

Diffusion Tensor Imaging

Lawrence R. Frank, Ph.D.

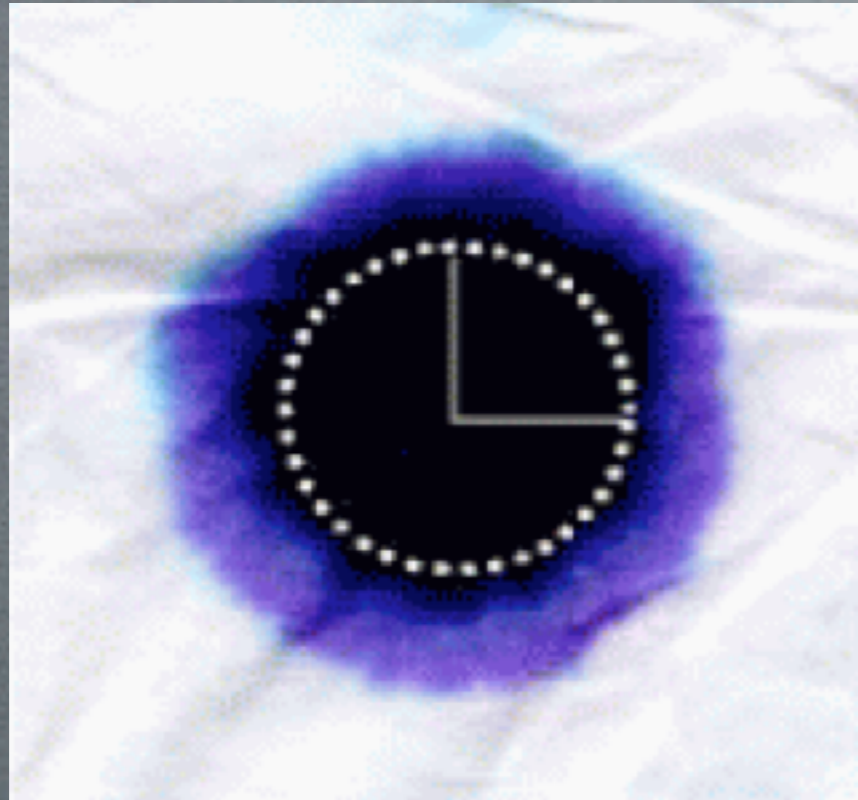
CENTER FOR SCIENTIFIC COMPUTATION IN
IMAGING
AND
UCSD CENTER FOR FMRI
UNIVERSITY OF CALIFORNIA, SAN DIEGO



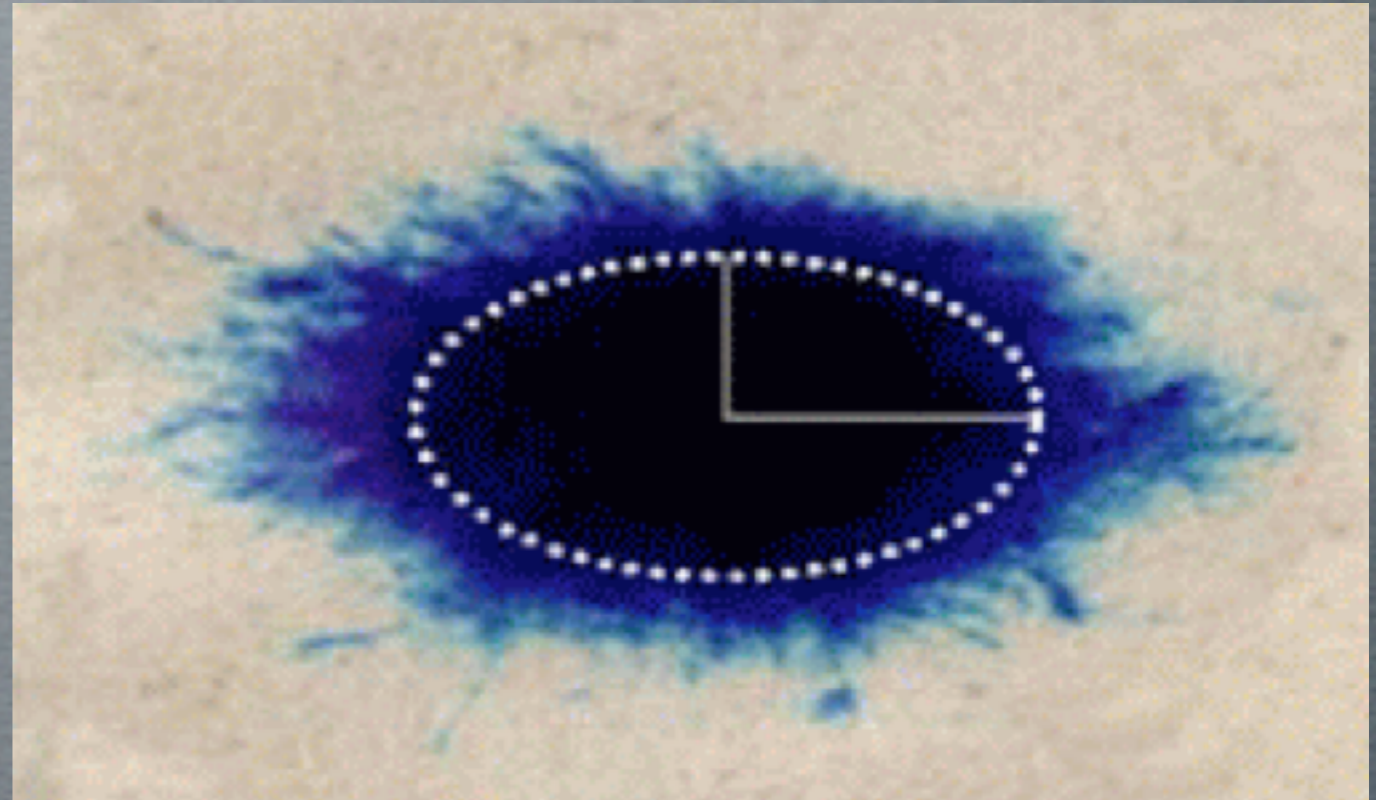
University of California
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MACROSCOPIC INFORMATION FROM MICROSCOPIC MEASUREMENTS



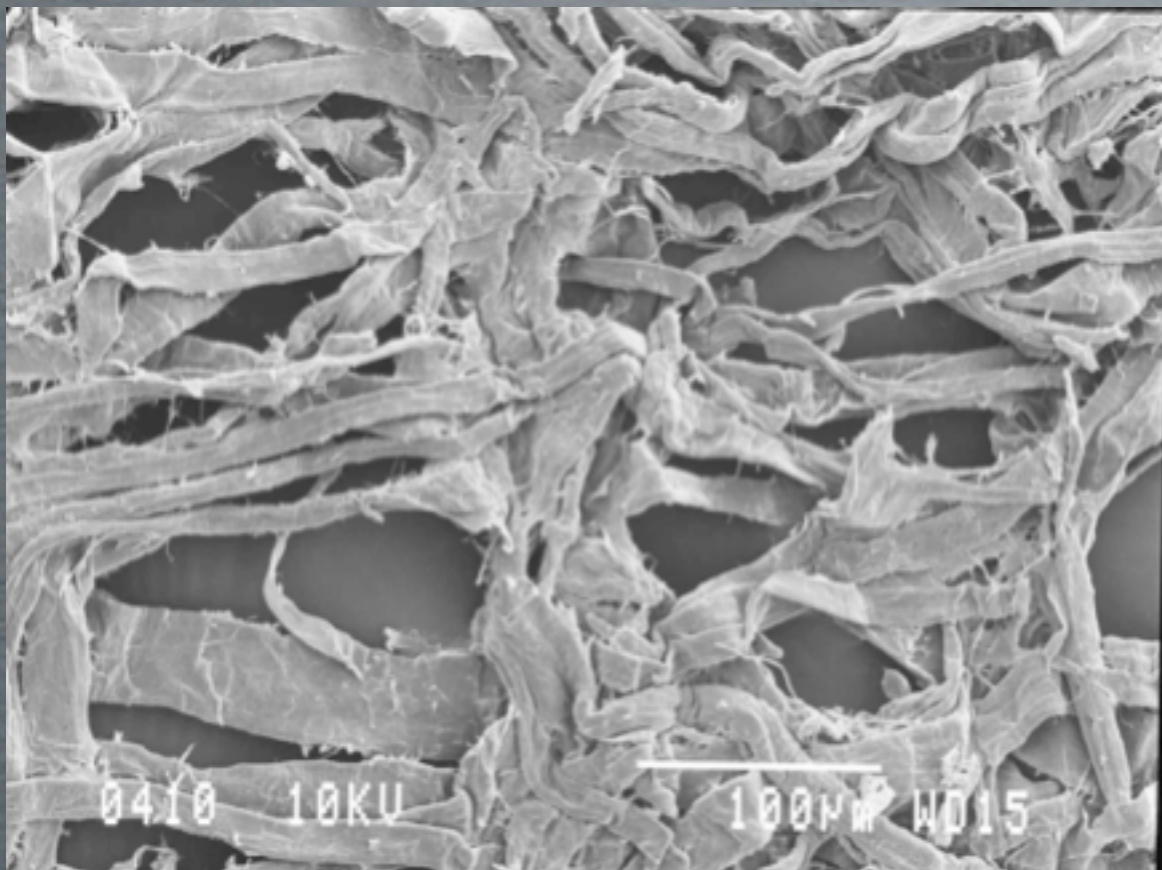
tissue paper



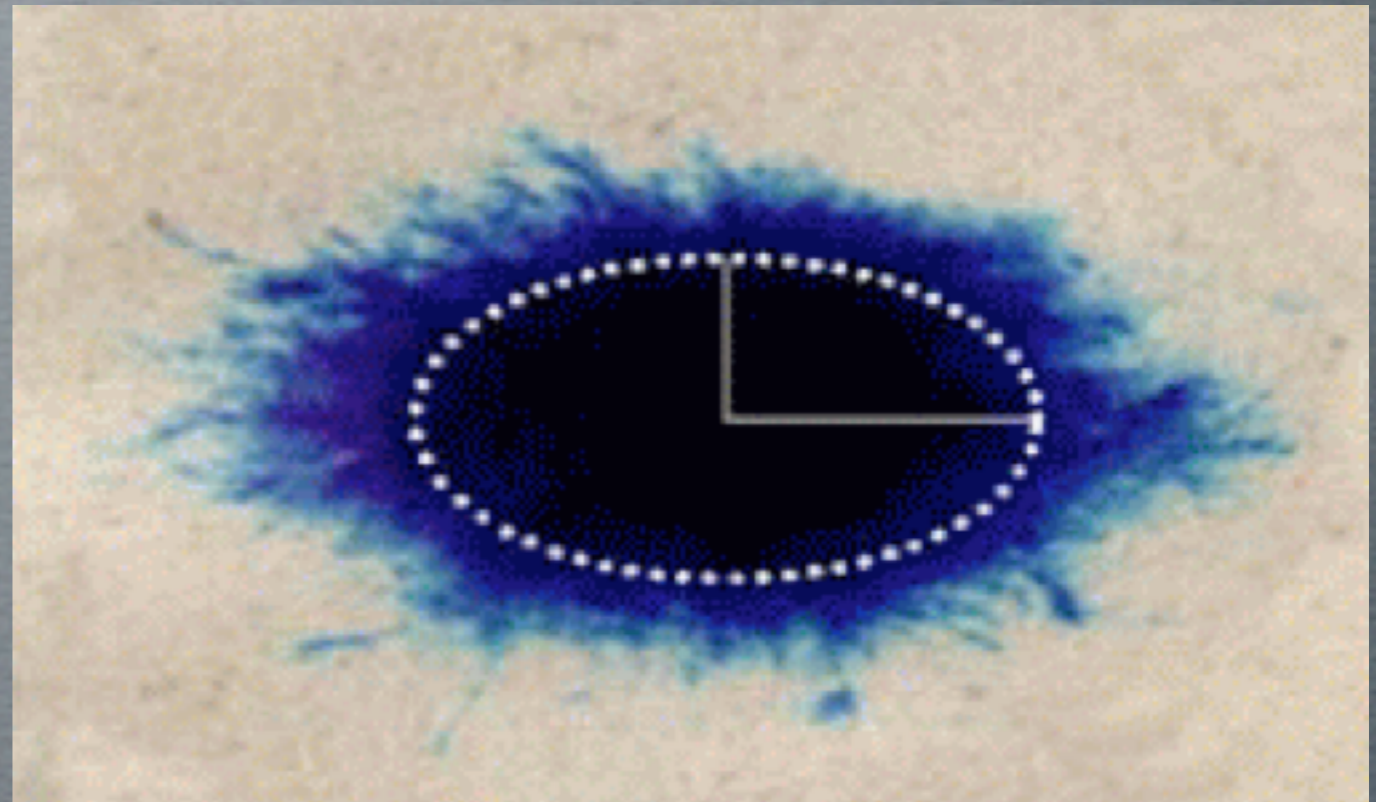
newspaper

diffusing ink in paper

MACROSCOPIC INFORMATION FROM MICROSCOPIC MEASUREMENTS



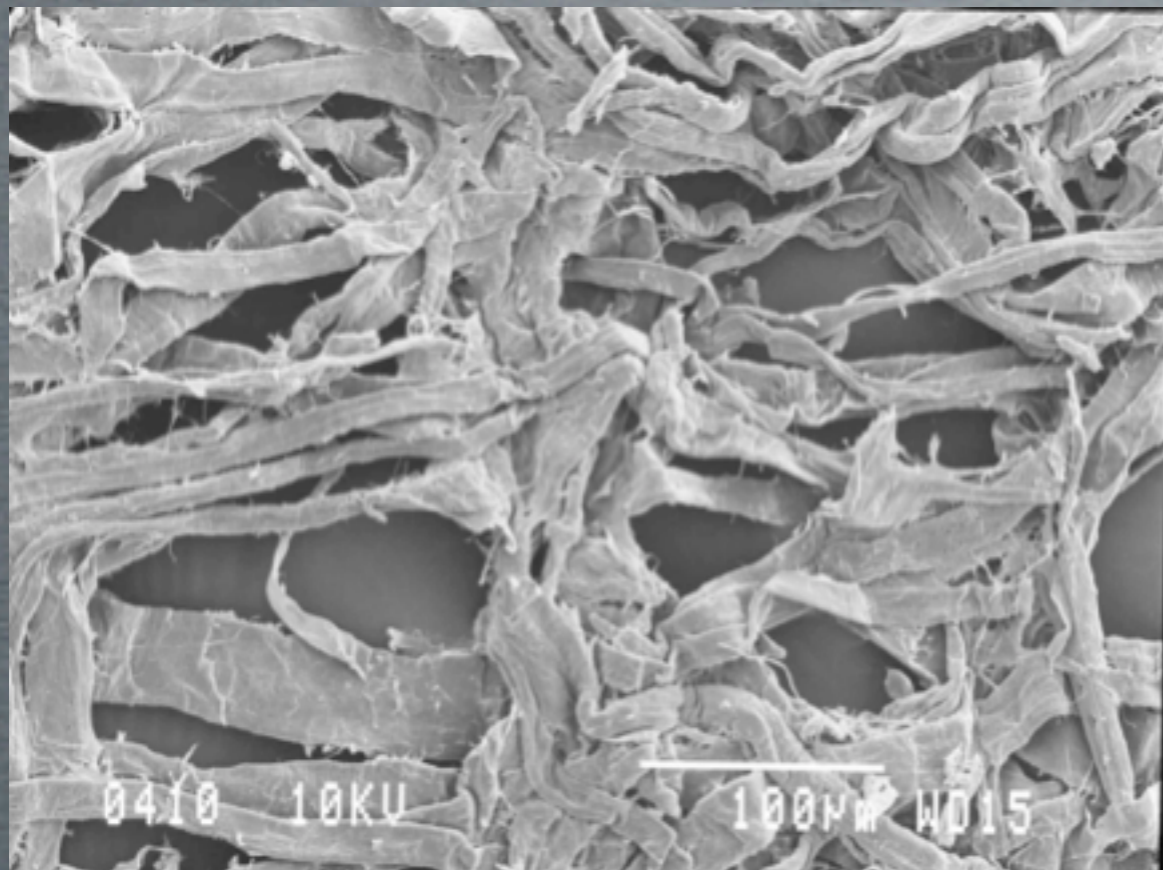
tissue paper



newspaper

diffusing ink in paper

MACROSCOPIC INFORMATION FROM MICROSCOPIC MEASUREMENTS



tissue paper



newspaper

diffusing ink in paper

WHAT IS DIFFUSION AND WHY DO WE CARE ABOUT IT?

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Self-diffusion is the thermally driven random motions of molecules that occurs in the absence of a concentration gradient

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The self-diffusion of water is ongoing in the human body and its characteristics depend on the local tissue architecture and physiology

WHAT IS DIFFUSION AND WHY DO WE CARE ABOUT IT?

Self-diffusion is the thermally driven random motions of molecules that occurs in the absence of a concentration gradient

The self-diffusion of water is ongoing in the human body and its characteristics depend on the local tissue architecture and physiology

Therefore the ability to measure self-diffusion offers the possibility of non-invasively measuring tissue structure and physiology

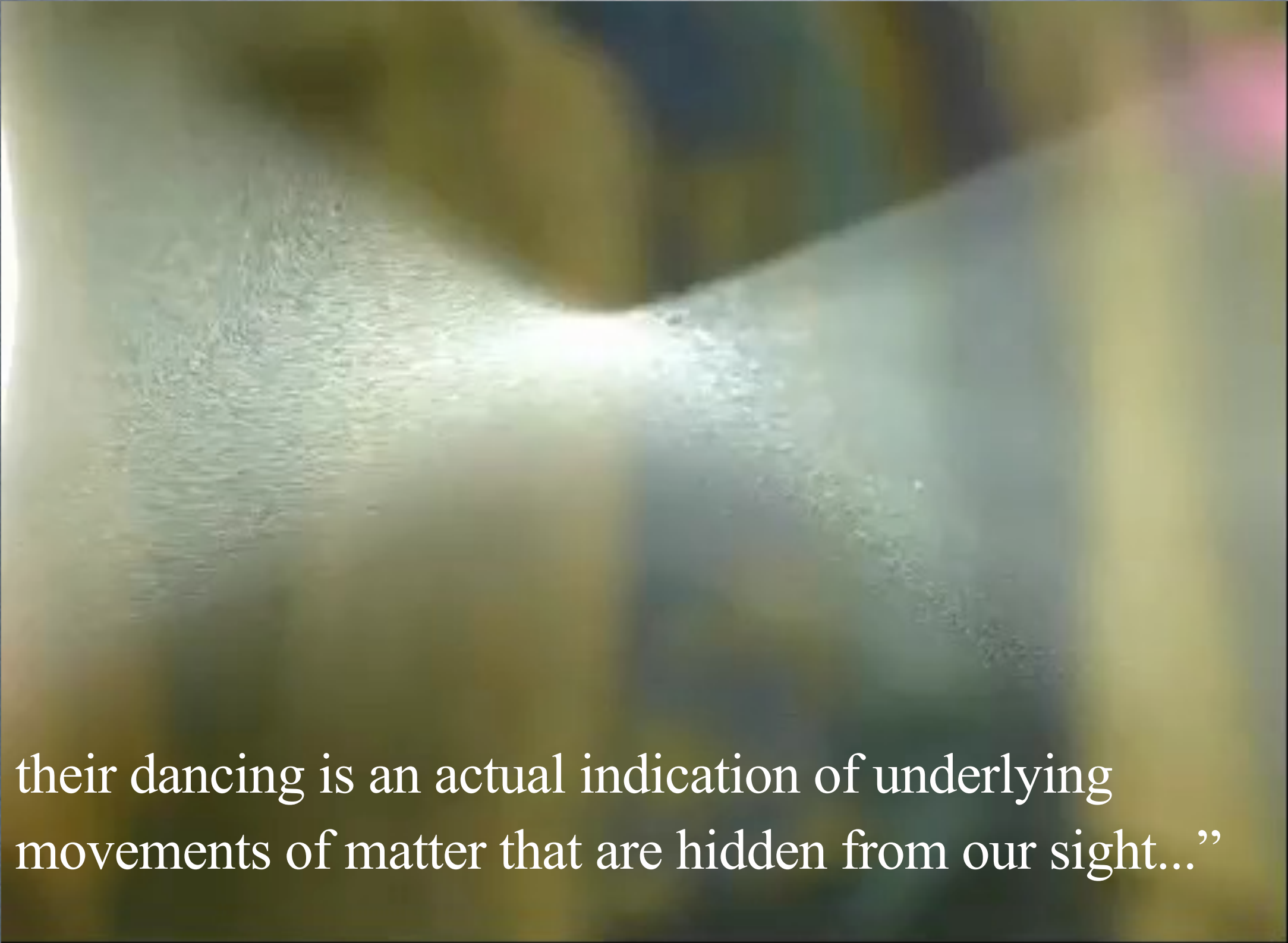
A BRIEF HISTORY OF DIFFUSION MEASUREMENT

A BRIEF HISTORY OF DIFFUSION MEASUREMENT



Lucretius (ca. 99BC-55BC)
Roman philosopher and poet

A BRIEF HISTORY OF DIFFUSION MEASUREMENT



their dancing is an actual indication of underlying movements of matter that are hidden from our sight...”

<http://www.youtube.com/eYeFractal>

CONVECTION VS DIFFUSION

A CAUTIONARY NOTE

CONVECTION VS DIFFUSION

A CAUTIONARY NOTE

The large scale swirling of the dust particles is primarily due to air currents (convection) but the *much* smaller scale jittery movements are diffusion

CONVECTION VS DIFFUSION

A CAUTIONARY NOTE



Convection

A BRIEF HISTORY OF DIFFUSION MEASUREMENT

A BRIEF HISTORY OF DIFFUSION MEASUREMENT

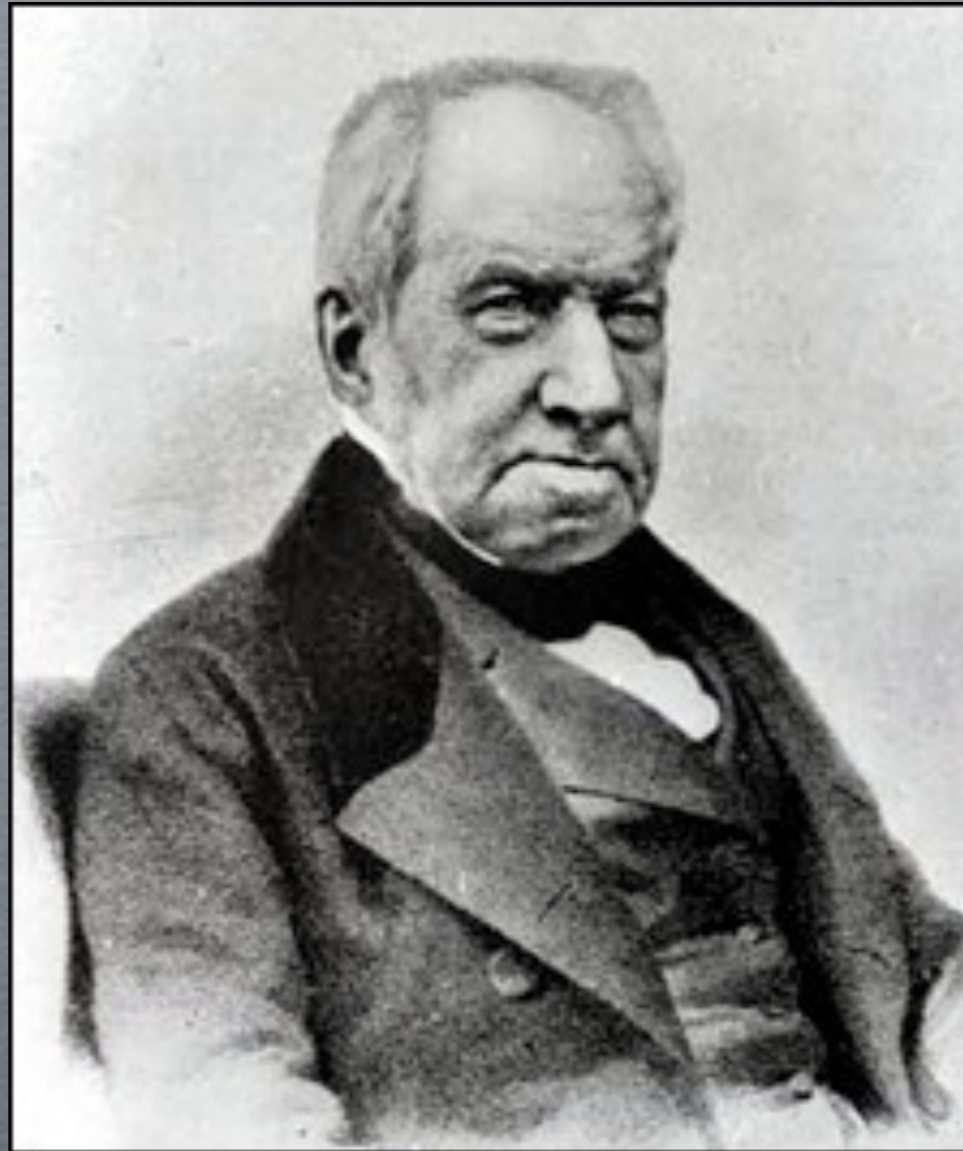


Jan Ingenhousz (1730 – 1799)
Dutch botanist and physiologist

Described the “irregular movements” of coal dust
on the surface of alcohol

A BRIEF HISTORY OF DIFFUSION MEASUREMENT

A BRIEF HISTORY OF DIFFUSION MEASUREMENT



Robert Brown (1773 – 1858)
British botanist and surgeon

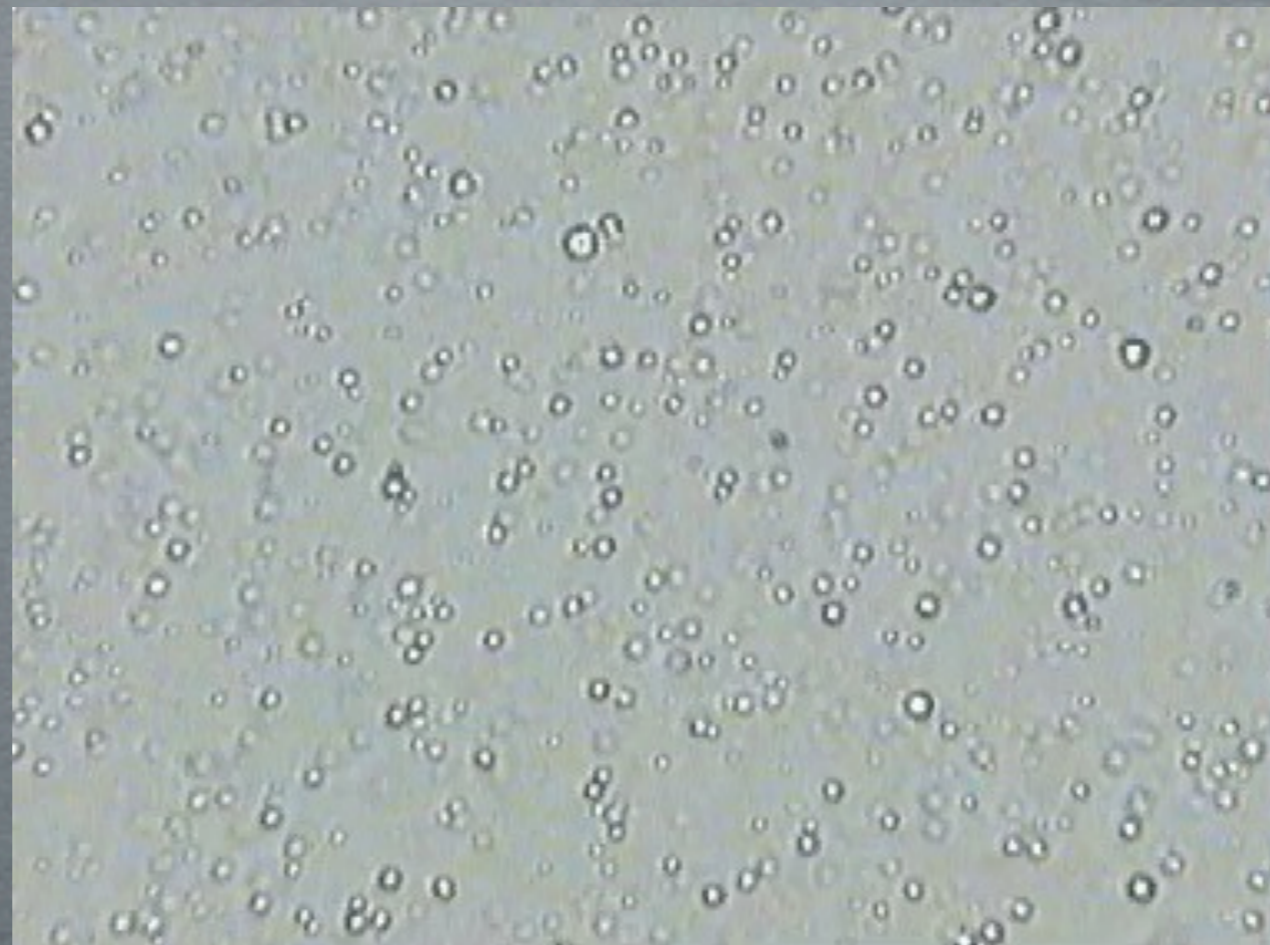
A BRIEF HISTORY OF DIFFUSION MEASUREMENT

Observation:

irregular movement of pollen granules in water

A BRIEF HISTORY OF DIFFUSION MEASUREMENT

“Brownian Motion”



Experiment: Repeat pollen experiment using tiny shards of window glass

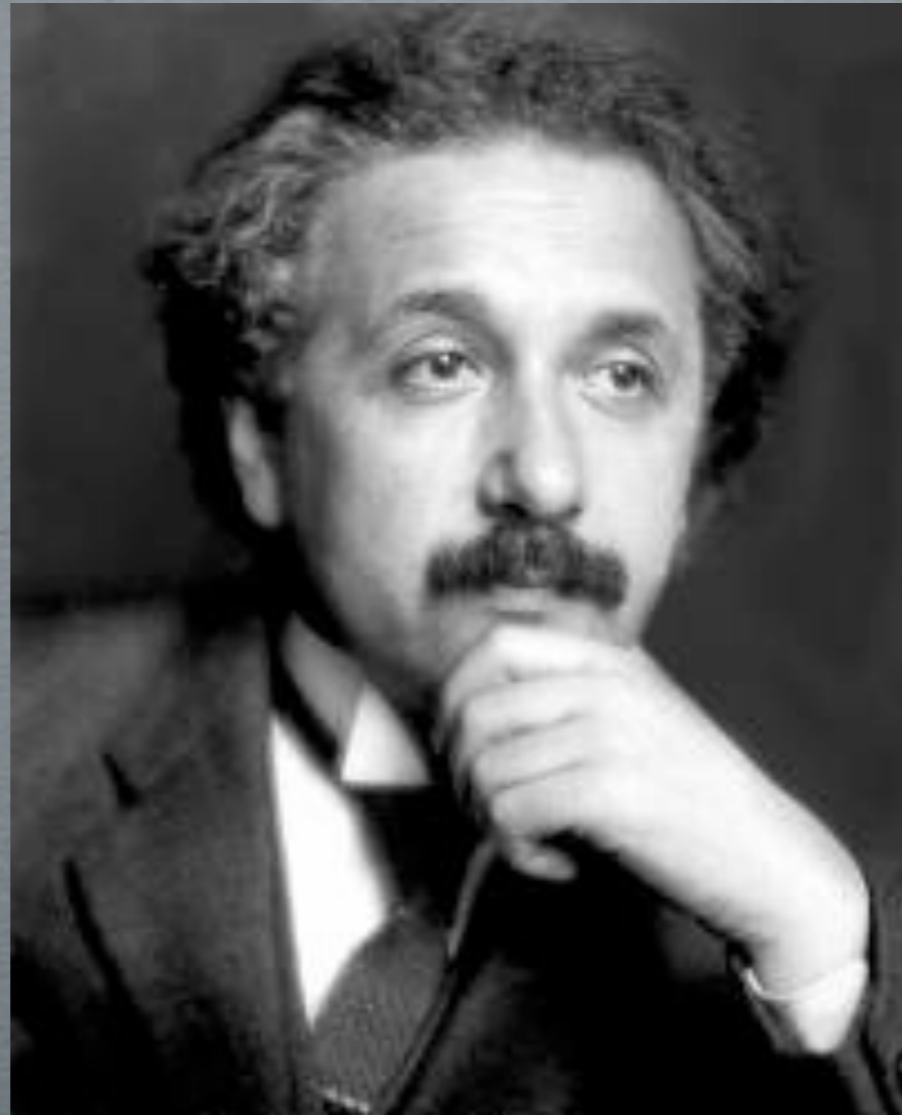
Result: Same!

Conclusion: Not alive

Theory: ???

EINSTEIN'S THEORY OF BROWNIAN MOTION

EINSTEIN'S THEORY OF BROWNIAN MOTION



Albert Einstein (1879 – 1955)
German physicist

EINSTEIN'S THEORY OF BROWNIAN MOTION

Einstein's Theory

Part 1: Equation describing motion of a Brownian particle

Part 2: Relate diffusion to experimentally measurable quantities

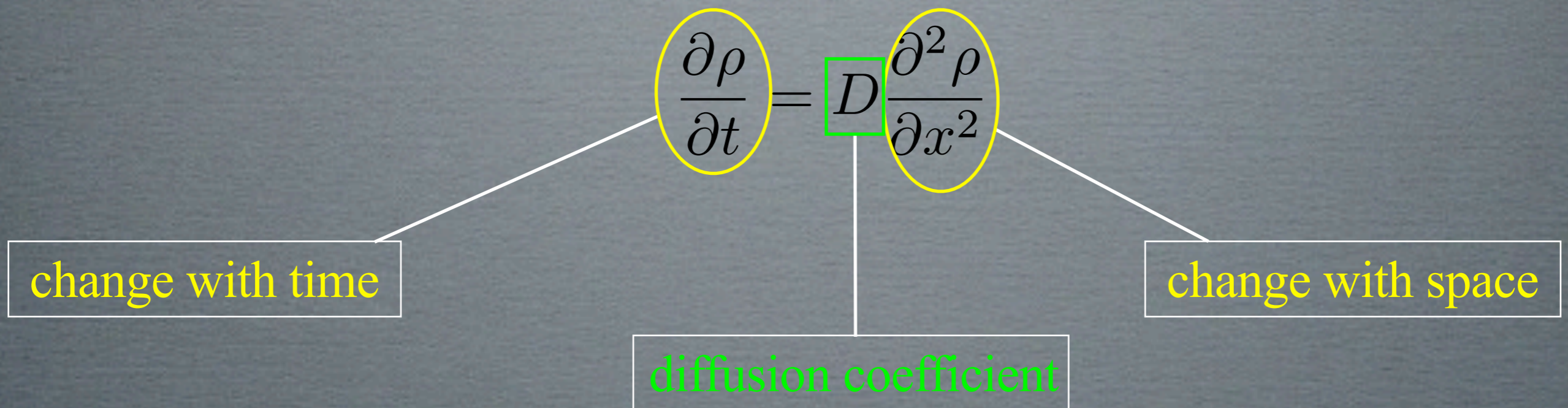
EINSTEIN THEORY OF BROWNIAN MOTION

PART I

EINSTEIN THEORY OF BROWNIAN MOTION

PART I

The particle density $\rho(x, t)$ at a position x at time t obeys



The Diffusion Equation

EINSTEIN THEORY OF BROWNIAN MOTION

PART I

EINSTEIN THEORY OF BROWNIAN MOTION

PART I

The solution to the Diffusion Equation
for particles initially at location x_0

$$\rho(x, t) = \frac{1}{\sqrt{4\pi Dt}} e^{-(x-x_0)^2/4Dt}$$

This is a Gaussian (or Normal) distribution
with mean position

$$\bar{x} = x_0$$

and variance in the position

$$\sigma_x^2 = \overline{(x - x_0)^2} = 2Dt$$

EINSTEIN THEORY OF BROWNIAN MOTION

PART I

EINSTEIN THEORY OF BROWNIAN MOTION

PART I

What does this mean?

$$\bar{x} = x_0$$

implies that, on *average*,
the particles do not move from their initial position

$$\sigma_x^2 = 2Dt$$

implies that the *variance* of a Brownian particle's
position is proportional to the diffusion coefficient D
and time t

EINSTEIN THEORY OF BROWNIAN MOTION

PART I

EINSTEIN THEORY OF BROWNIAN MOTION

PART I

Einstein argued that the *displacement* of a Brownian particle is thus the RMS distance

$$\Delta x = \sqrt{(x - x_0)^2} = \sqrt{2Dt}$$

and thus *not* linearly proportional to time (like flow), but to the *square root of time*

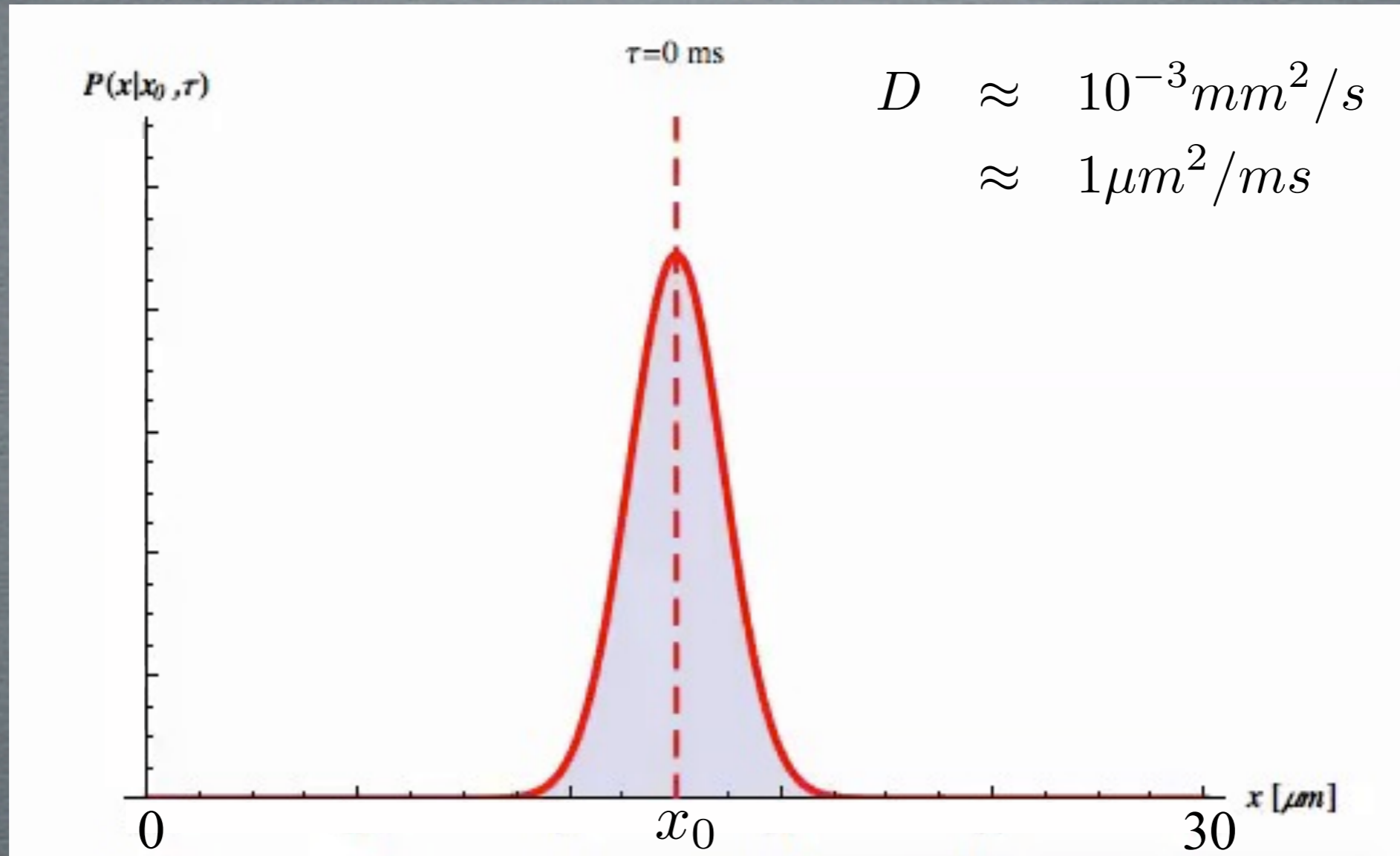
Diffusion in Brain Tissue:

$$D \cong 1 \mu^2 / \text{ms} = (0.001 \text{ mm}^2/\text{s})$$

$$\text{For } t=100 \text{ msec, } \Delta x \cong 14 \mu$$

GAUSSIAN DIFFUSION

GAUSSIAN DIFFUSION



$$P(x|x_0, \tau) = \frac{1}{\sqrt{4\pi D\tau}} e^{-\frac{(x-x_0)^2}{4\pi D\tau}}$$

$$\sigma = \sqrt{2D\tau}$$

EINSTEIN THEORY OF BROWNIAN MOTION

PART I

EINSTEIN THEORY OF BROWNIAN MOTION

PART I

DIFFUSION VS FLOW

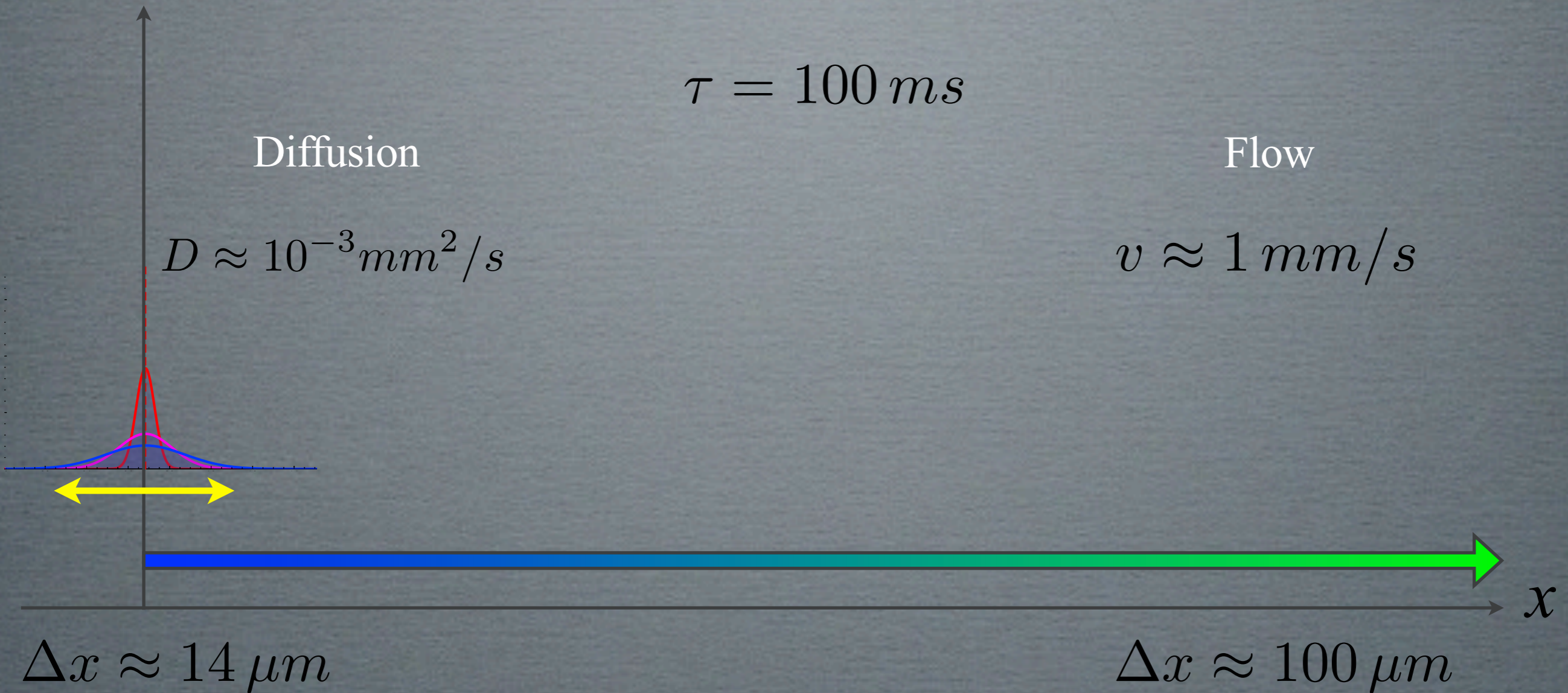
$$\tau = 100 \text{ ms}$$

Diffusion

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

Flow

$$v \approx 1 \text{ mm/s}$$



$$\Delta x \approx 14 \mu\text{m}$$

$$\Delta x \approx 100 \mu\text{m}$$

EINSTEIN THEORY OF BROWNIAN MOTION

PART II

EINSTEIN THEORY OF BROWNIAN MOTION

PART II

The diffusion coefficient is

$$D = \alpha \frac{T}{\eta r}$$

Diffusion coefficient goes **up** with **temperature**
and **down** with **viscosity** and **particle radius**

It's sensitive to the local environment!

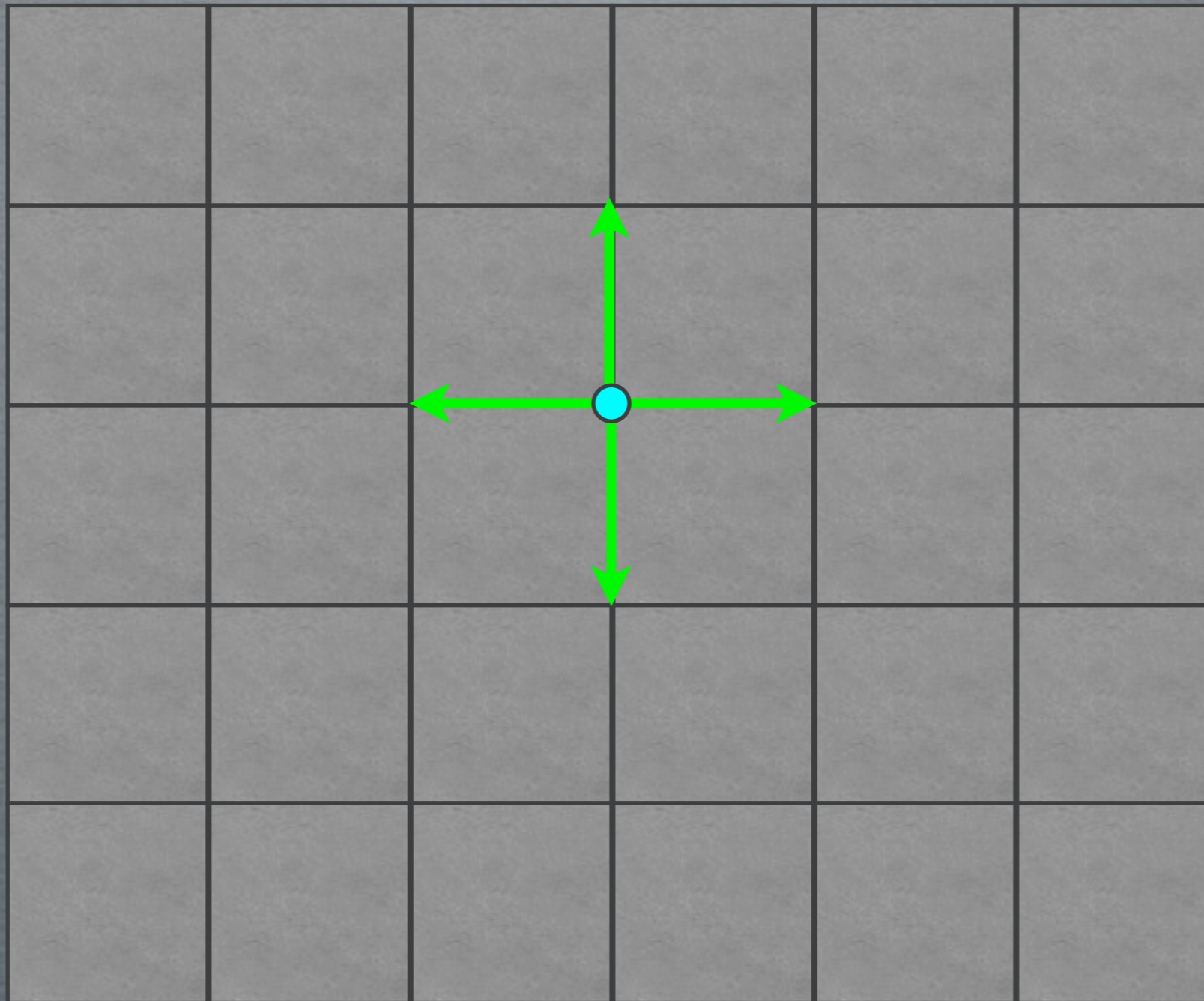
MODELING DIFFUSION: RANDOM WALK

MODELING DIFFUSION: RANDOM WALK

MRI is all about mapping the locations of molecules ...

... we need a way to model the spatial locations of Brownian molecules as a function of time

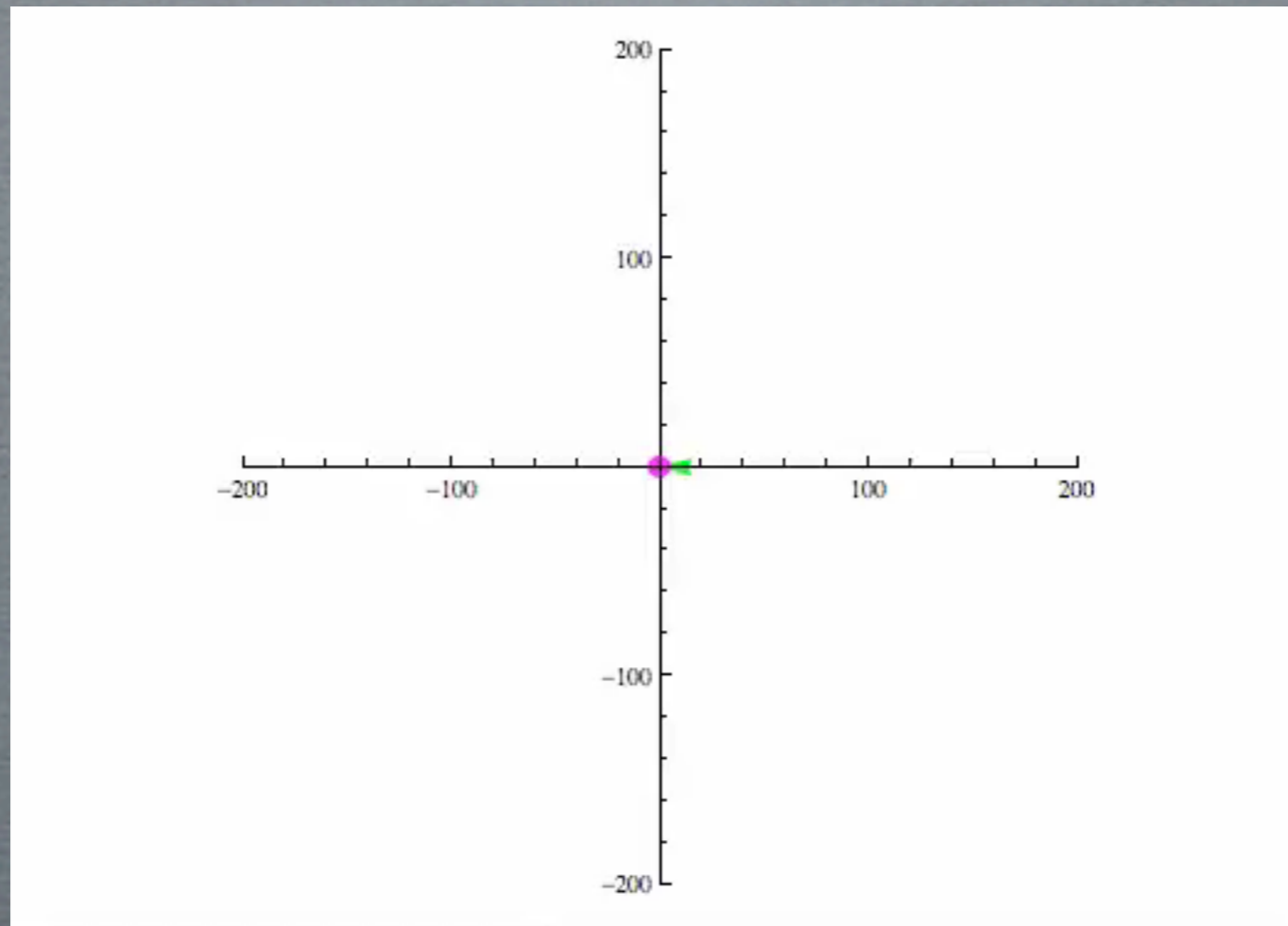
MODELING DIFFUSION: RANDOM WALK



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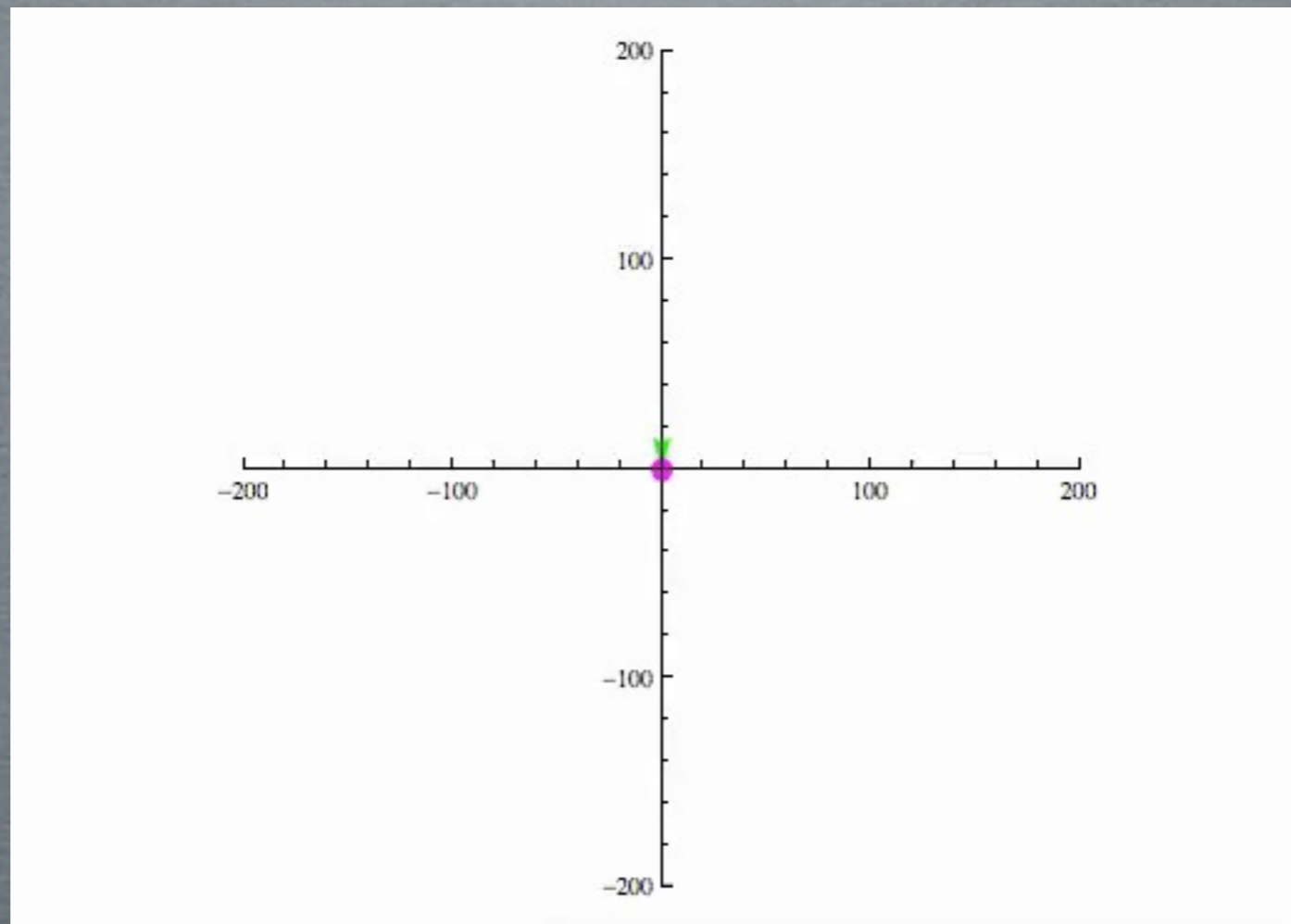
$$\tau = \text{constant}$$

MODELING DIFFUSION: RANDOM WALK



$$\tau = \text{constant}$$

MODELING DIFFUSION: RANDOM WALK

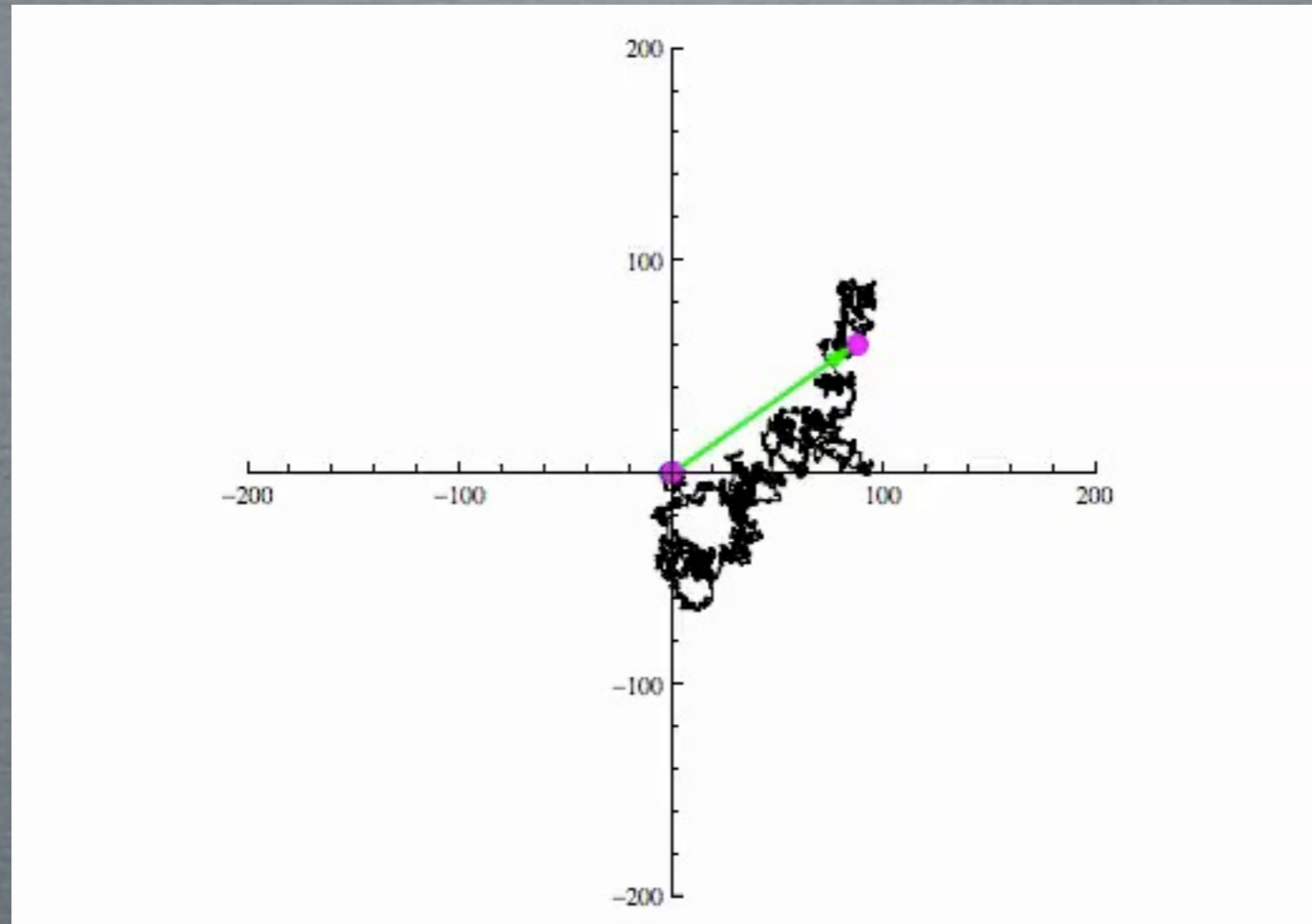


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MODELING DIFFUSION: RANDOM WALK

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MODELING DIFFUSION: RANDOM WALK

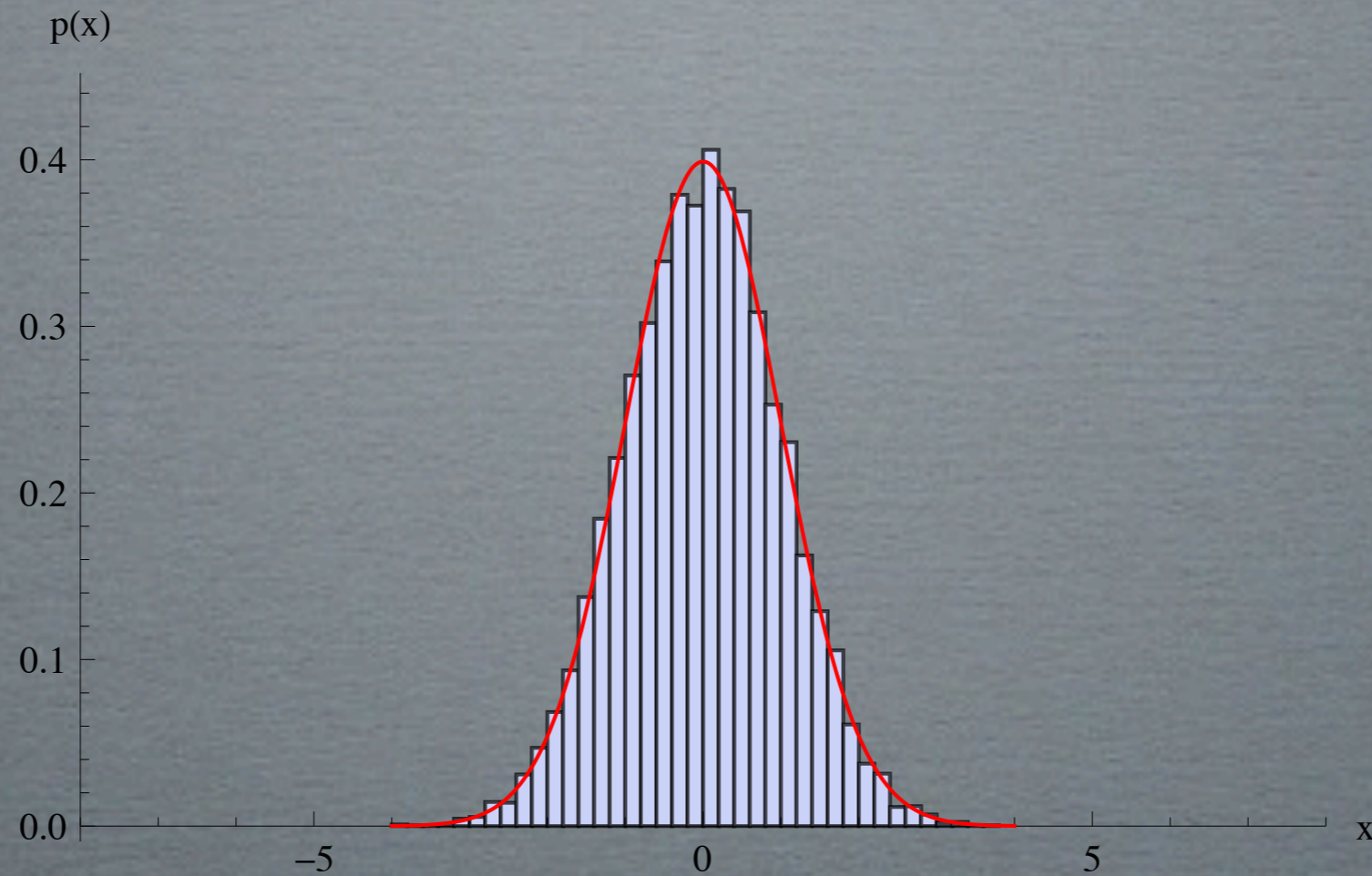
MODELING DIFFUSION: RANDOM WALK

The distribution of particles after a time τ



MODELING DIFFUSION: RANDOM WALK

The distribution of particles after a time τ

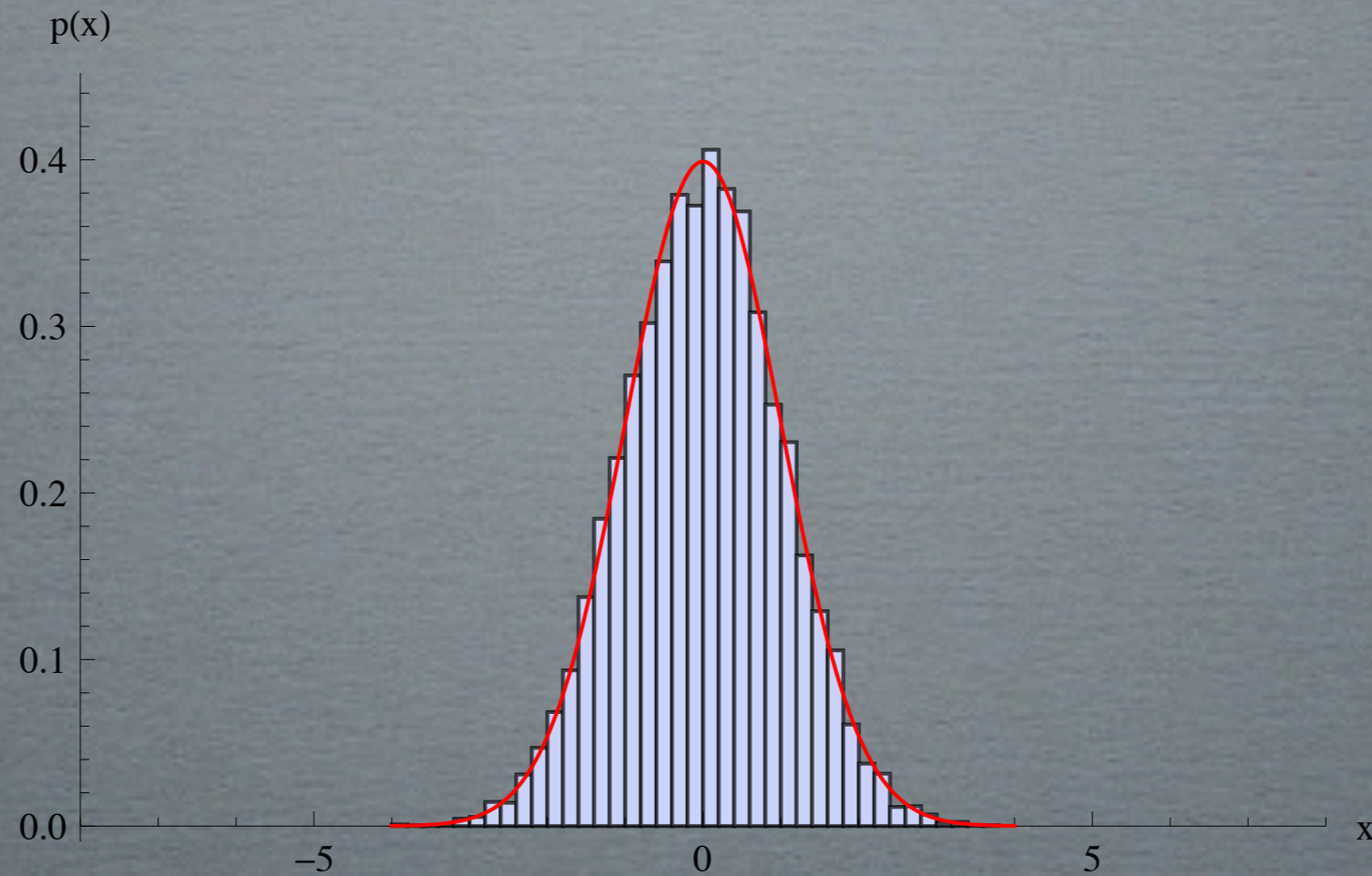


GAUSSIAN DIFFUSION

$$P(x|x_0, \tau) = \frac{1}{\sqrt{4\pi D\tau}} e^{-\frac{(x-x_0)^2}{4\pi D\tau}}$$

