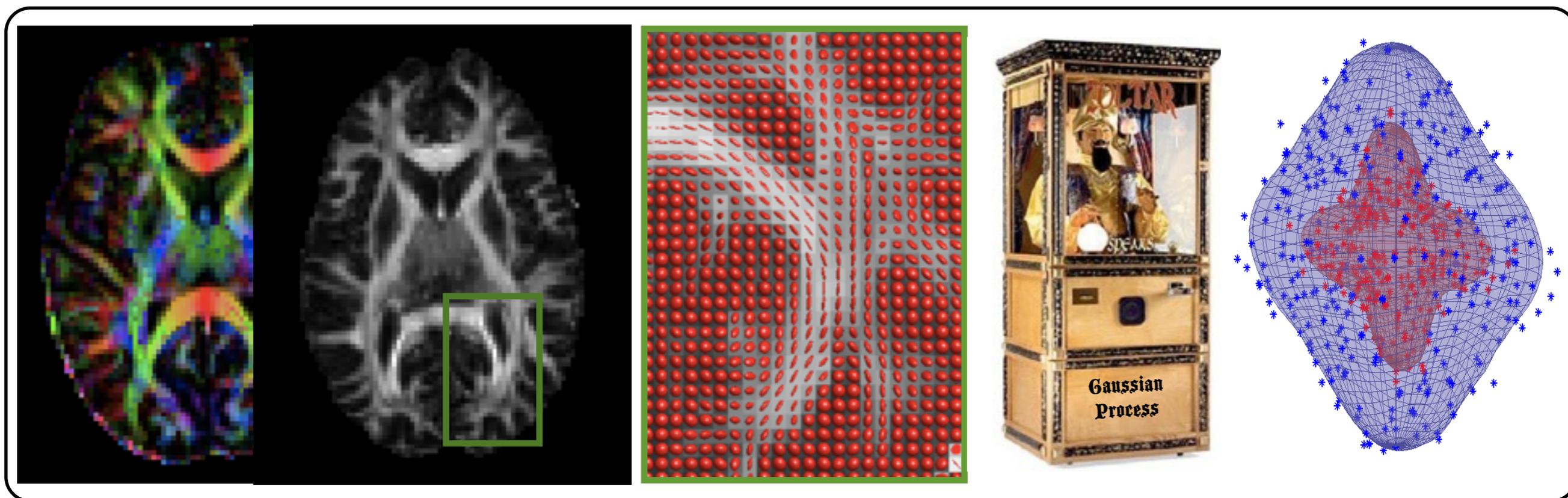
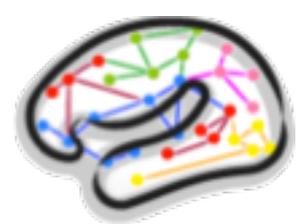


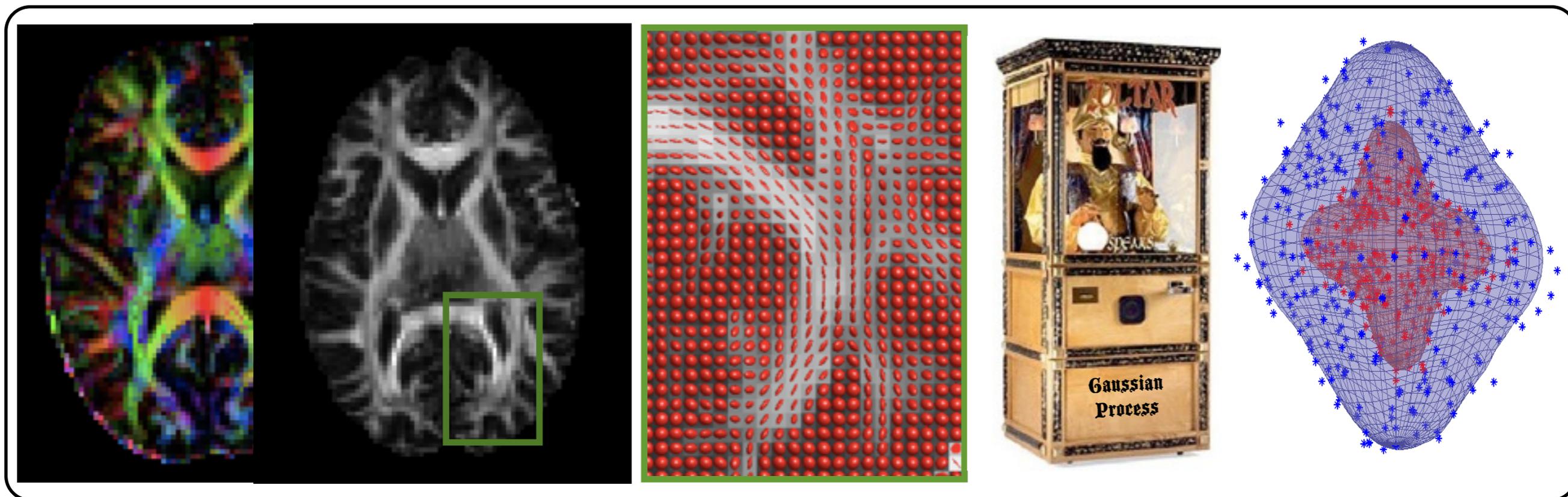
# Diffusion MRI, Distortion Correction & DTI

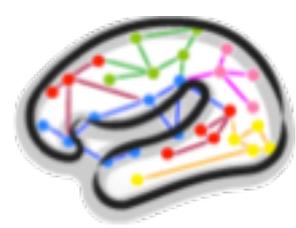




# Overview

- What is Diffusion? Diffusion-weighted MRI
- Diffusion Tensor Model and DTI
- Pre-processing of Diffusion data

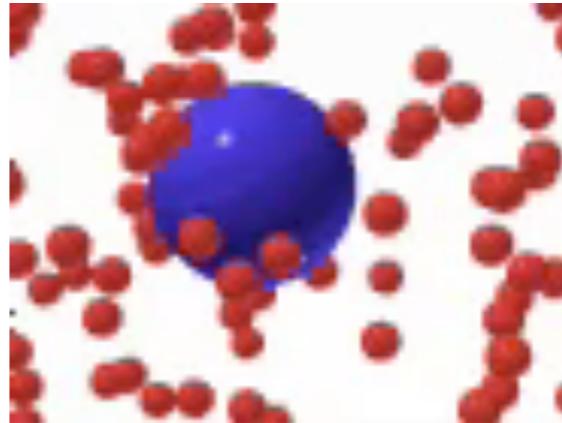




# Diffusion - Brownian Motion

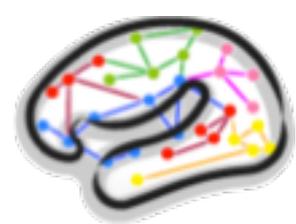


Robert Brown (1773-1858)



**Molecules are in constant motion at non-zero absolute temperatures**

**Diffusion = thermally-driven random motion**



# Diffusion - Brownian Motion



Albert Einstein (1879-1955)

How can we describe this motion?  
For an ensemble of molecules, in  $n$ -dimensional space:

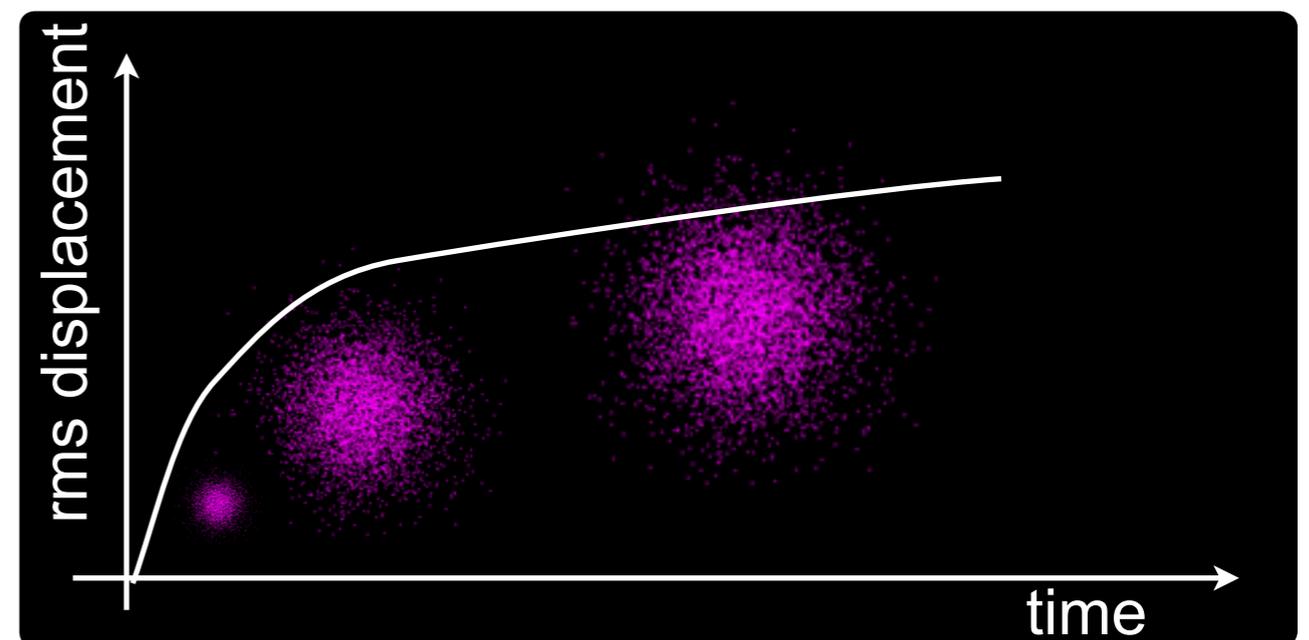
$$\langle x^2 \rangle = 2nDt$$

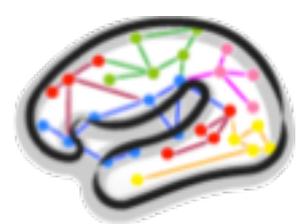
mean squared displacement

Diffusion coefficient

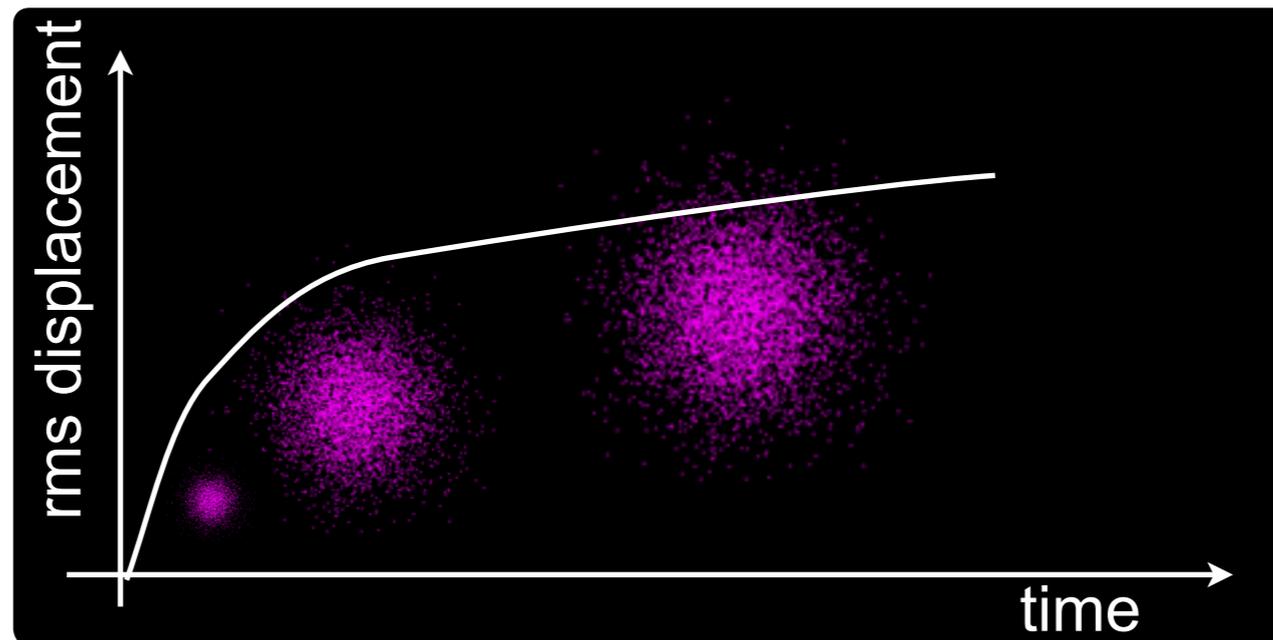
time

Valid for a homogeneous, barrier-free medium.





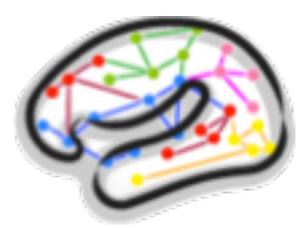
# Diffusion - Brownian Motion



$$\langle x^2 \rangle = 2nDt$$

$$D \sim 2.4 \mu\text{m}^2/\text{ms}$$
$$t \sim 50\text{ms}$$

$$\Rightarrow x = \sqrt{6Dt} \sim 27\mu\text{m}$$

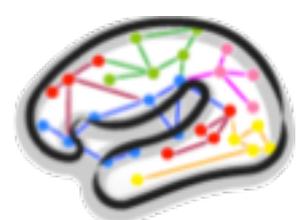


## Diffusion - Brownian Motion

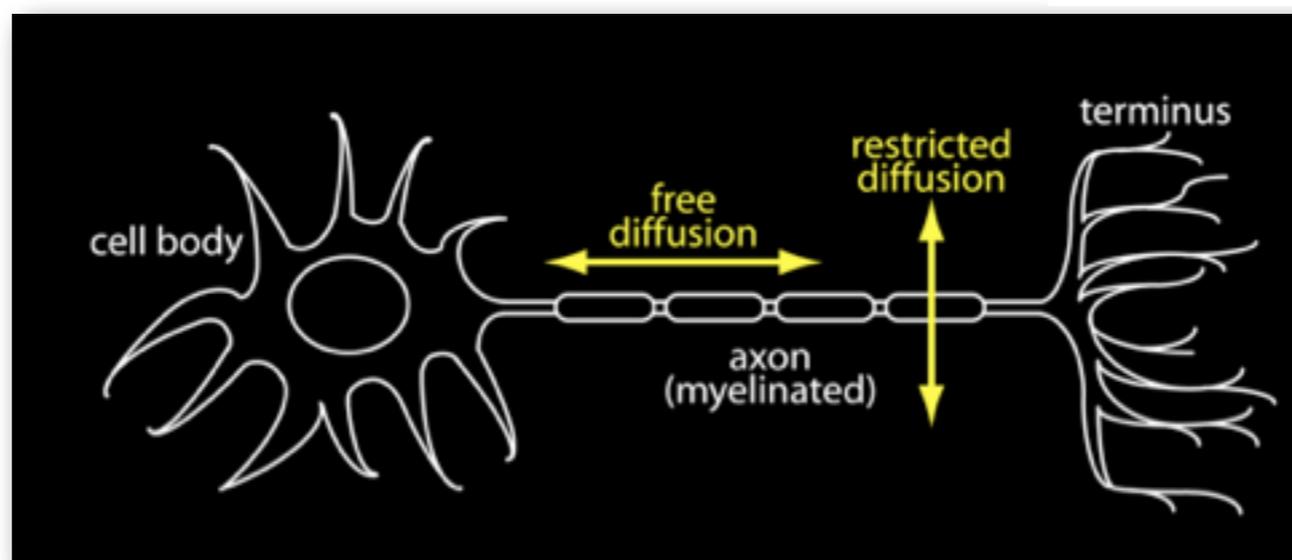
Another way to describe Einstein's equation:

For a barrier-free medium, **diffusion displacements of an ensemble follow a Normal distribution** with  $N(0, 2tD)$ :

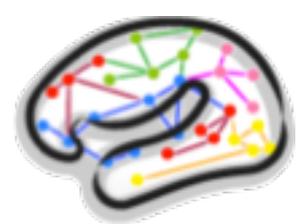
- Zero-mean displacement  
(some will diffuse left, some will diffuse right, equal distances on average)
- Variance proportional to time and the diffusion coefficient



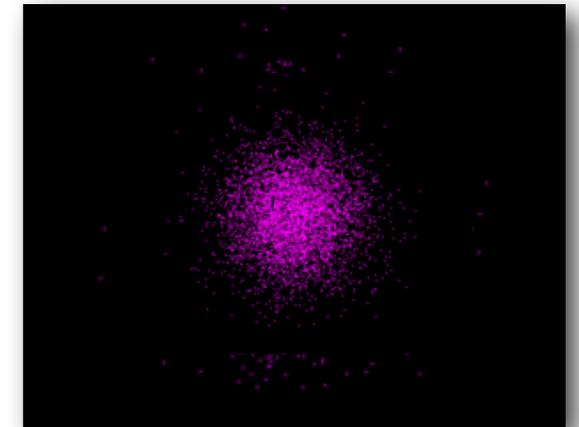
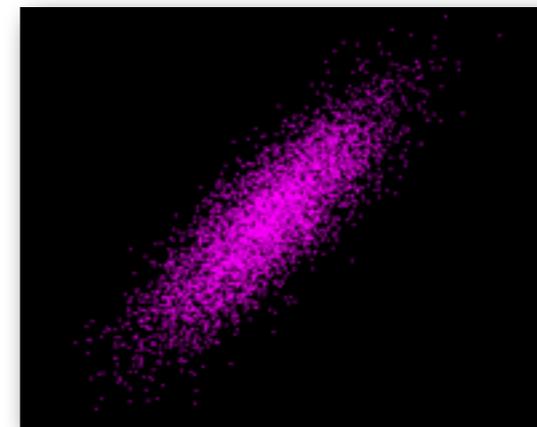
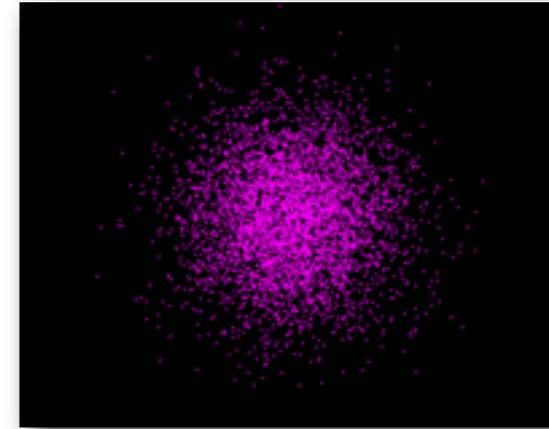
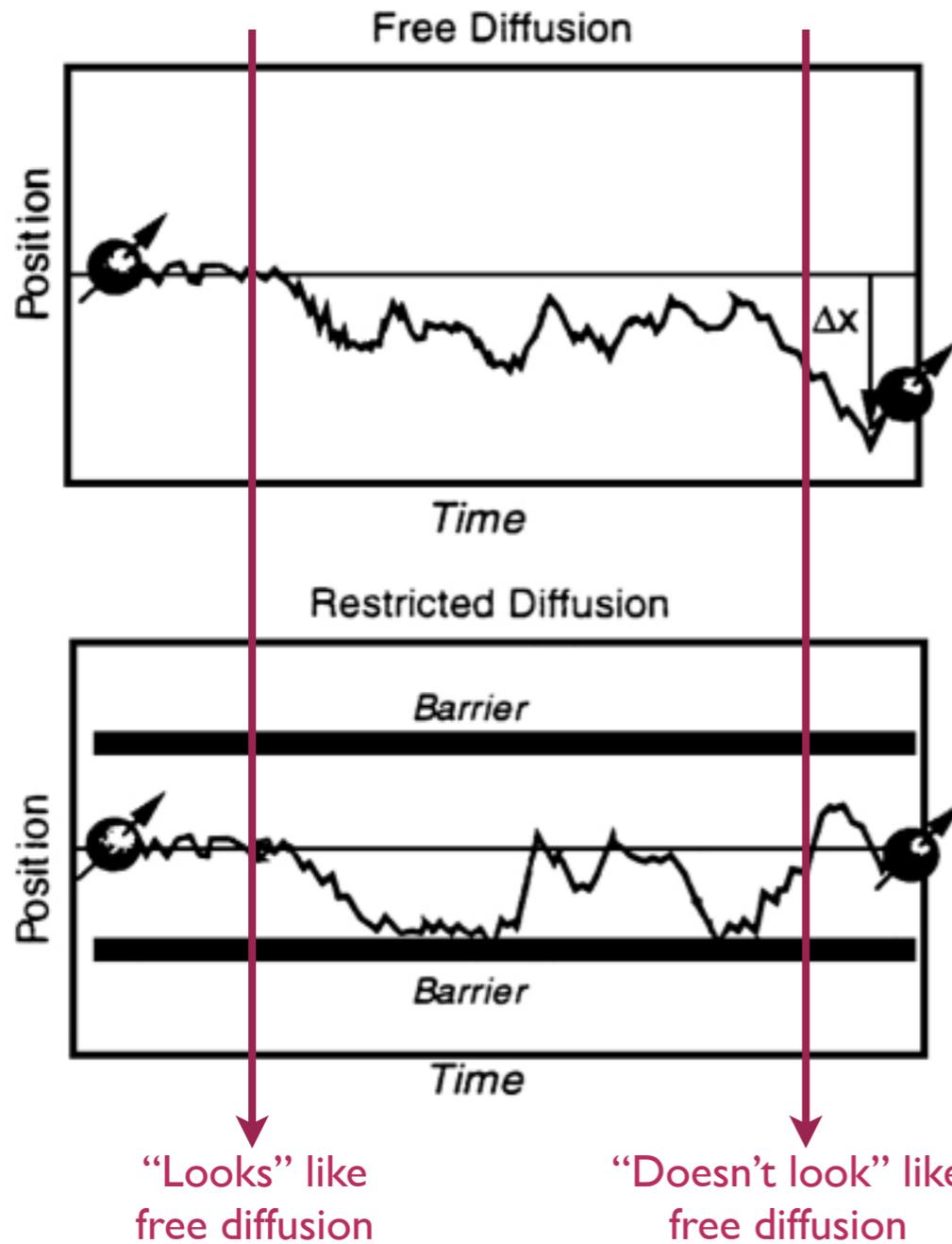
# Water Diffusion in the Brain. Why is it Interesting?



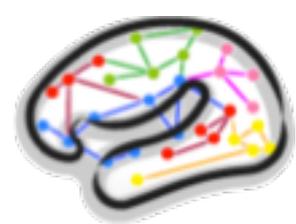
Diffusion is restricted by tissue boundaries, membranes, etc.  
Marker for tissue microstructure (healthy and pathology)  
Diffusion is **anisotropic** in white matter



# Apparent Diffusion



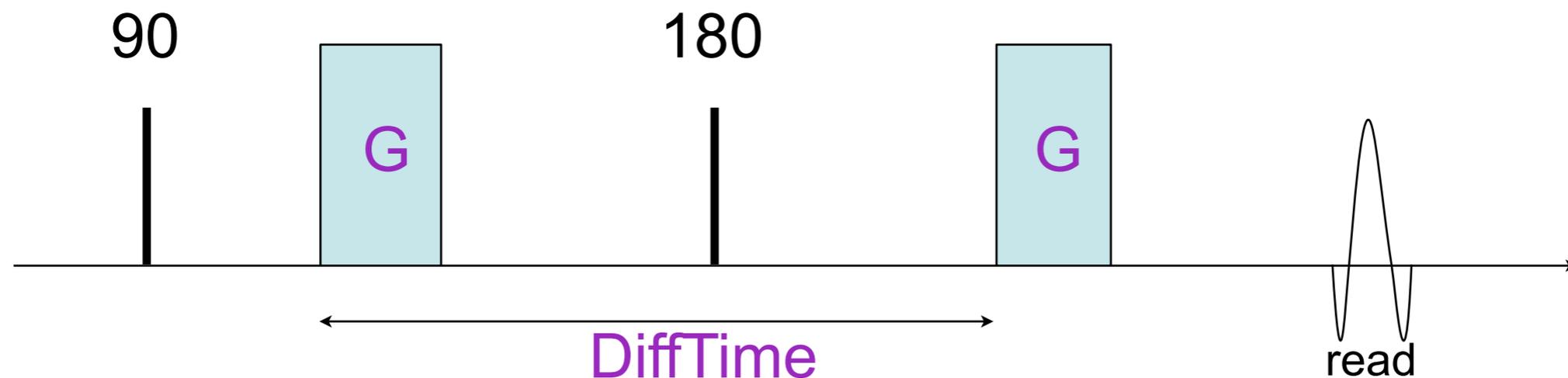
Observed diffusion in tissues depends on the experiment =  
“Apparent diffusion” &  
“Apparent diffusion coefficient” (ADC)



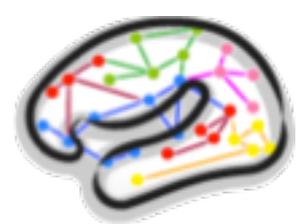
## Measuring Diffusion with MRI: Diffusion-Weighted Imaging (DWI)

Pulsed-Gradient Spin-Echo Sequence:

To achieve diffusion-weighting along a direction  $\mathbf{x}$ , apply strong magnetic field gradients along  $\mathbf{x}$ .



