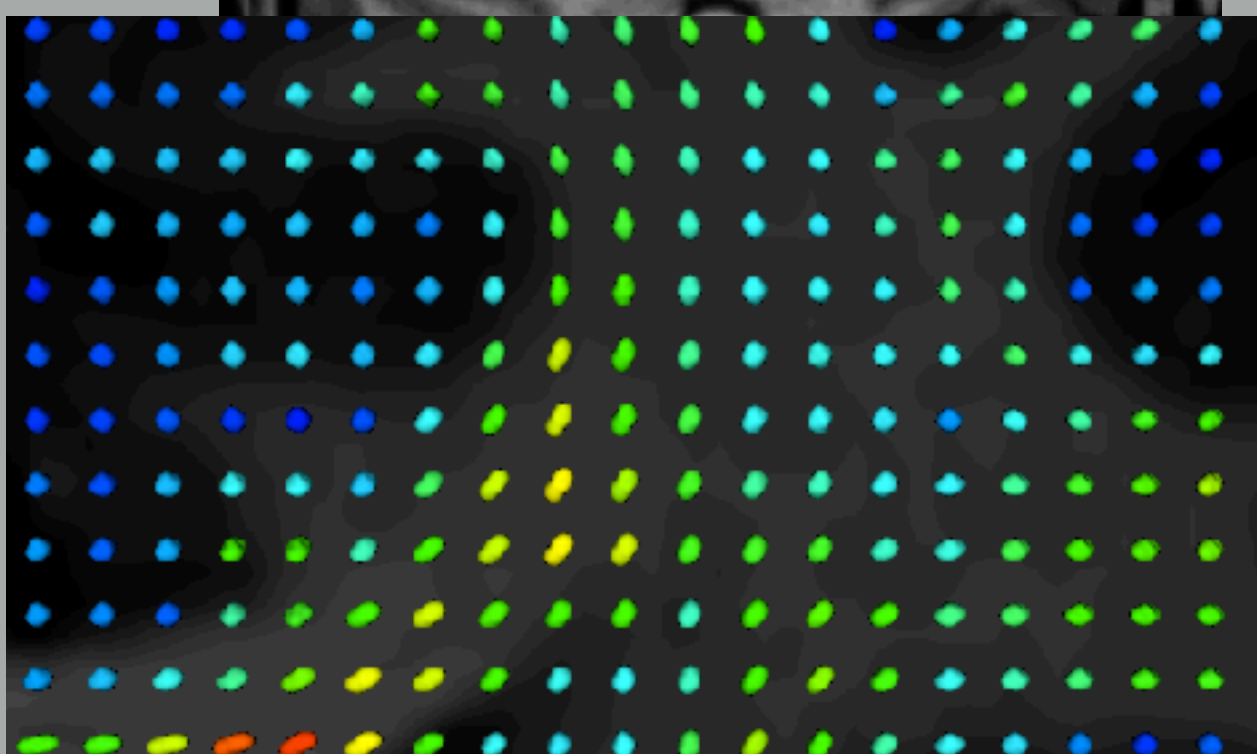
High Angular Resolution DTI (HARDI)