MODELING DIFFUSION: RANDOM WALK

The distribution of particles after a time τ

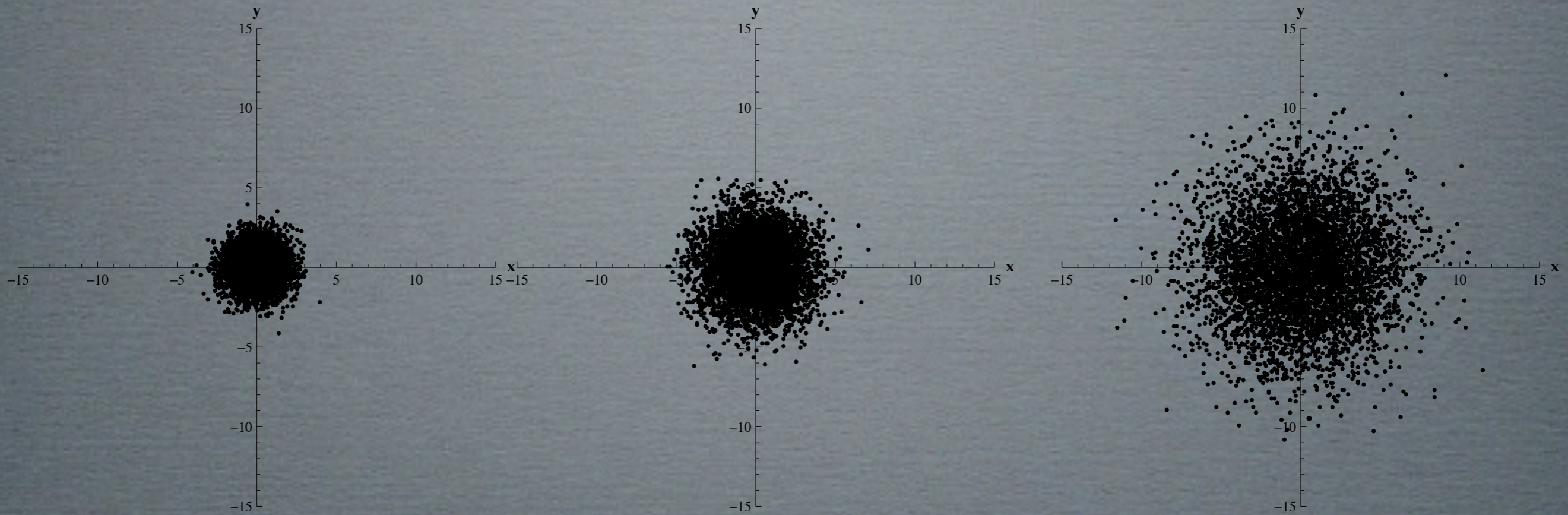


GAUSSIAN DIFFUSION

$$P(x|x_0, \tau) \sim N(x_0, \sigma^2)$$

ISOTROPIC DIFFUSION IN 2D

ISOTROPIC DIFFUSION IN 2D

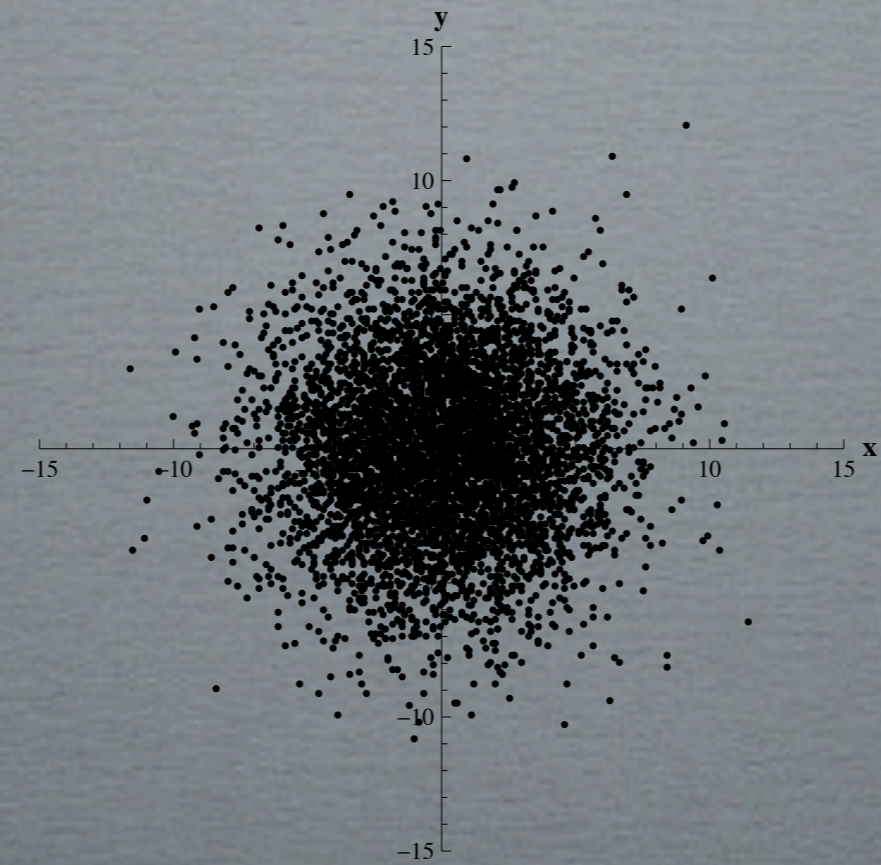


$$\tau = 1 \text{ ms}$$

$$\tau = 10 \text{ ms}$$

$$\tau = 100 \text{ ms}$$

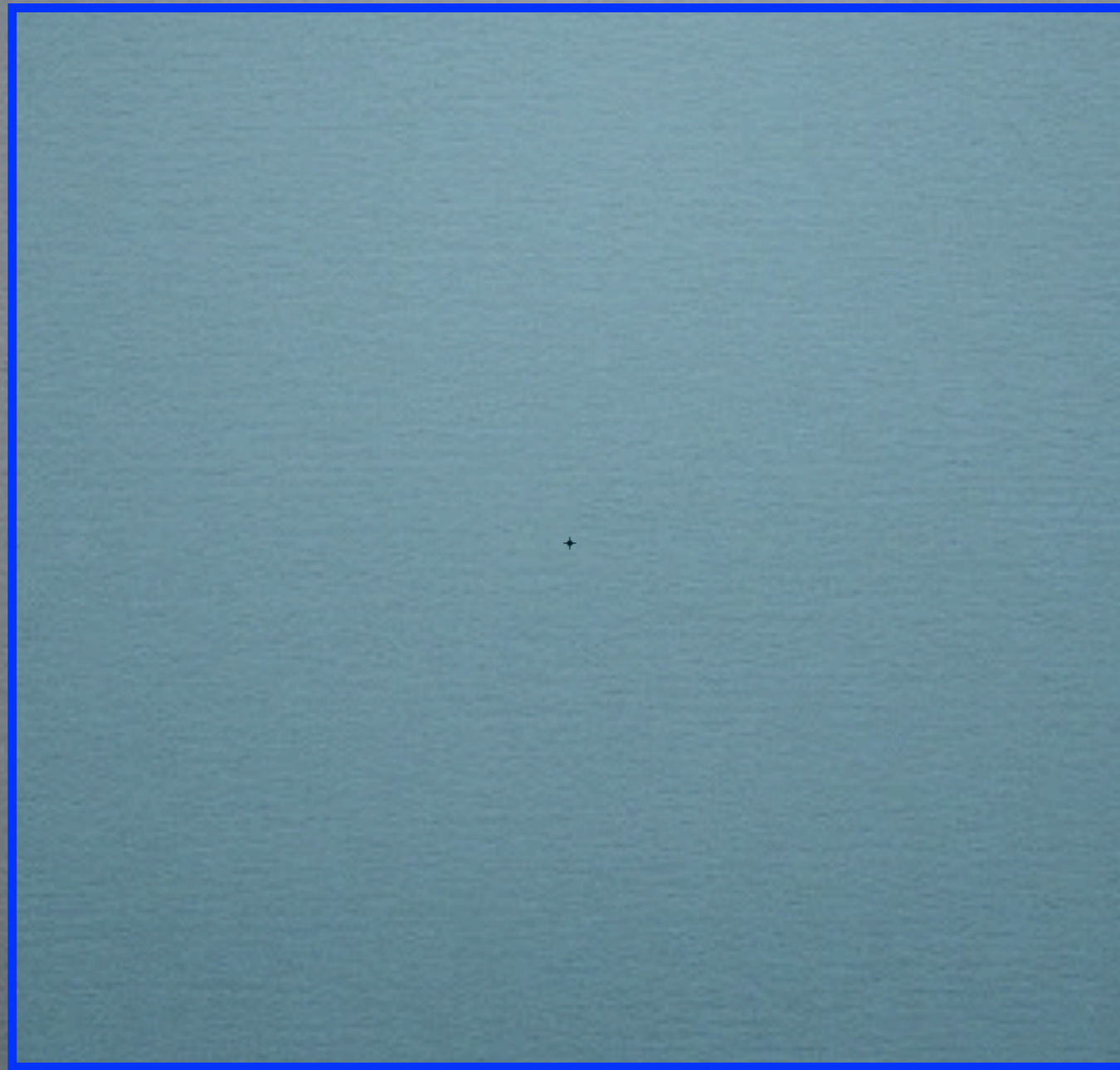
DIFFUSION DIMENSIONS



DIFFUSION DIMENSIONS

$$\tau = 100 \text{ ms}$$

voxel

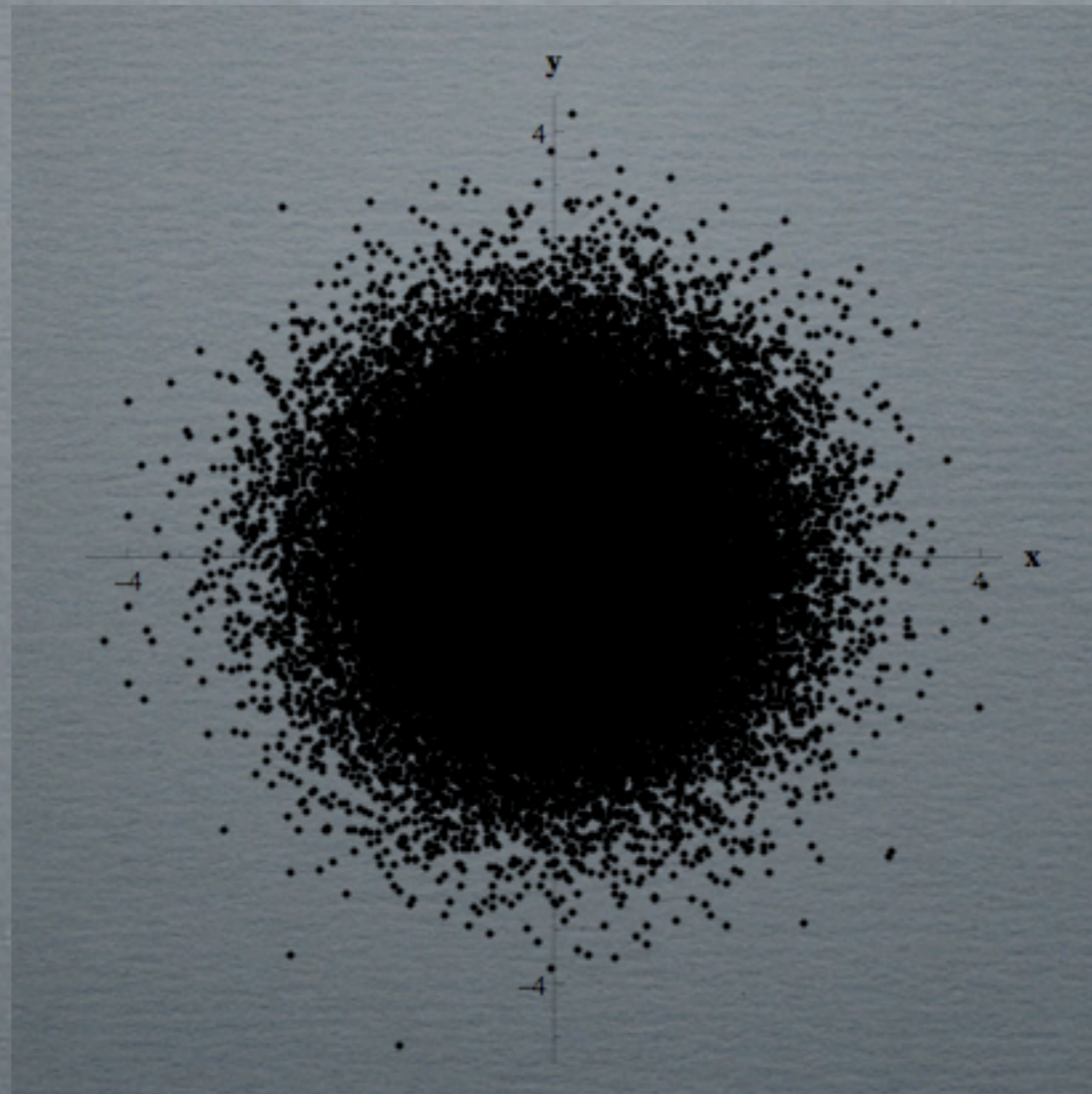


1.5 mm

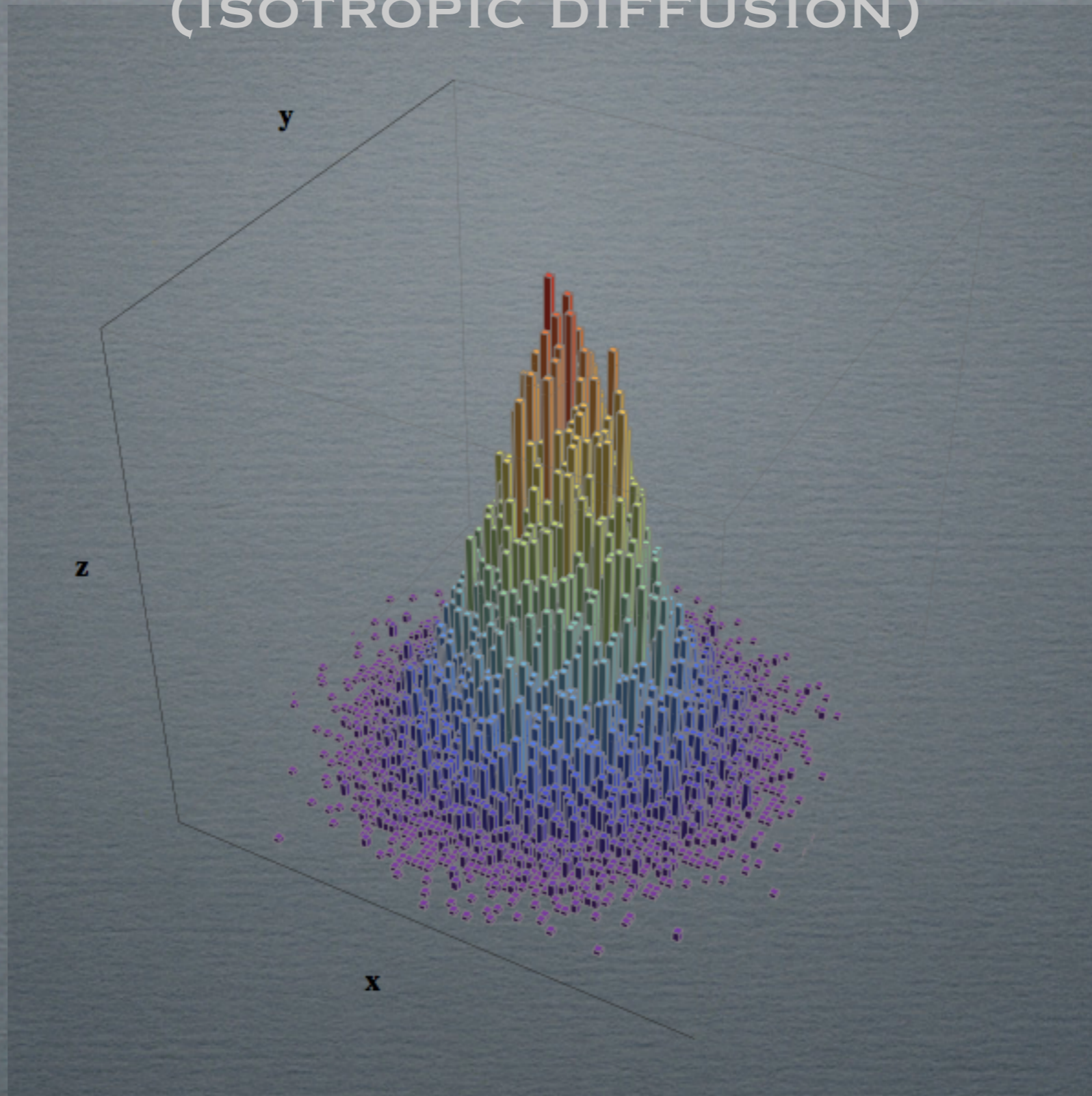
$\Delta x \approx \left(\frac{1}{1000} \right)$ a typical imaging voxel dimension

PROBABILITY CONTOURS (ISOTROPIC DIFFUSION)

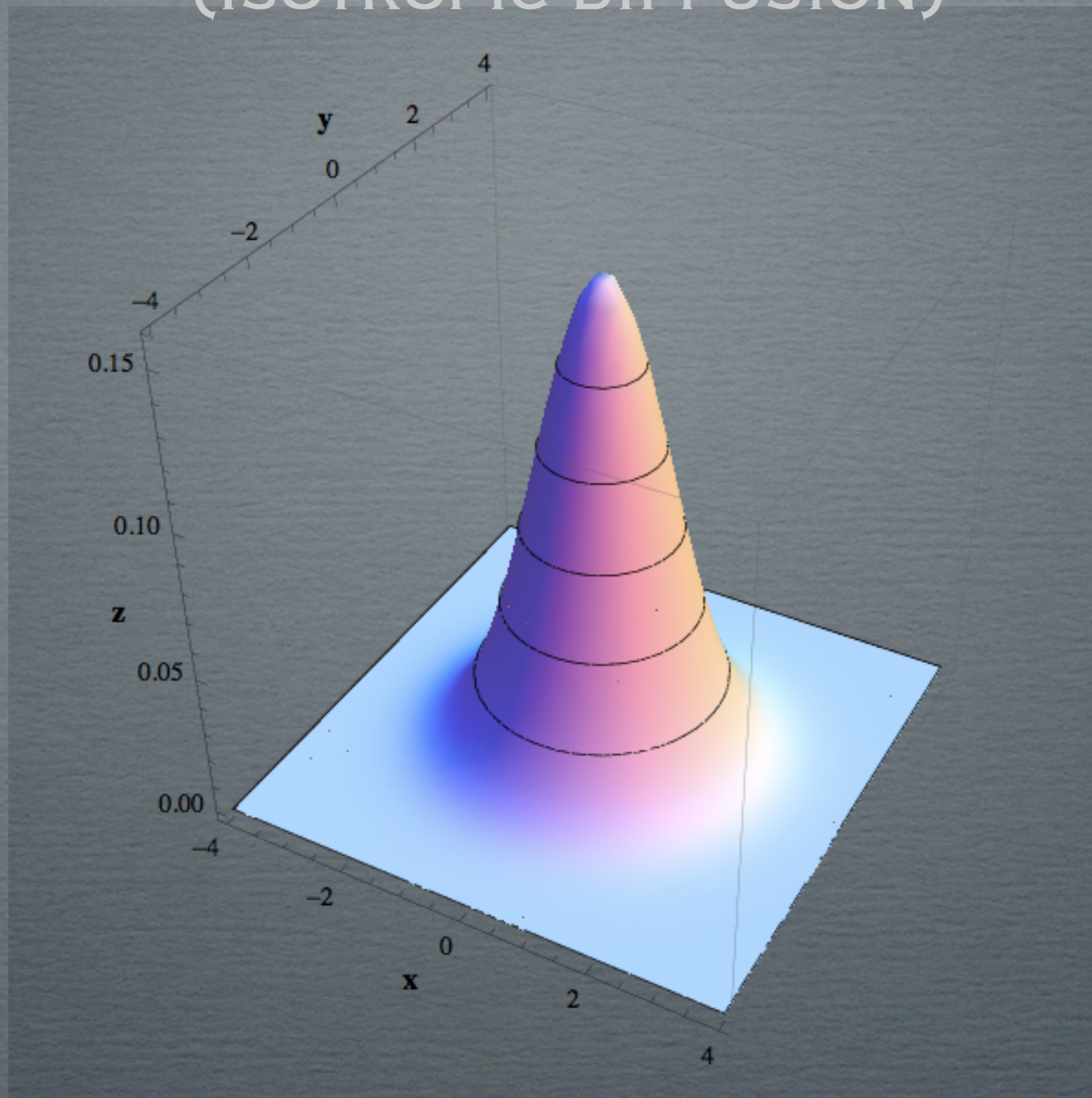
PROBABILITY CONTOURS (ISOTROPIC DIFFUSION)



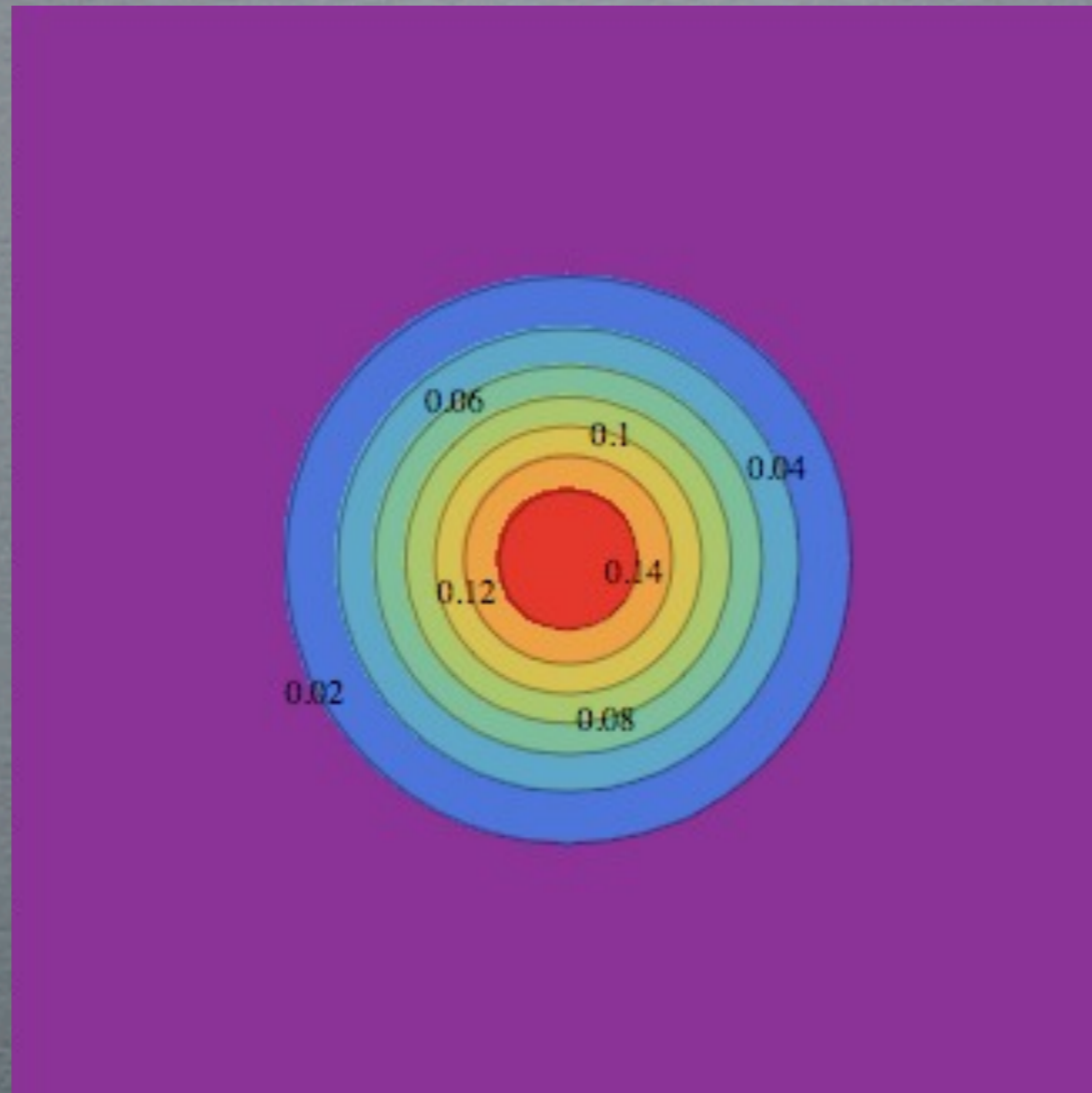
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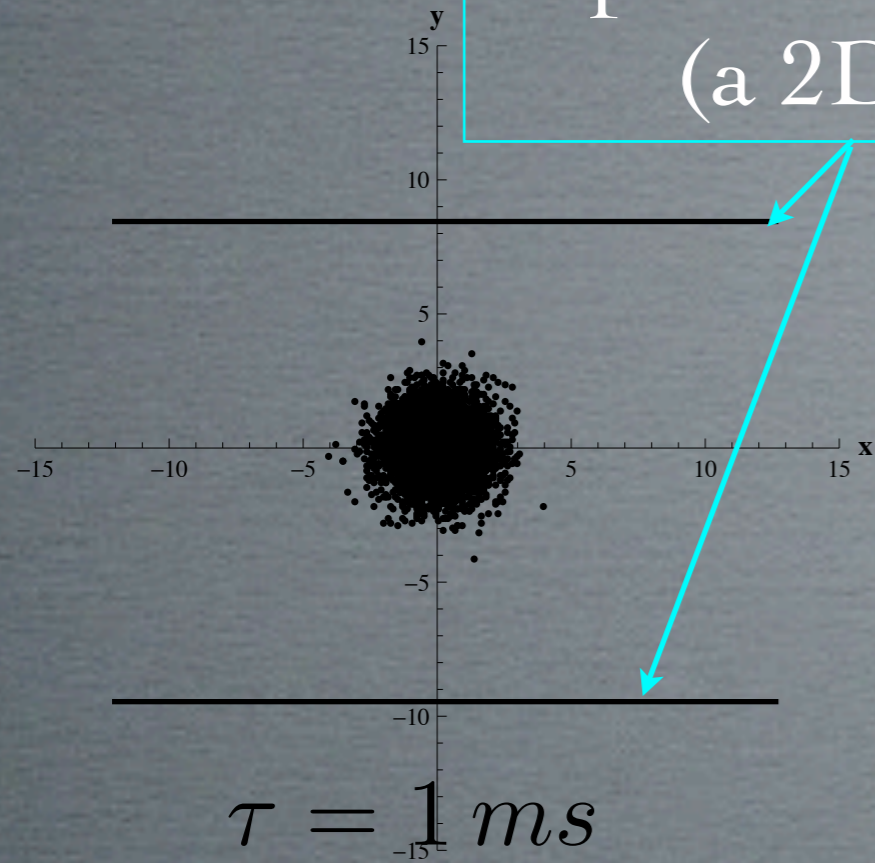
PROBABILITY CONTOURS (ISOTROPIC DIFFUSION)



ANISOTROPIC DIFFUSION IN 2D

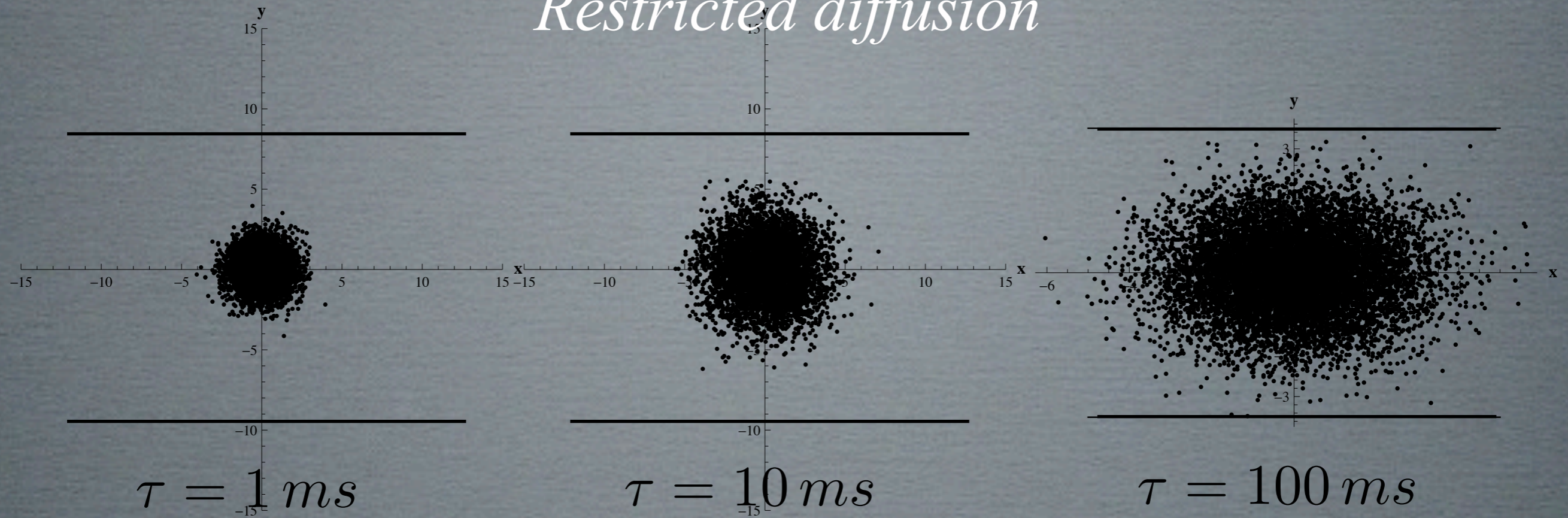
ANISOTROPIC DIFFUSION IN 2D

Impermeable barriers
(a 2D tube)



ANISOTROPIC DIFFUSION IN 2D

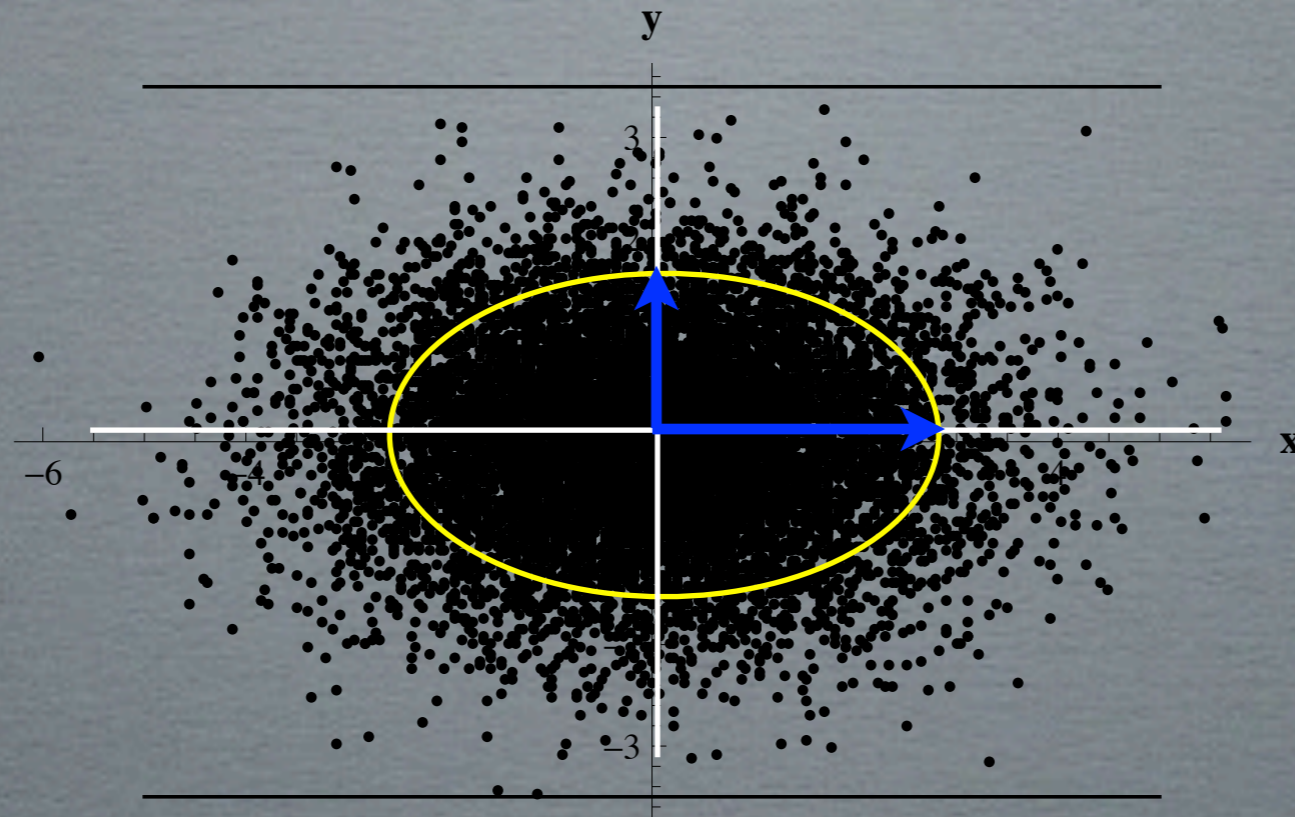
Restricted diffusion



ANISOTROPIC DIFFUSION IN 2D

ANISOTROPIC DIFFUSION IN 2D

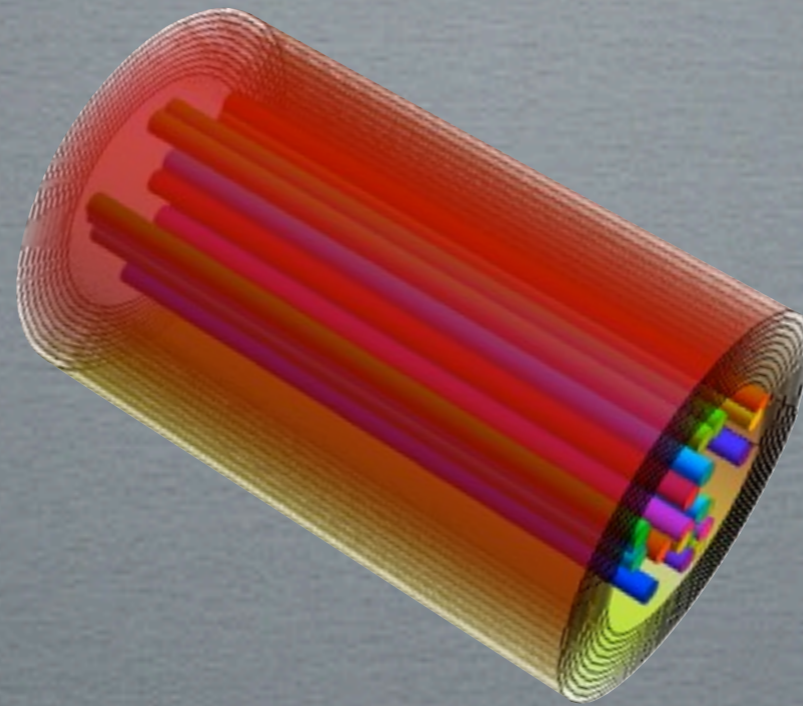
$$P(\mathbf{r}|\mathbf{r}_0, \tau) \sim N(\mathbf{r}_0, \Sigma)$$



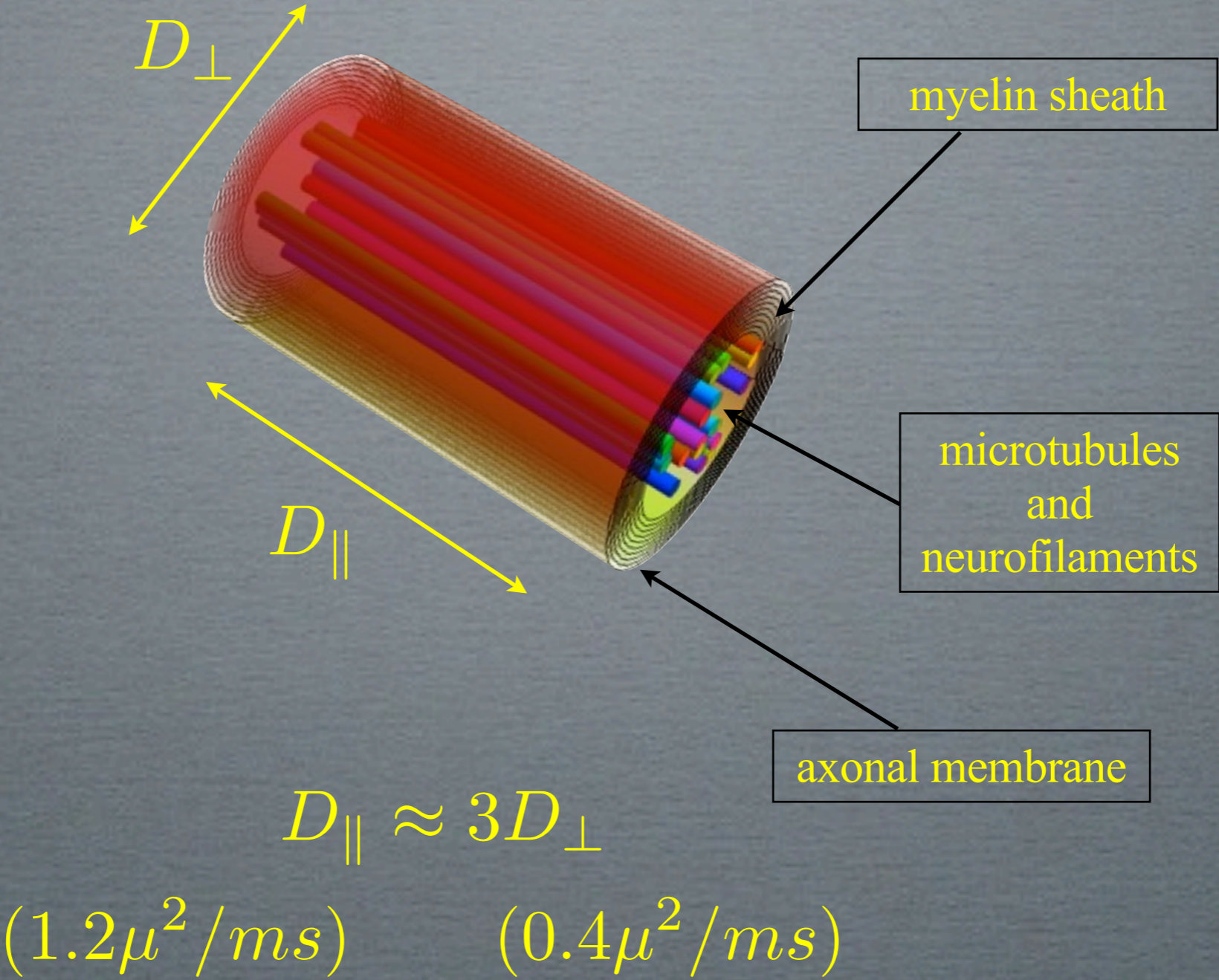
Covariance matrix

$$\Sigma = \begin{pmatrix} \sigma_x^2 & 0 \\ 0 & \sigma_y^2 \end{pmatrix}$$

DIFFUSION ANISOTROPY IN NEURAL TISSUES

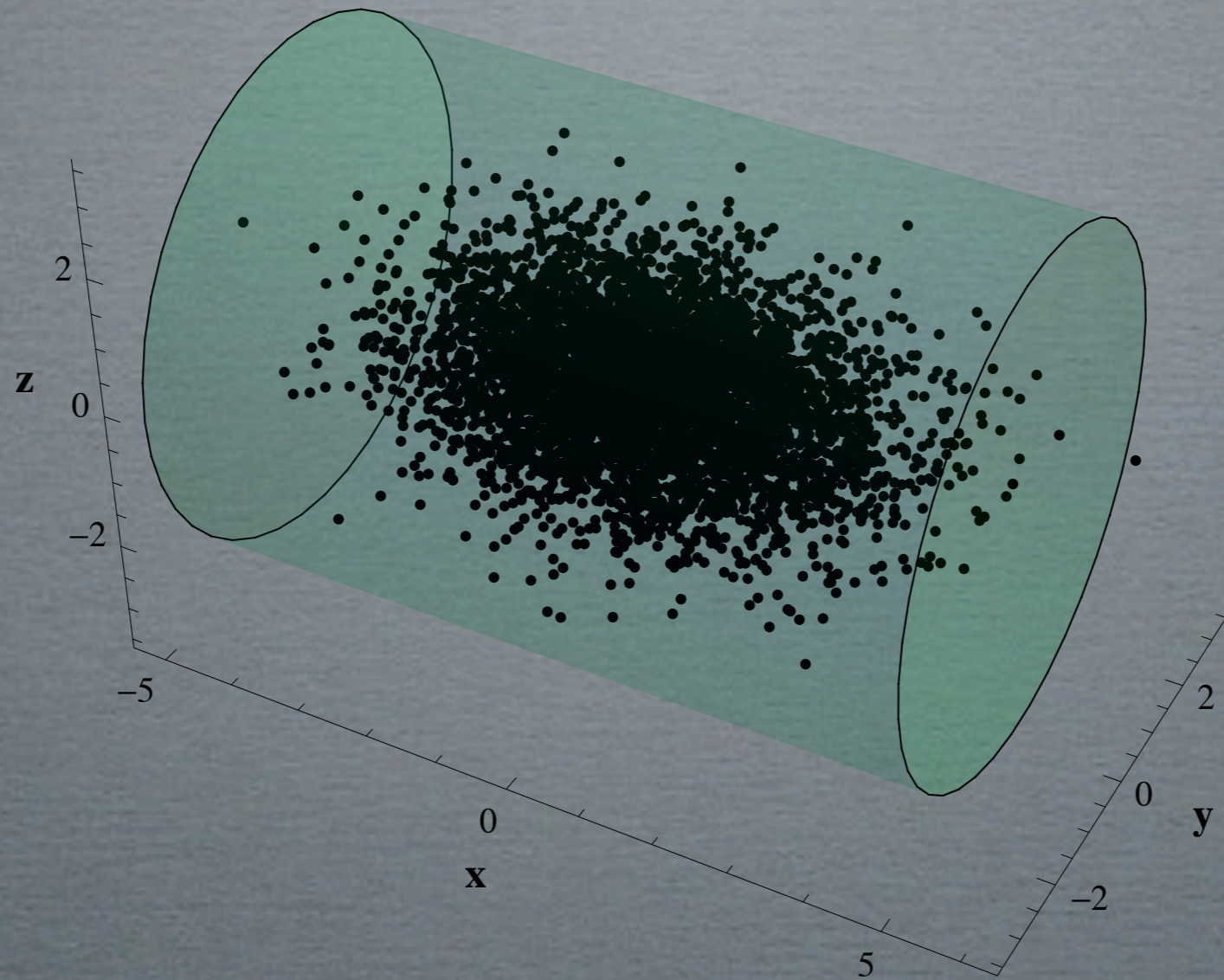


DIFFUSION ANISOTROPY IN NEURAL TISSUES

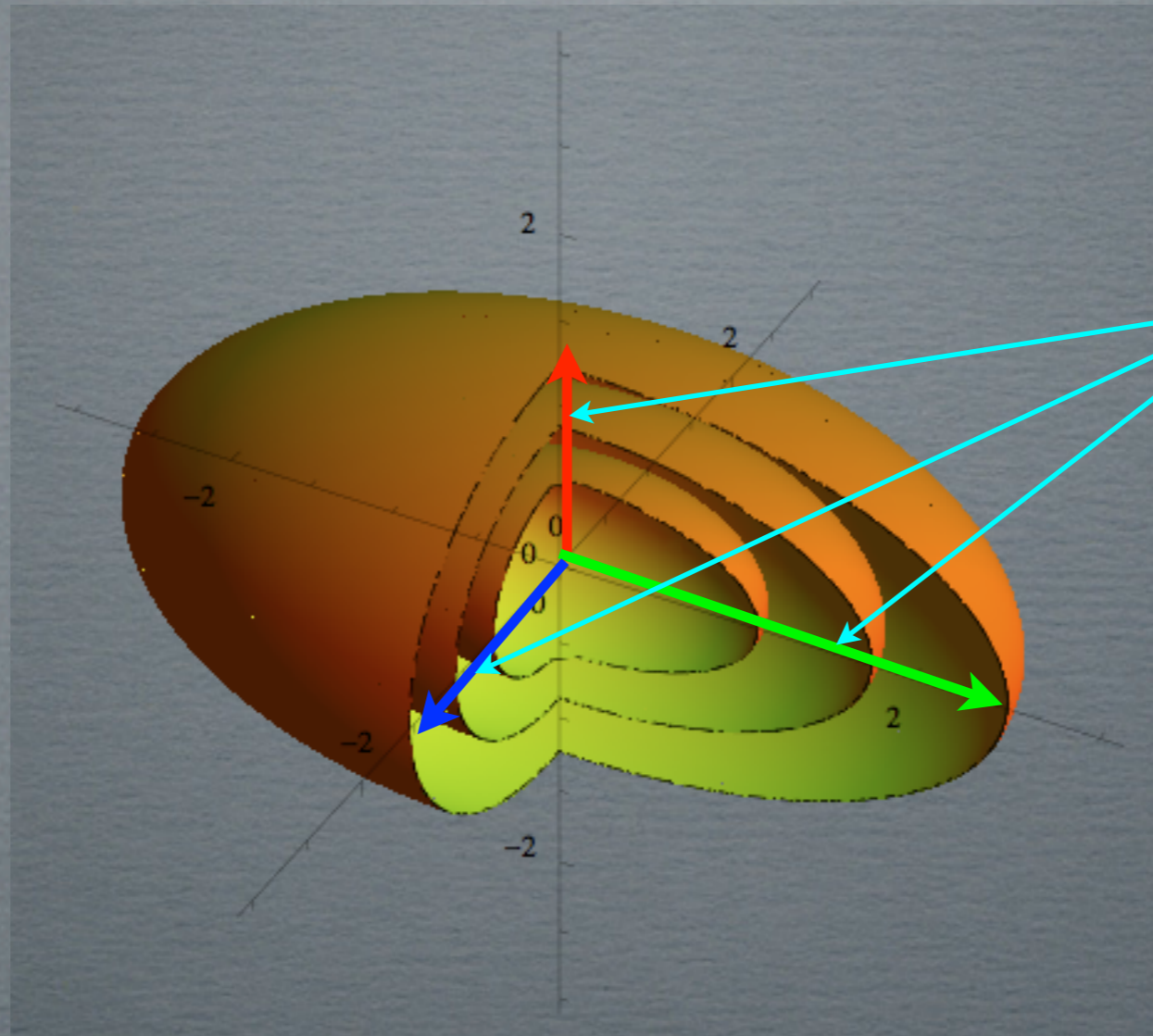


DIFFUSION ANISOTROPY IN 3D

DIFFUSION ANISOTROPY IN 3D



DIFFUSION ANISOTROPY IN 3D



eigenvectors

probability contours in 3D

THE SENSITIVITY OF MRI TO DIFFUSION

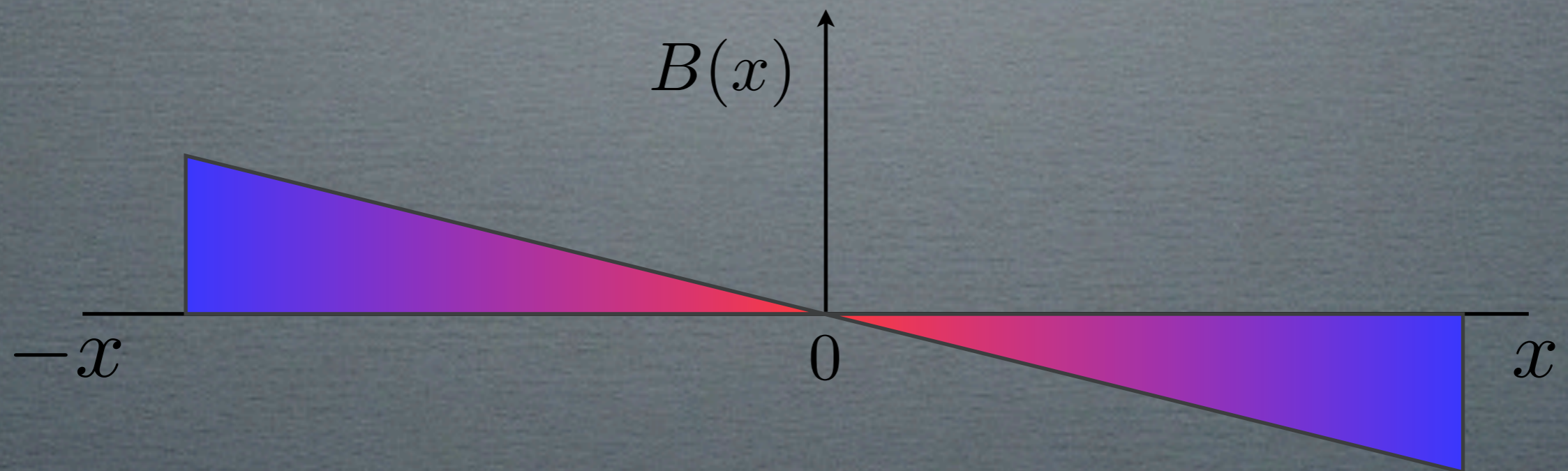
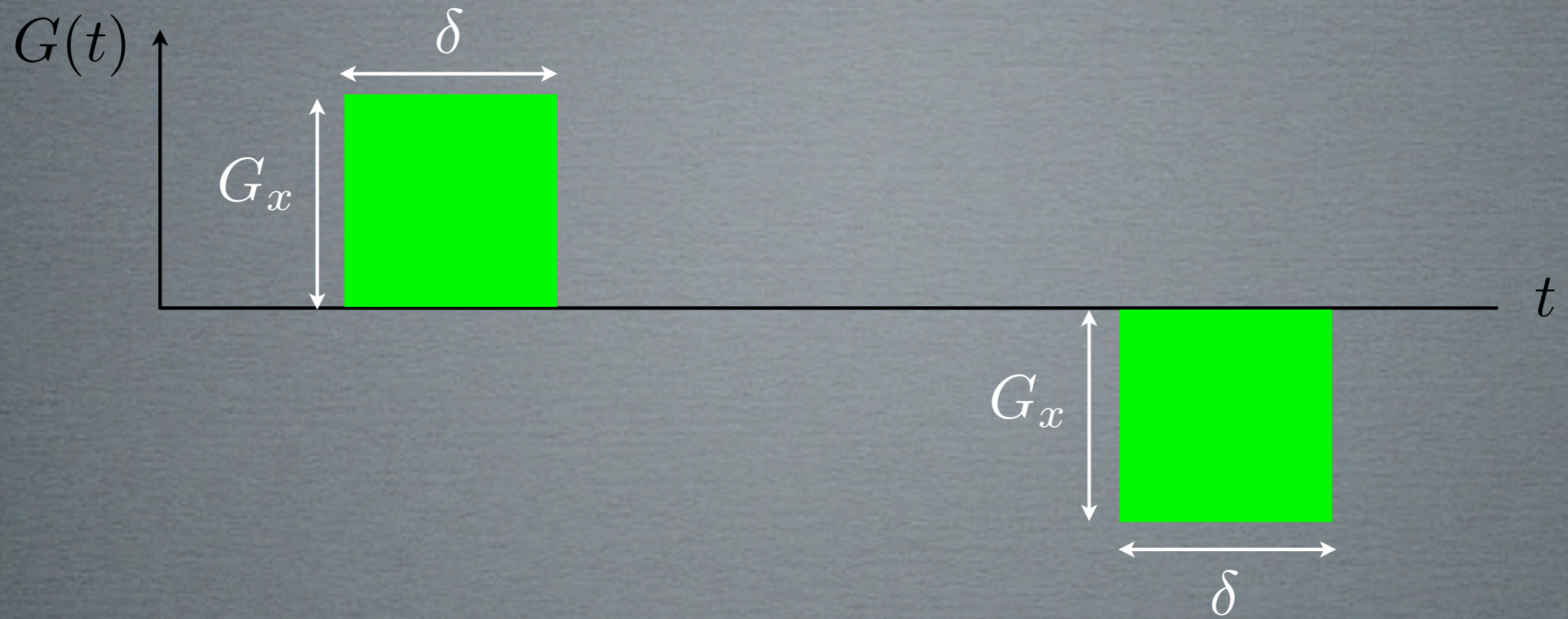
THE SENSITIVITY OF MRI TO DIFFUSION

WE'VE DESCRIBED THE SPATIAL AND
TEMPORAL CHARACTERISTICS OF THE
MOLECULES.

WHAT IS THE INFLUENCE OF THIS ON THE
MRI SIGNAL?

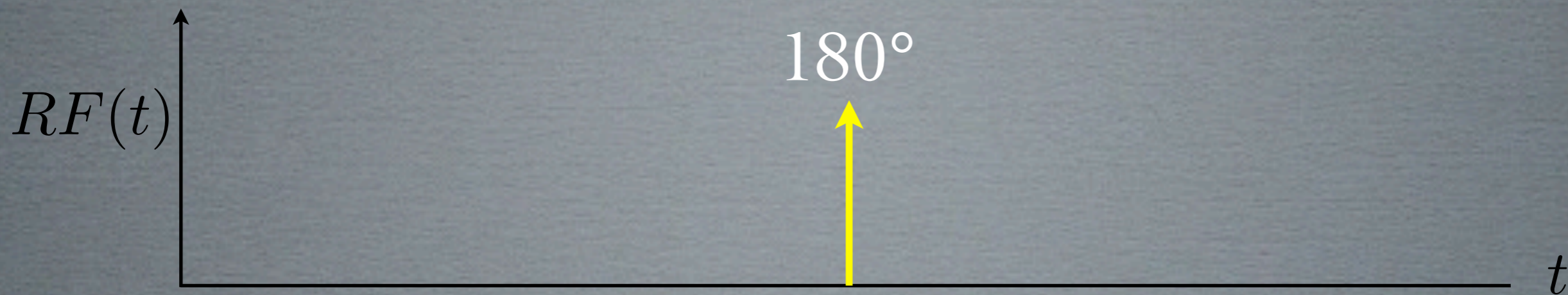
THE BIPOLAR GRADIENT PULSE (GRADIENT ECHO)

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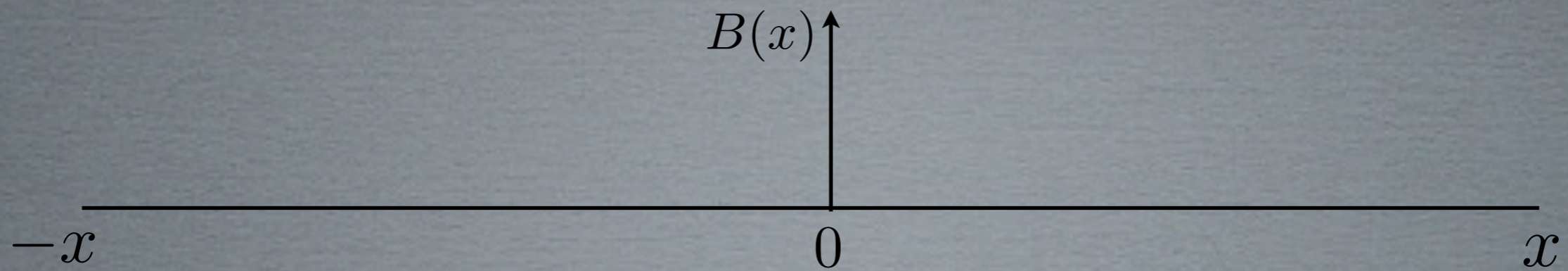


THE BIPOLAR GRADIENT PULSE (SPIN ECHO)

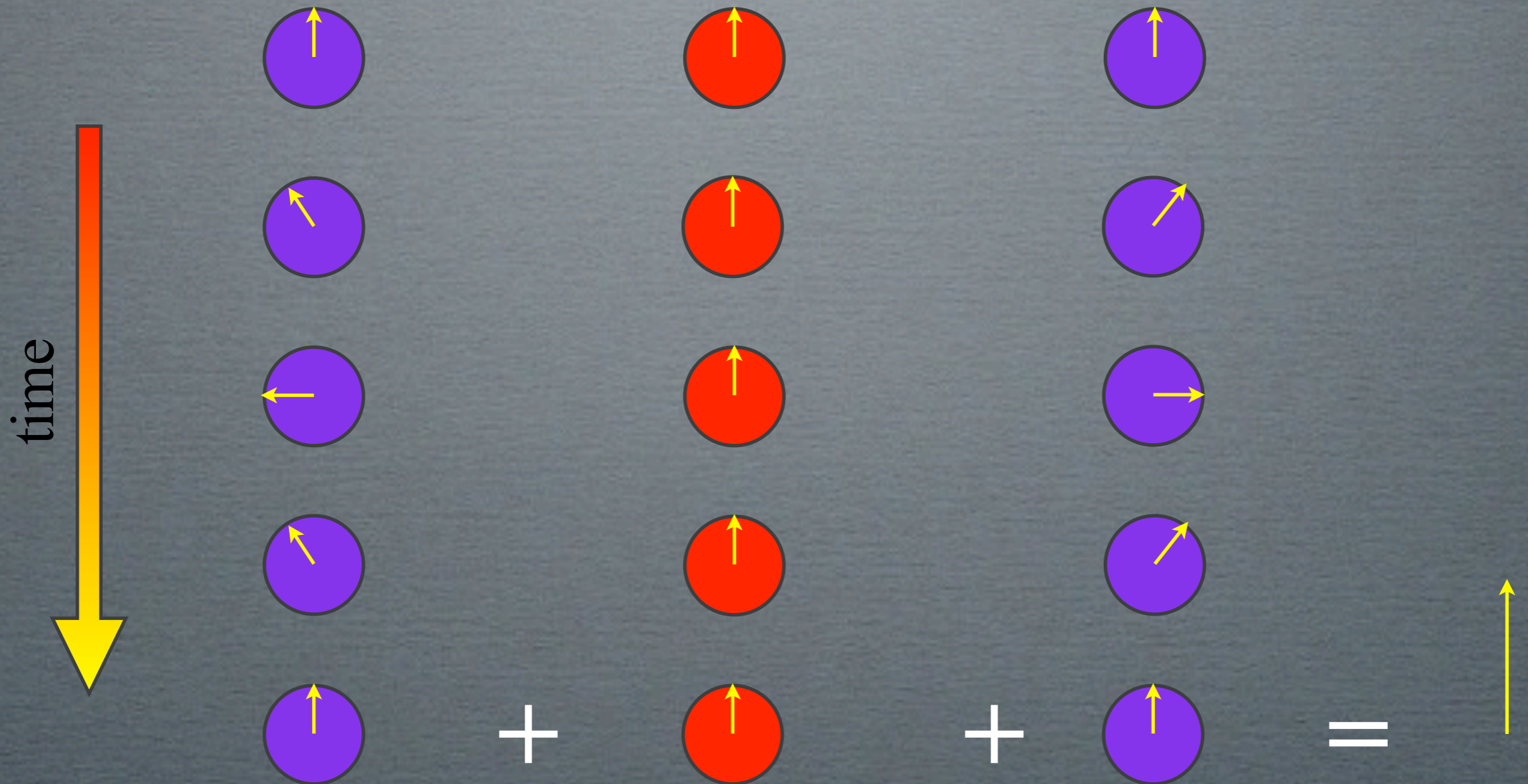
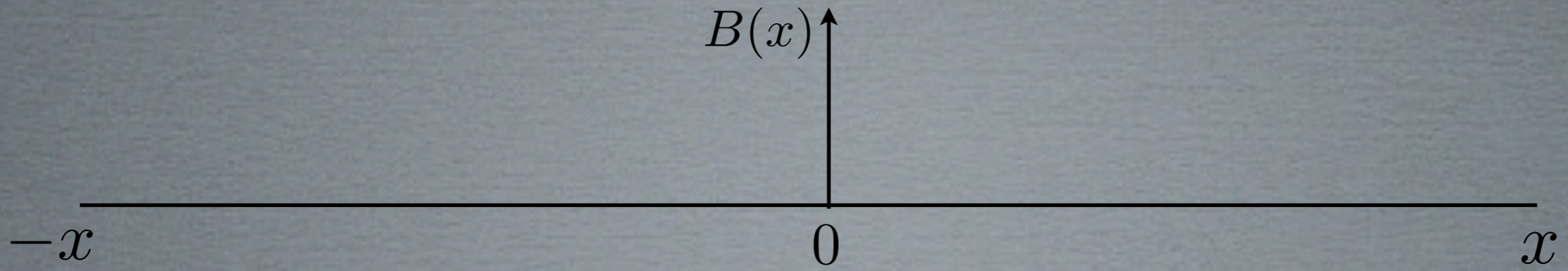
THE BIPOLAR GRADIENT PULSE (SPIN ECHO)



STATIONARY SPINS IN BIPOLAR PULSE



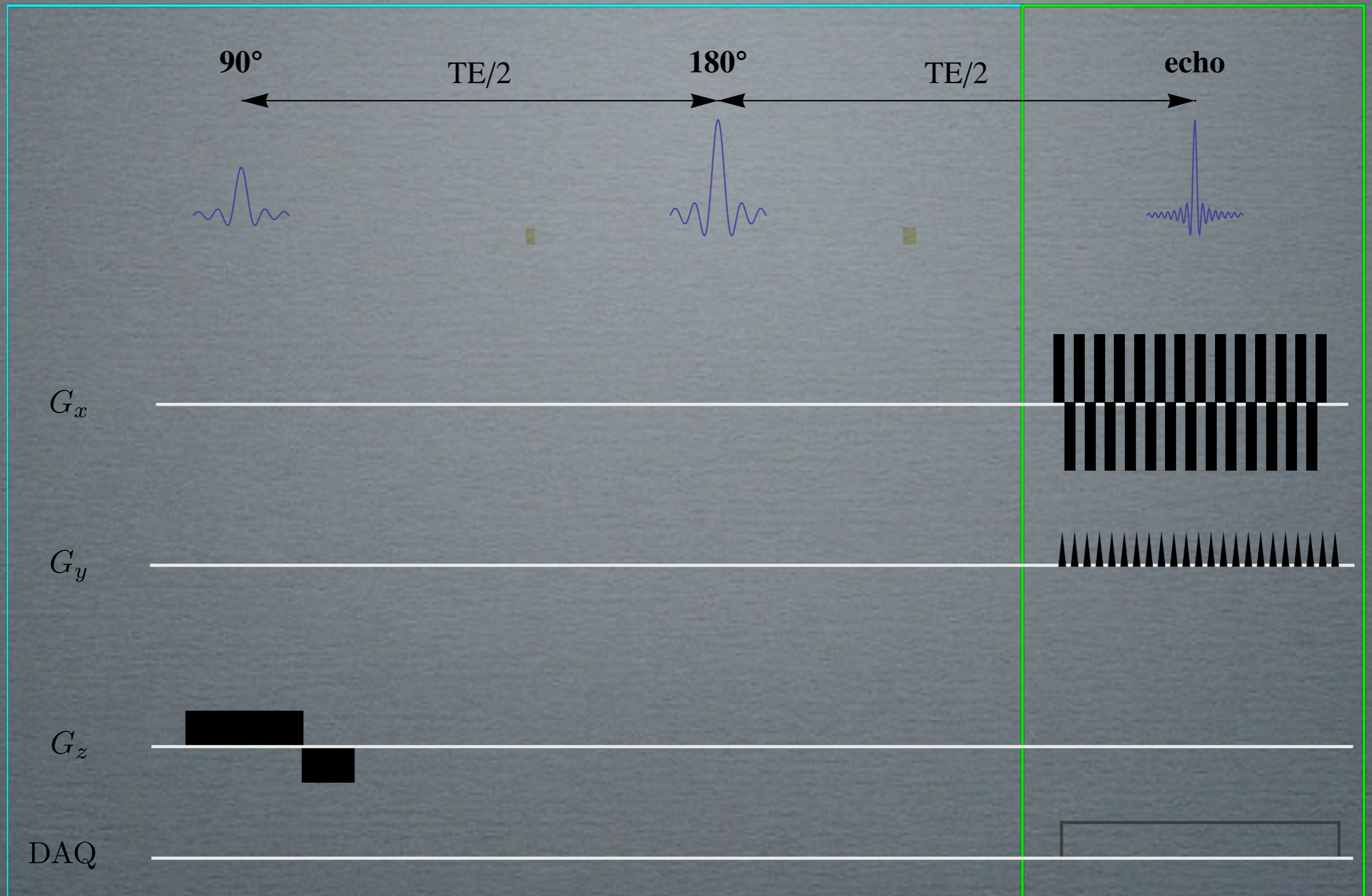
STATIONARY SPINS IN BIPOLAR PULSE



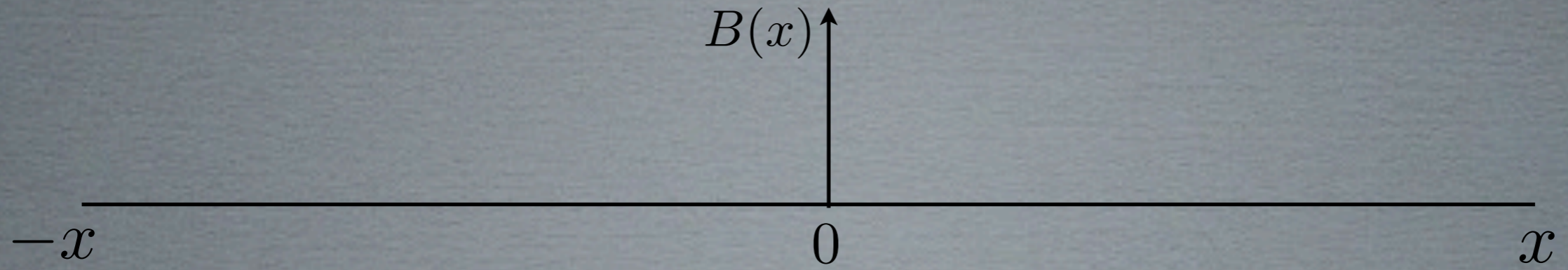
ECHO-PLANAR IMAGING

Preparation

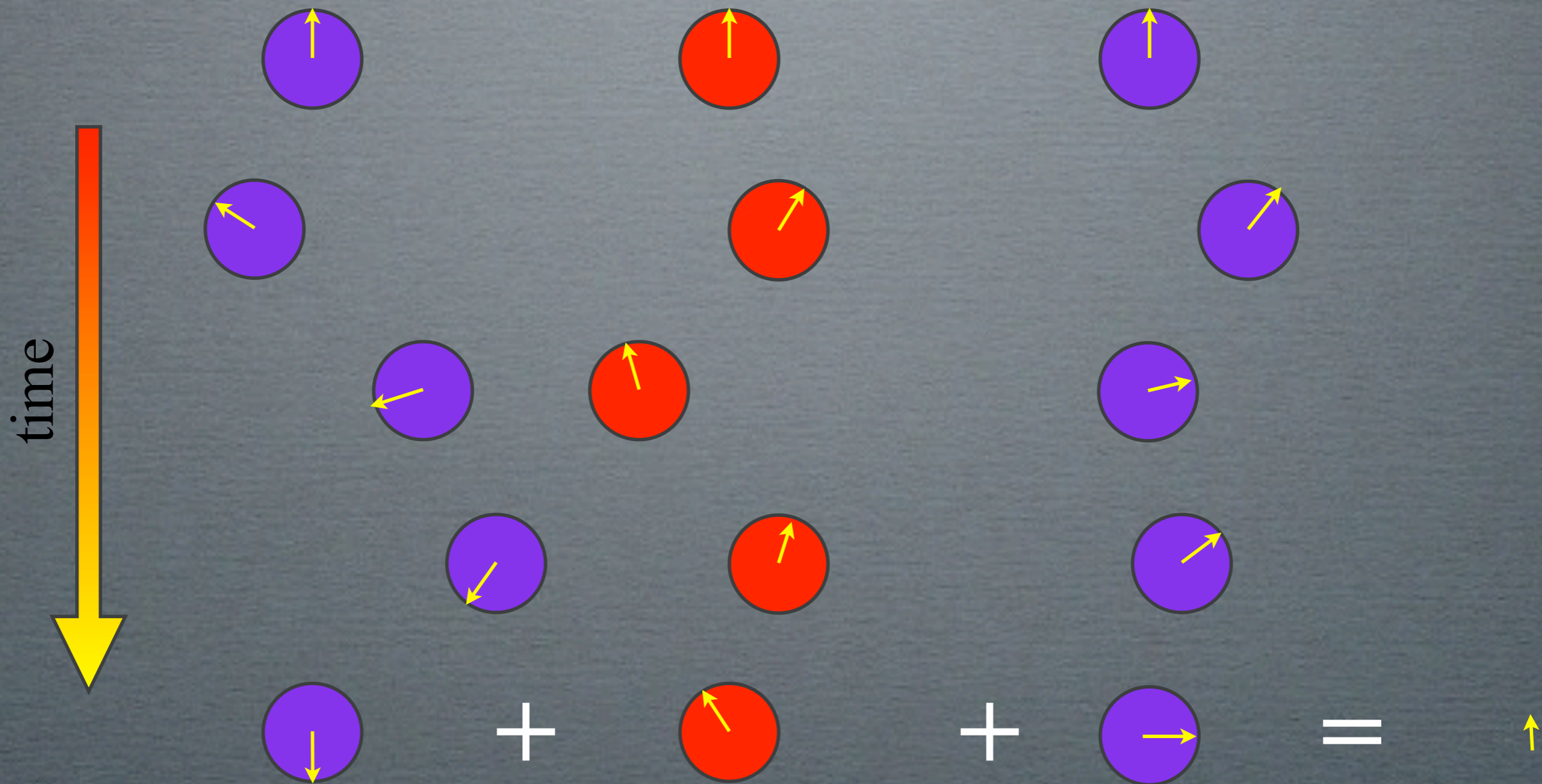
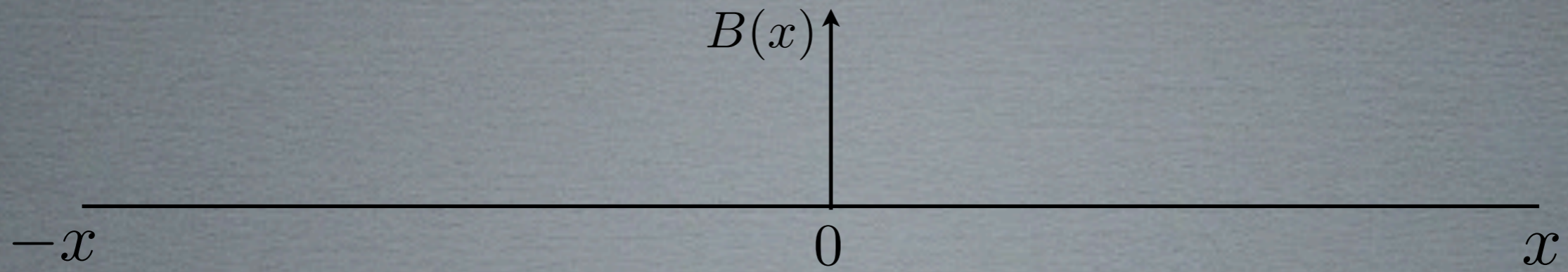
Acquisition



DIFFUSING SPINS IN BIPOLAR PULSE



DIFFUSING SPINS IN BIPOLAR PULSE



KEY FACT

KEY FACT

Only diffusion along the direction of the applied gradient has an effect

EARLY NMR MEASUREMENTS OF DIFFUSION

EARLY NMR MEASUREMENTS OF DIFFUSION

PHYSICAL REVIEW

VOLUME 80, NUMBER 4

NOVEMBER 15, 1950

Spin Echoes*†

E. L. HAHN‡

Physics Department, University of Illinois, Urbana, Illinois

(Received May 22, 1950)

Intense radiofrequency power in the form of pulses is applied to an ensemble of spins in a liquid placed in a large static magnetic field H_0 . The frequency of the pulsed r-f power satisfies the condition for nuclear magnetic resonance, and the pulses last for times which are short compared with the time in which the nutating macroscopic magnetic moment of the entire spin ensemble can decay. After removal of the pulses a non-equilibrium configuration of isochromatic macroscopic moments remains in which the moment vectors precess freely. Each moment vector has a magnitude at a given precession frequency which is determined by the distribution of Larmor frequencies imposed upon the ensemble by inhomogeneities in H_0 . At times determined by pulse sequences applied in the past the constructive interference of these moment vectors gives rise to observable spontaneous nuclear induction signals. The properties and underlying principles of these spin echo signals are discussed with use of the Bloch theory. Relaxation times are measured directly and accurately from the measurement of echo amplitudes. An analysis includes the effect on relaxation measurements of the self-diffusion of liquid molecules which contain resonant nuclei. Preliminary studies are made of several effects associated with spin echoes, including the observed shifts in magnetic resonance frequency of spins due to magnetic shielding of nuclei contained in molecules.

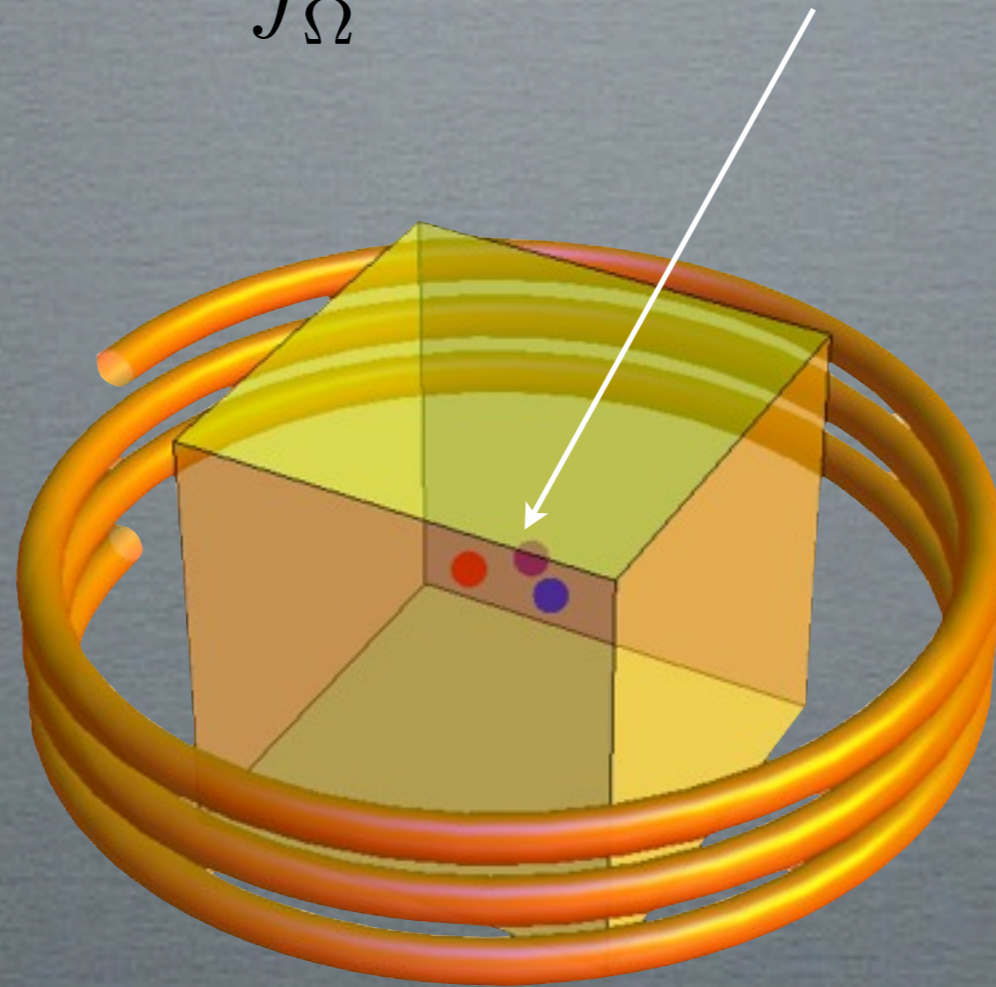
Since there is an established gradient of the magnetic field over the volume of the sample, a molecule whose nuclear moment has been flipped initially in a field H_0 , may, in the course of time 2τ , drift by Brownian motion into a randomly differing field H_0 . Therefore, as τ is increased, a lesser number of moments participate in the generation of in-phase nuclear radio-frequency signals.