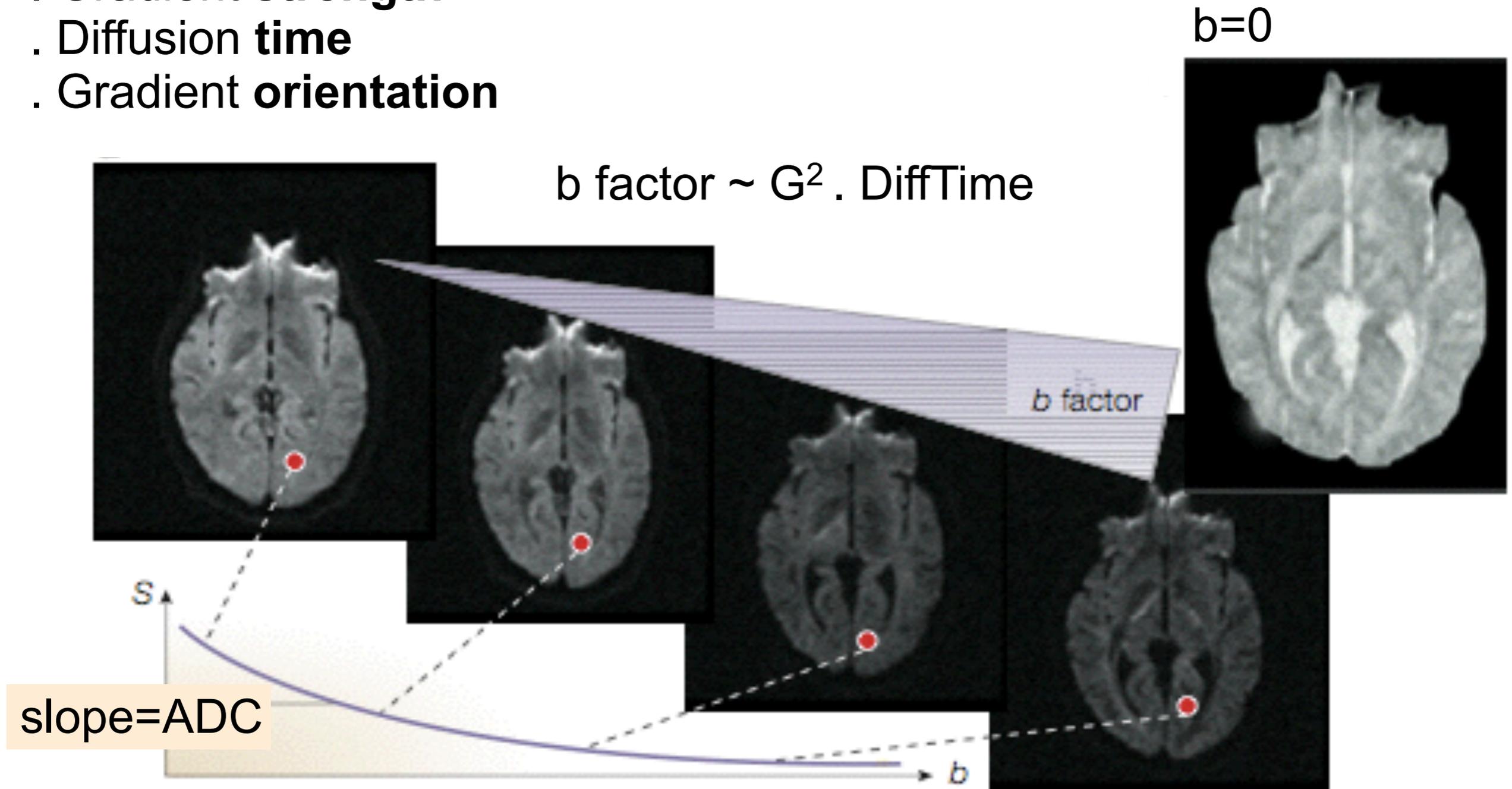
If particles diffuse during the allowed time (DiffTime), a signal attenuation is observed, compared to the signal with  $G=0$ .



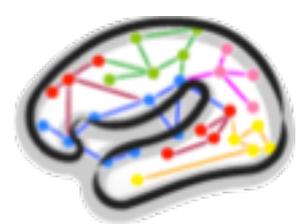
# Measuring Diffusion with MRI: Diffusion-Weighted Imaging (DWI)

Diffusion-weighting is modulated by:

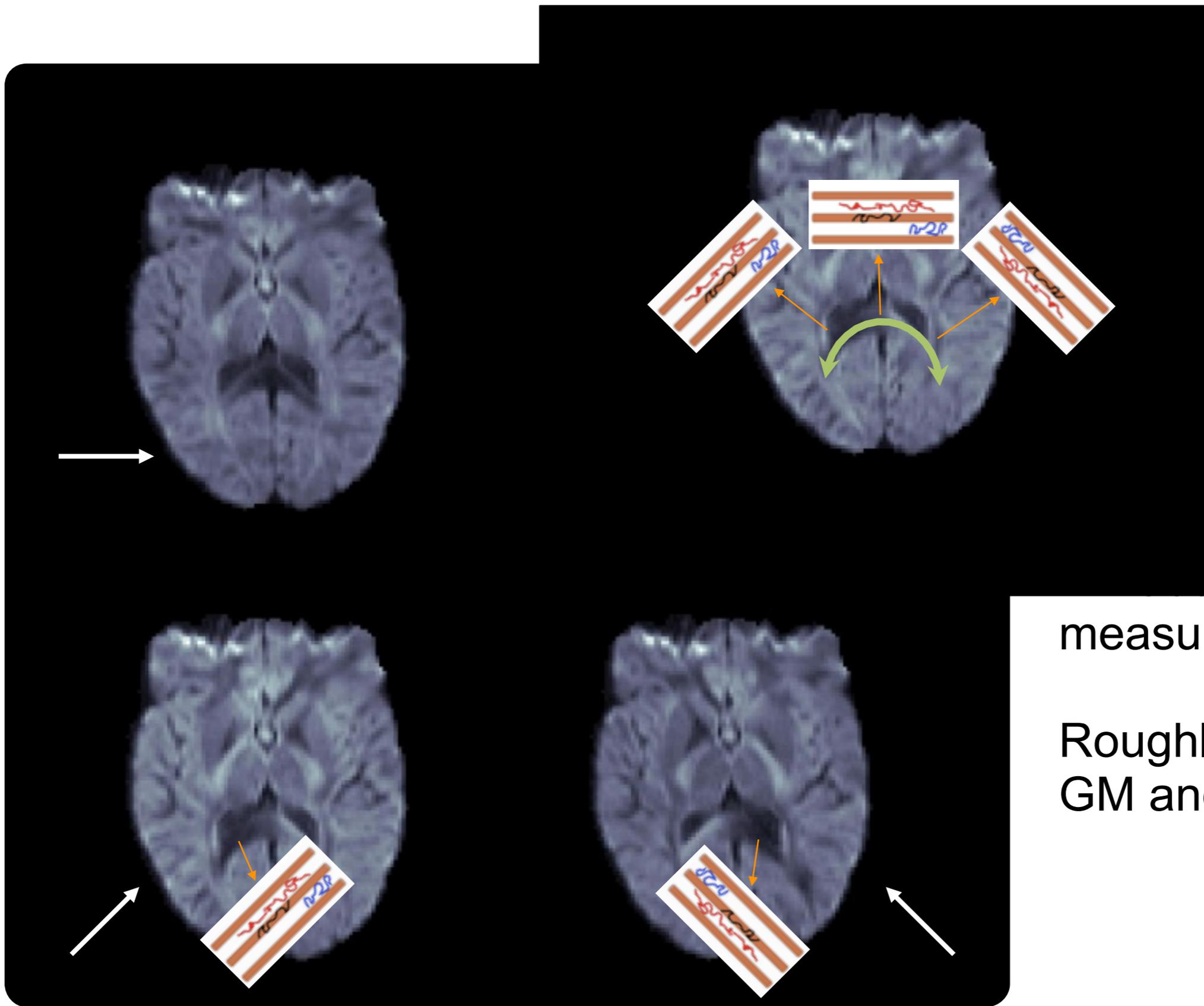
- . Gradient **strength**
- . Diffusion **time**
- . Gradient **orientation**



$$S = S_0 \exp(-b \cdot \text{ADC})$$



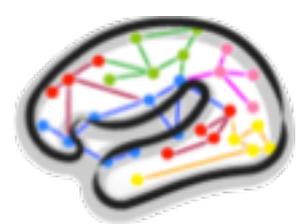
# Orientation Contrast in DWI



...e diffusion is  
...ropic in WM,  
...g a gradient  $G$   
...ifferent  
...ns  $x$ , gives  
...t contrast in

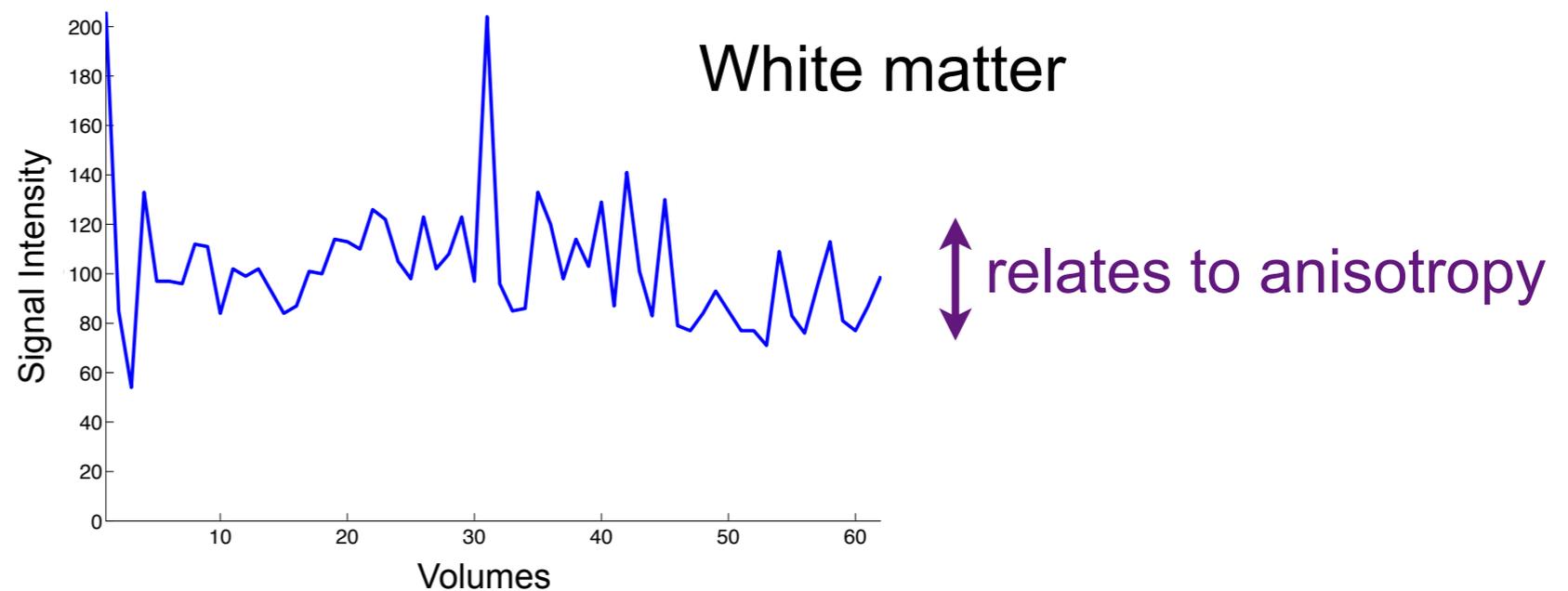
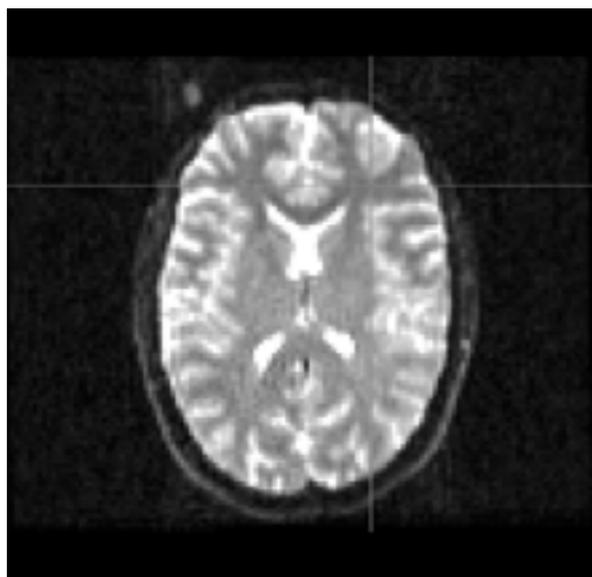
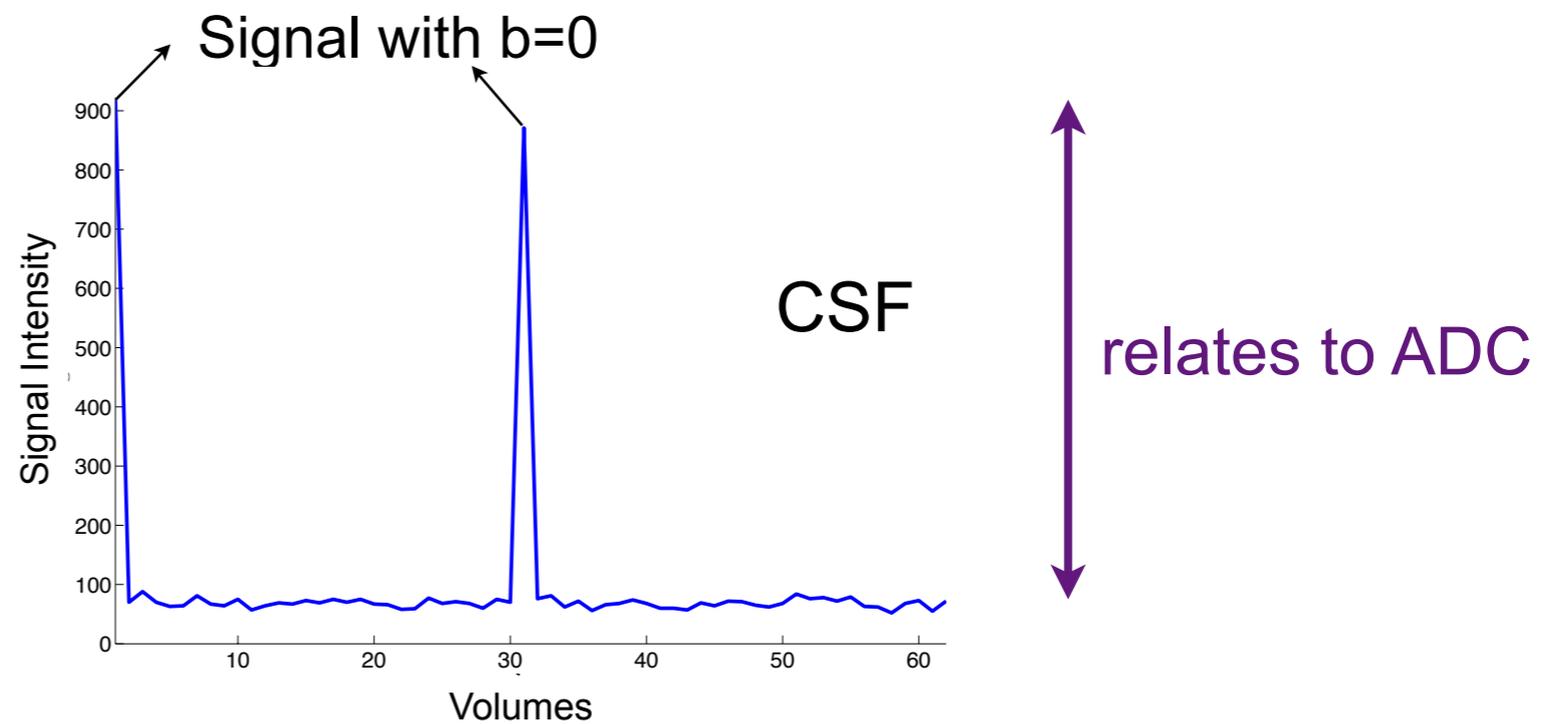
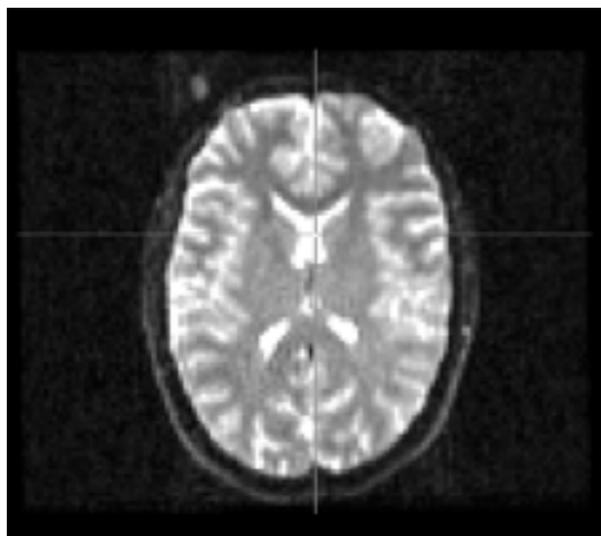
**Isotropic**  
measurements in WM

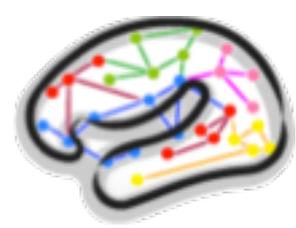
Roughly **Isotropic** in  
GM and CSF.



# A Typical DWI Protocol

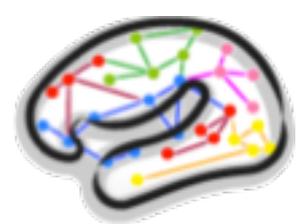
- Normally a few (at least one)  $b=0$  volumes acquired, along with volumes at higher  $b$  ( $\sim 1000$   $\text{s}/\text{mm}^2$ ).
- Different gradient directions are applied for the high  $b$  volumes.



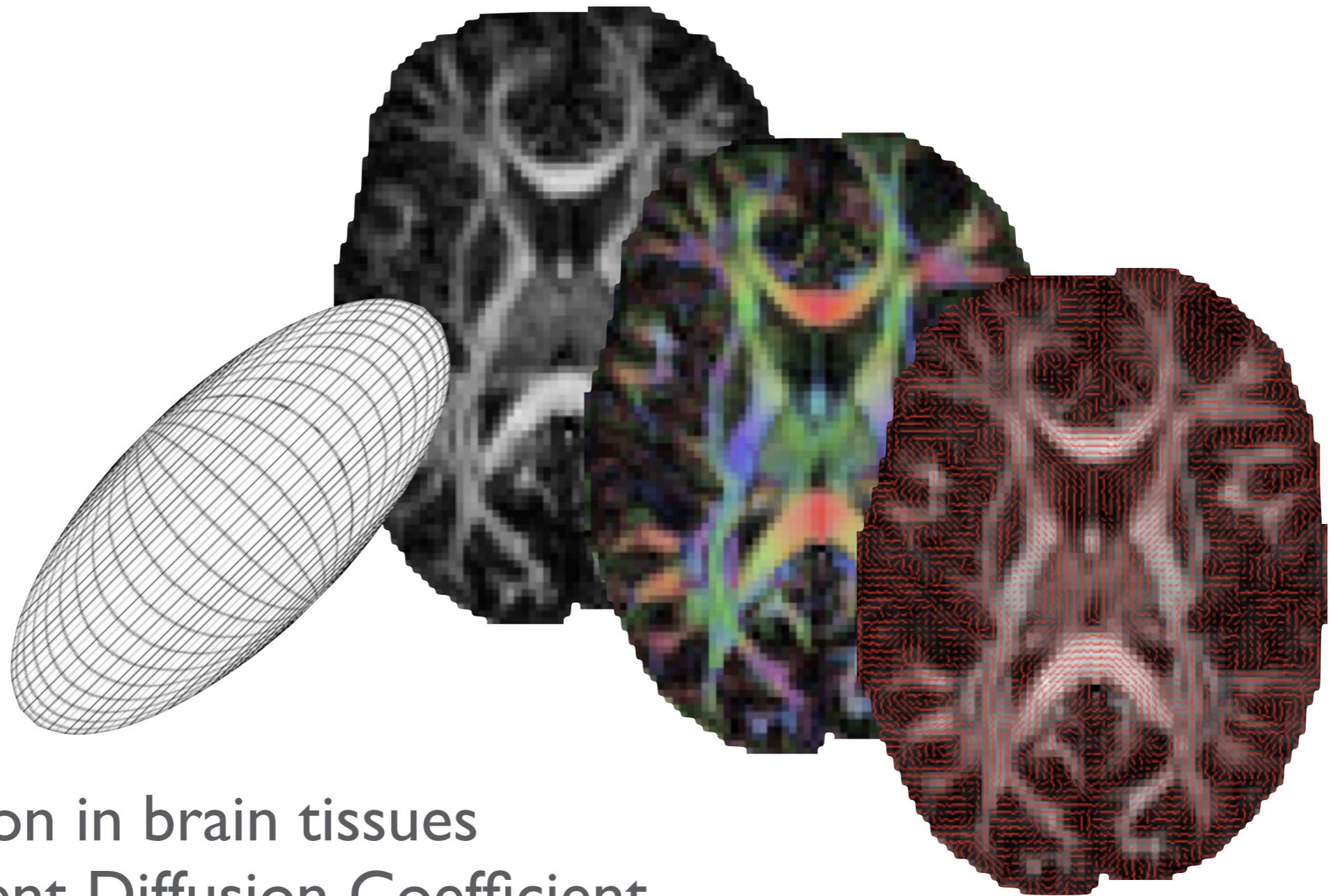


## DWI Summary

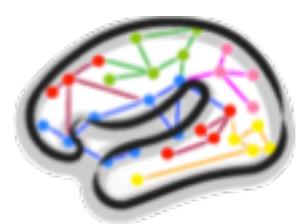
- Images acquired with a Gradient along  $\mathbf{x}$ , have contrast that is sensitive to diffusion of water molecules along  $\mathbf{x}$ .
- When diffusion occurs, signal is attenuated compared to the one with no diffusion-weighting.
- In WM, measurements are anisotropic.
- In GM and CSF, measurements are roughly isotropic.