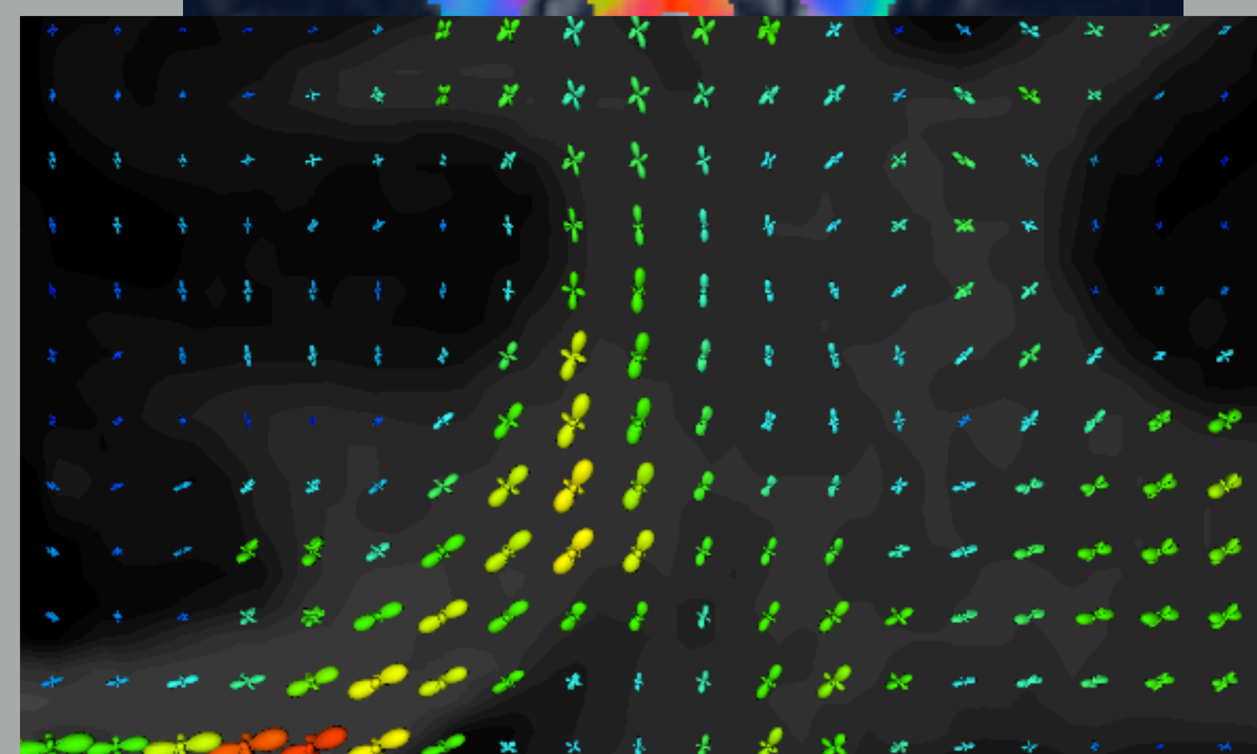
principal eigenvector



2nd order diffusion tensor

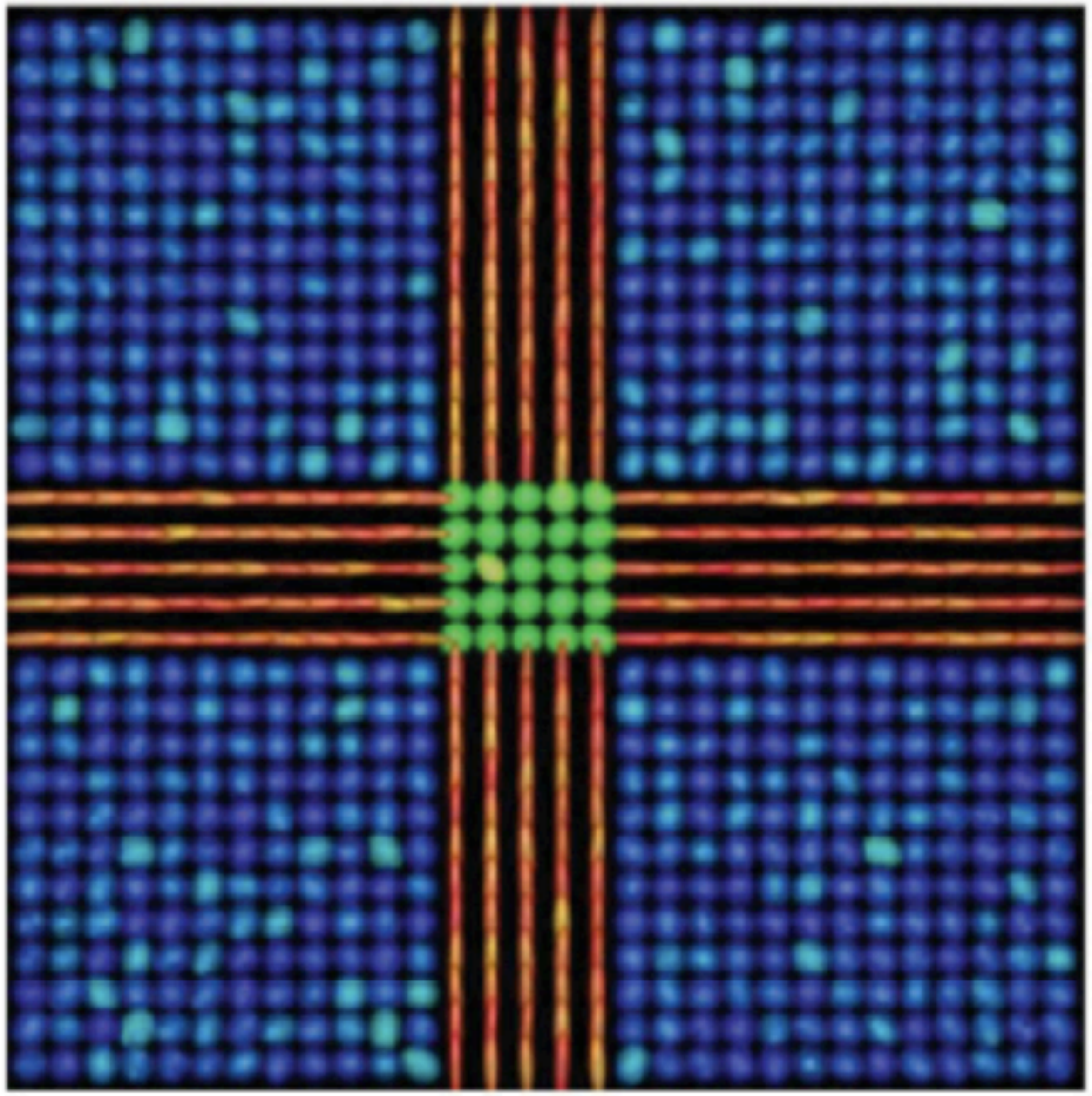


ODF

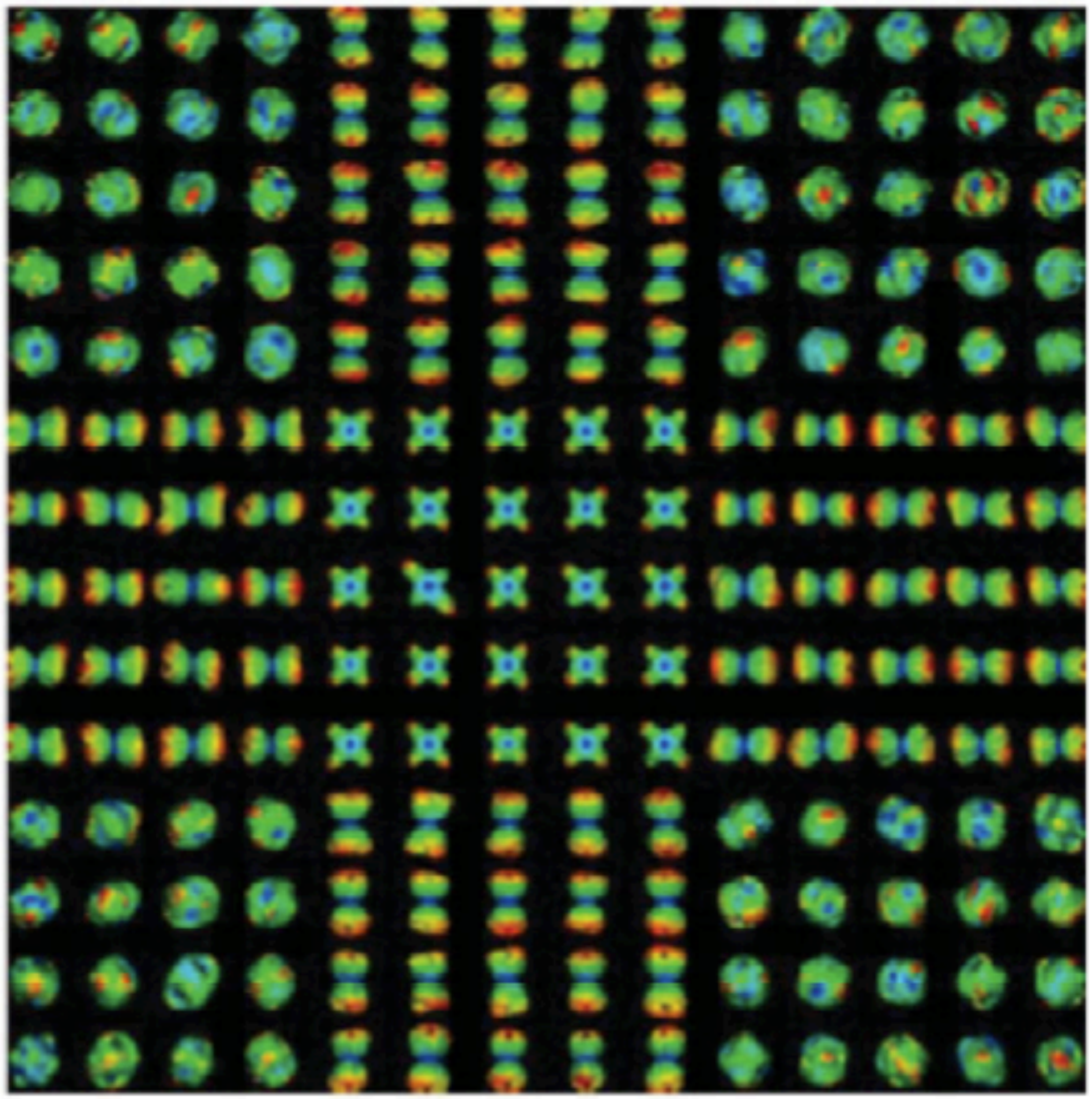


anisotropic components of ODF

HARDI Simulation



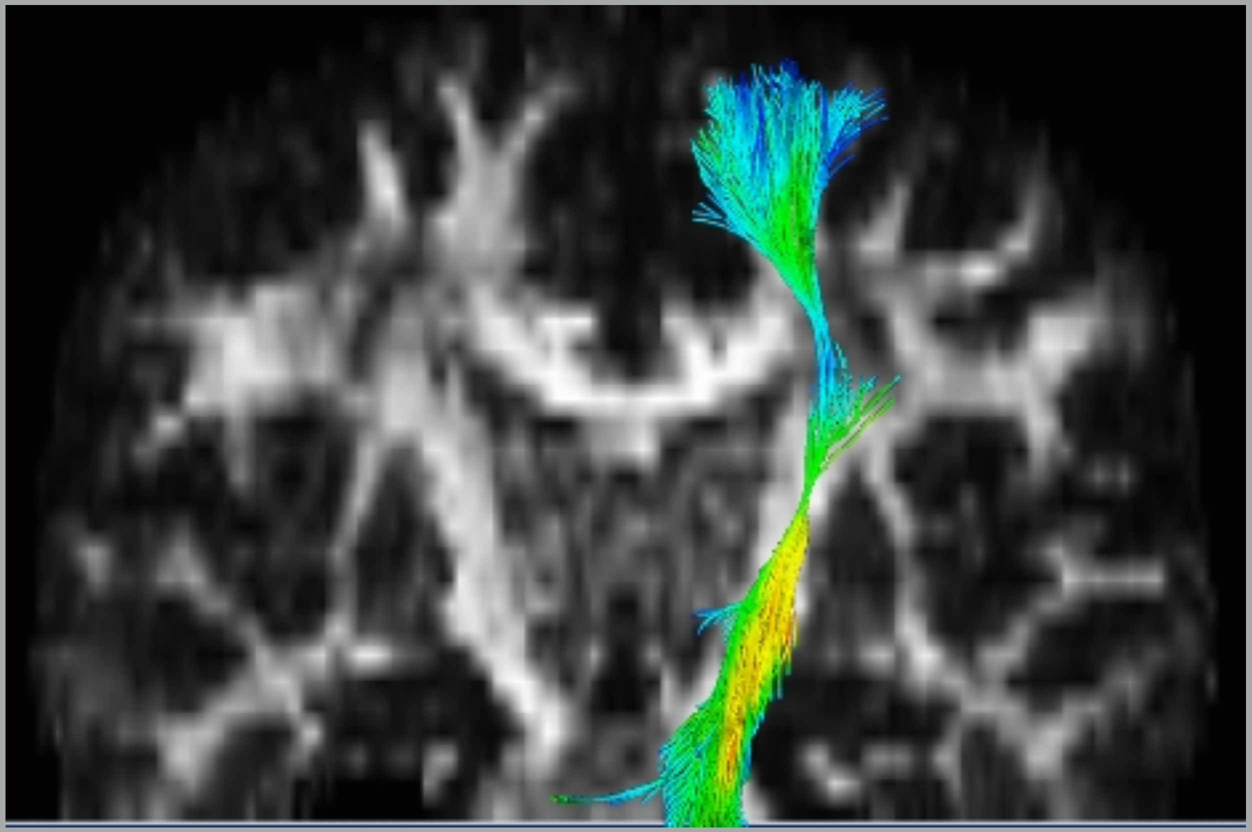
DTI ellipsoids

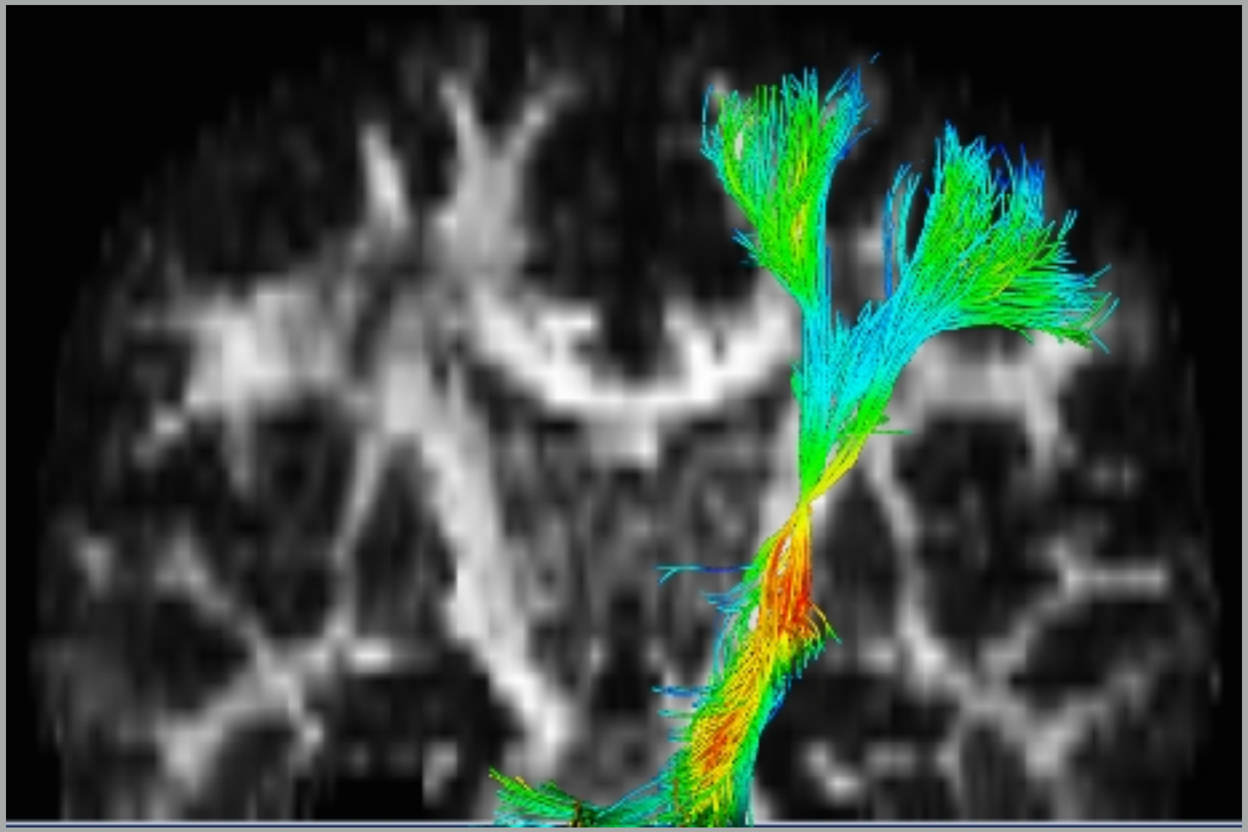


HARDI field of diffusion profiles

Descataux, et. al. MRM 2005

High Angular Resolution DTI (HARDI)





The FORECAST Model

$$\boxed{\text{Fiber orientation by SHD of signal spherical harmonic representation of fiber orientation function but with the assumption of cylindrical symmetry}}$$

the signal

$$S(\theta, \phi) = \sum_{l=0}^{\infty} \sum_{m=-l}^{l} s_{lm} Y_{lm}(\theta, \phi)$$

the angular distribution of fibers

$$P(\vartheta, \varphi) = \sum_{l=0}^{\infty} \sum_{m=-l}^{l} p_{lm} Y_{lm}(\vartheta, \varphi)$$

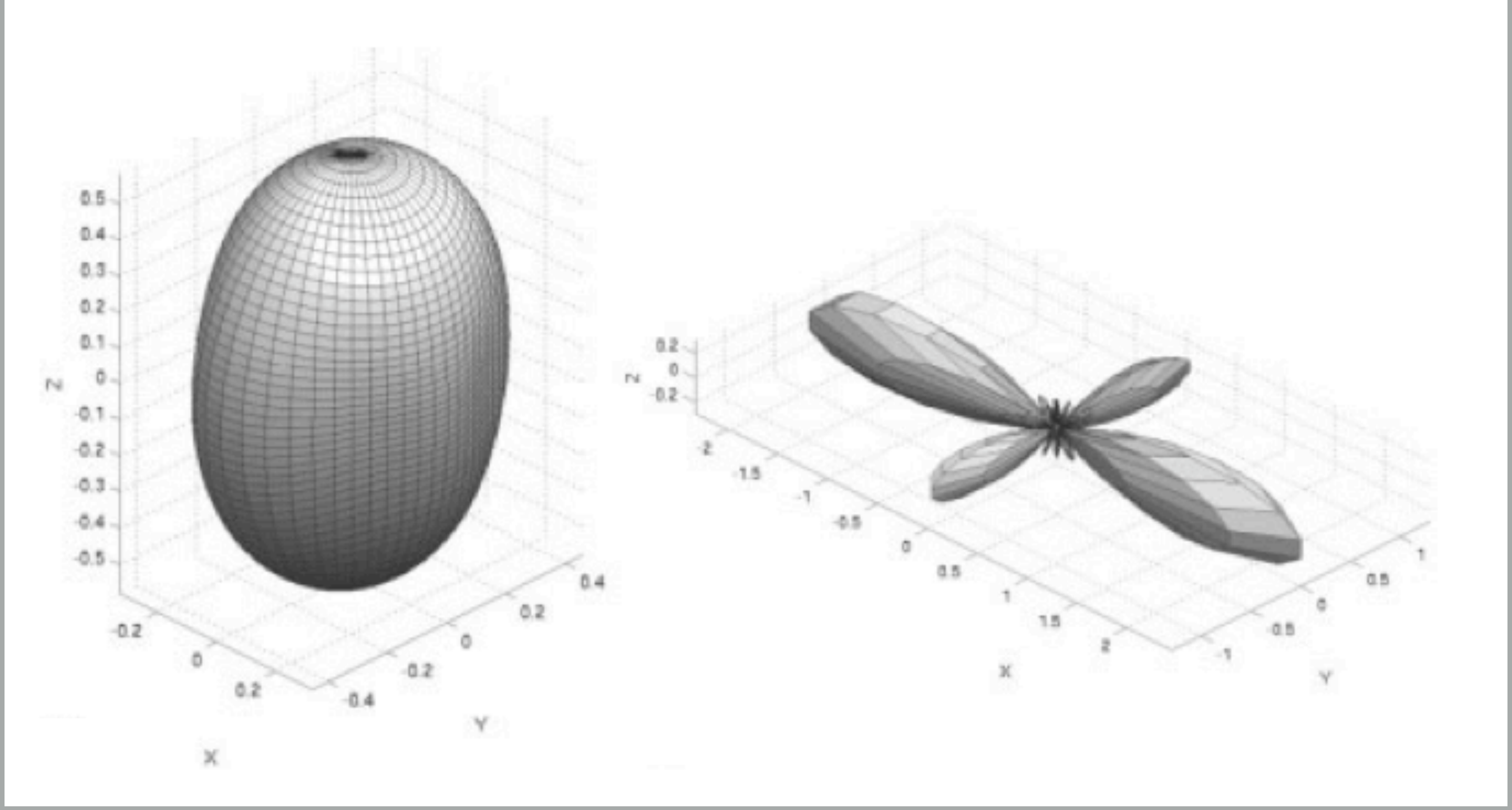
The FORECAST Model

Assumption of cylindrical symmetry

$$\boldsymbol{D} = \begin{pmatrix} \lambda_\perp & 0 & 0 \\ 0 & \lambda_\perp & 0 \\ 0 & 0 & \lambda_\| \end{pmatrix}$$

Anderson, MRM 54:1194 (2005)

The FORECAST Model

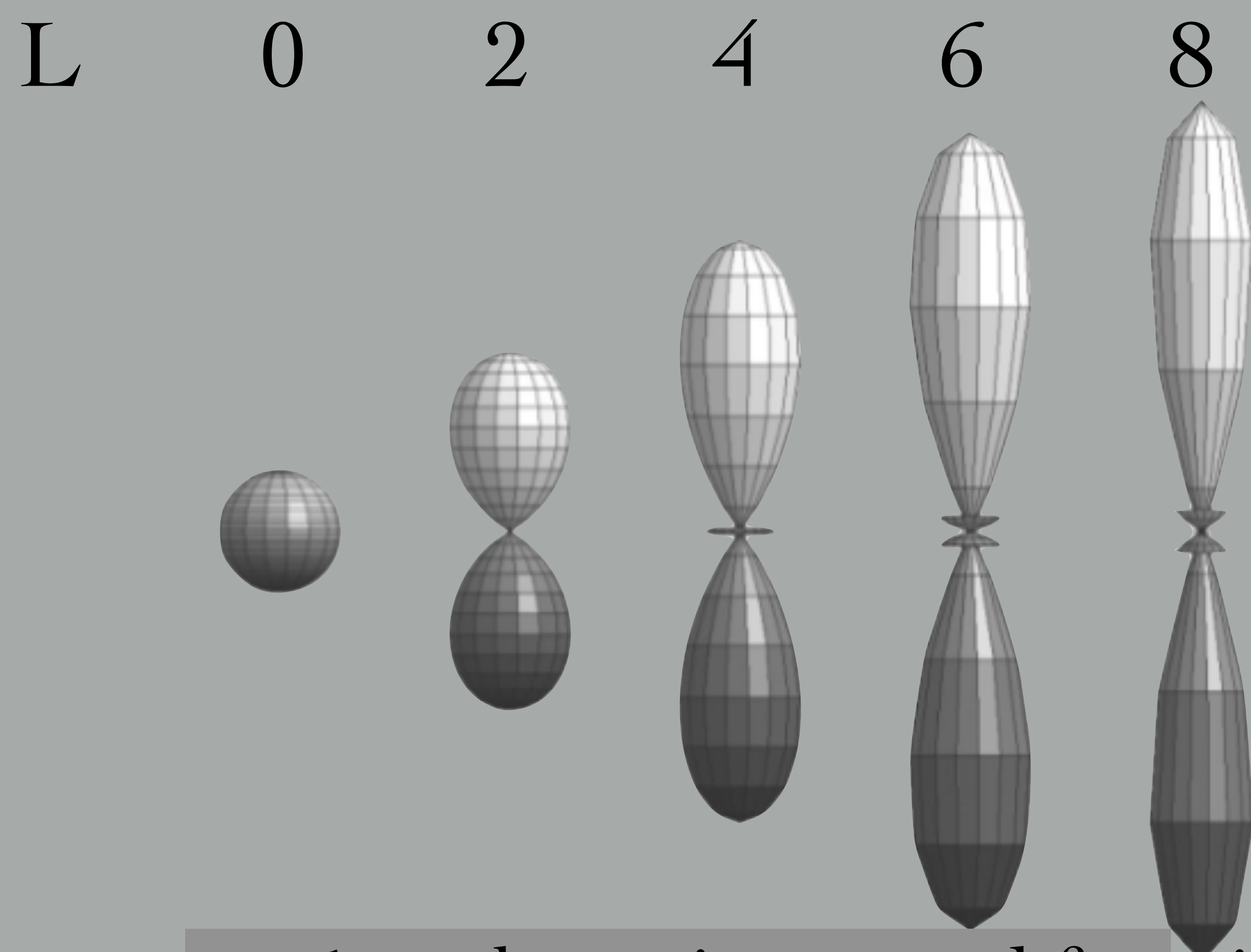


signal

orientation and
volume fraction (2/3 & 1/3)