THE MRI SIGNAL

THE MRI SIGNAL

signal = Sum over all spins

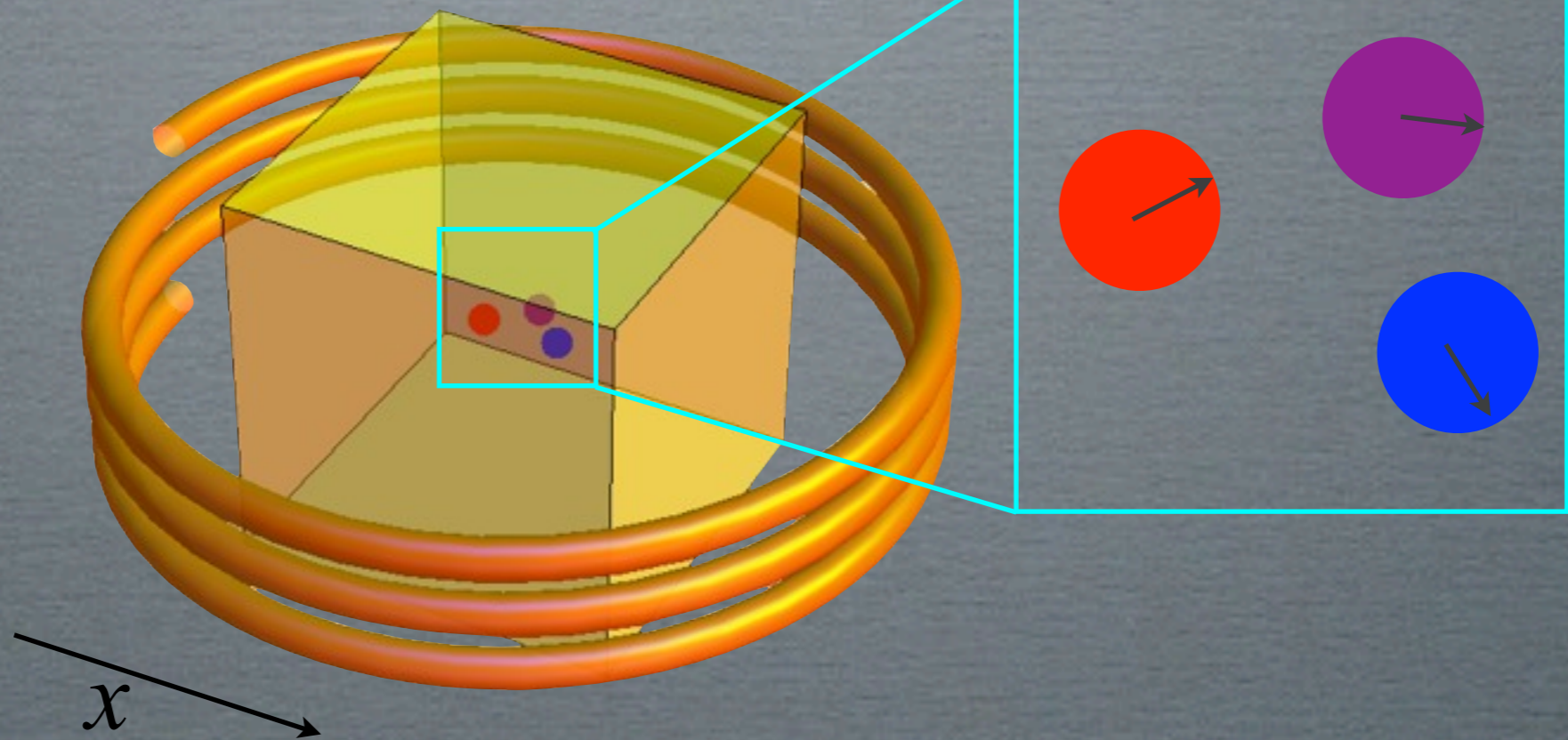
$$S(\varphi) = \int_{\Omega} dx \text{ spins}(\text{location}, \text{phase})$$



THE MRI SIGNAL

signal = Sum over all spins

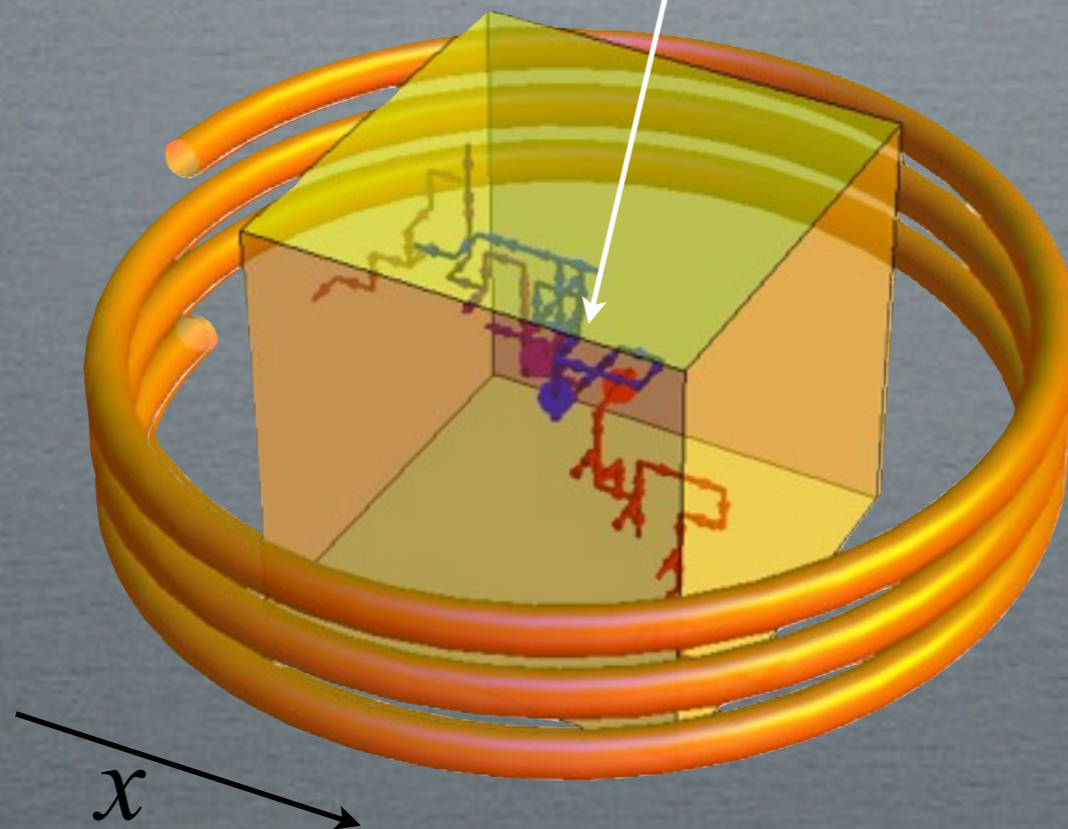
$$S(\varphi) = \int_{\Omega} dx \rho(x) e^{-i\varphi(x,t)}$$



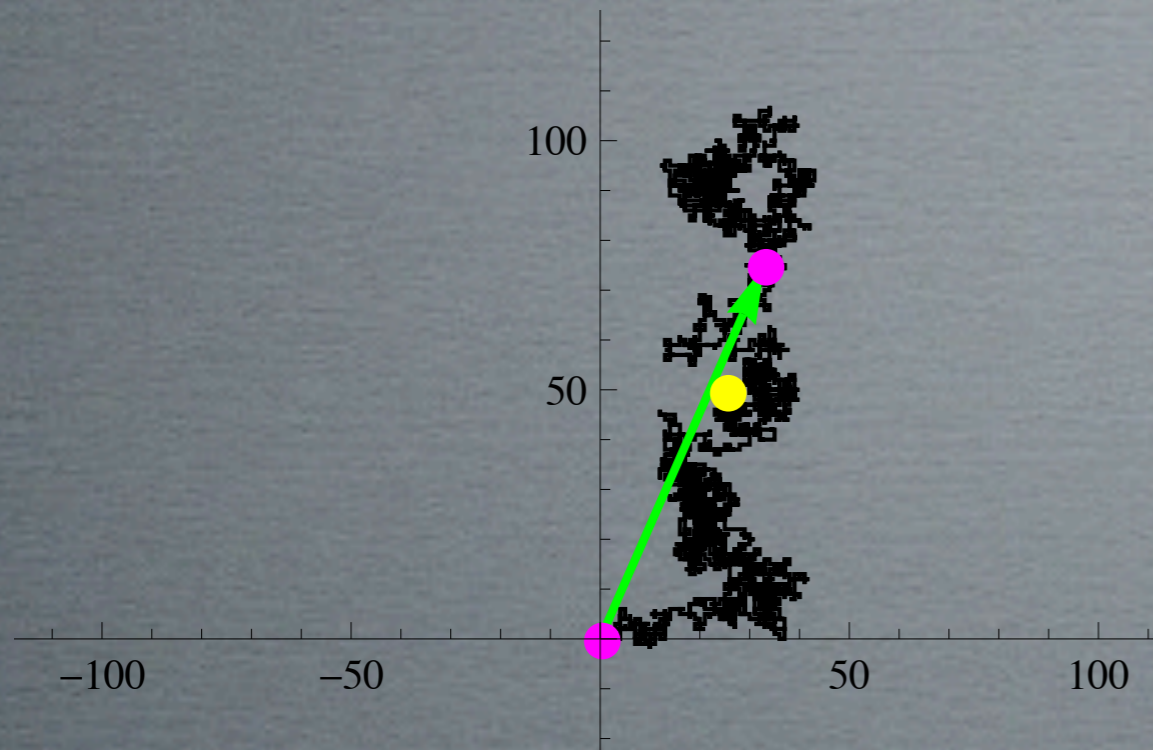
THE MRI SIGNAL

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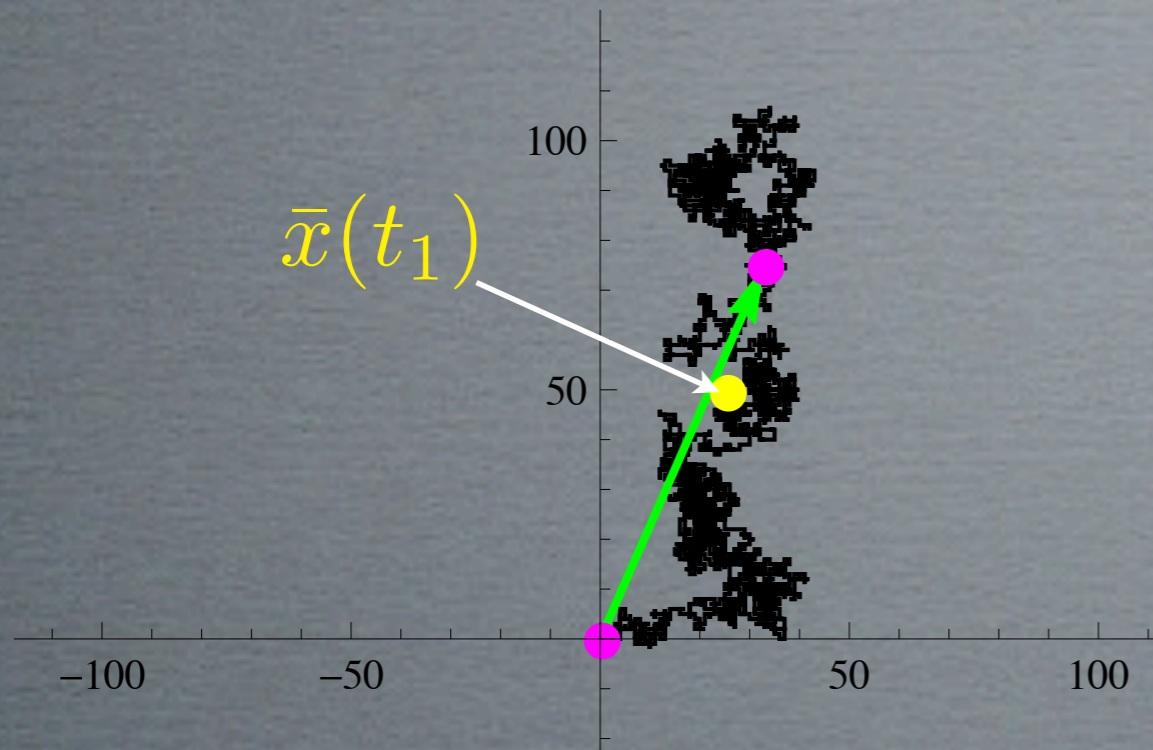
$$S(\varphi) = \int_{\Omega} dx P(x, t) e^{-i\varphi(x, t)}$$



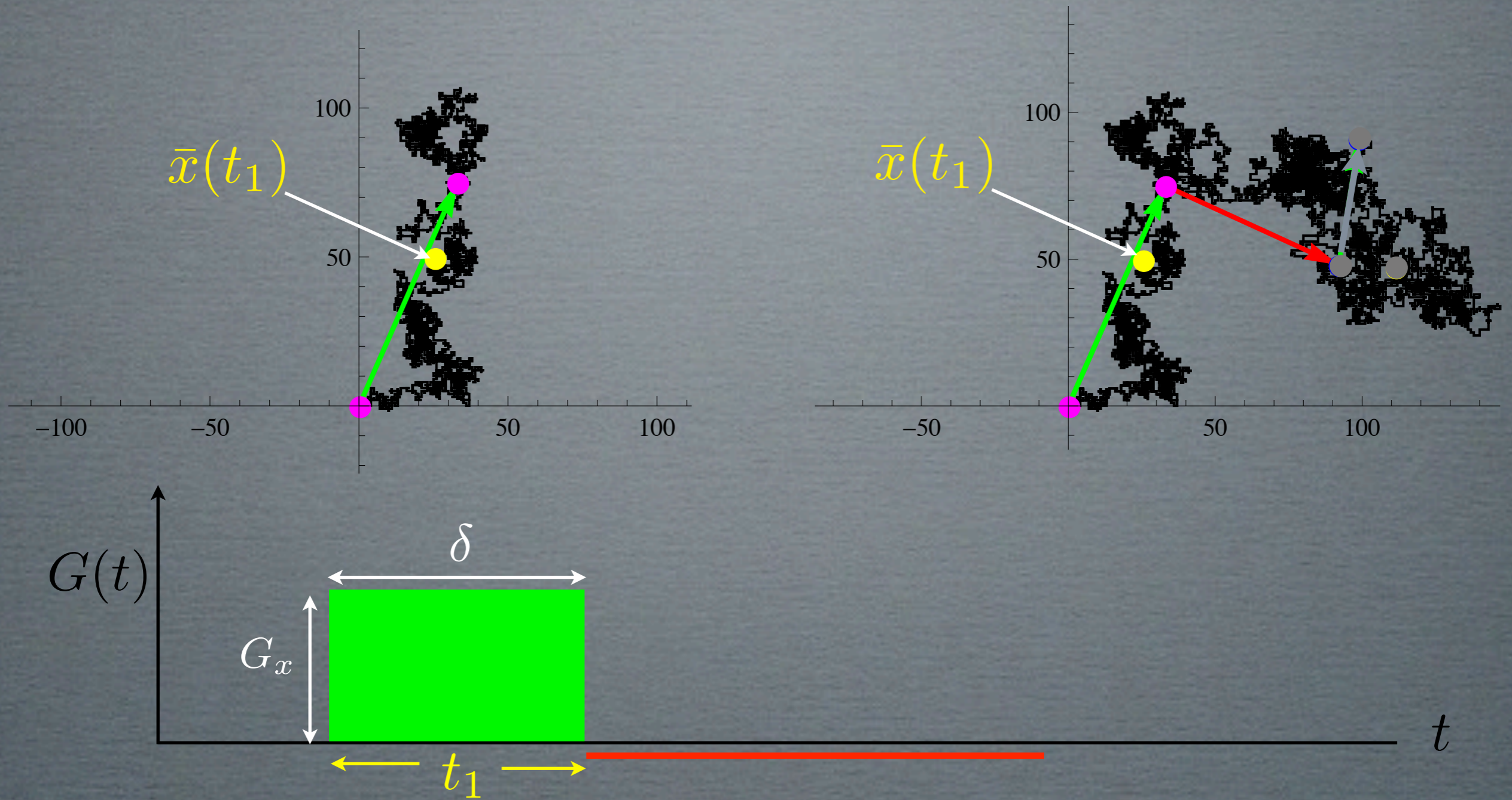
DIFFUSION PHASE IN A BIPOLAR PULSE



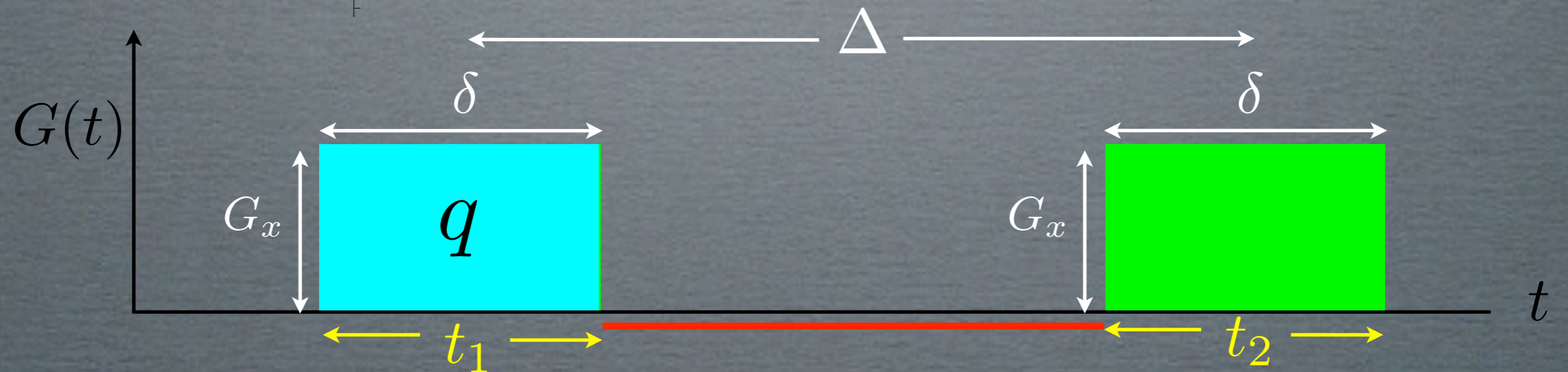
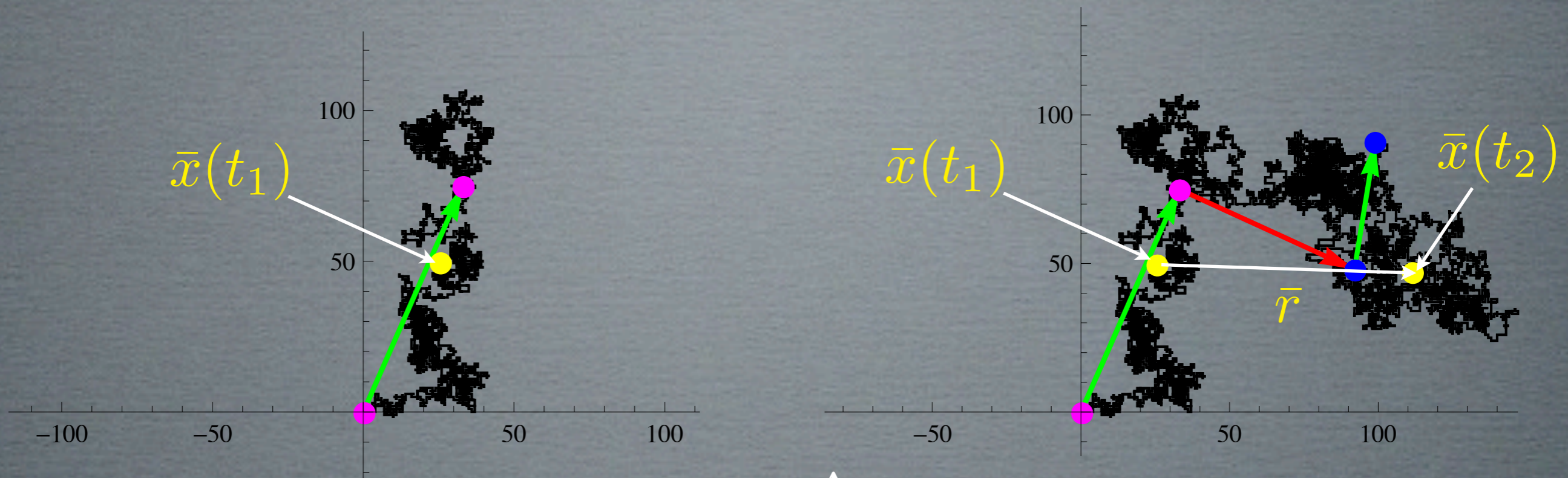
DIFFUSION PHASE IN A BIPOLAR PULSE



DIFFUSION PHASE IN A BIPOLAR PULSE



DIFFUSION PHASE IN A BIPOLAR PULSE



$$\varphi(x, t) = \underbrace{G\delta}_q \underbrace{[\bar{x}(t_2) - \bar{x}(t_1)]}_{\bar{r}} = q\bar{r}$$

THE DIFFUSION WEIGHTED SIGNAL

THE DIFFUSION WEIGHTED SIGNAL

Signal and Distribution are
Fourier Transform pairs

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



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

So, in principal, you can measure $P(r, \tau)$ by collecting data throughout q -space, just like imaging.

In practice, *very* time consuming

THE ESTIMATION PROBLEM FOR GAUSSIAN DIFFUSION

THE ESTIMATION PROBLEM FOR GAUSSIAN DIFFUSION

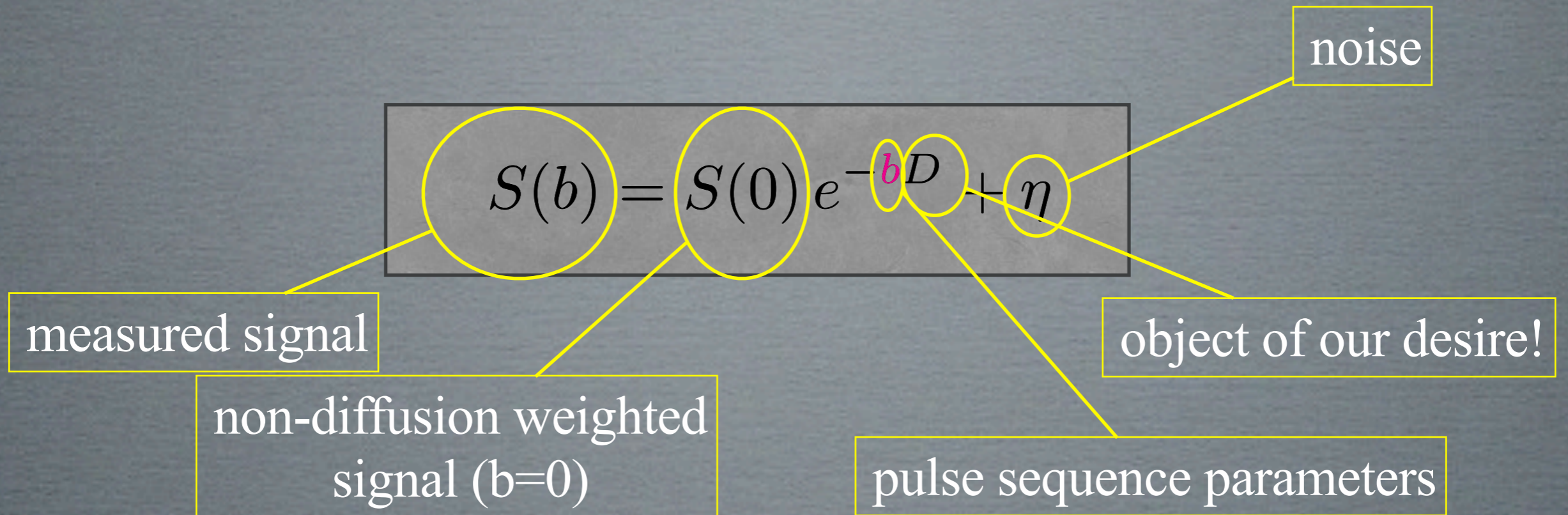
$$S(\varphi) = \int_{\Omega} dx P(x, t) e^{-i\varphi(x, t)}$$

THE ESTIMATION PROBLEM FOR GAUSSIAN DIFFUSION

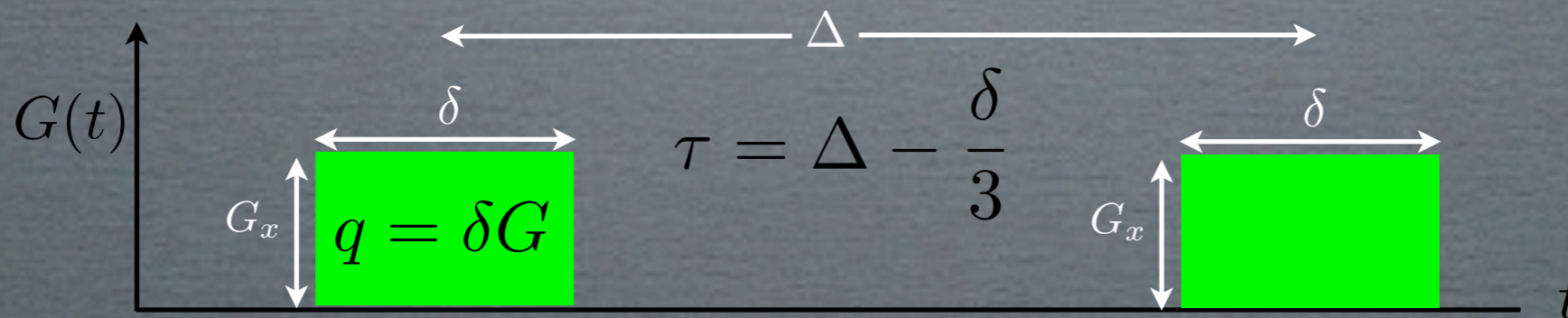
$$S(\varphi) = \int_{\Omega} d\bar{r} P(\bar{r}, t) e^{-i q \bar{r}}$$

Gaussian

THE ESTIMATION PROBLEM FOR GAUSSIAN DIFFUSION

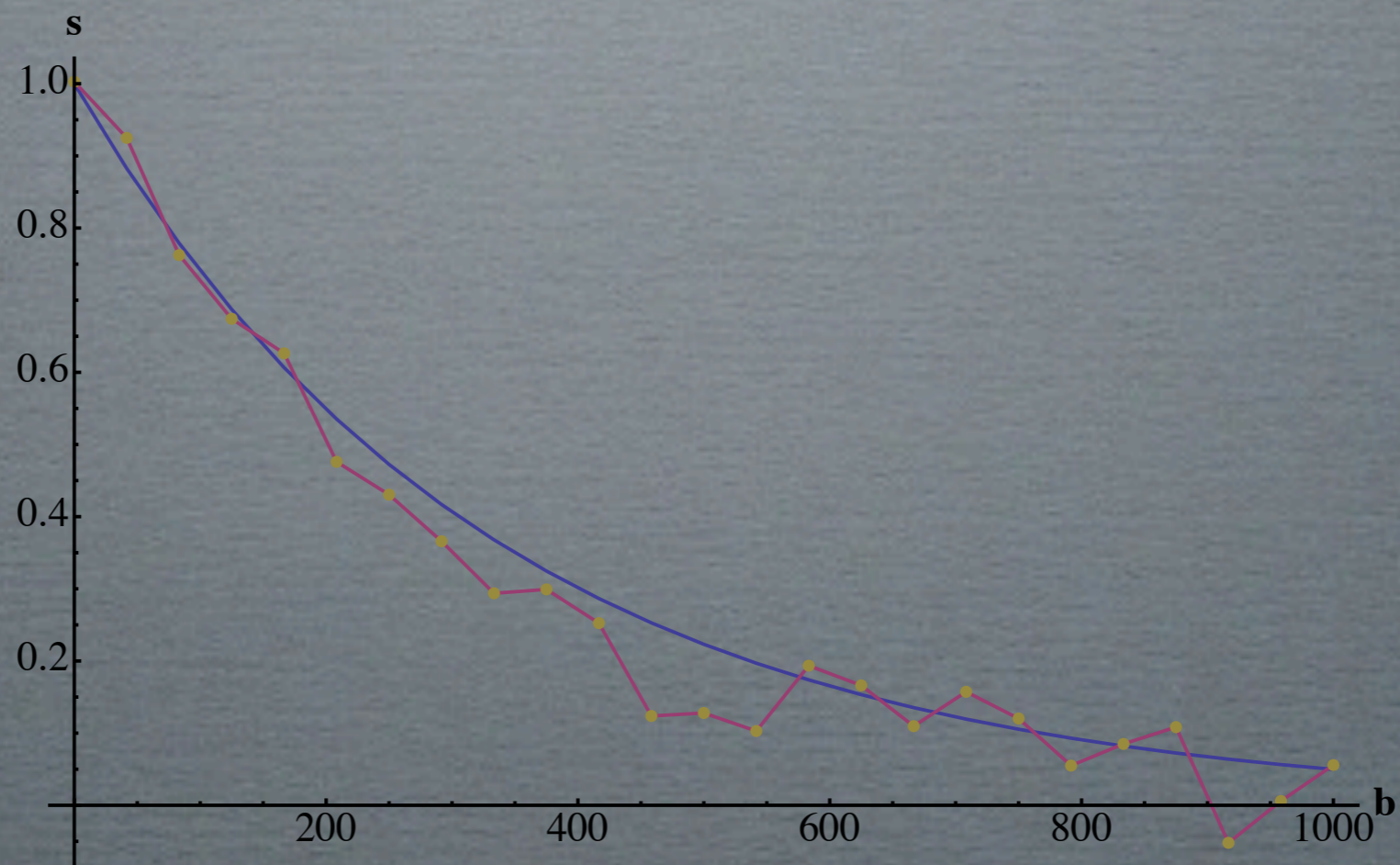


$$b = q^2 \tau$$



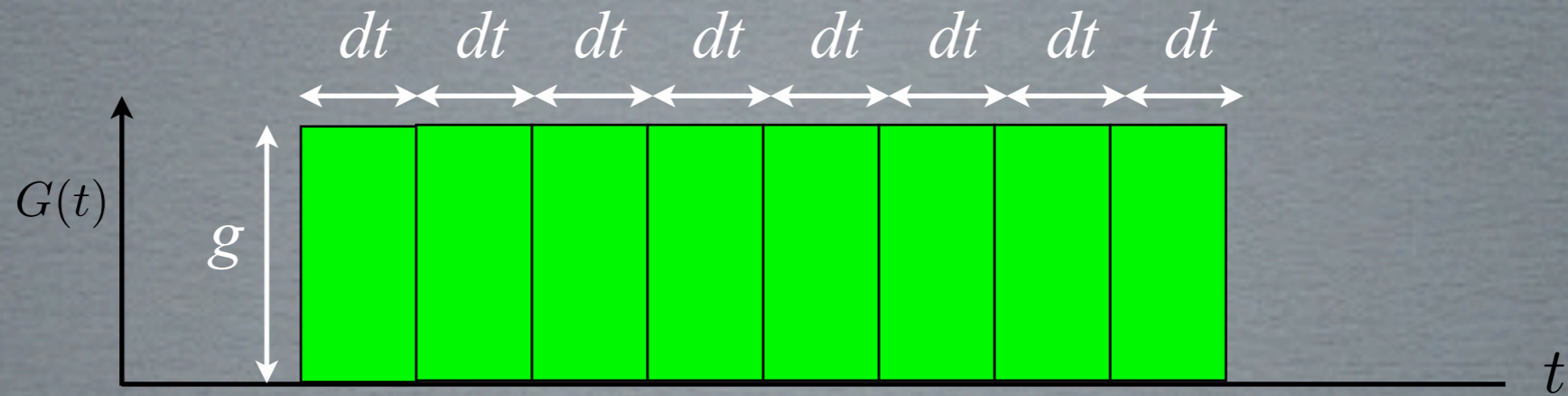
The signal from Gaussian Diffusion

$$s(b) = s(0)e^{-bD} + \eta(b)$$



THE B-VALUE

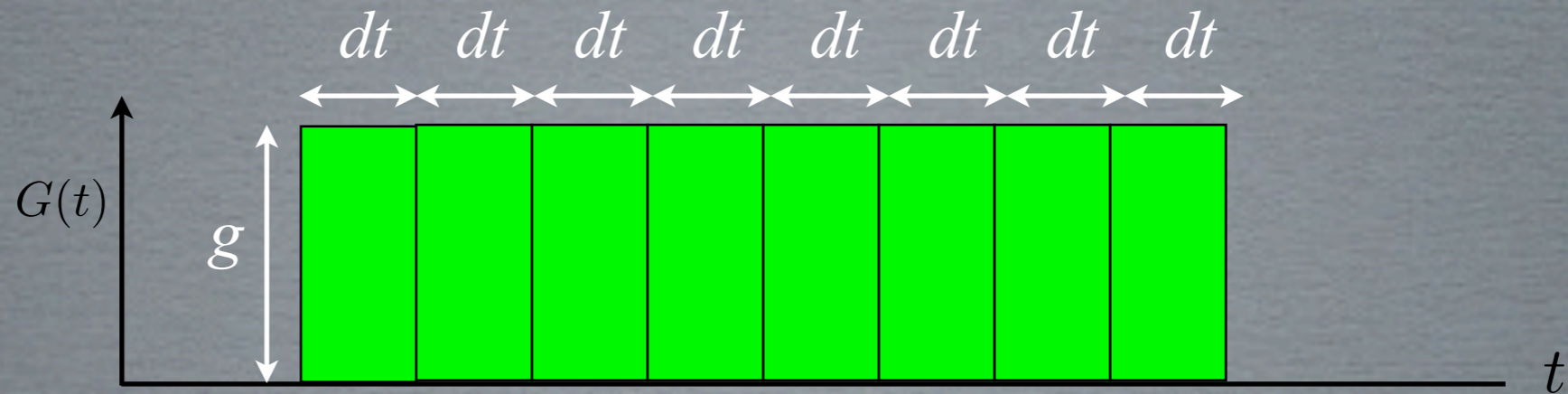
THE B-VALUE



attenuation for each
little time interval:

A_1 A_2 • • • A_n

THE B-VALUE



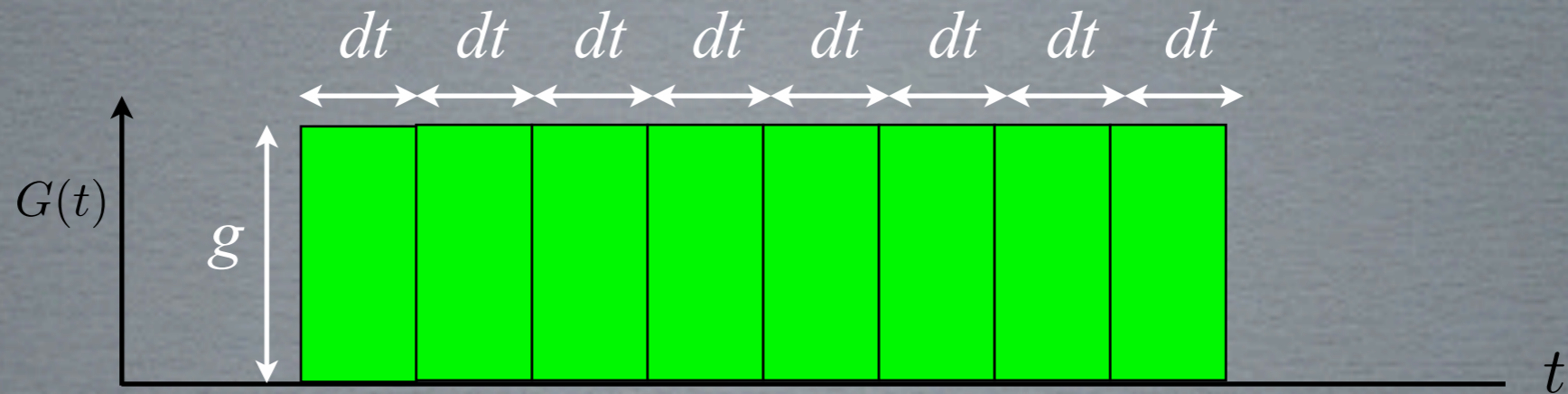
attenuation for each
little time interval:

$$A_1 \quad A_2 \quad \cdot \quad \cdot \quad \cdot \quad A_n$$

total attenuation

$$A_\tau = \prod_{i=1}^n A_i \quad \text{where} \quad A_i = e^{-k^2 D dt}$$

THE B-VALUE



attenuation for each little time interval:

$$A_1 \quad A_2 \quad \bullet \quad \bullet \quad \bullet \quad A_n$$

total attenuation

$$A_\tau = \prod_{i=1}^n A_i \quad \text{where} \quad A_i = e^{-k^2 D dt}$$

$$A_\tau = \prod_{i=1}^n e^{-k^2 D dt} = e^{-D \sum_{i=1}^n k^2 dt} = e^{-D \int k^2 dt}$$

$dt \rightarrow \epsilon$

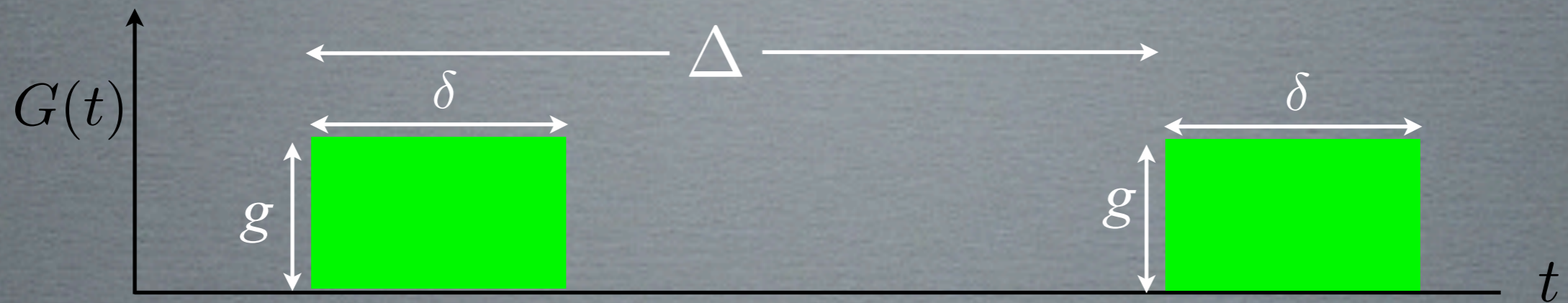
$$A_\tau = e^{-D \int k^2 dt}$$

b

THE B-VALUE

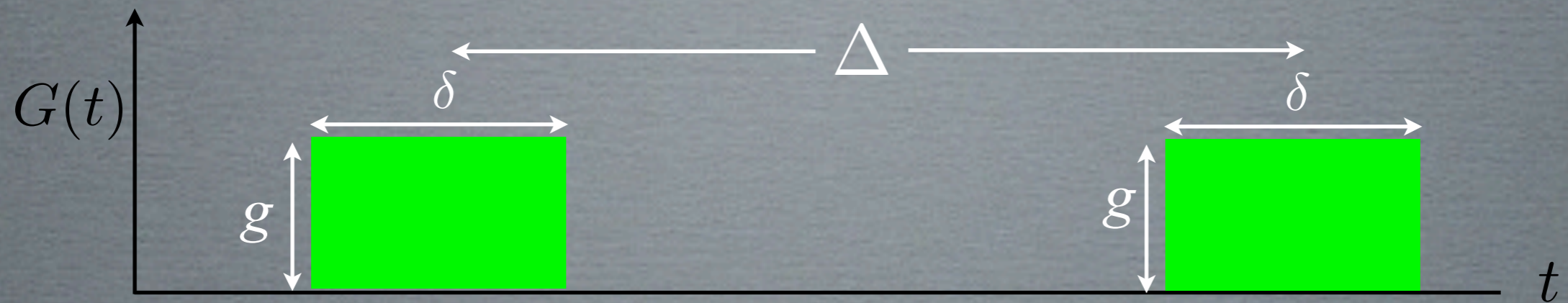
THE B-VALUE

$$b = g^2 \delta^2 \left(\Delta - \frac{1}{3} \delta \right)$$



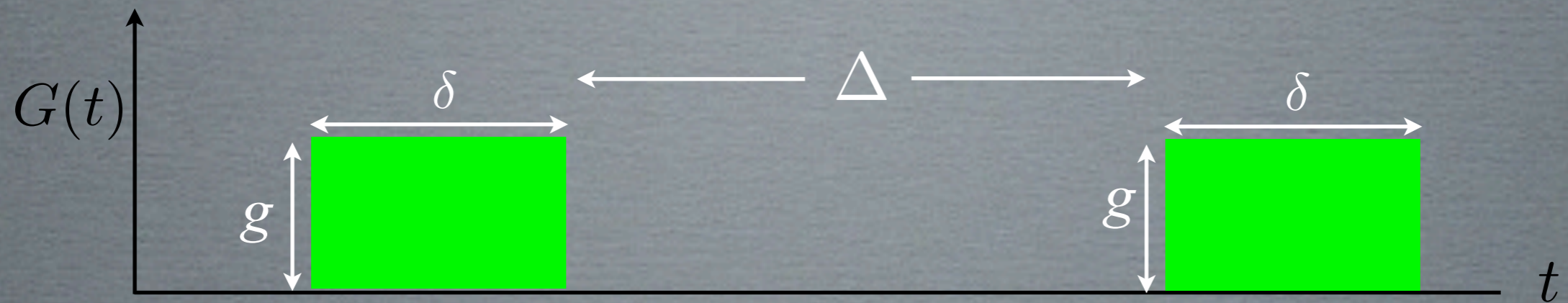
THE B-VALUE

$$b = g^2 \delta^2 \left(\Delta - \frac{1}{3} \delta \right)$$



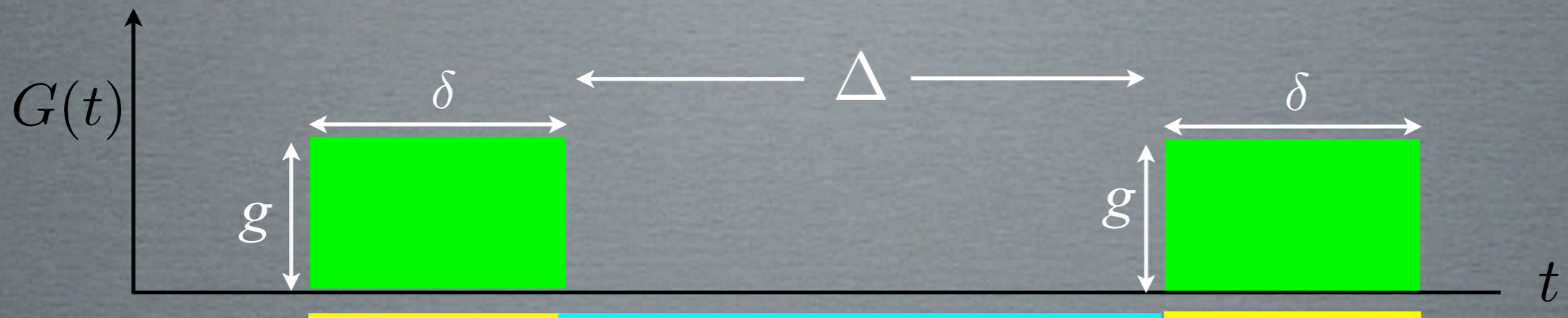
THE B-VALUE

$$b = g^2 \delta^2 \left(\Delta + \frac{2}{3} \delta \right)$$



THE B-VALUE

$$b = g^2 \delta^2 \left(\Delta + \frac{2}{3} \delta \right)$$



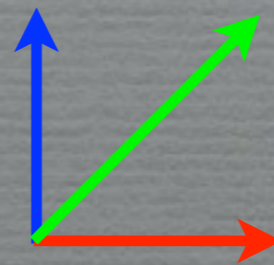
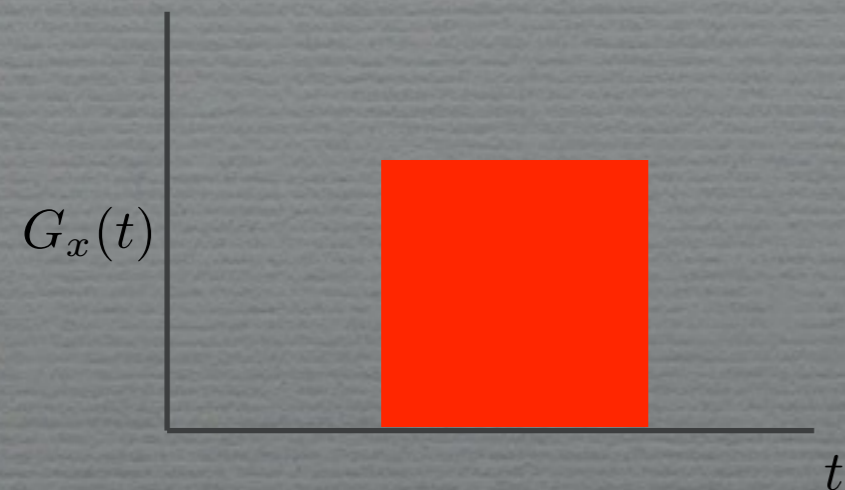
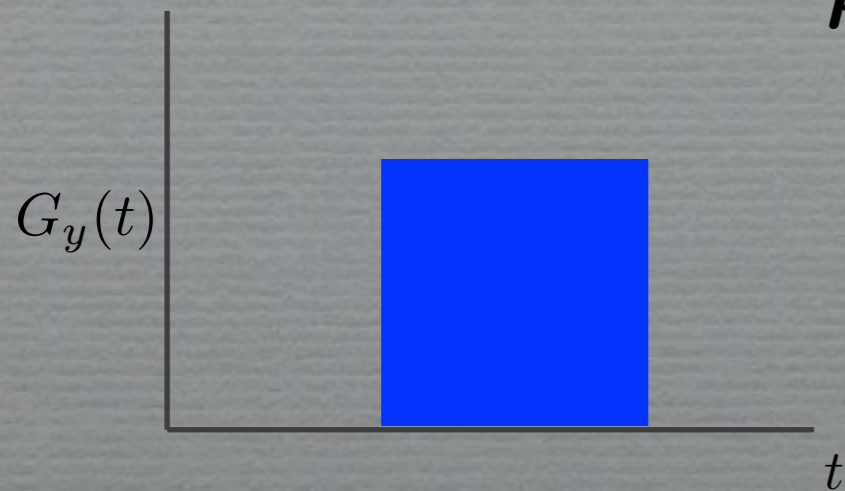
$$\int k^2 dt = g^2 \int_0^{\delta} t^2 dt + g^2 \delta^2 \int_0^{\Delta} dt + g^2 \int_0^{\delta} t^2 dt$$

$$b = g^2 \frac{\delta^3}{3} + g^2 \delta^2 \Delta + g^2 \frac{\delta^3}{3}$$

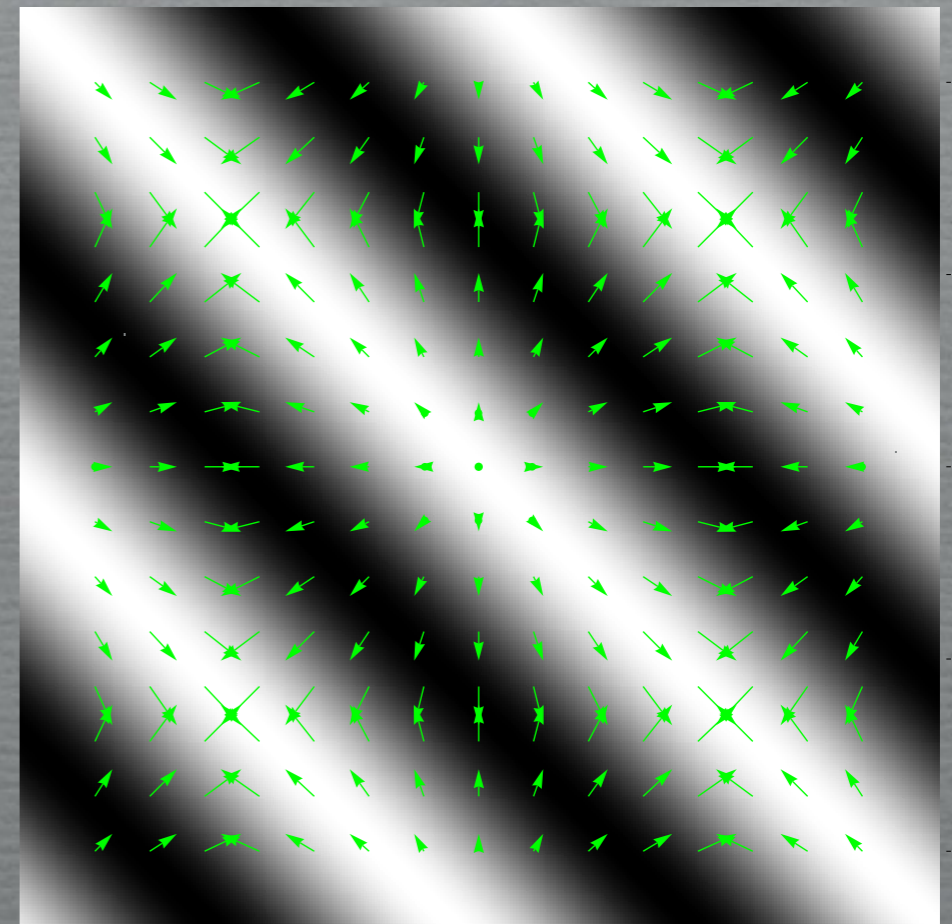
What gradients are doing to k-space

What gradients are doing to k-space

$$\mathbf{k} \cdot \mathbf{x} = k_x x + k_y y = \gamma G_x t x + \gamma G_y t y$$



y

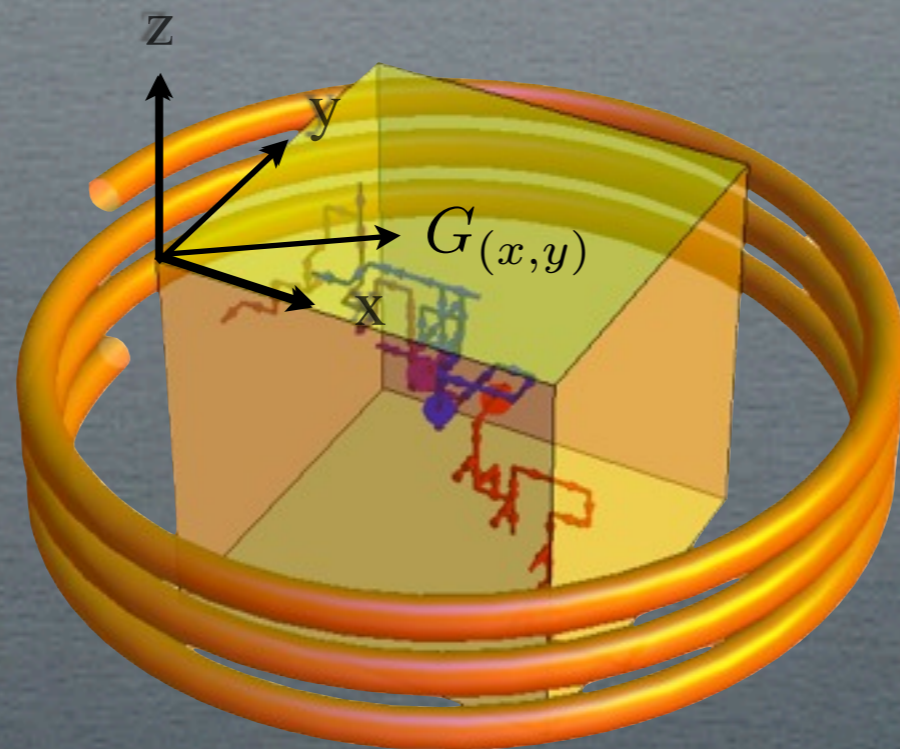
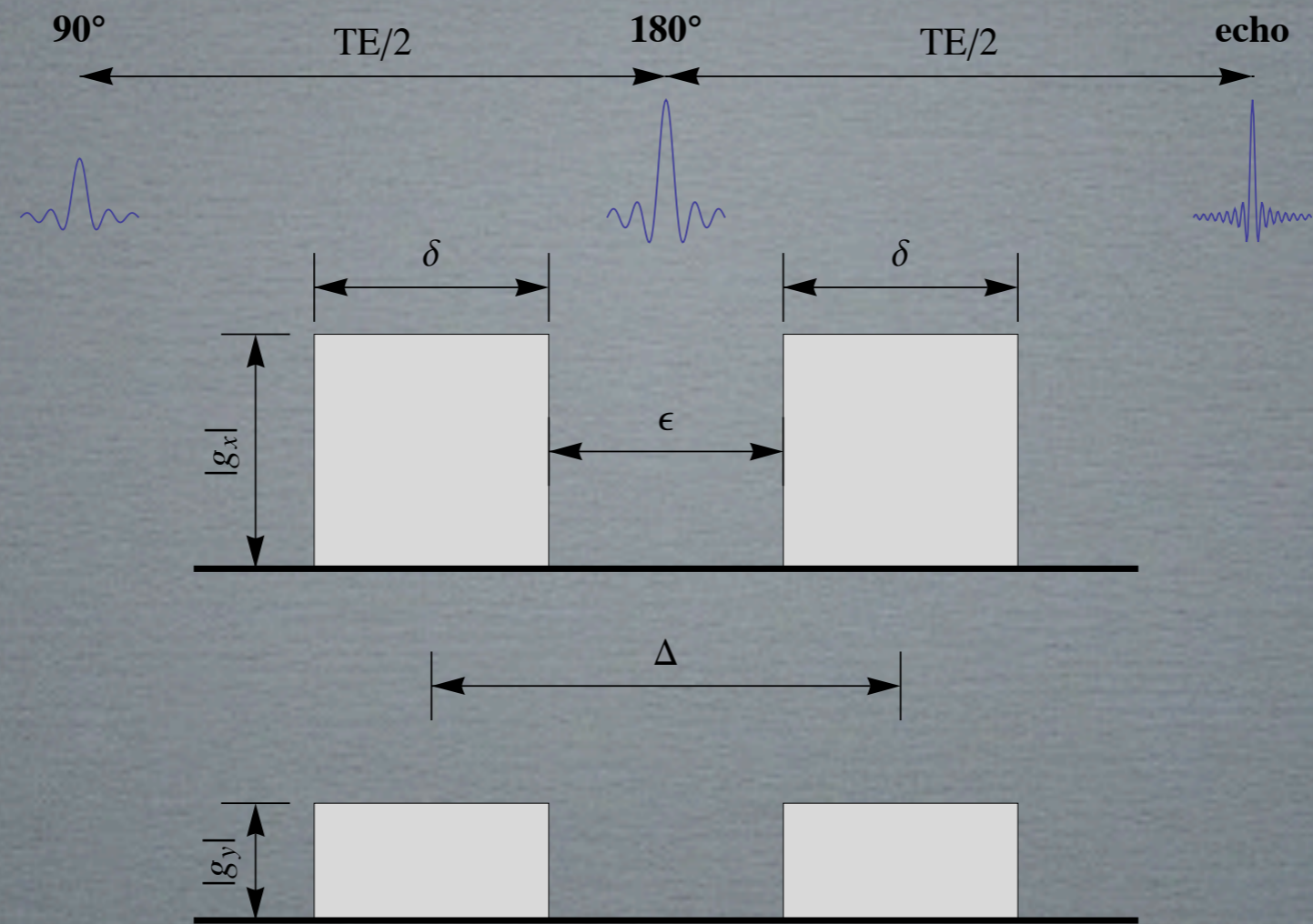


spatial modulation of the phase \mathbf{x}

gradients alter the k-space representation of the object

DIRECTIONAL DIFFUSION ENCODING

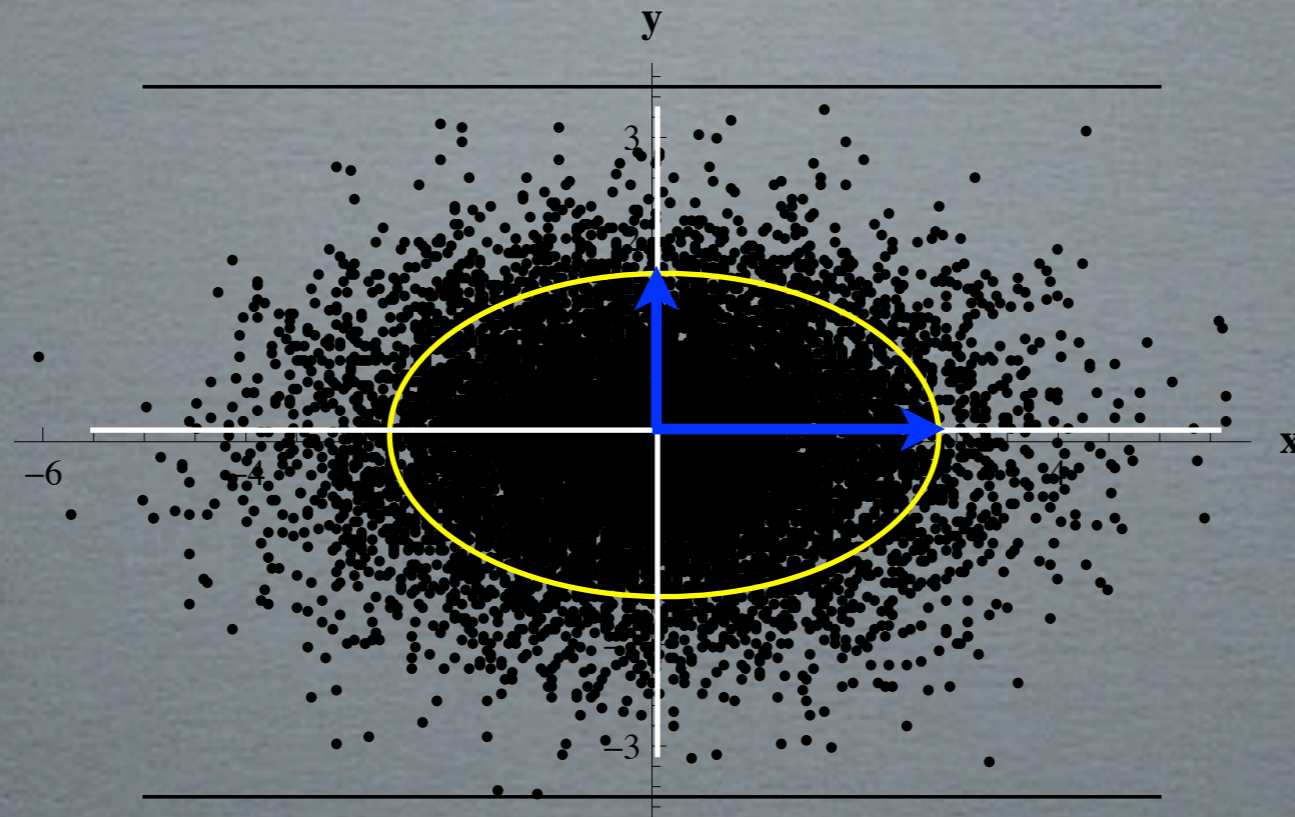
DIRECTIONAL DIFFUSION ENCODING



ANISOTROPIC DIFFUSION IN 2D

ANISOTROPIC DIFFUSION IN 2D

$$P(\mathbf{r}|\mathbf{r}_0, \tau) \sim N(\mathbf{r}_0, \Sigma)$$

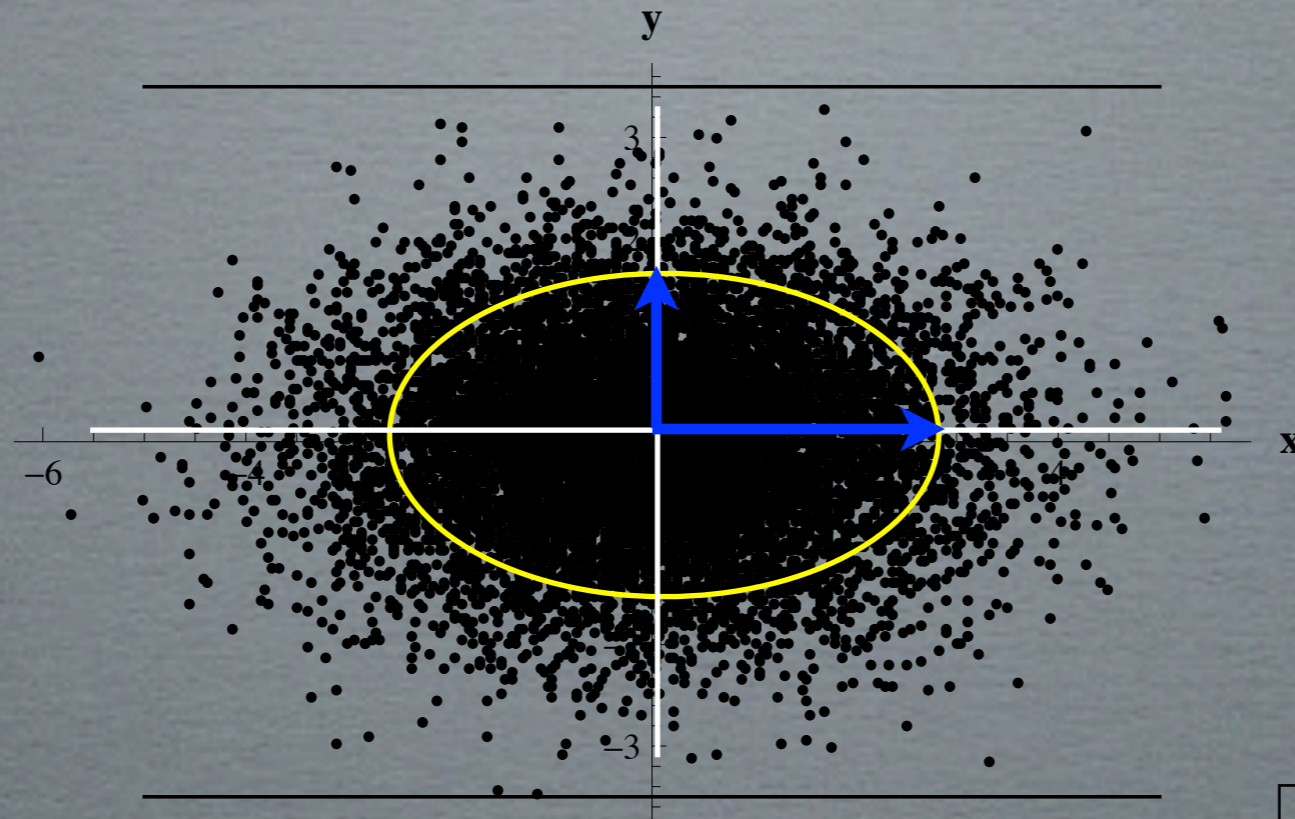


Covariance matrix

$$\Sigma = \begin{pmatrix} \sigma_x^2 & 0 \\ 0 & \sigma_y^2 \end{pmatrix}$$

ANISOTROPIC DIFFUSION IN 2D

$$P(\mathbf{r}|\mathbf{r}_0, \tau) \sim N(\mathbf{r}_0, \Sigma)$$



Covariance matrix

Diffusion Tensor

$$\Sigma = \begin{pmatrix} \sigma_x^2 & 0 \\ 0 & \sigma_y^2 \end{pmatrix} = 2\tau \begin{pmatrix} D_x & 0 \\ 0 & D_y \end{pmatrix}$$

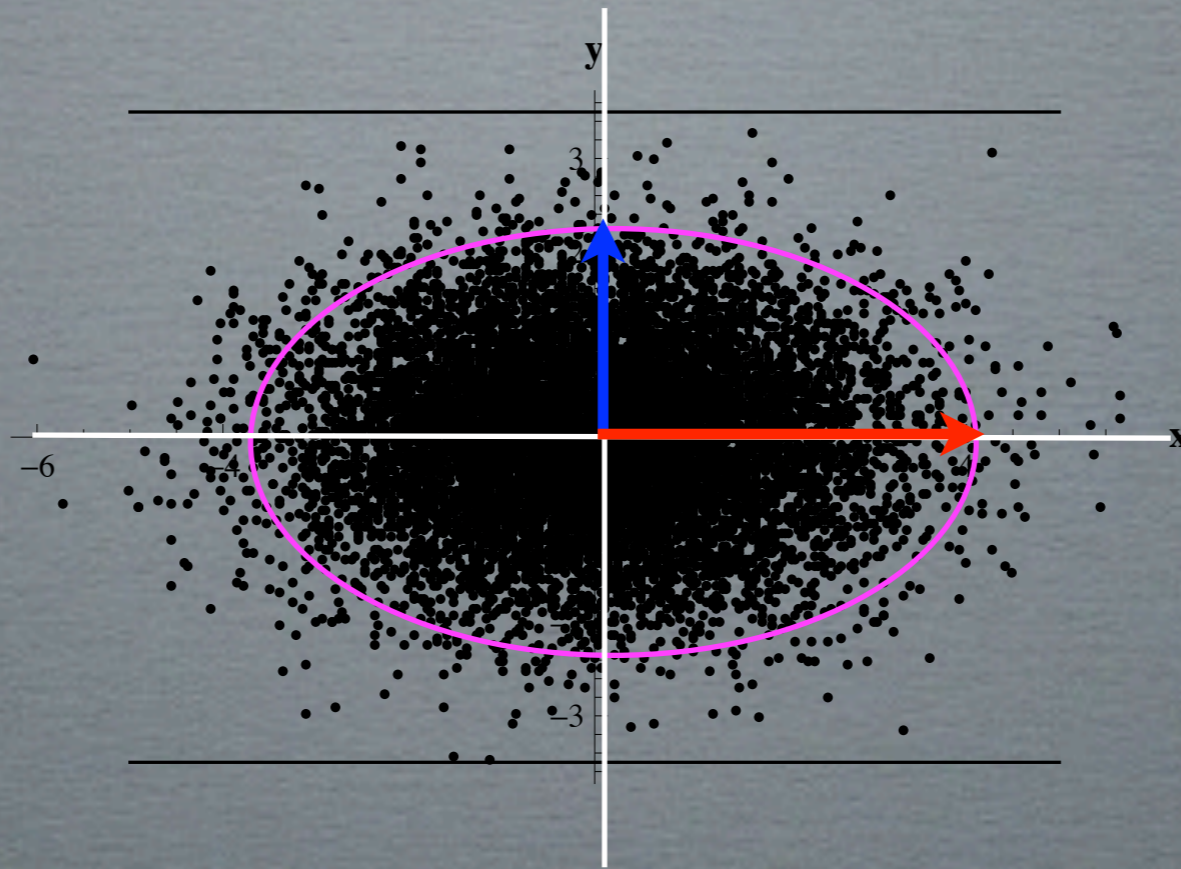
$\{D_x, D_y\}$ are the *principal diffusivities*

MEASURING THE DIFFUSION TENSOR

MEASURING THE DIFFUSION TENSOR

$$S(b, \hat{r}) = S(0)e^{-b\tilde{D}} + \eta$$

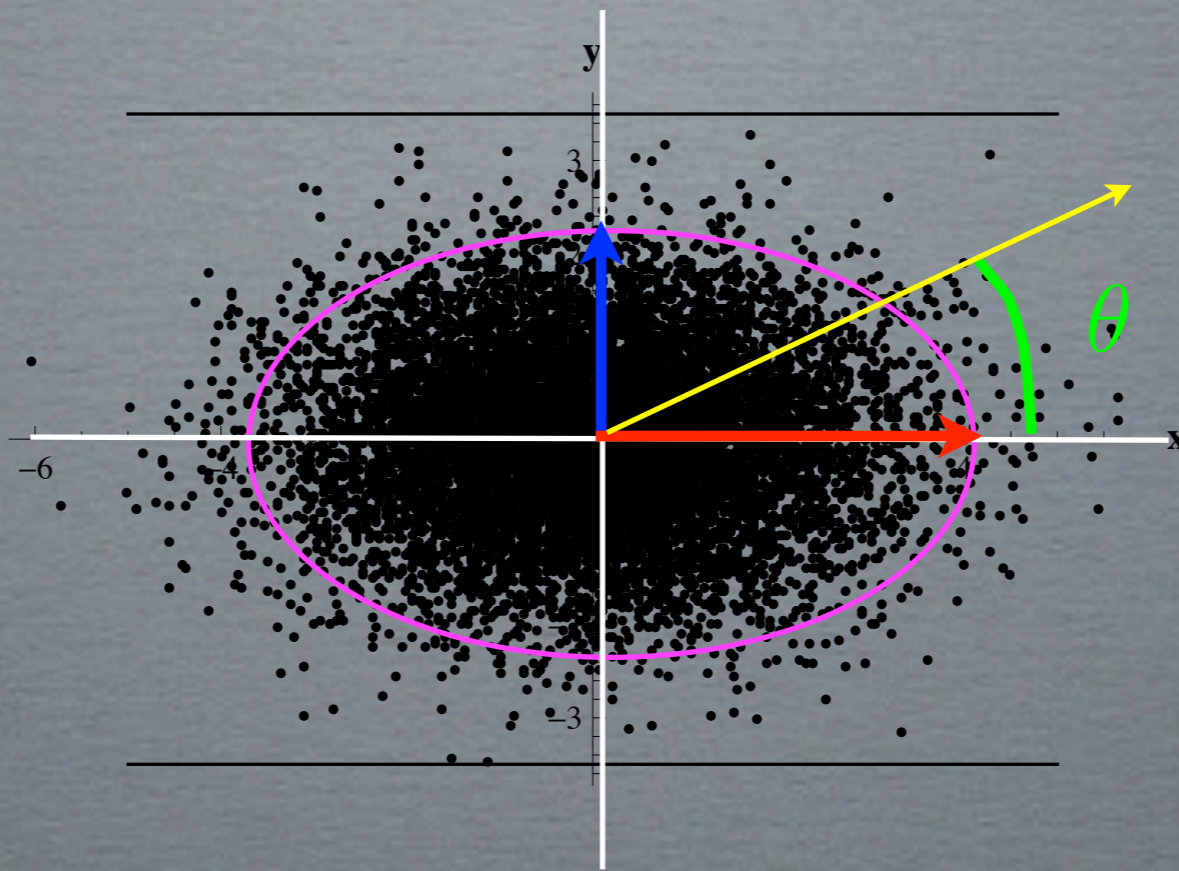
$$D = \begin{pmatrix} D_x & 0 \\ 0 & D_y \end{pmatrix}$$