# Diffusion Tensor Imaging - basic principles

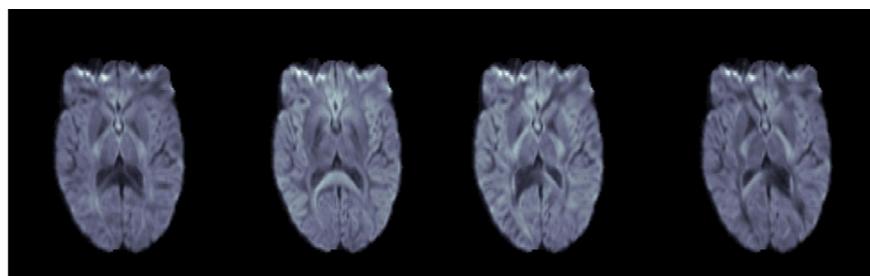


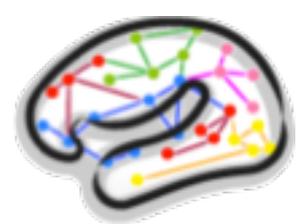
- Diffusion in brain tissues
- Apparent Diffusion Coefficient
- Diffusion Tensor model
- Tensor-derived measures



# Diffusion Tensor Imaging (DTI)

- Apply **the diffusion tensor model** to a set of DWI images.



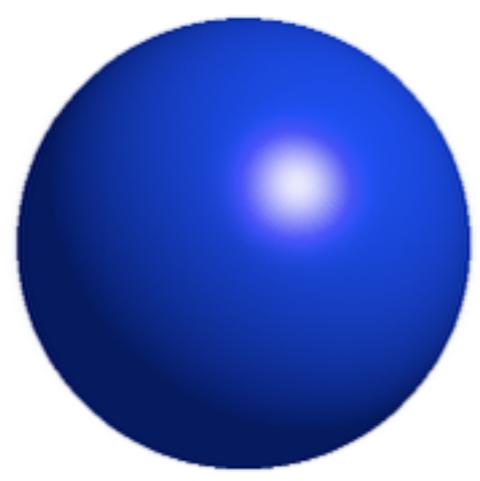
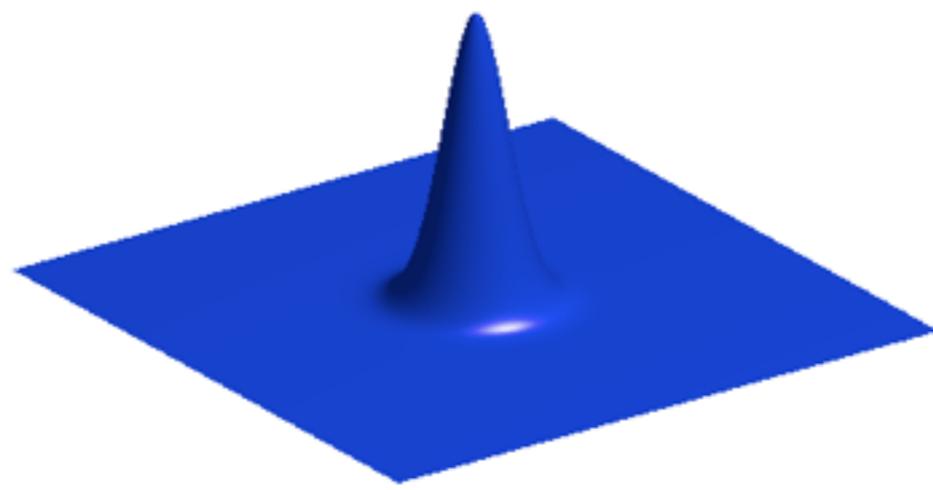


# Diffusion Tensor Imaging (DTI)

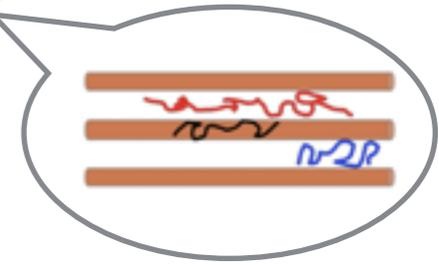
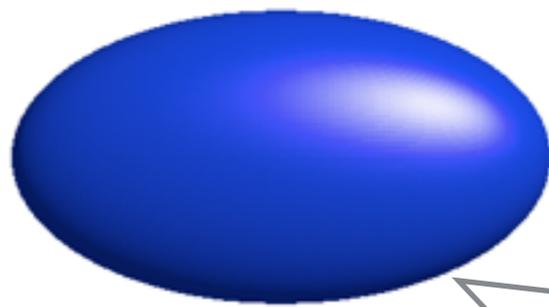
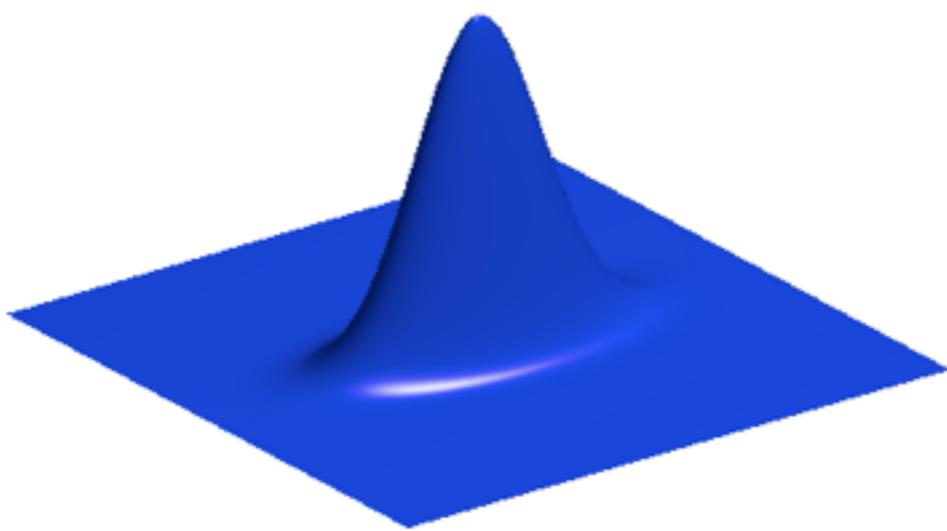
Two dimensions

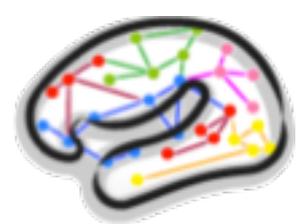
Three dimensions

Scalar D (same D for all directions)



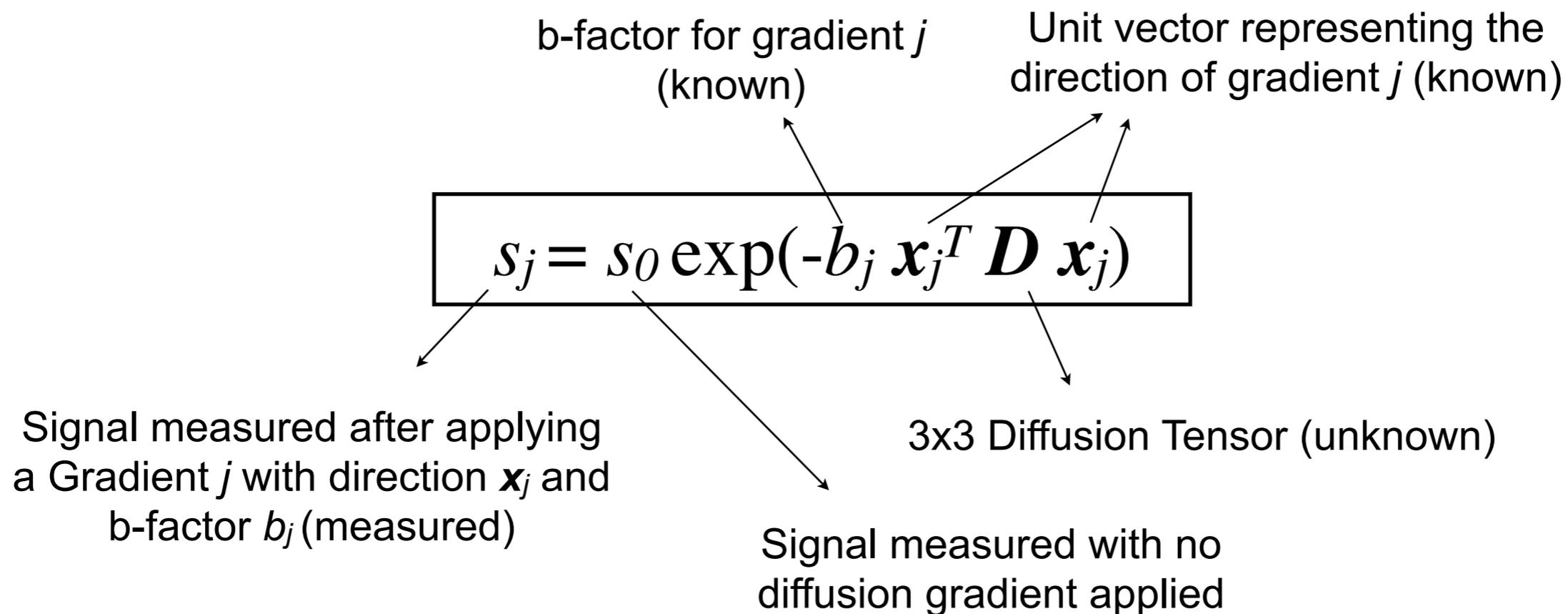
Tensor D - DTI (D can be different for different directions)

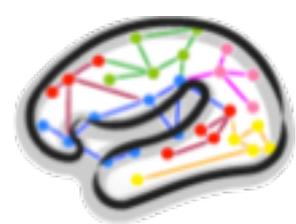




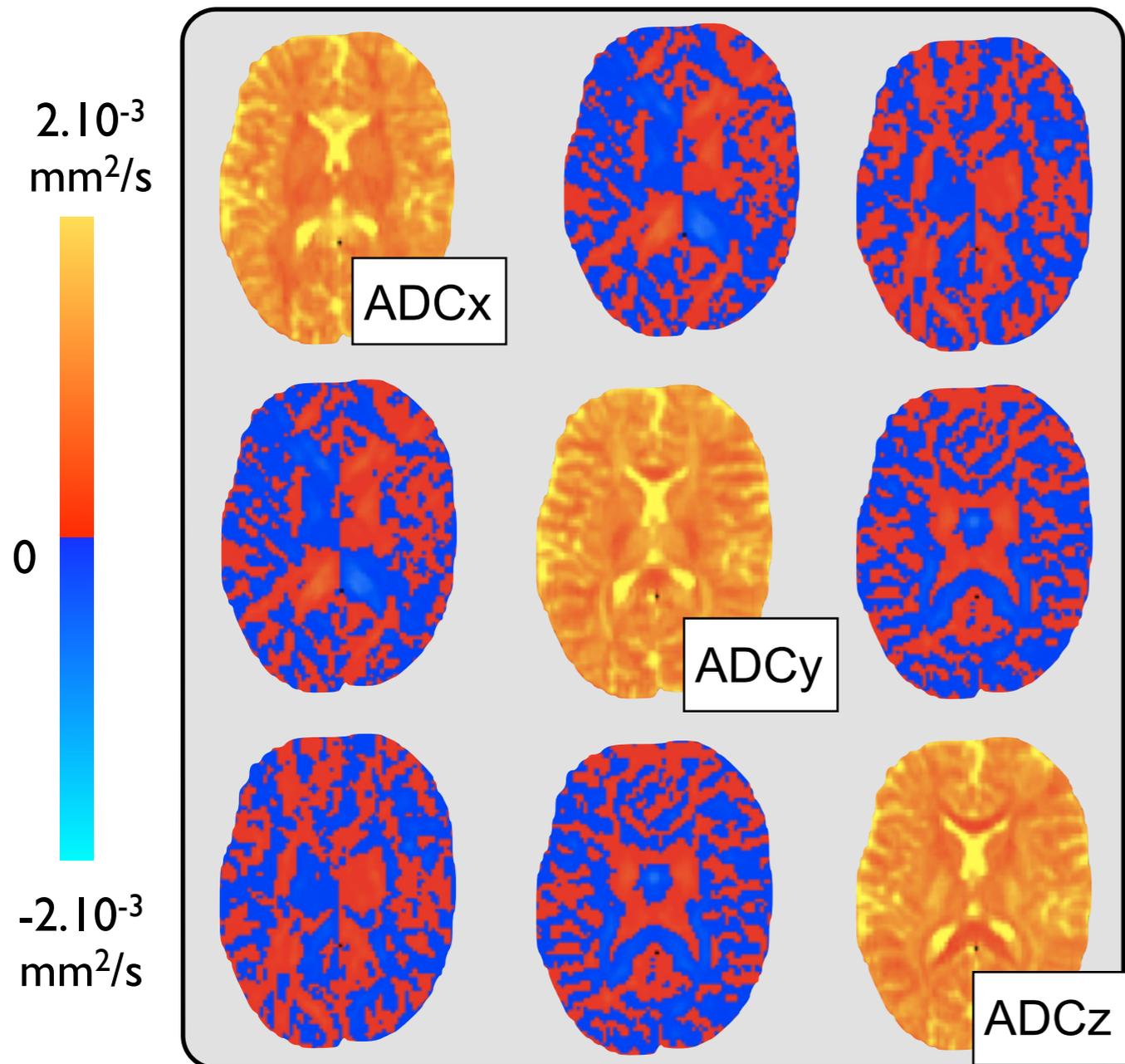
# Diffusion Tensor Imaging (DTI)

## Diffusion Tensor Model. In each voxel:





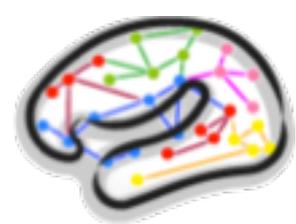
# The Elements of the Diffusion Tensor



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

- Tensor is **symmetric** (6 unknowns)
- **Diagonal Elements** are proportional to the diffusion displacement variances (**ADCs**) along the three directions of the experiment coordinate system
- **Off-diagonal Elements** are proportional to the **correlations** (covariances) of displacements along these directions

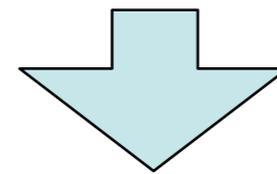
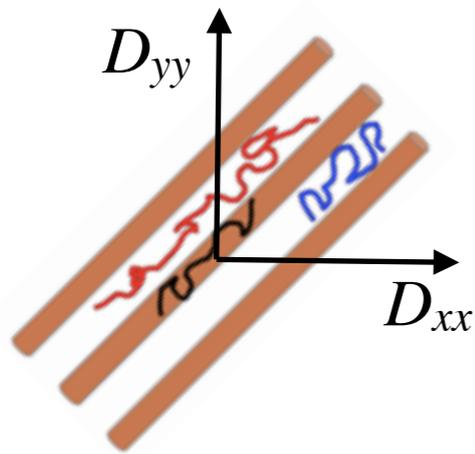
$N_3(0, 2t\mathbf{D})$



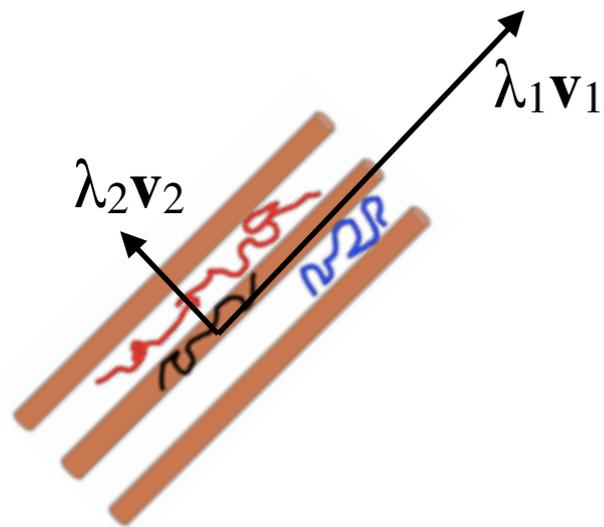
# The Diffusion Tensor Eigenspectrum

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

Once  $\mathbf{D}$  is estimated, we get ADCs along the scanner's coordinate system. But we want ADCs along a local coordinate system in each voxel, determined by the anatomy.



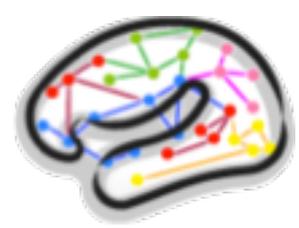
Diagonalize the estimated tensor in each voxel



$$\mathbf{D} = [\mathbf{v}_1 | \mathbf{v}_2 | \mathbf{v}_3]^T \begin{bmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{bmatrix} [\mathbf{v}_1 | \mathbf{v}_2 | \mathbf{v}_3]$$

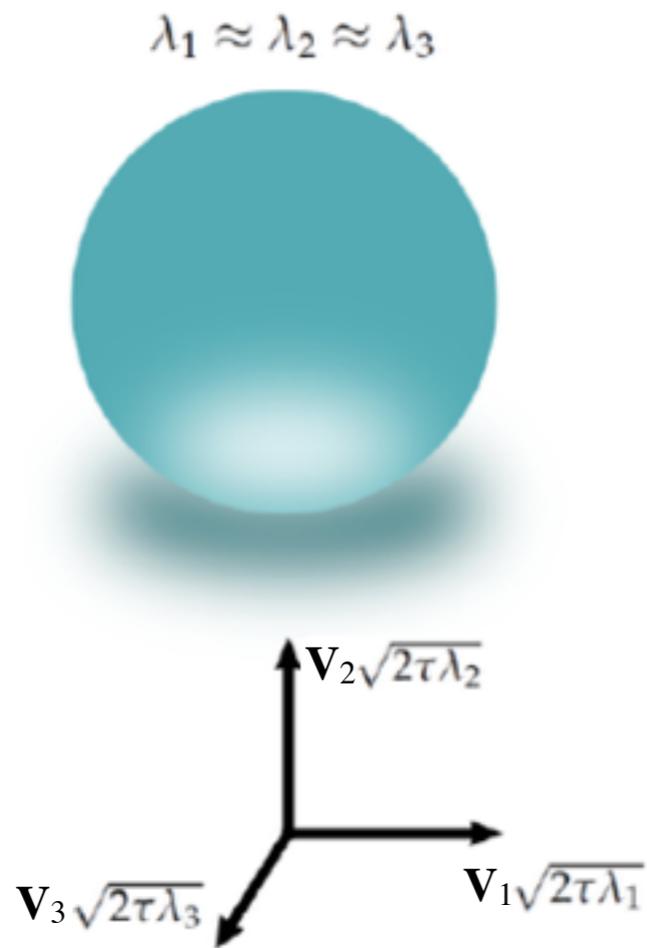
eigenvalues: ADCs along  $\mathbf{v}_1, \mathbf{v}_2, \mathbf{v}_3$