Anderson, MRM 54:1194 (2005)

The FORECAST Model

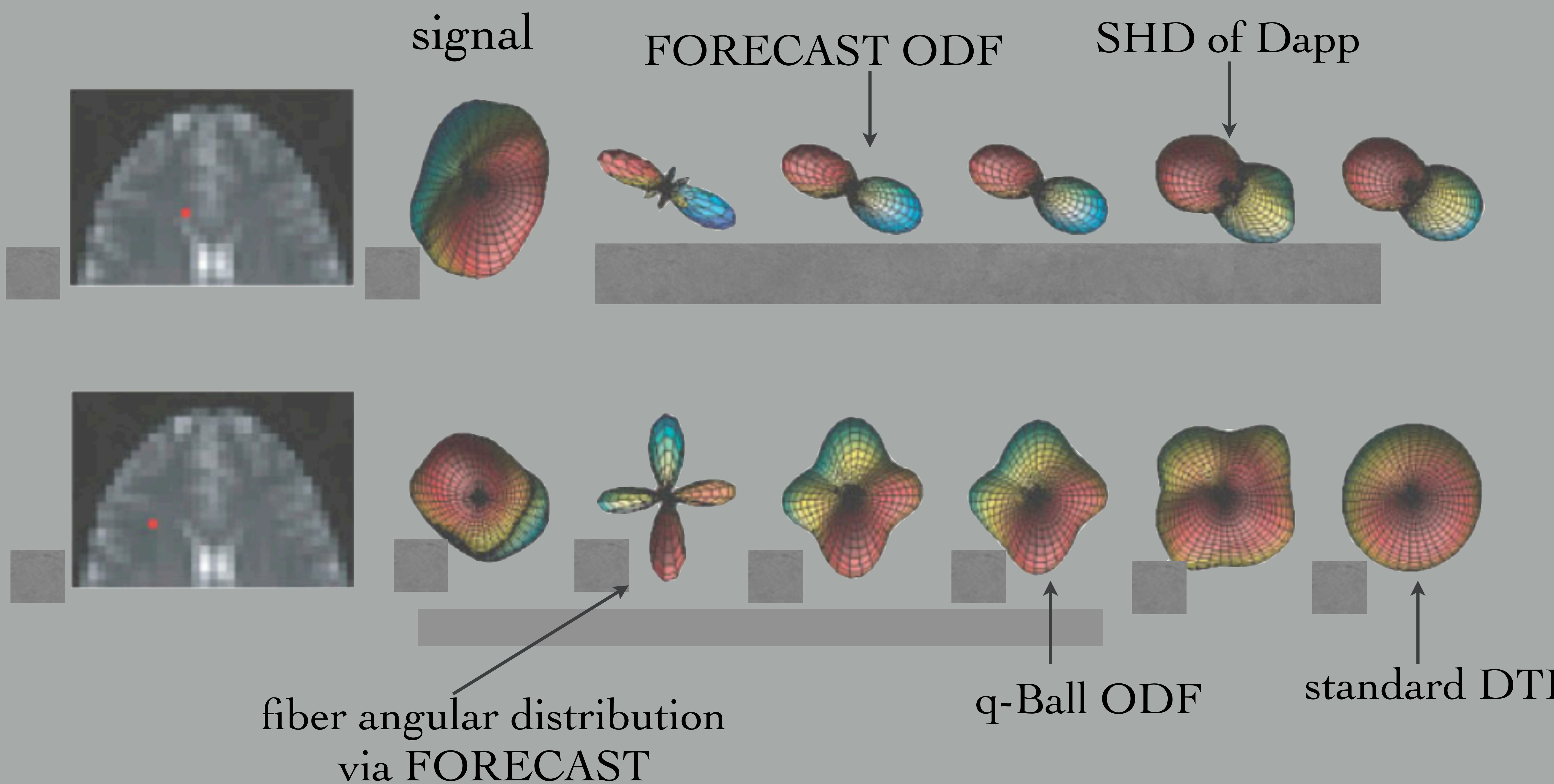


Angular point spread function

Higher order gives higher resolution but is more sensitive to noise as the coefficients are smaller

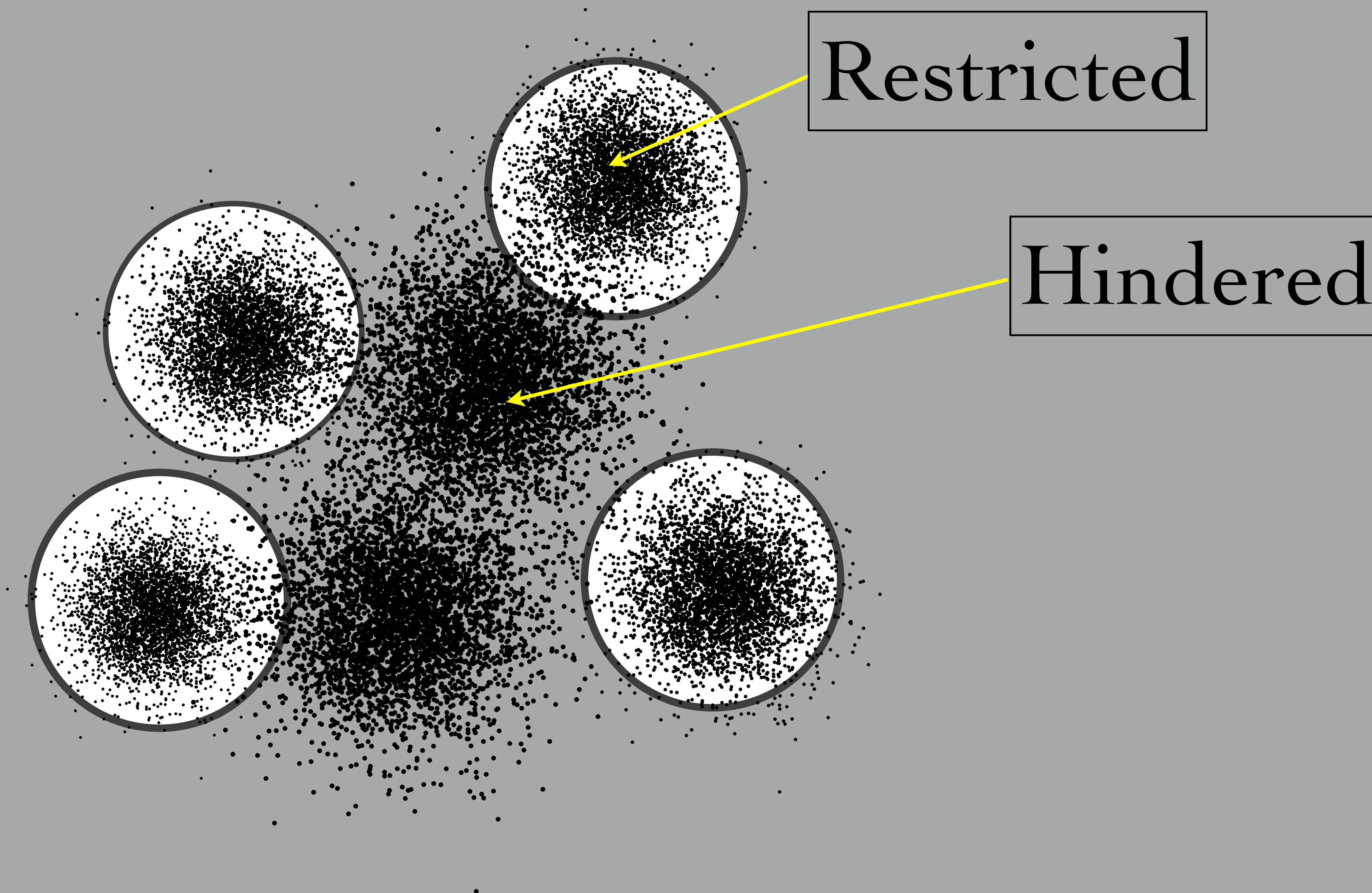
Anderson, MRM 54:1194 (2005)

The FORECAST Model



Anderson, MRM 54:1194 (2005)

The CHARMED Model



Assaf, et. al. MRM 52:965 (2004)

The CHARMED Model

$$E(q,\Delta) = f_h E_h(q,\Delta) + \sum_{j=1}^{n} f_r^j E_r^j(q,\Delta)$$

Signal decay

Hindered decay

Restricted decay

hindered volume fraction

restricted volume fraction

Assaf, et. al. MRM 52:965 (2004)

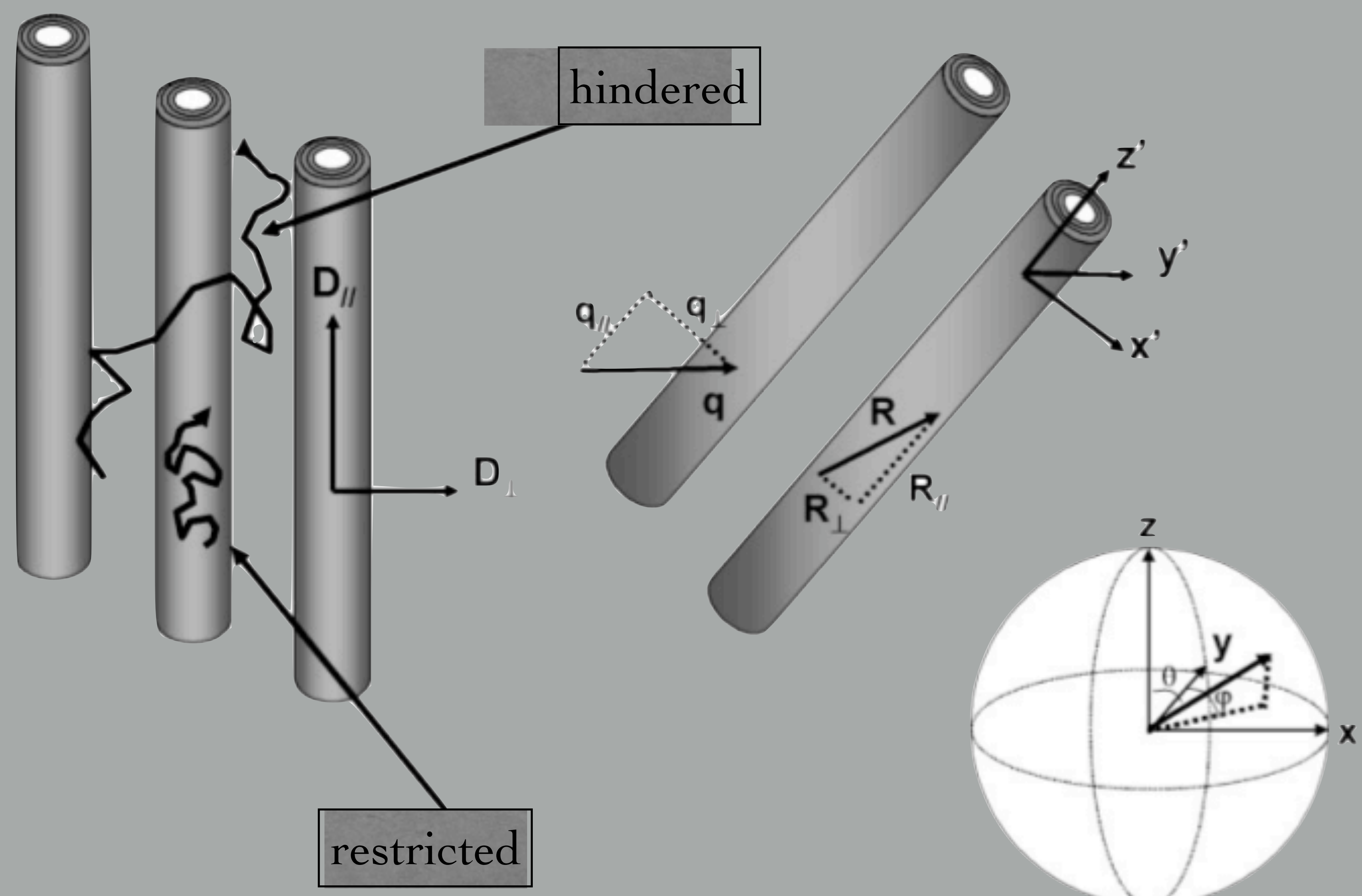
The CHARMED Model

Assume cylindrical symmetry

$$\boldsymbol{D} = \begin{pmatrix} \lambda_\perp & 0 & 0 \\ 0 & \lambda_\perp & 0 \\ 0 & 0 & \lambda_\parallel \end{pmatrix}$$

Assaf, et. al. MRM 52:965 (2004)

The CHARMED Model



Assume cylindrical symmetry

Assaf, et. al. MRM 52:965 (2004)

The CHARMED Model

Decoupling of $\boldsymbol{D}_{\parallel}$ and $\boldsymbol{D}_{\perp}$ in restricted compartment

$$E_R(\boldsymbol{q}, \Delta) = \int \overline{P}(\boldsymbol{r}, \Delta) e^{i\boldsymbol{q}\cdot\boldsymbol{r}} d\boldsymbol{r}$$

$$\Downarrow$$

$$P_R(\boldsymbol{r}, \Delta) = P_{\perp}(\boldsymbol{r}_{\perp}, \Delta) P_{\parallel}(\boldsymbol{r}_{\parallel}, \Delta)$$

$$\Downarrow$$

$$E_R(\boldsymbol{q}, \Delta) = E_{\perp}(\boldsymbol{q}_{\perp}, \Delta) E_{\parallel}(\boldsymbol{q}_{\parallel}, \Delta)$$

Assaf, et. al. MRM 52:965 (2004)