MEASURING THE DIFFUSION TENSOR

$$S(b, \hat{r}) = S(0)e^{-b\tilde{D}} + \eta$$

$$D = \begin{pmatrix} D_x & 0 \\ 0 & D_y \end{pmatrix}$$



$$\hat{r} = \begin{pmatrix} \cos \theta \\ \sin \theta \end{pmatrix}$$

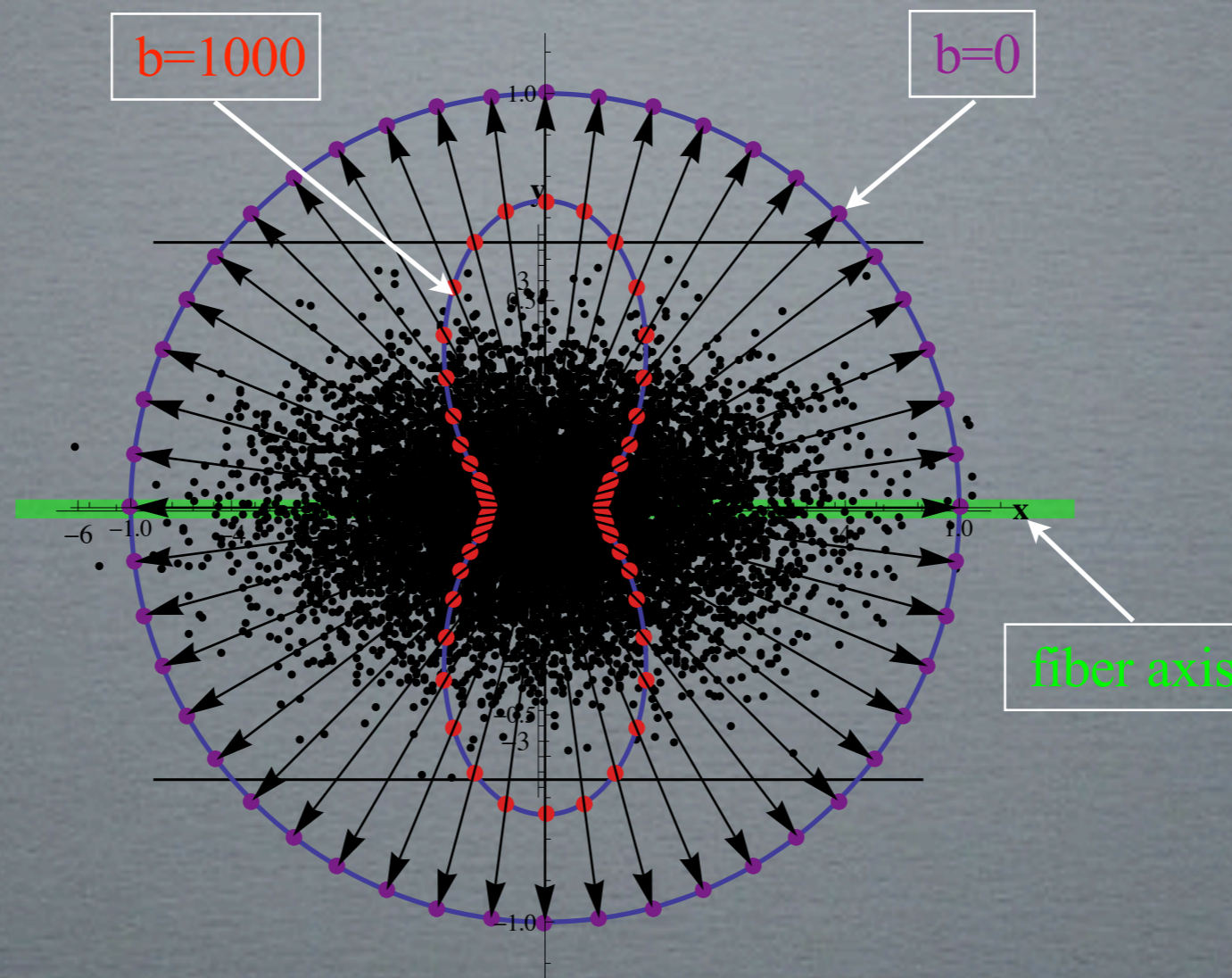
measurement direction

$$\tilde{D} = \hat{r}^t D \hat{r} = D_x \cos^2 \theta + D_y \sin^2 \theta$$

projection of an ellipsoid!
not like projection of a vector

MEASURING THE DIFFUSION TENSOR

MEASURING THE DIFFUSION TENSOR

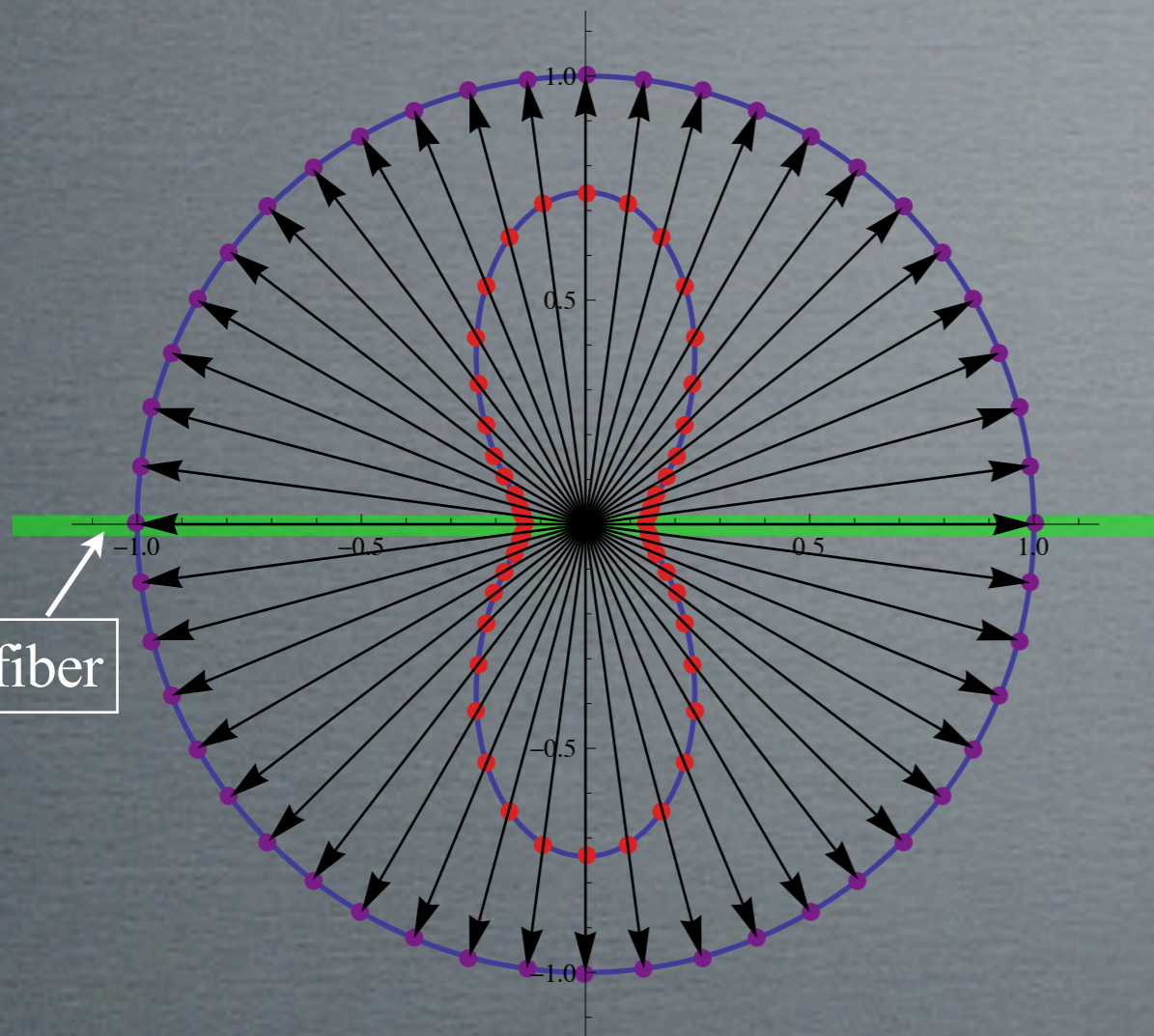


$$S(b, \theta) = S(0)e^{-bD(\theta)} + \eta$$

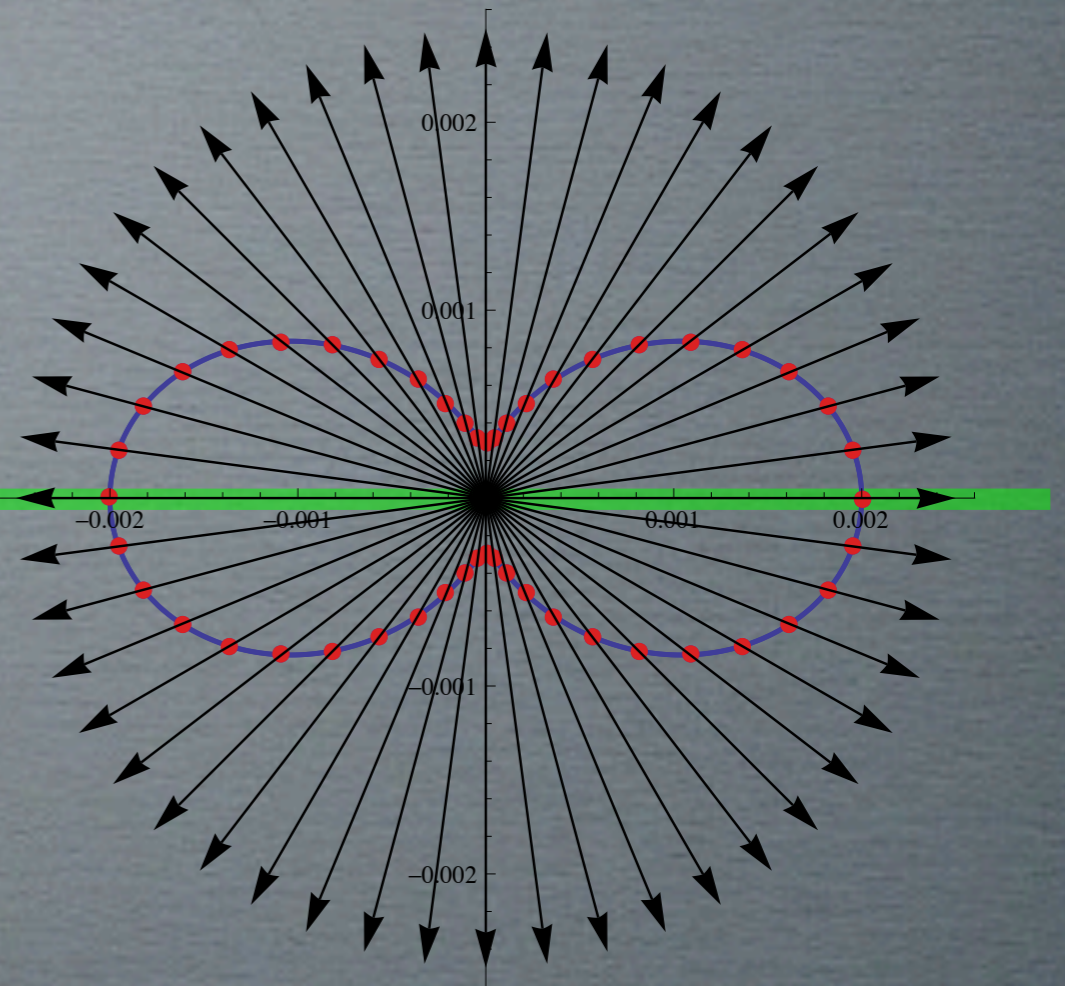
$$D(\theta) = \lambda_x \cos^2 \theta + \lambda_y \sin^2 \theta$$

THE SHAPE OF DIFFUSION

THE SHAPE OF DIFFUSION



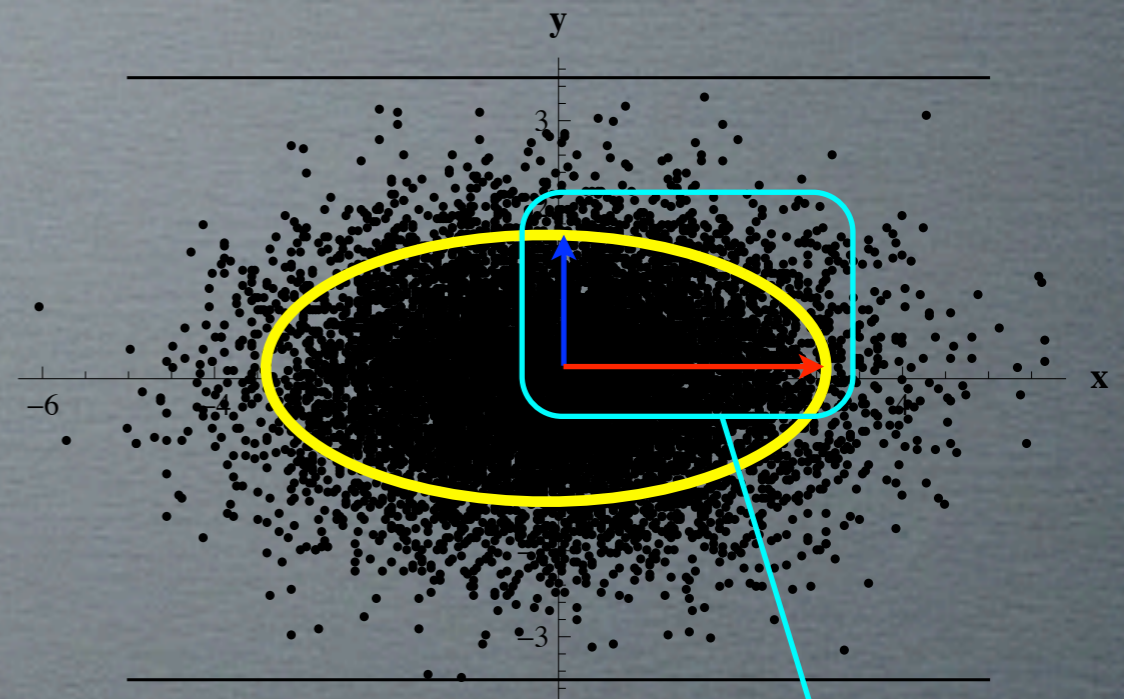
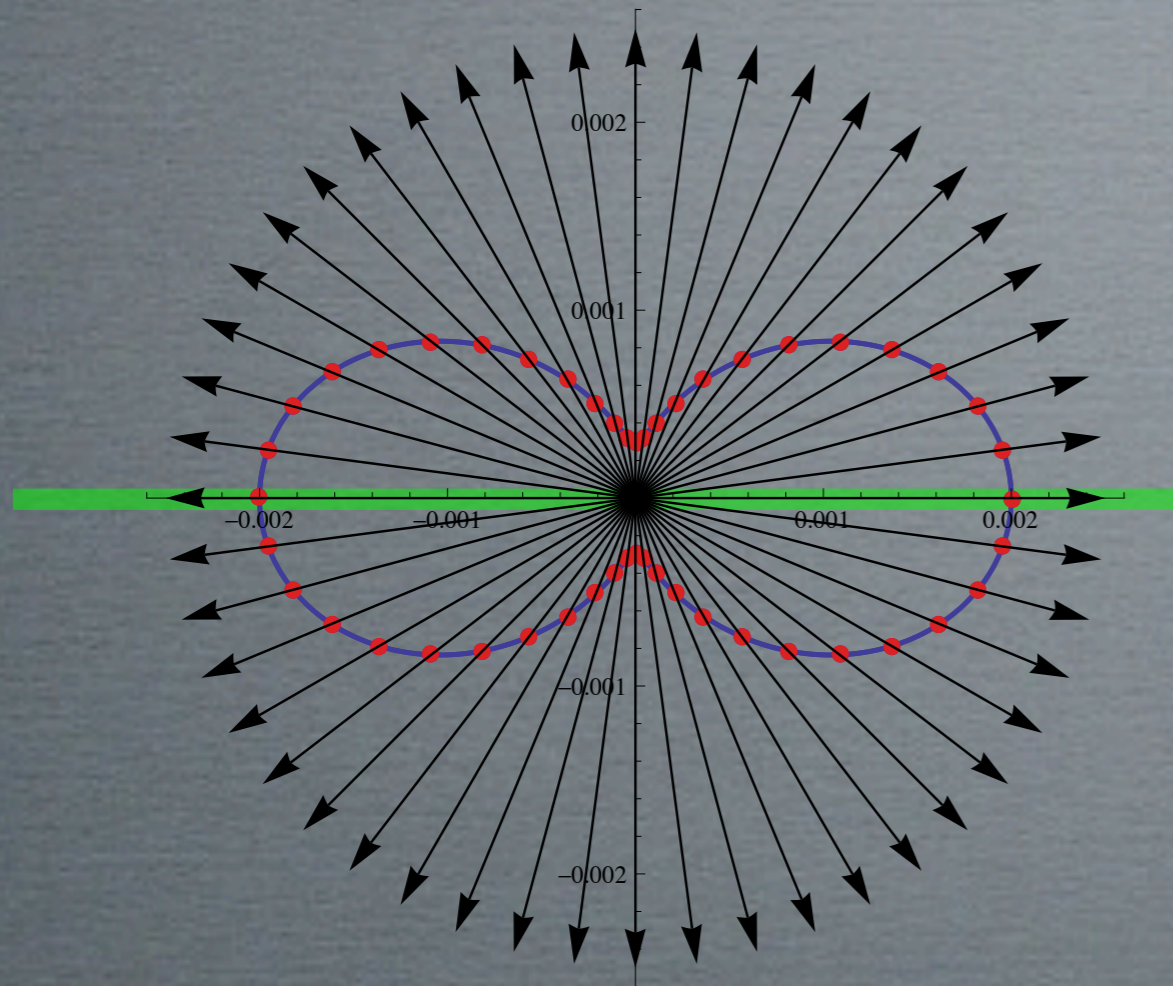
signal $S_b(\theta)$



$$D_{app}(\theta) = -\frac{1}{b} \log \left(\frac{S_b}{S_0} \right)$$

THE ESTIMATION OF DIFFUSION

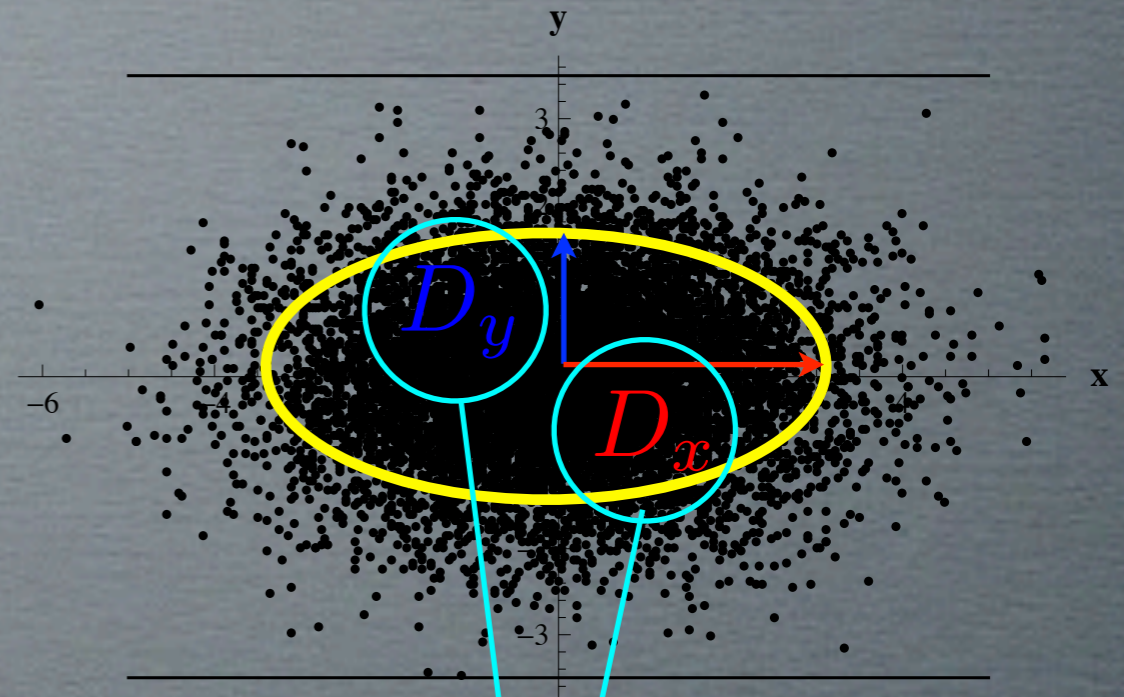
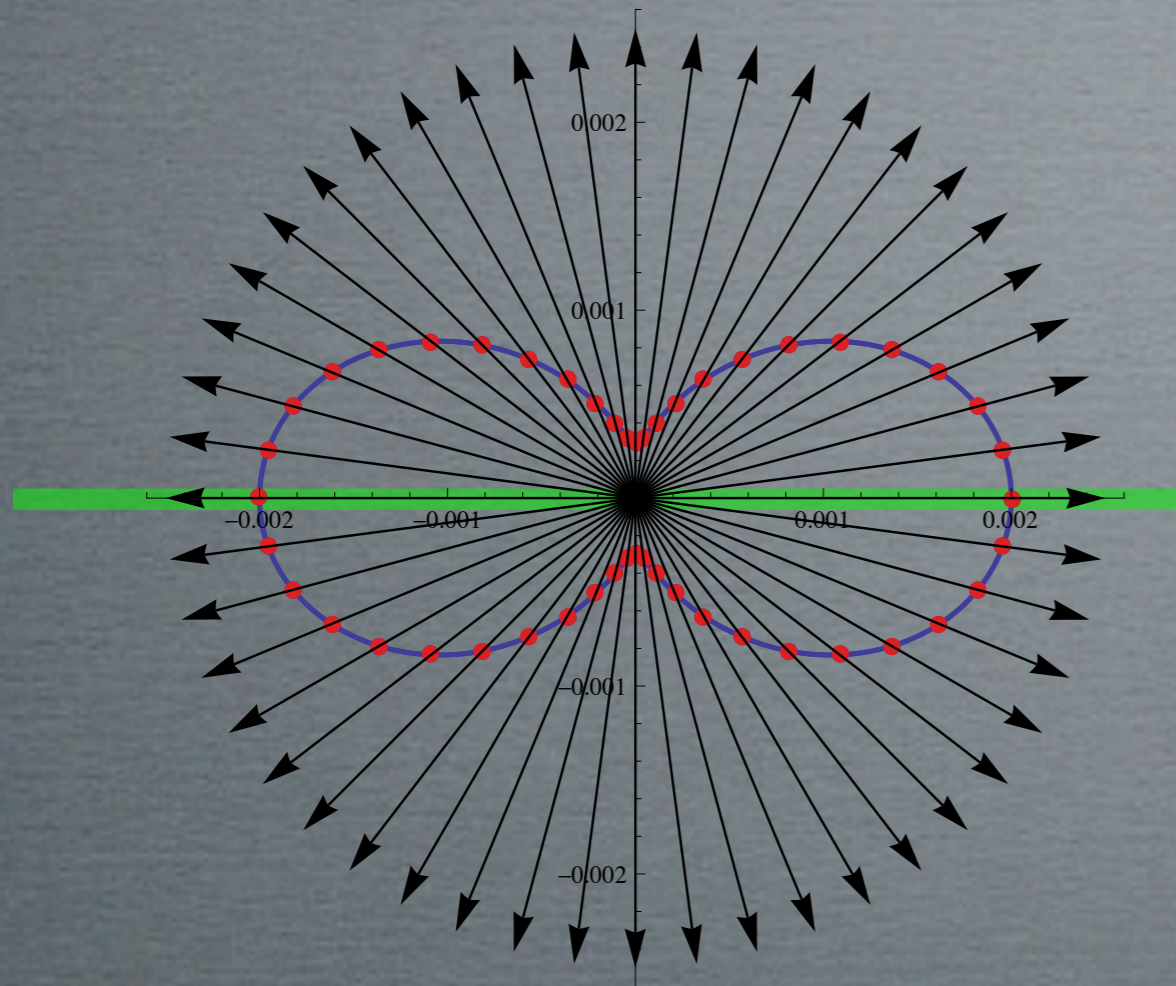
THE ESTIMATION OF DIFFUSION



eigenvectors

$$D_{app}(\theta) = -\frac{1}{b} \log \left(\frac{S_b}{S_0} \right)$$

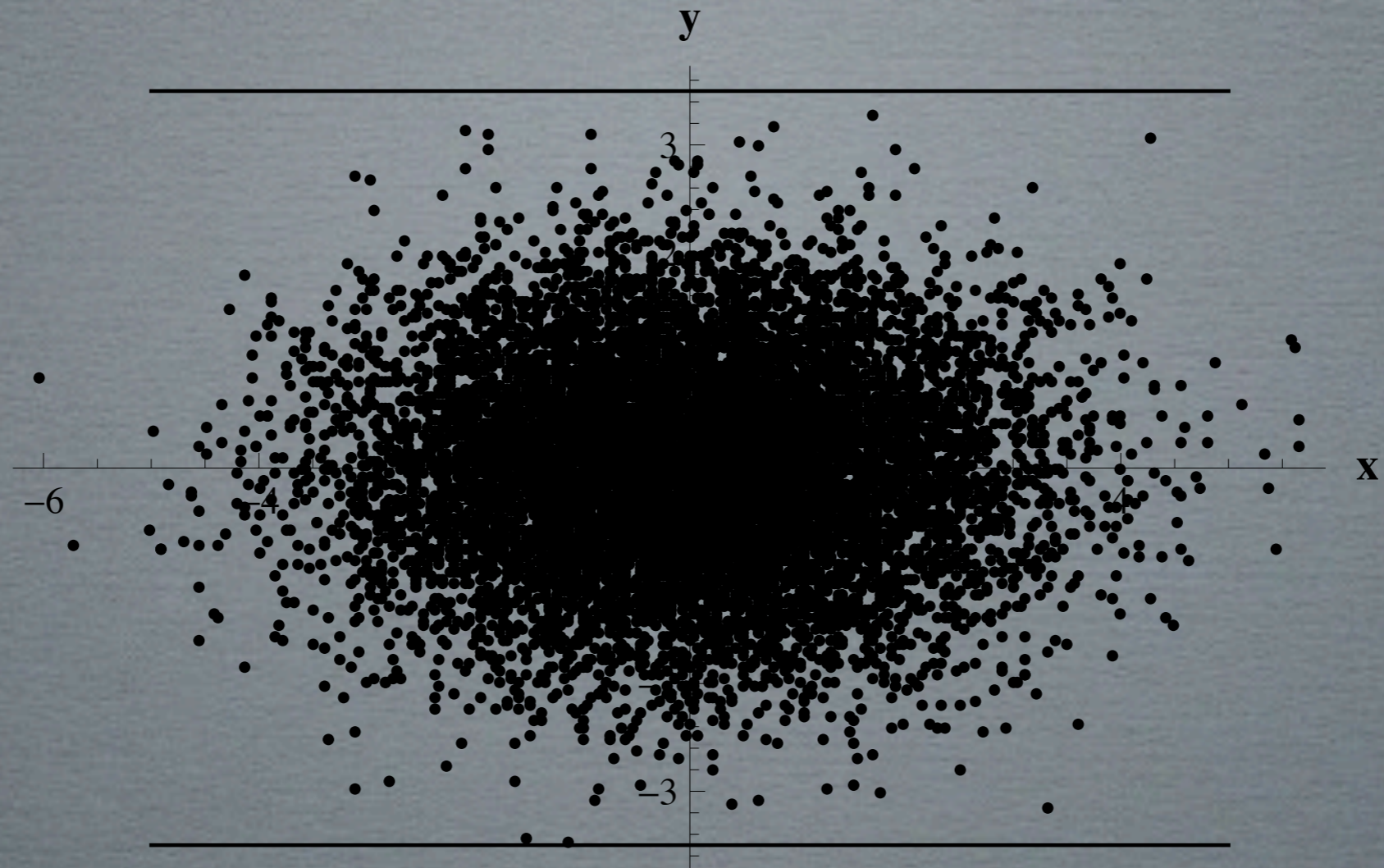
THE ESTIMATION OF DIFFUSION



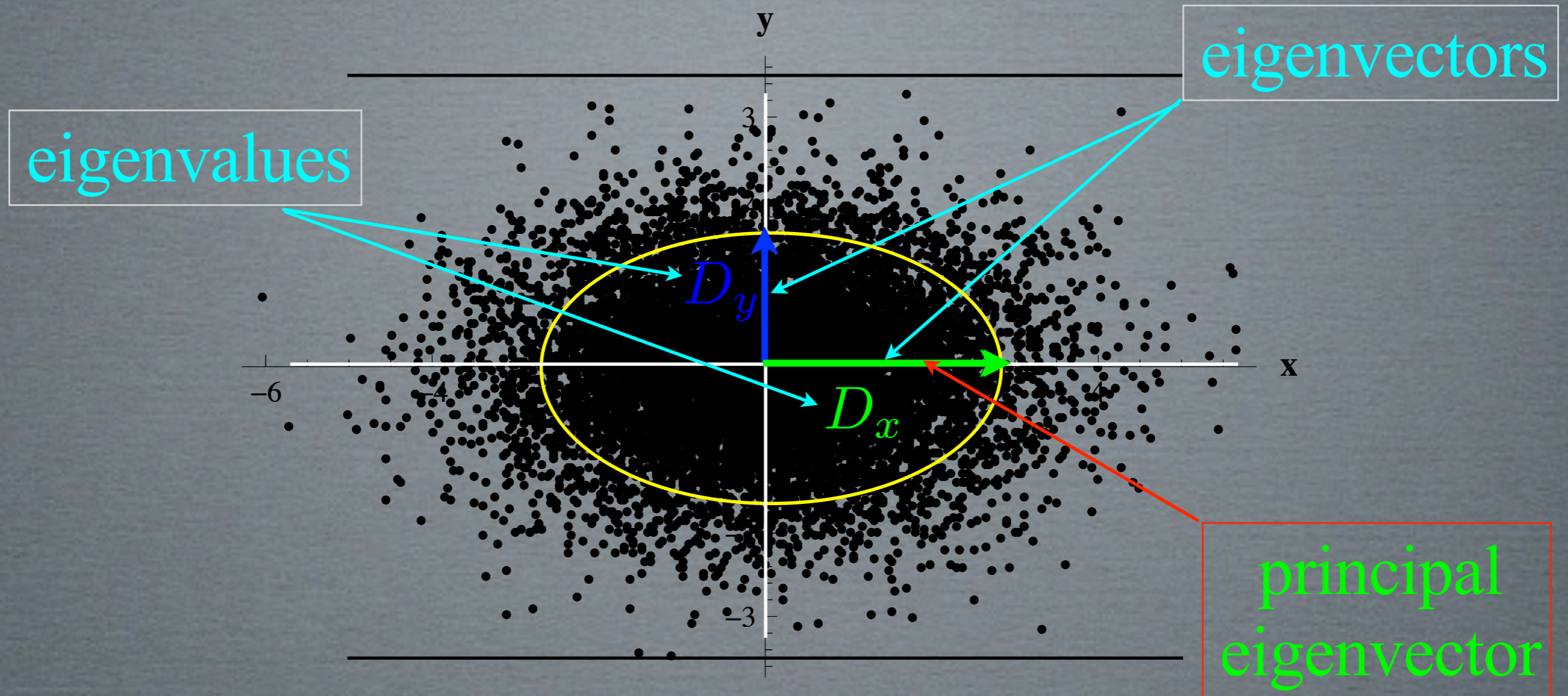
$$D_{app}(\theta) = -\frac{1}{b} \log \left(\frac{S_b}{S_0} \right)$$

eigenvalues

ANISOTROPIC GAUSSIAN DIFFUSION



ANISOTROPIC GAUSSIAN DIFFUSION

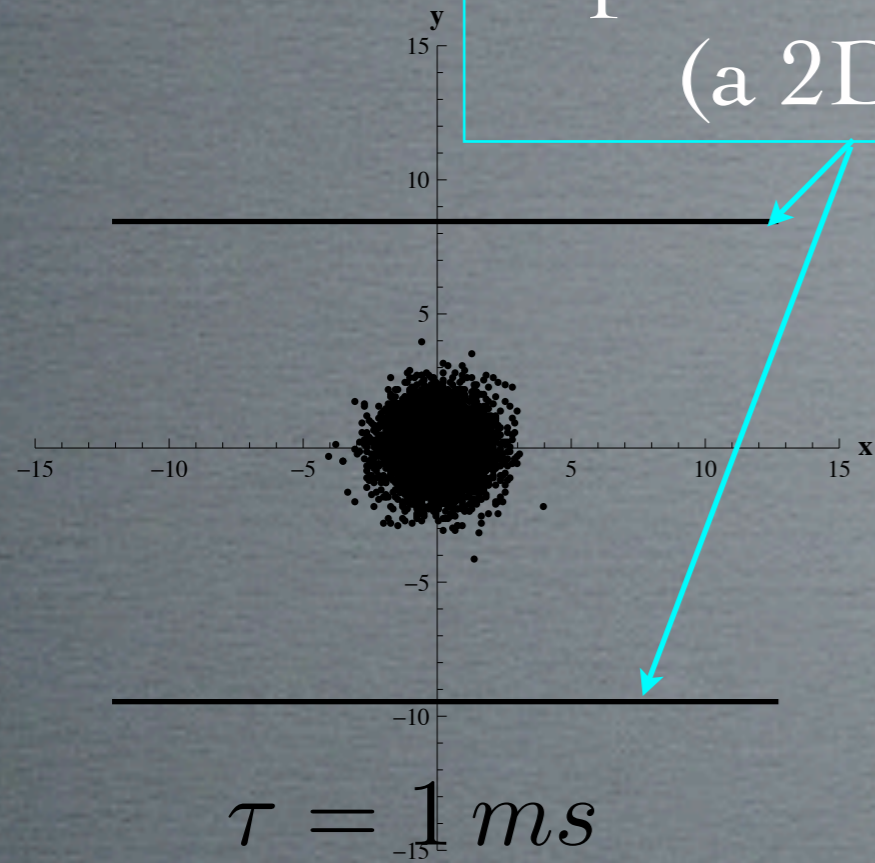


1. The relative dimensions of the contours tells us about local structure
2. The orientation of the eigenvectors is related to the orientation of the structure

ANISOTROPIC DIFFUSION IN 2D

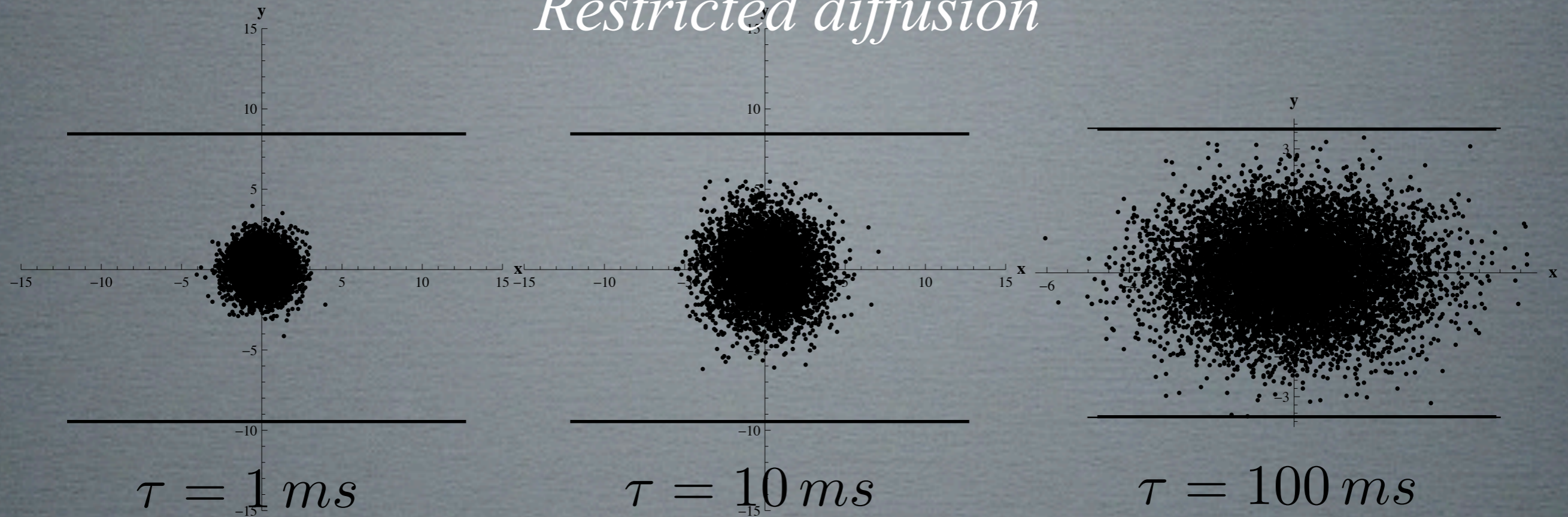
ANISOTROPIC DIFFUSION IN 2D

Impermeable barriers
(a 2D tube)



ANISOTROPIC DIFFUSION IN 2D

Restricted diffusion

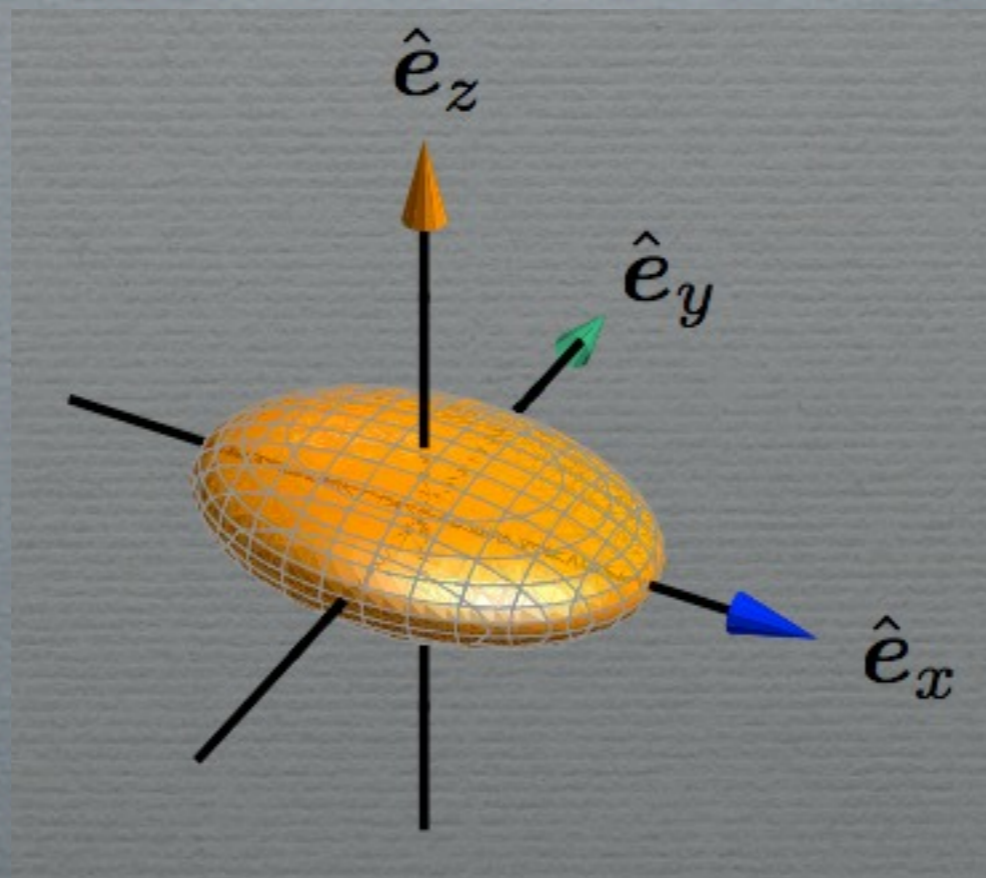


1. Anisotropy induced by local geometry
2. Sensitivity to geometry depends upon diffusion time τ
3. While the D of the liquid may be a constant, there is an *apparent diffusion coefficient (ADC)* that varies with direction

THE 3D GAUSSIAN DISTRIBUTION:

THE 3D GAUSSIAN DISTRIBUTION:

$$P(\mathbf{r}|\mathbf{r}_0, \tau) \sim N(\mathbf{r}_0, \mathbf{\Sigma})$$



Covariance matrix

Diffusion Tensor

$$\mathbf{\Sigma} = \begin{pmatrix} \sigma_{xx}^2 & 0 & 0 \\ 0 & \sigma_{yy}^2 & 0 \\ 0 & 0 & \sigma_{zz}^2 \end{pmatrix} = 6\tau \begin{pmatrix} D_x & 0 & 0 \\ 0 & D_y & 0 \\ 0 & 0 & D_z \end{pmatrix}$$

THE DIFFUSION TENSOR

THE DIFFUSION TENSOR

The three eigenvectors of D

$$\{\vec{e}_1, \vec{e}_2, \vec{e}_3\}$$

are the three unique directions along which the molecular displacements are uncorrelated

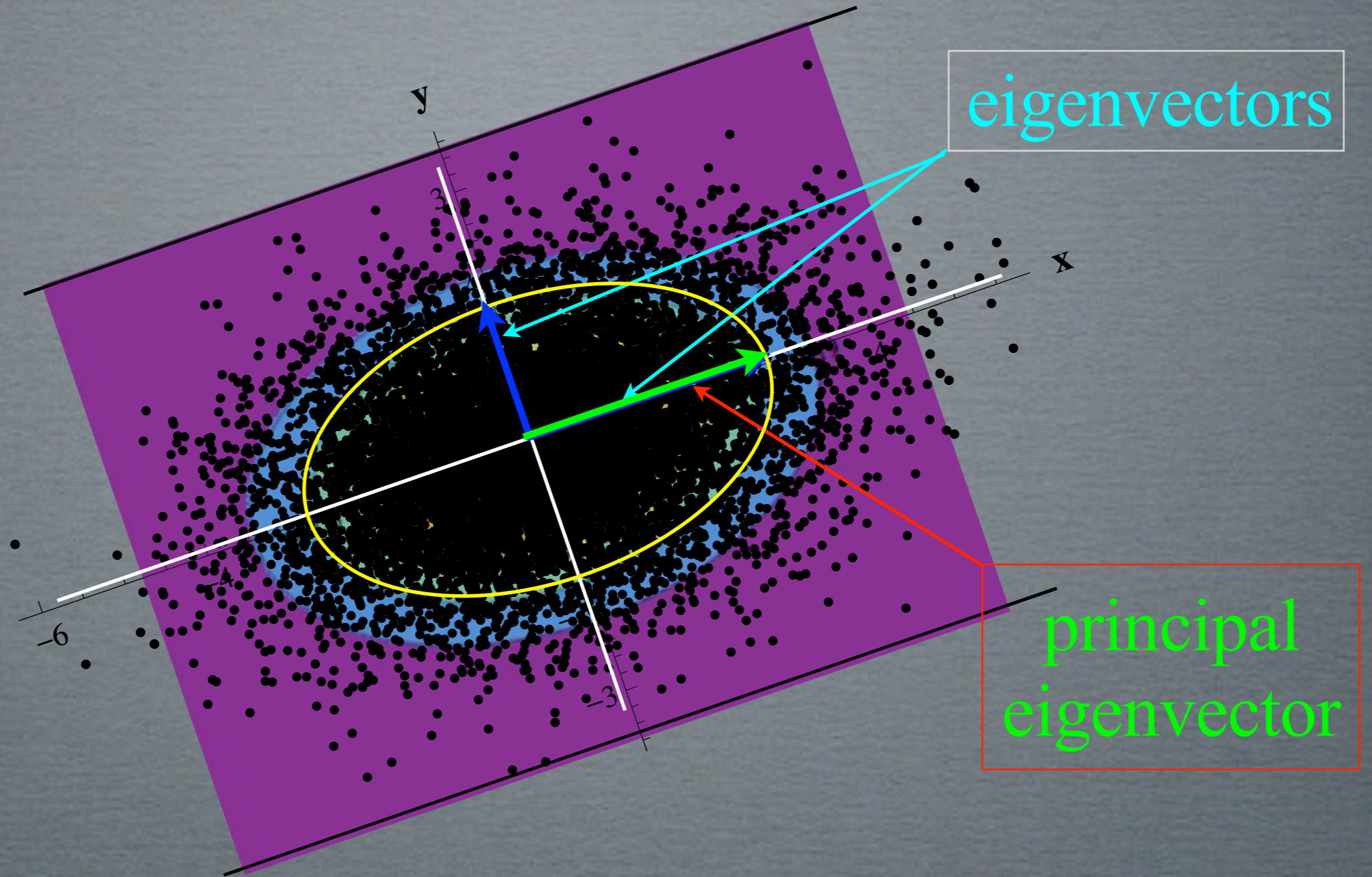
The three eigenvalues of D

$$\{D_x, D_y, D_z\}$$

are the principle diffusivities

ROTATED TUBE

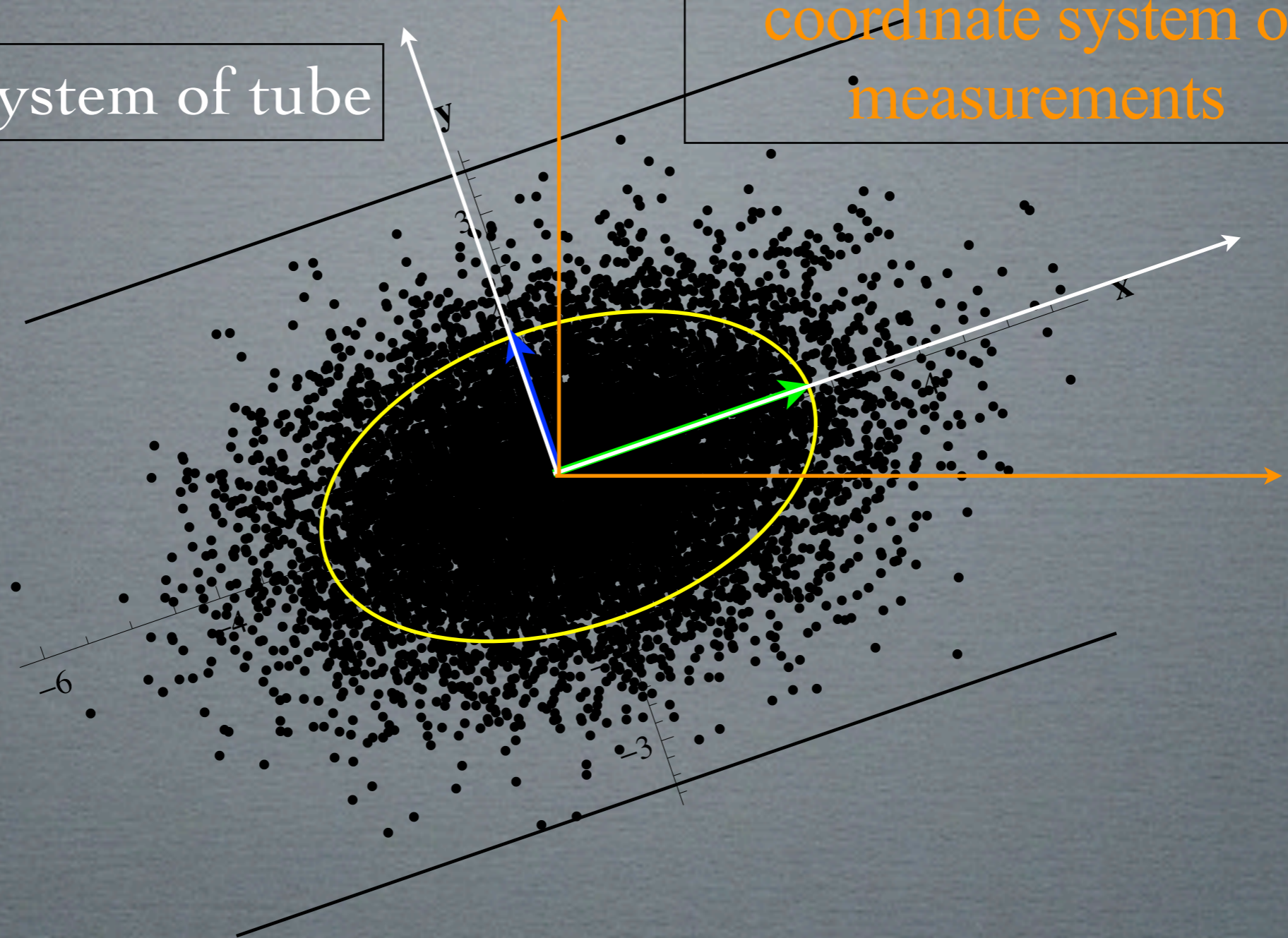
ROTATED TUBE



ROTATED TUBE

coordinate system of tube

coordinate system of measurements



If the tube is not aligned with the coordinate system of the measurements, the diffusion along the measurement axes appears correlated

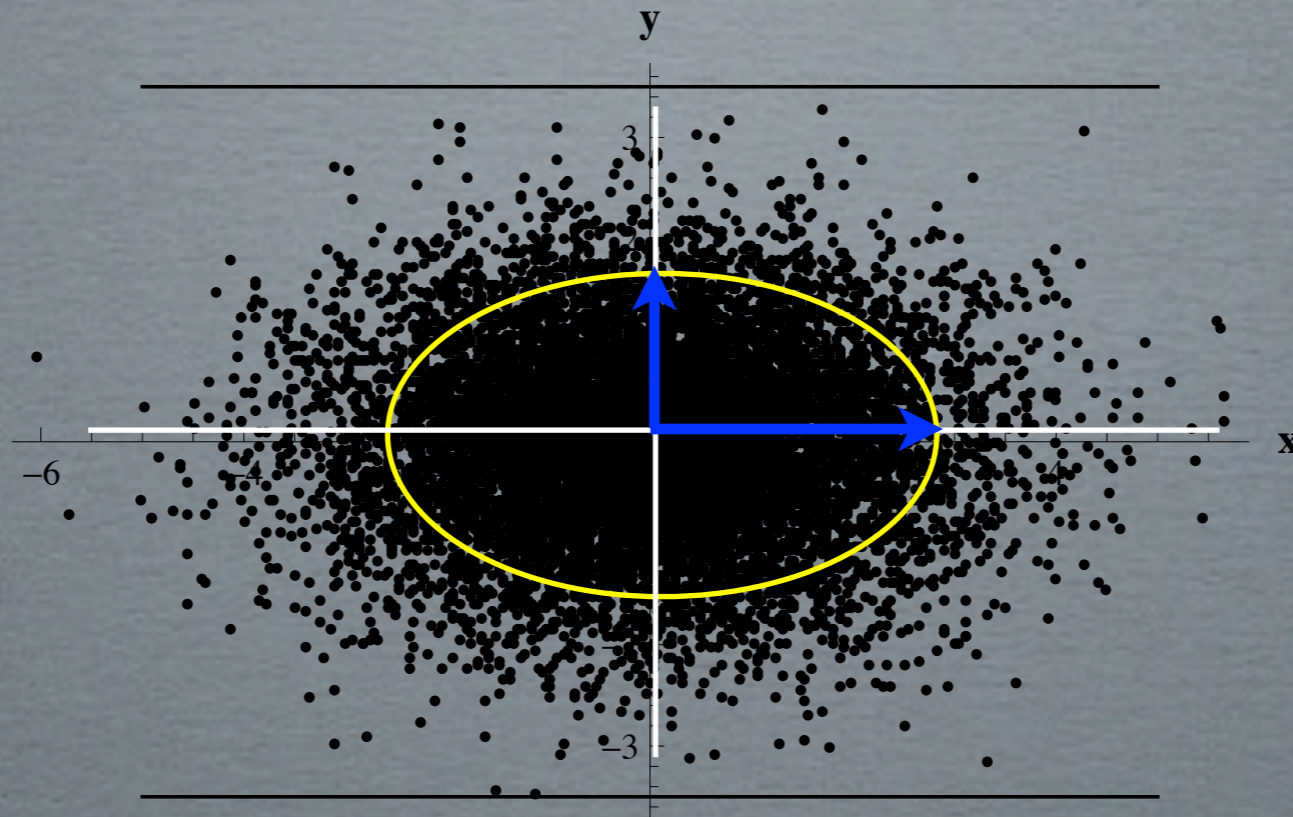
THE 2D GAUSSIAN DISTRIBUTION:

$$P(\mathbf{r}|\mathbf{r}_0, \tau) \sim N(\mathbf{r}_0, \Sigma)$$

THE 2D GAUSSIAN DISTRIBUTION:

$$P(\mathbf{r}|\mathbf{r}_0, \tau) \sim N(\mathbf{r}_0, \Sigma)$$

$$\mathbf{r} = \{x, y\}$$



Covariance matrix

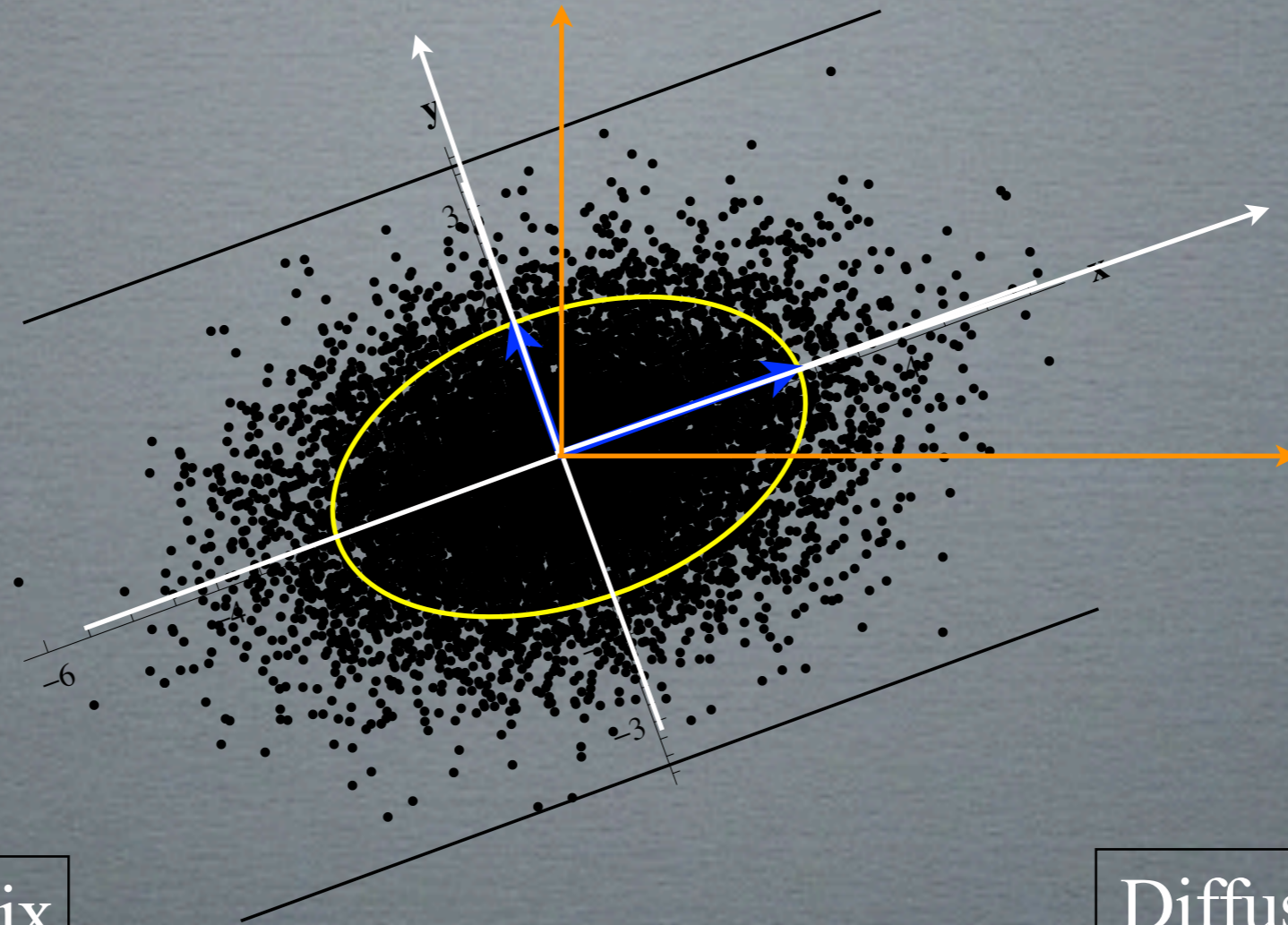
Diffusion Tensor

$$\Sigma = \begin{pmatrix} \sigma_x^2 & 0 \\ 0 & \sigma_y^2 \end{pmatrix} = 4\tau \begin{pmatrix} D_x & 0 \\ 0 & D_y \end{pmatrix}$$

THE 2D GAUSSIAN DISTRIBUTION:

$$P(\mathbf{r}|\mathbf{r}_0, \tau) \sim N(\mathbf{r}_0, \Sigma)$$

$$\mathbf{r} = \{x, y\}$$



Covariance matrix

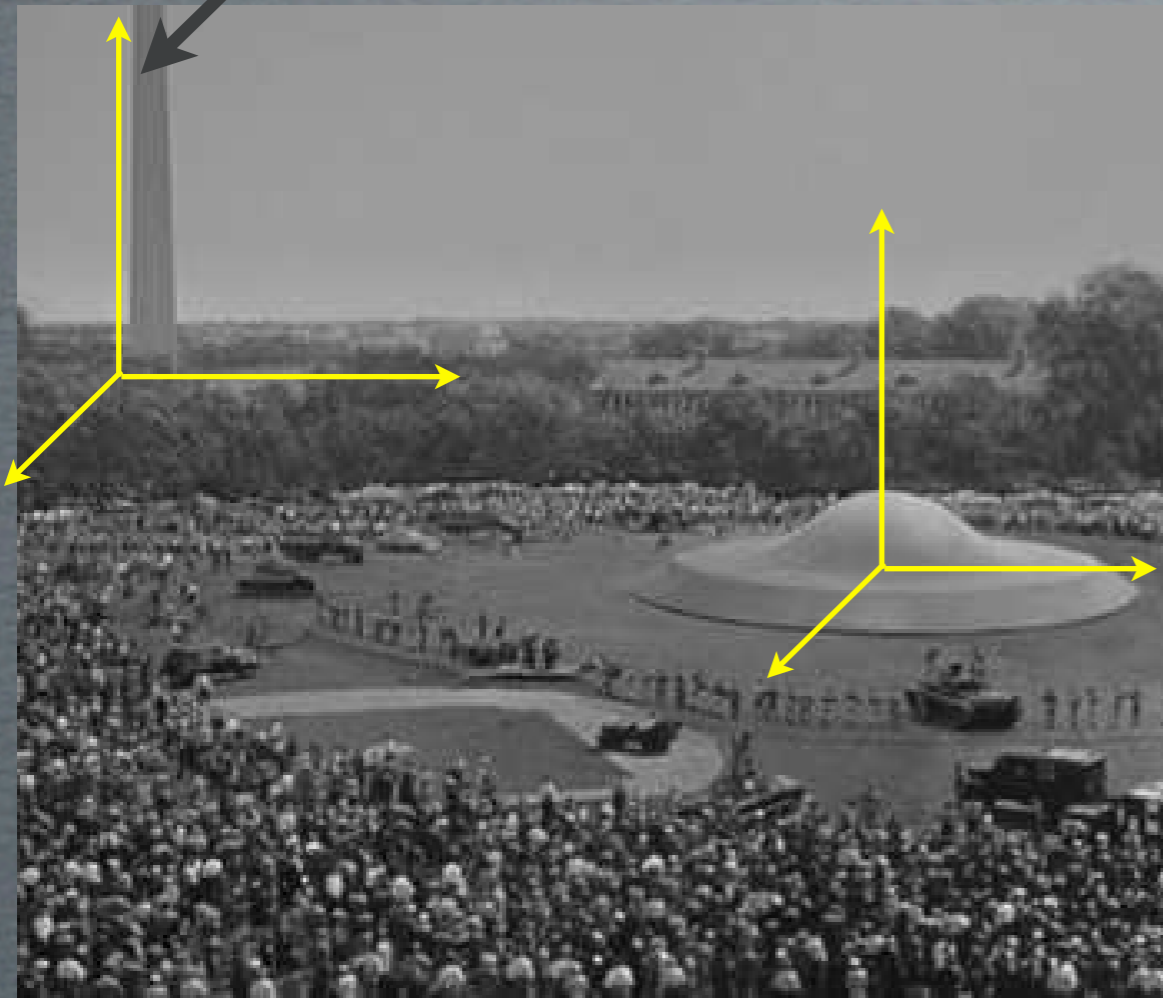
Diffusion Tensor

$$\Sigma = \begin{pmatrix} \sigma_{xx}^2 & \sigma_{xy}^2 \\ \sigma_{yx}^2 & \sigma_{yy}^2 \end{pmatrix} = 4\tau \begin{pmatrix} D_{xx} & D_{xy} \\ D_{yx} & D_{yy} \end{pmatrix}$$

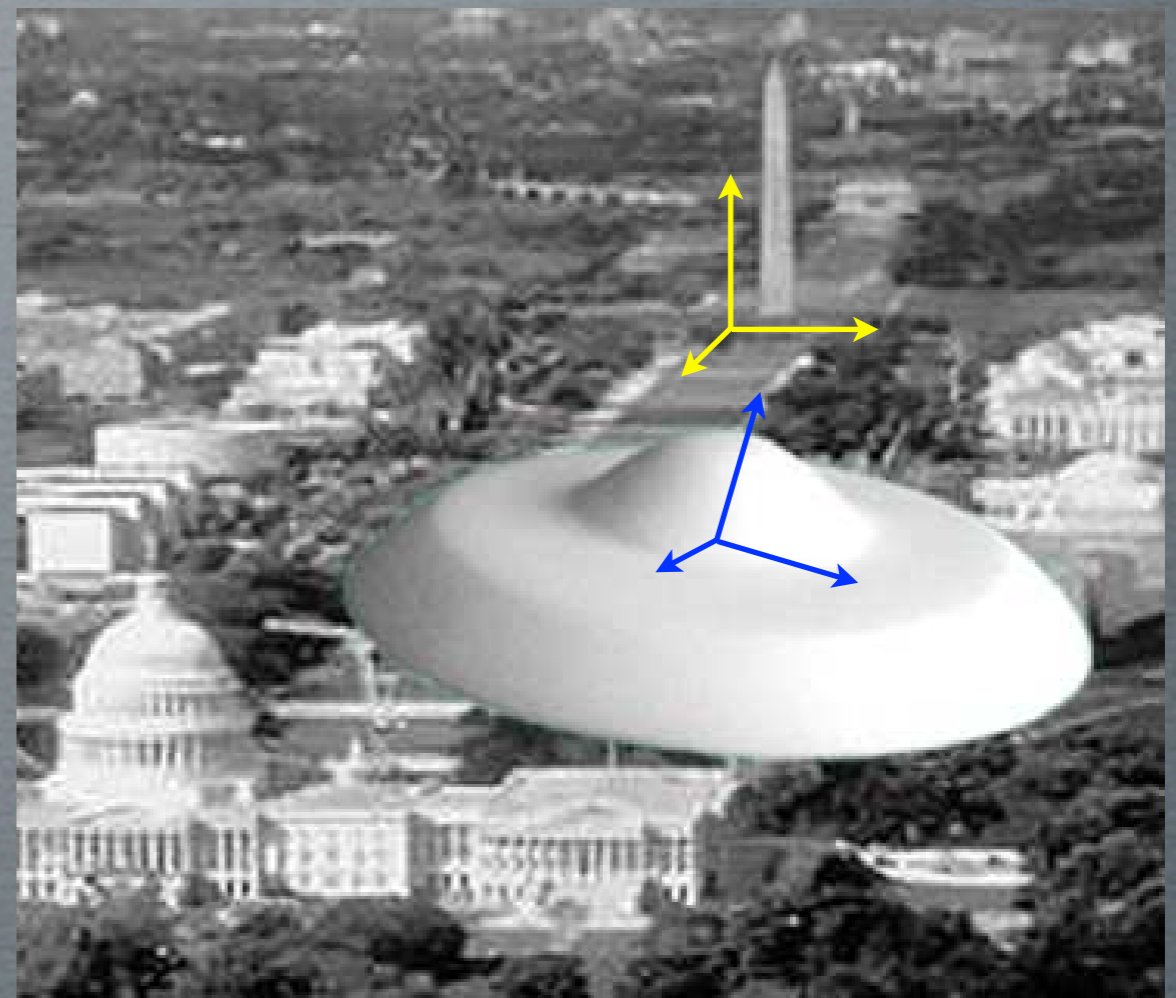
**GENERALLY FIBERS ARE NOT ALIGNED
ALONG MAGNET COORDINATES!**

GENERALLY FIBERS ARE NOT ALIGNED ALONG MAGNET COORDINATES!

laboratory
coordinate system



same orientation as laboratory
coordinate system



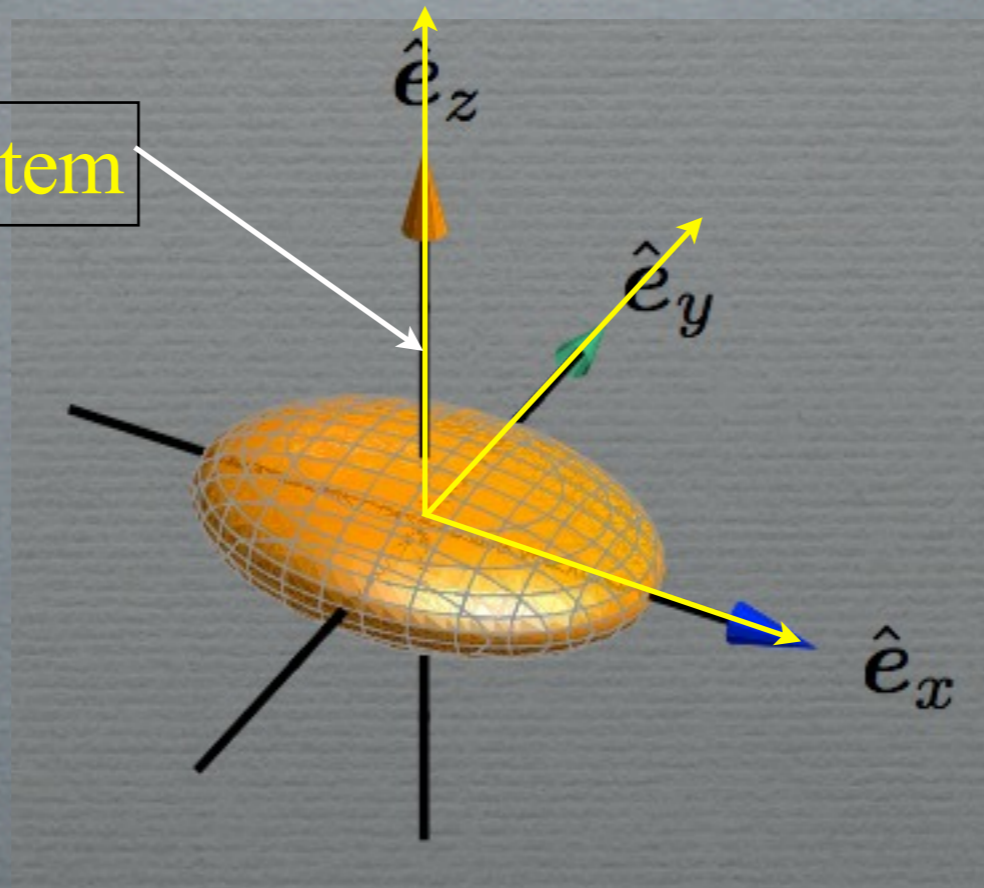
rotated relative to laboratory
coordinate system

THE 3D GAUSSIAN DISTRIBUTION:

THE 3D GAUSSIAN DISTRIBUTION:

$$P(\mathbf{r}|\mathbf{r}_0, \tau) \sim N(\mathbf{r}_0, \Sigma)$$

scanner coordinate system



Covariance matrix

$$\Sigma = \begin{pmatrix} \sigma_{xx}^2 & 0 & 0 \\ 0 & \sigma_{yy}^2 & 0 \\ 0 & 0 & \sigma_{zz}^2 \end{pmatrix} = 6\tau \begin{pmatrix} D_x & 0 & 0 \\ 0 & D_y & 0 \\ 0 & 0 & D_z \end{pmatrix}$$

Diffusion Tensor

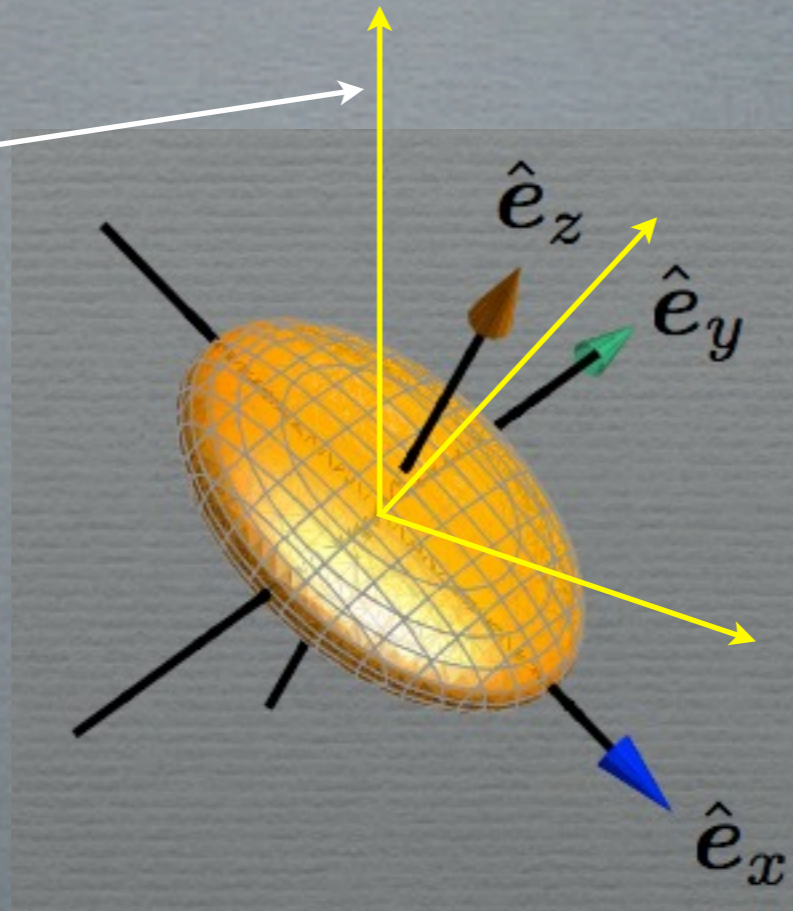
THE 3D GAUSSIAN DISTRIBUTION:

$$P(\mathbf{r}|\mathbf{r}_0, \tau) \sim N(\mathbf{r}_0, \Sigma)$$

THE 3D GAUSSIAN DISTRIBUTION:

$$P(\mathbf{r}|\mathbf{r}_0, \tau) \sim N(\mathbf{r}_0, \Sigma)$$

scanner coordinate system



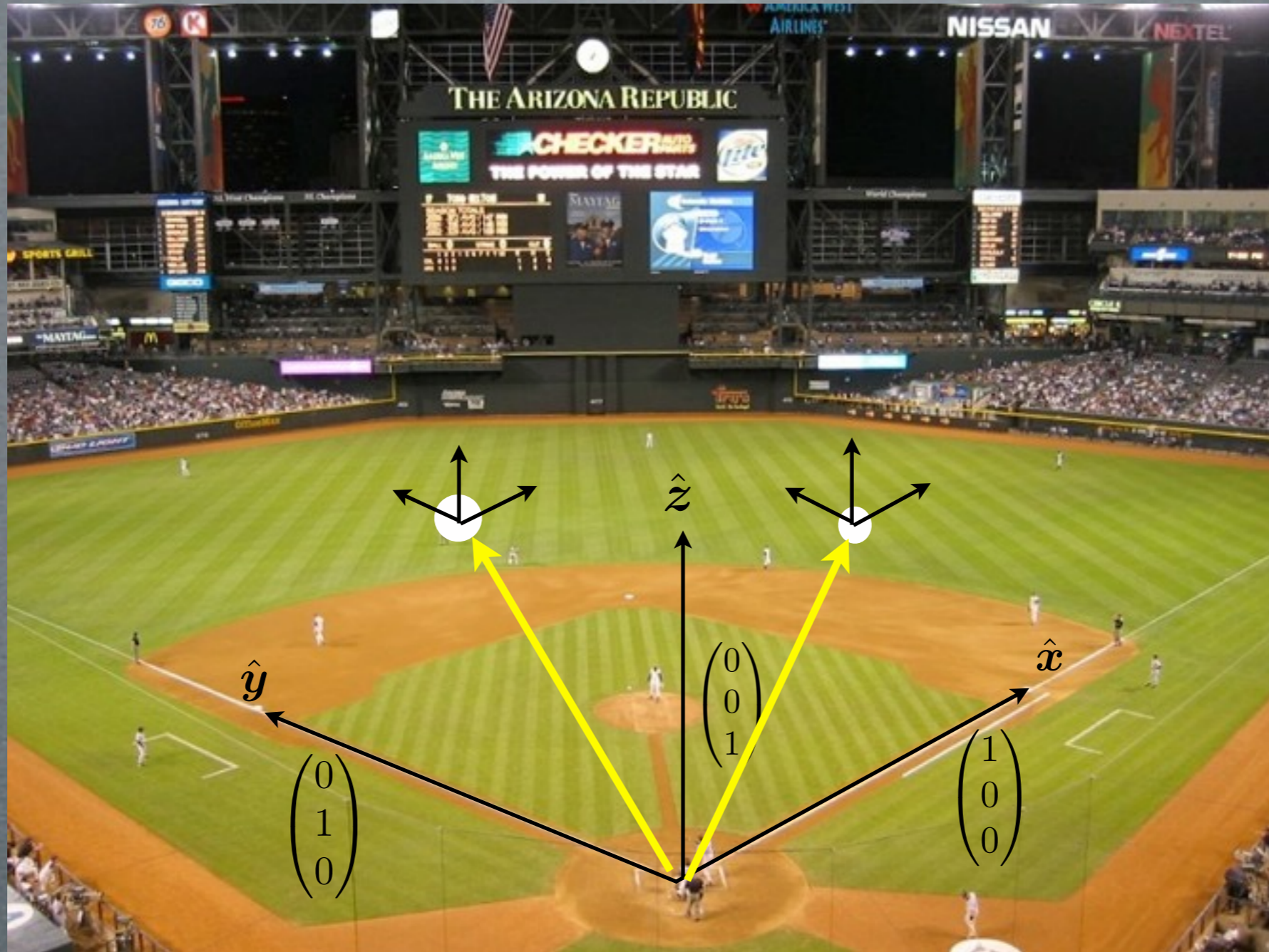
Covariance matrix

$$\Sigma = \begin{pmatrix} \sigma_{xx}^2 & \sigma_{xy}^2 & \sigma_{xz}^2 \\ \sigma_{yx}^2 & \sigma_{yy}^2 & \sigma_{yz}^2 \\ \sigma_{zx}^2 & \sigma_{zy}^2 & \sigma_{zz}^2 \end{pmatrix} = 6\tau \underbrace{\begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{pmatrix}}_D$$

Diffusion Tensor

TENSOR ROTATIONS

TENSOR ROTATIONS



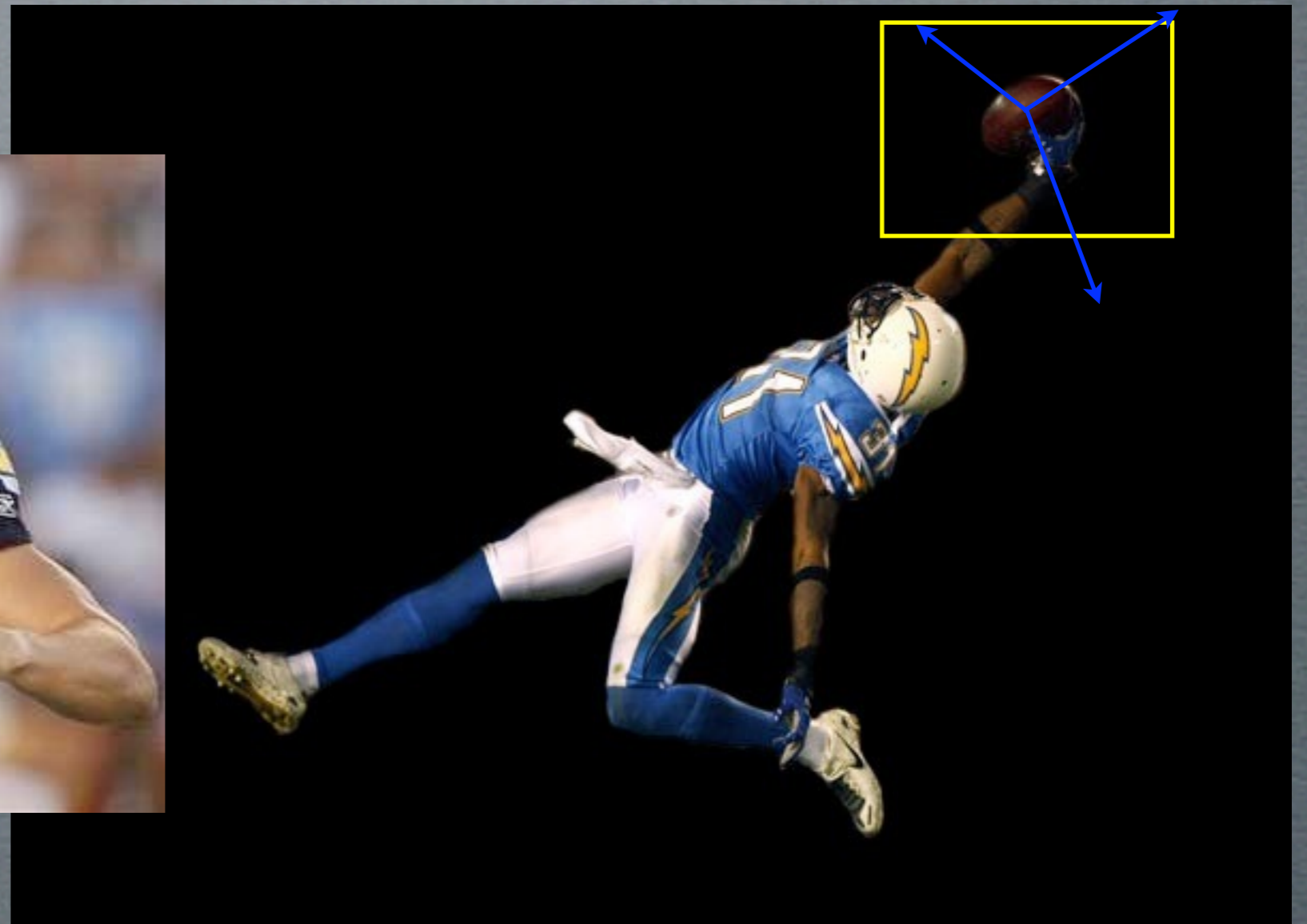
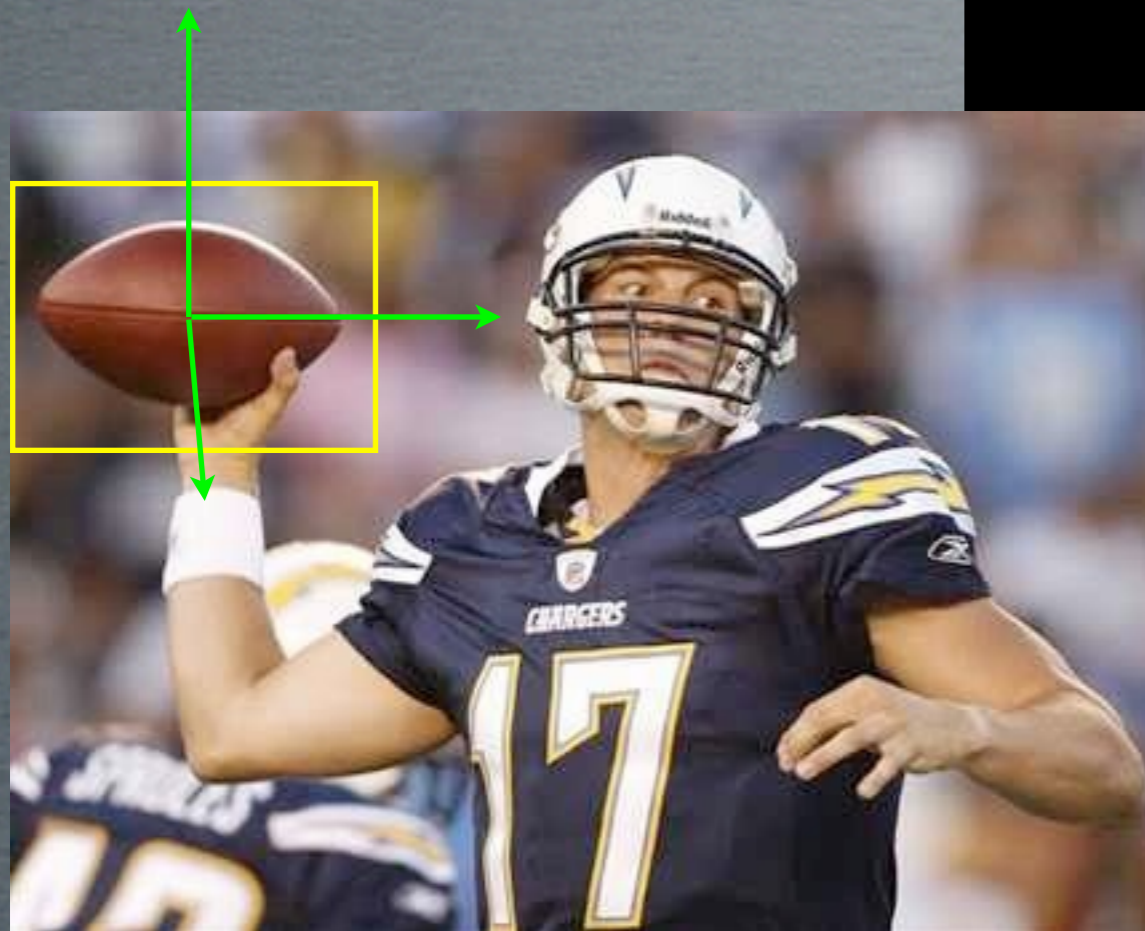
A baseball is spherical - it has no sense of orientation

TENSOR ROTATIONS

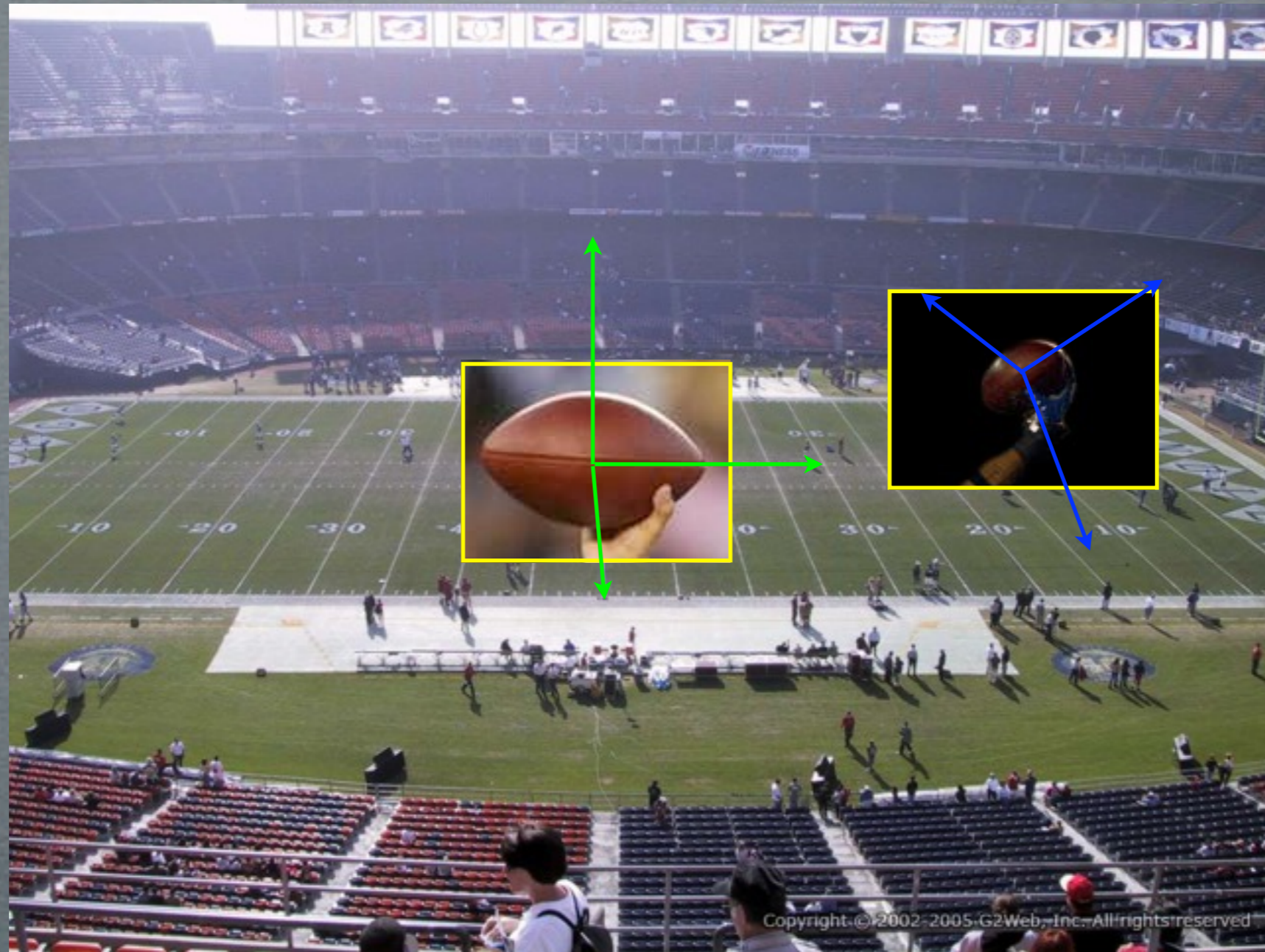


... but a football is ellipsoidal, and does!