eigenvectors -  $\mathbf{v}_1$ =direction of max diffusivity

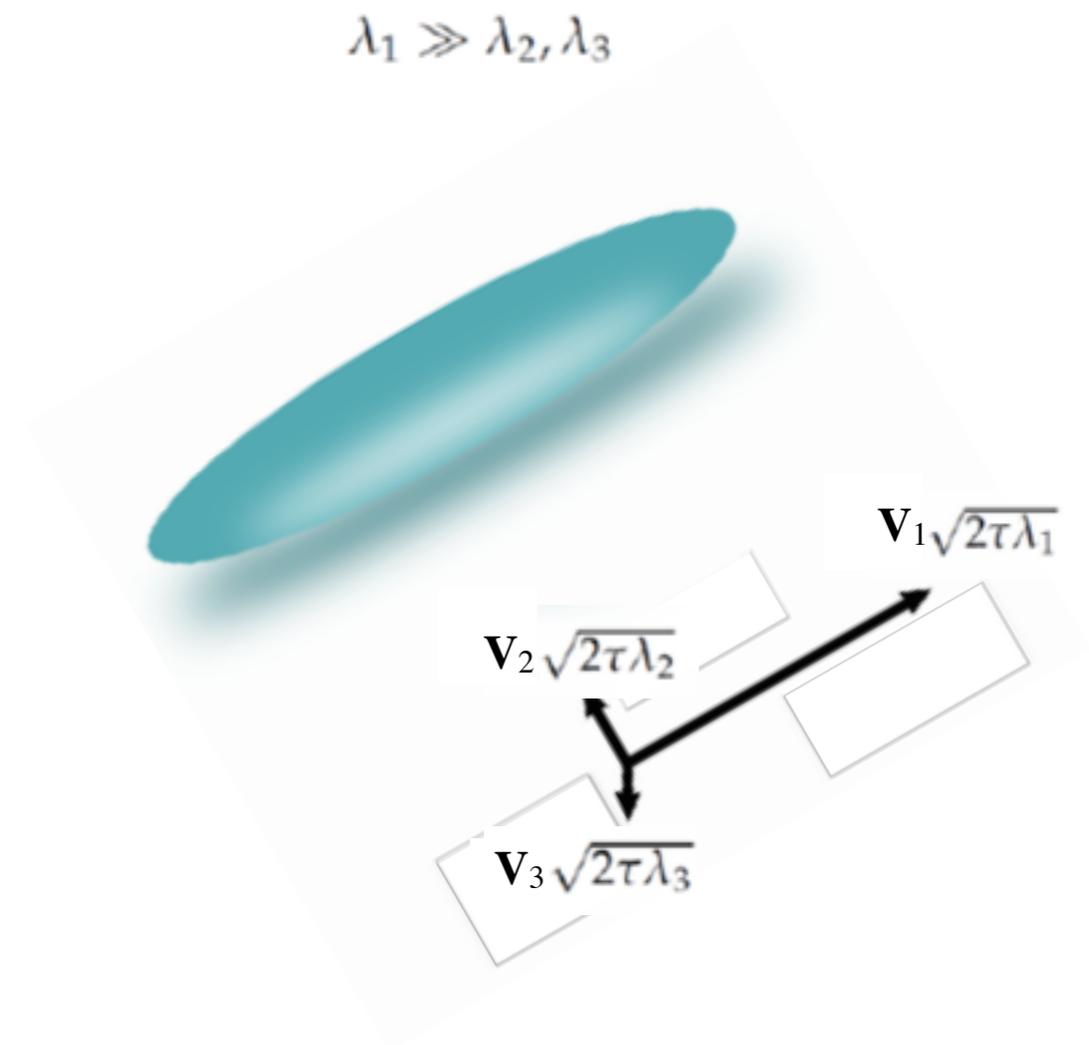


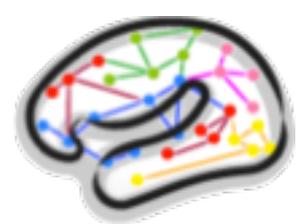
# The Diffusion Tensor Ellipsoid

Isotropic voxel

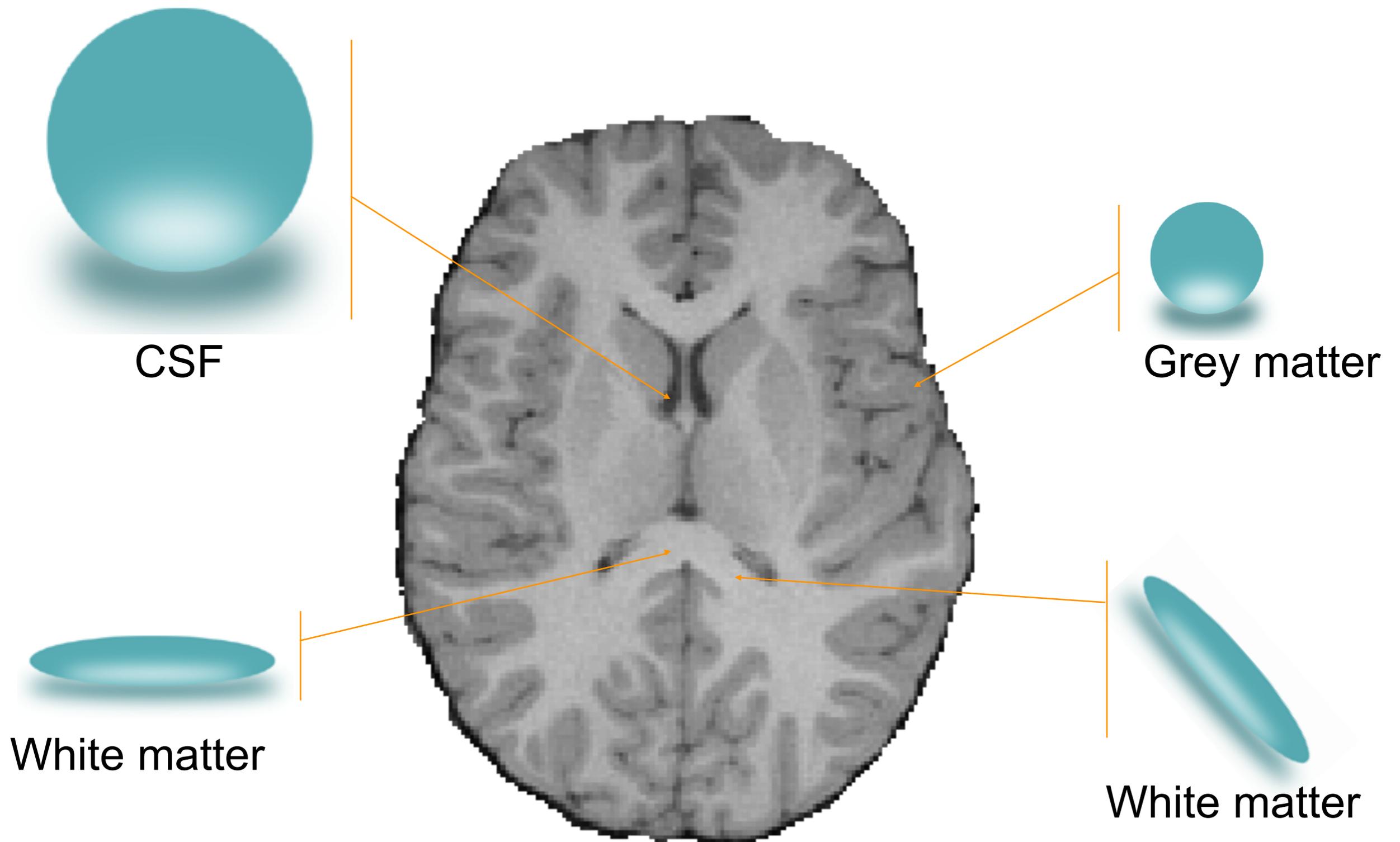


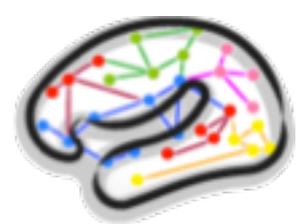
Anisotropic voxel





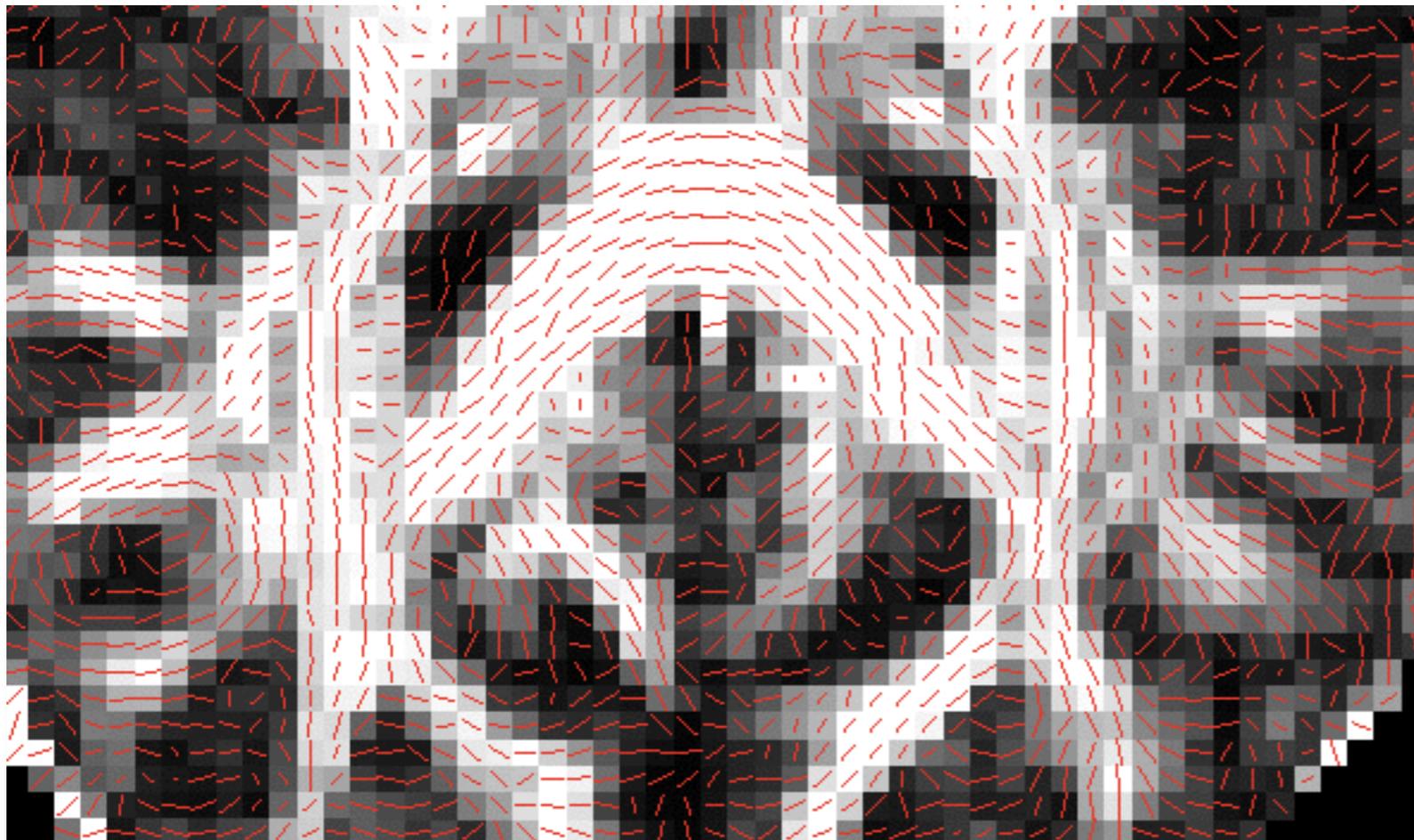
# The Diffusion Tensor Ellipsoid



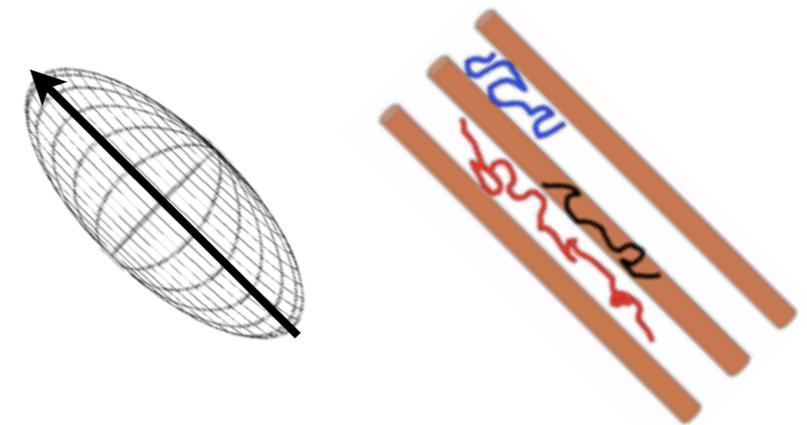


# Estimates of Principal Fibre Orientation in WM

$v_1$  map  
Principal Diffusion Direction

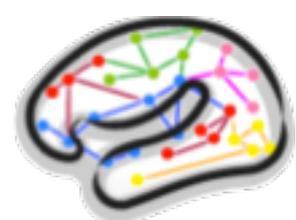


Principal Diffusion  
Direction

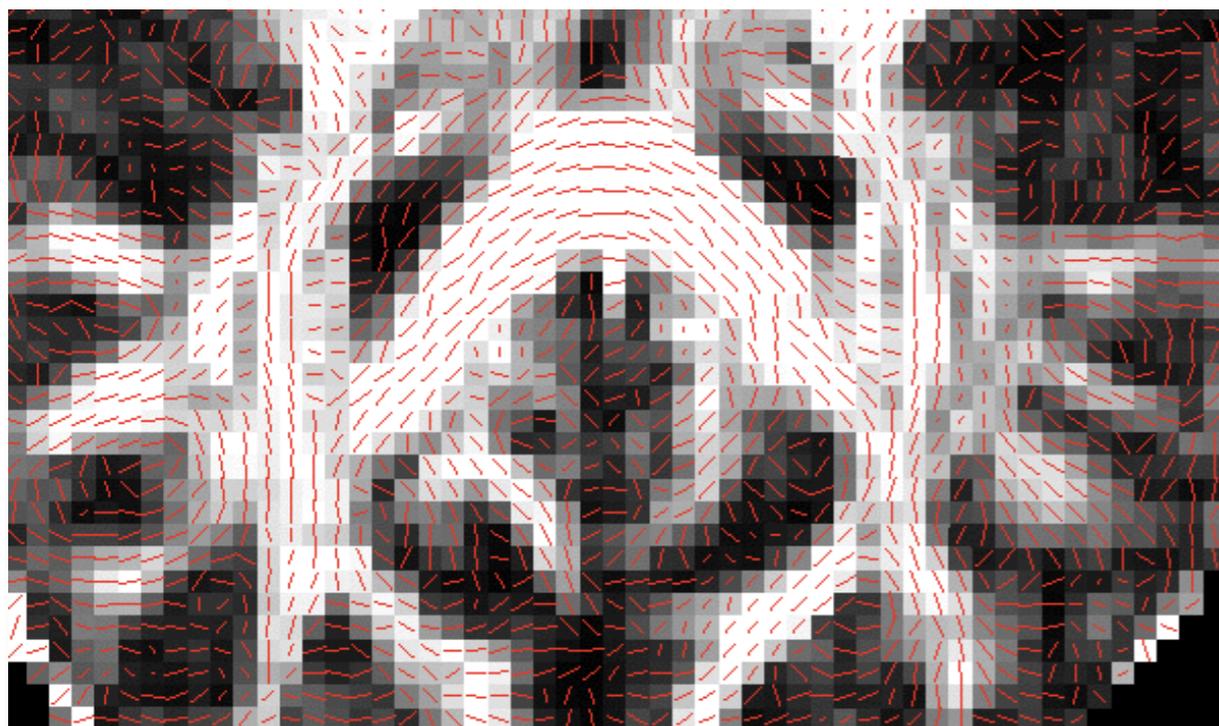


**Assumption!!**

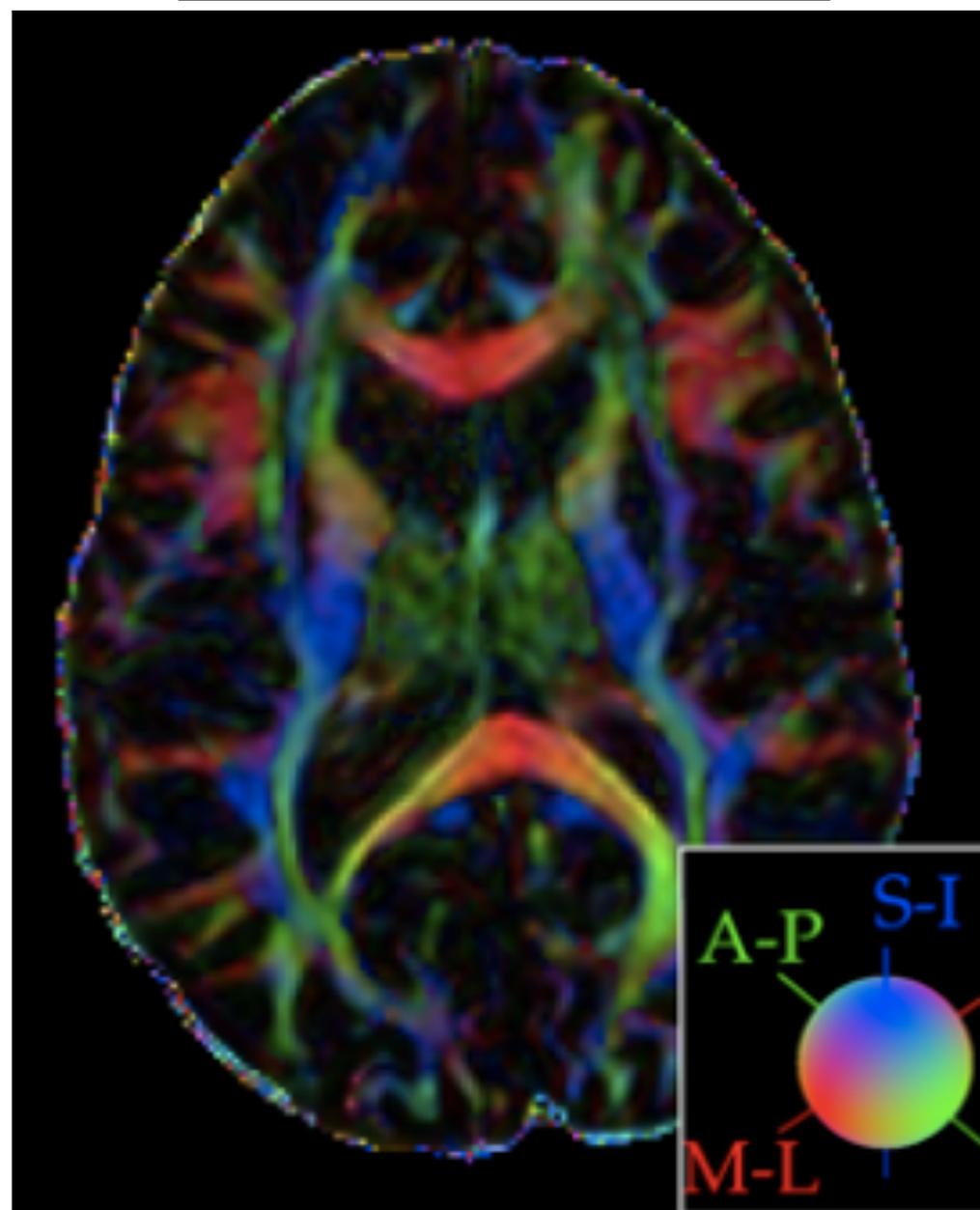
**Direction of maximum diffusivity in voxels with anisotropic profile is an estimate of the major fibre orientation.**

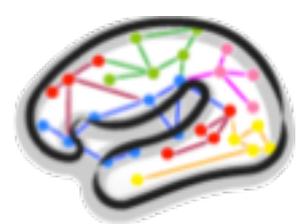


# Estimates of Principal Fibre Orientation in WM

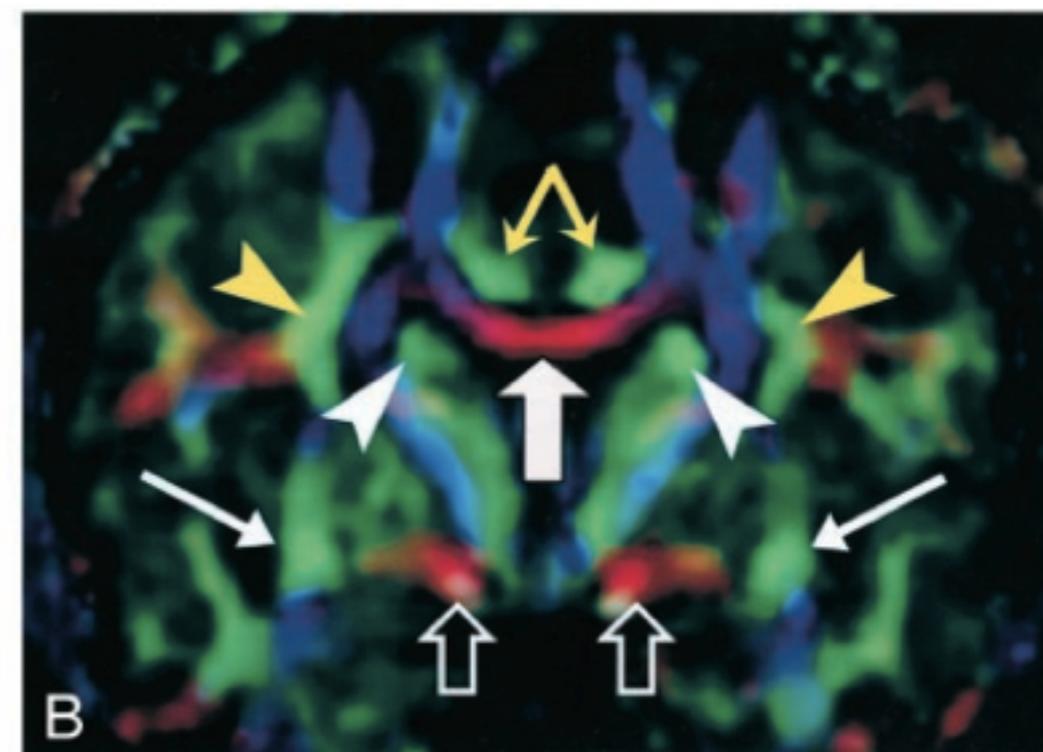
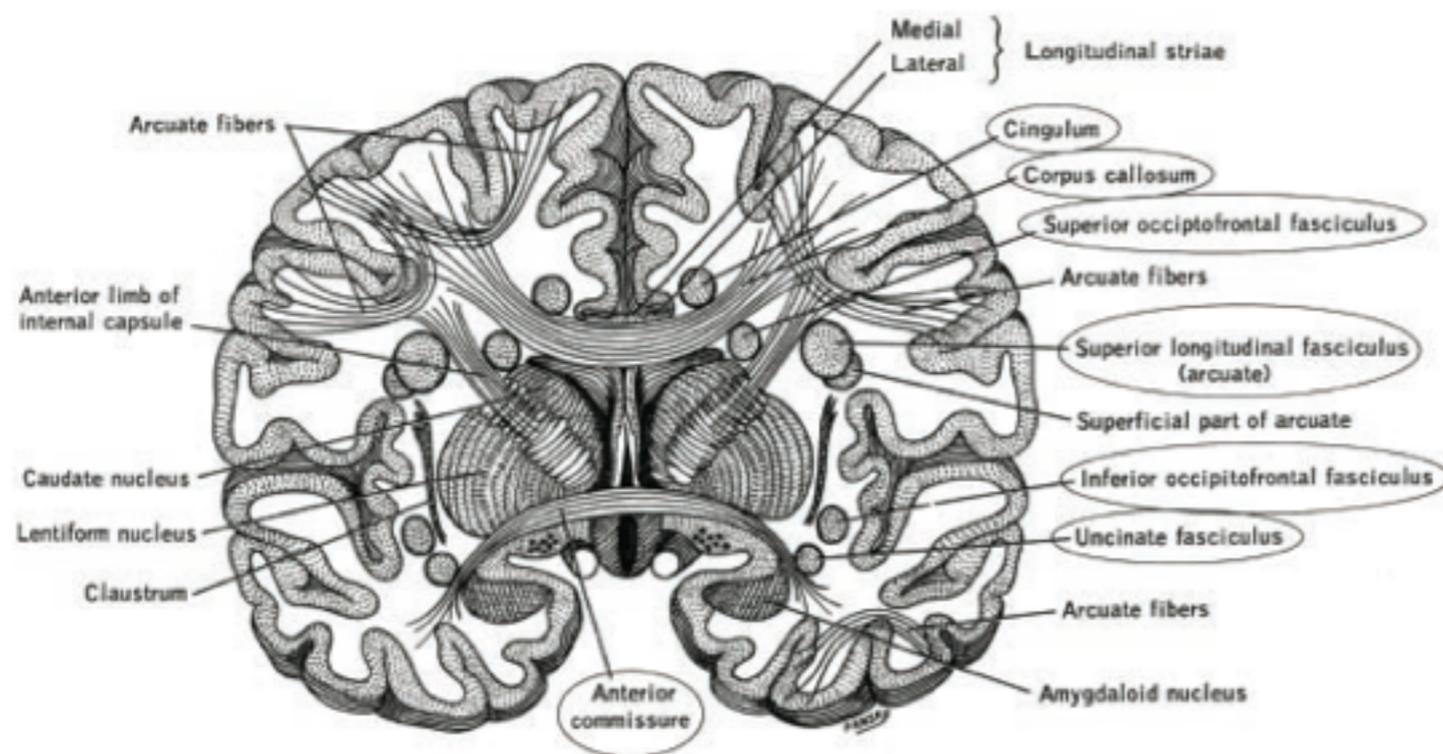


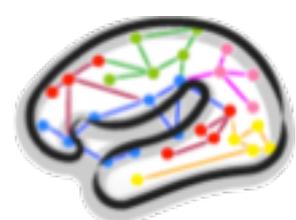
Colour-coded  $v_1$  map



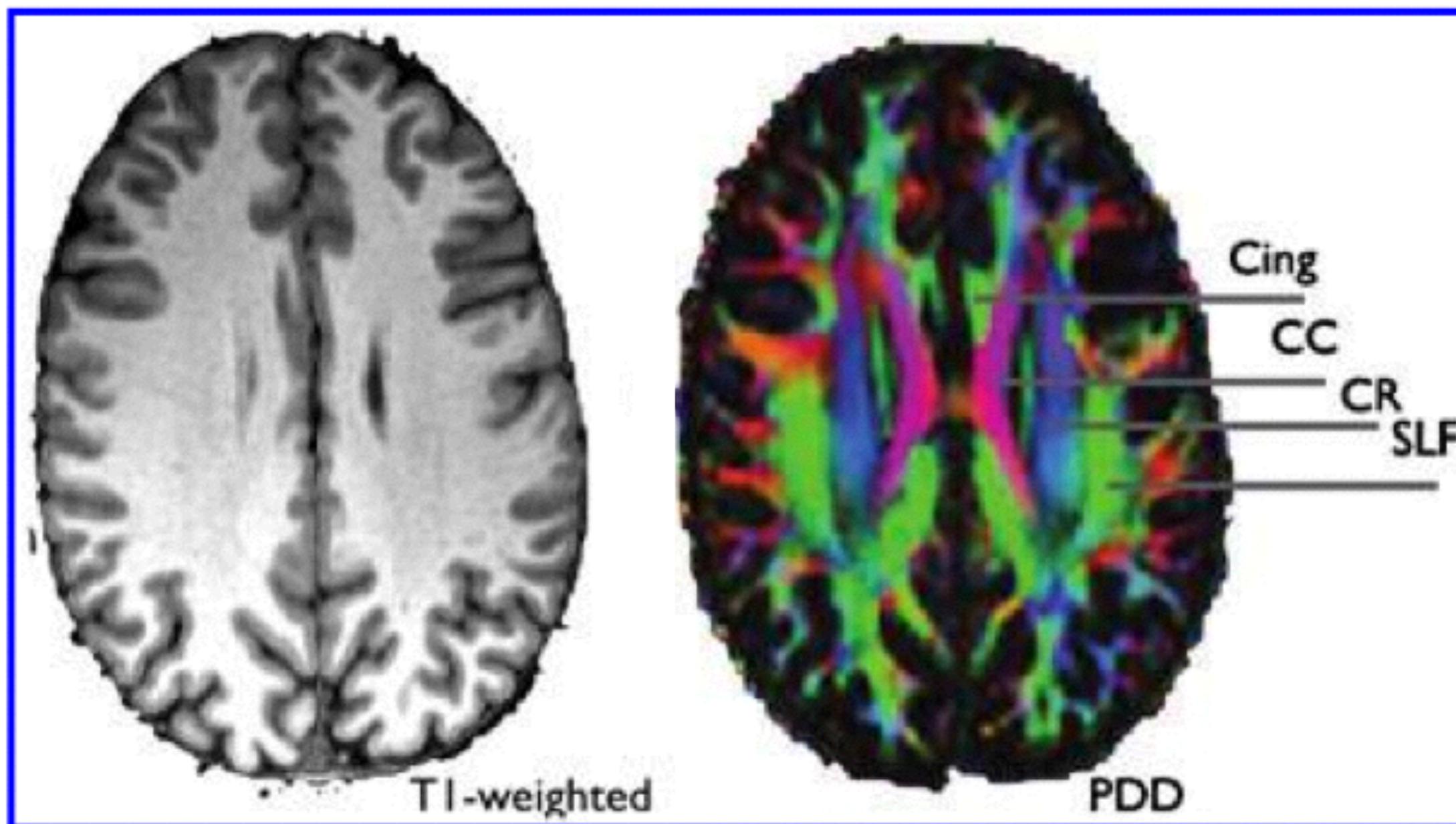


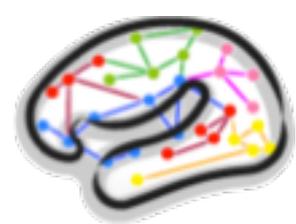
# Estimates of Principle Fibre Orientation in WM