The CHARMED Model

Form of $E_{\|}$ and $E_{\perp}$ in restricted compartment

$$E_{\|}(\boldsymbol{q}_{\|}, \Delta) = e^{-4\pi^2|\boldsymbol{q}_{\|}|^2\tau D_{\|}}$$

$$\tau = \Delta - \delta/3$$

messy!

$$E_{\perp}(\boldsymbol{q}_{\perp}, \Delta) = e^{f(D_{\perp})} = \text{restricted diffusion in a cylinder (Neuman)}$$

Assaf, et. al. MRM 52:965 (2004)

The CHARMED Model

Form of E_h in hindered compartment

$$E_h(\boldsymbol{q}, \Delta) = e^{-4\pi^2 \tau \boldsymbol{q}^t \boldsymbol{D} \boldsymbol{q}}$$

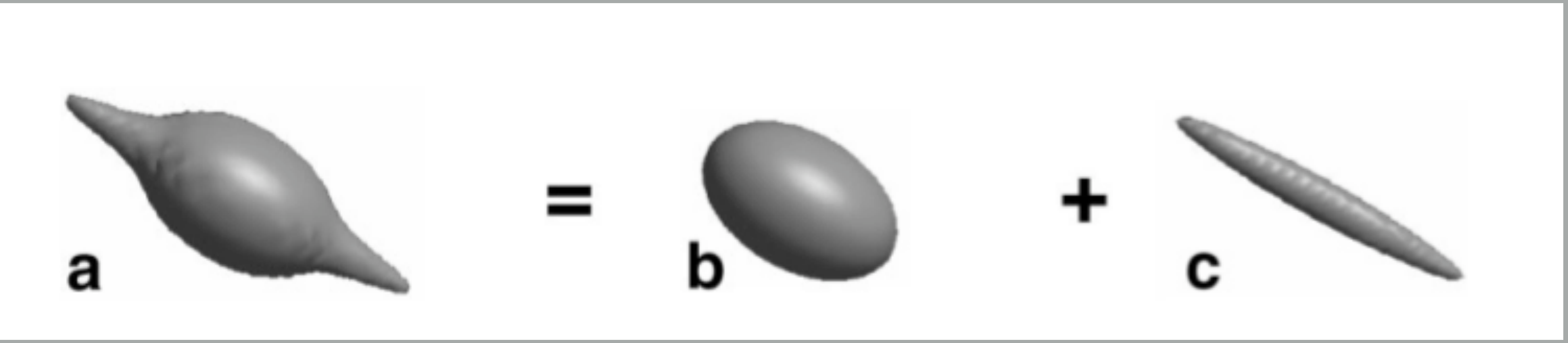
$$\boldsymbol{q} = \boldsymbol{q}_{\|} + \boldsymbol{q}_{\perp}$$

$$E_h(\boldsymbol{q}, \Delta) = e^{-4\pi^2 \tau (|\boldsymbol{q}_{\|}|^2 \lambda_{\|} + |\boldsymbol{q}_{\perp}|^2 \lambda_{\perp})}$$

Assaf, et. al. MRM 52:965 (2004)

The CHARMED Model

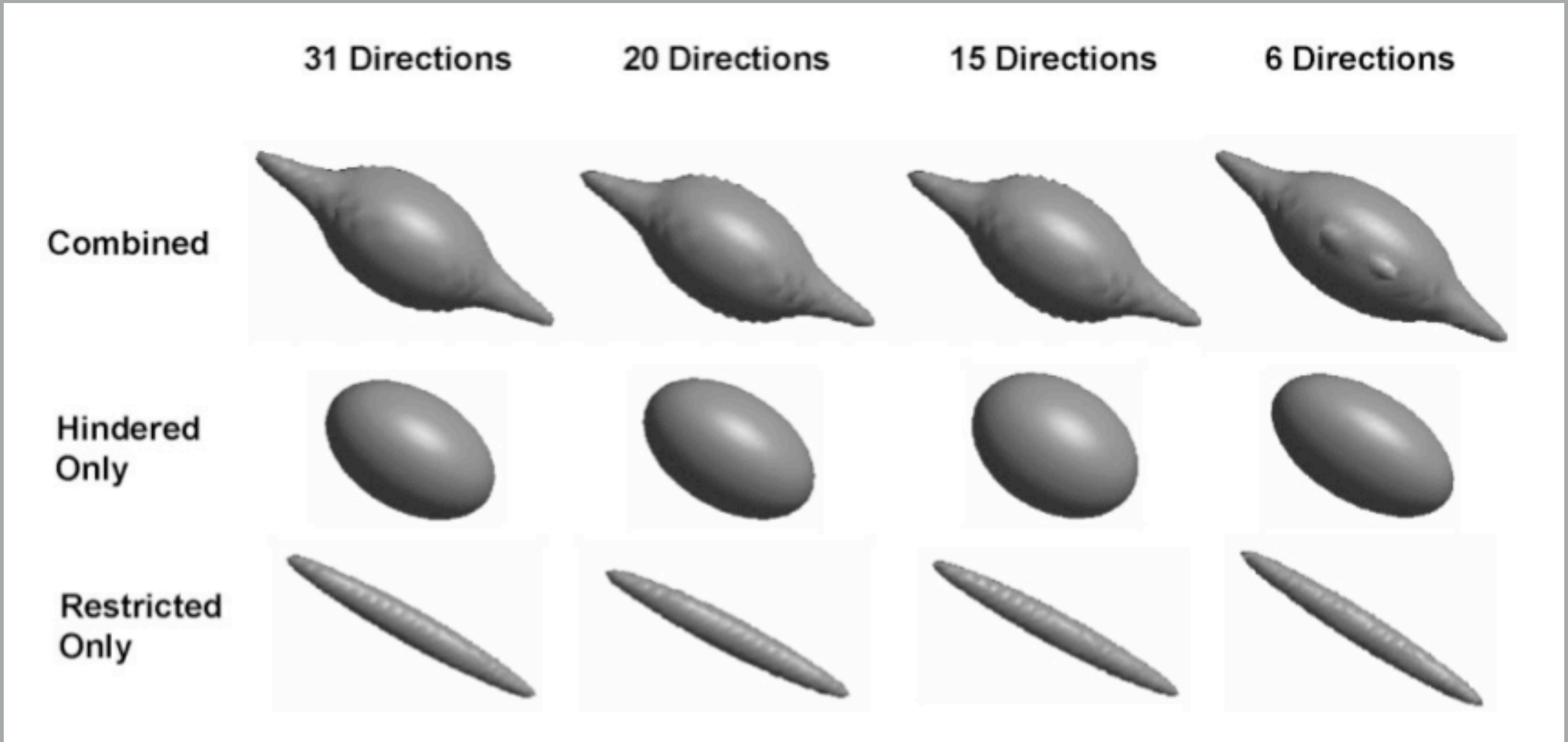
3D-FFT of simulated signal



Assaf, et. al. MRM 52:965 (2004)

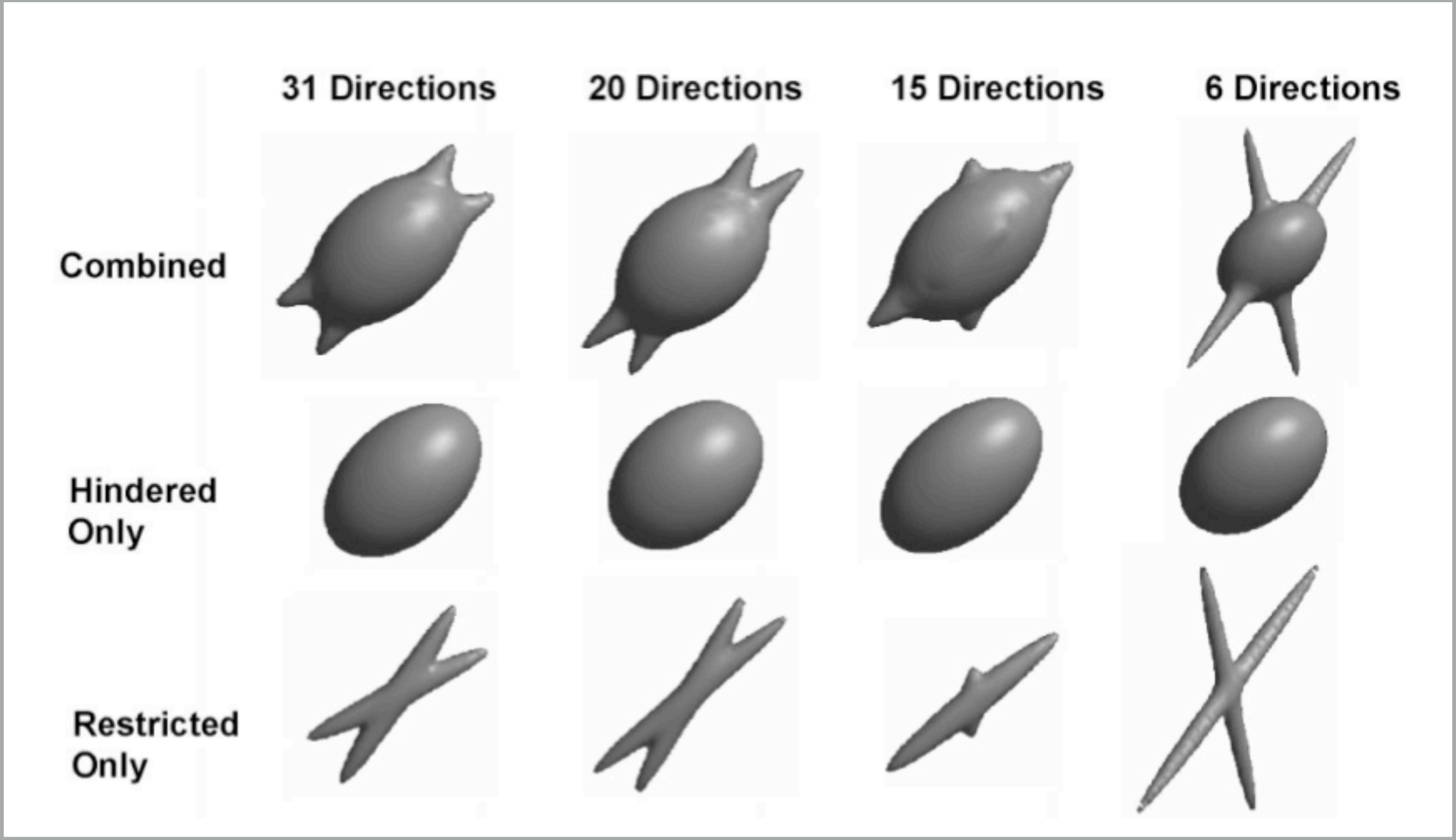
The CHARMED Model

3D-FFT of simulated signal



Assaf, et. al. MRM 52:965 (2004)

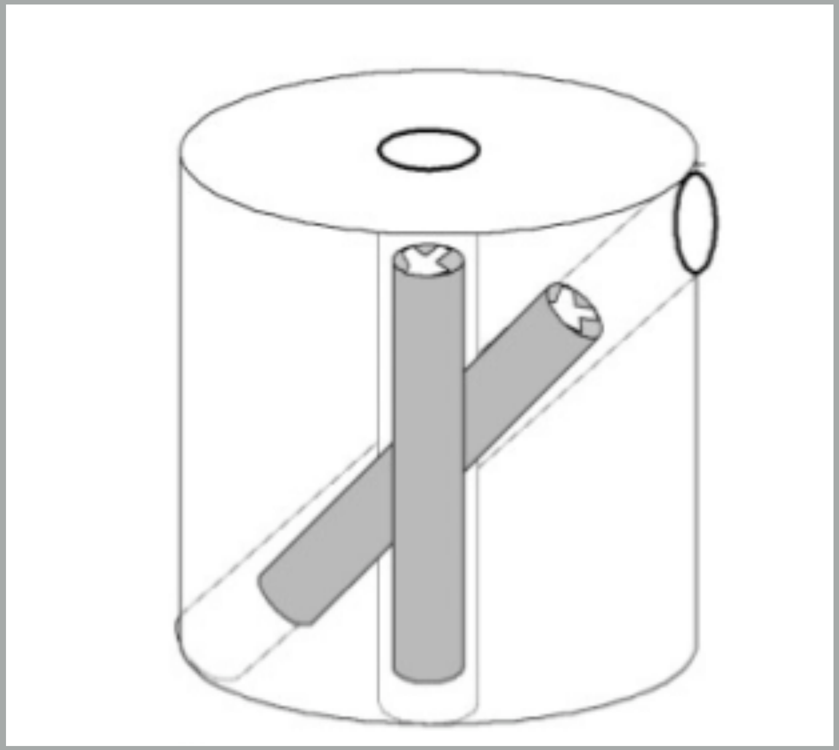
The CHARMED Model



Assaf, et. al. MRM 52:965 (2004)