TENSOR ROTATIONS

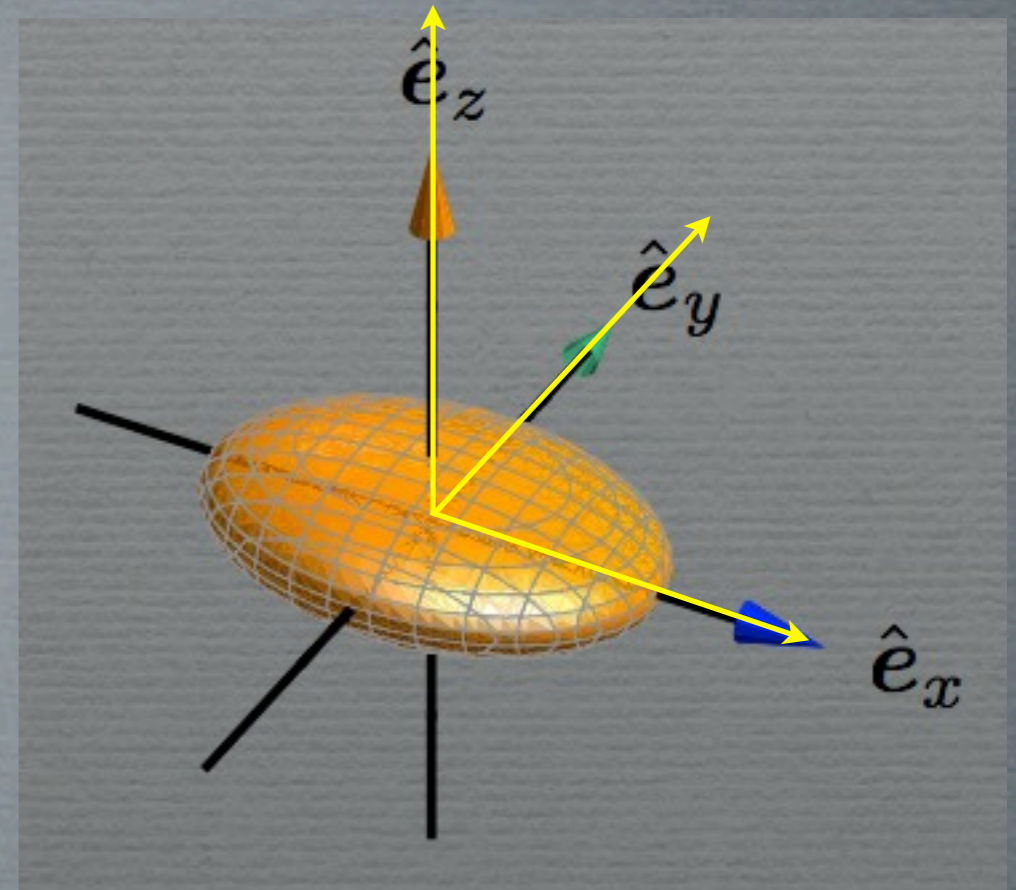
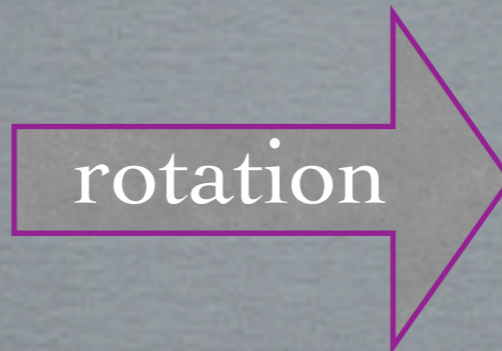
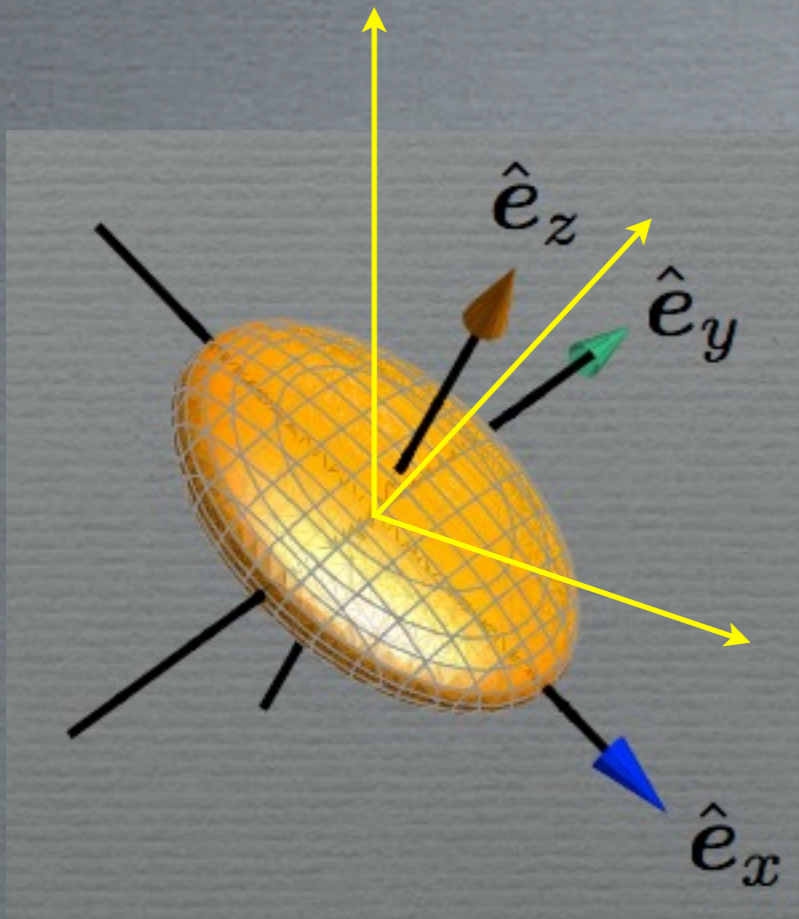


TENSOR ROTATIONS



WHAT WE WANT

WHAT WE WANT



$$D = \begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{pmatrix} \xrightarrow{\text{rotation}} D = \begin{pmatrix} D_x & 0 & 0 \\ 0 & D_y & 0 \\ 0 & 0 & D_z \end{pmatrix}$$

This is what eigenvector routines do!

THE ESTIMATION OF DIFFUSION CAUTION

THE ESTIMATION OF DIFFUSION CAUTION

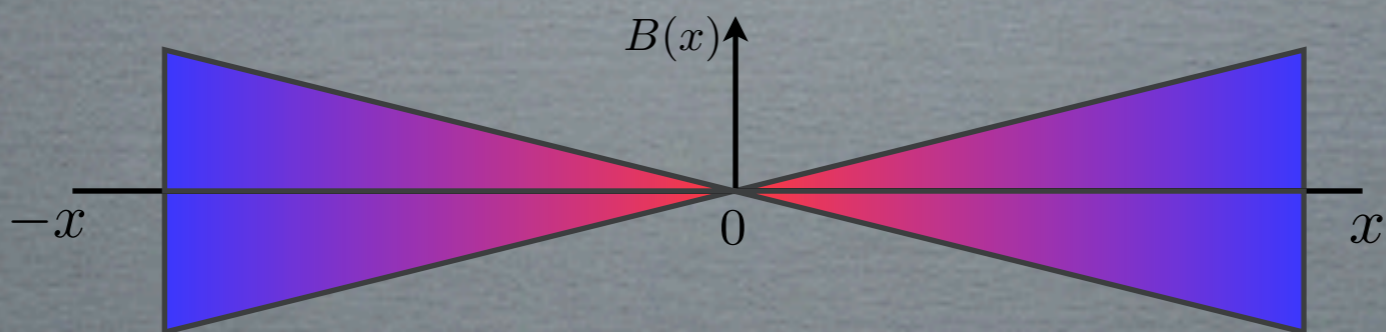
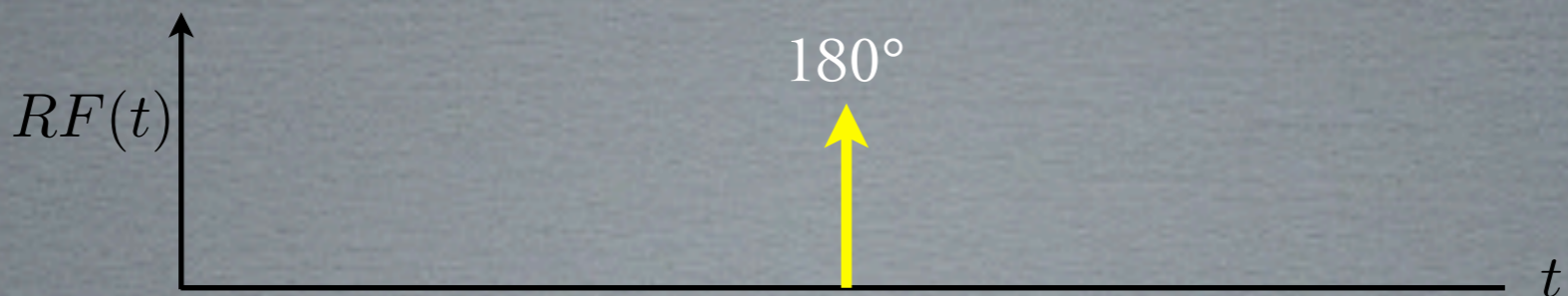
$$S(b, \hat{r}) = S(0)e^{-bD(\hat{r})} + \eta$$



$$D(\hat{r}) = -\frac{1}{b} \log \left(\frac{S(b, \hat{r})}{S(0)} - \eta \right)$$

Not additive noise anymore!

THE BIPOLAR GRADIENT PULSE (SPIN ECHO)

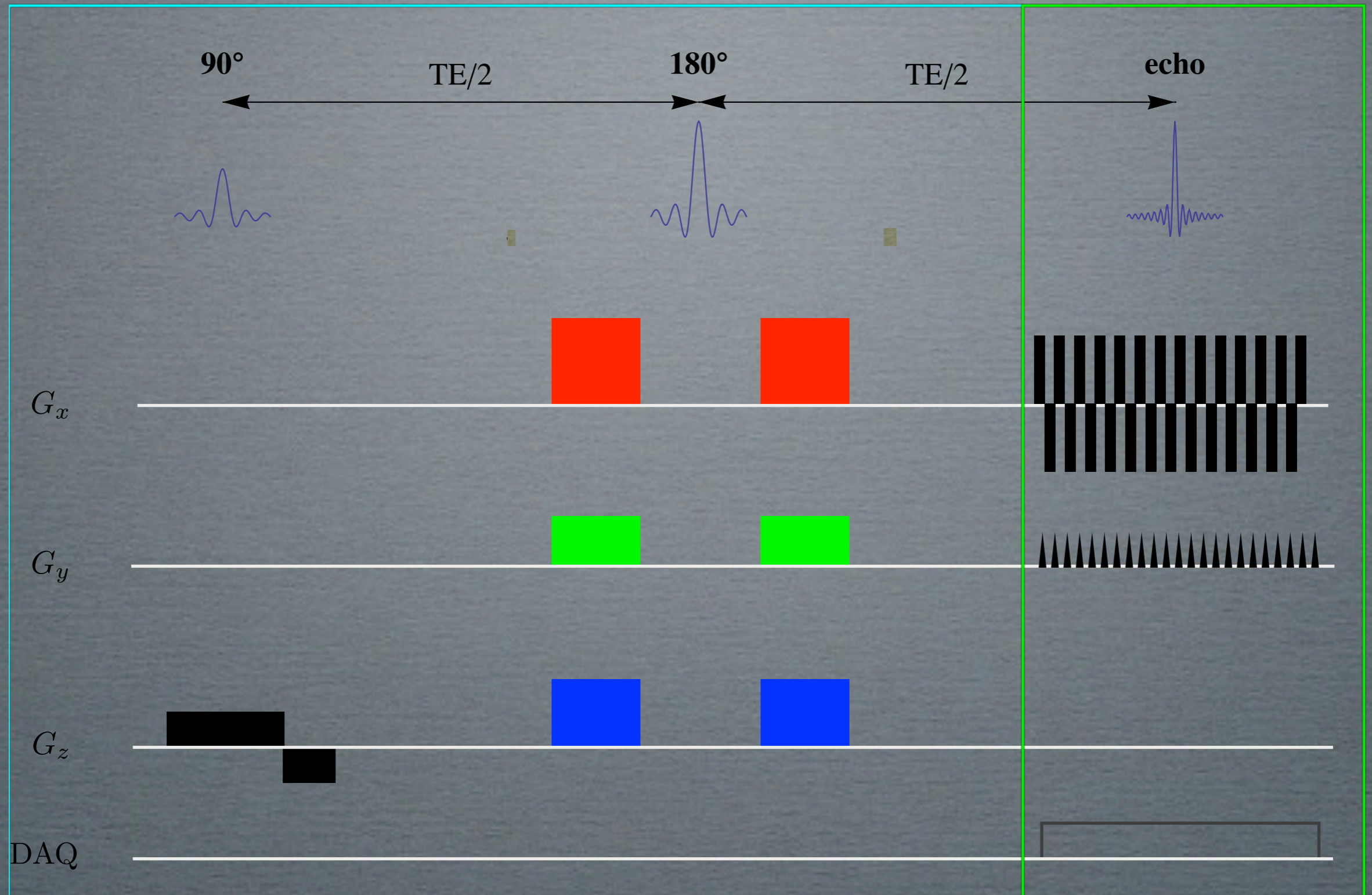


EXTENSION TO IMAGING

EXTENSION TO IMAGING

Preparation

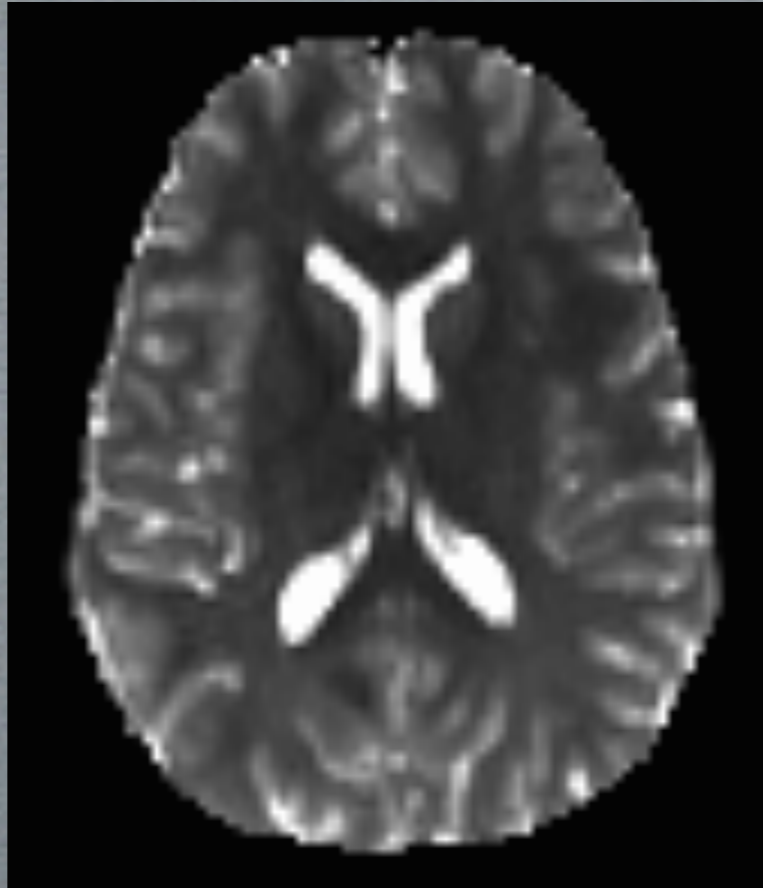
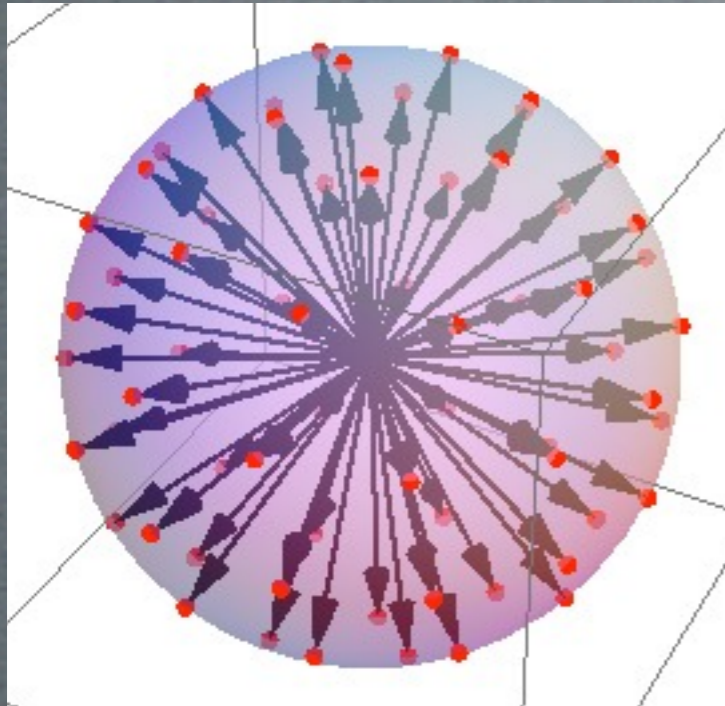
Acquisition



Because the diffusion weighting does not interfere with the stationary tissue signal, we can “insert” it into a standard imaging procedure

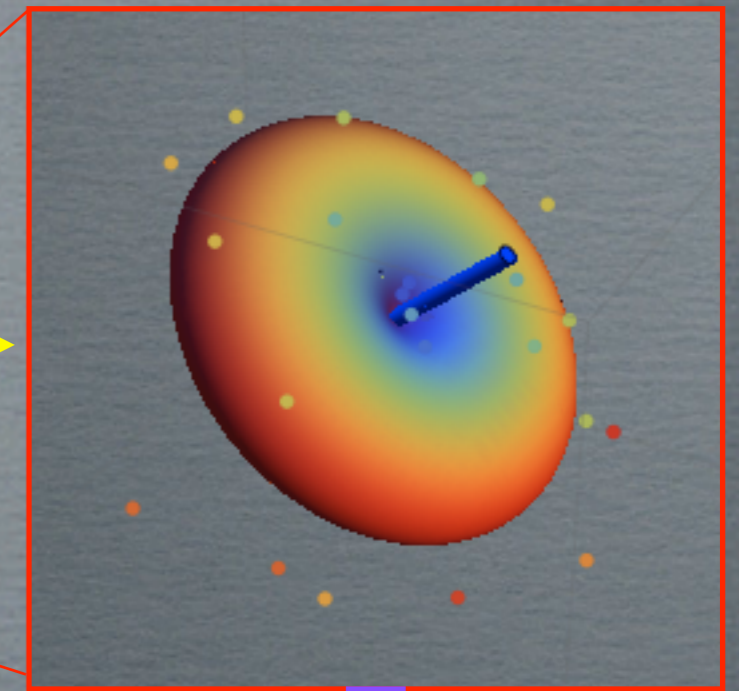
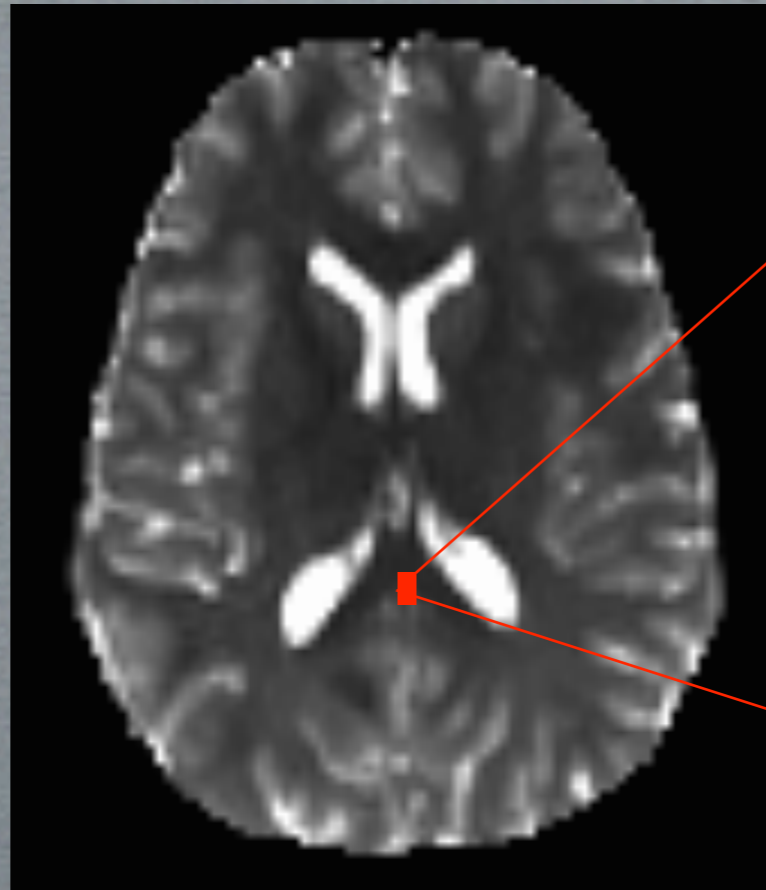
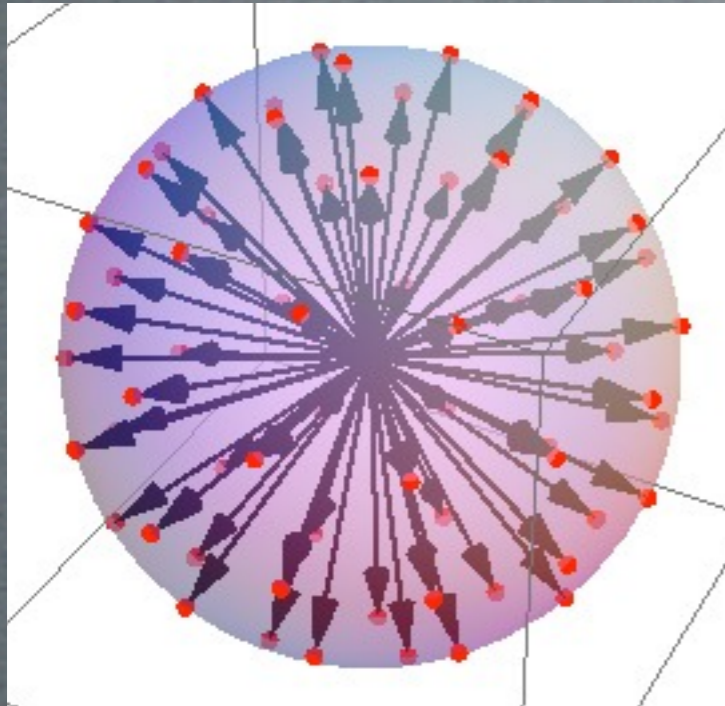
DTI

DTI

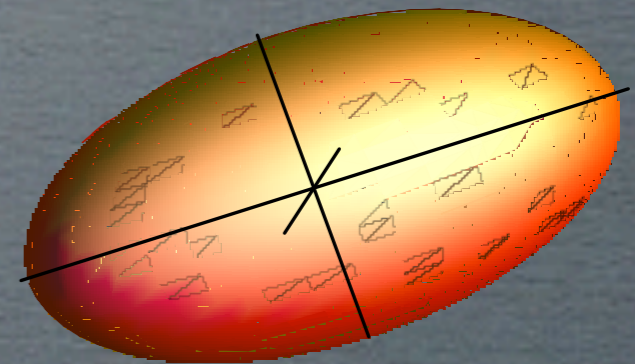


DTI

voxel signal
from multiple images at
different directions

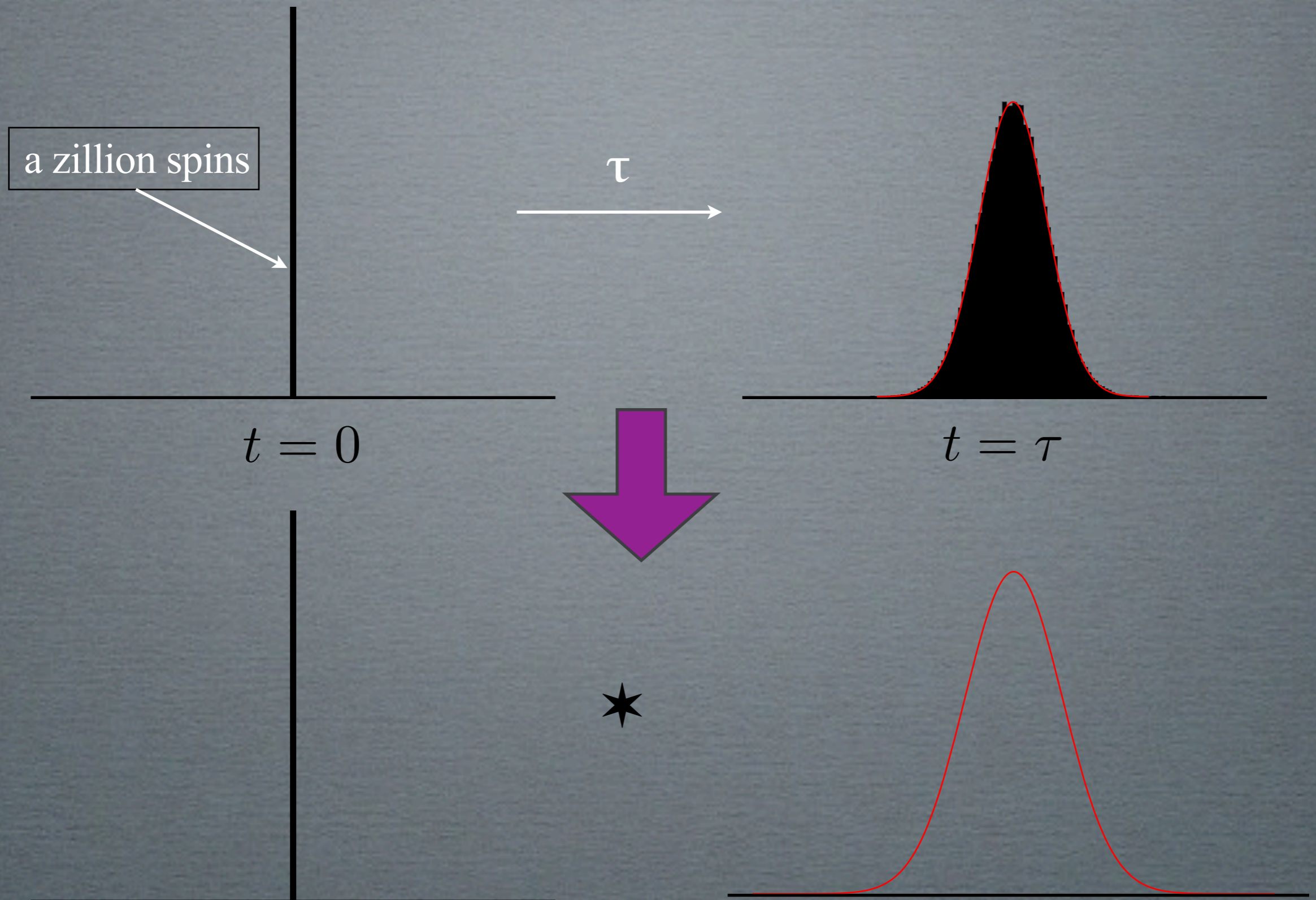


reconstruct D
(diffusion ellipsoid)

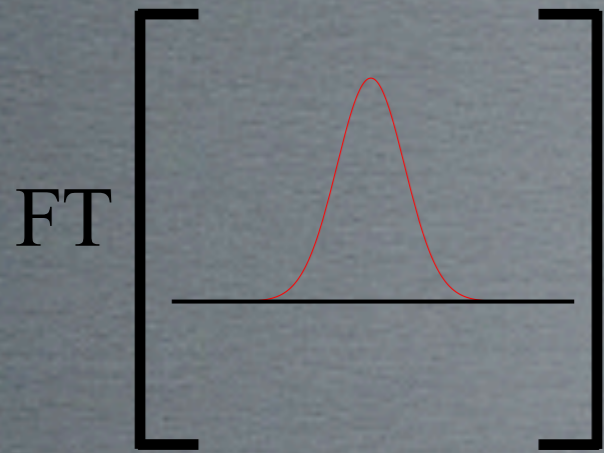


Diffusion acts as a convolution in the image domain

Diffusion acts as a convolution in the image domain



$\sigma \approx 15\mu m \ll$ voxel dimensions

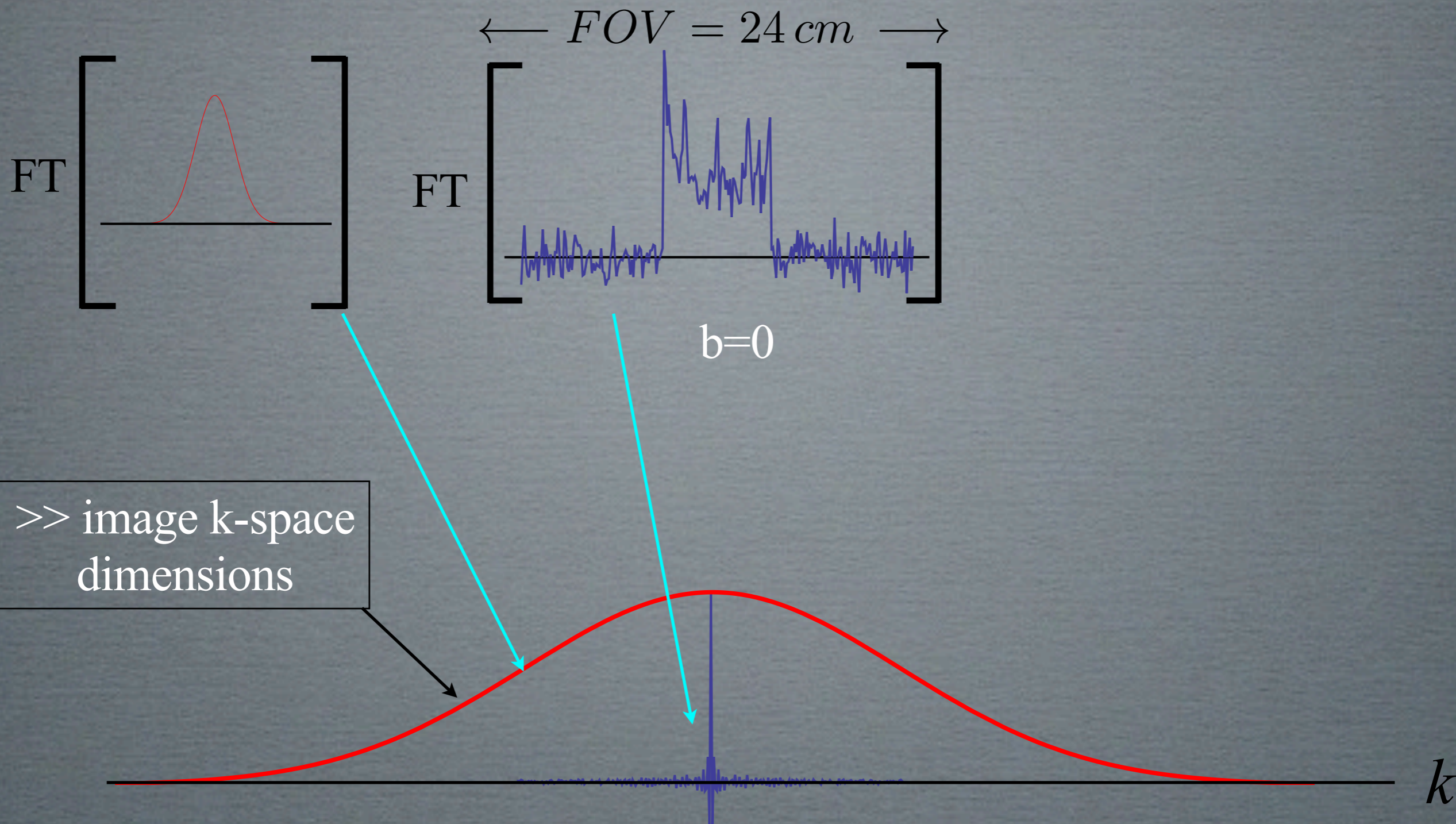


\gg image k-space dimensions



$$e^{-x^2 / D dt} \Leftrightarrow e^{-k^2 D dt}$$

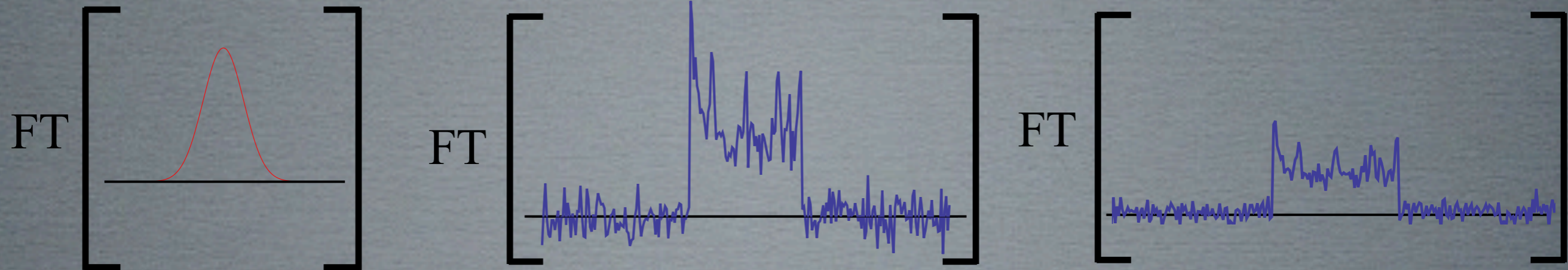
$\sigma \approx 15\mu m \ll$ voxel dimensions



$$e^{-x^2 / D dt} \Leftrightarrow e^{-k^2 D dt}$$

$\sigma \approx 15\mu m \ll$ voxel dimensions

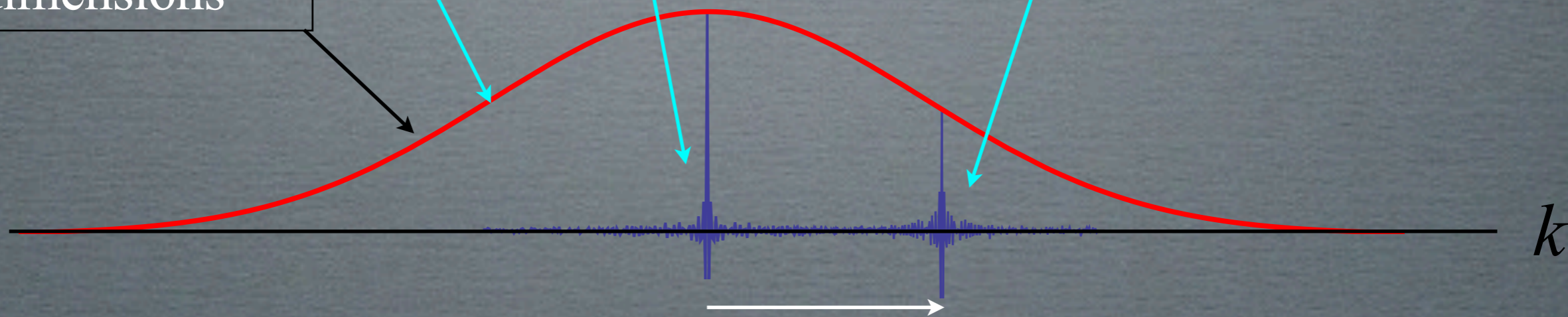
$\leftarrow FOV = 24\text{ cm} \rightarrow$



$b=0$

DWI

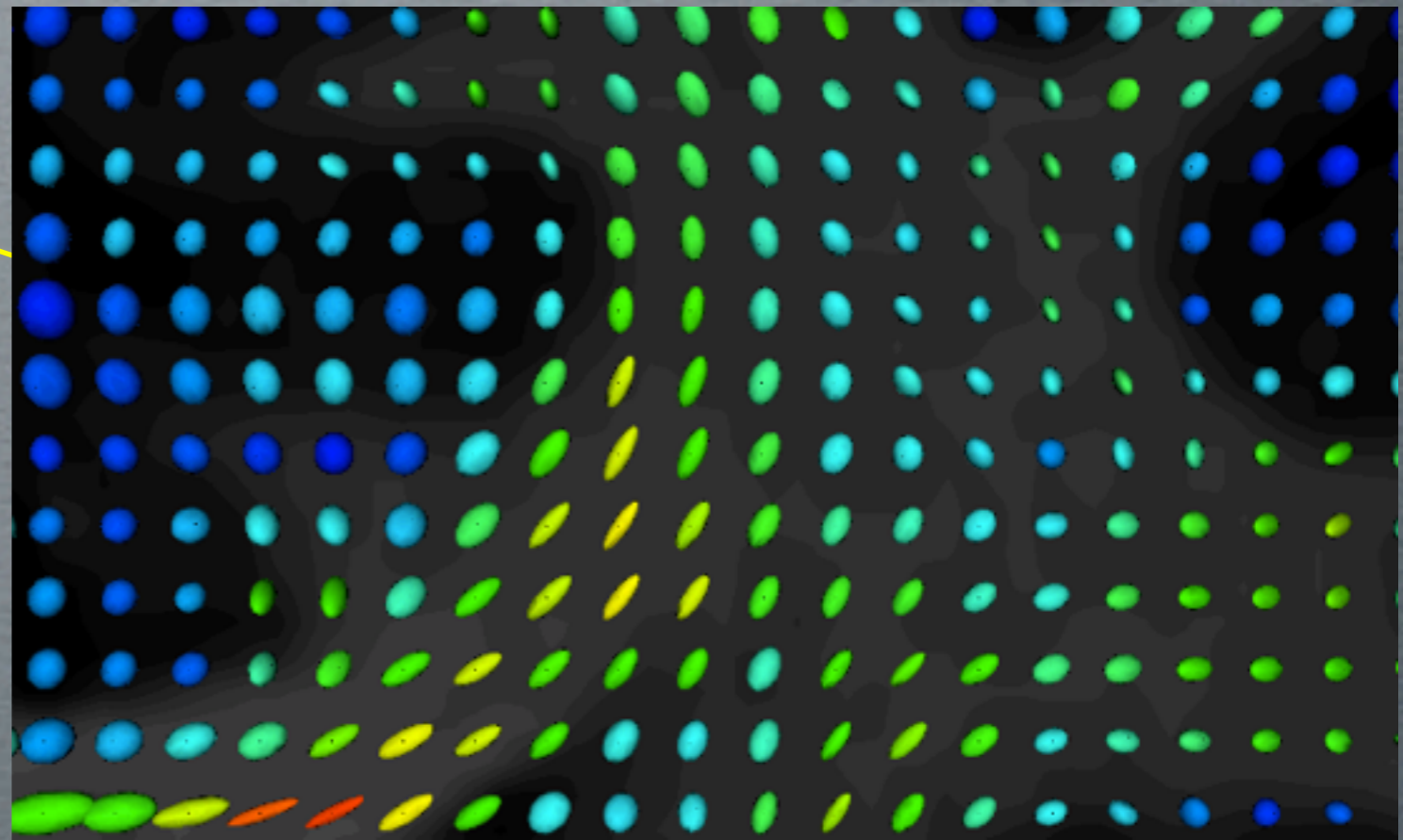
\gg image k-space dimensions



$$e^{-x^2 / D dt} \Leftrightarrow e^{-k^2 D dt}$$

DIFFUSION ELLIPSOID

DIFFUSION ELLIPSOID



diffusion ellipsoids

AVERAGE DIFFUSION IN A VOXEL

Three eigenvalues of D are the three principle mean-squared displacements along its three principal directions

$$D = \begin{pmatrix} \lambda_x & 0 & 0 \\ 0 & \lambda_y & 0 \\ 0 & 0 & \lambda_z \end{pmatrix}$$

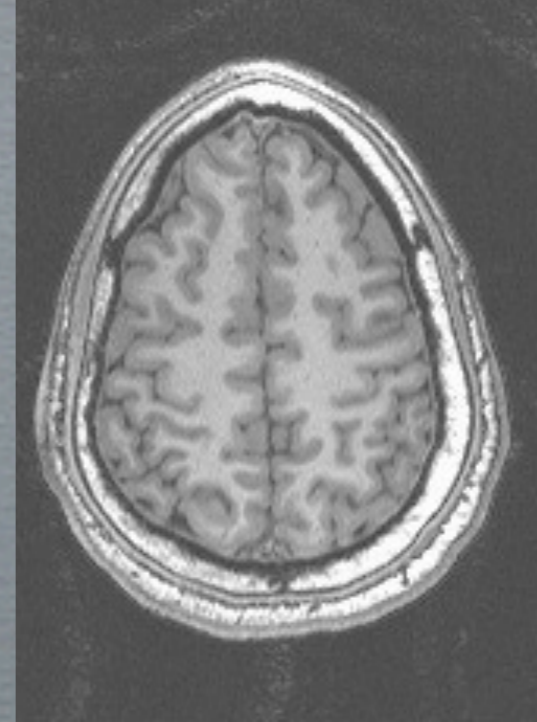
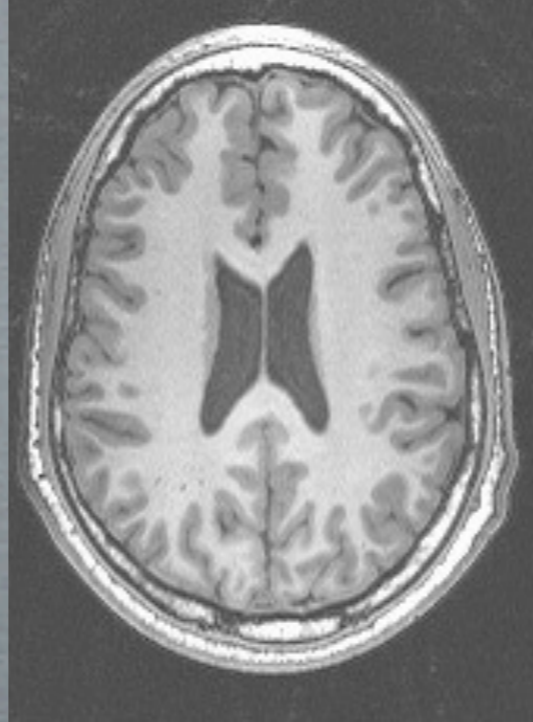
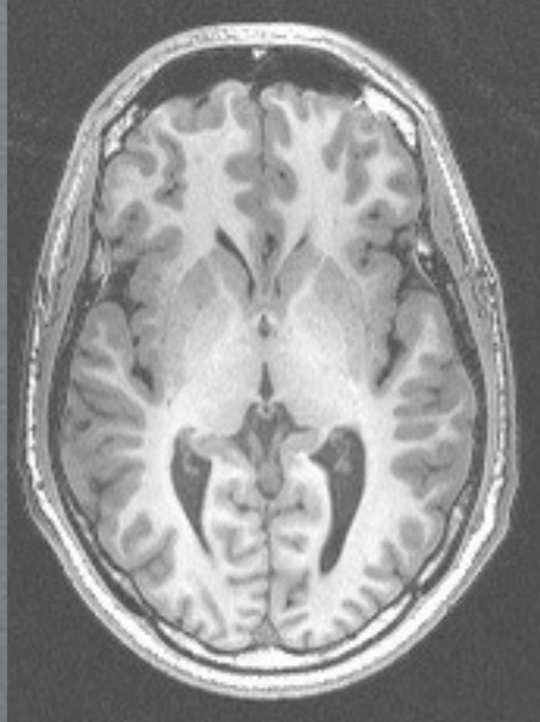
$$\begin{aligned} \langle D \rangle &= (\lambda_1 + \lambda_2 + \lambda_3) / 3 = \langle \lambda \rangle \\ &= \text{Tr}(D) \end{aligned}$$

Tr = Trace = sum of diagonal elements

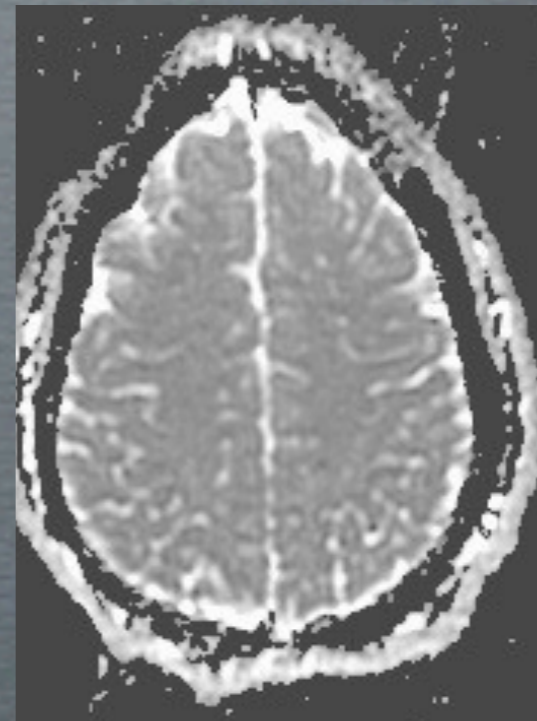
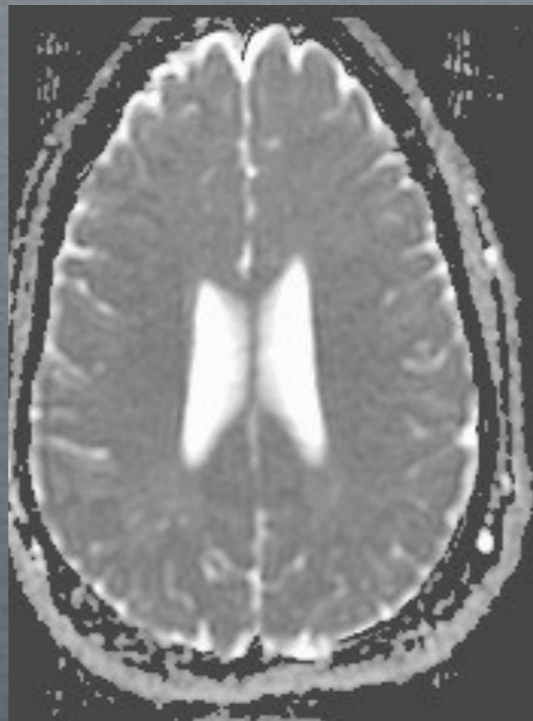
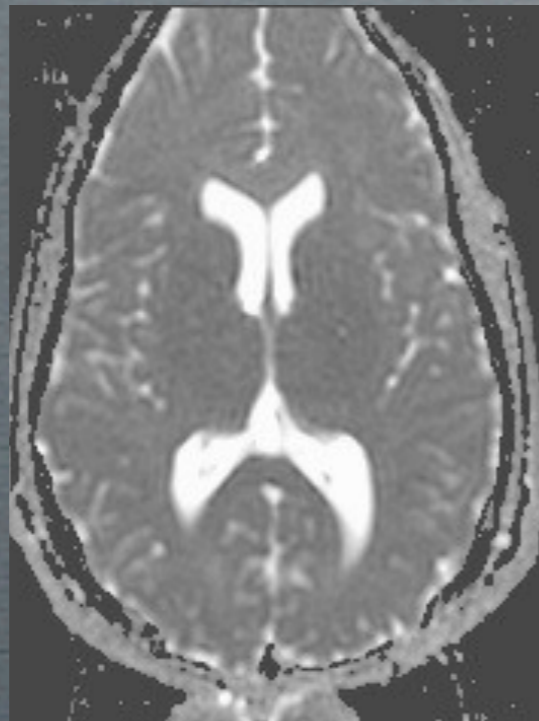
AVERAGE DIFFUSION IN A VOXEL

AVERAGE DIFFUSION IN A VOXEL

anatomical



mean D



DIFFUSION ANISOTROPY IN A VOXEL

One measure of diffusion anisotropy is the variance of the eigenvalues, normalized to the mean-squared eigenvalue

$$\text{anisotropy} \propto \frac{(\lambda_x - \bar{\lambda})^2 + (\lambda_y - \bar{\lambda})^2 + (\lambda_z - \bar{\lambda})^2}{\bar{\lambda}^2}$$

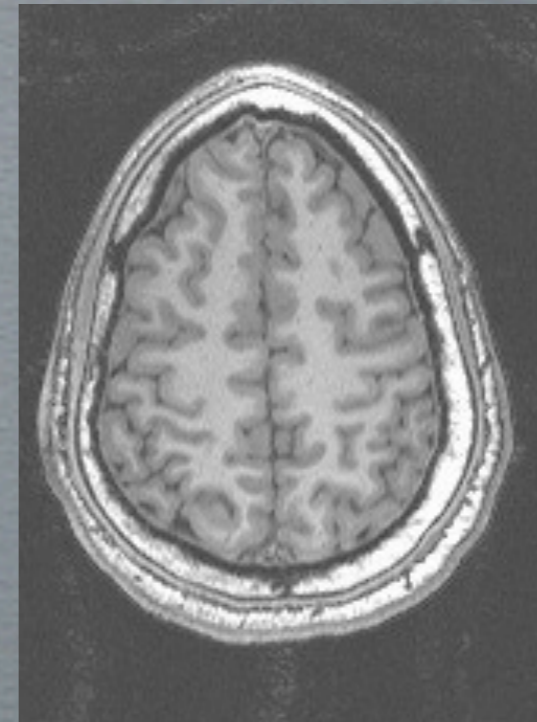
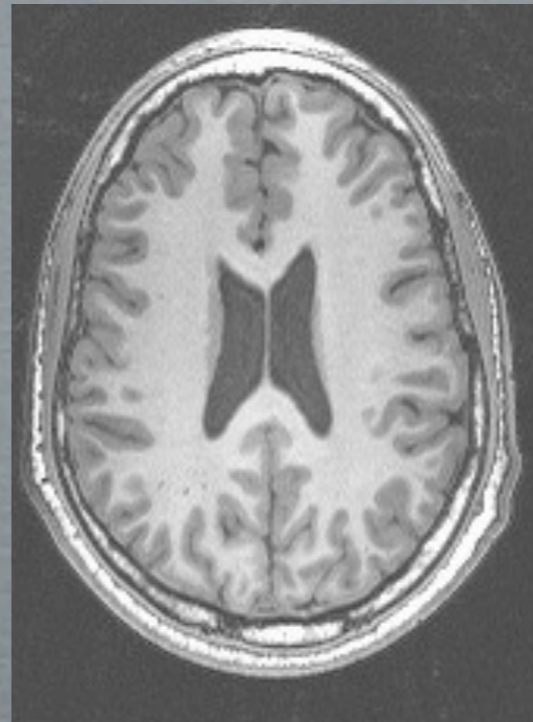
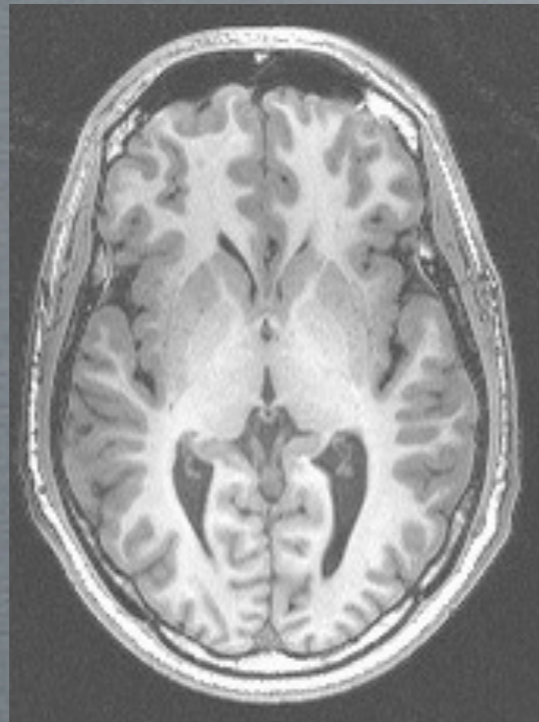
Fractional Anisotropy

$$FA \equiv \sqrt{\frac{3 \sigma_{\lambda}^2}{2 \bar{\lambda}^2}}$$

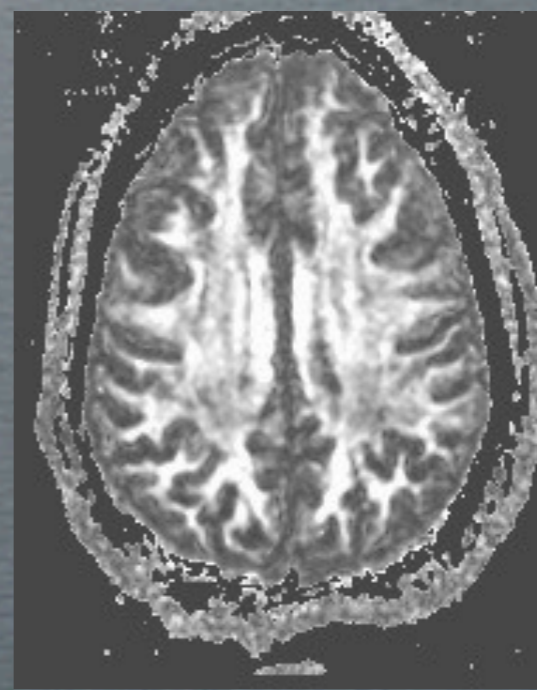
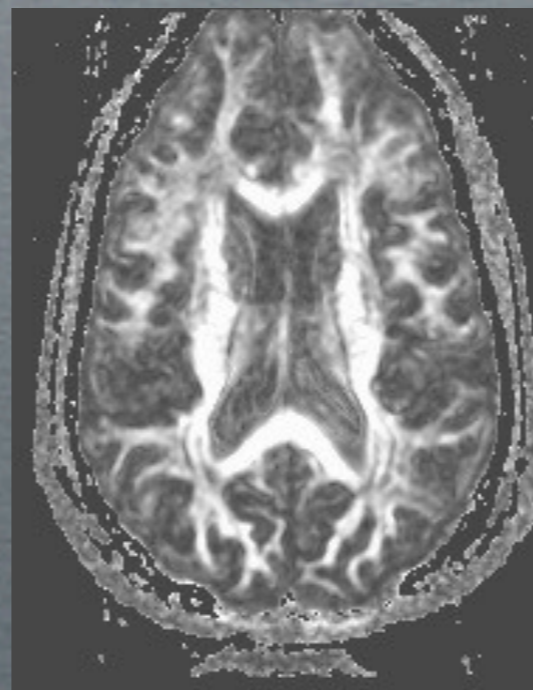
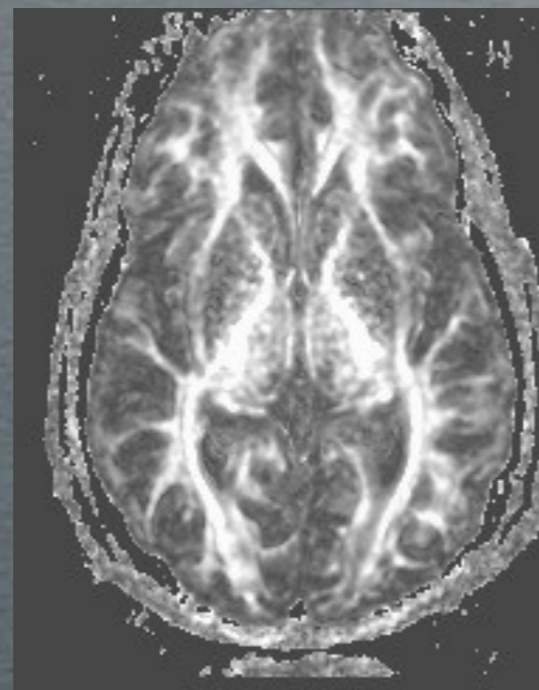
DIFFUSION ANISOTROPY IN A VOXEL

DIFFUSION ANISOTROPY IN A VOXEL

anatomical

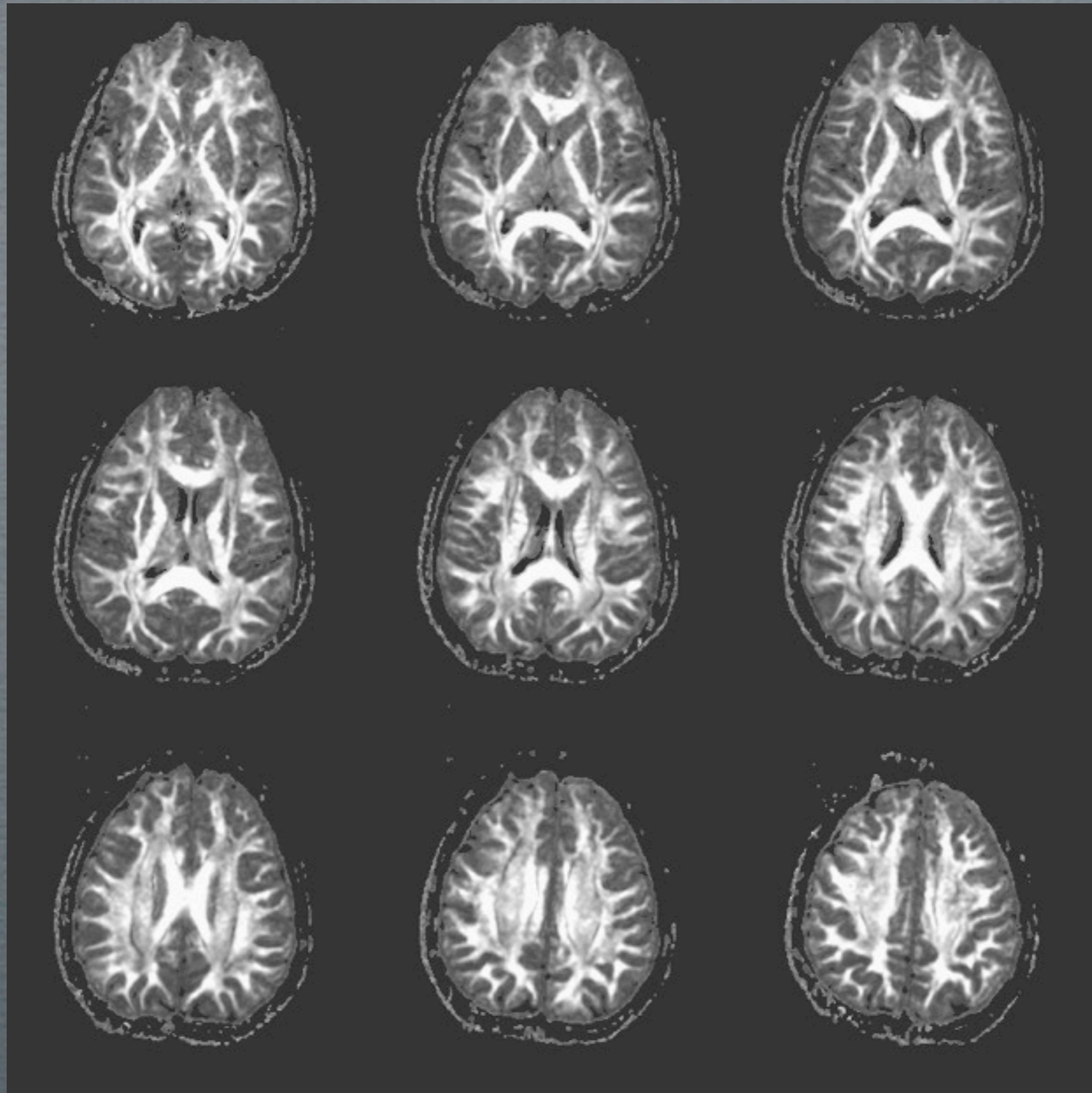


FA

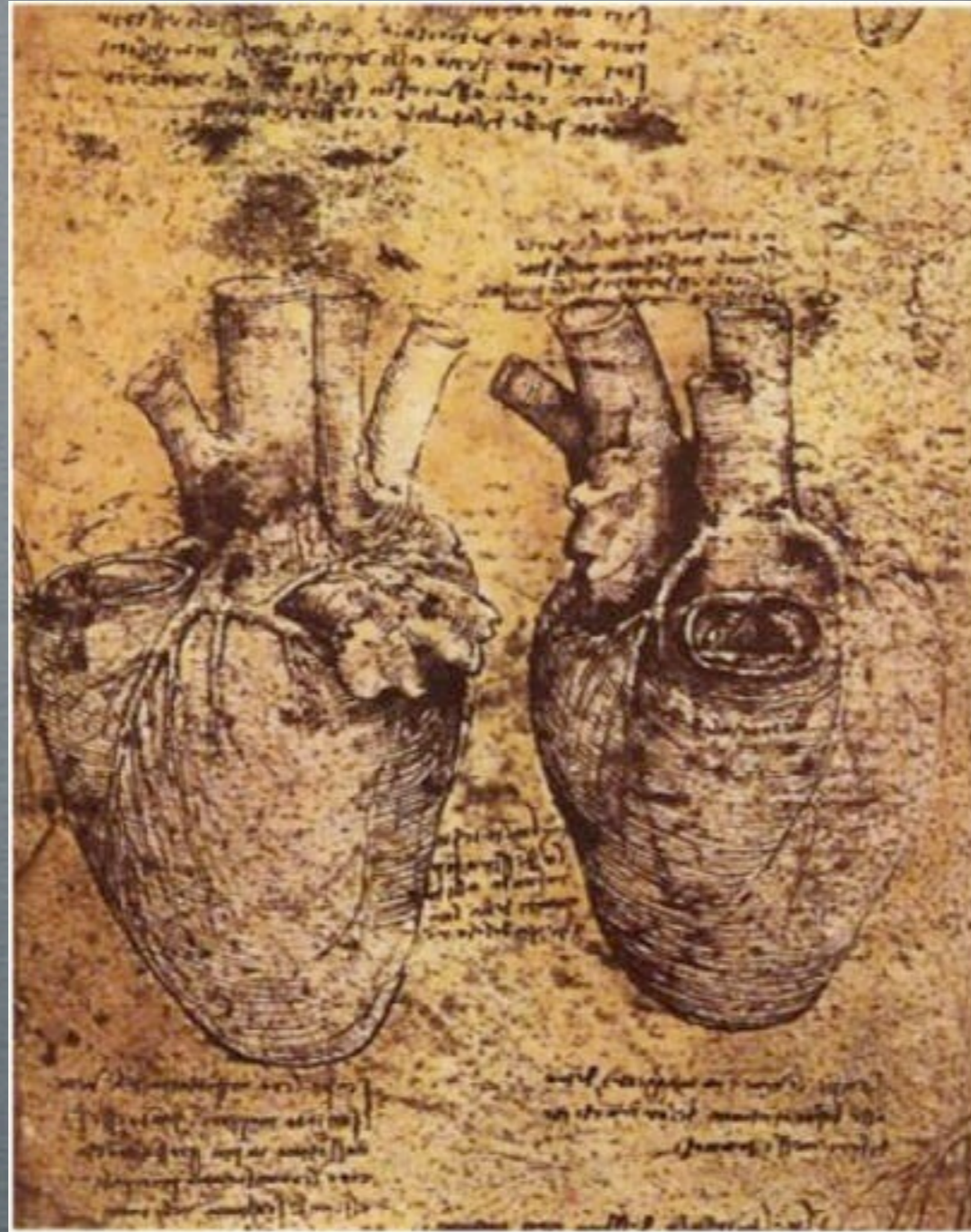


DIFFUSION ANISOTROPY

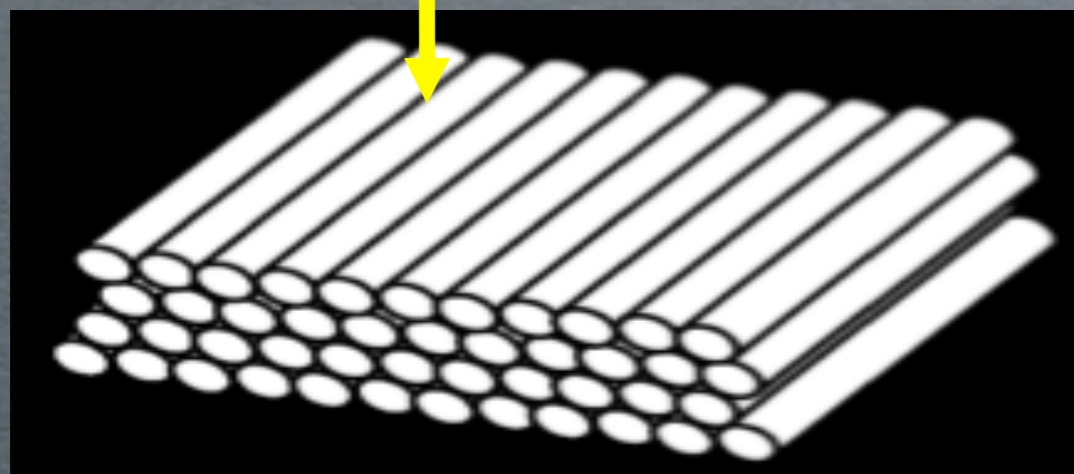
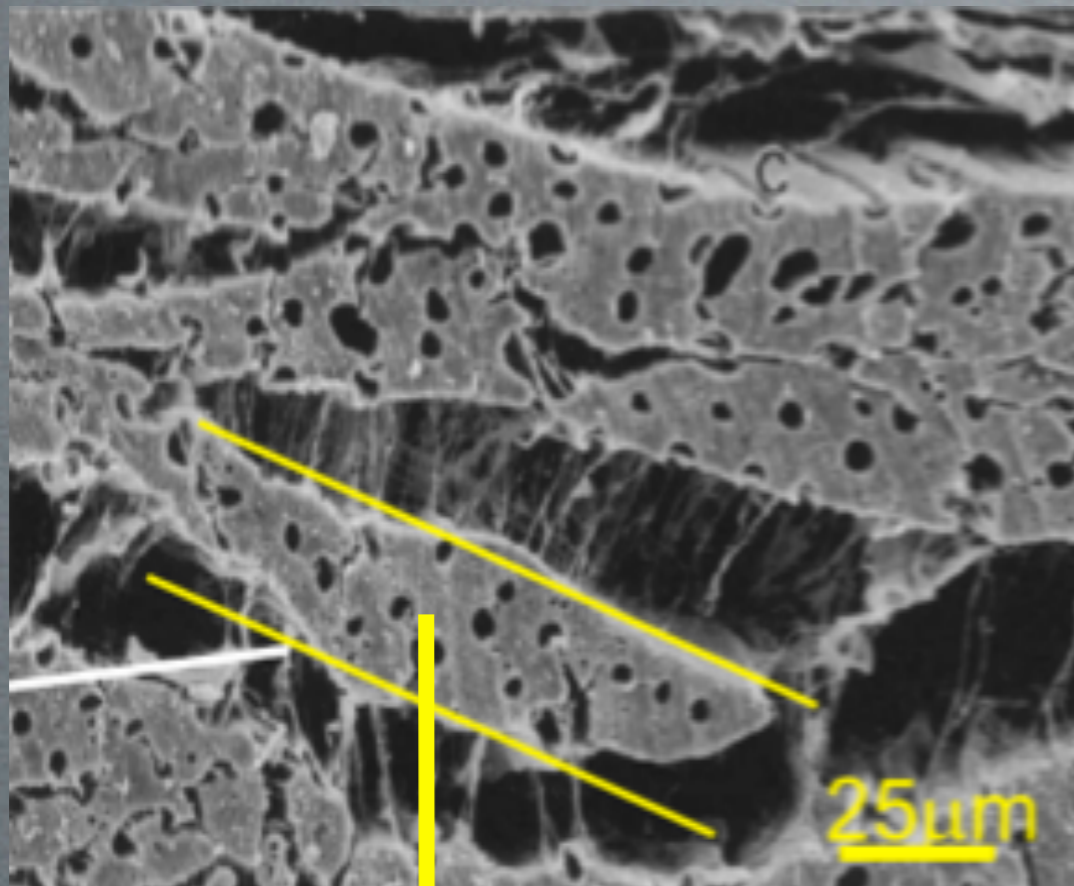
DIFFUSION ANISOTROPY