# Directional contrast in DTI



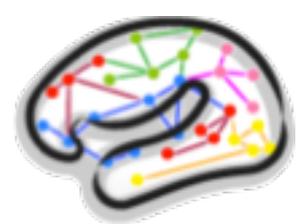


# Quantitative Diffusion Maps

Fractional Anisotropy (FA) ~ Eigenvalues Variance (normalised)  
Mean Diffusivity (MD) = Eigenvalues Mean

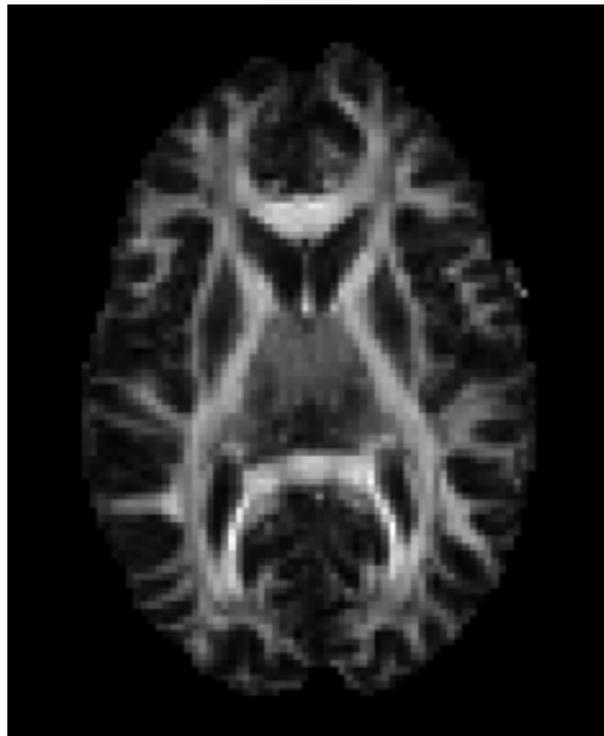
$$FA = \sqrt{\frac{3 \sum_{i=1}^3 (\lambda_i - \bar{\lambda})^2}{2 \sum_{i=1}^3 \lambda_i^2}}, \quad FA \text{ in } [0,1]$$

$$MD = \frac{D_{xx} + D_{yy} + D_{zz}}{3} = \frac{\lambda_1 + \lambda_2 + \lambda_3}{3}$$



# Quantitative Diffusion Maps

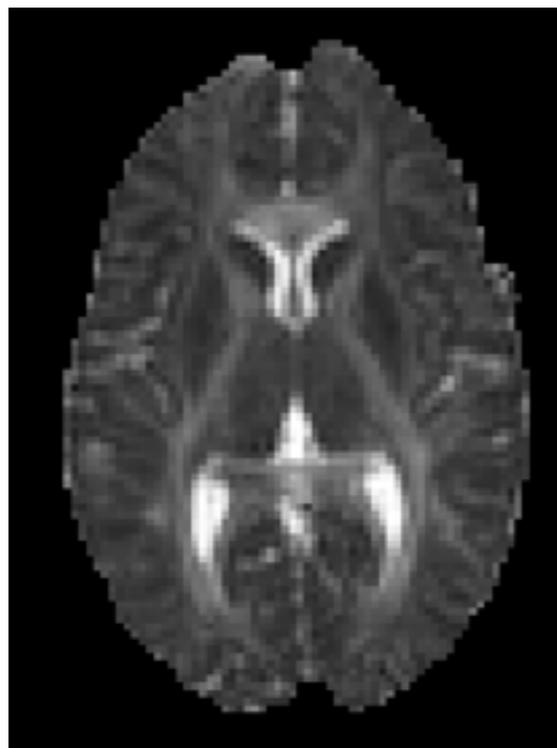
FA



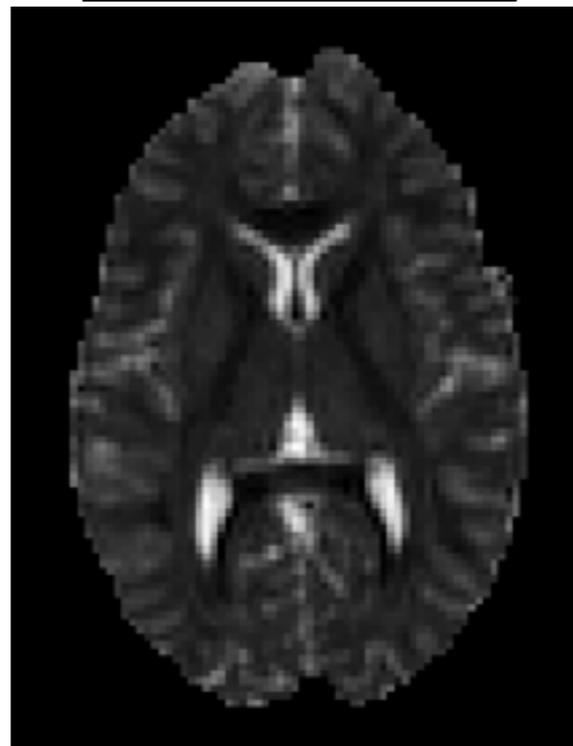
MD

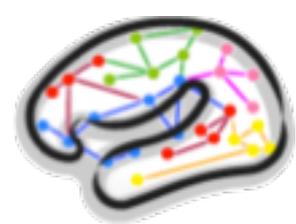


Longitudinal ADC  
( $\lambda_1$ )



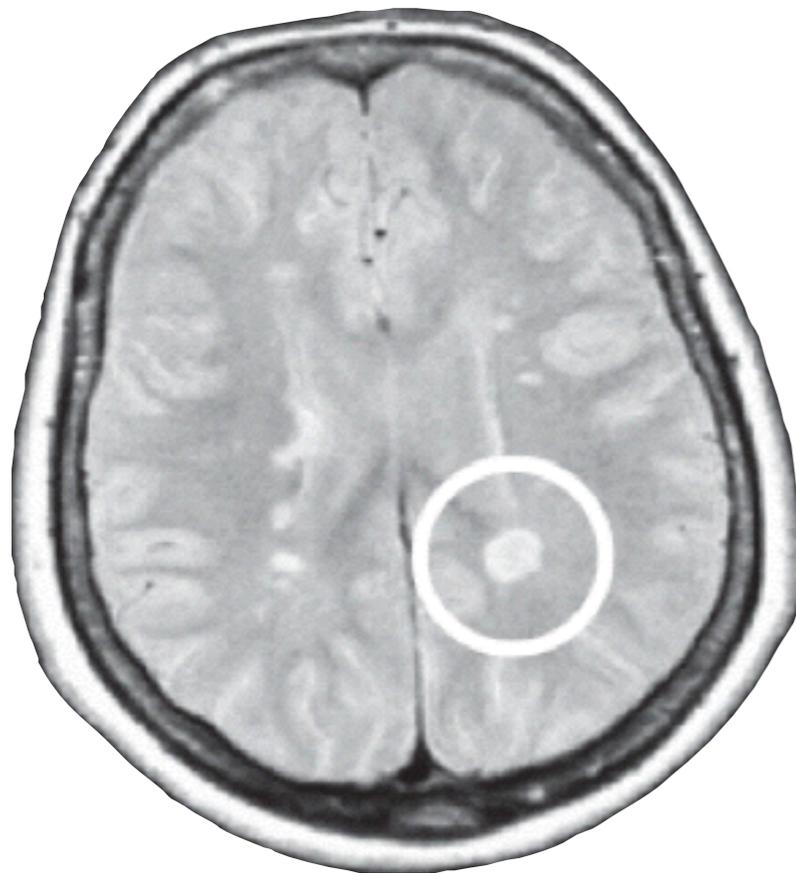
Transverse ADC  
( $(\lambda_2 + \lambda_3)/2$ )



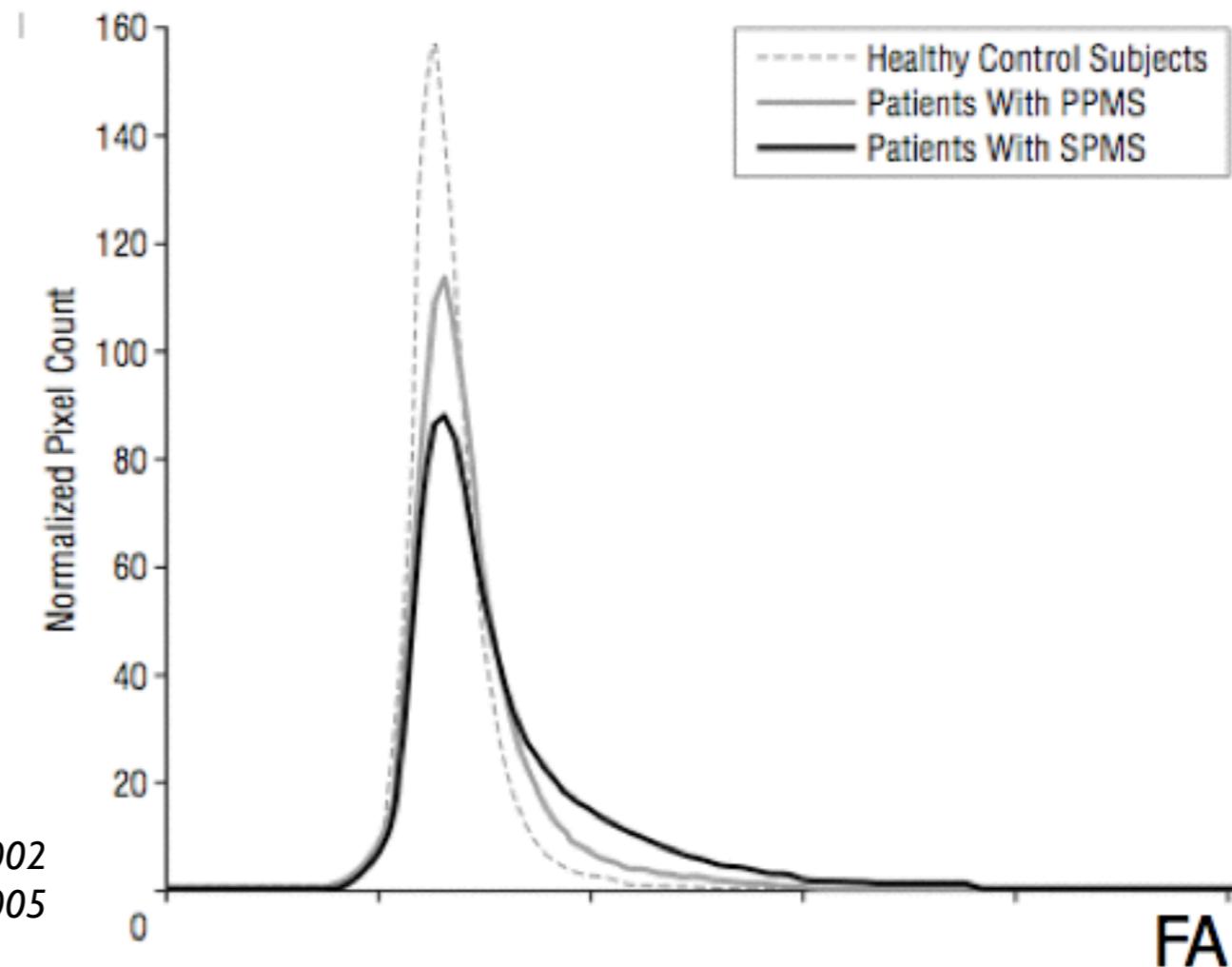


# Quantitative Diffusion Maps

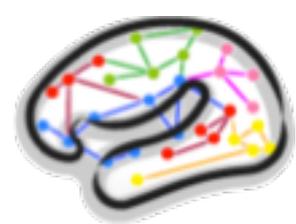
FA decrease/ MD increase has been associated in many studies with tissue breakdown (loss of structure).



*Rovaris et al, Arch Neurol 2002*  
*Gallo et al, Arch Neurol 2005*



Fractional Anisotropy changes in MS normal appearing white matter



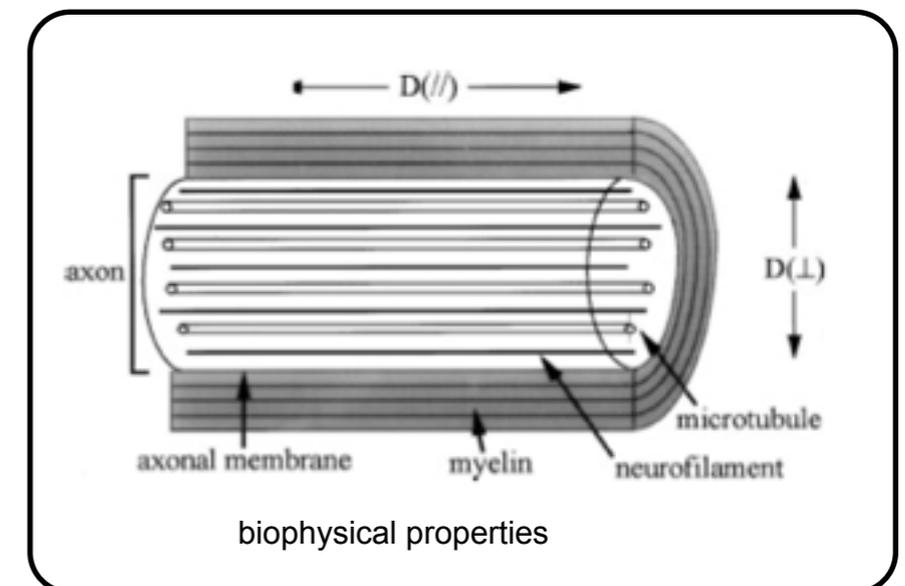
# Quantitative Diffusion Maps

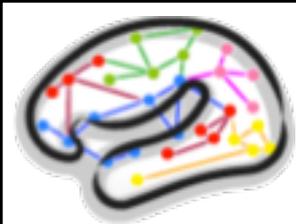
FA decrease in WM can be caused:

a) Decrease of longitudinal ADC.  
Axonal breakdown?

b) Increase of transverse ADC.  
Myelin breakdown?

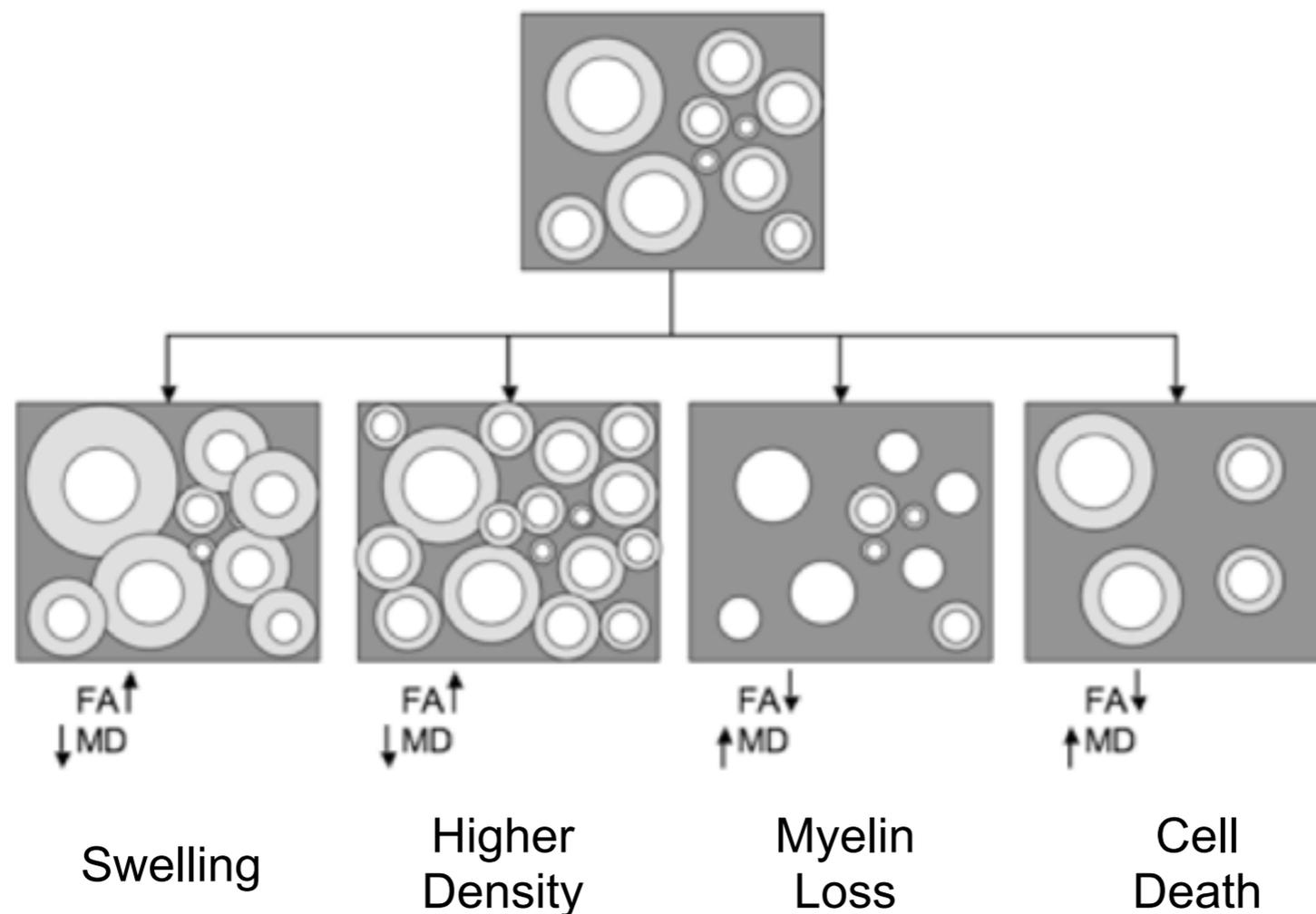
But do not overinterpret your results!  
Always keep in mind that the DTI  
model is an oversimplification of  
reality!

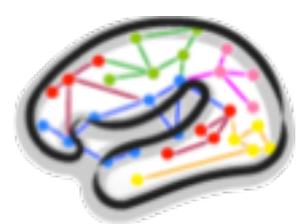




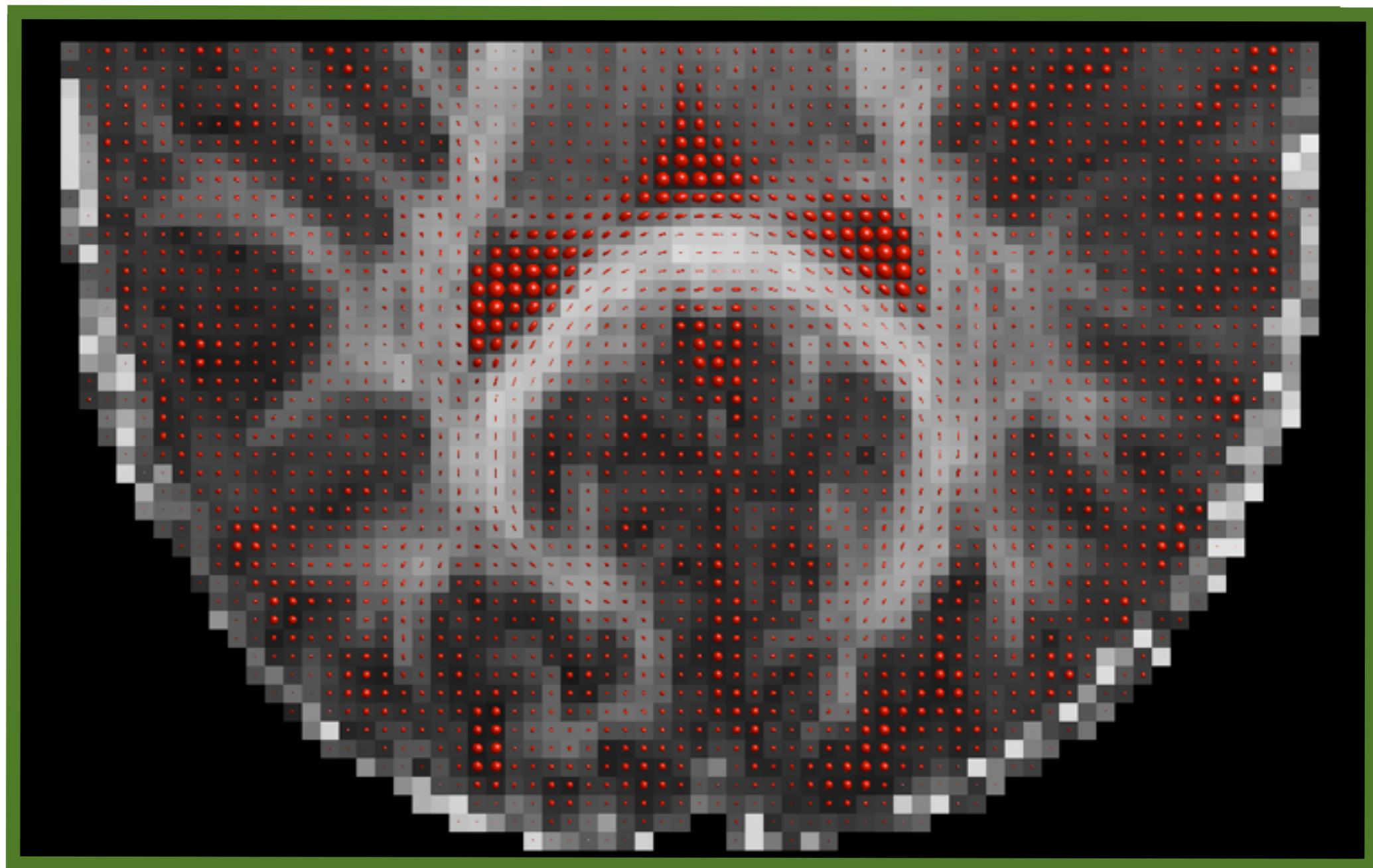
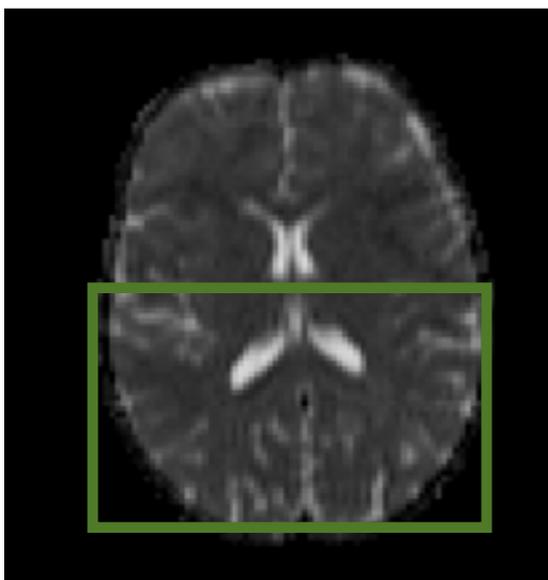
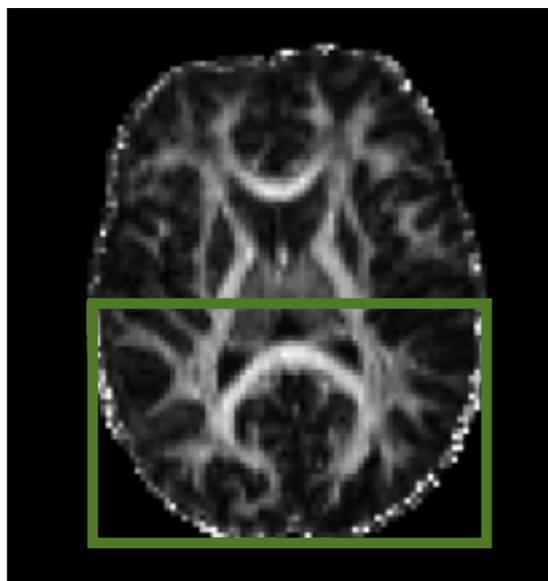
# Quantitative Diffusion Maps

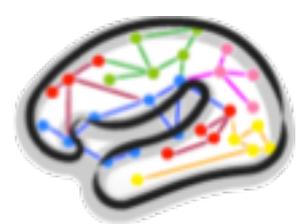
But do not overinterpret your results! Always keep in mind that the DTI model is an oversimplification of reality! Different configurations can have same effect on FA, MD!