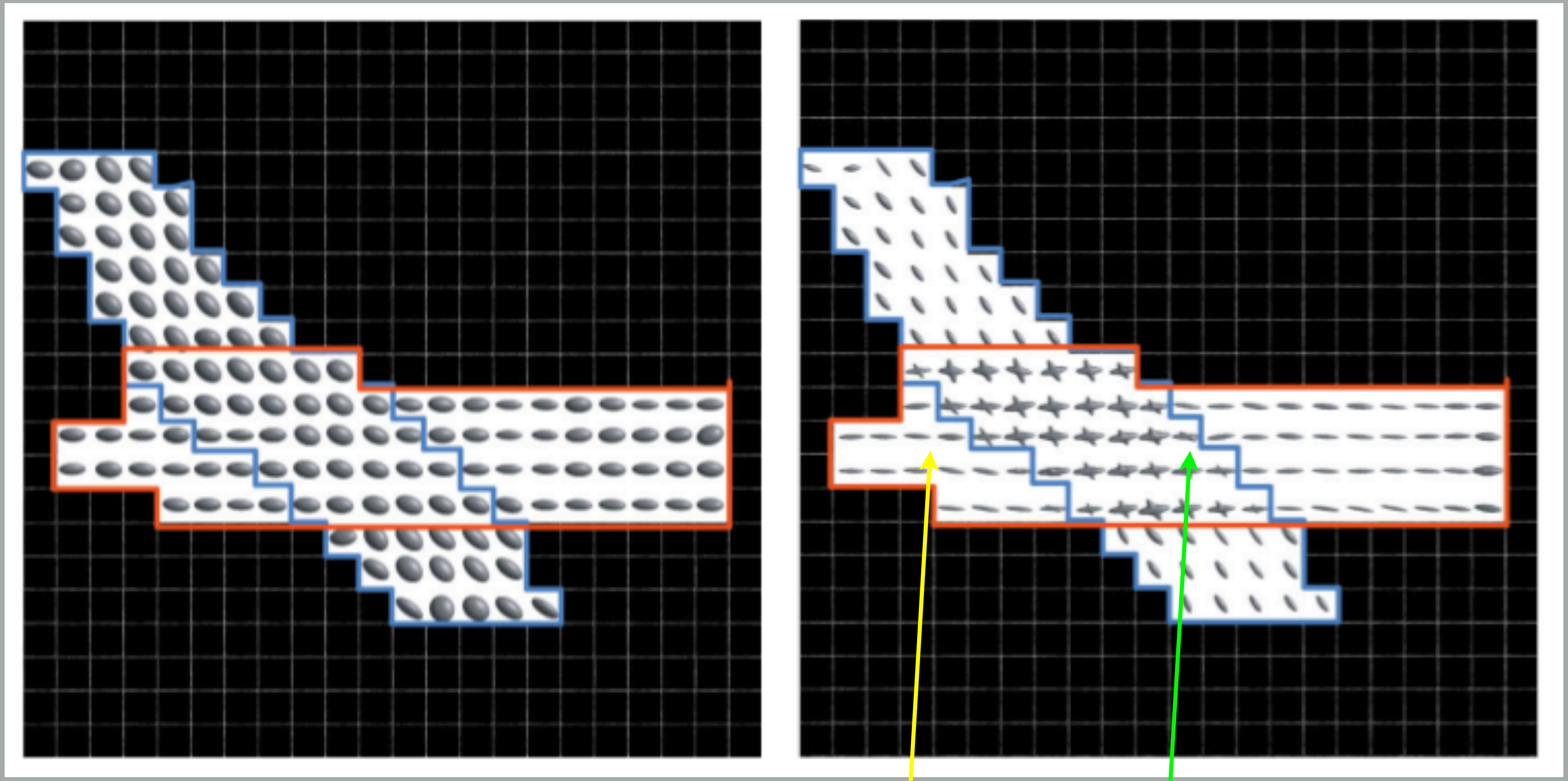
The CHARMED Model

pig spinal cord phantom



Assaf, et. al. MRM 52:965 (2004)

The CHARMED Model



one hindered
(i.e., standard DTI)

one hindered
one and two restricted

Assaf, et. al. MRM 52:965 (2004)

The CHARMED Model

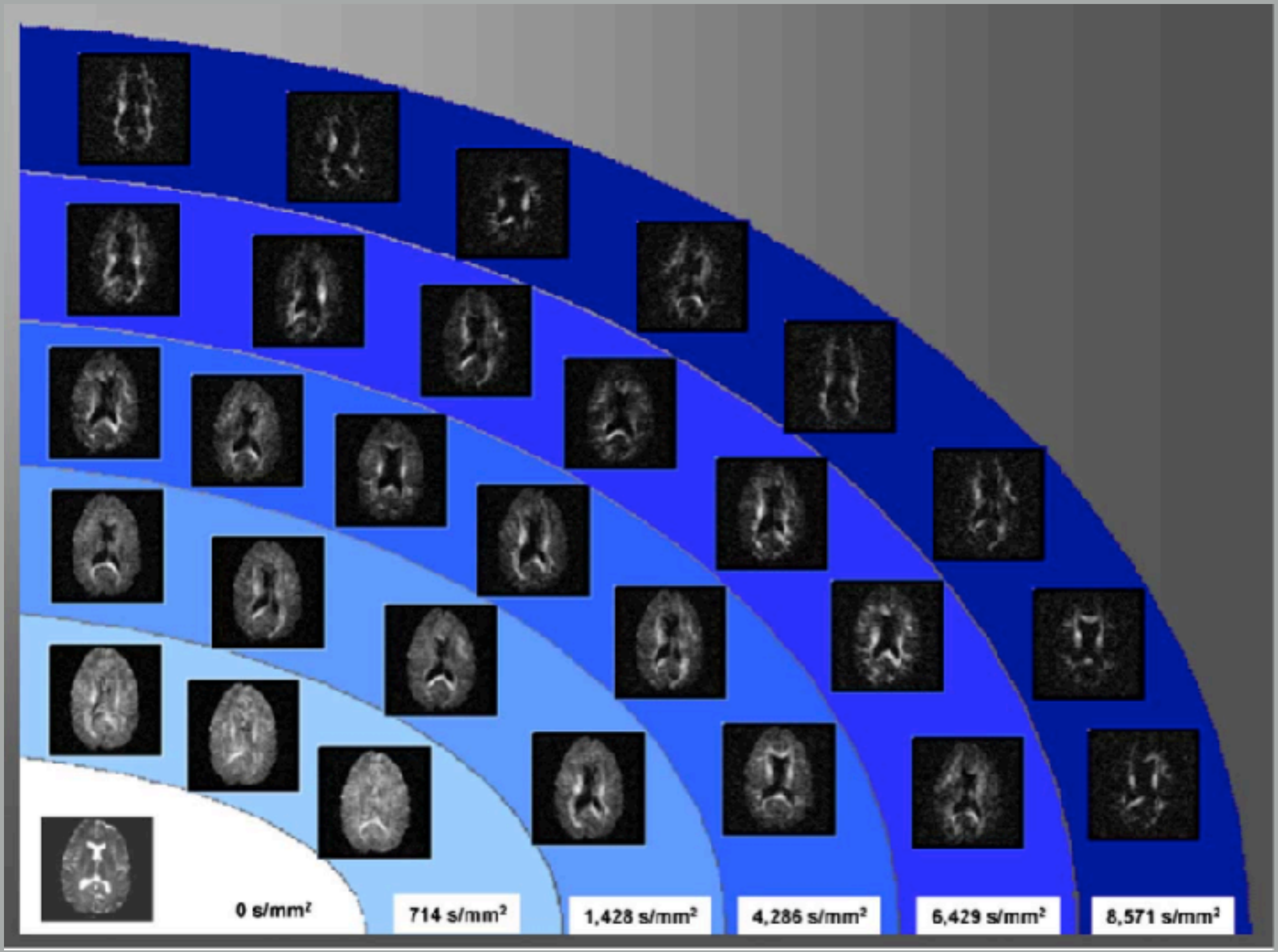
Three configurations

1. One hindered and no restricted (n=0)
2. One hindered and one restricted (n=1)
3. One hindered and two restricted (n=2)

Assaf and Basser, Neuroimage 27:48 (2005)

Assaf and Basser, Neuroimage 27:48 (2005)

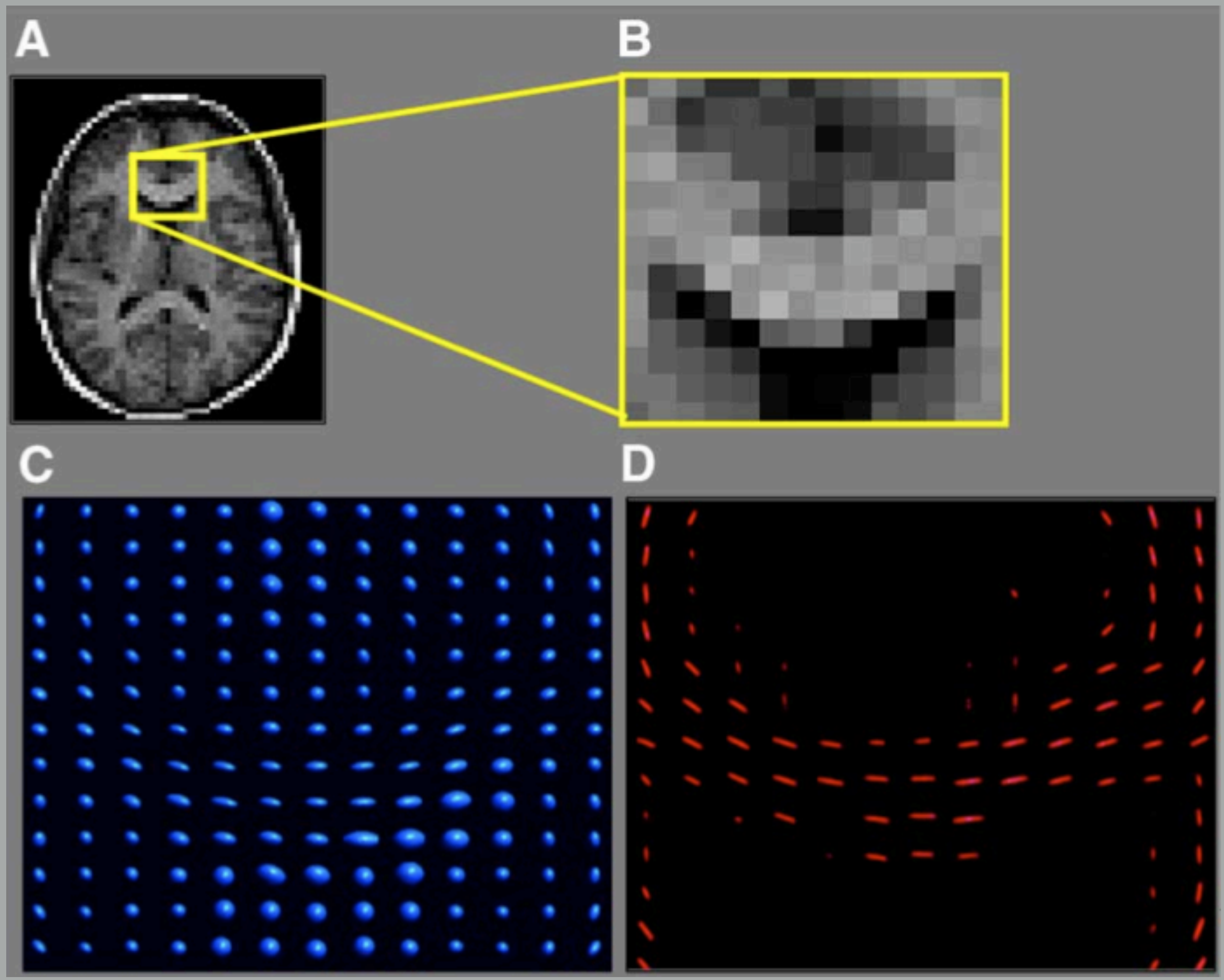
The CHARMED Model



10 shells of b-values from 0-10,000 s/mm^2,
from 6 directions (inner shell) to 30 directions (outer shell)

Assaf and Basser, Neuroimage 27:48 (2005)

The CHARMED Model



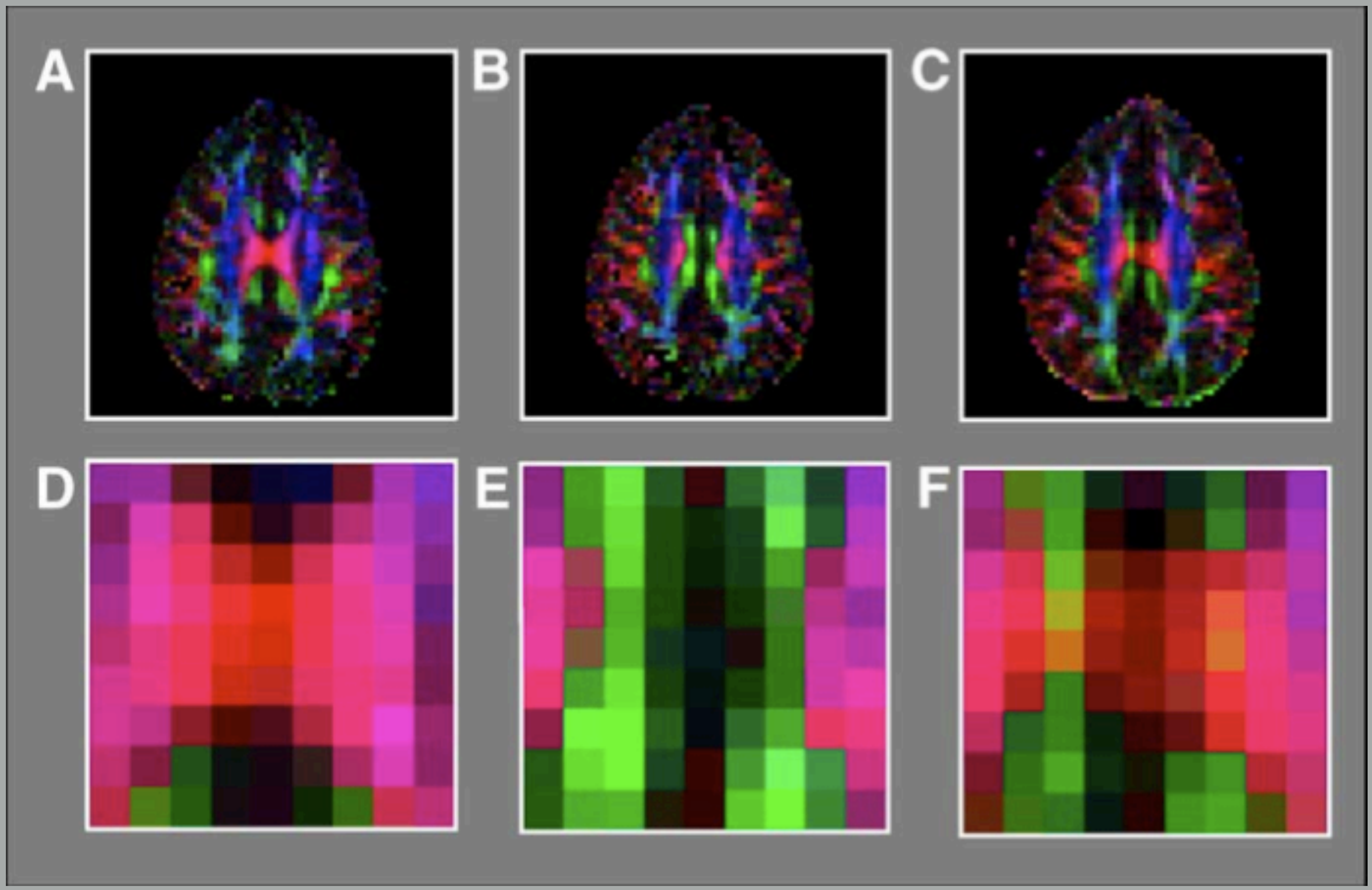
Hindered component

Restricted component

Assaf and Basser, Neuroimage 27:48 (2005)