THE USES OF ANISOTROPY: CARDIAC MECHANICS

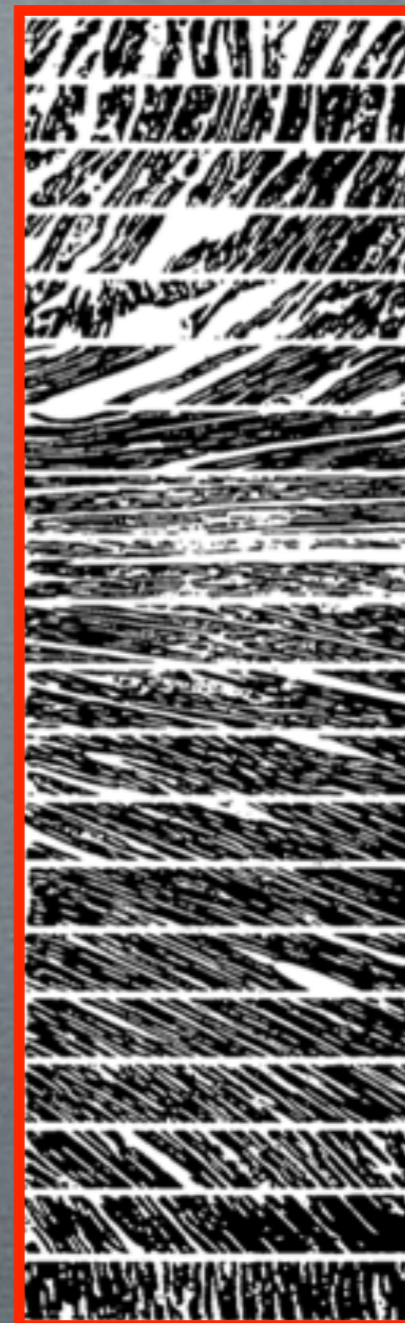


THE USES OF ANISOTROPY: CARDIAC MECHANICS



Legrice et al. 1994

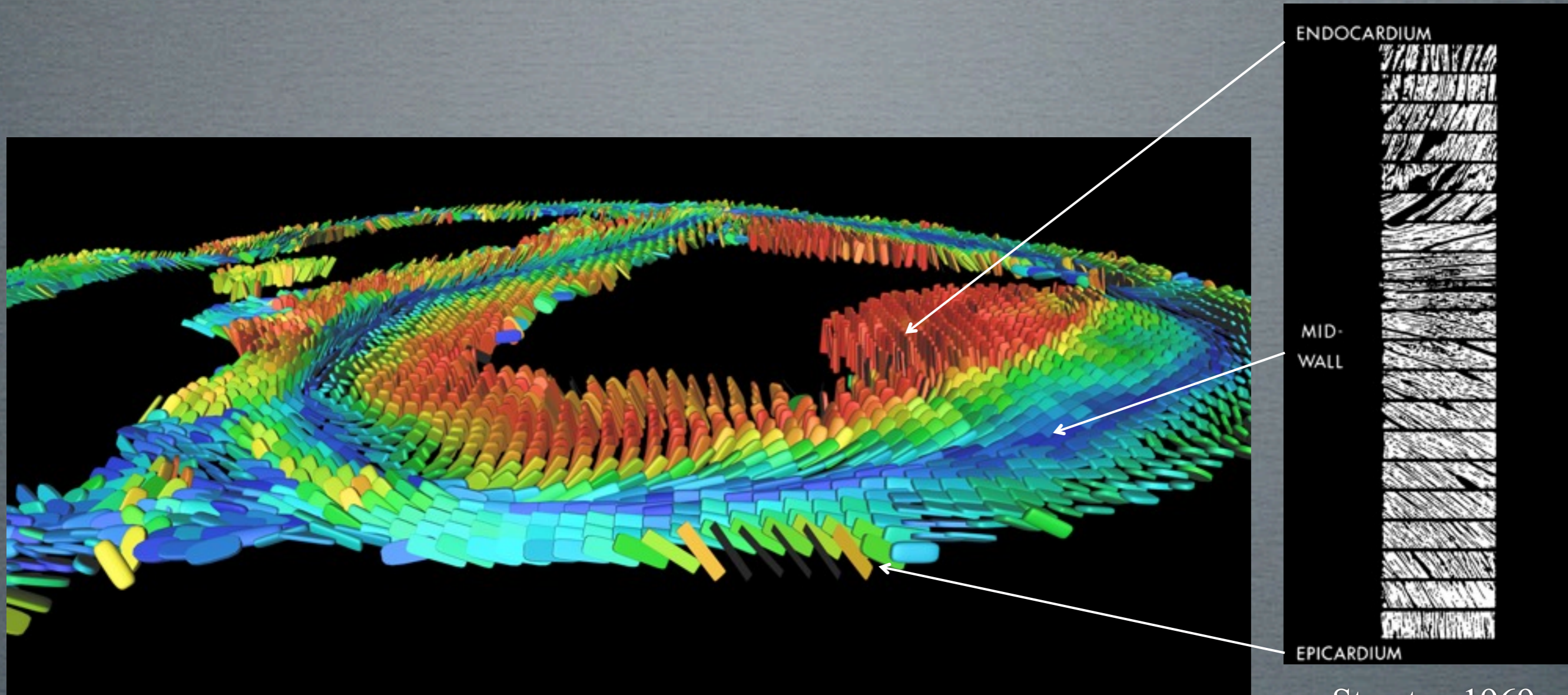
Endocardium



Epicardium

Streeter et al. 1969

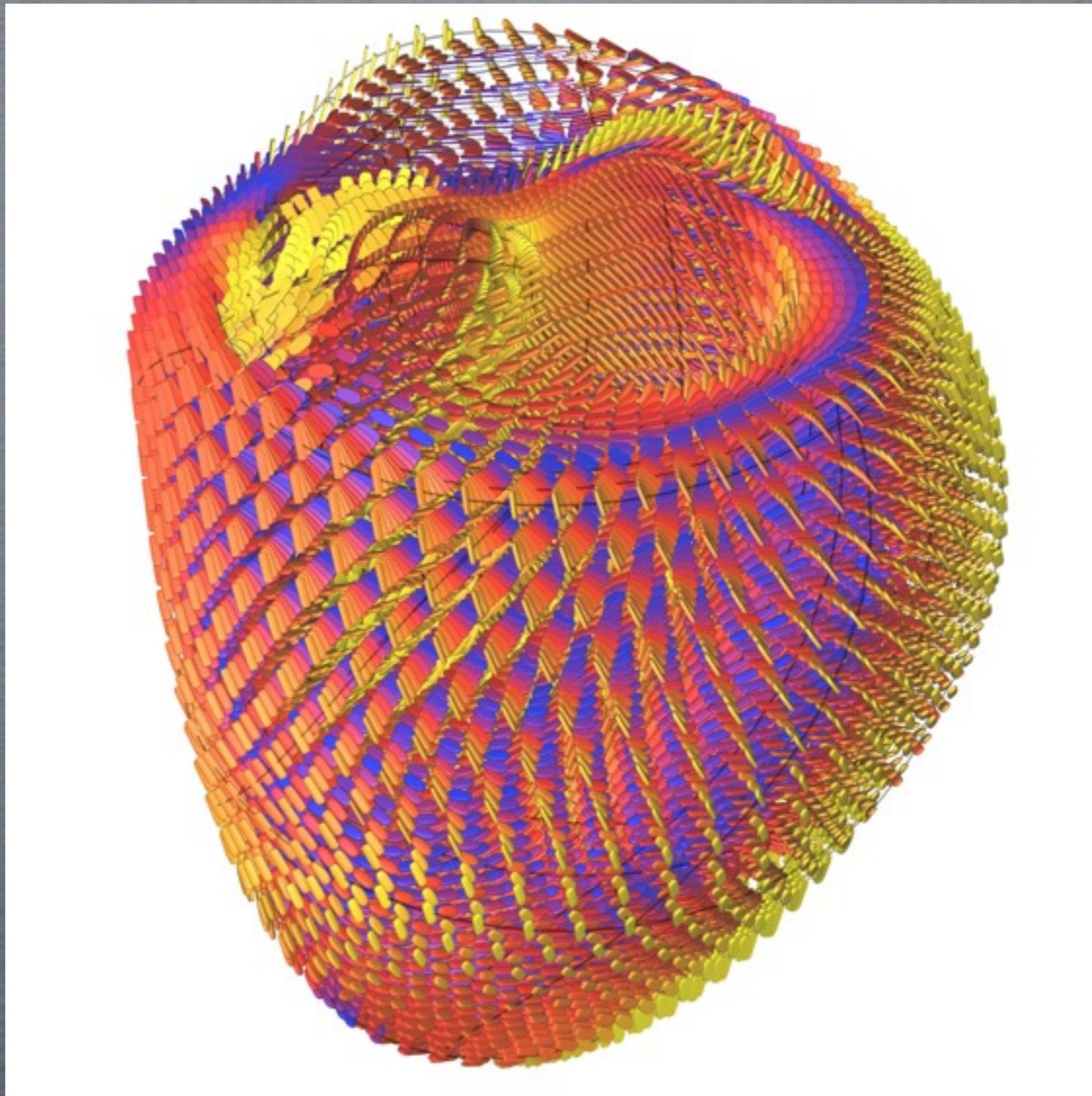
THE USES OF ANISOTROPY: CARDIAC MECHANICS



Streeter, 1969

Excised canine heart (Howard, UCSD Cardiac Biomechanics Group 2011) using
3D Spiral FSE DTI sequence (Frank et al, Neuroimage 2010)

THE USES OF ANISOTROPY: CARDIAC MECHANICS

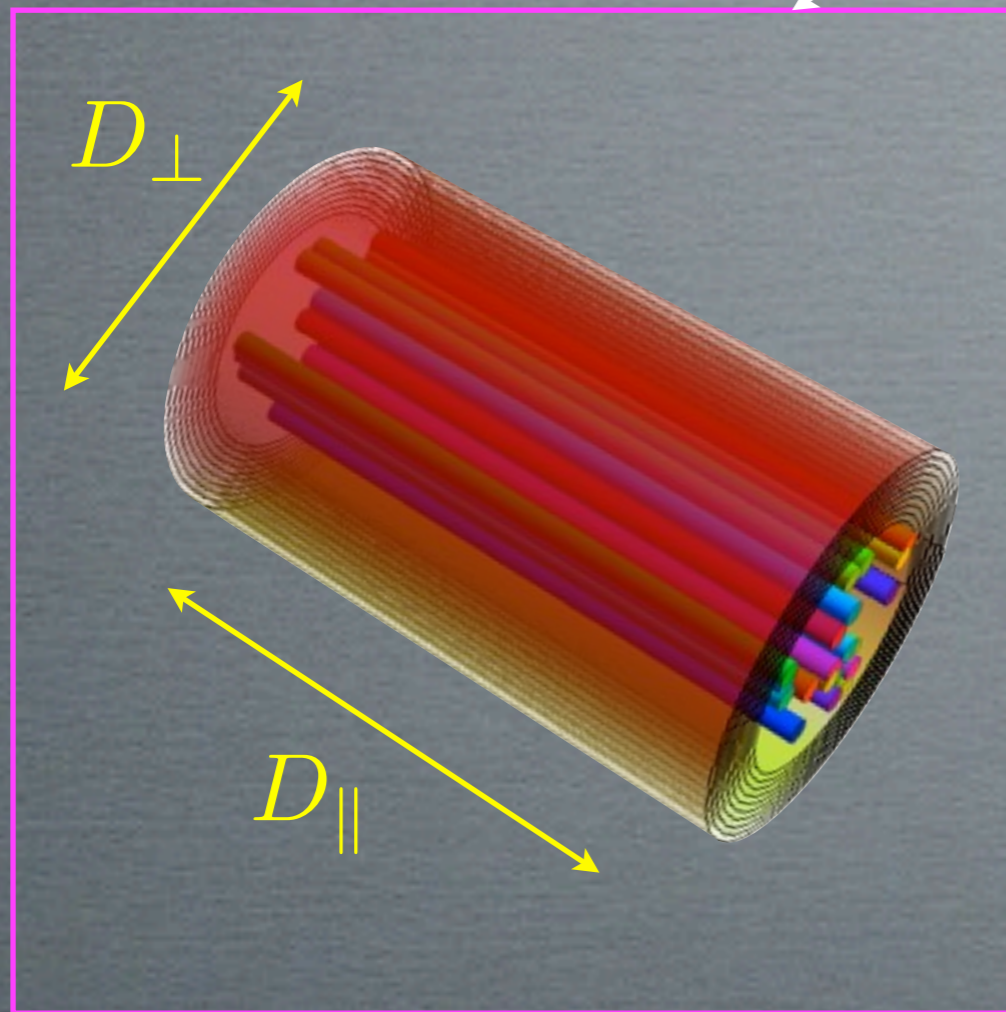


Our first whole human heart DTI (ex vivo)

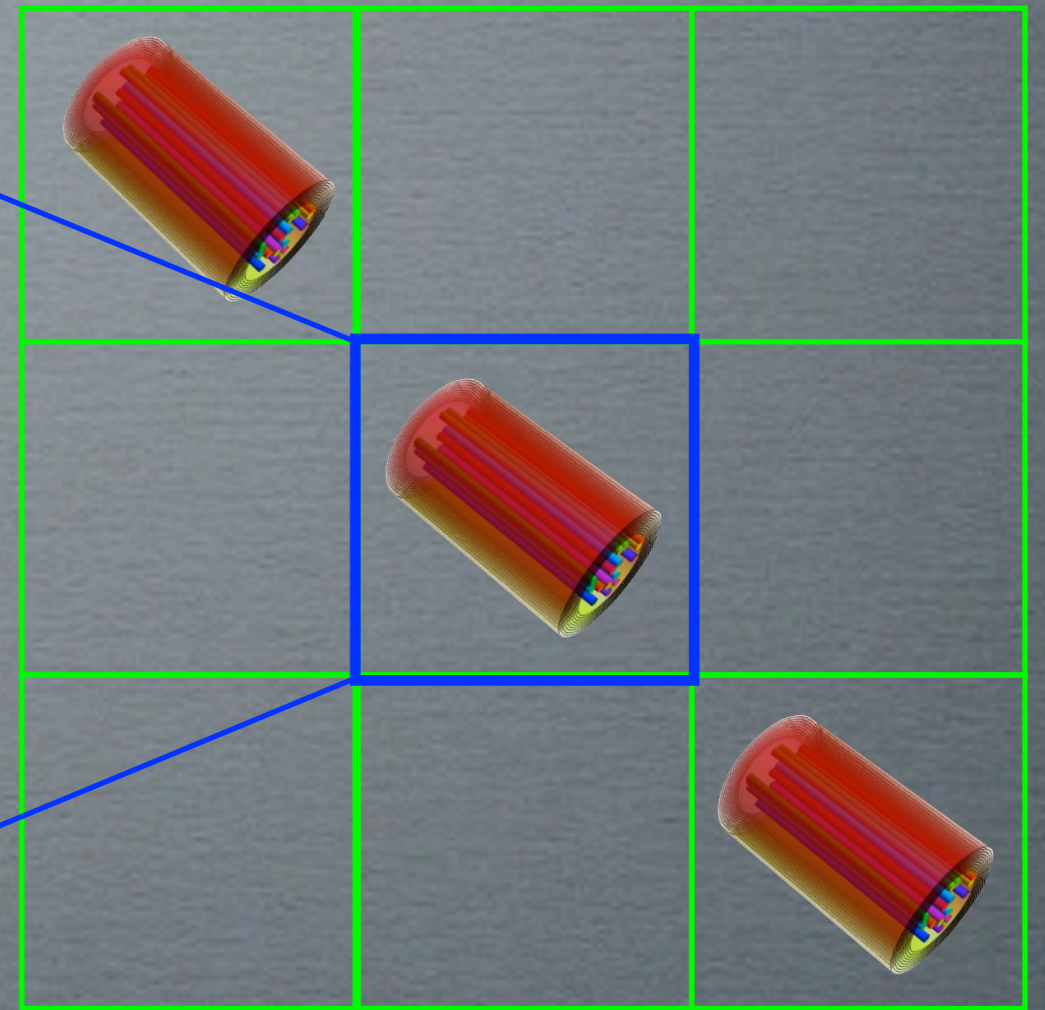
FROM LOCAL (VOXEL) ANISOTROPY TO EXTENDED SPATIALLY COHERENT ANISOTROPY: TRACTOGRAPHY

FROM LOCAL (VOXEL) ANISOTROPY TO EXTENDED SPATIALLY COHERENT ANISOTROPY: TRACTOGRAPHY

Local Anisotropy voxel



Local/Global Coherence



$$D_{\parallel} \approx 3D_{\perp}$$

$$(1.2\mu^2/ms) \quad (0.4\mu^2/ms)$$

STREAMLINES

STREAMLINES

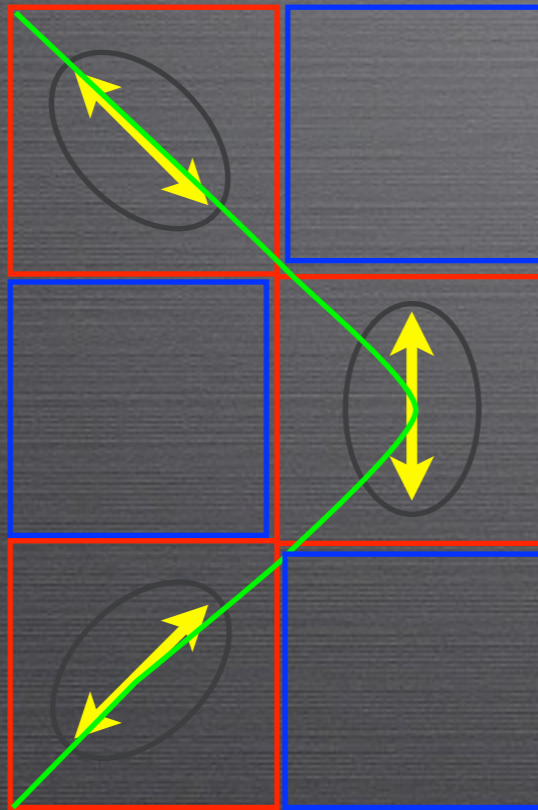
Anisotropy

high



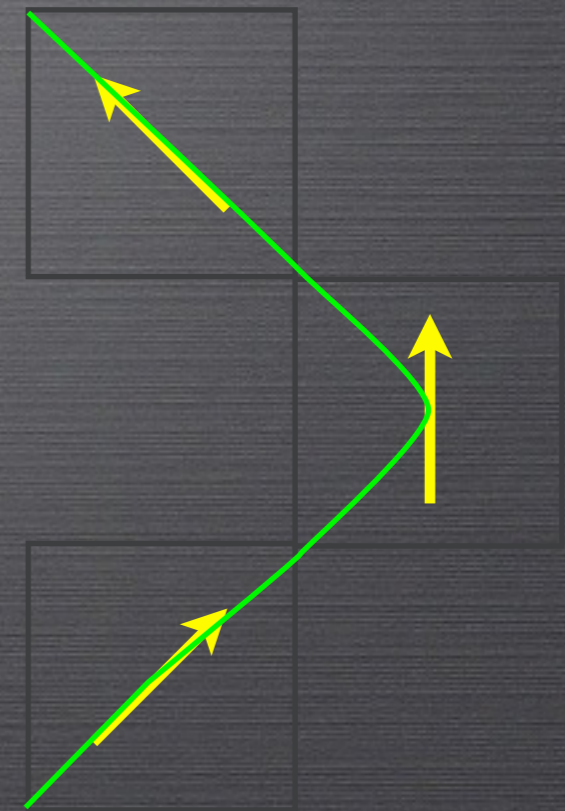
low

Estimated orientation



analogy

Flow vector field

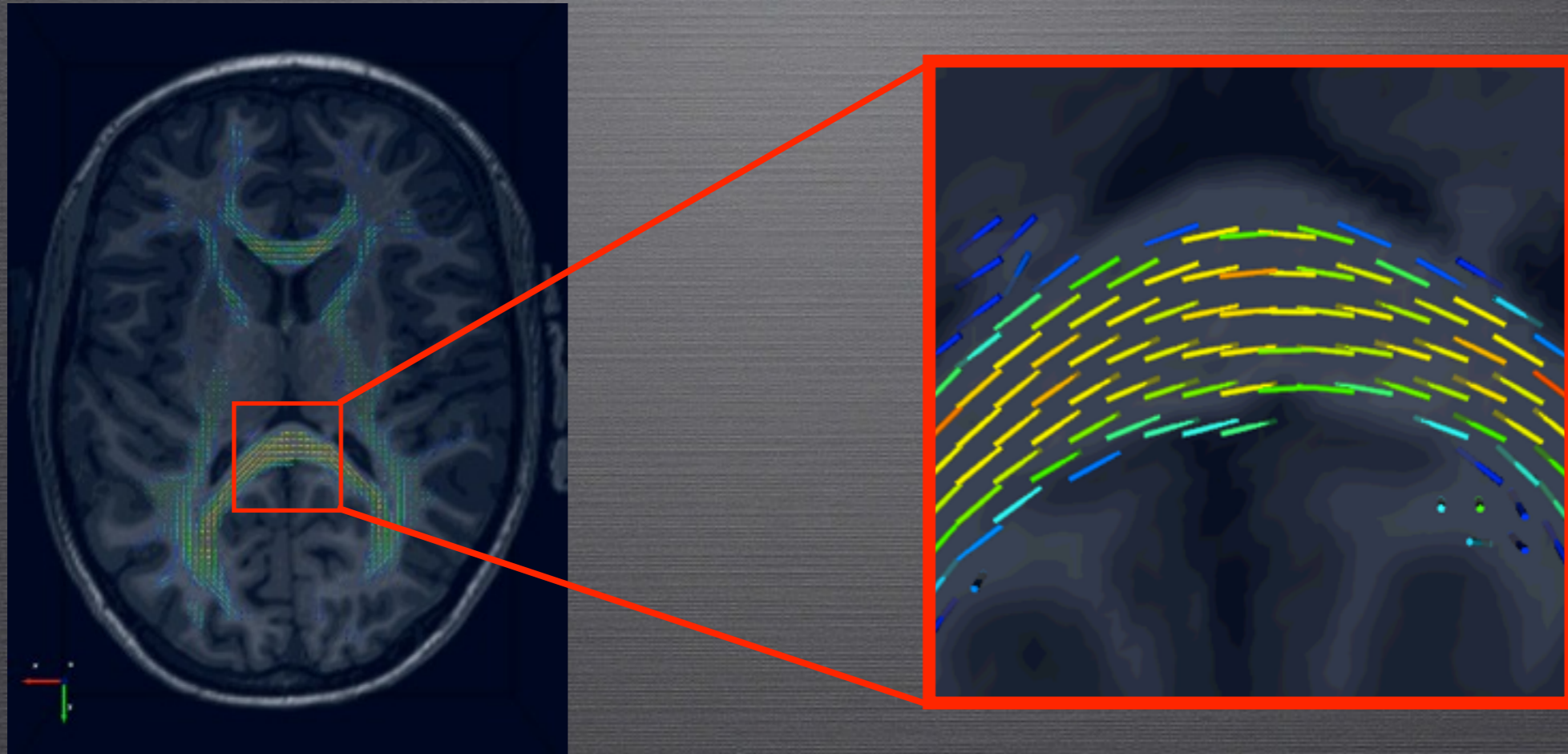


(principal eigenvector)

WHAT WE EXPECT OF DIFFUSION IMAGING

WHAT WE EXPECT OF DIFFUSION IMAGING

Some information about the microscopic structure



For voxels with aligned fibers (as in the corpus callosum)...

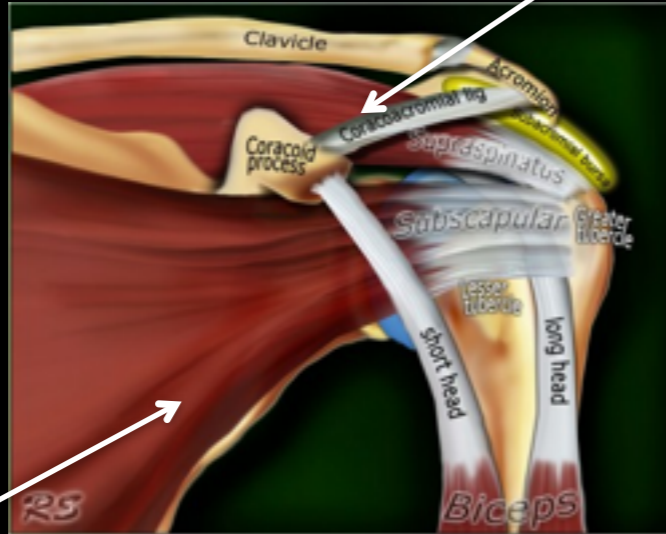
...the primary diffusion direction should be oriented in the same direction as the fiber.

**A. RODRIGUES-SOTO,
WARD GROUP**

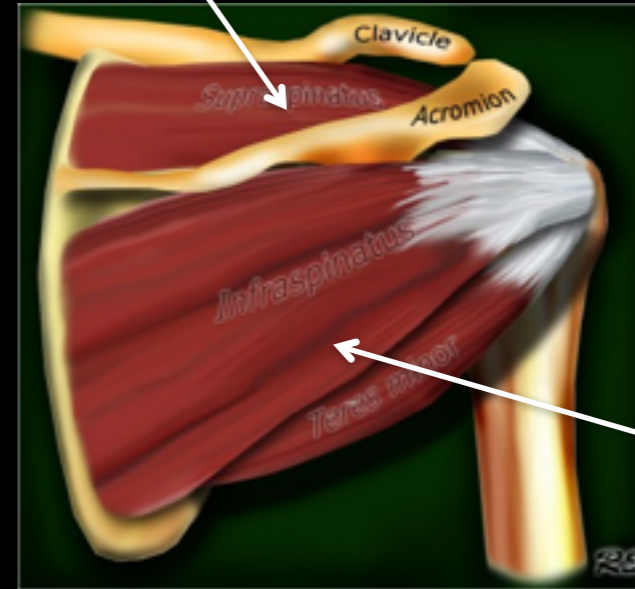
Supraspinatus DTI

Supraspinatus

Anterior



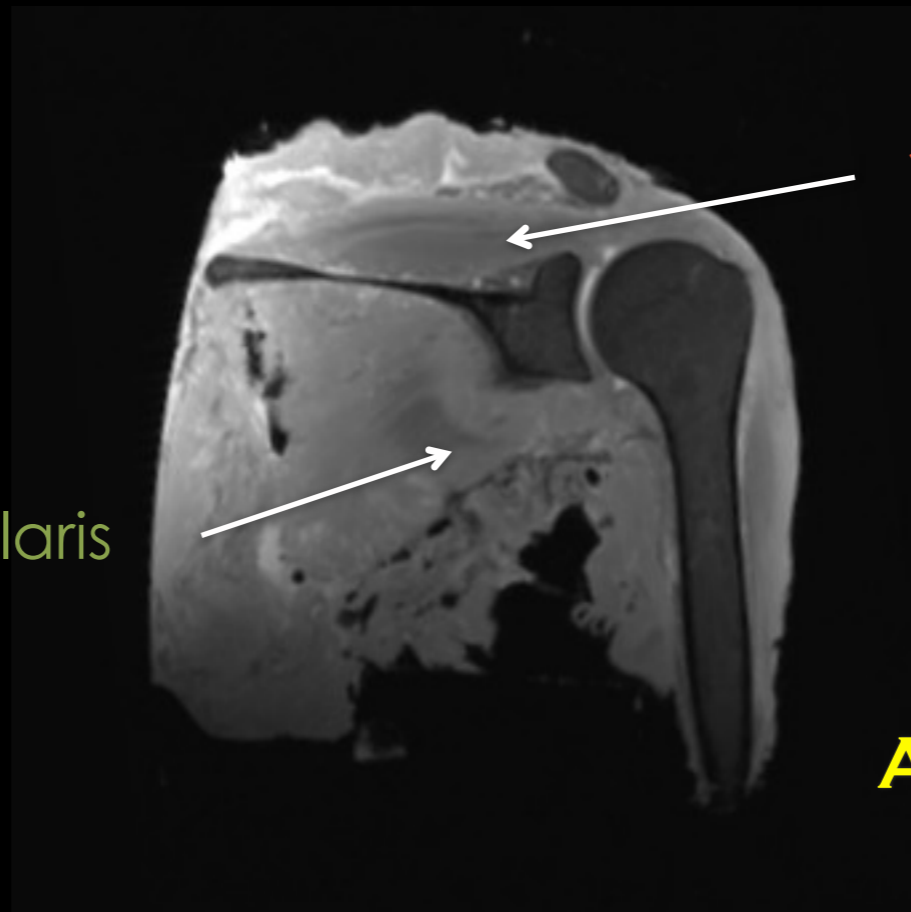
Posterior



Infraspinatus + Teres Minor

Subscapularis

Subscapularis



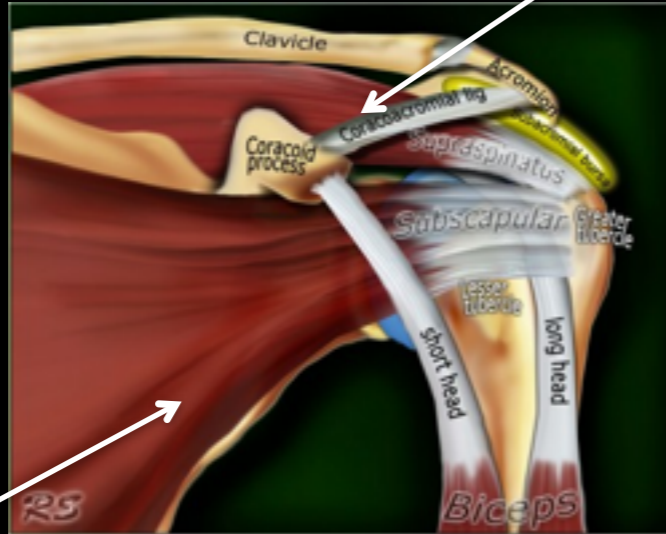
Supraspinatus

**A. RODRIGUES-SOTO,
WARD GROUP**

Supraspinatus DTI

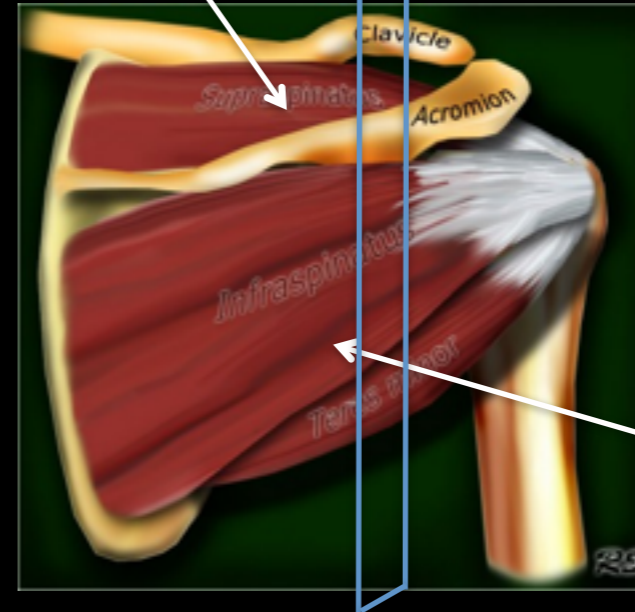
Supraspinatus

Anterior

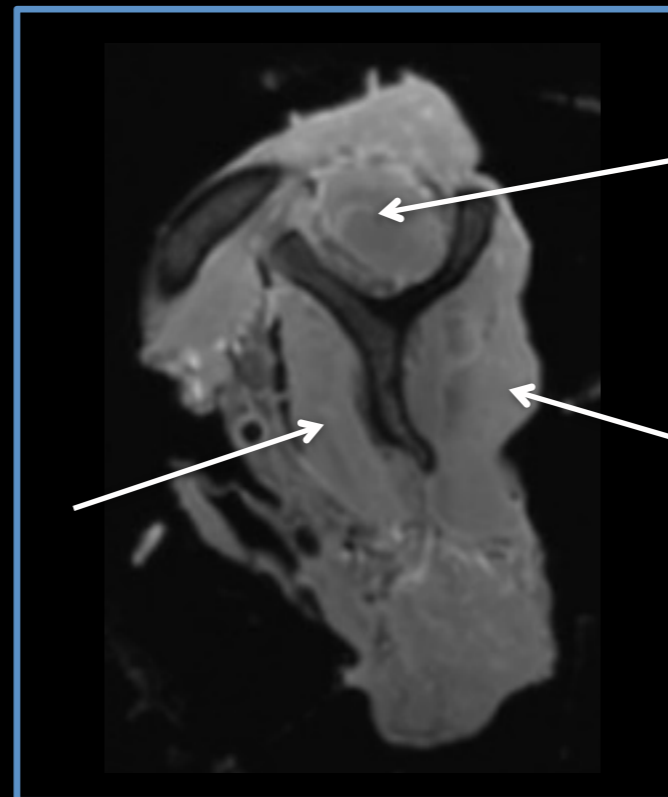


Subscapularis

Posterior



Infraspinatus + Teres Minor



Supraspinatus

Subscapularis

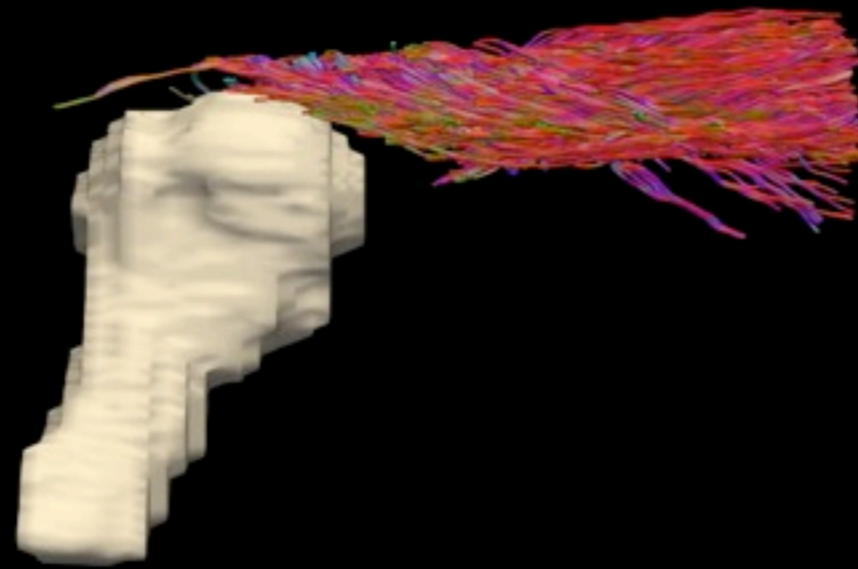
Infraspinatus

**A. RODRIGUES-SOTO,
WARD GROUP**

Supraspinatus Tractography @60 directions

**A. RODRIGUES-SOTO,
WARD GROUP**

Supraspinatus Tractography @60 directions



**A. RODRIGUES-SOTO,
WARD GROUP**

P

Supraspinatus Tractography @60 directions

**A. RODRIGUES-SOTO,
WARD GROUP**

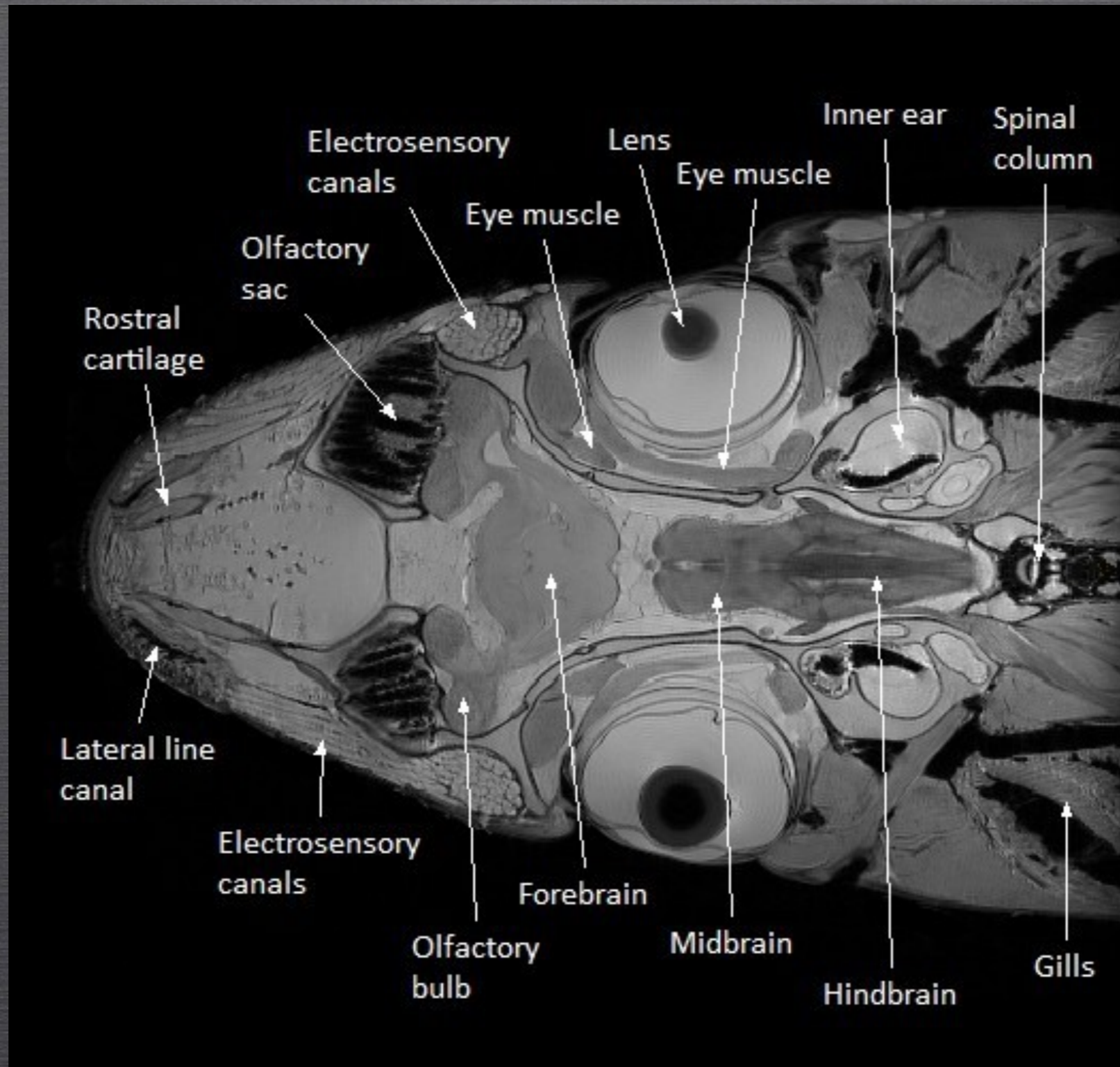
WHAT IS THE NEURAL STRUCTURE OF ELASMOBRANCHS?

WHAT IS THE NEURAL STRUCTURE OF ELASMOBRANCHS?



Mustelus henlei

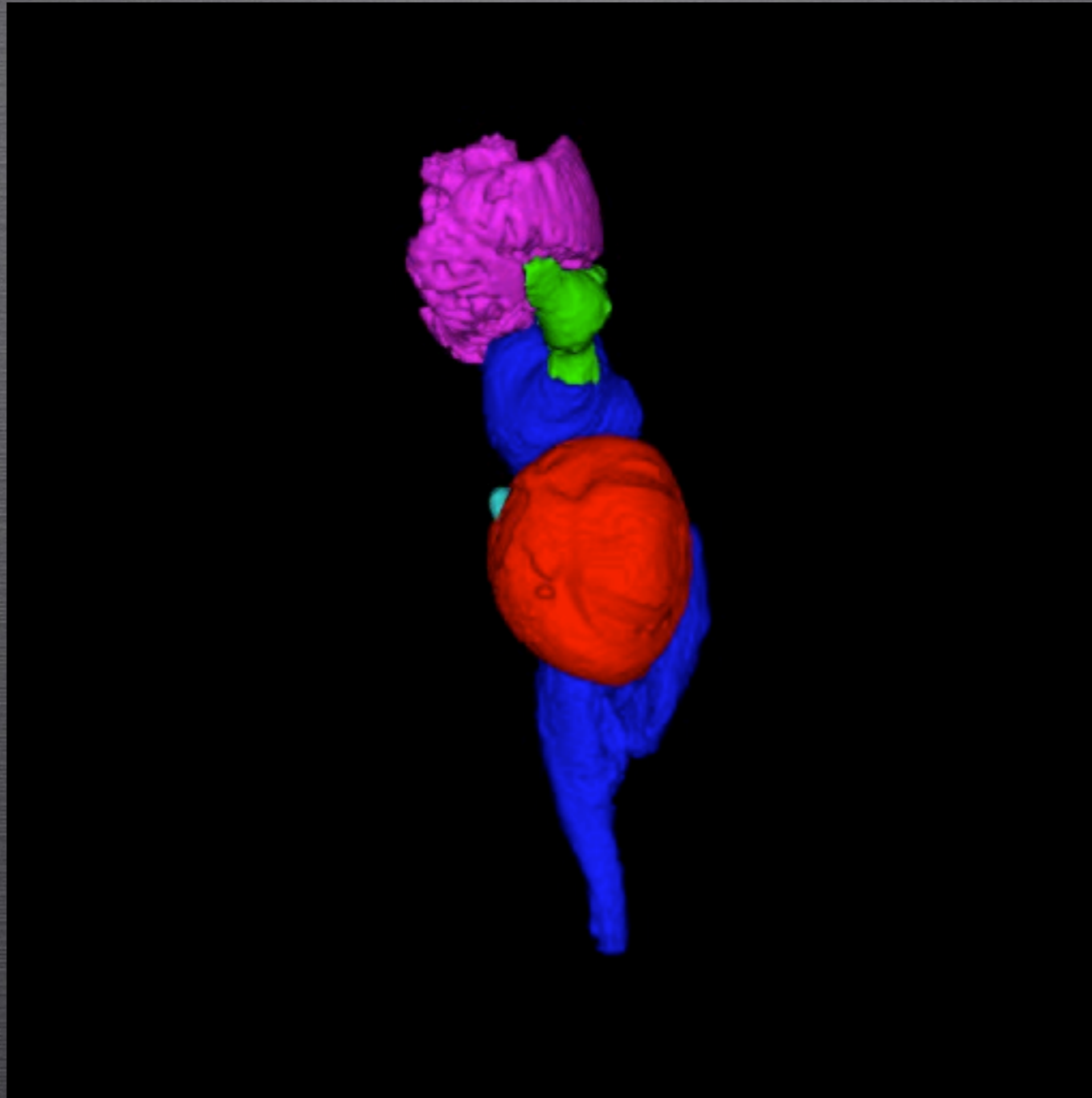
WHAT IS THE NEURAL STRUCTURE OF ELASMOBRANCHS?



Mustelus henlei

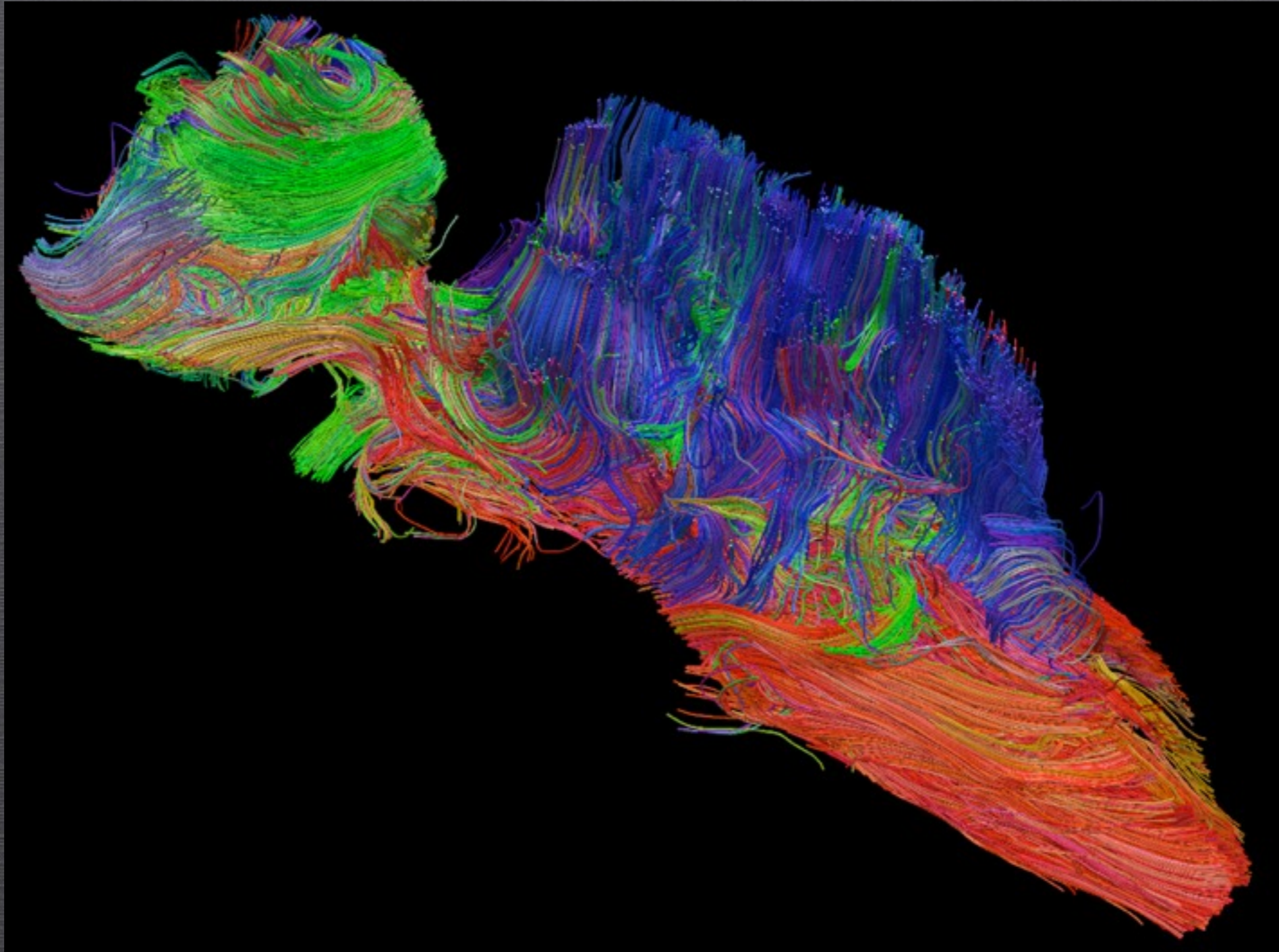
Data: M. Tyszka, CalTech
R. Berquist, CSCI

WHAT IS THE NEURAL STRUCTURE OF ELASMOBRANCHS?



Segmentation: K. Yopak, CSCI

WHAT IS THE NEURAL STRUCTURE OF ELASMOBRANCHS?

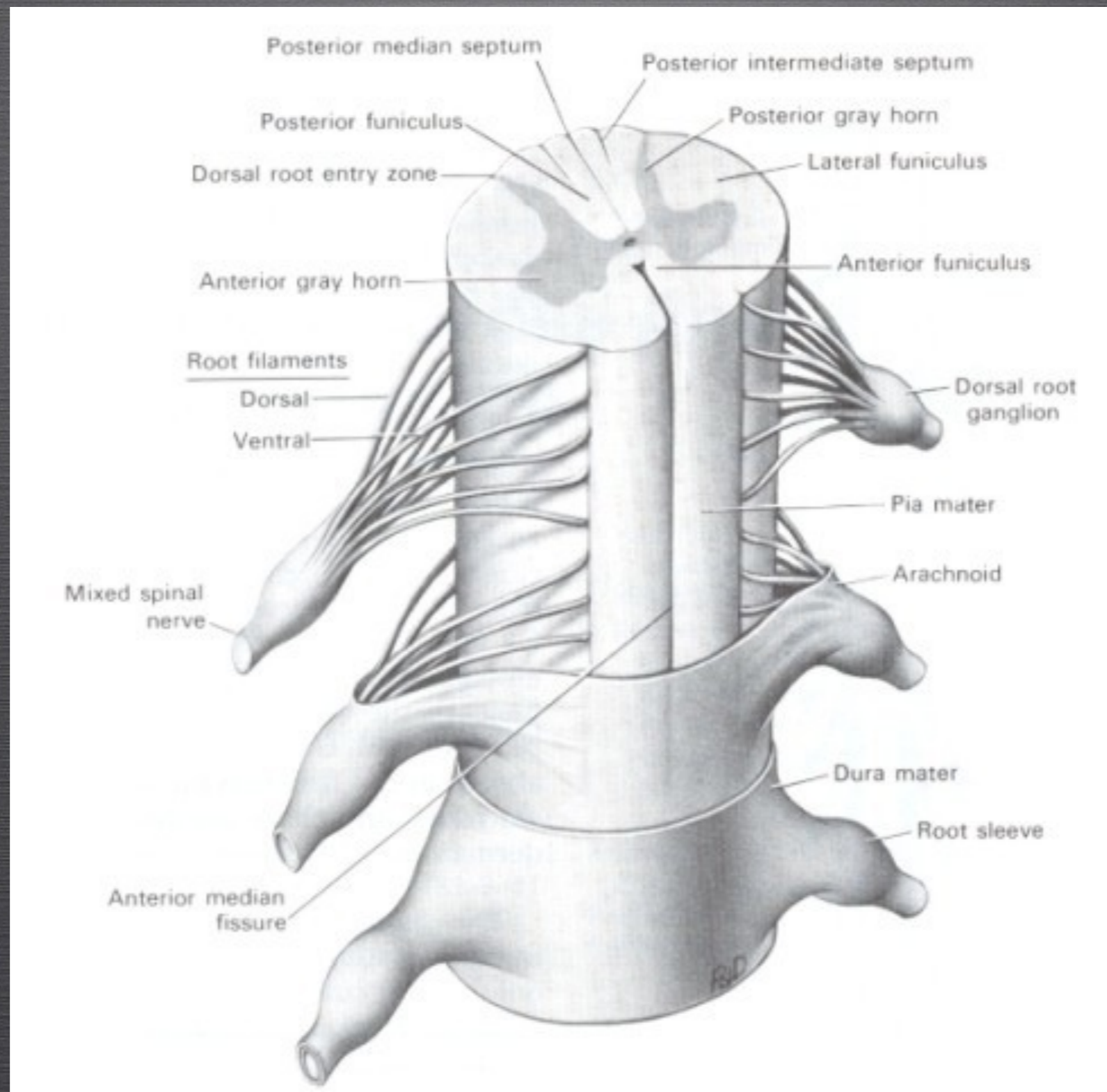


DTI @ 11.7T

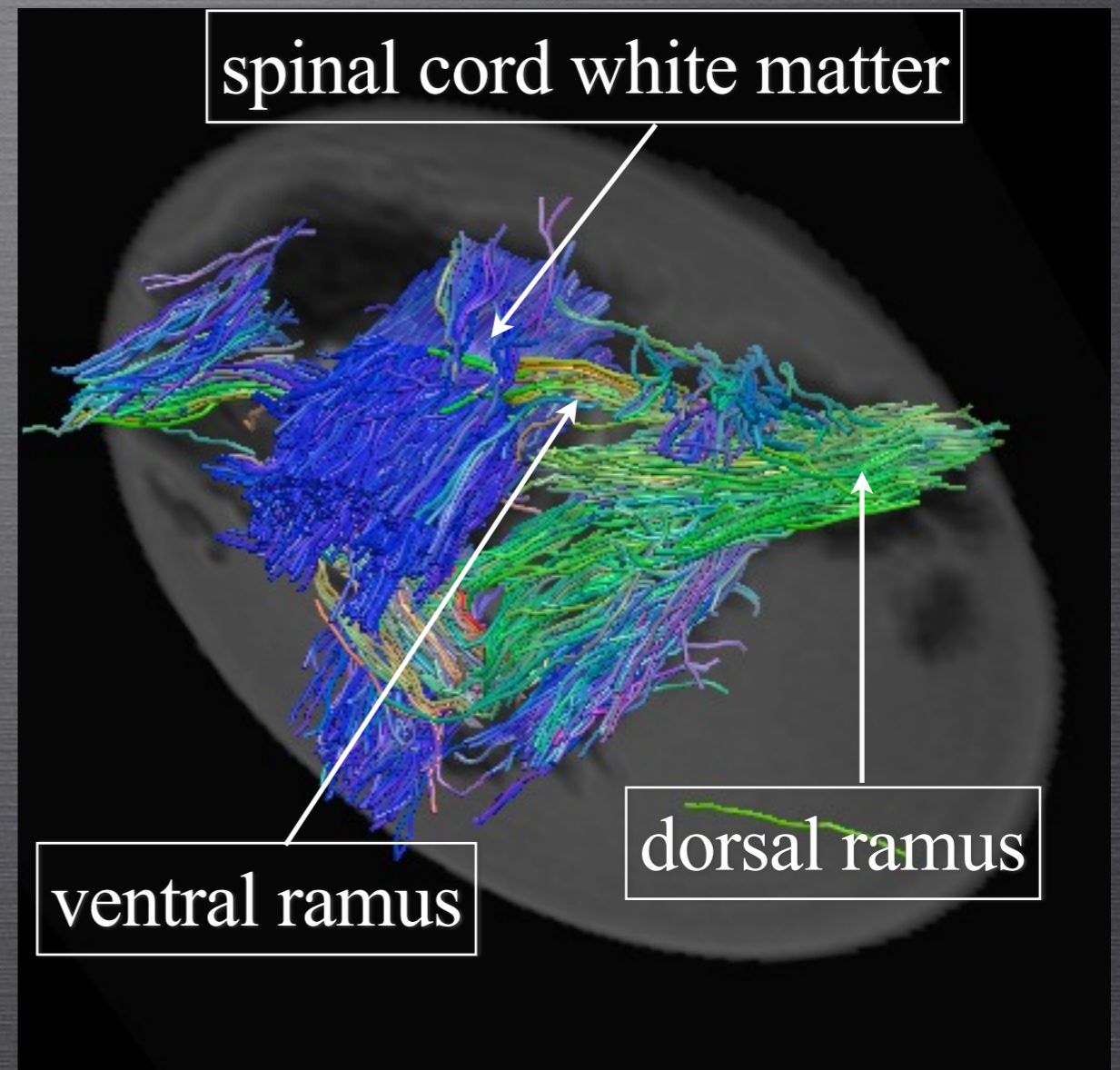
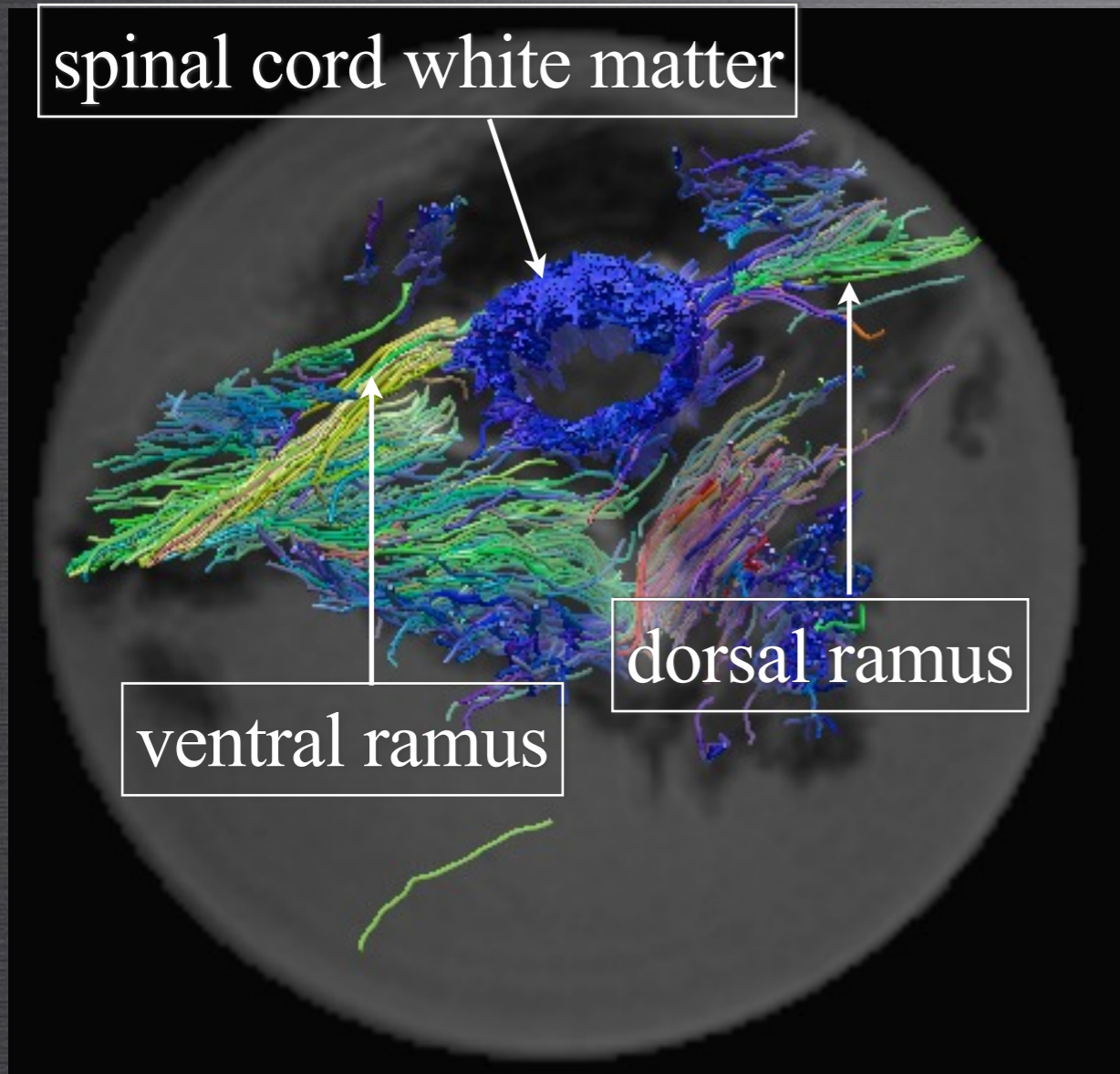
Data: M. Tyszka, CalTech
R. Berquist, CSCI

SPINAL CORD INJURY (RAT MODEL AT 7T)

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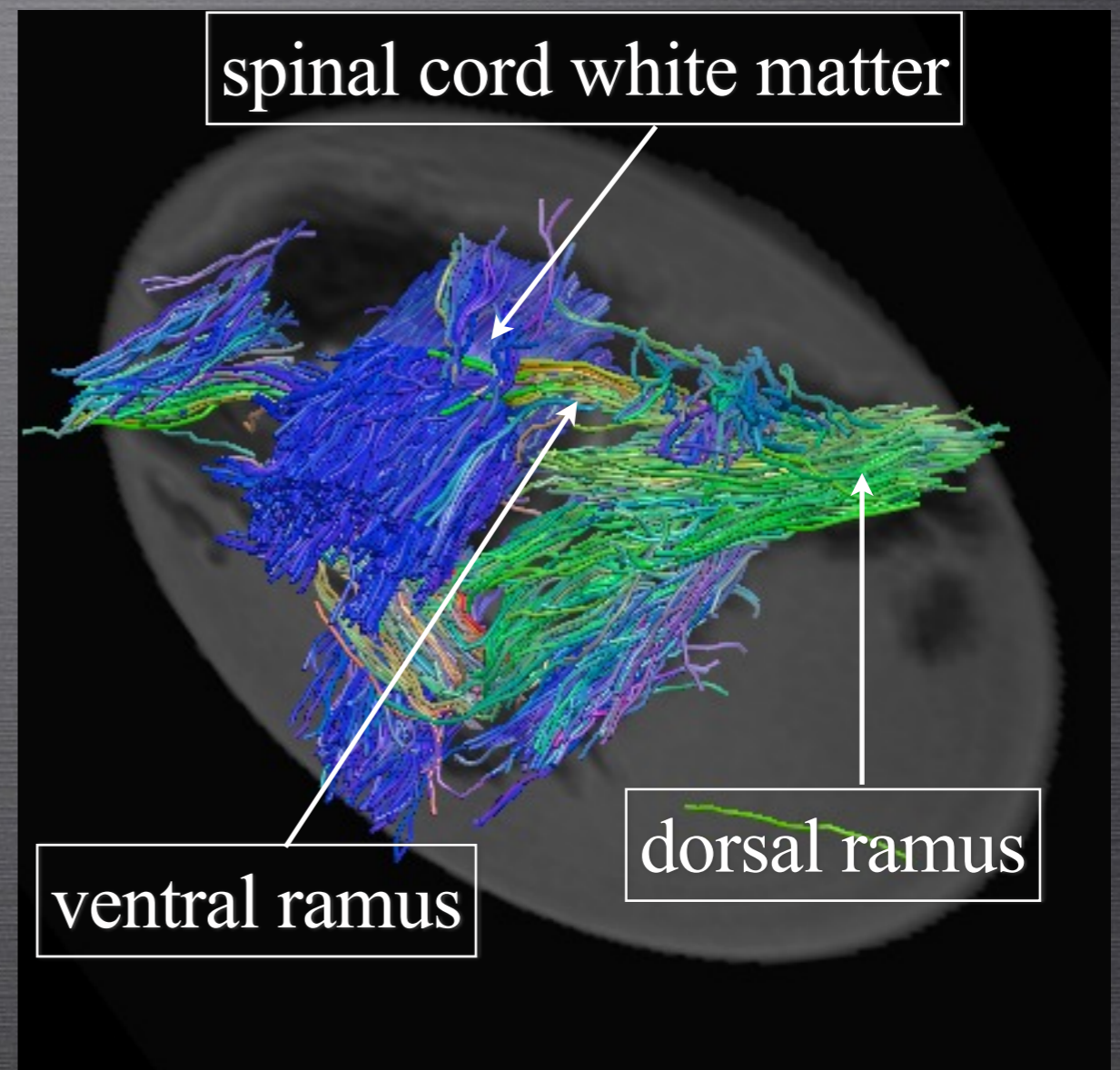
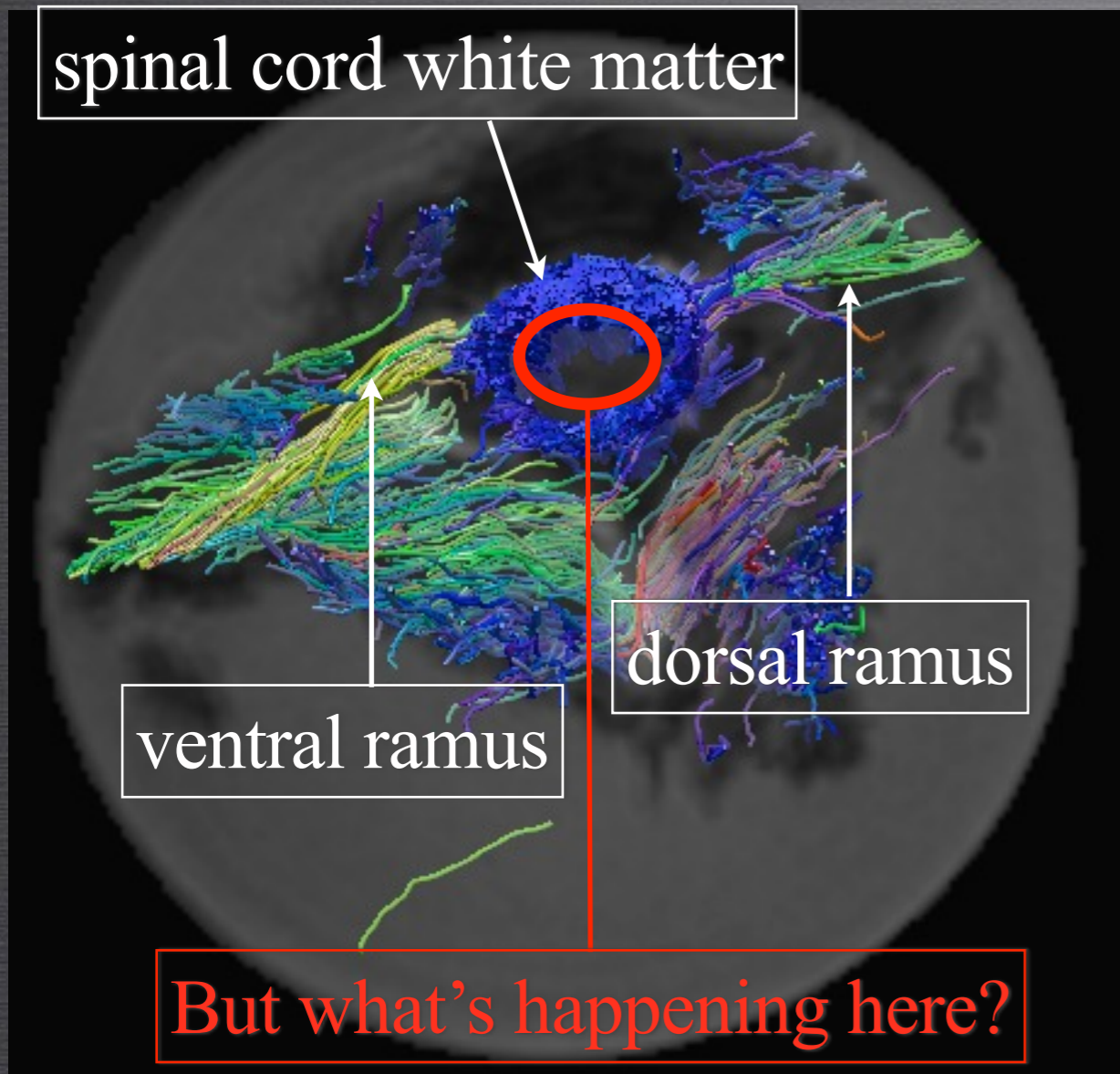


SPINAL CORD INJURY (RAT MODEL AT 7T)



Jacob Koffler, Ph.D.
Mark H. Tuszynski, M.D., Ph.D.
Center for Neural Repair
University of California, San Diego

SPINAL CORD INJURY (RAT MODEL AT 7T)



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HOW MUCH INFORMATION CAN WE EXTRACT?

HOW MUCH INFORMATION CAN WE EXTRACT?

UFODIGEST

UFO AND PARANORMAL NEWS FROM AROUND THE WORLD



Giant Monolith Photographed On Mars



Submitted by [Dirk Vander Ploeg](#) on Mon, 04/16/2012 - 09:02

Dirk Vander Ploeg is the publisher of UFODigest.com and other paranormal and UFO related websites. He is the author of the non-fiction book "Quest for Middle-earth" and is currently writing a new book. He has worked in marketing for the Toronto Star and the [Hamilton Spectator](#) and as a publisher and writer for [travel](#) related and other magazines.

By: Natalie Wolchover

Published: 04/11/2012 05:50 PM EDT on Lifes Little Mysteries

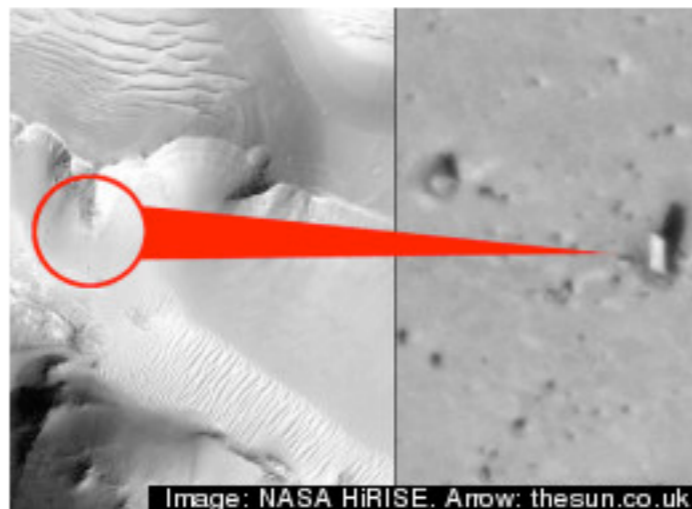
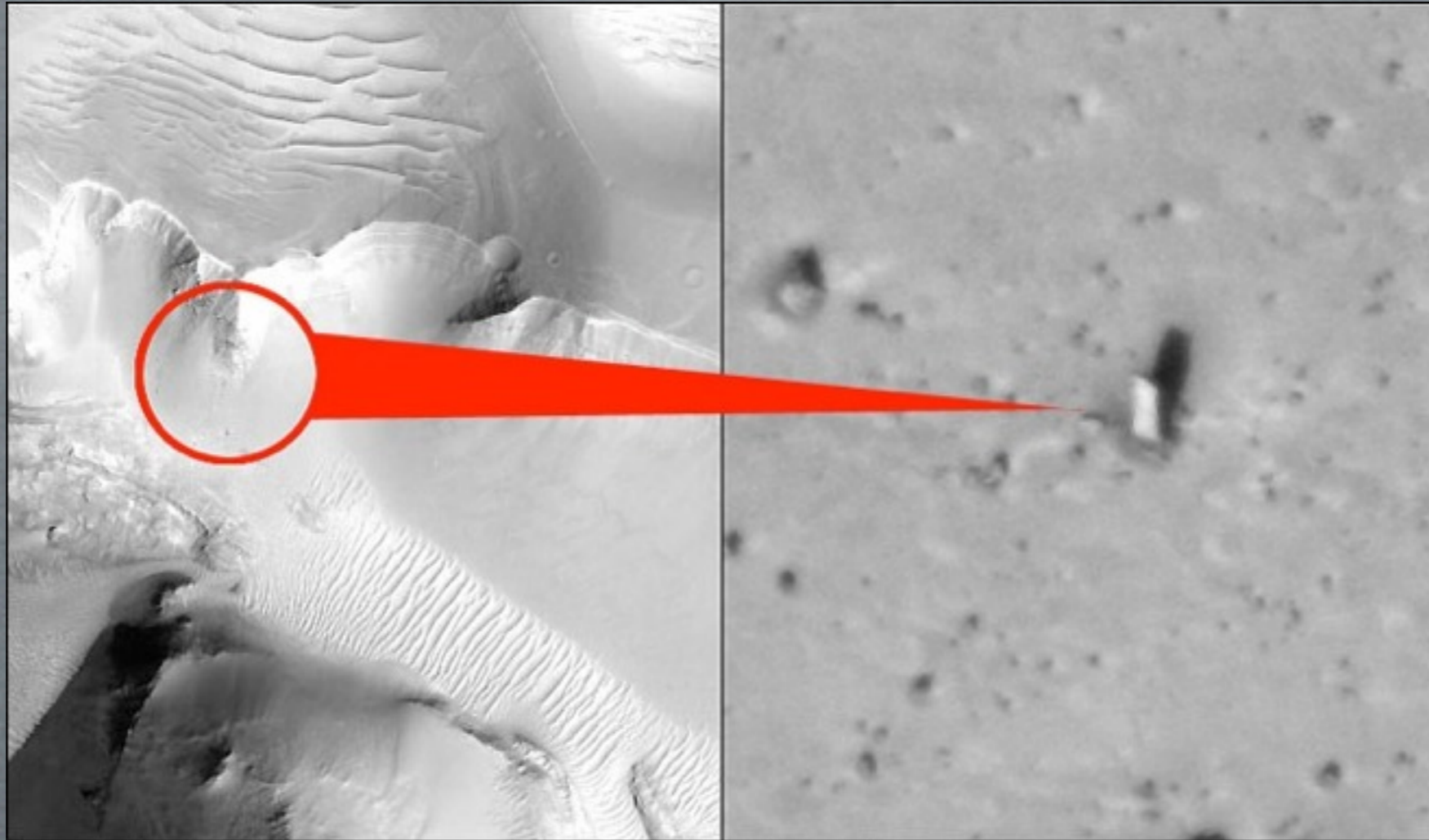


Image: NASA HiRISE. Arrow: thesun.co.uk

HOW MUCH INFORMATION CAN WE EXTRACT?