# Diffusion Tensor Ellipsoids





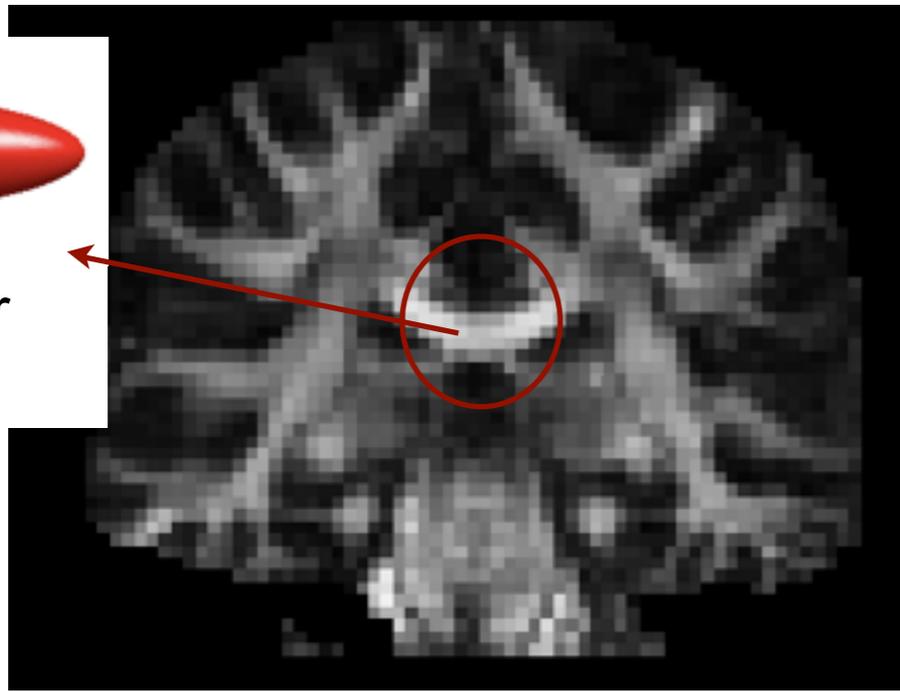
# Tensor and FA in Crossing Regions

- In voxels containing two crossing bundles, FA is low and the tensor ellipsoid is pancake-shaped (oblate, planar tensor).



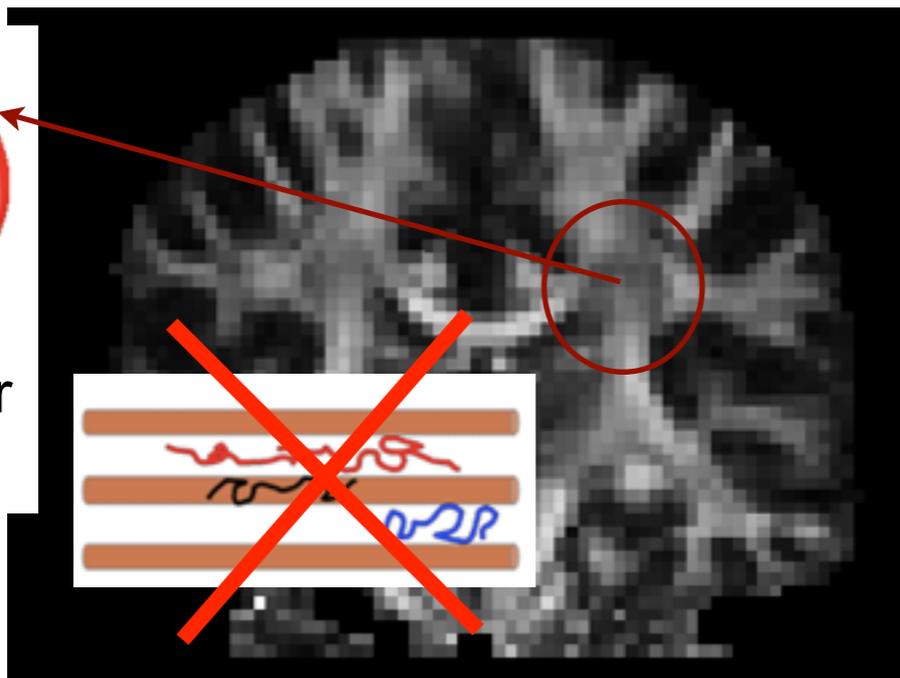
Prolate Tensor

$$\lambda_1 \gg \lambda_2, \lambda_3$$



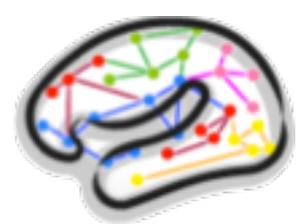
Oblate Tensor

$$\lambda_1 = \lambda_2 \gg \lambda_3$$



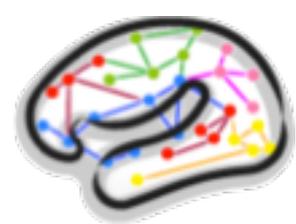
Consequences:

- PDD not necessarily = direction of fibres
- FA changes difficult to interpret



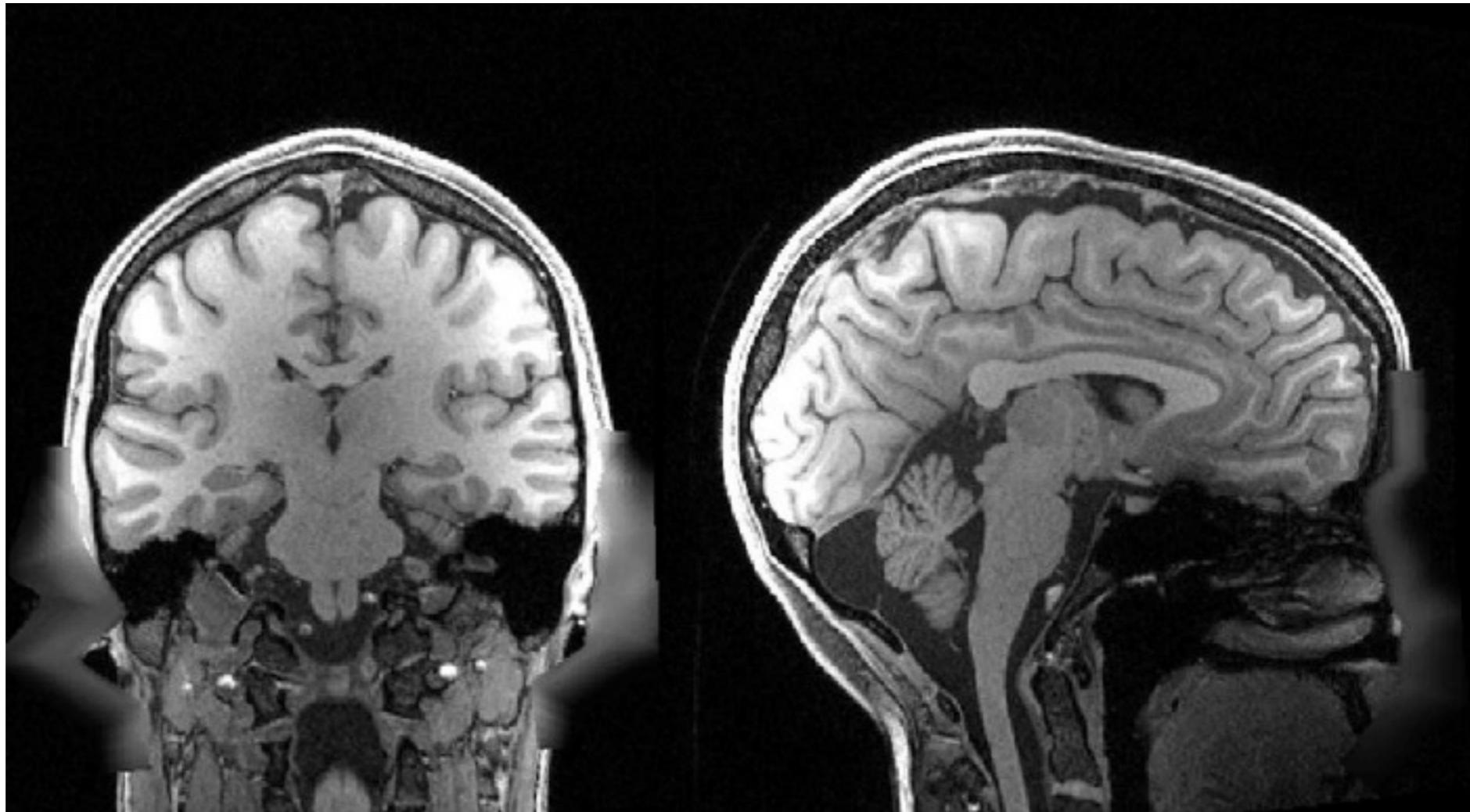
# “Problems” with diffusion data

- Gradient non-linearities
  - Distortions
    - Susceptibility-induced (topup)
    - Eddy current-induced
  - Subject movement
    - Gross movement
    - Signal dropout
- } (eddy)

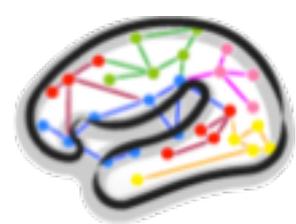


# Gradient non-linearities

Gradients are not perfectly linear

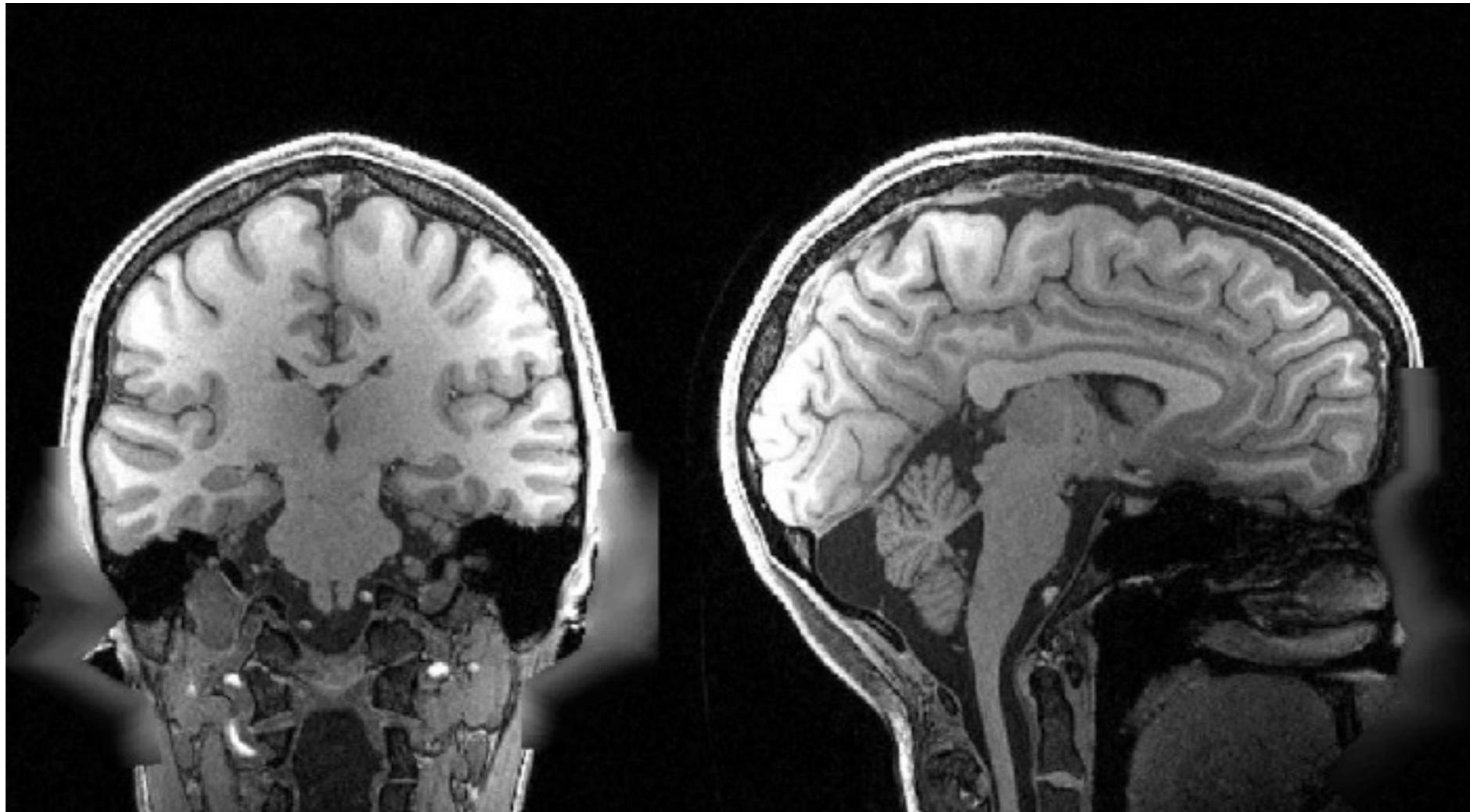


If we take a subject like this and scan with “typical” gradients.

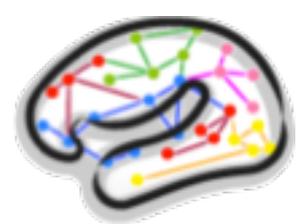


# Gradient non-linearities

Gradients are not perfectly linear

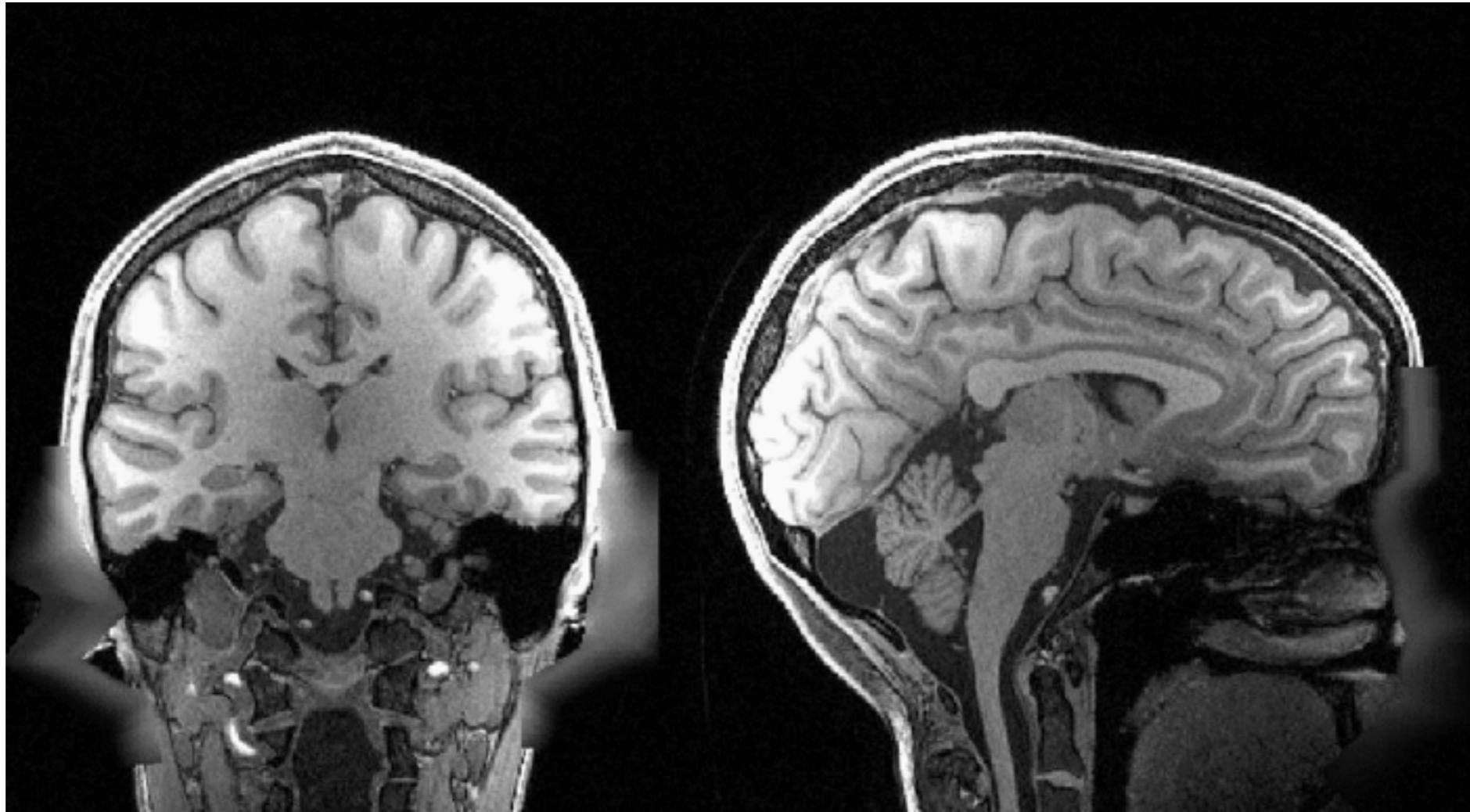


He/she will look like this

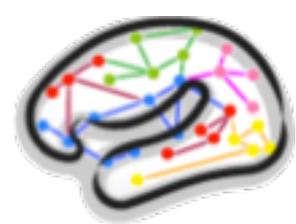


# Gradient non-linearities

This is (mostly) fixed by your scanner

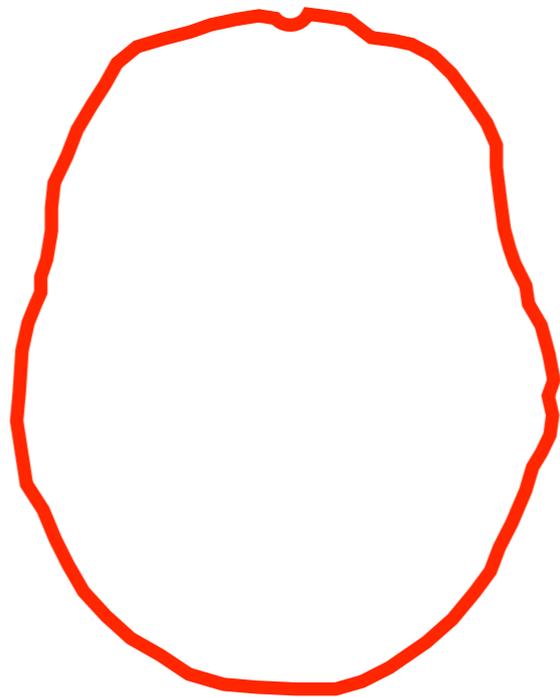


**BUT**, what about the diffusion encoding?

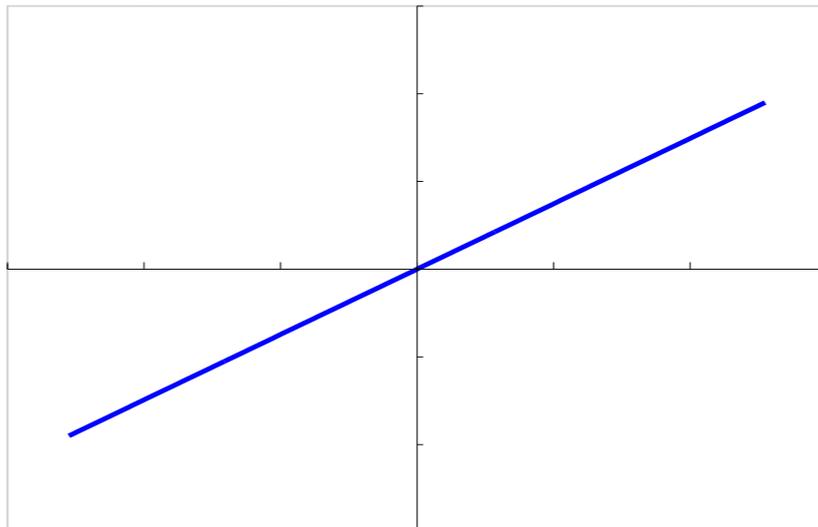


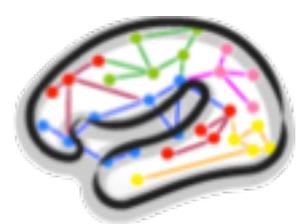
# Gradient non-linearities and diffusion encoding

(Bammer et al., 2003)



x-gradient

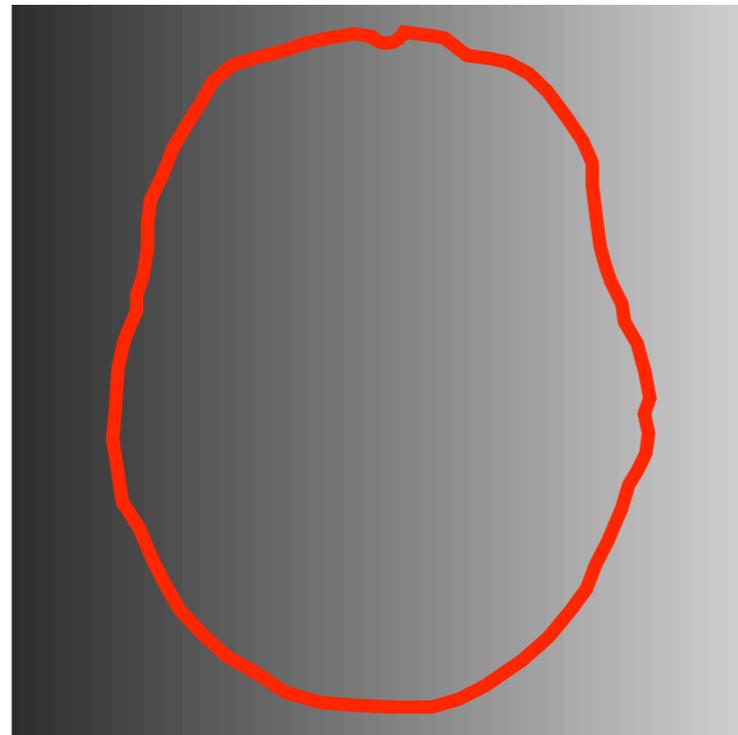




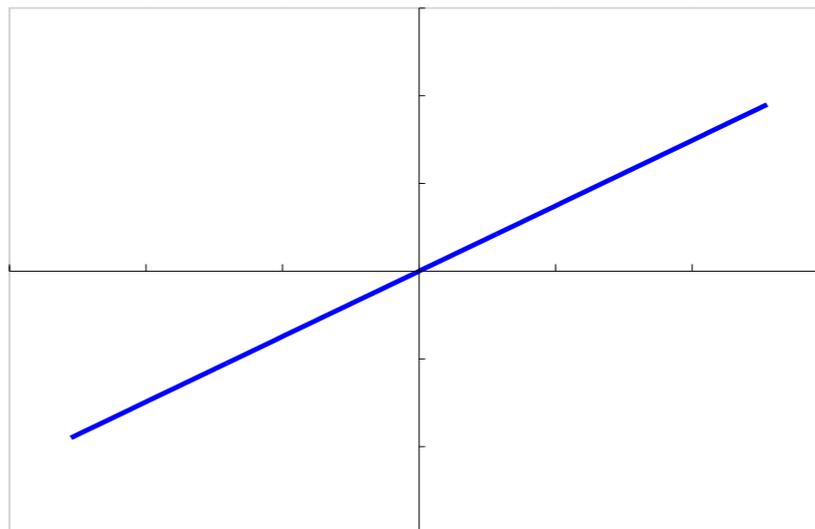
# Gradient non-linearities and diffusion encoding