The CHARMED Model

Directionality Map



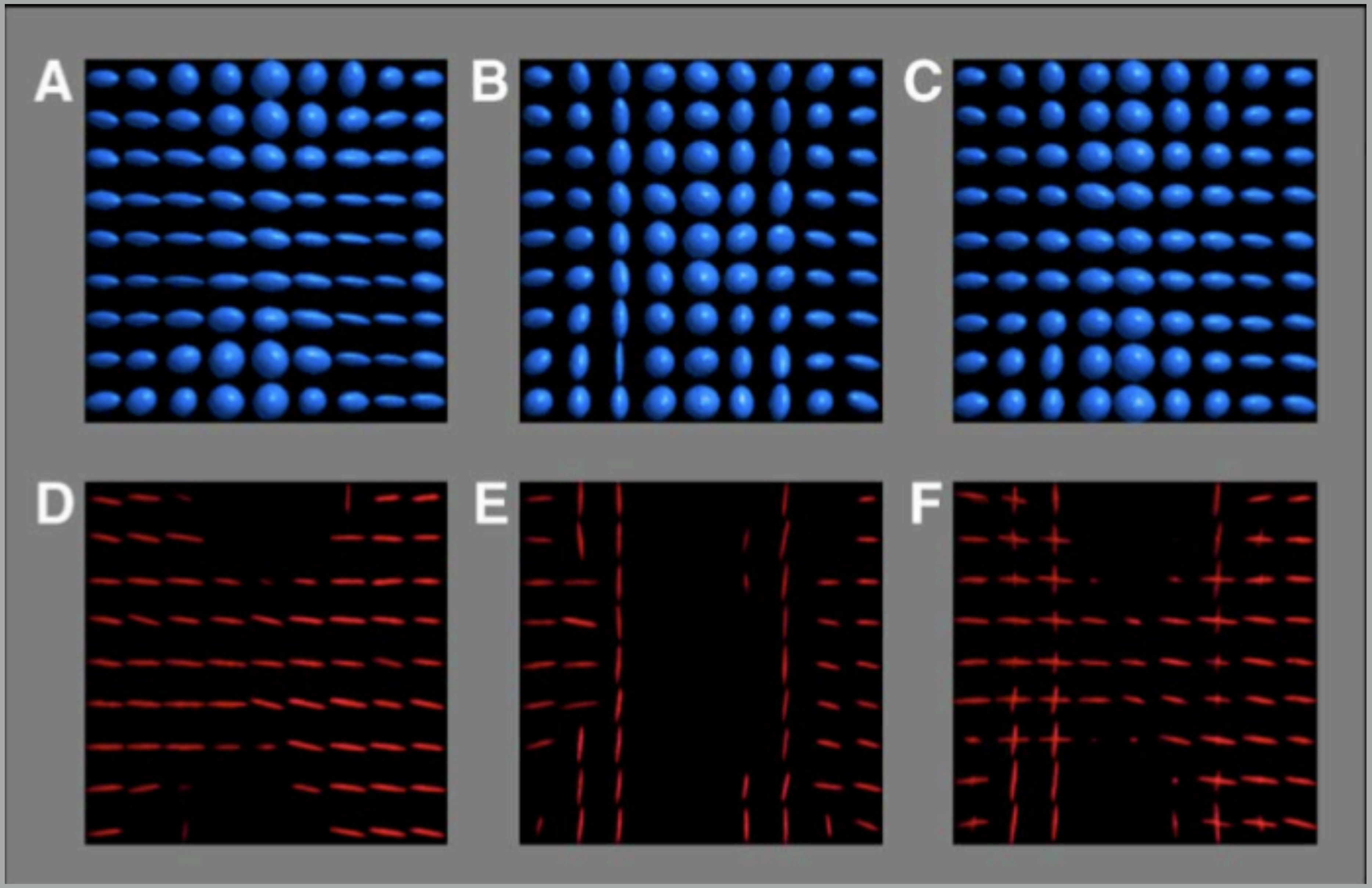
Corpus callosum Cingulum A+B

Assaf and Basser, Neuroimage 27:48 (2005)

The CHARMED Model

Hindered

Restricted



Corpus callosum

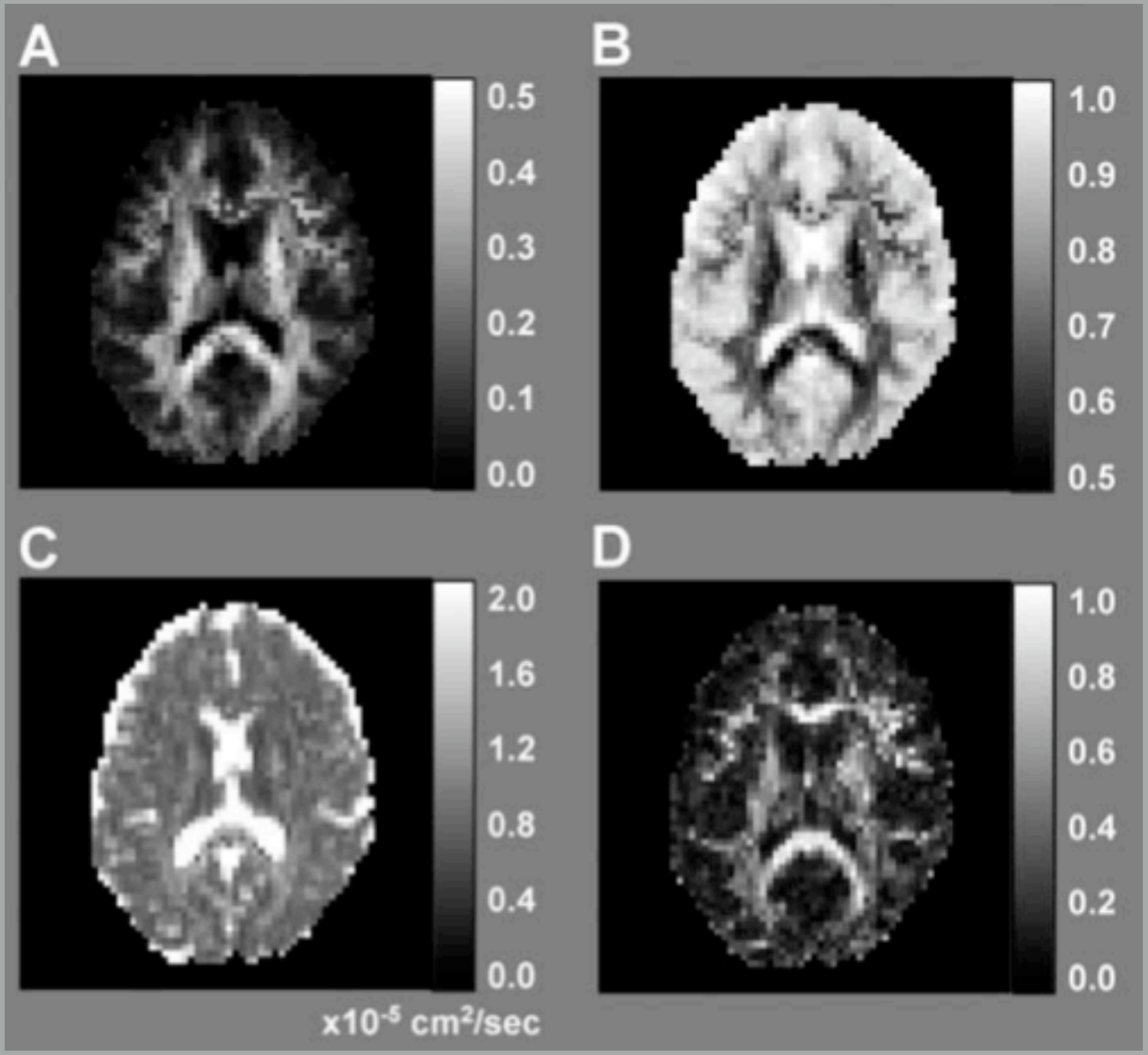
Cingulum

A+B

The CHARMED Model

Restricted

Hindered

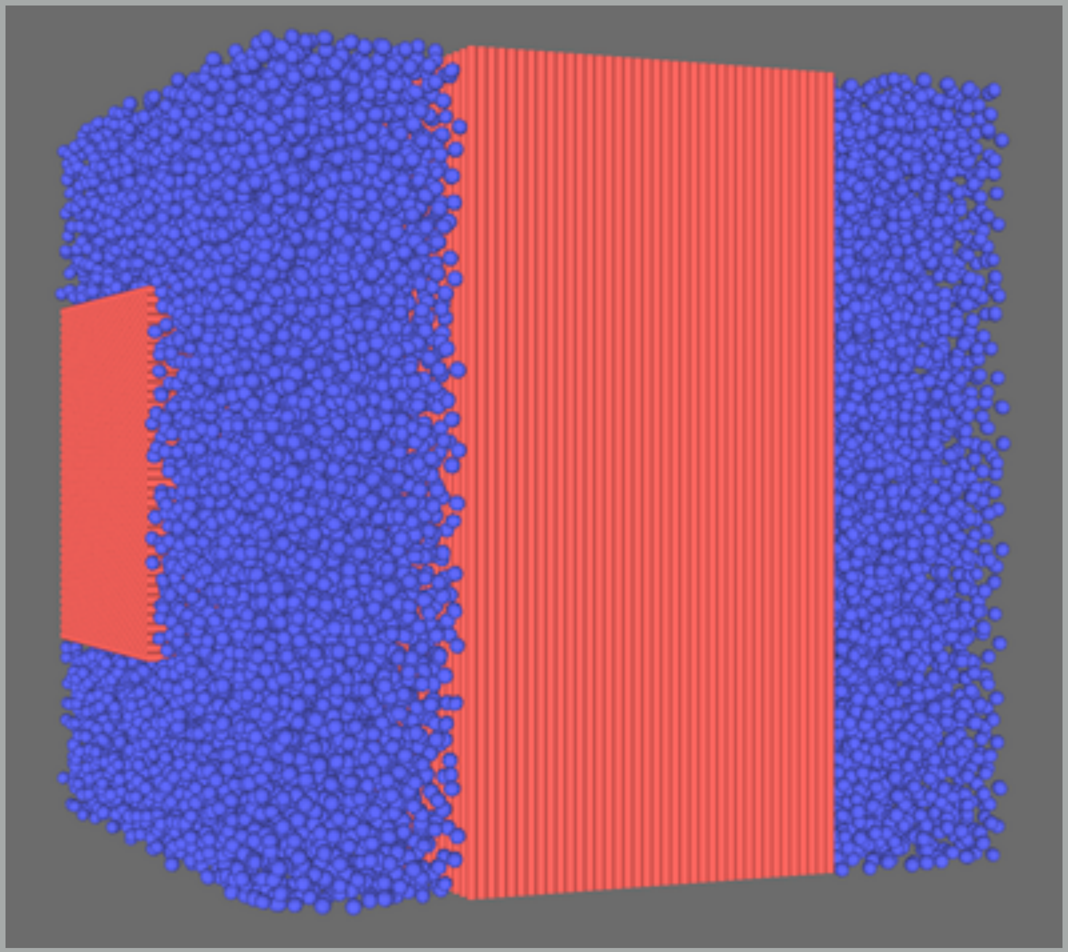


Mean diffusivity

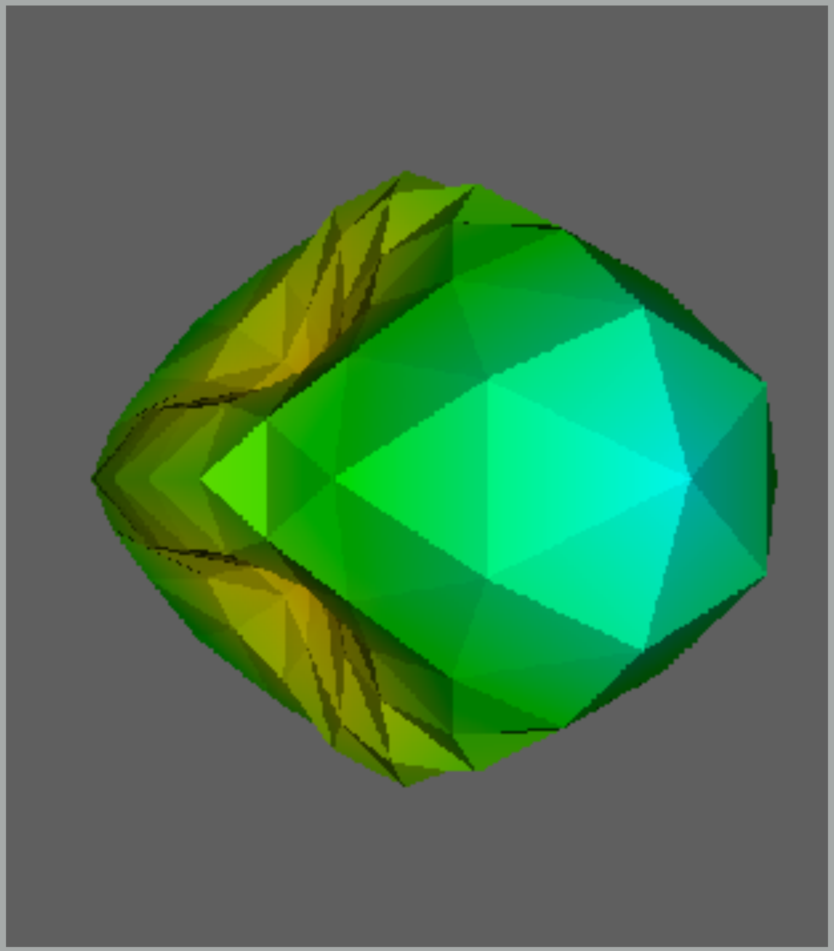
FA

Assaf and Basser, Neuroimage 27:48 (2005)