HOW MUCH INFORMATION CAN WE EXTRACT?

Science on  msnbc.com

Mars 'monolith' isn't the work of Martians

Object in NASA images looks just like one in '2001: A Space Odyssey' — but it's just a rock



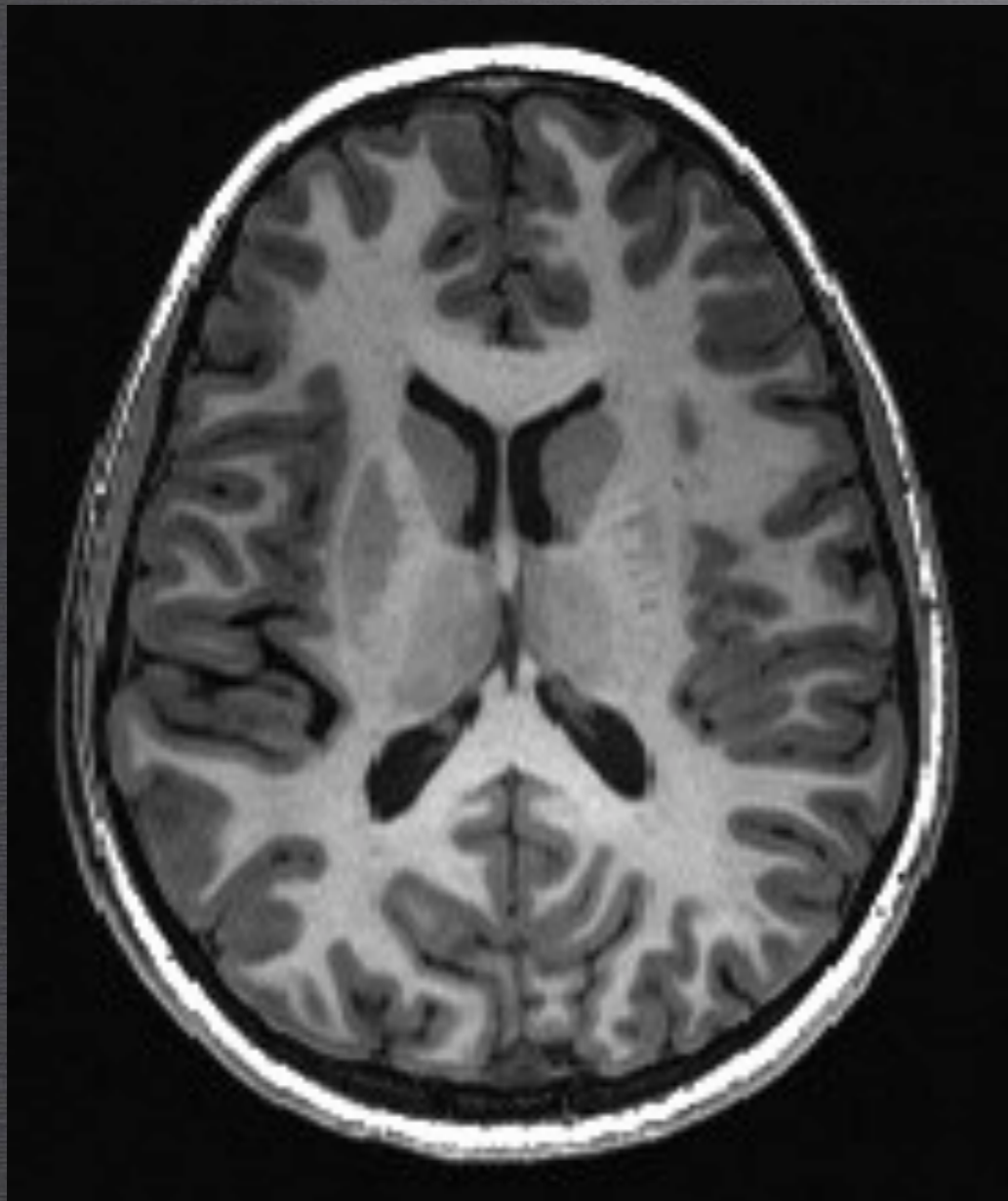
HOW MUCH INFORMATION CAN WE EXTRACT?



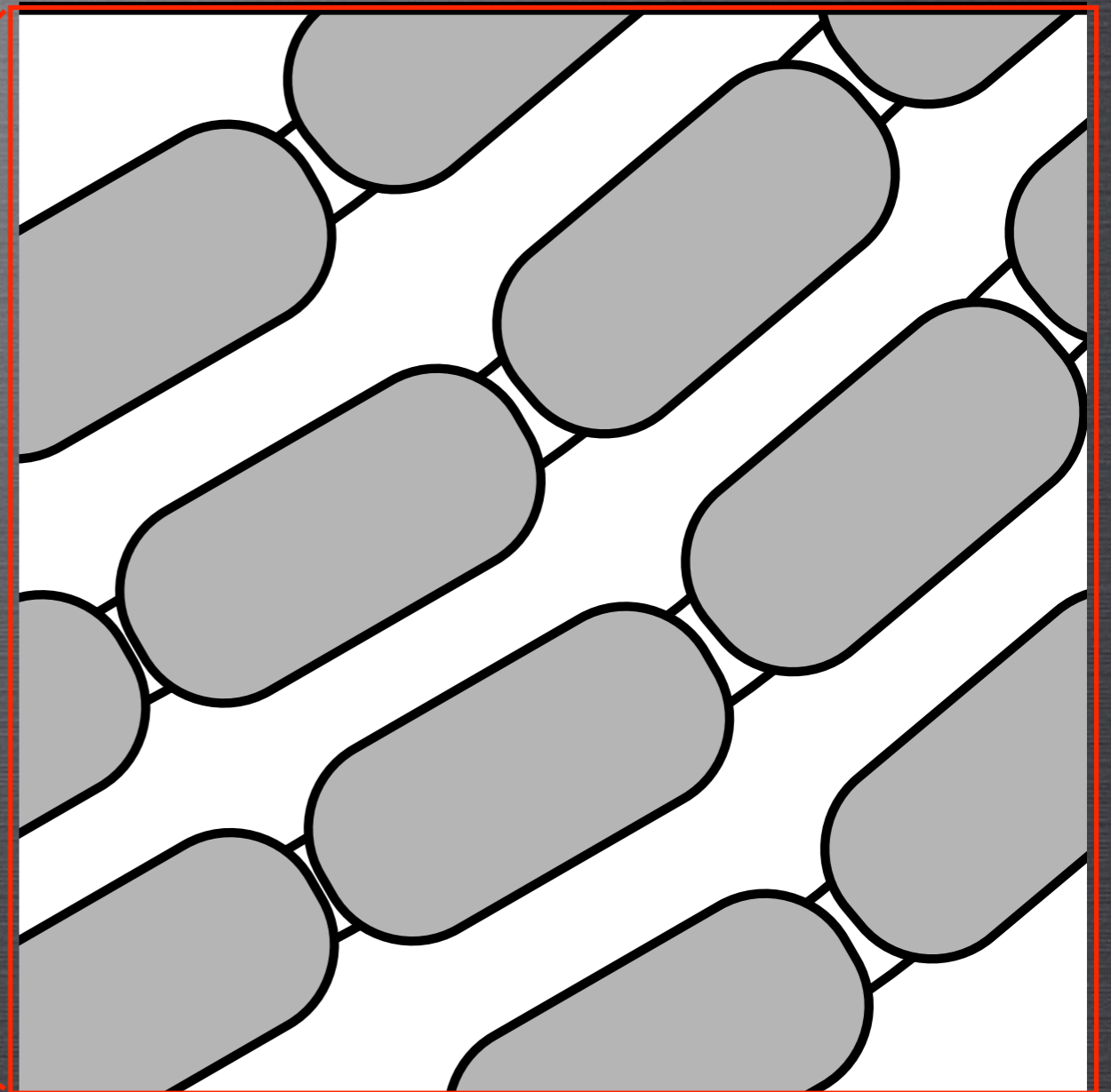
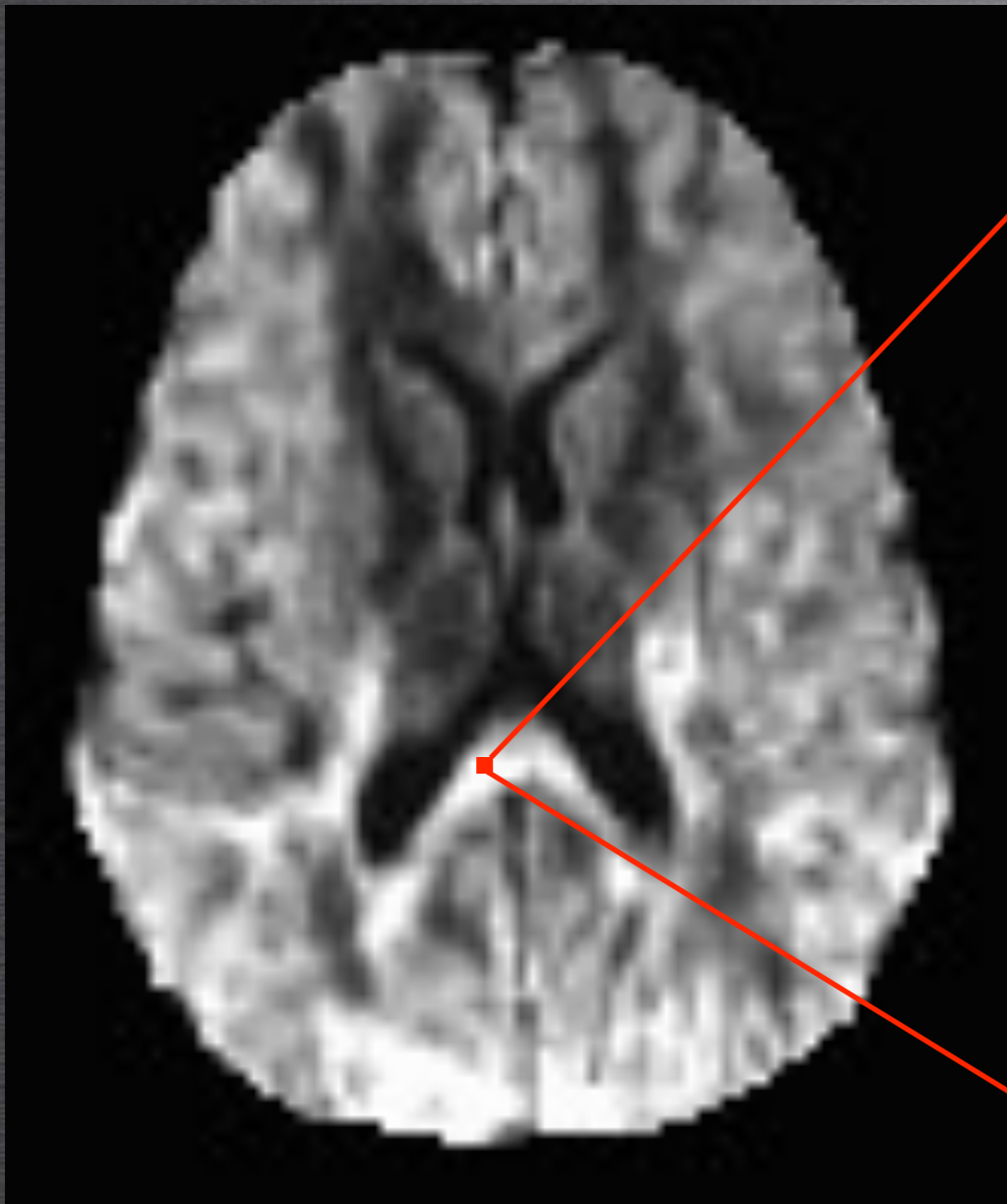
According to Jonathon Hill of Arizona State University, the reason that the rock looks like an artificial construction is very simple: *lack of resolution in the image.*

WHAT'S THE PROBLEM?

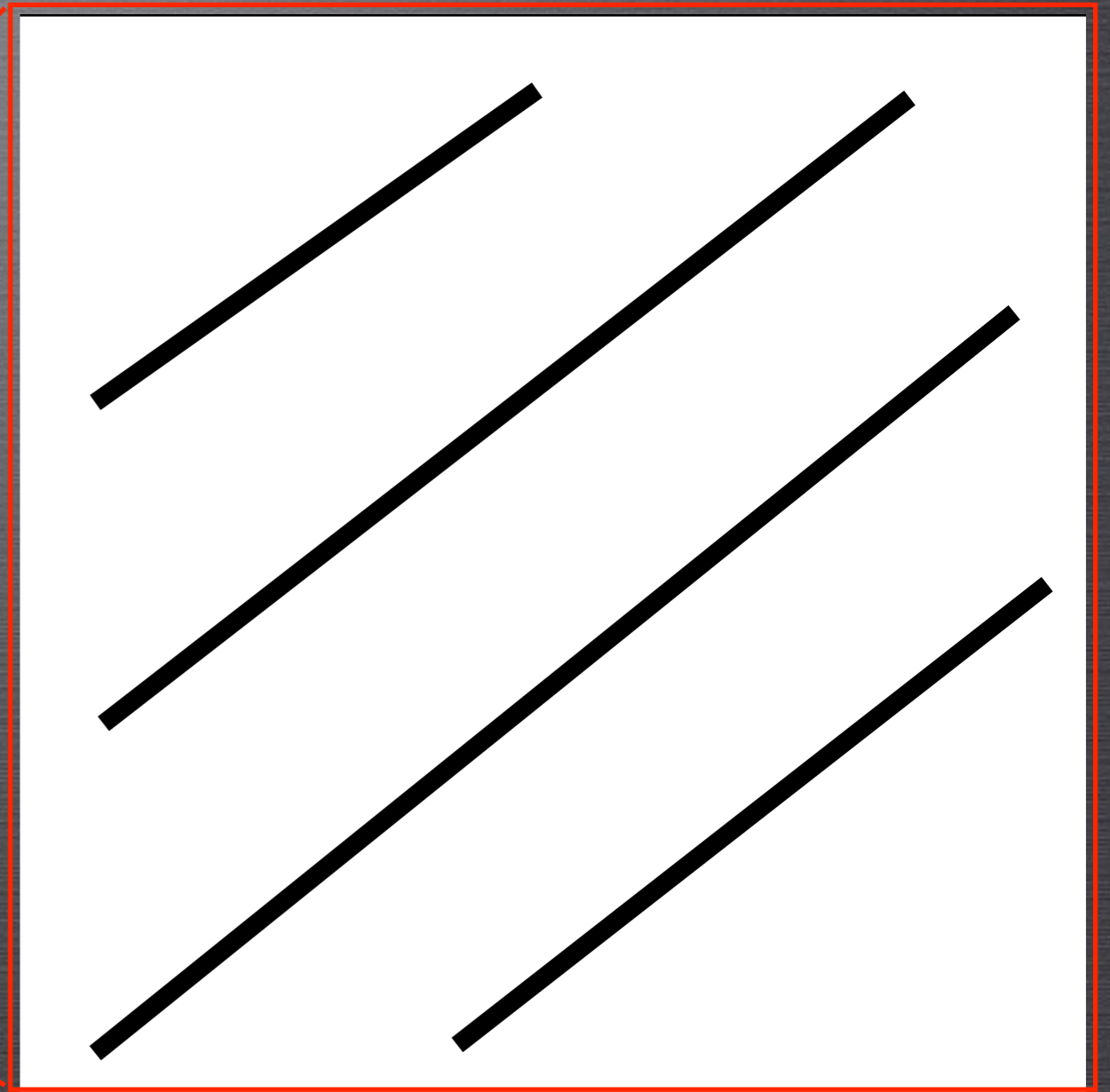
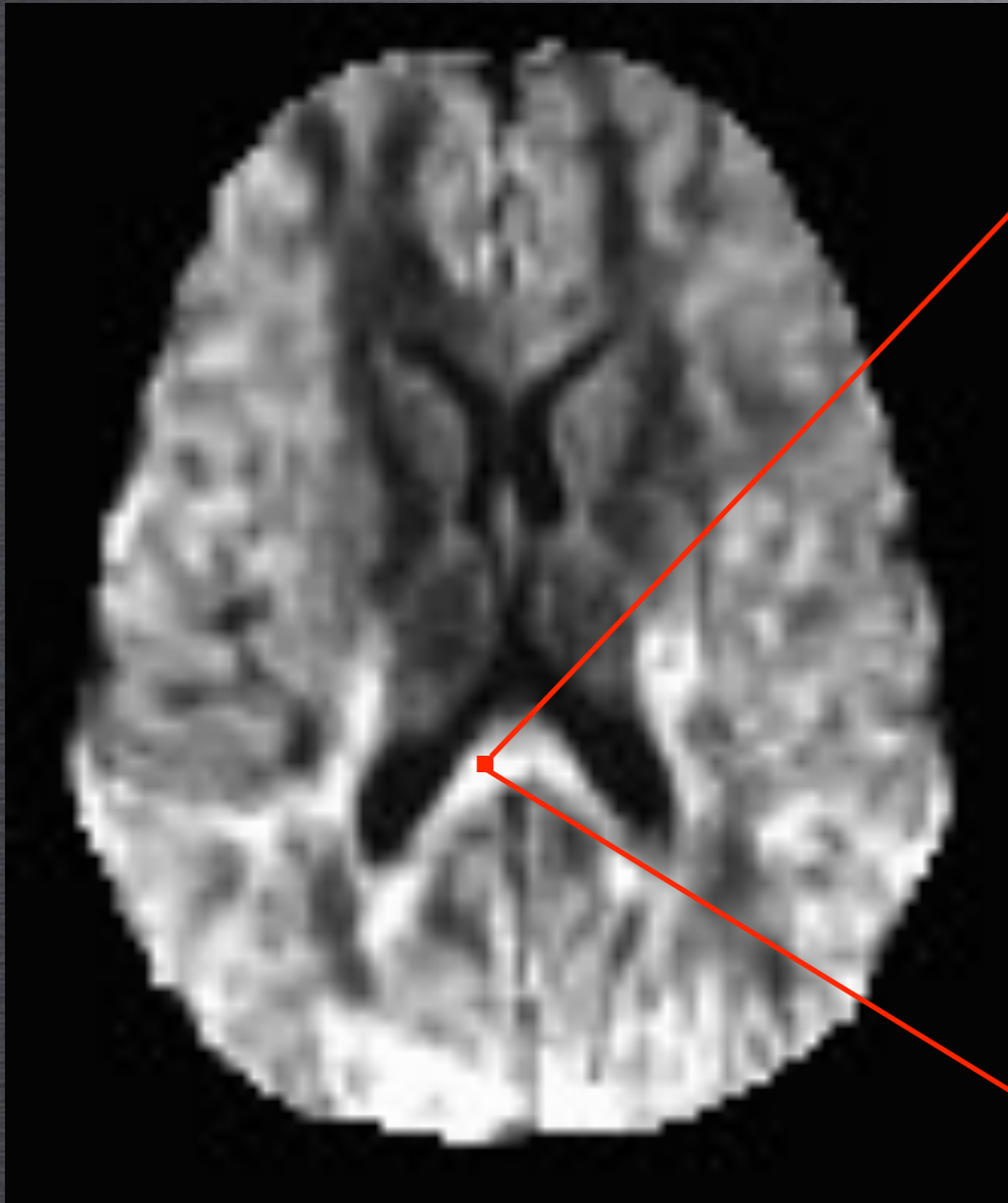
WHAT'S THE PROBLEM?



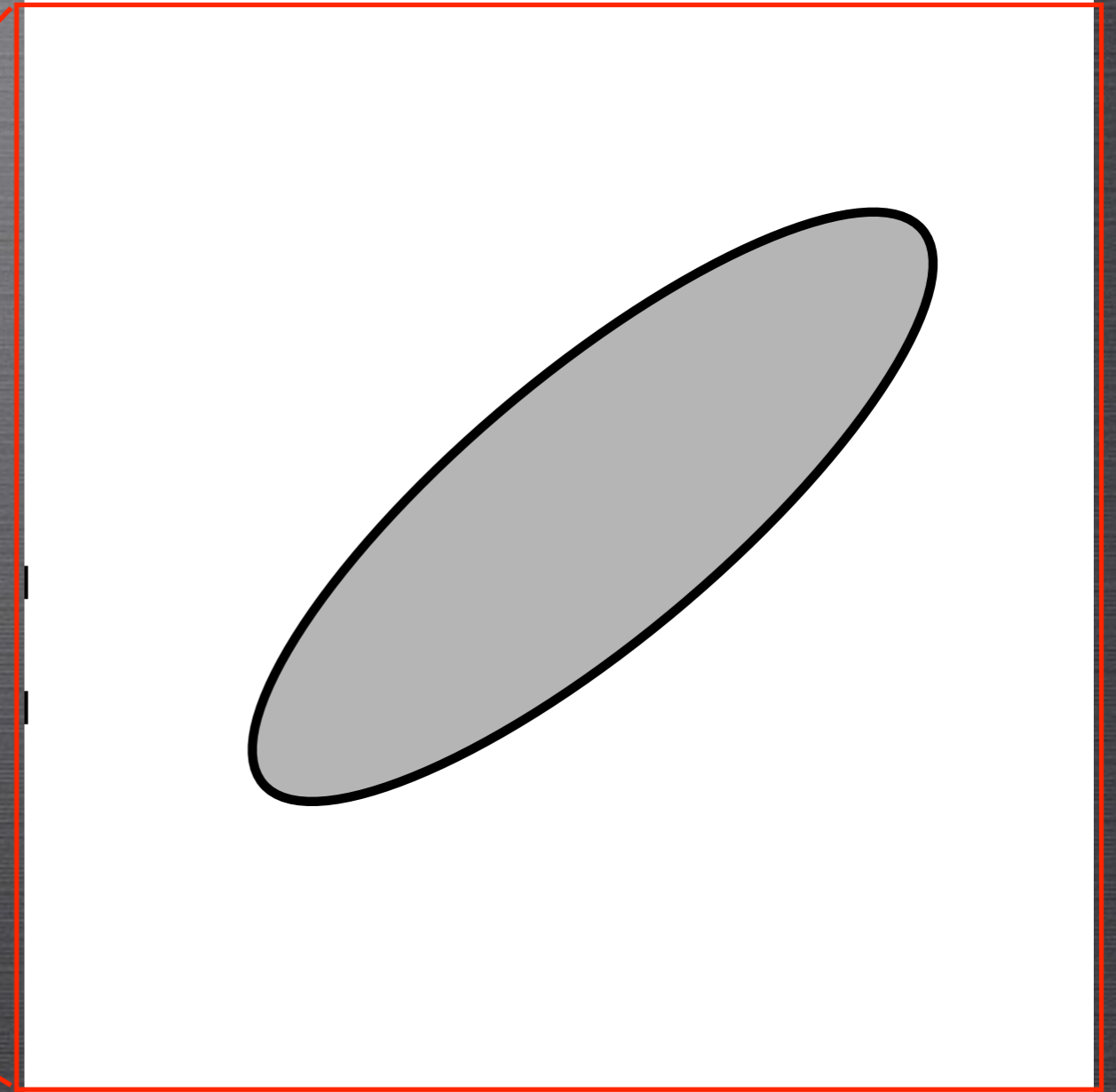
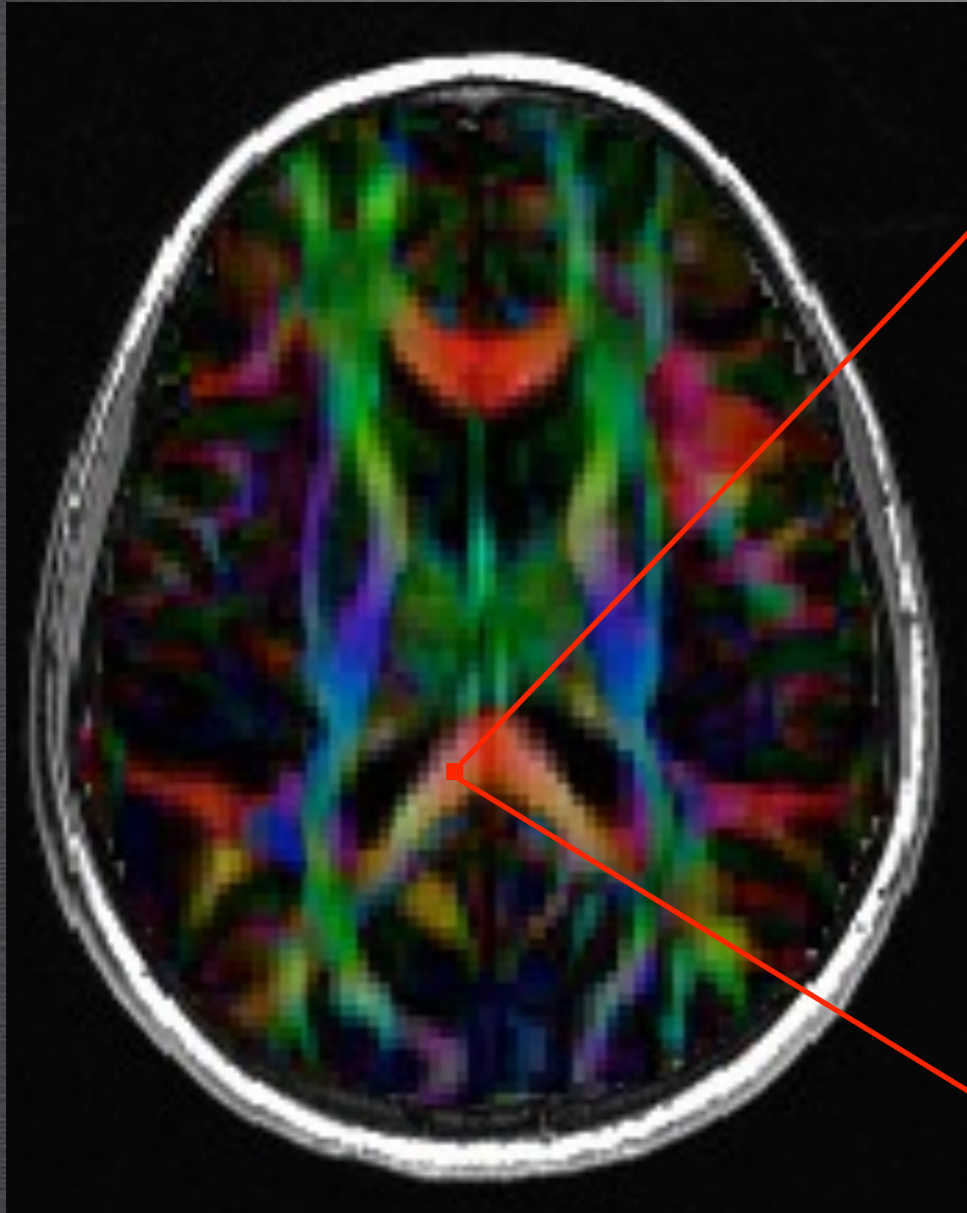
WHAT'S THE PROBLEM?



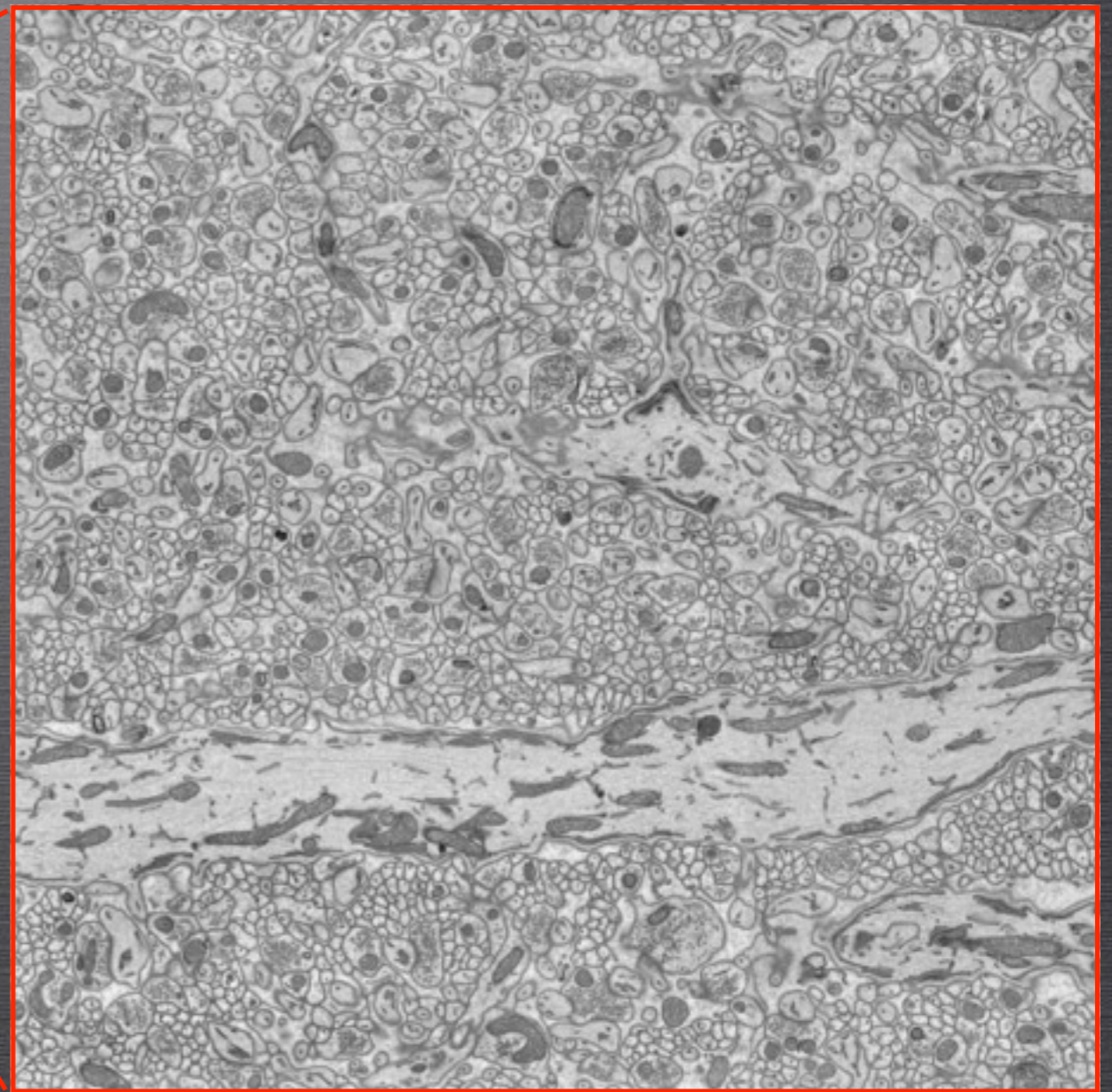
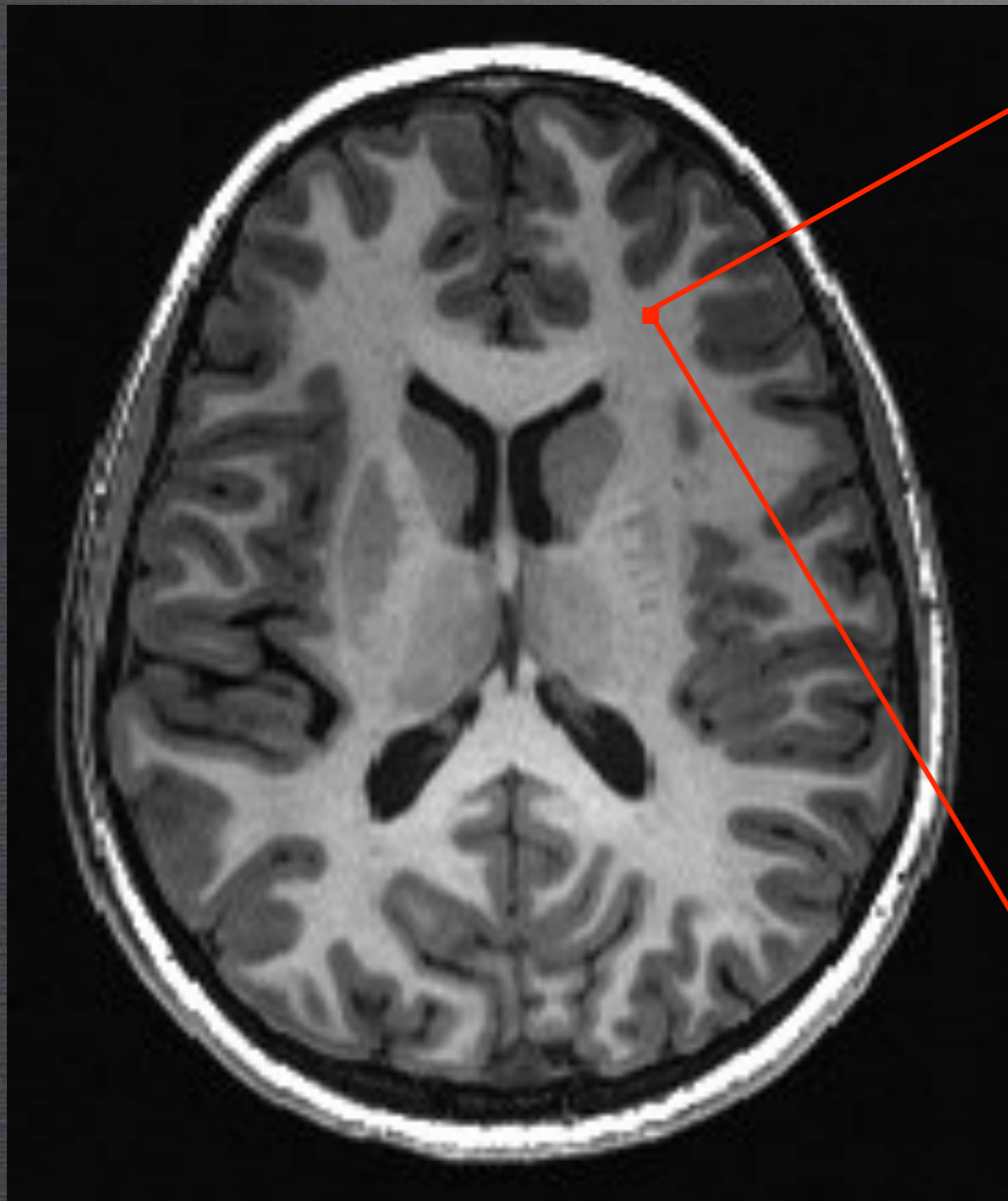
WHAT'S THE PROBLEM?



WHAT'S THE PROBLEM?



BUT WE KNOW NEURAL TISSUES
AREN'T THAT SIMPLE

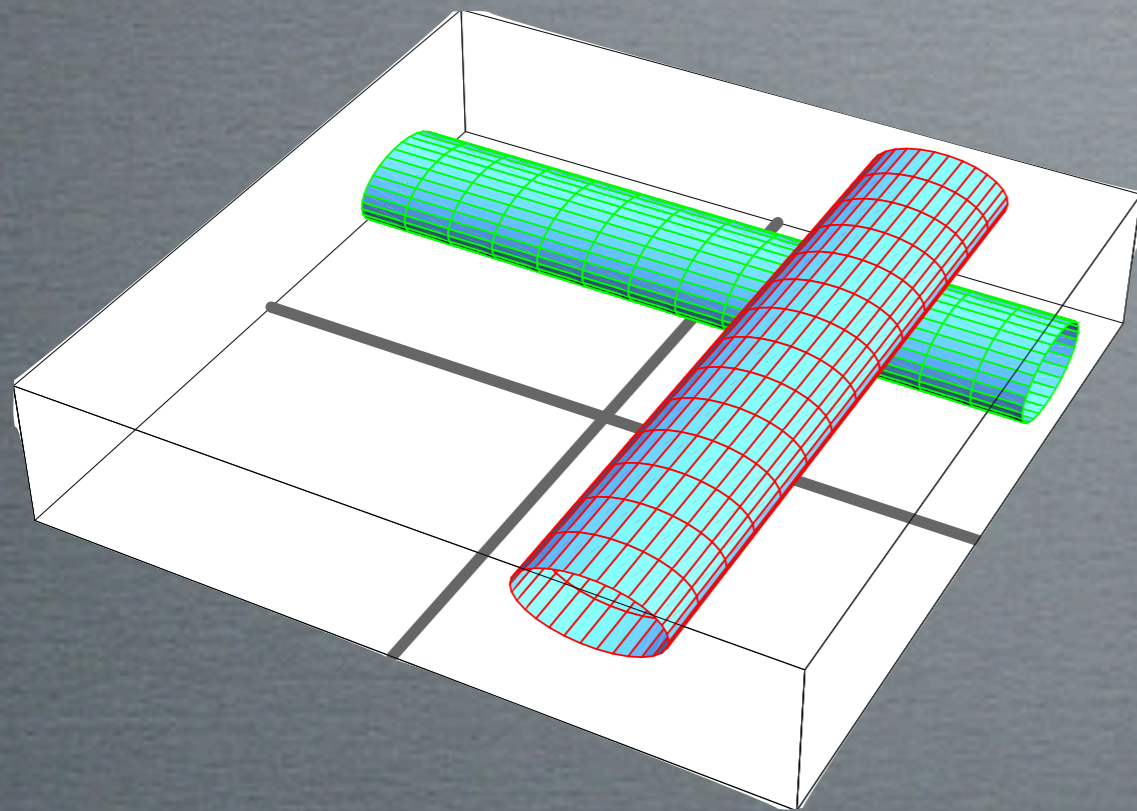


Rat WM electron microscopic image
Courtesy, M. Ellisman, UCSD

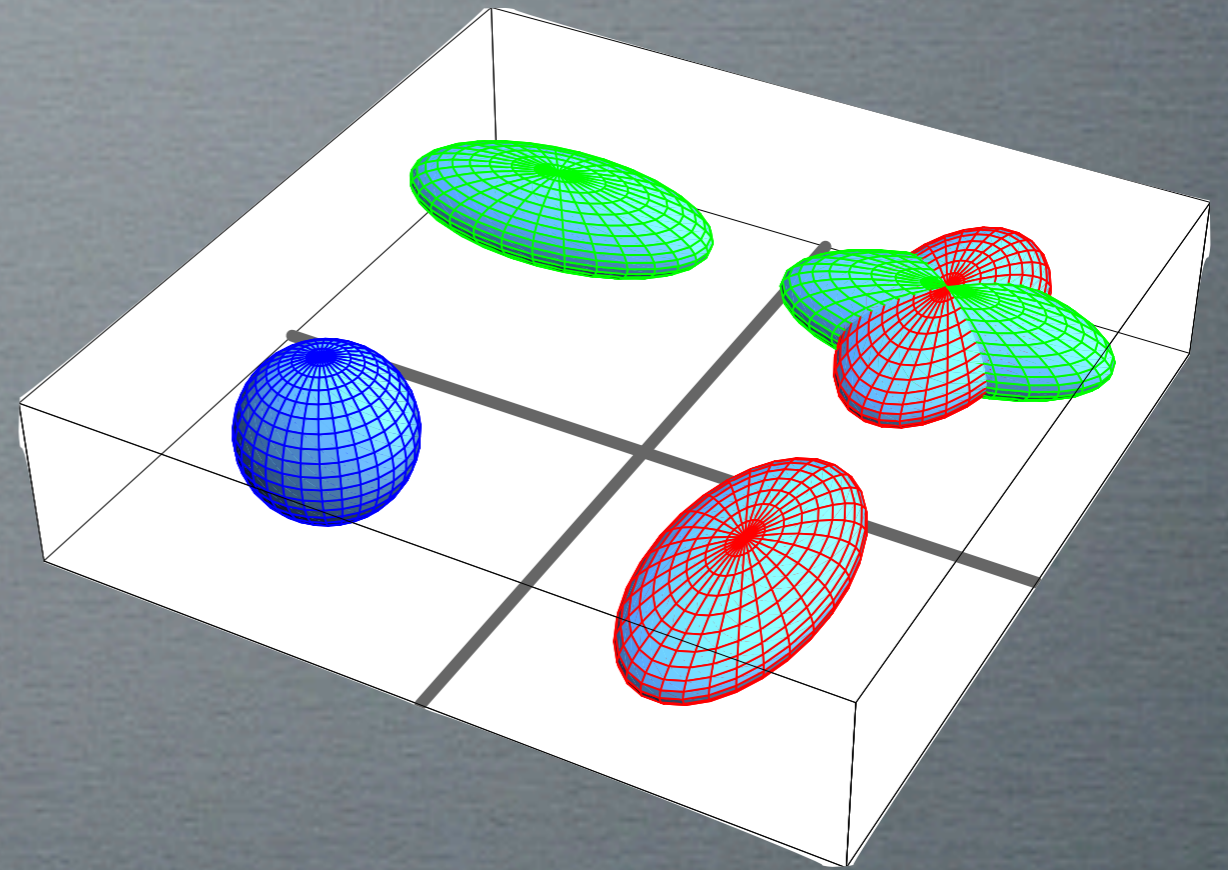
FAILURE OF THE STANDARD MODEL

FAILURE OF THE STANDARD MODEL

A simple partial-volume model



Two crossing fibers

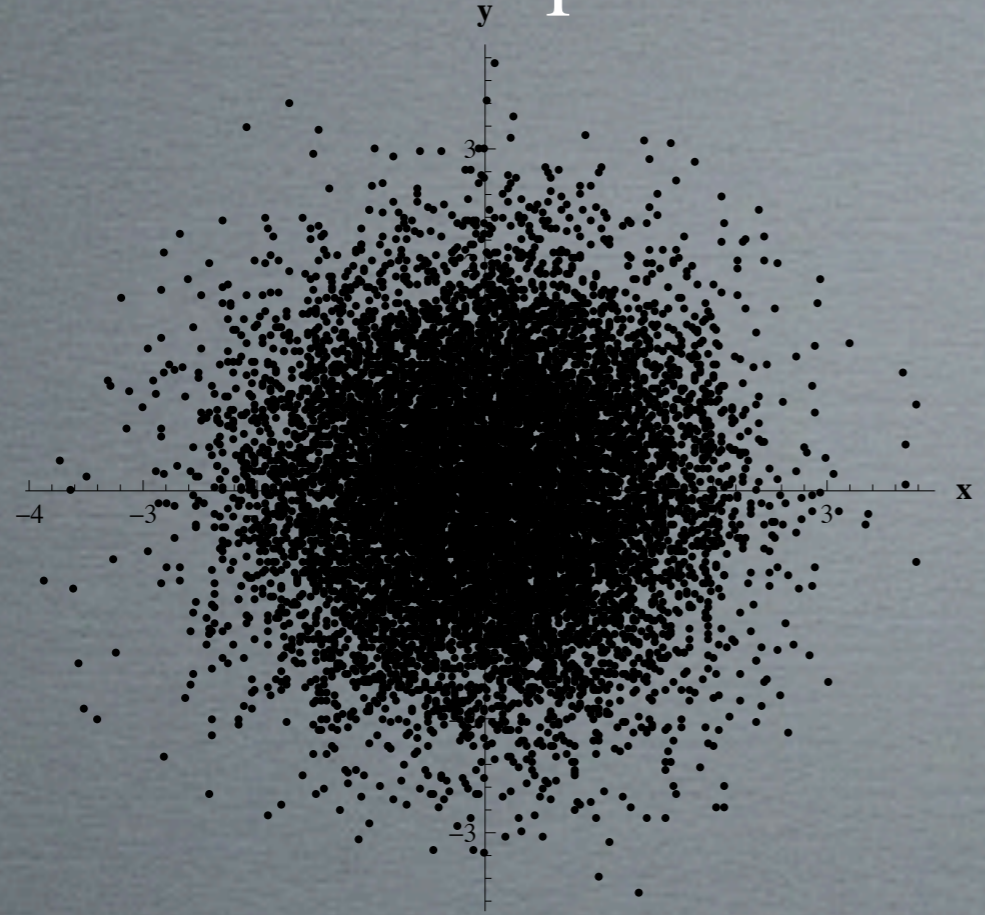


resulting distributions

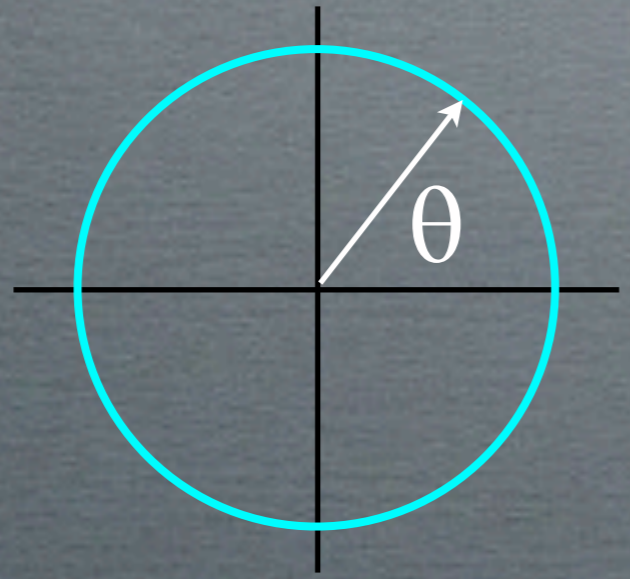
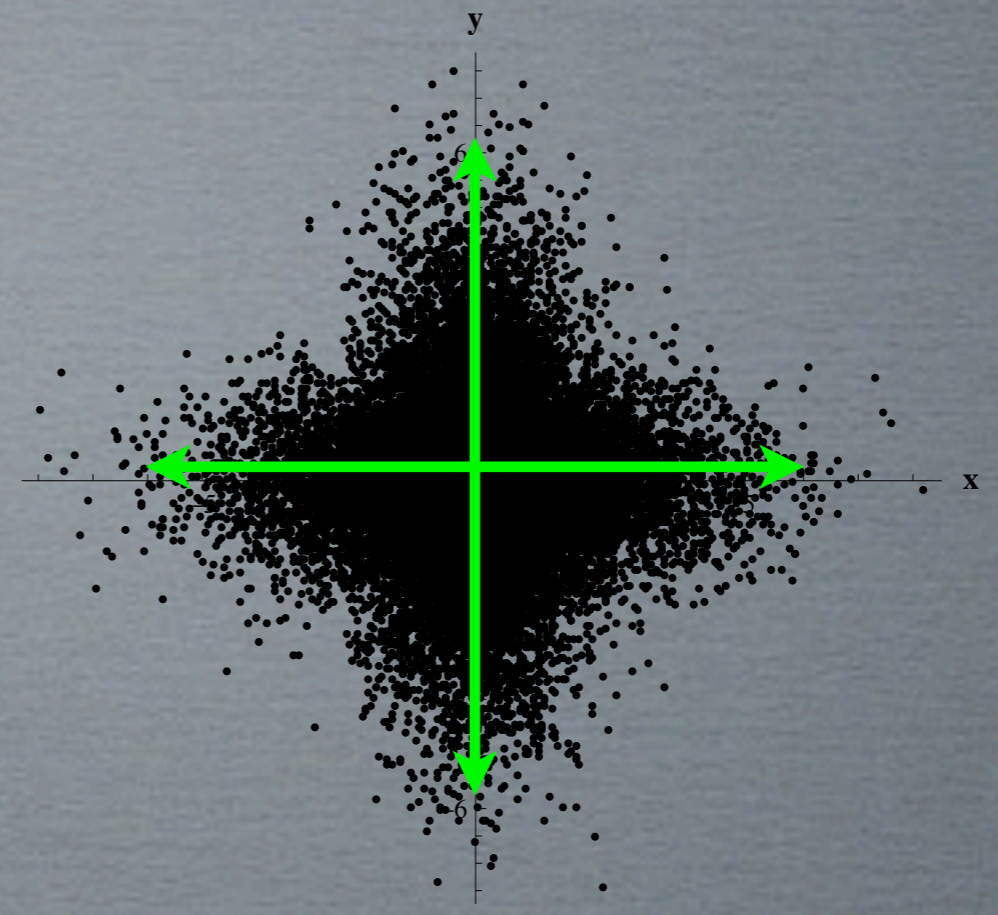
AMBIGUITIES IN THE STANDARD MODEL

AMBIGUITIES IN THE STANDARD MODEL

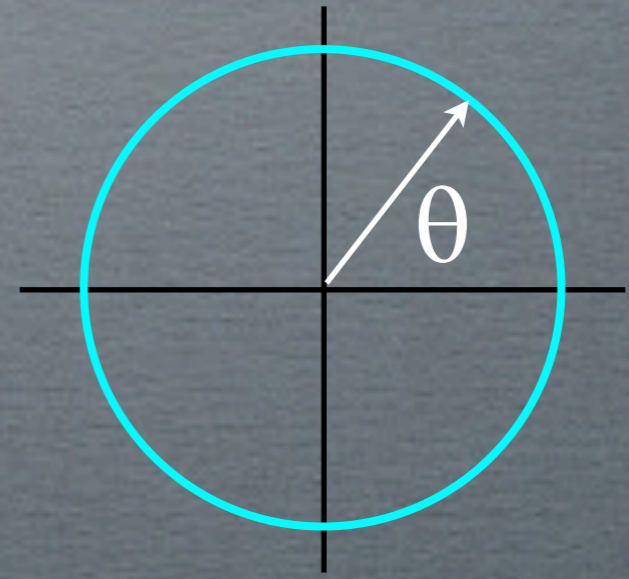
isotropic



crossed fibers 90°



$D(\theta)$

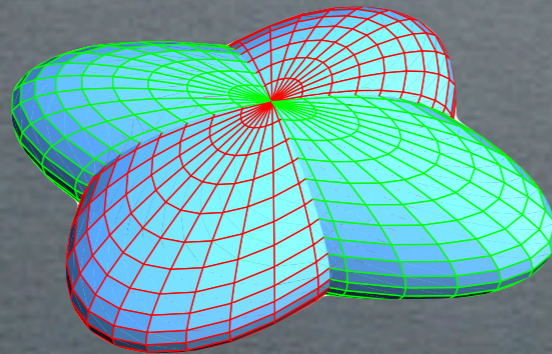
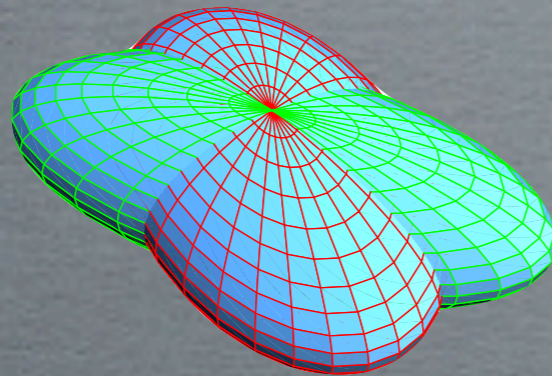
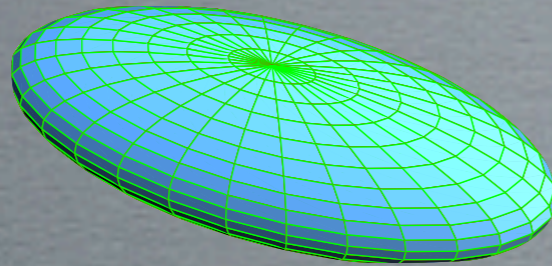


$D(\theta)$

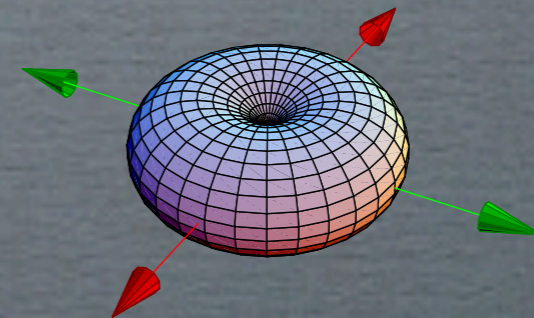
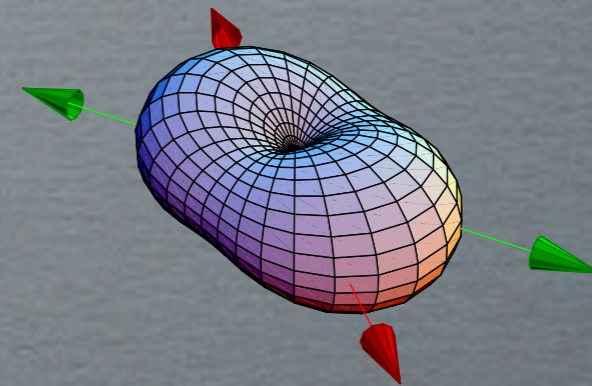
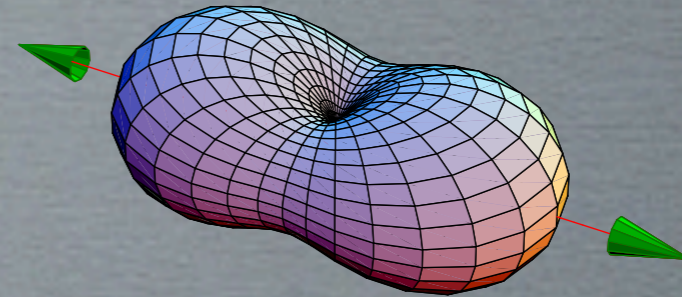
FAILURE OF THE STANDARD MODEL

FAILURE OF THE STANDARD MODEL

Distribution of spins



Estimated D

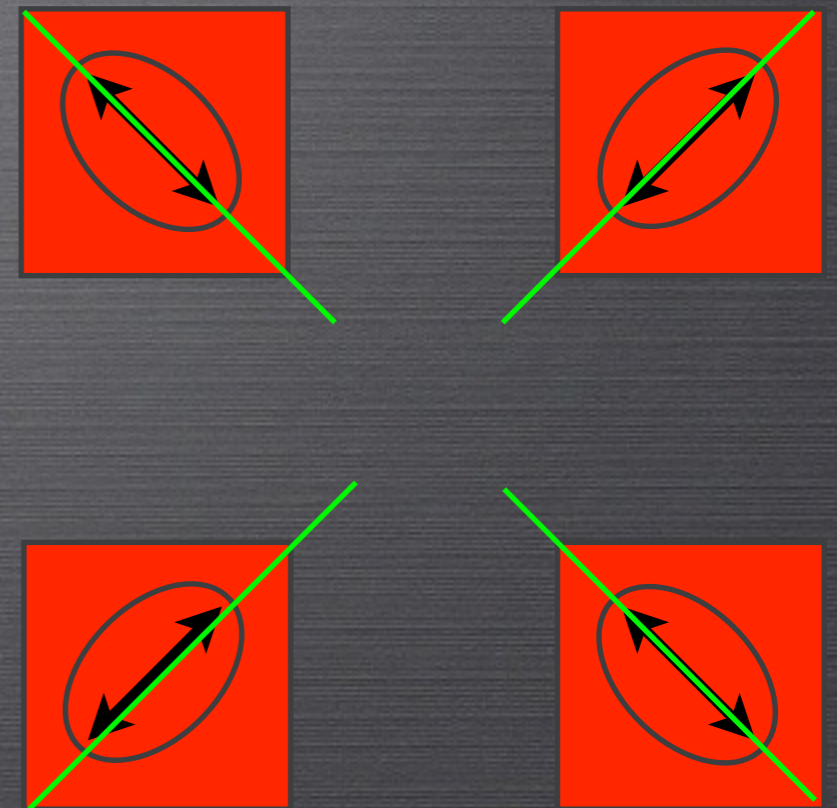
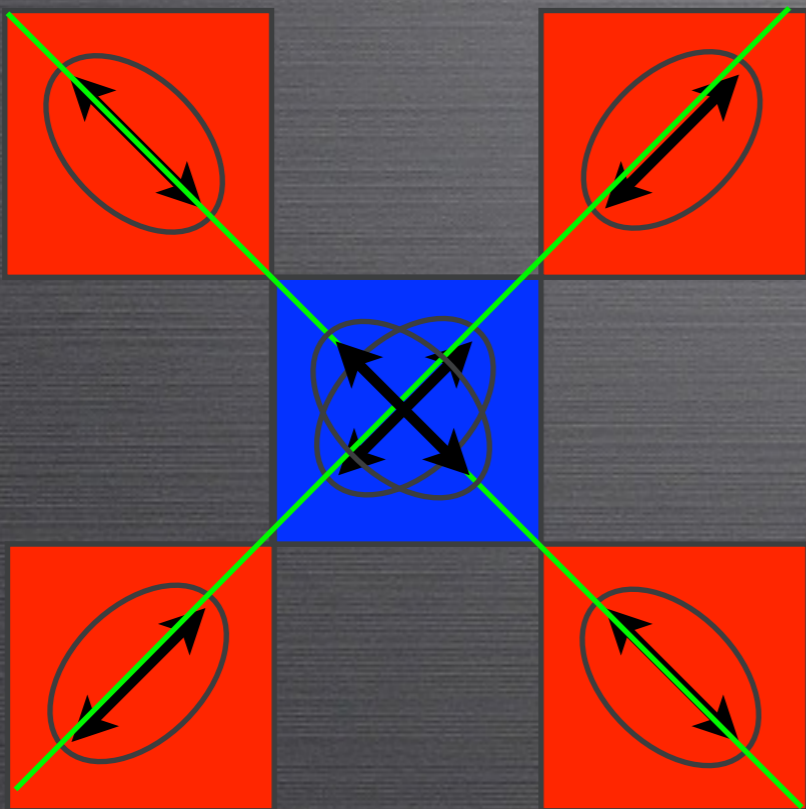


THE MAJOR PROBLEM: HETEROGENEOUS VOXELS

THE MAJOR PROBLEM: HETEROGENEOUS VOXELS

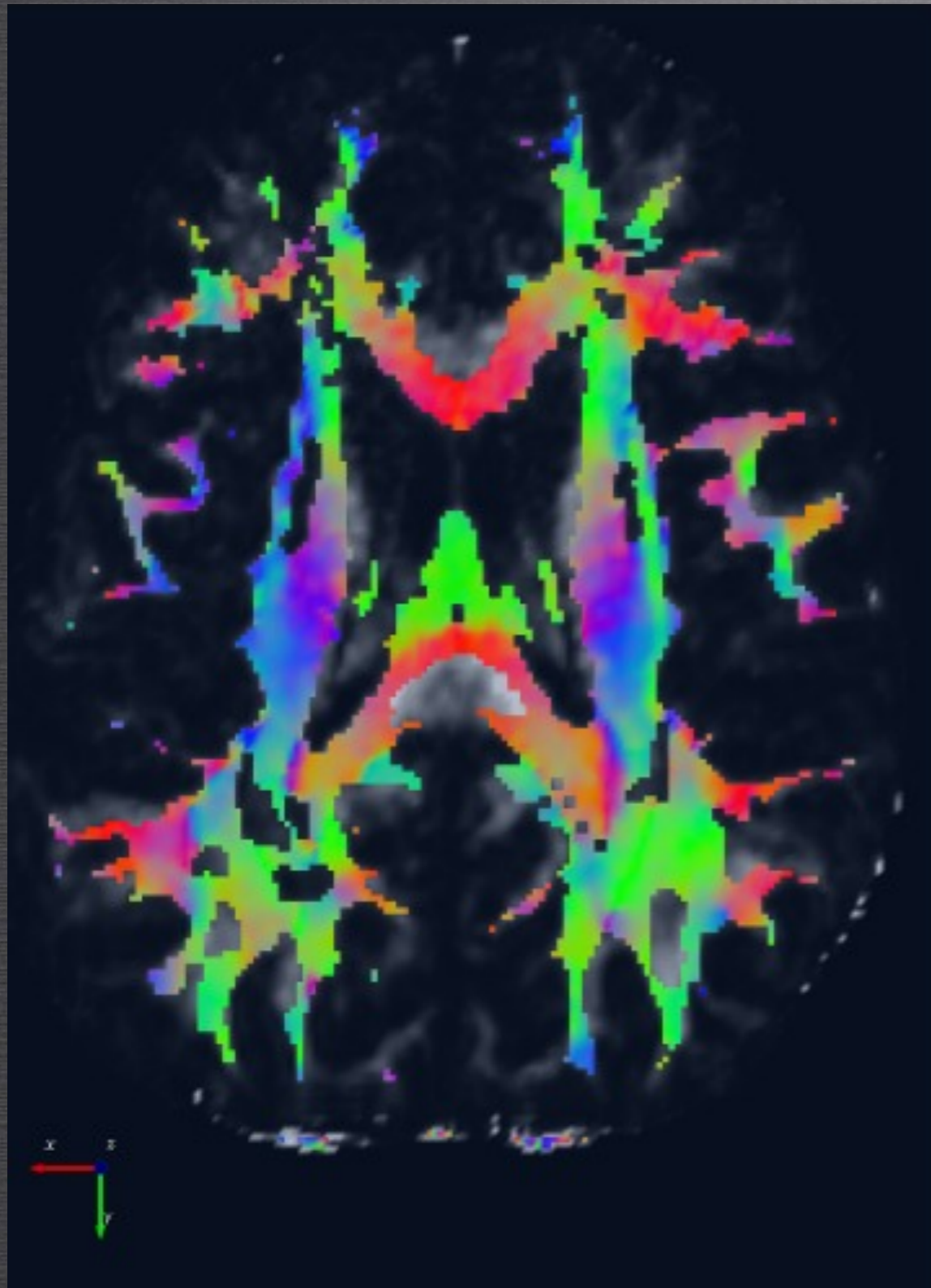
Anisotropy

high

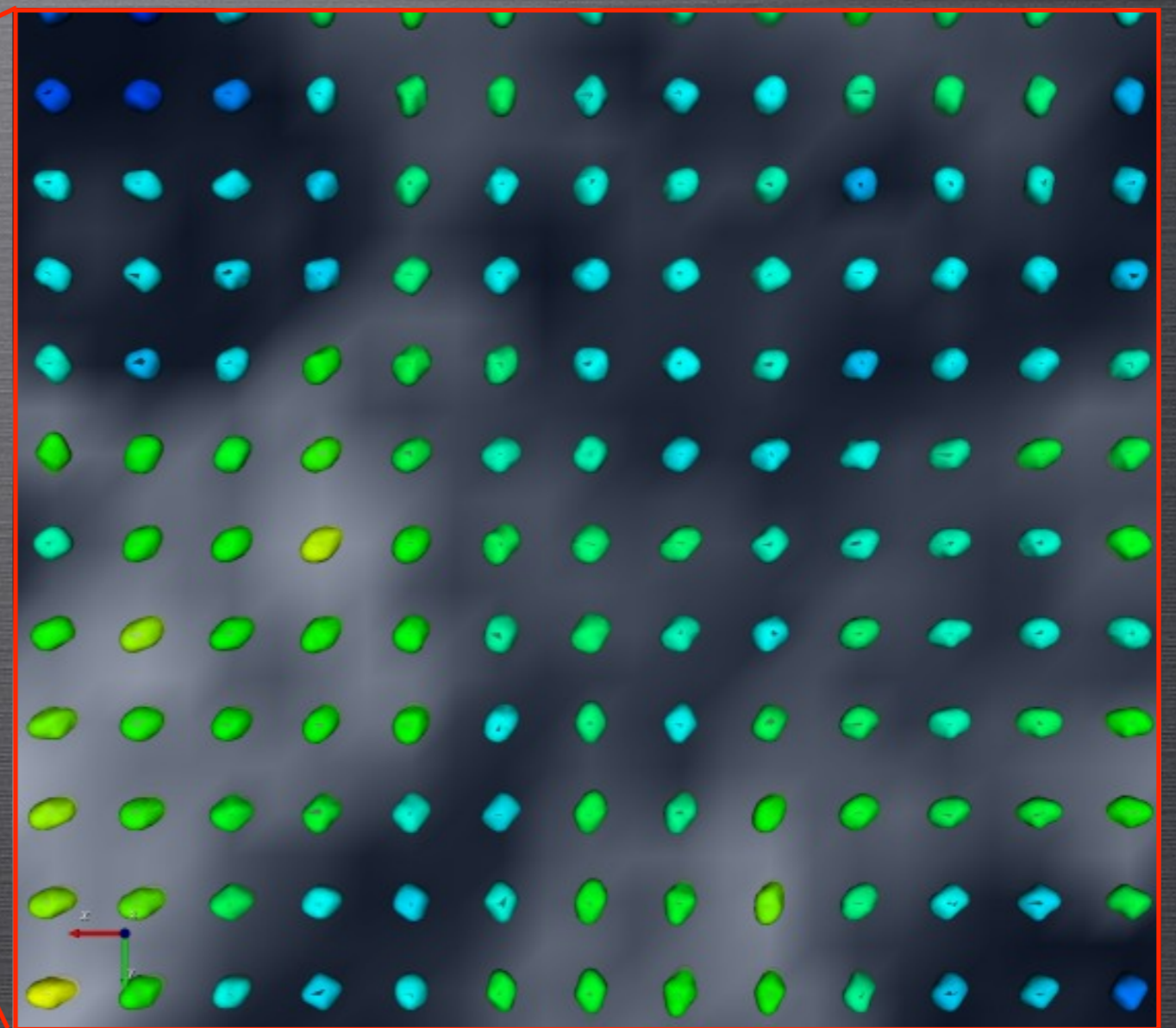
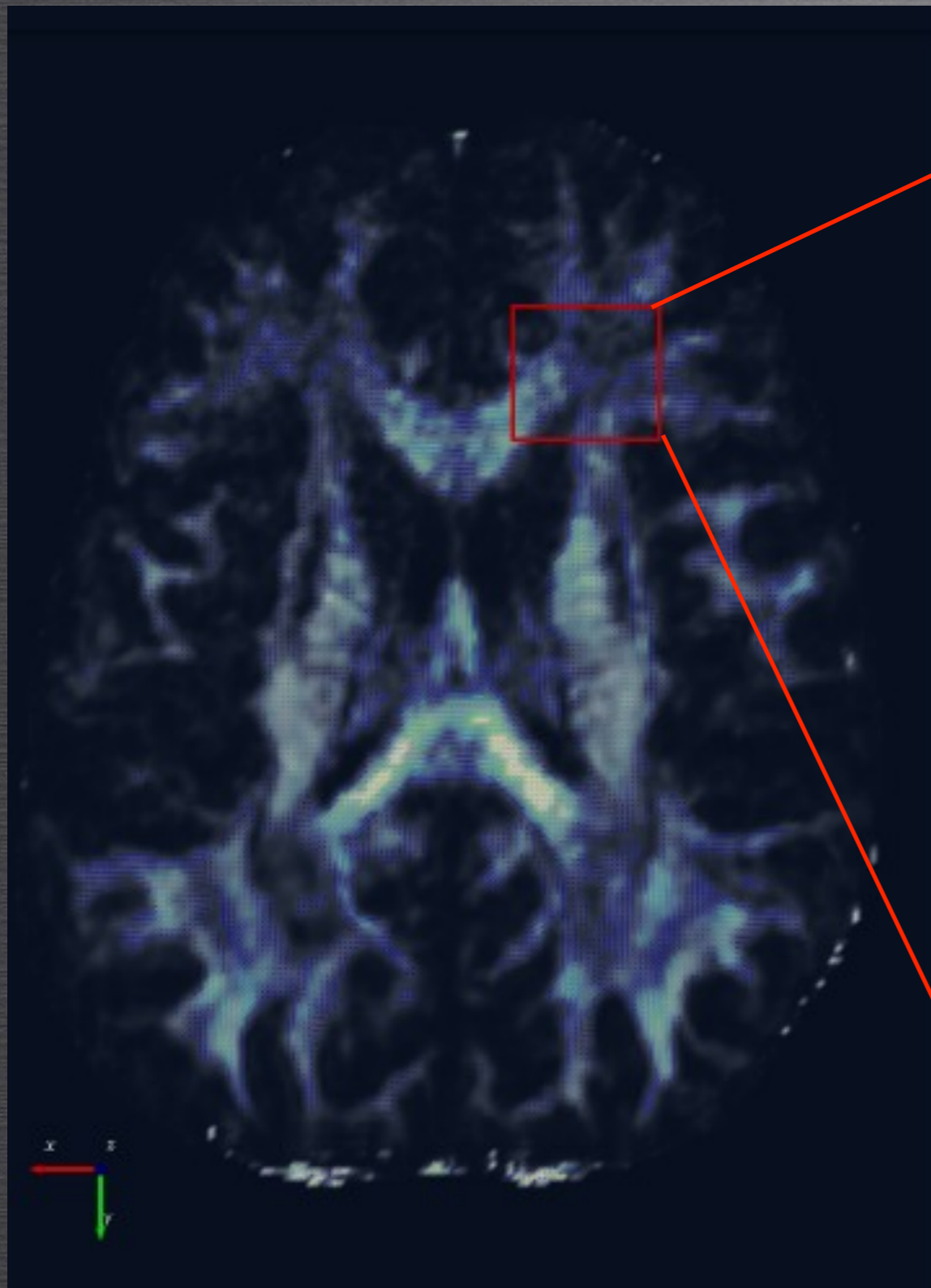


TRACTOGRAPHY PROBLEM

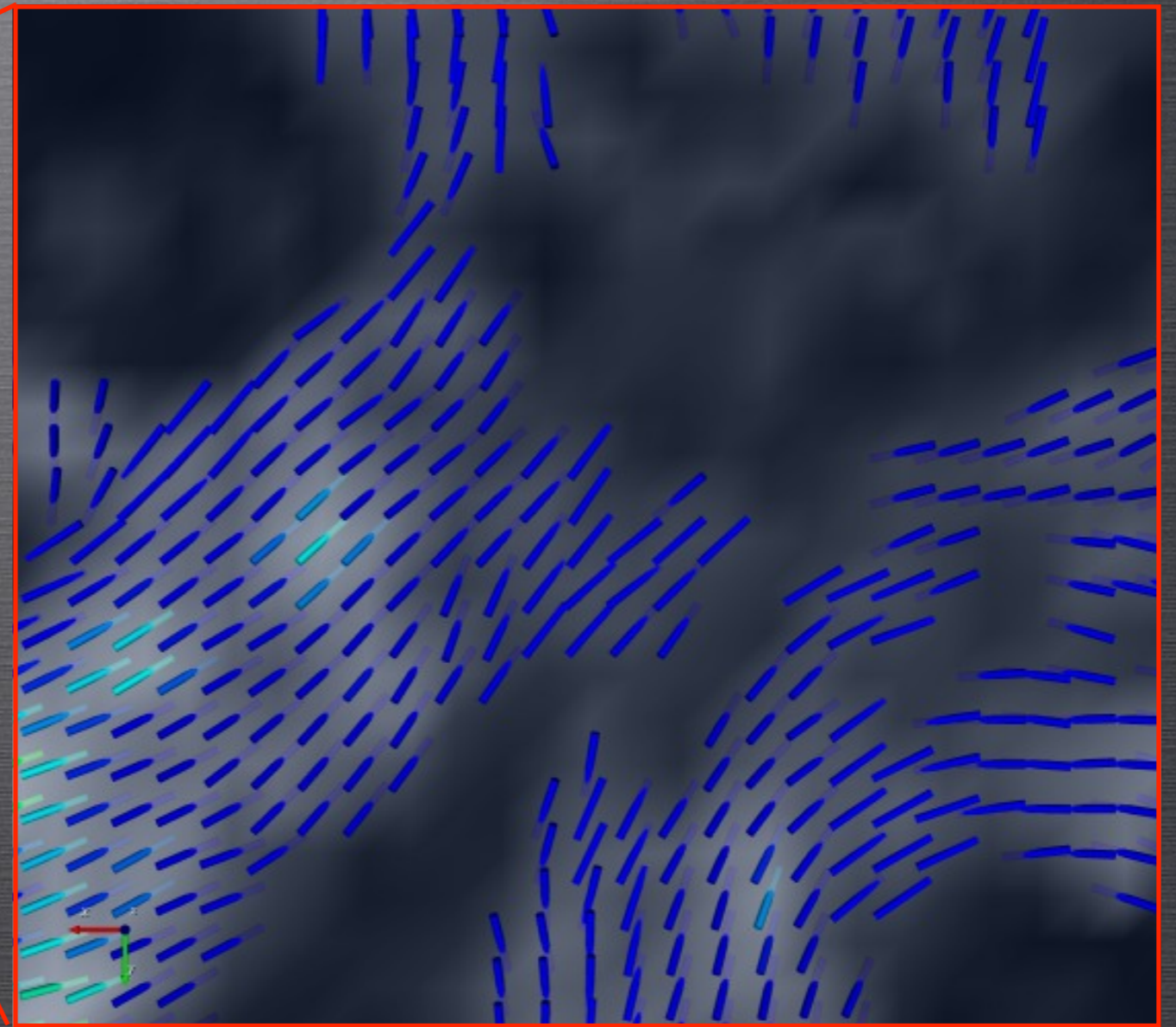
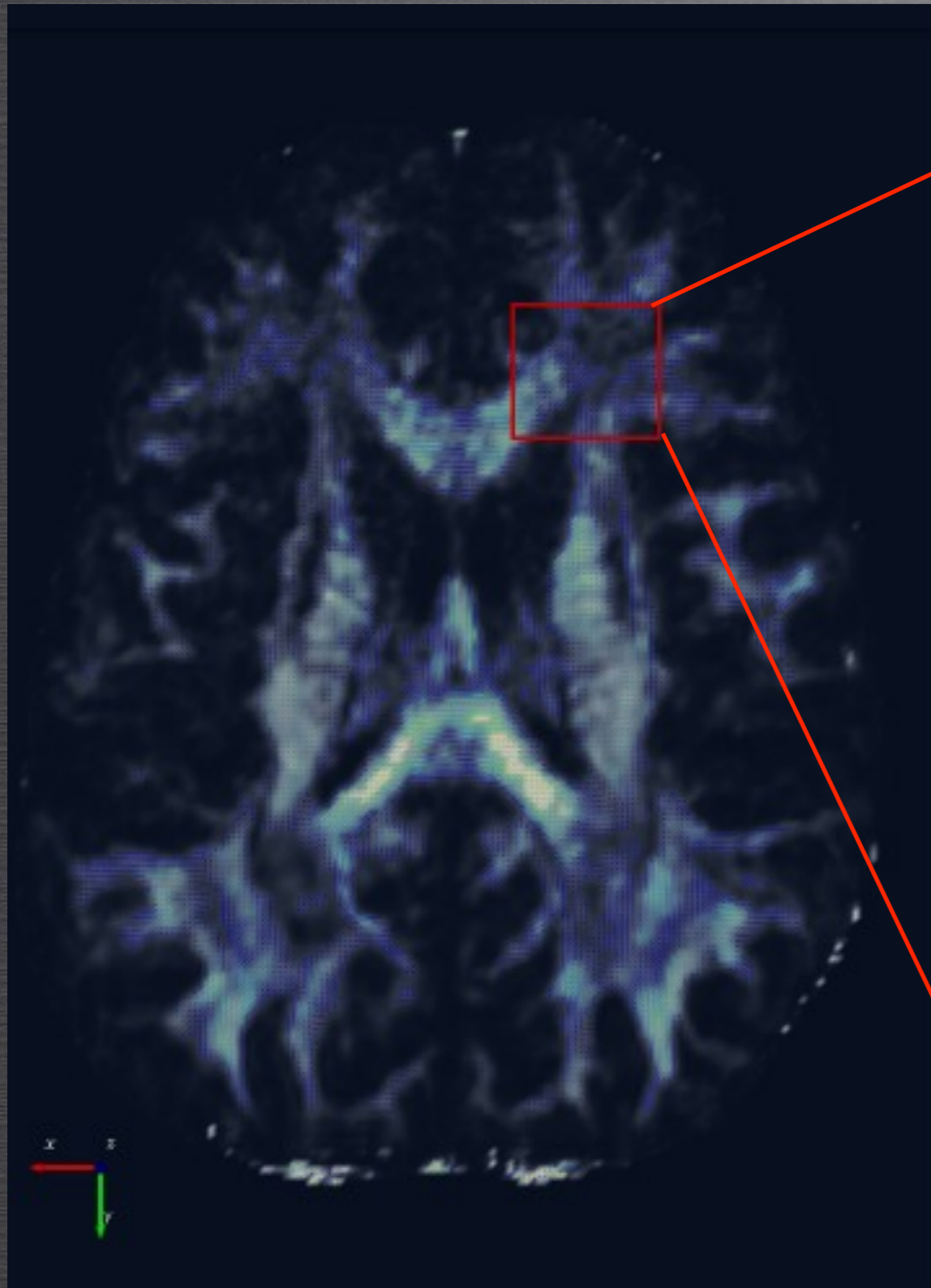
TRACTOGRAPHY PROBLEM