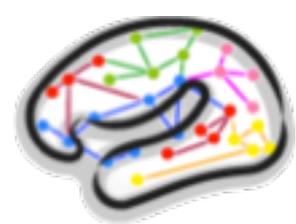
(Bammer et al., 2003)

field



x-gradient



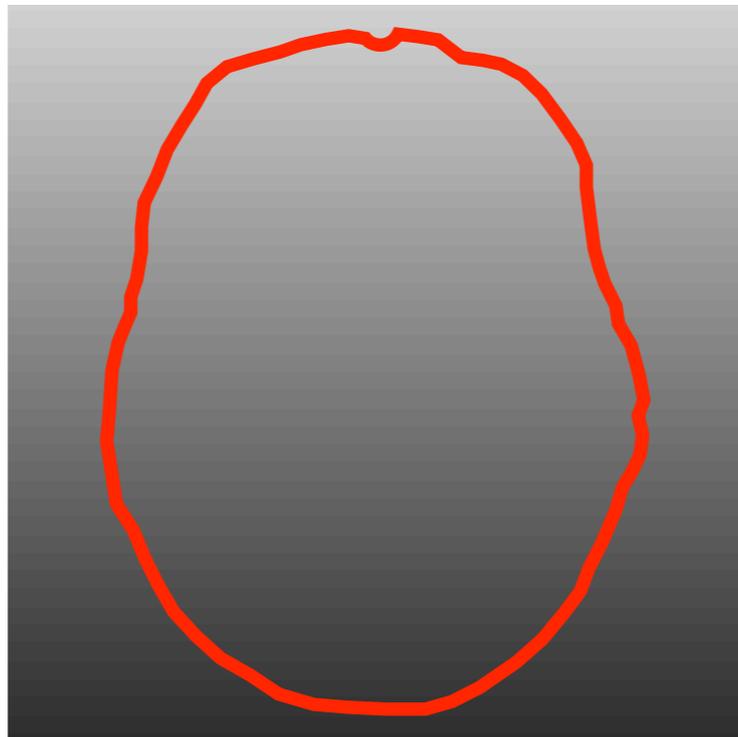
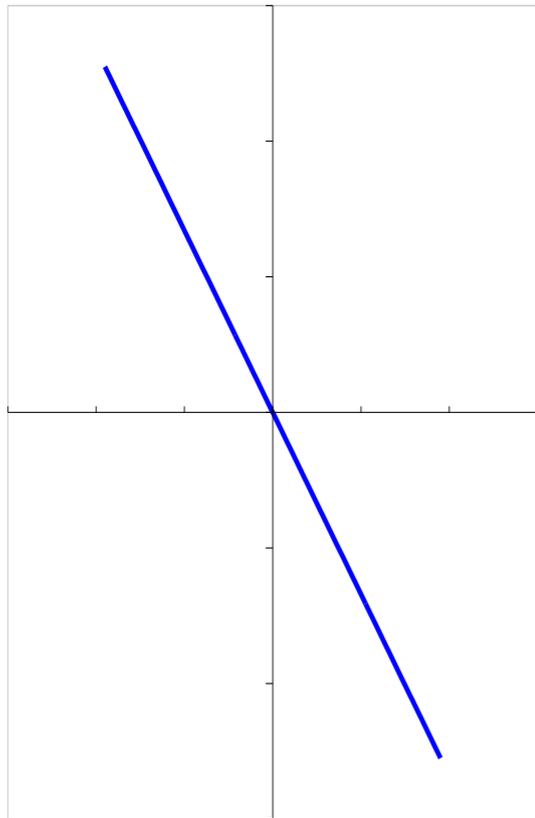


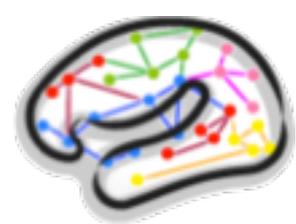
# Gradient non-linearities and diffusion encoding

(Bammer et al., 2003)

field

y-gradient



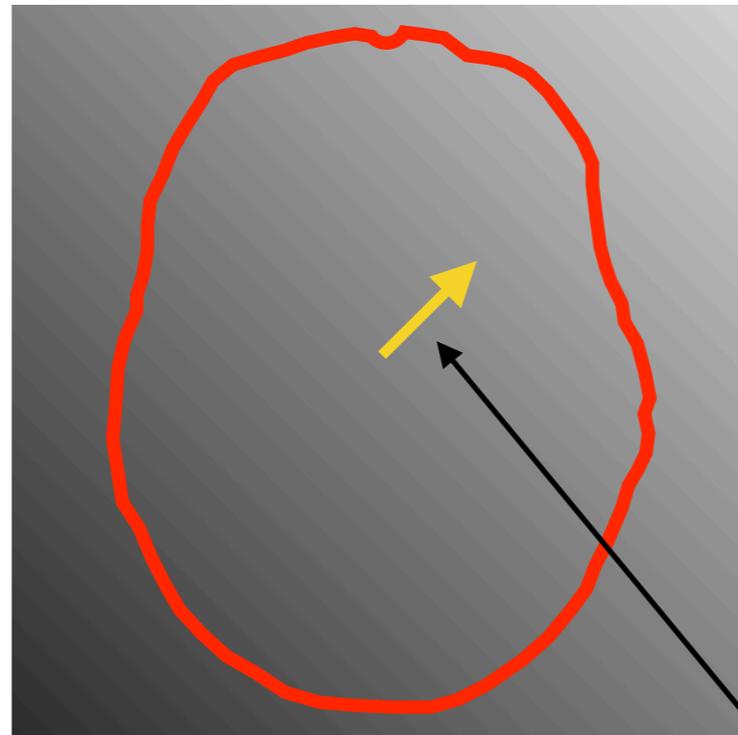
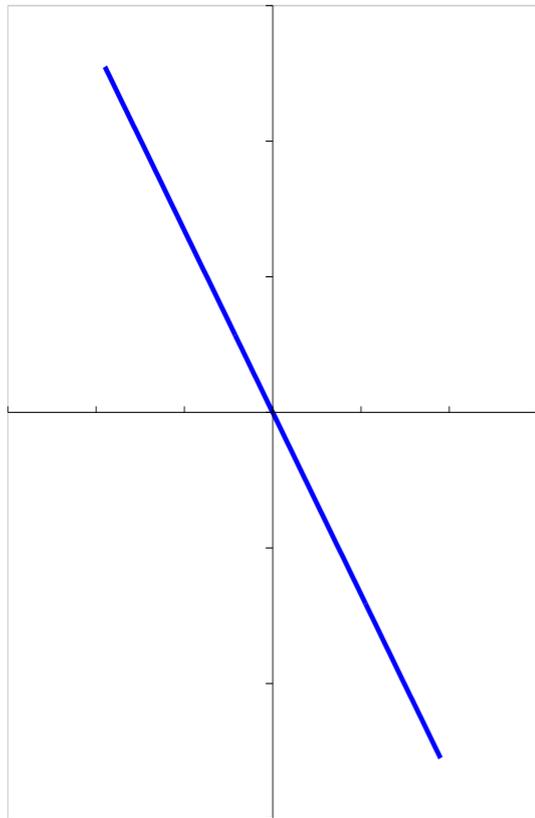


# Gradient non-linearities and diffusion encoding

(Bammer et al., 2003)

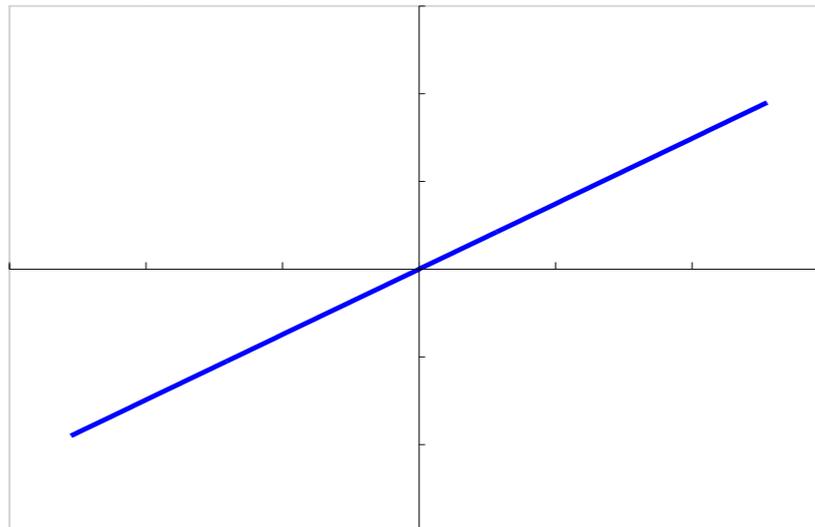
field

y-gradient

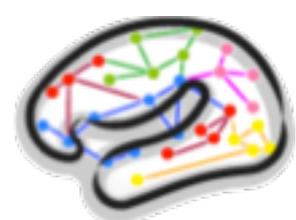


So when we  
play out a  
diffusion  
gradient [.7 .7]  
we get this

x-gradient



**b-vector, same  
everywhere in  
the brain**

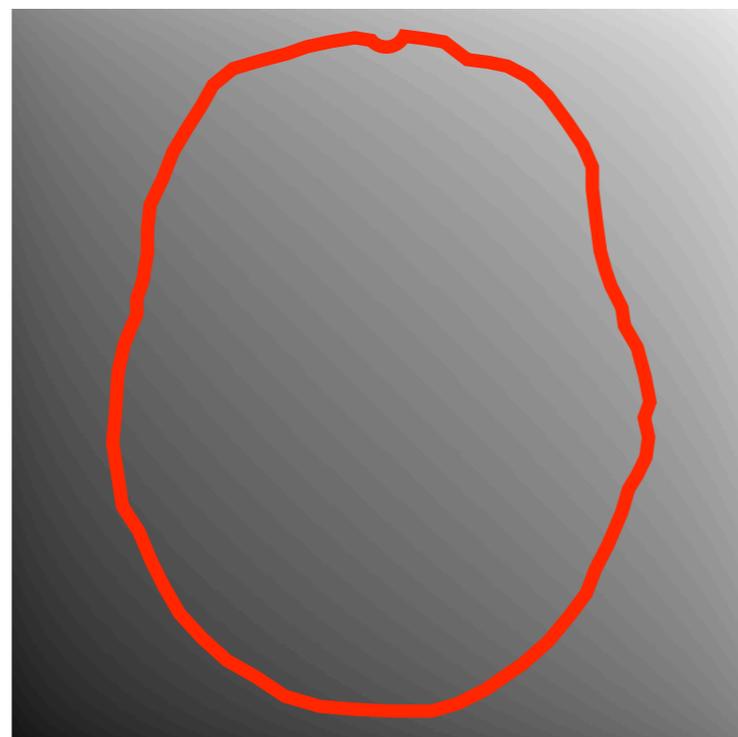
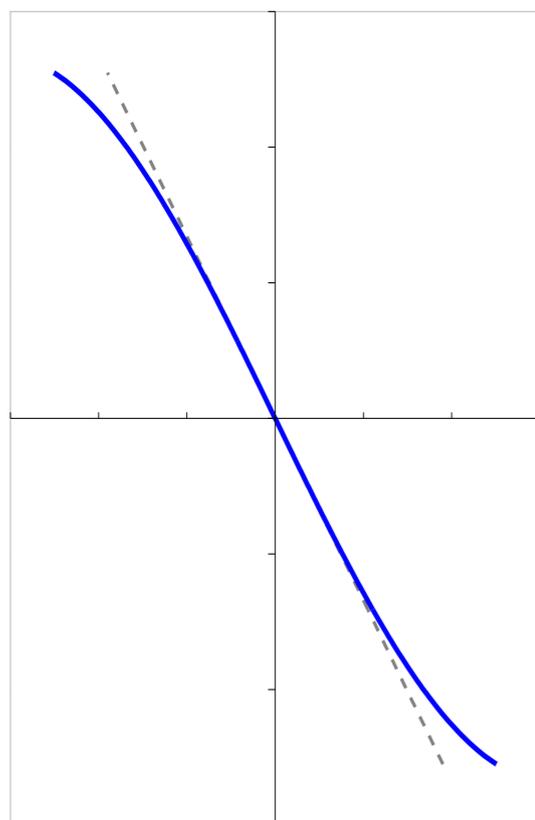


# Gradient non-linearities and diffusion encoding

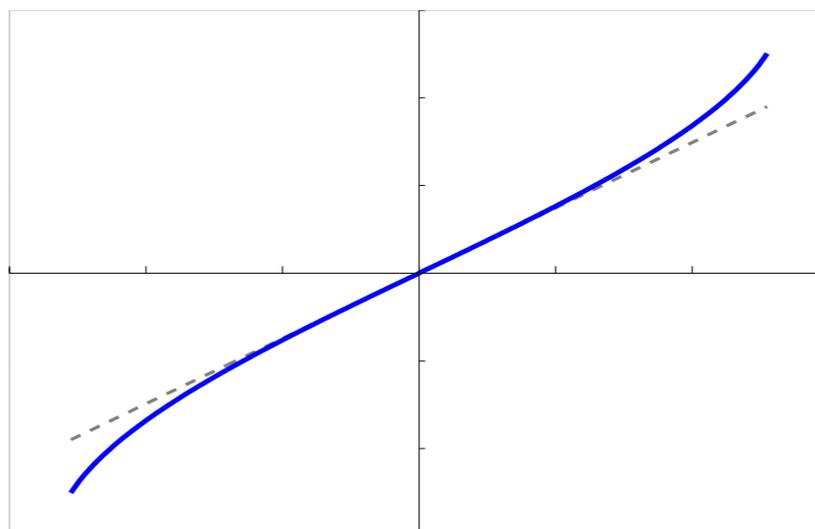
(Bammer et al., 2003)

field

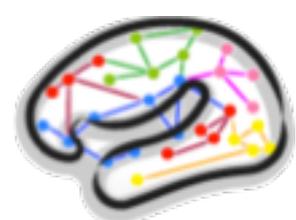
y-gradient



x-gradient



But what if  
the gradients  
really look  
like this?

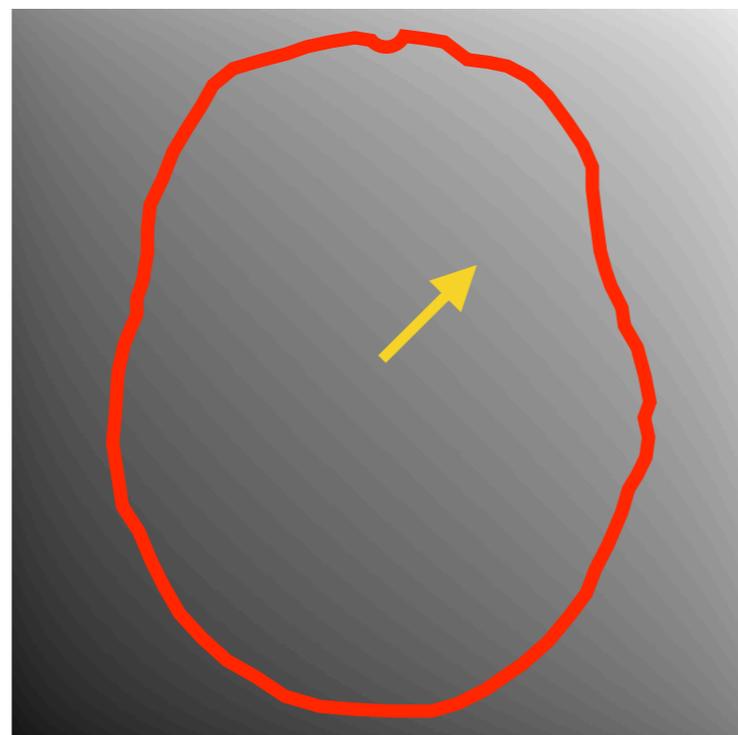
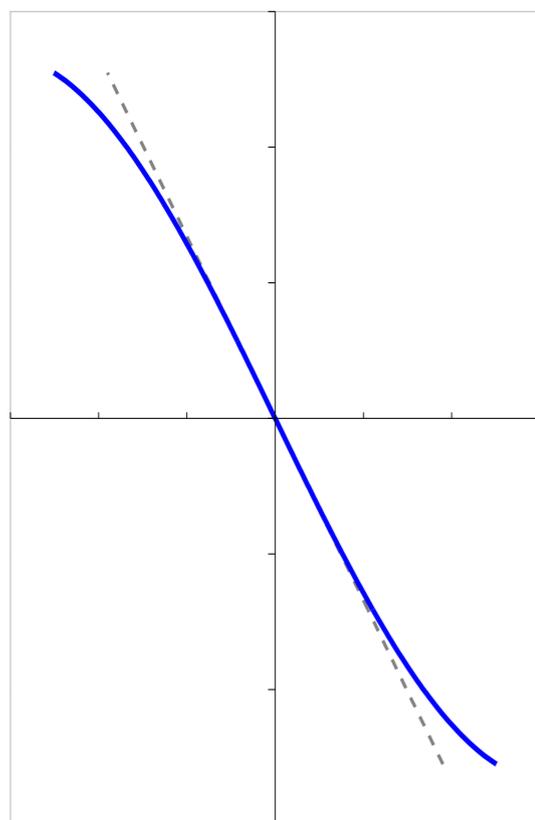


# Gradient non-linearities and diffusion encoding

(Bammer et al., 2003)

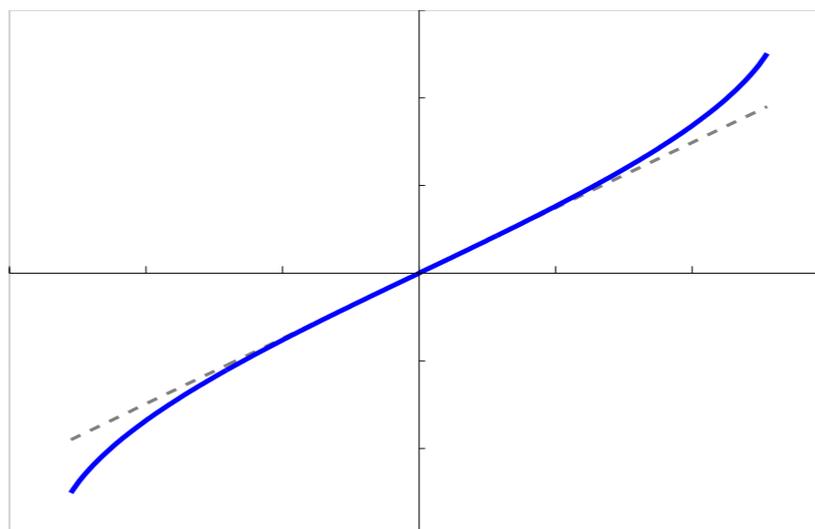
field

y-gradient

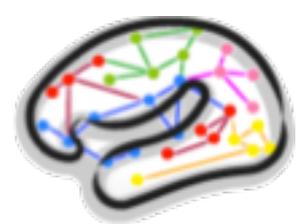


In the centre  
the b-vector is  
the same as  
before

x-gradient



But what if  
the gradients  
really look  
like this?

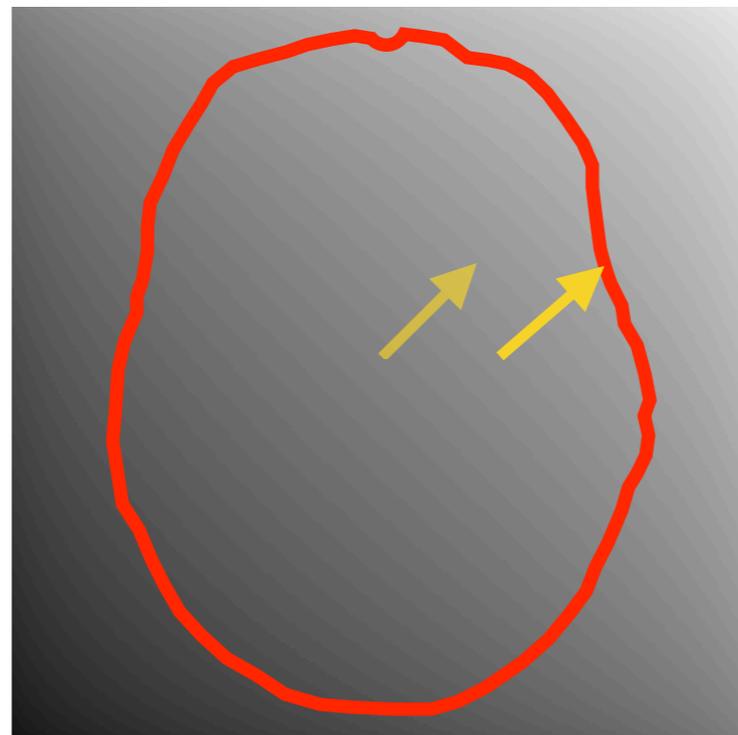
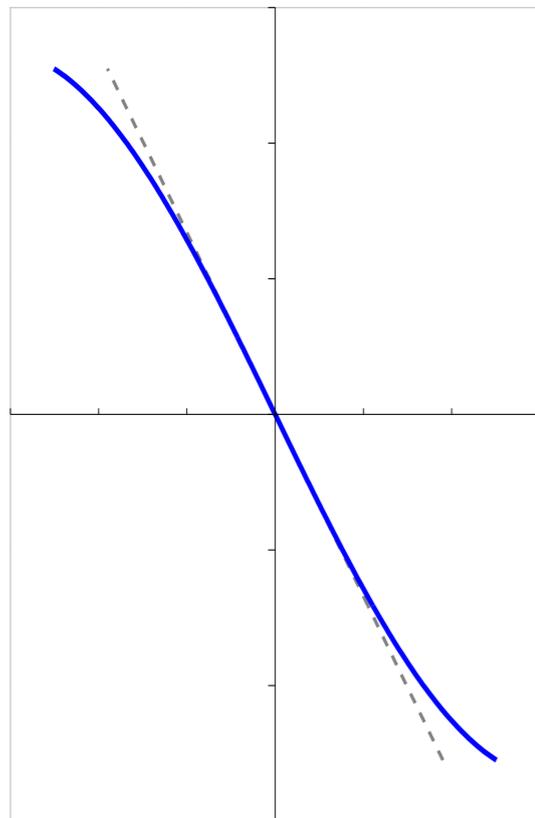


# Gradient non-linearities and diffusion encoding

(Bammer et al., 2003)

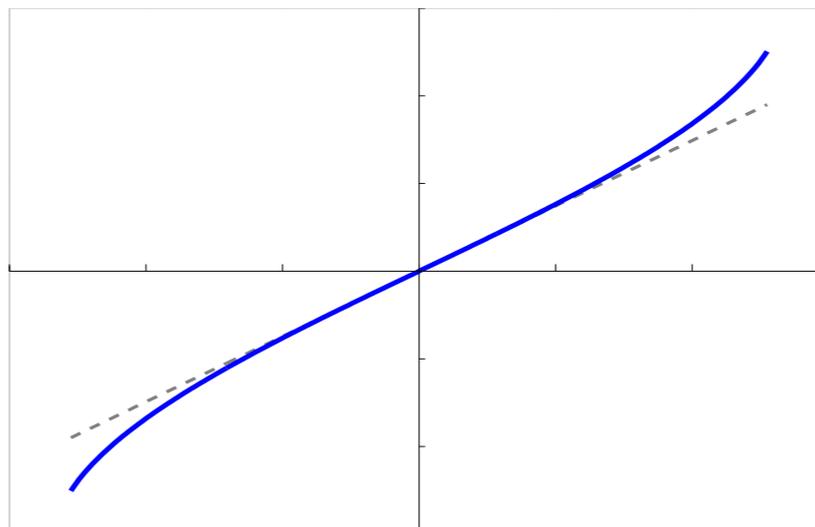
field

y-gradient

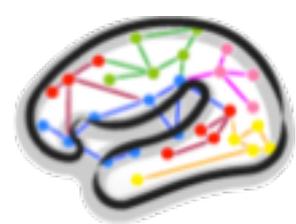


But as we  
move in the  
x-direction ...

x-gradient



But what if  
the gradients  
really look  
like this?