Heterogeneous Voxels and High Angular Resolution Sampling

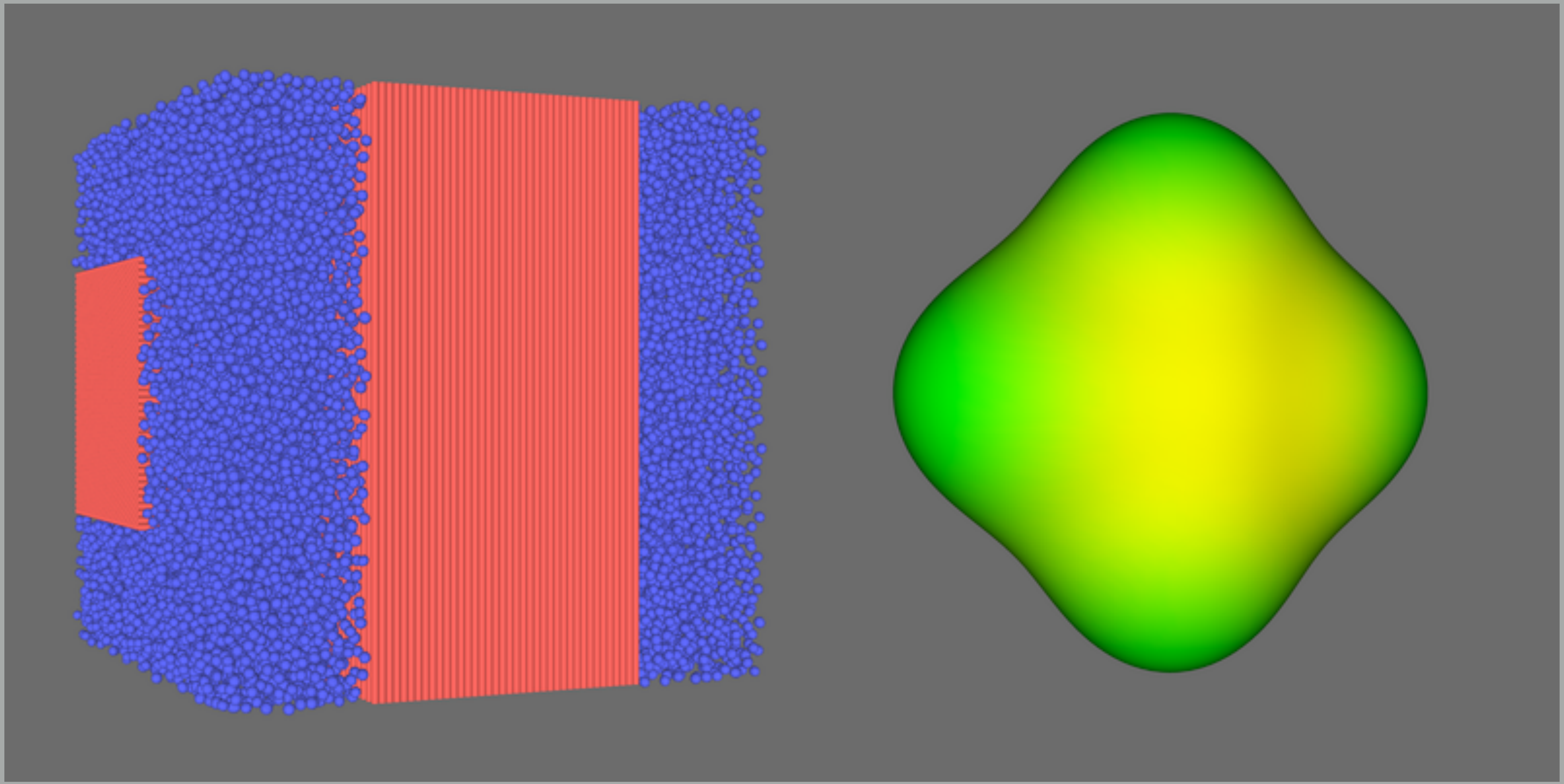


a voxel with crossing fiber bundles and random spherical cells...



signal from 162 directions

Quasi-realistic HARDI simulation

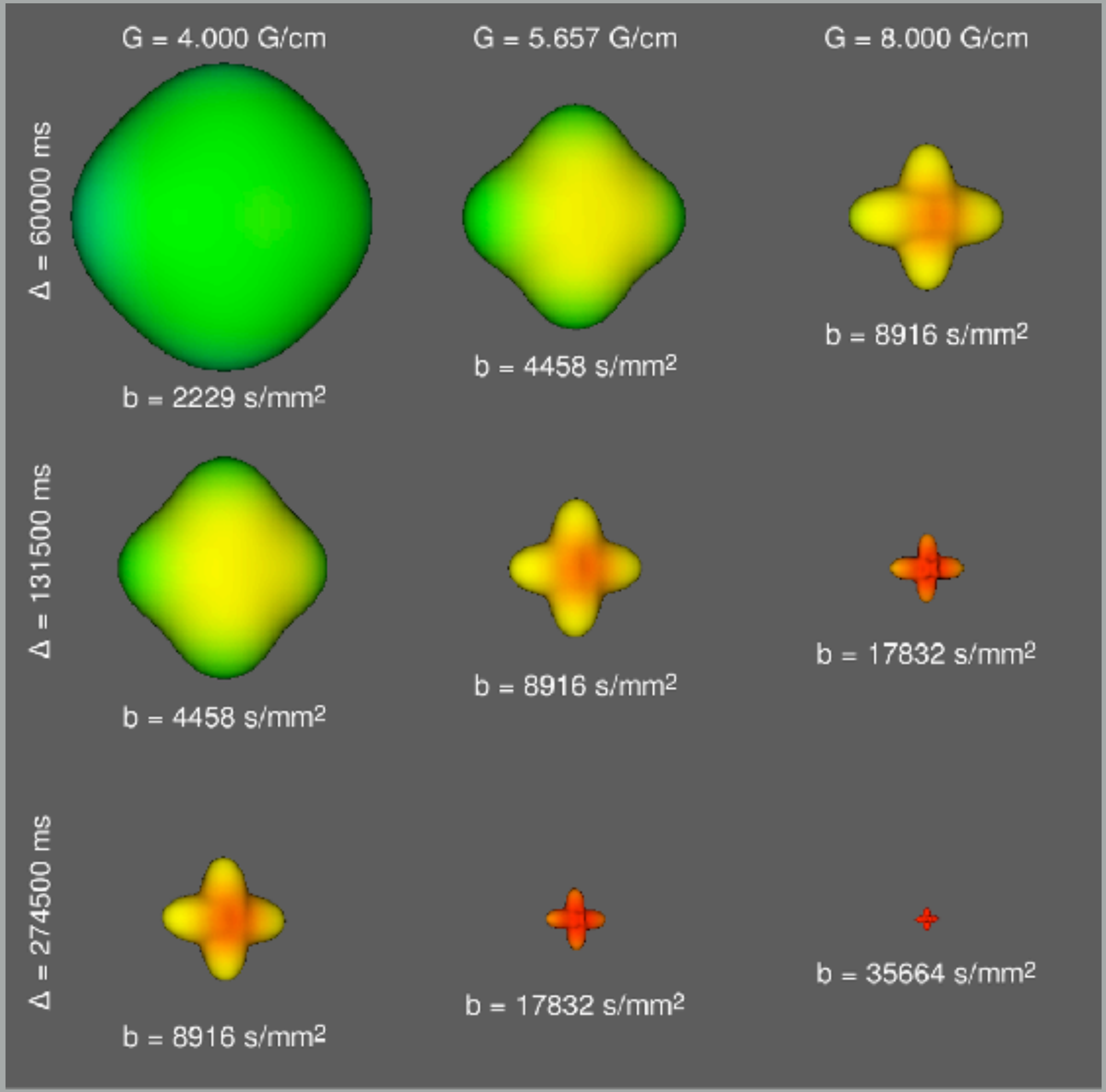


a voxel with crossing fiber bundles and random spherical cells...

...the orientation distribution function

Balls and Frank, Magn. Reson. Med. 62:(2009)

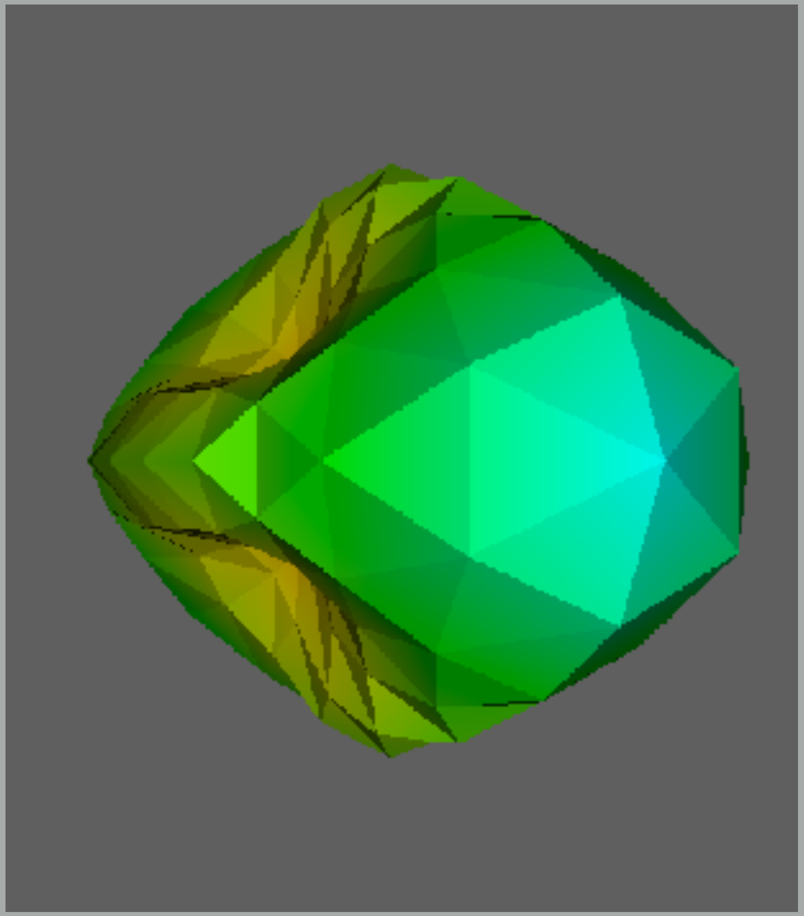
The interplay of Parameters



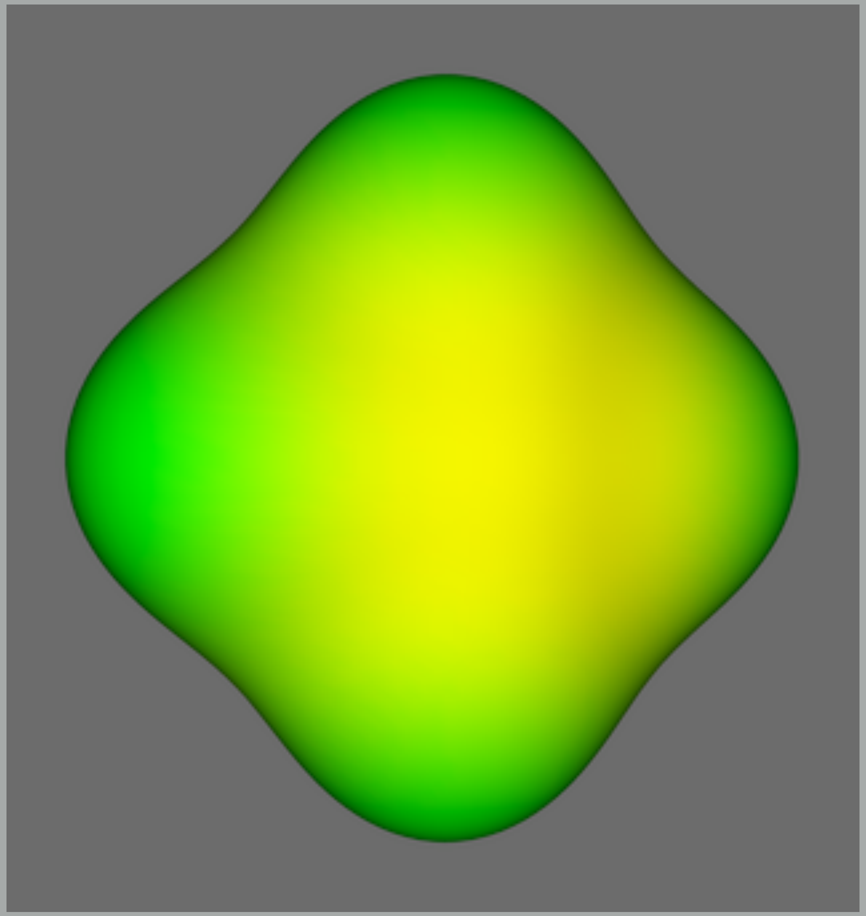
The ability to discriminate fiber content dependent on diffusion sampling scheme

And there are multiple fibers/voxel, relative orientations, volume fractions, etc!