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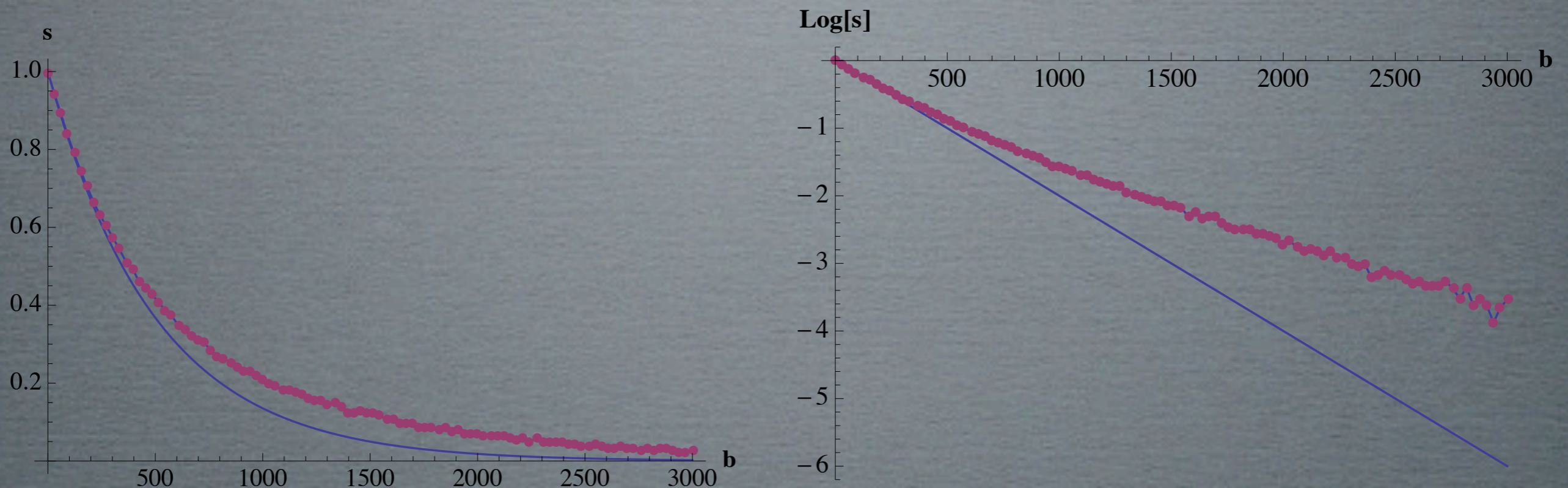
TRACTOGRAPHY PROBLEM



FAILURE OF THE STANDARD MODEL

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

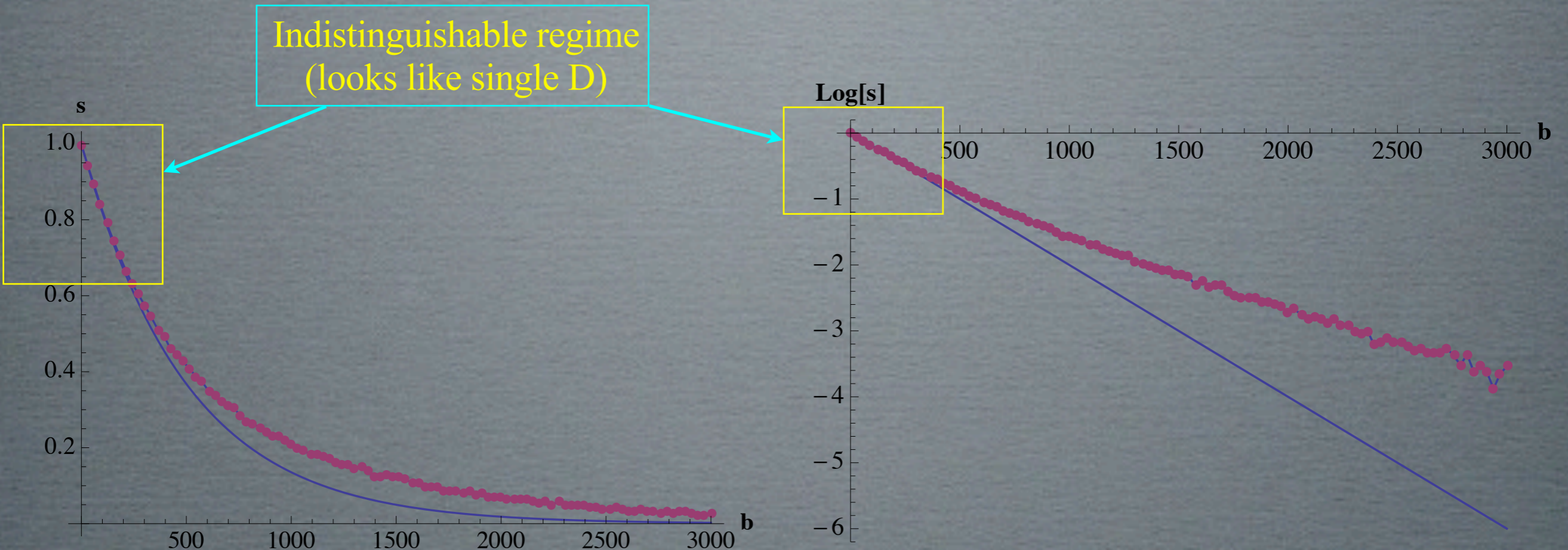


$$\frac{S(b)}{S(0)} = f e^{-bD_1} + (1 - f) e^{-bD_2}$$

simple two diffusion coefficient model

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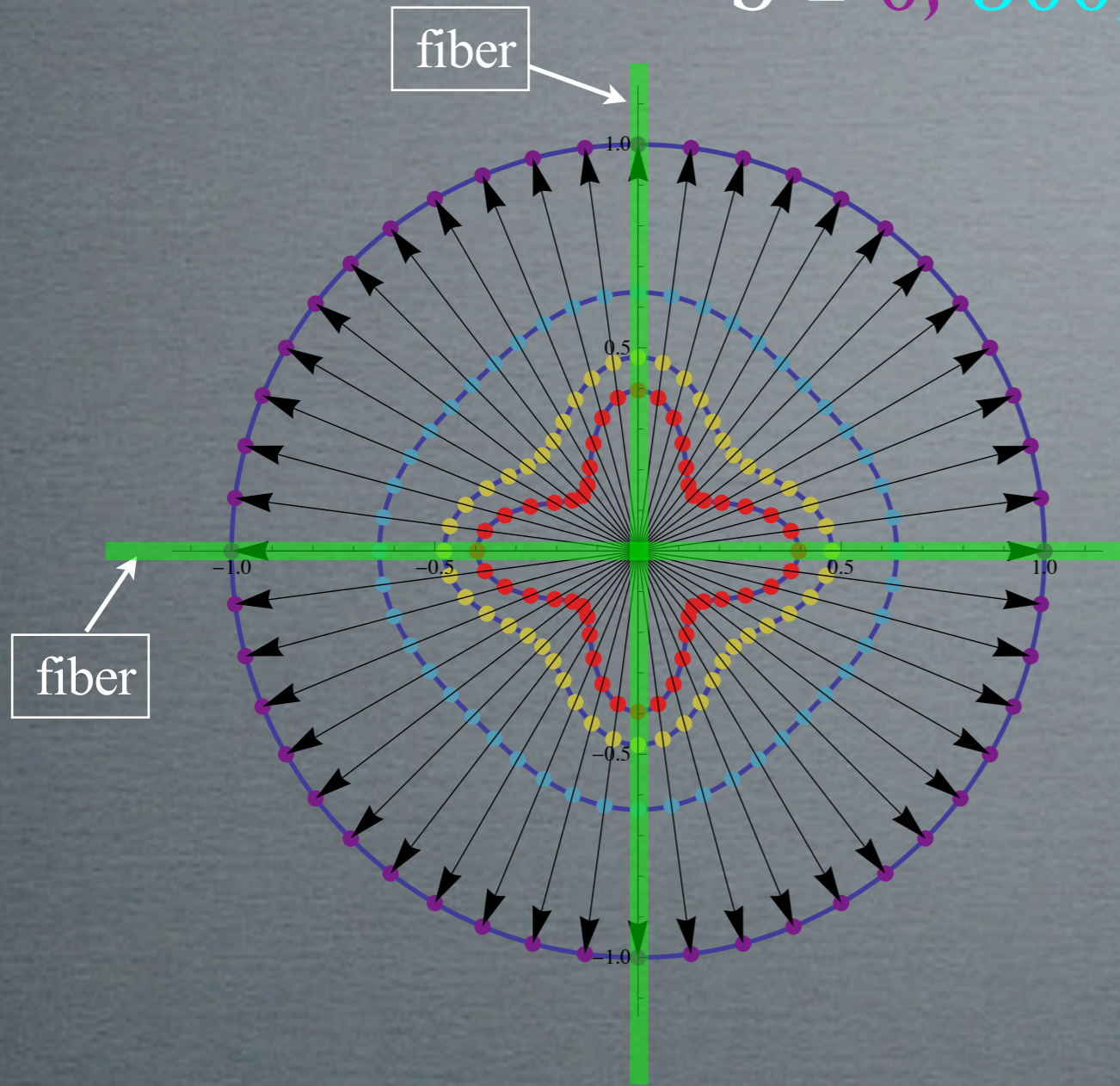
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simple two diffusion coefficient model

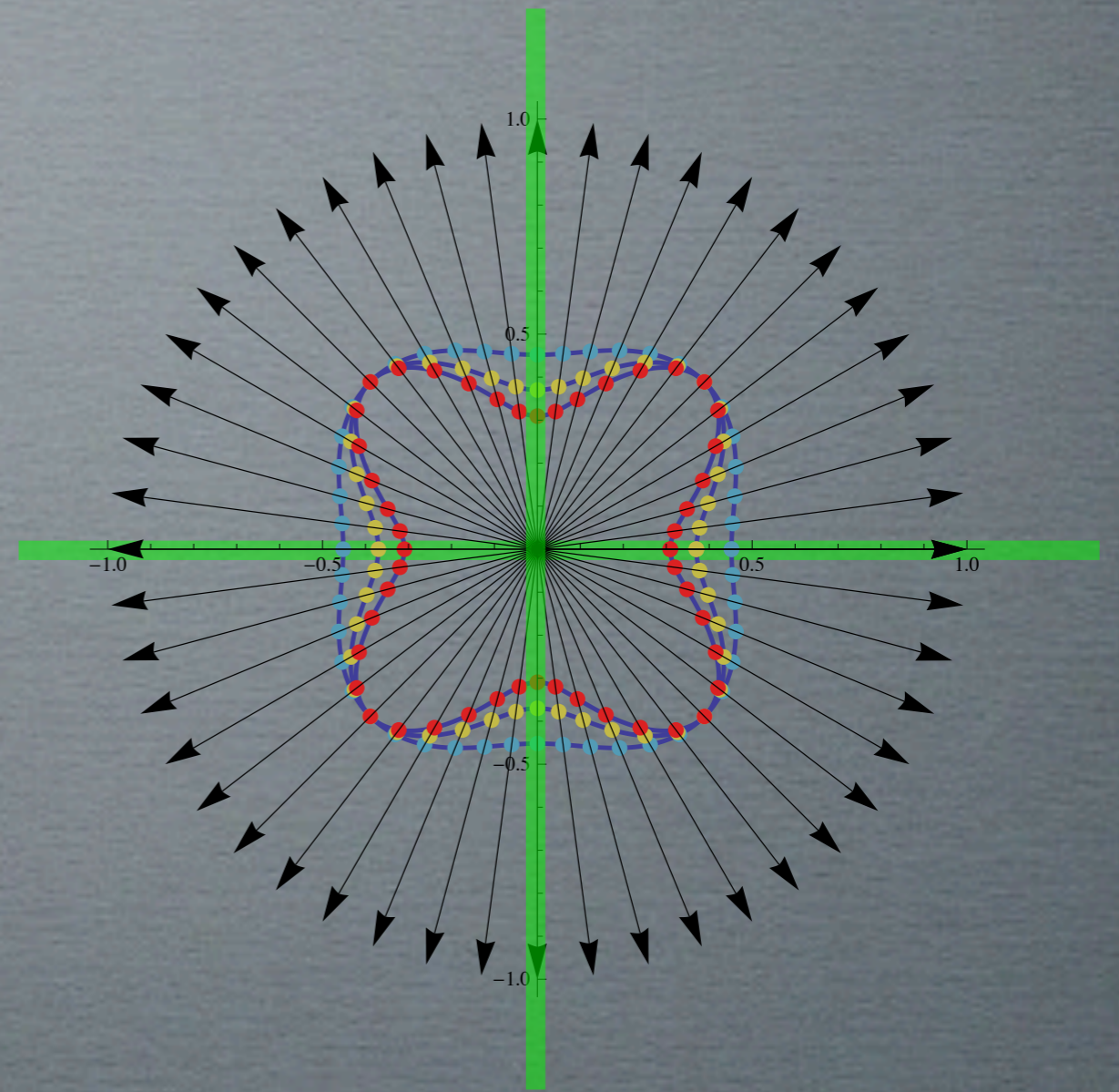
HIGH ANGULAR RESOLUTION DTI (HARDI)

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$b = 0, 500, 1000, 1500$



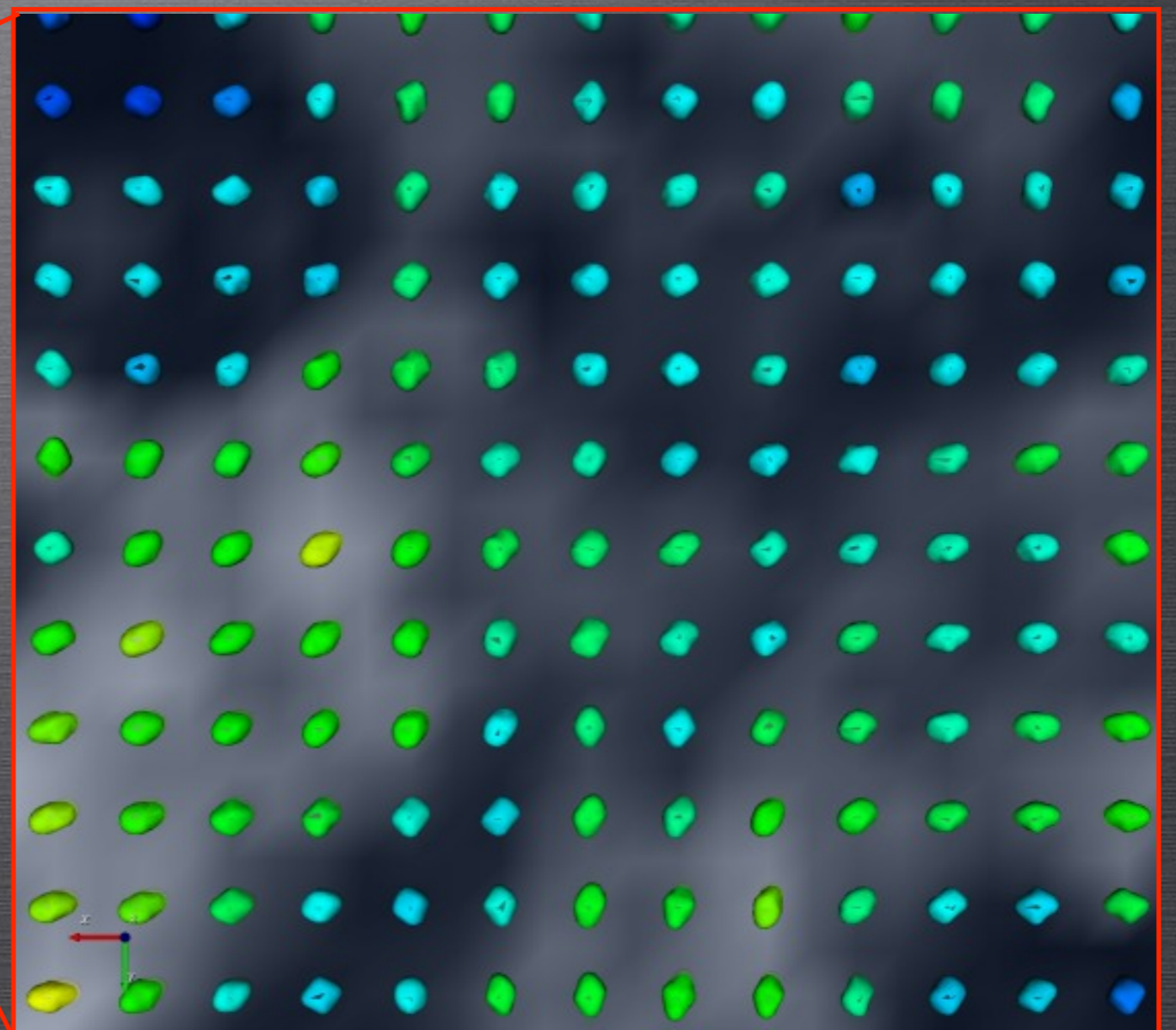
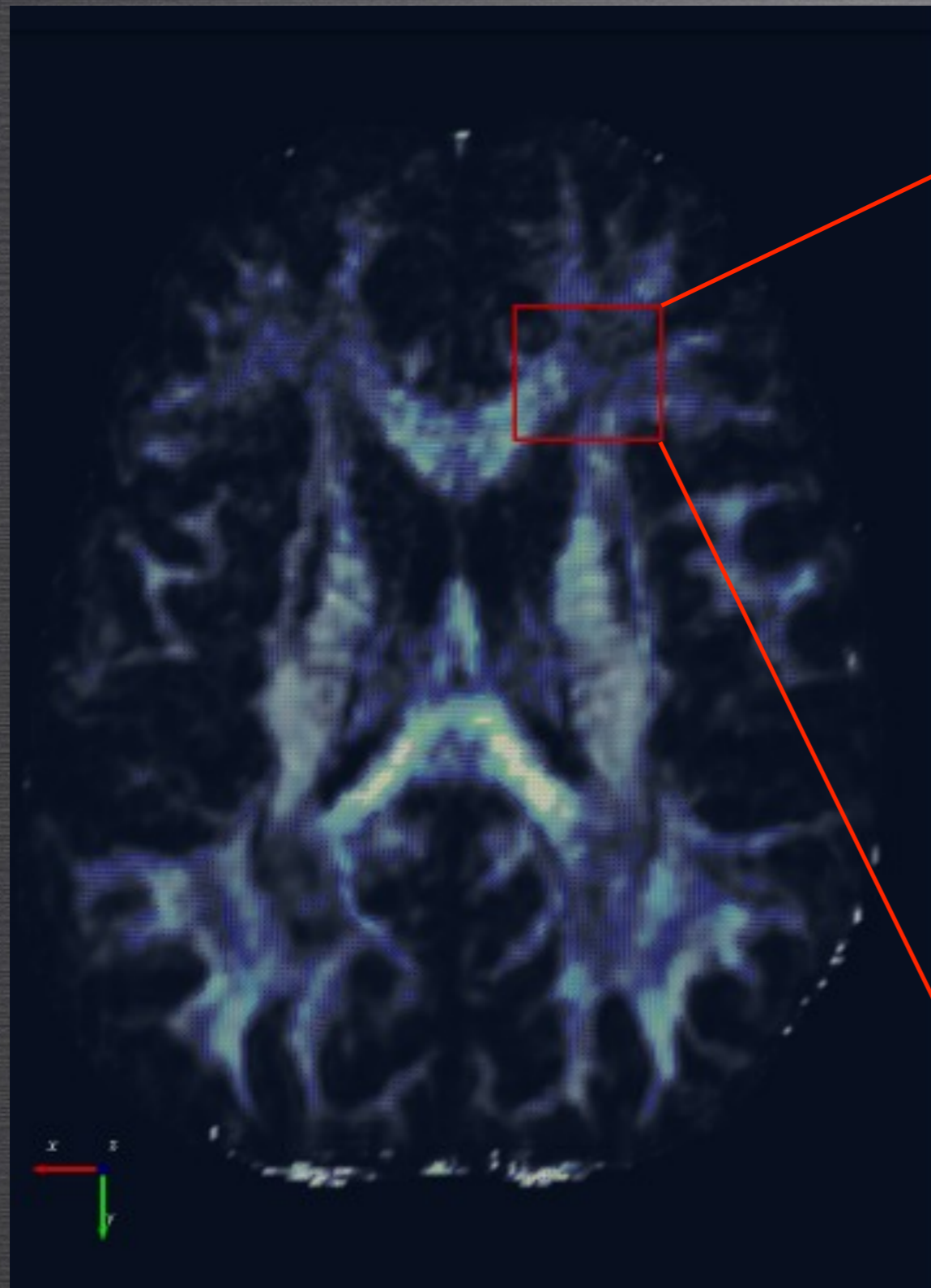
signal



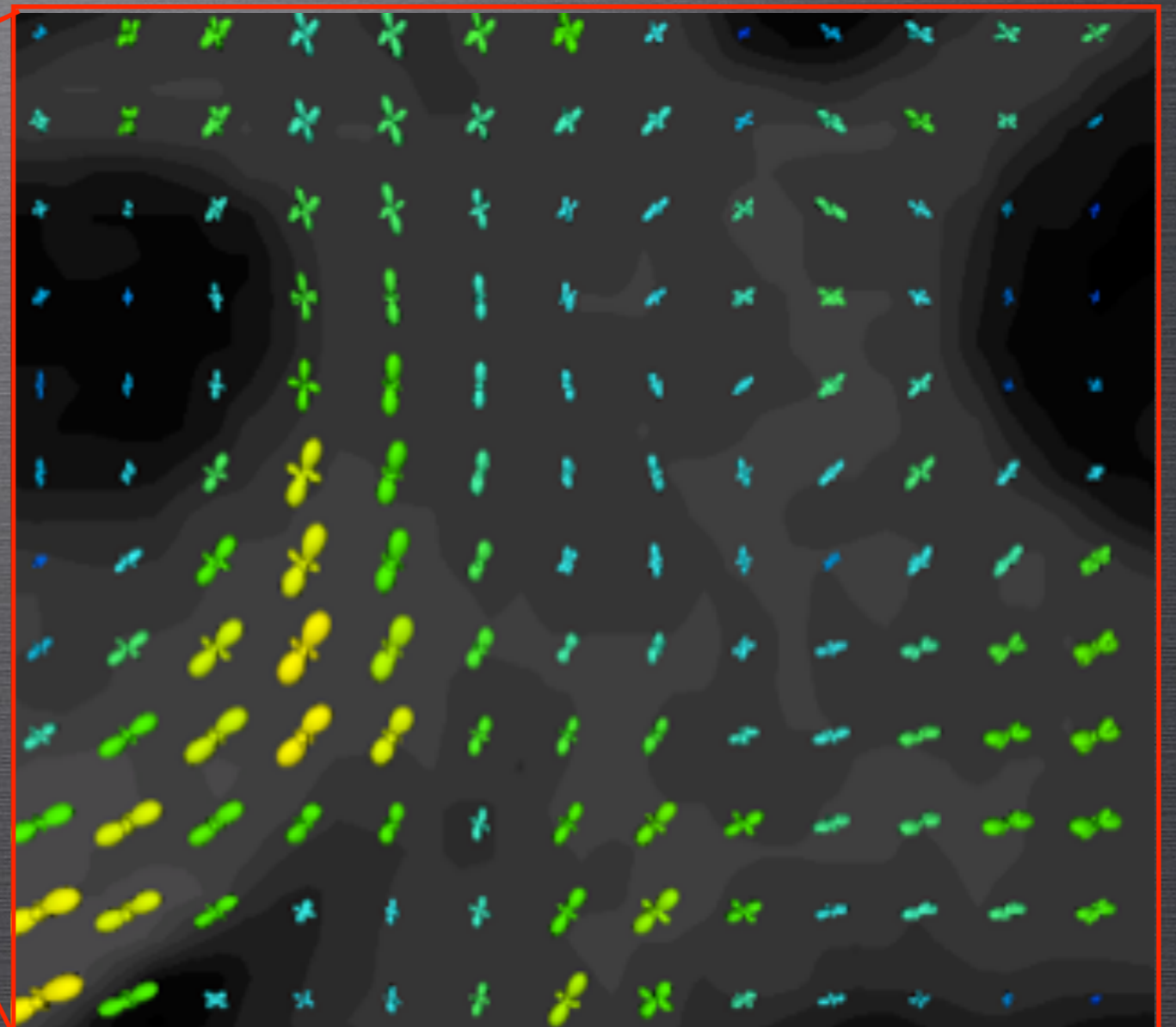
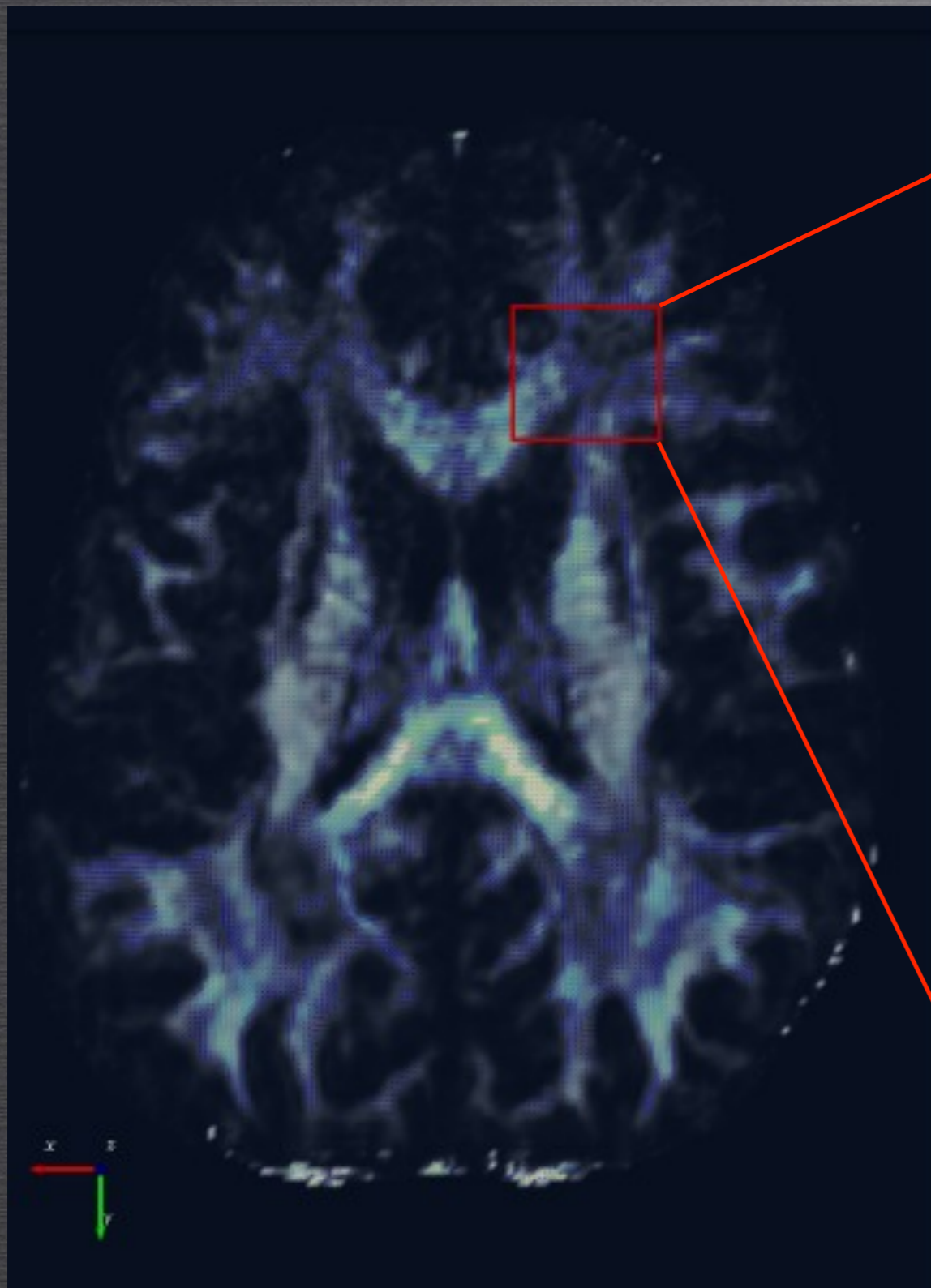
$D_{app}(\theta)$

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

TRACTOGRAPHY PROBLEM, REVISITED

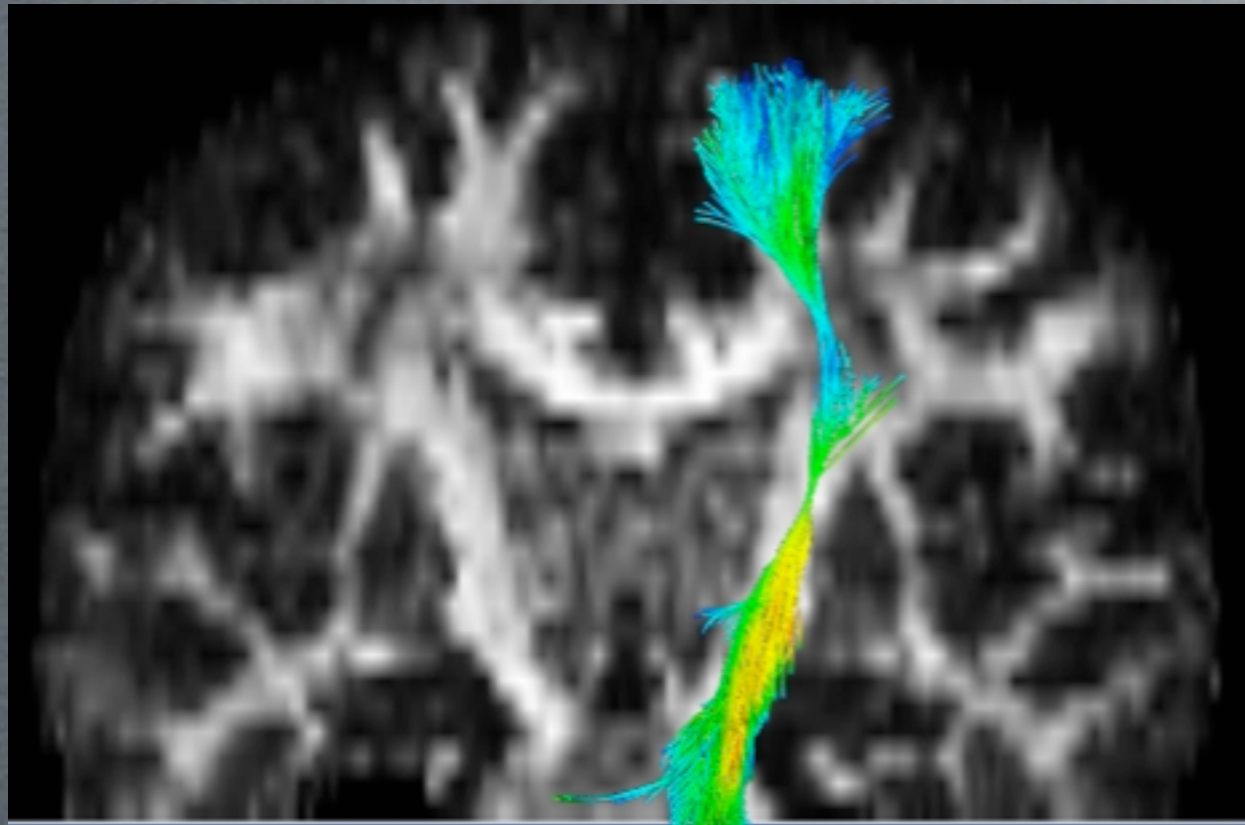


TRACTOGRAPHY PROBLEM, REVISITED

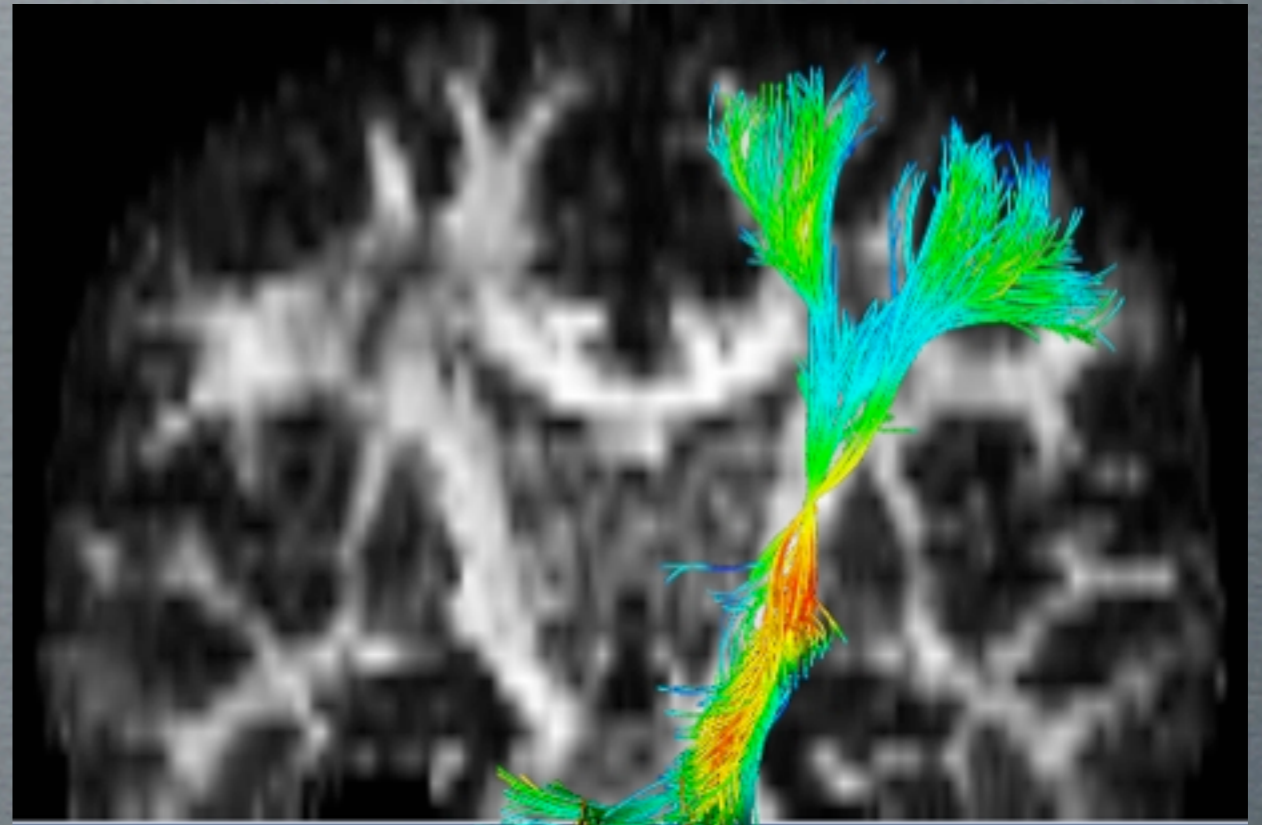


Higher order tensor fit to data

HIGH ANGULAR RESOLUTION DTI (HARDI)



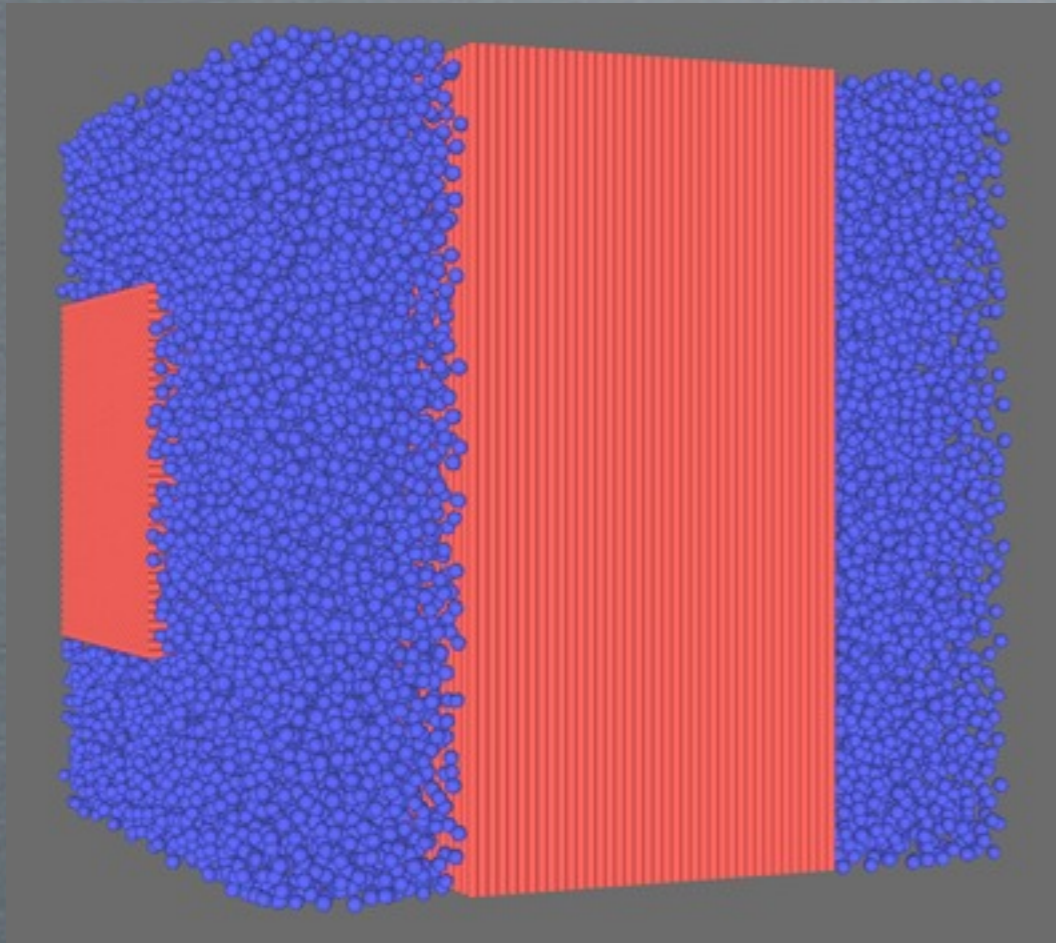
Standard DTI



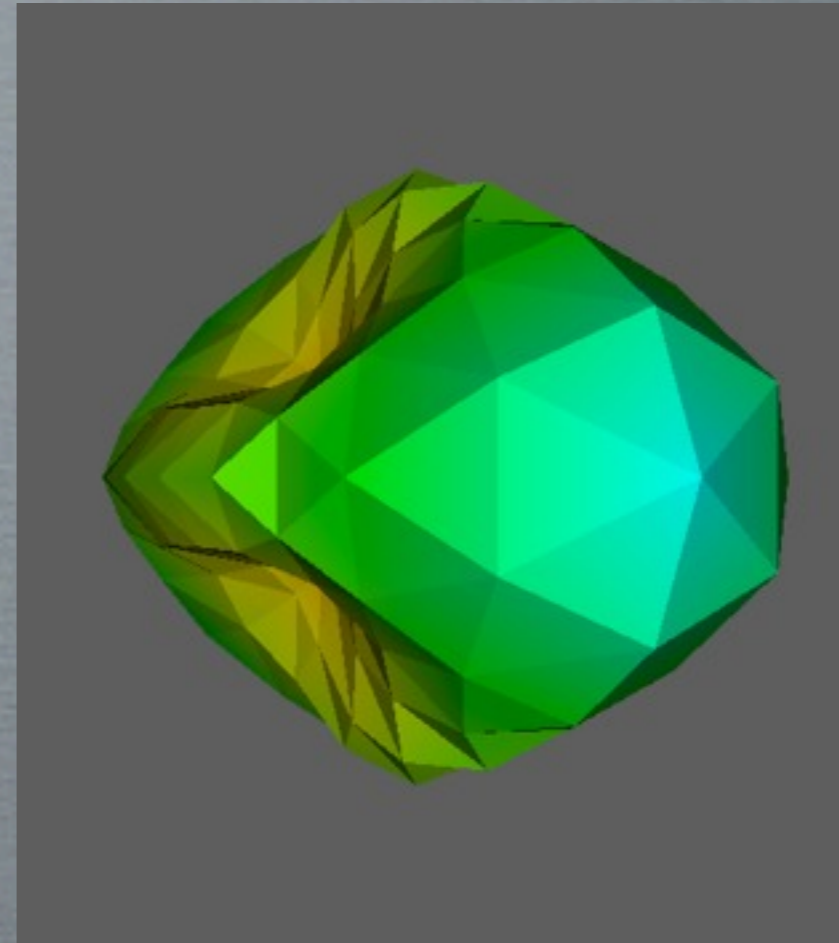
HARDI

HETEROGENEOUS VOXELS AND HIGH ANGULAR RESOLUTION SAMPLING

HETEROGENEOUS VOXELS AND HIGH ANGULAR RESOLUTION SAMPLING



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



signal from 162 directions

CONCLUSION

Diffusion MRI has a unique sensitivity
to tissue architecture and physiology

...and diffusion sensitivity is relatively easy
to incorporate into standard sequences

However ...

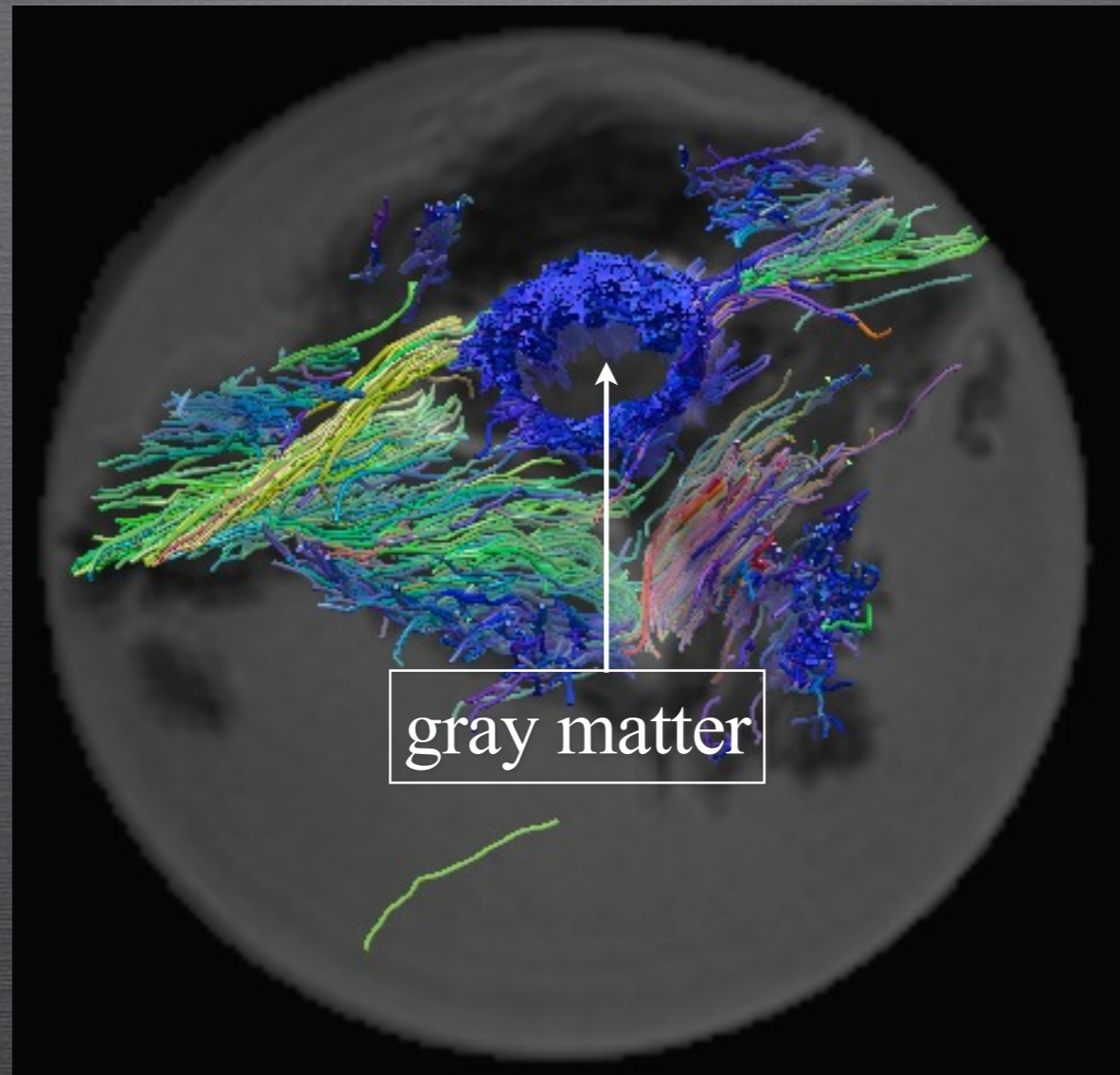
- Data artifact correction non-trivial
- Analysis is complicated
- Interpretation is difficult

But it's really cool!

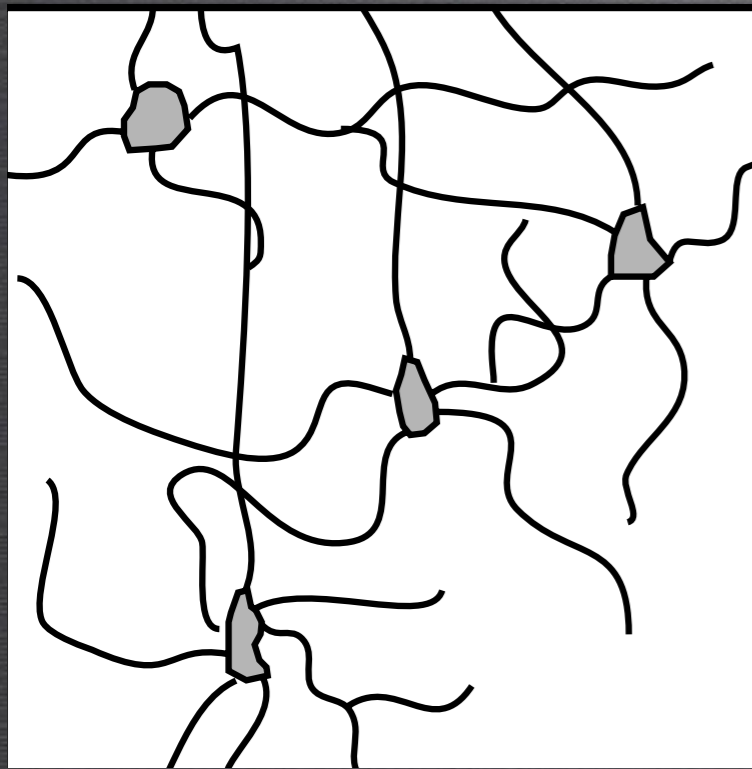
BREAK

FUNDAMENTAL LIMITATION OF DTI HETEROGENEOUS VOXELS

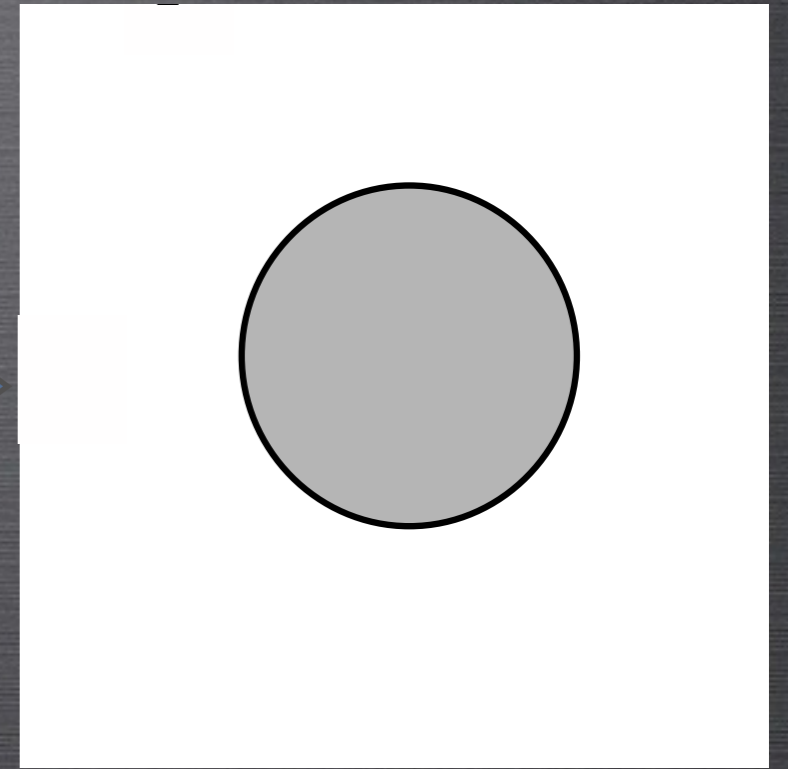
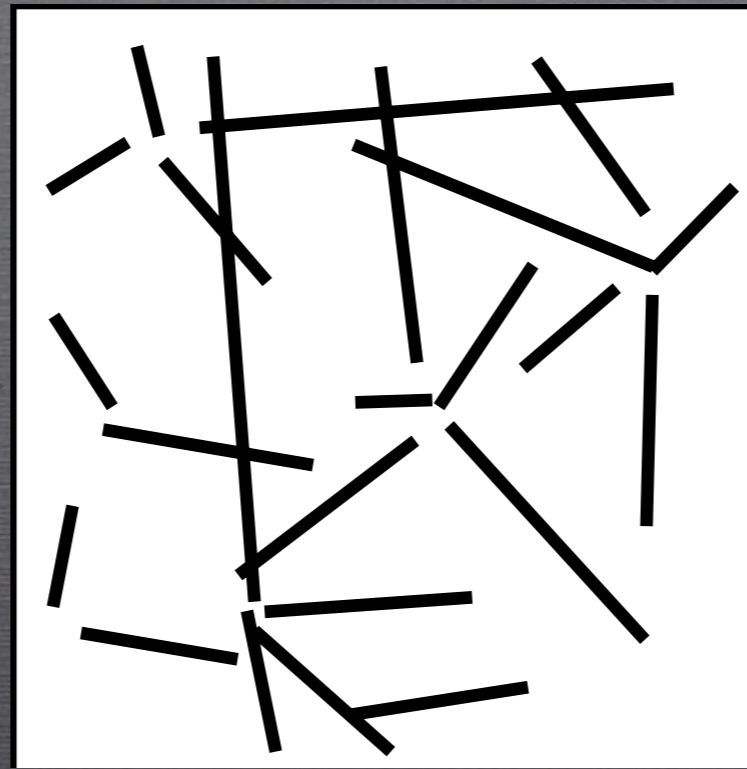
FUNDAMENTAL LIMITATION OF DTI HETEROGENEOUS VOXELS



FUNDAMENTAL LIMITATION OF DTI HETEROGENEOUS VOXELS



Gray matter



microscopically anisotropic but macroscopically (voxel) isotropic

RECAP

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Key point #1: Diffusion is influenced by local geometry and physiology.

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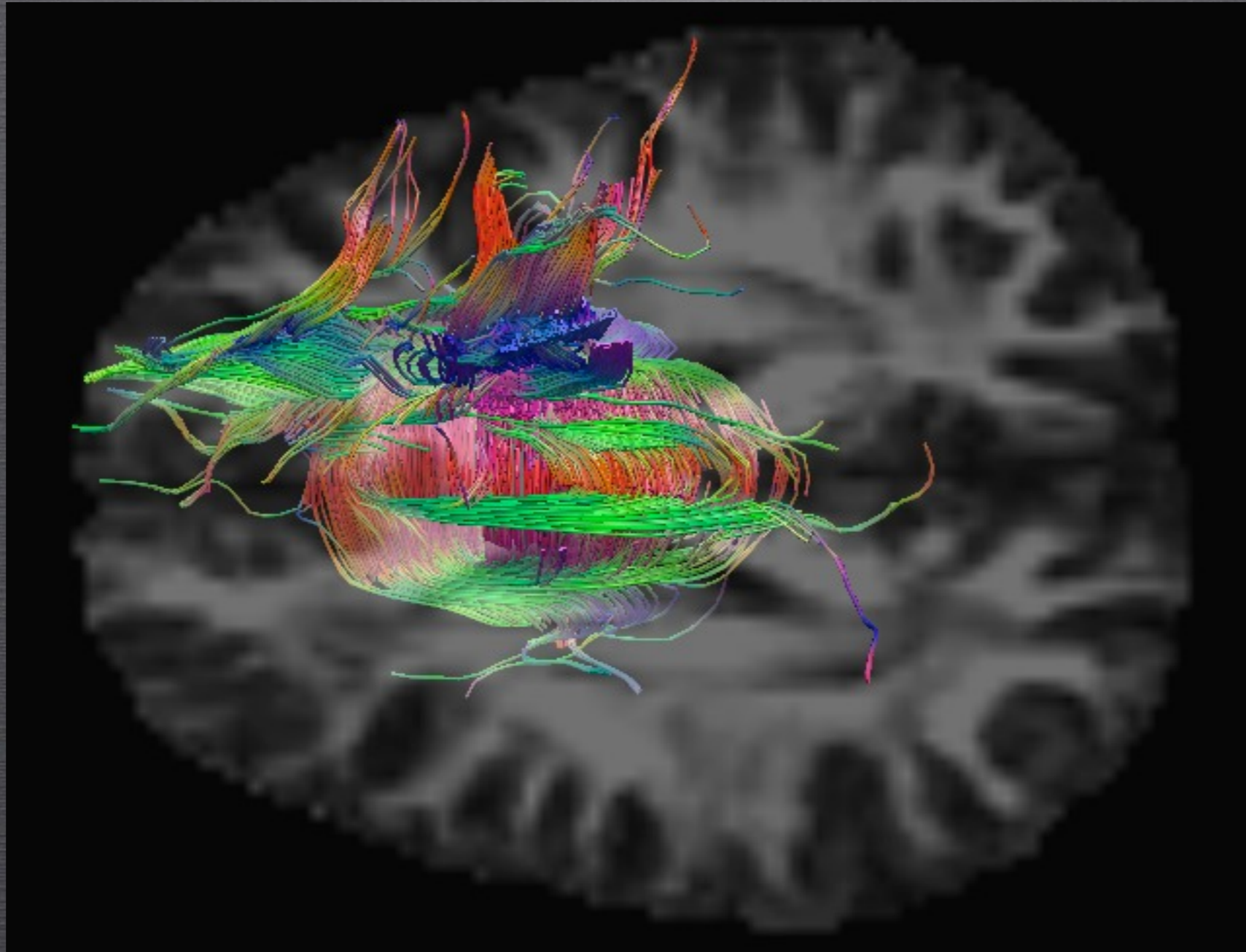
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STREAMLINES

Data courtesy Drs S. Tapert and J. Jacobus, UCSD

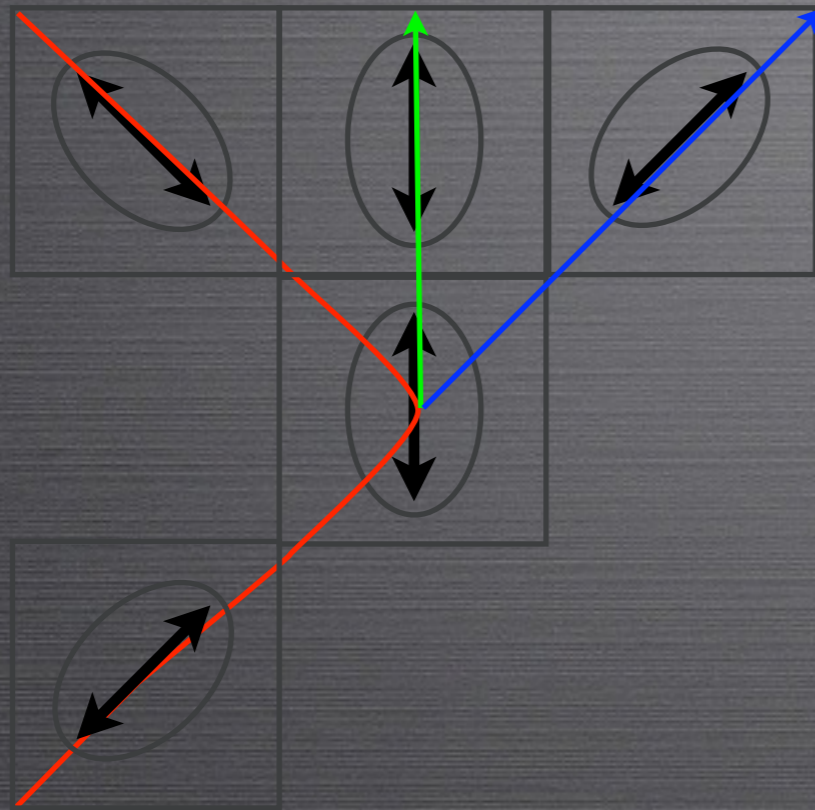
STREAMLINES



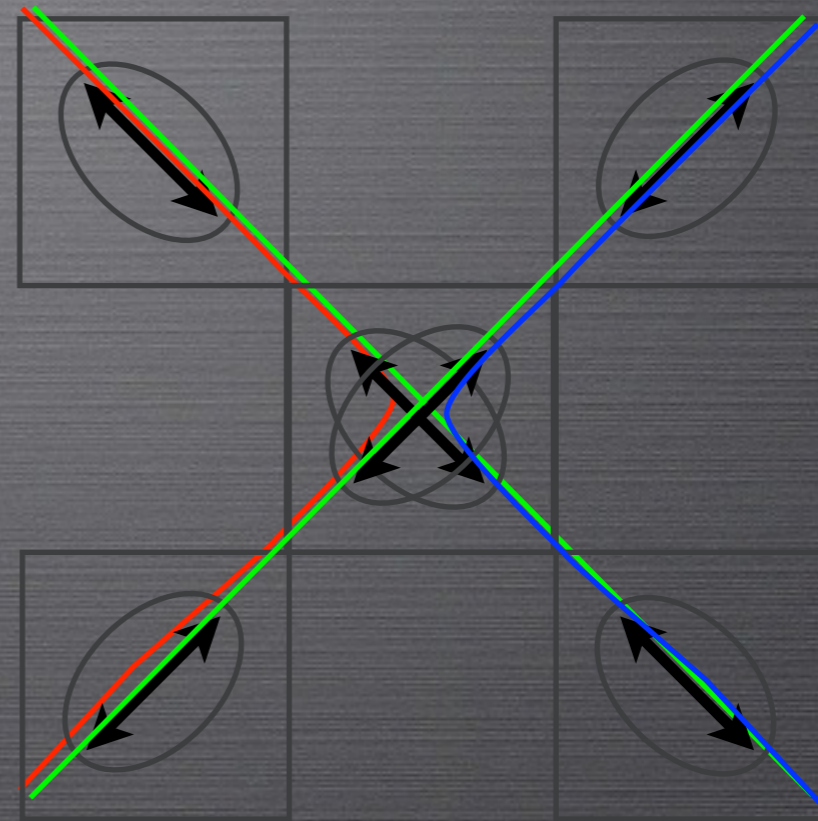
Data courtesy Drs S. Tapert and J. Jacobus, UCSD

TRACKING AMBIGUITY

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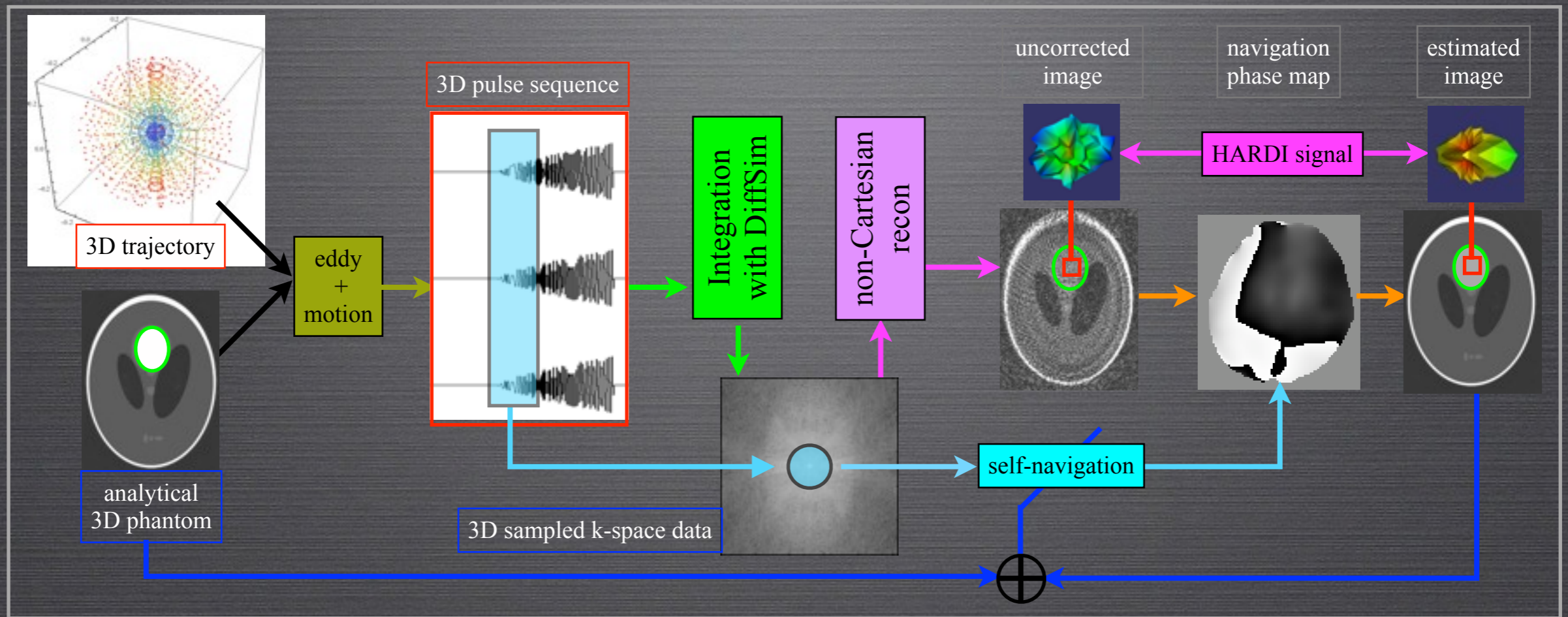
single fibers



crossing/kissing fibers

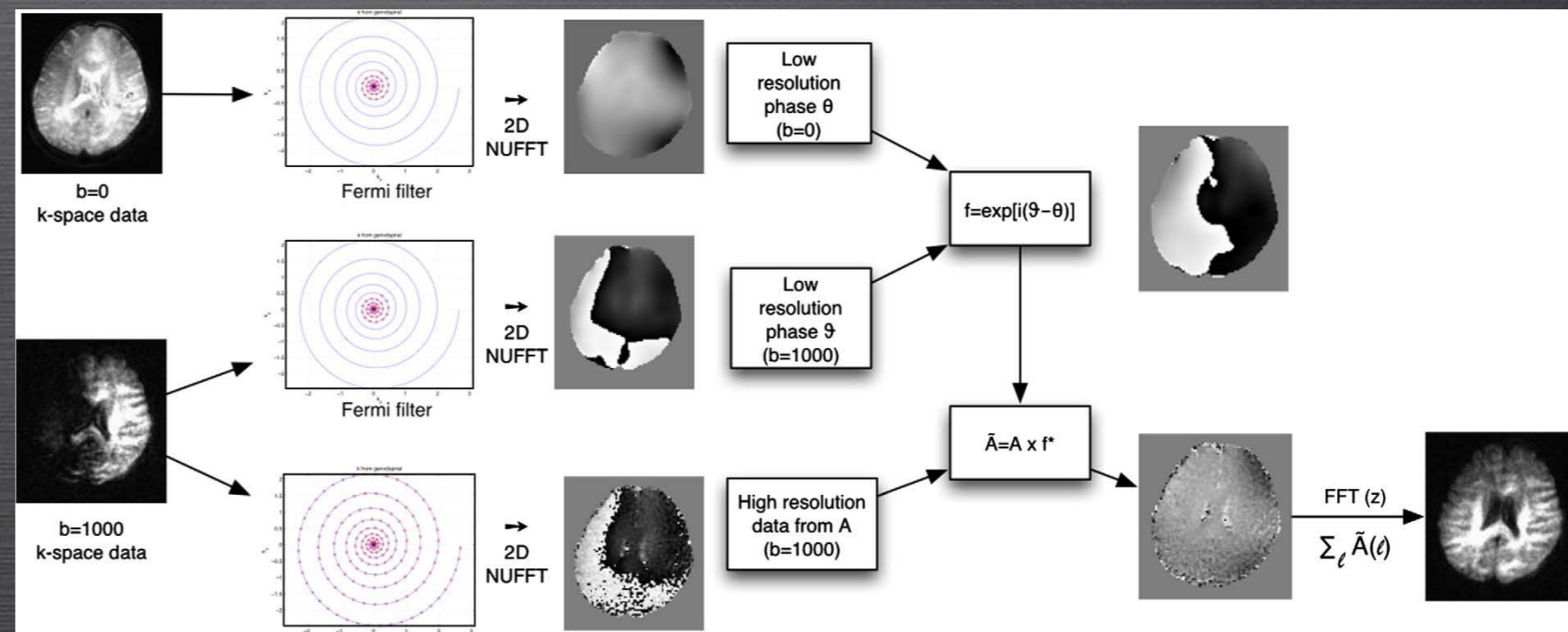
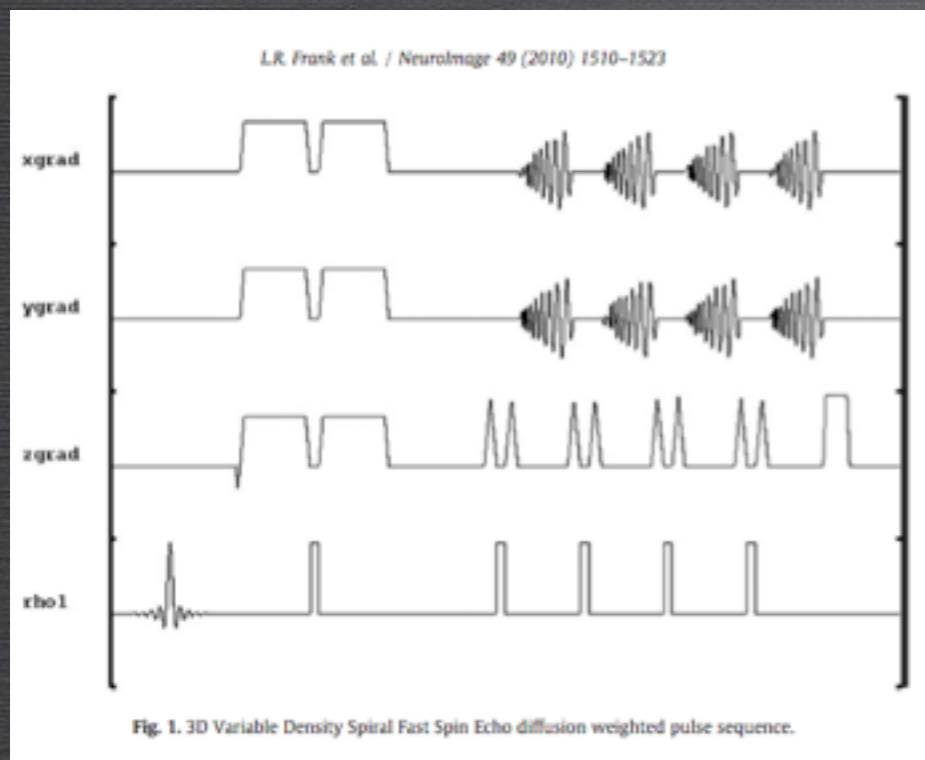
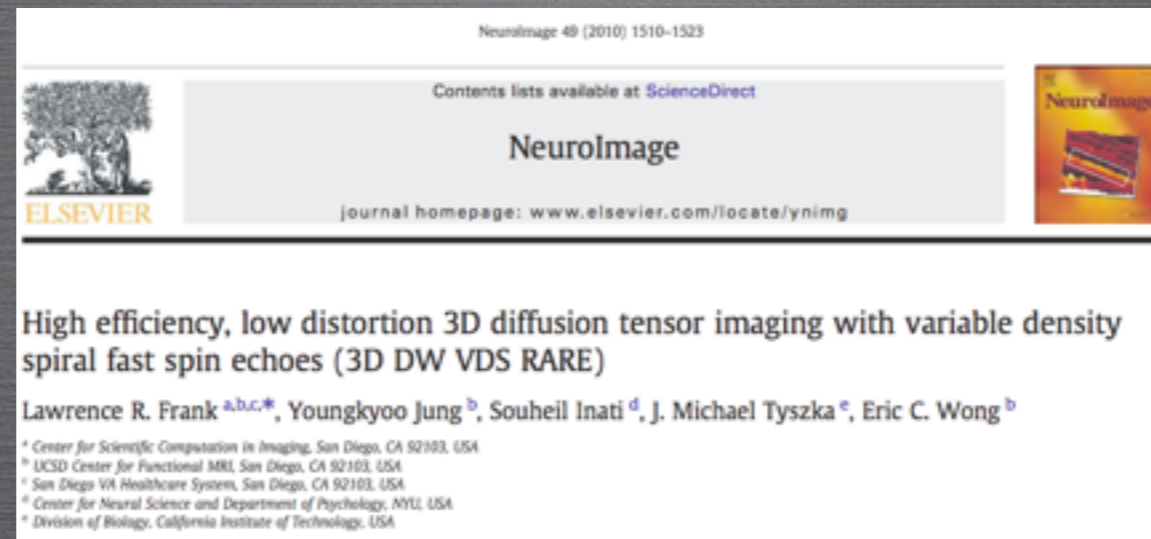
DIFFUSION TENSOR IMAGING (UNDER THE HOOD)

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Pulse sequence, reconstruction, and analysis

DIFFUSION TENSOR IMAGING (UNDER THE HOOD)



Pulse sequence, reconstruction, and analysis

DIFFUSION TENSOR IMAGING (UNDER THE HOOD)

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