High Angular Resolution DTI (HARDI)



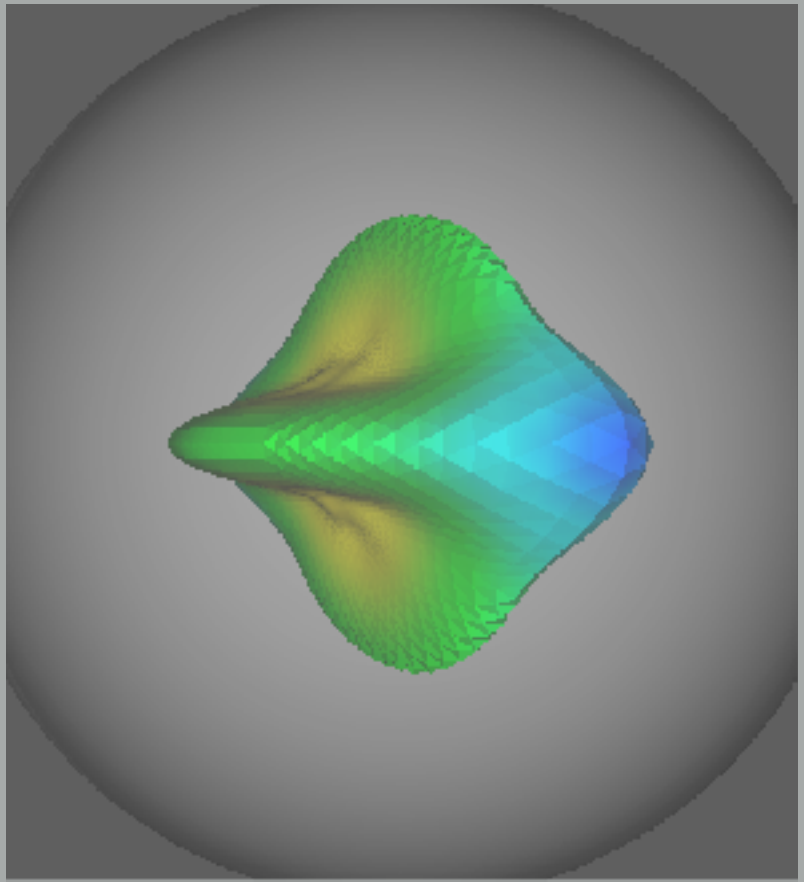
signal



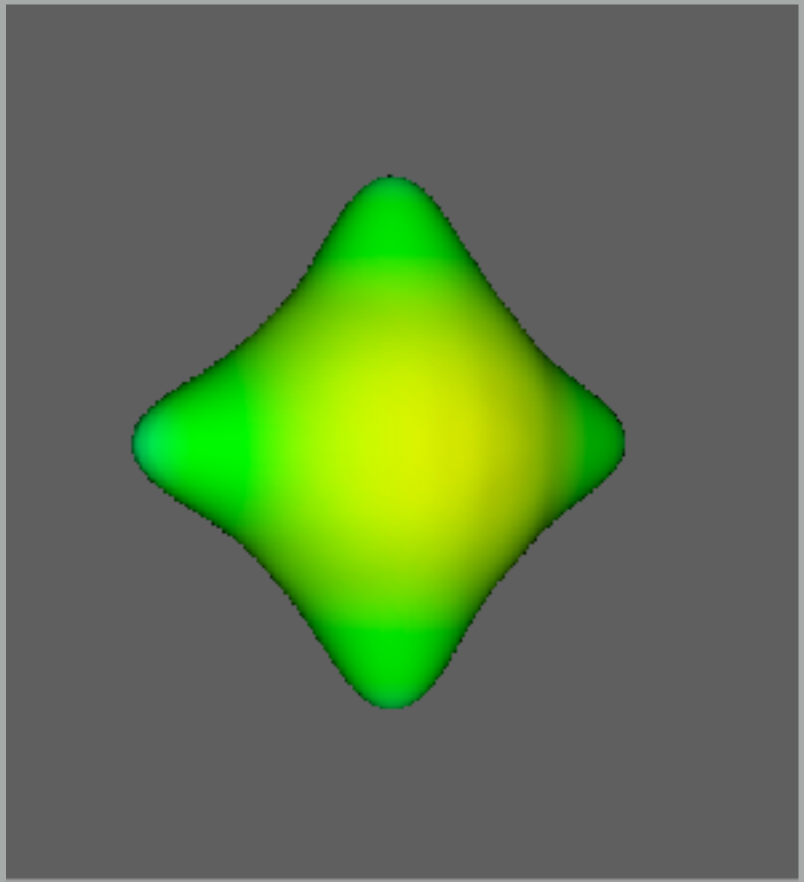
ODF

162 directions

High Angular Resolution DTI (HARDI)



signal



ODF

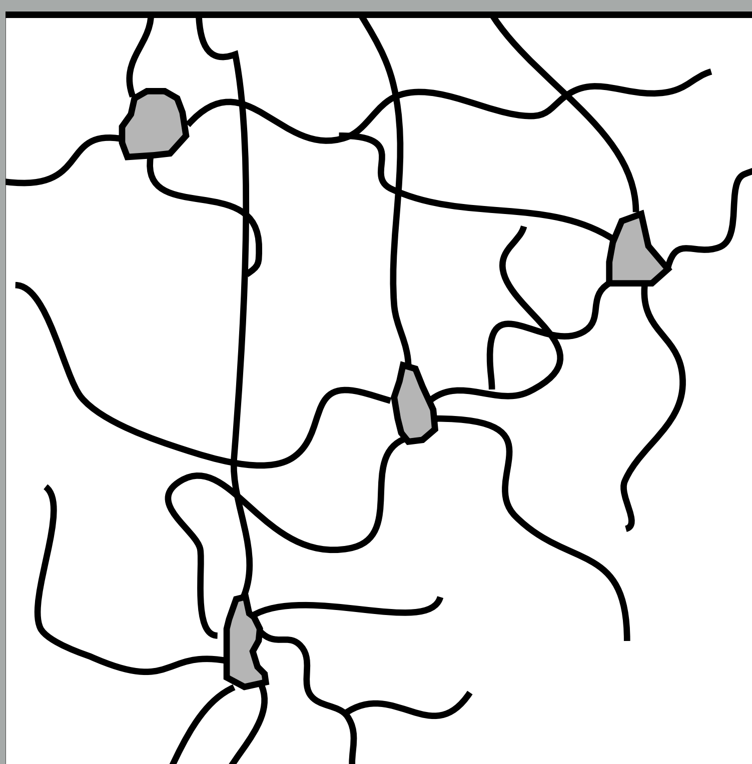
2562 directions

End

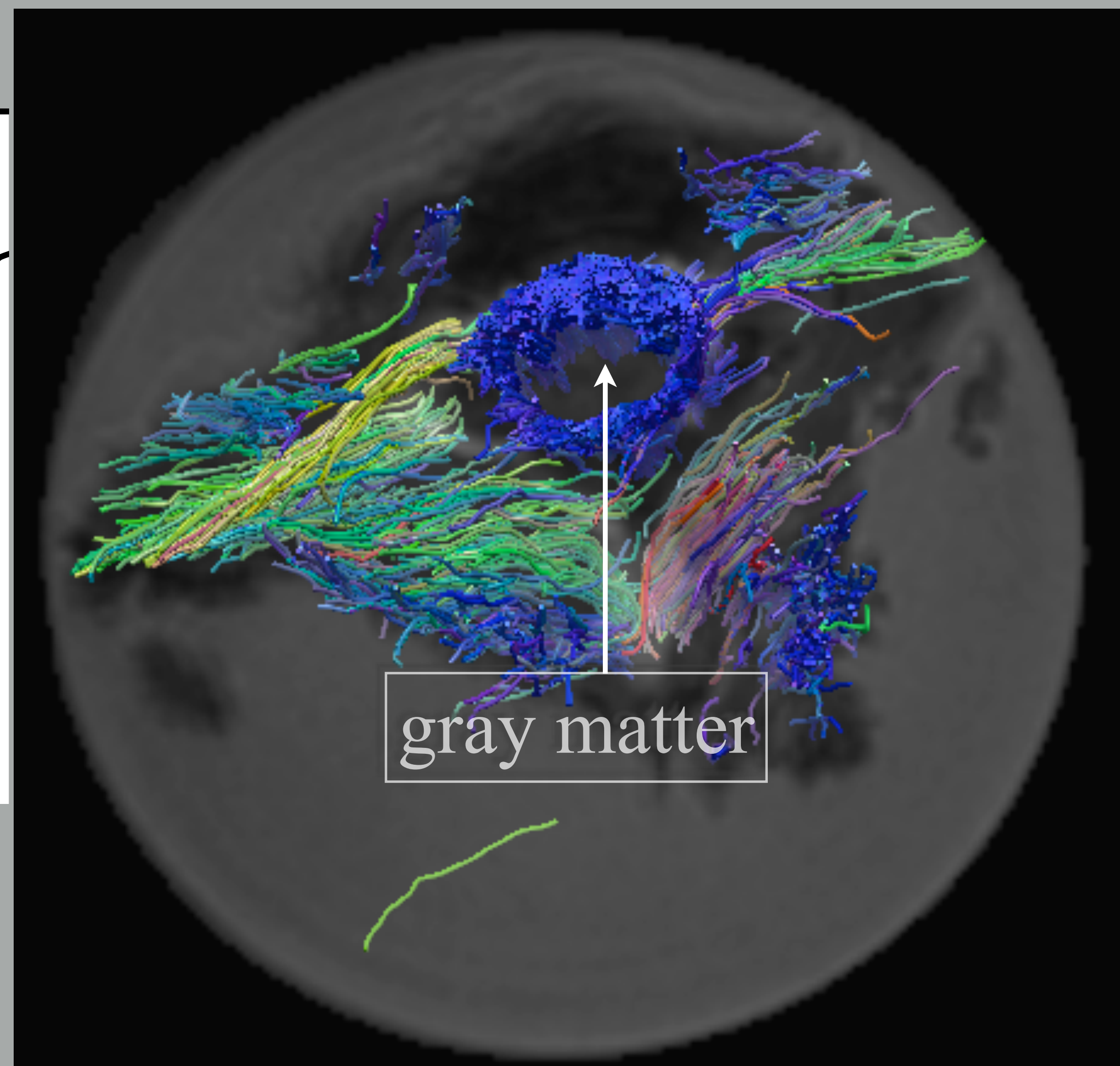
Next Lecture

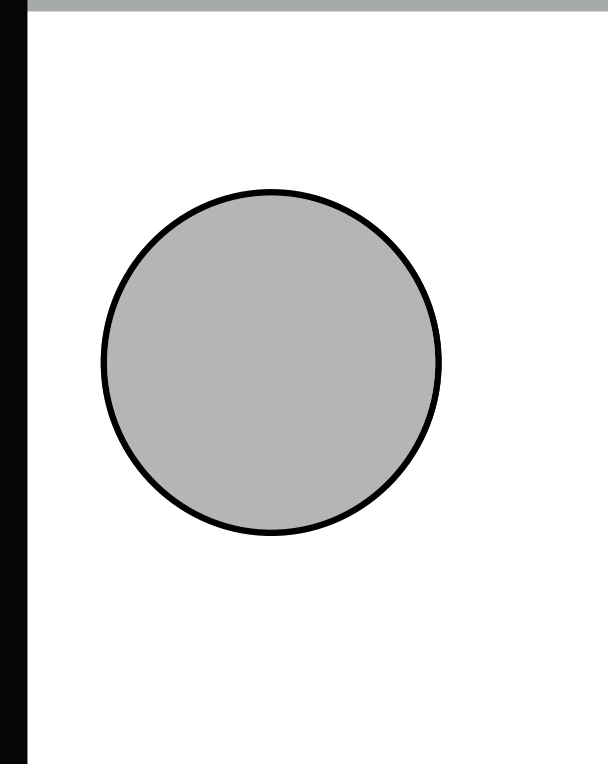
A General Approach to DTI

Fundamental Limitation of DTI
Heterogeneous Voxels



Gray matter



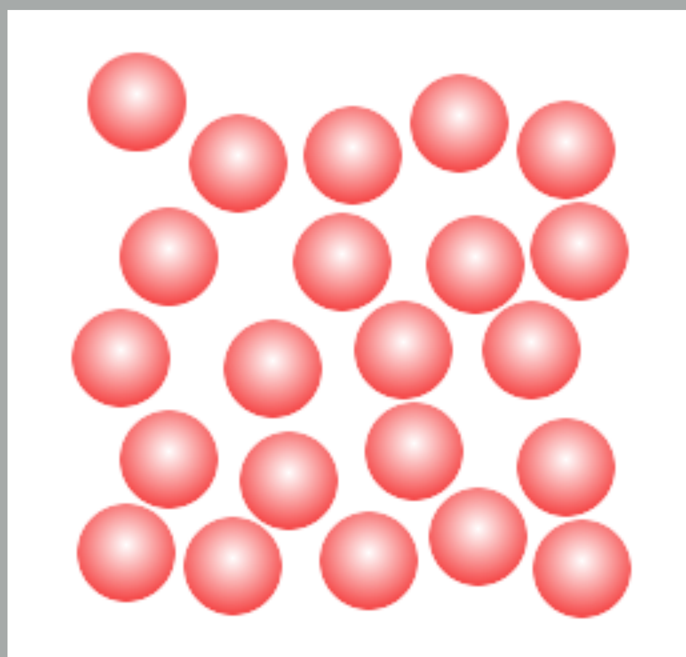


microscopically anisotropic but macroscopically (voxel) isotropic

Komlosh, 2009

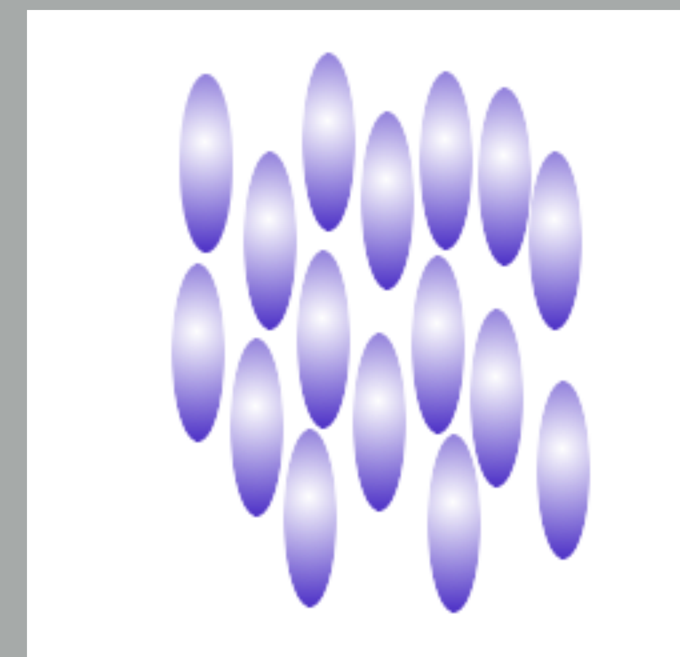
What if HARDI doesn't show anisotropy?

Anisotropy on the microscopic scale requires "multiple scattering"[1,2]



(a). **Microscopic**

(b). **Compartment Scale**



(c). **Ensemble**

Of the examples shown, only (c) would appear to have anisotropy using standard DTI techniques.

1. Özarslan, J. Magn. Reson. 199 (2009)
2. Özarslan and Basser, J. Chem. Phys. 128 (2008)