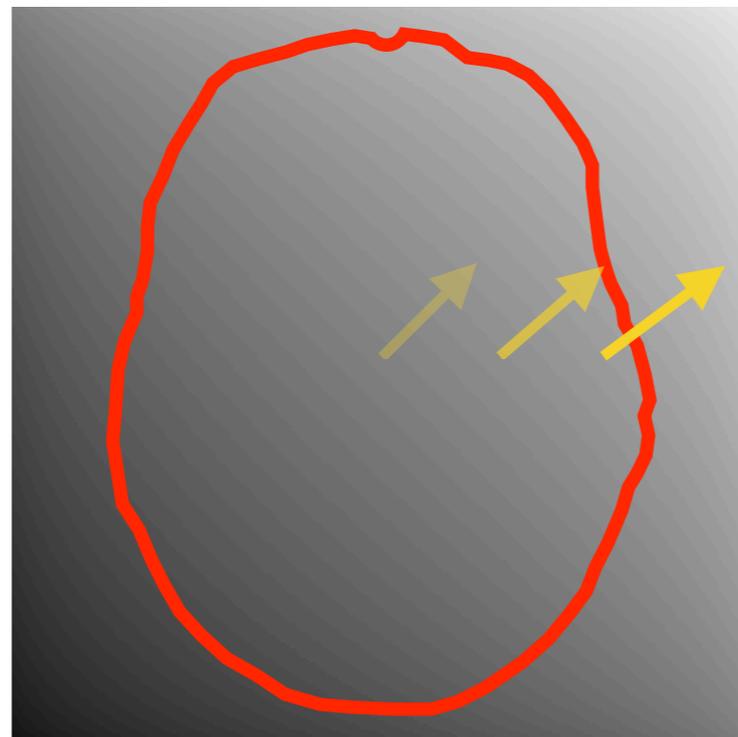
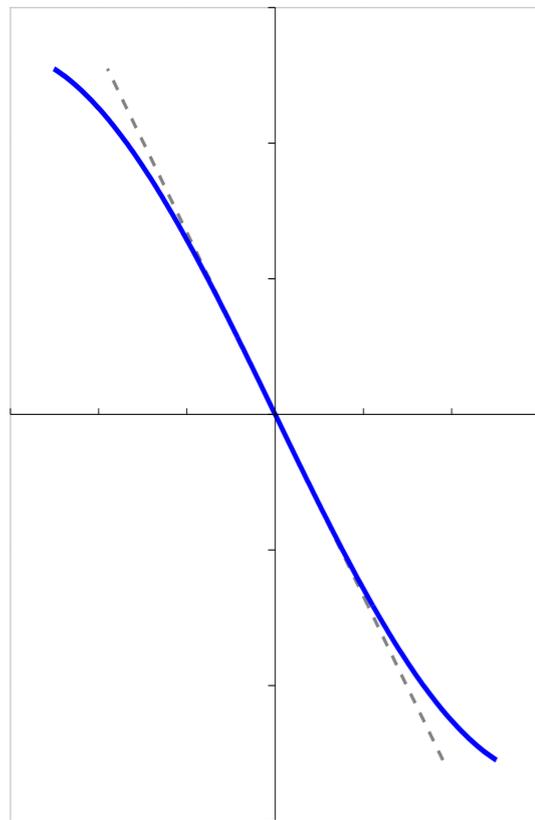


# Gradient non-linearities and diffusion encoding

(Bammer et al., 2003)

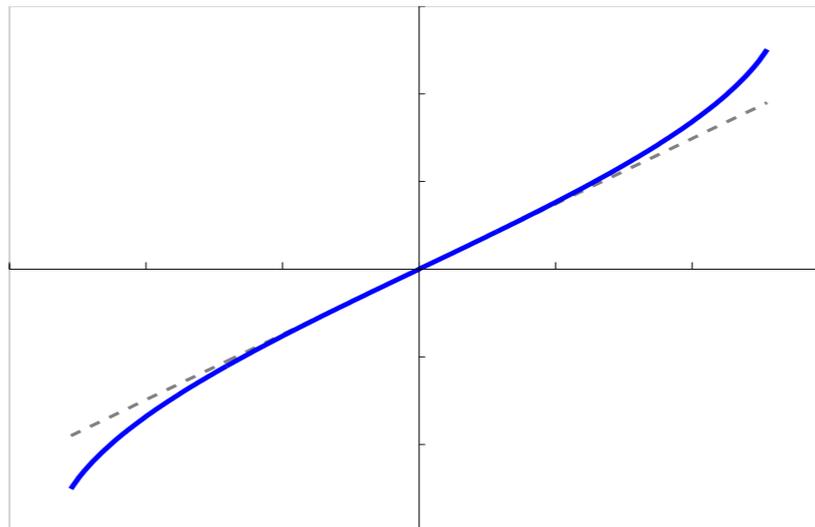
field

y-gradient

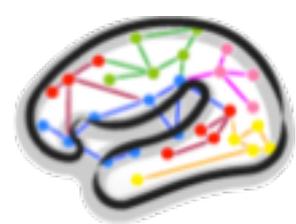


But as we  
move in the  
x-direction ...

x-gradient



But what if  
the gradients  
really look  
like this?

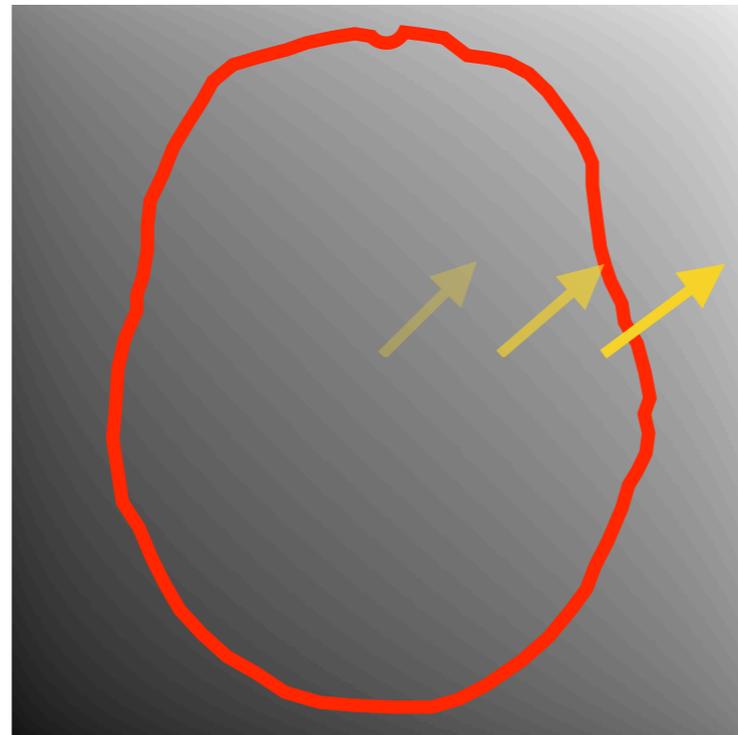
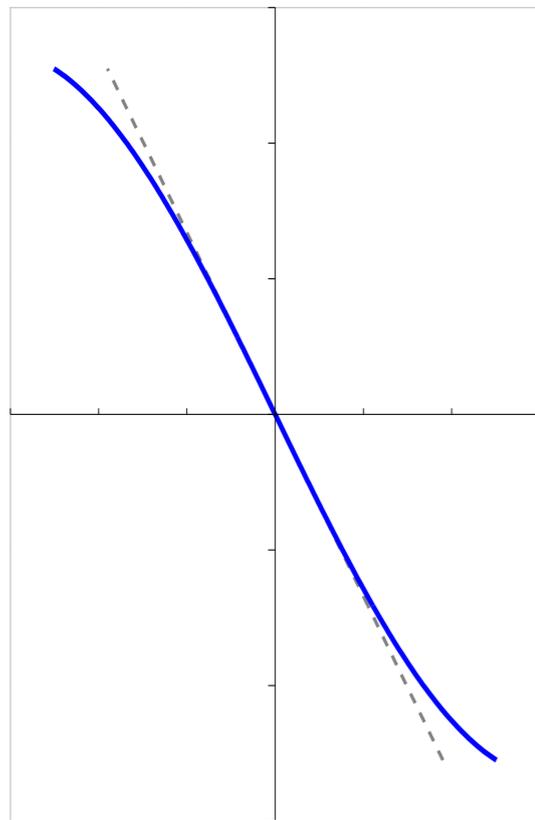


# Gradient non-linearities and diffusion encoding

(Bammer et al., 2003)

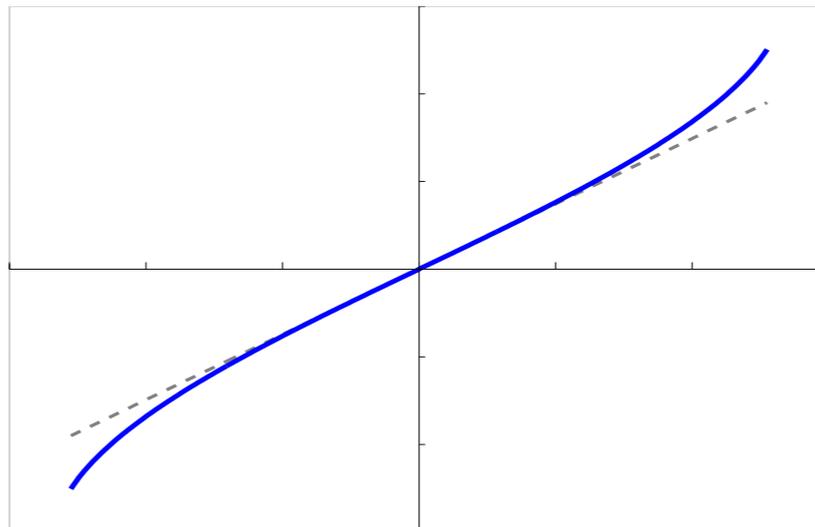
field

y-gradient

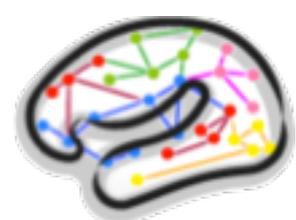


It grows  
(b-value  
increases) and  
rotates

x-gradient



But what if  
the gradients  
really look  
like this?

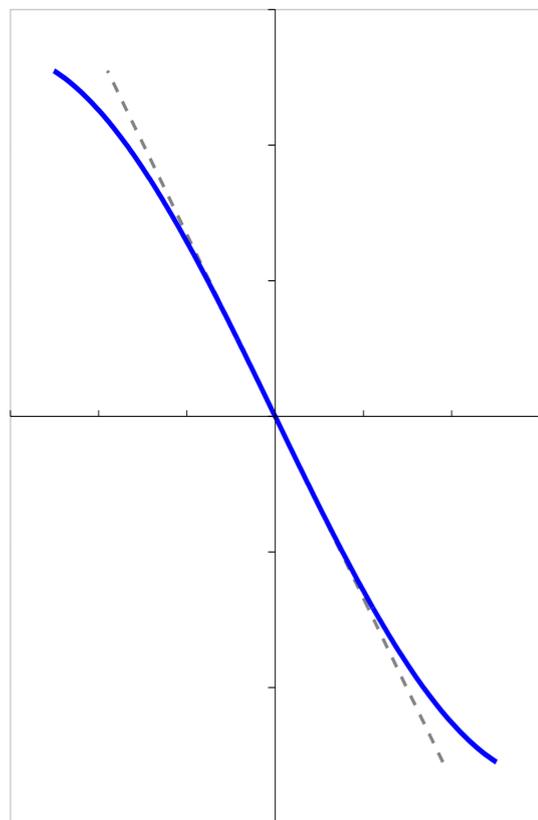


# Gradient non-linearities and diffusion encoding

(Bammer et al., 2003)

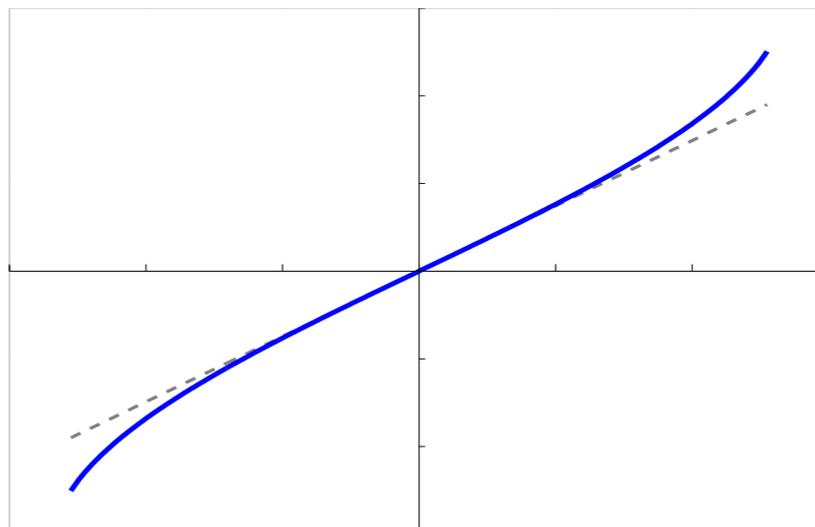
field

y-gradient

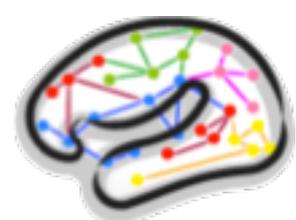


And if we move  
in the  
y-direction

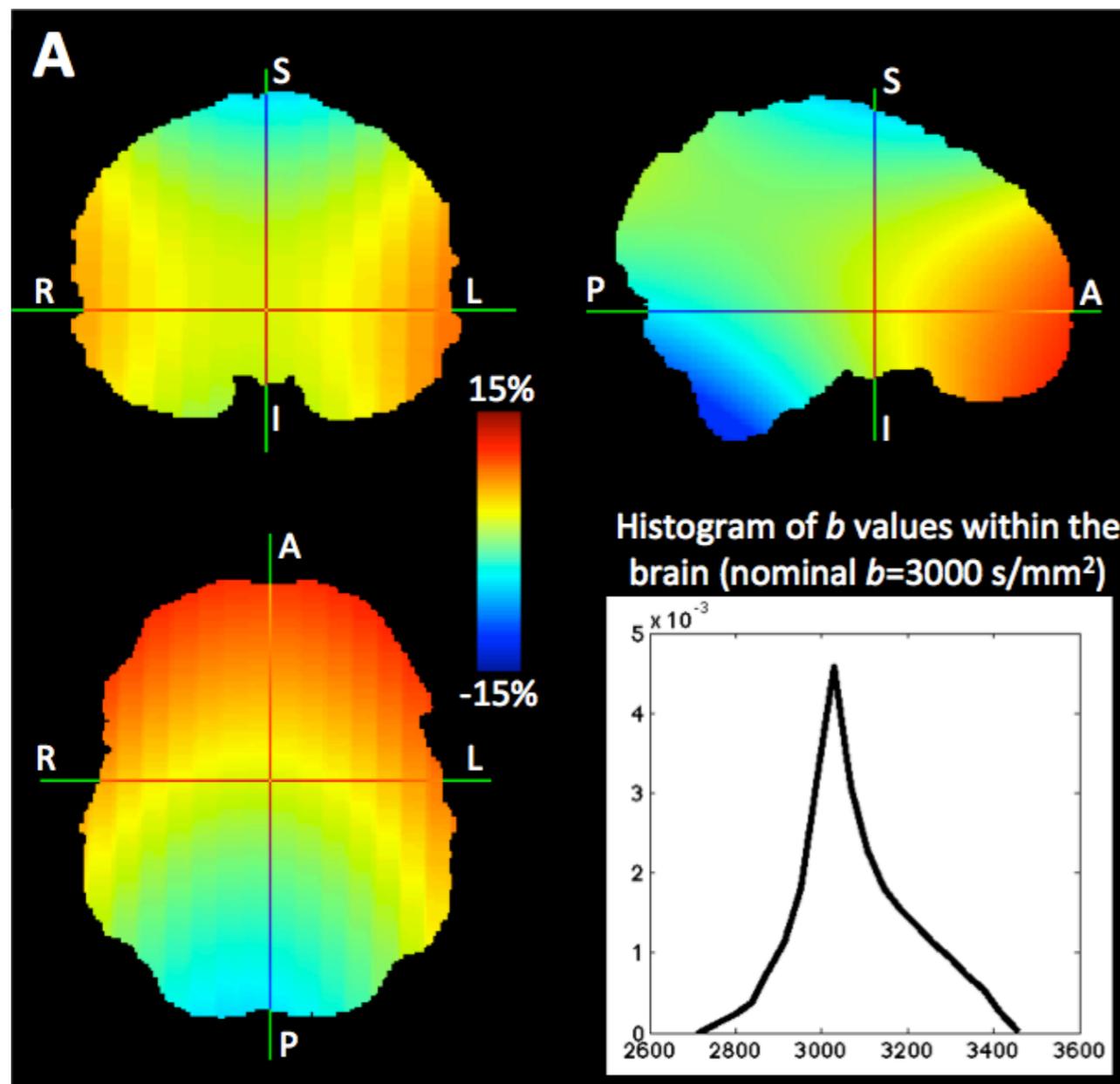
x-gradient



But what if  
the gradients  
really look  
like this?

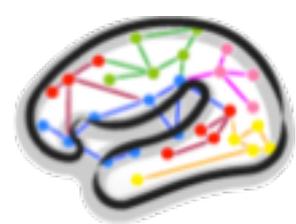


# Gradient non-linearities and diffusion encoding (Bammer et al., 2003)



HCP data comes with gradient specifications and code to correct for this.

To do this at home you need gradient specifications from your vendor

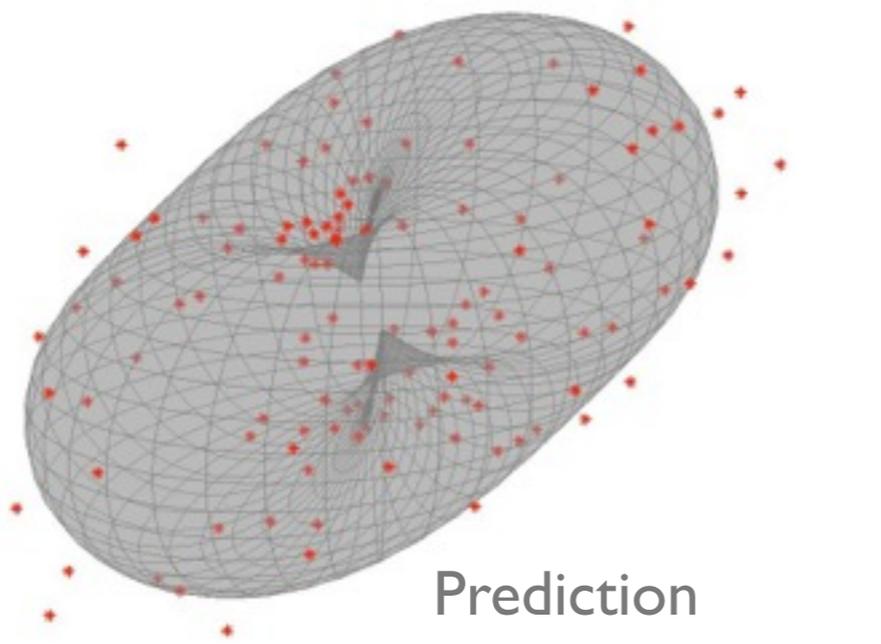


# eddy and topup - tools for processing of diffusion data



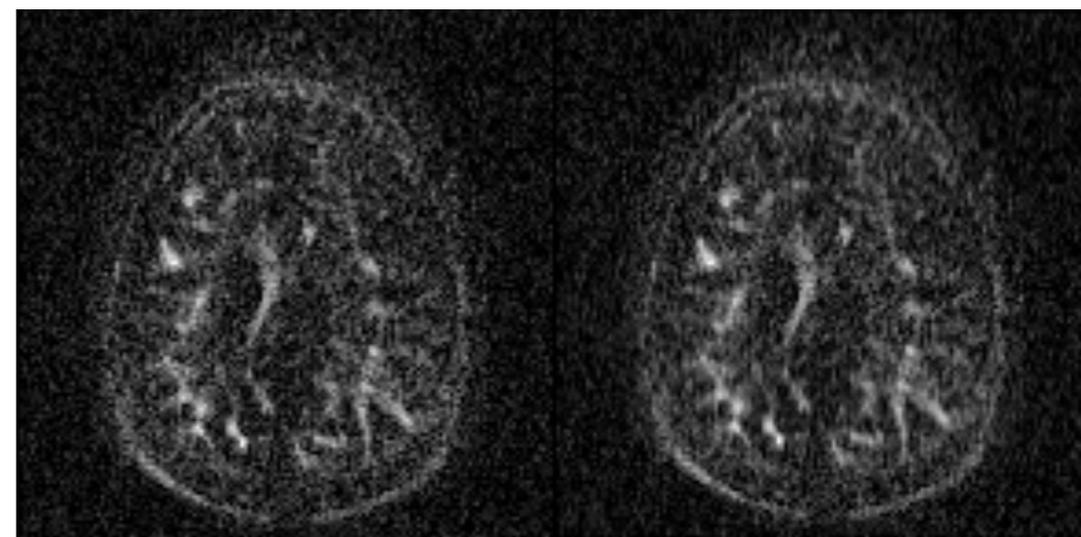
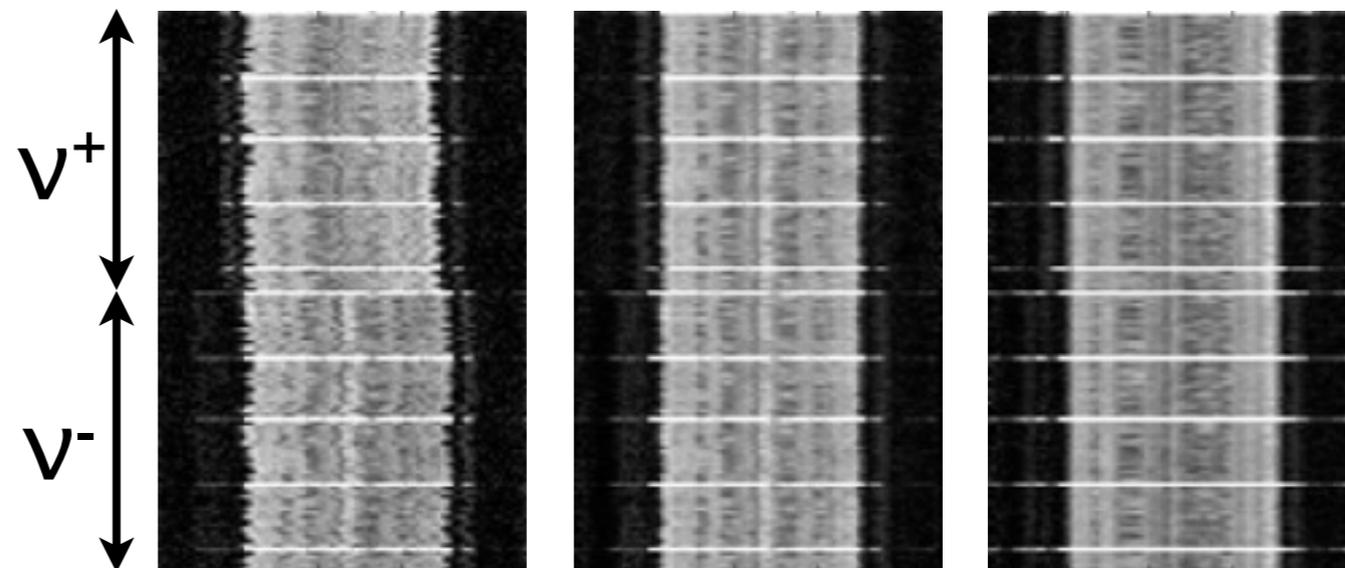
y-component of diffusion gradient

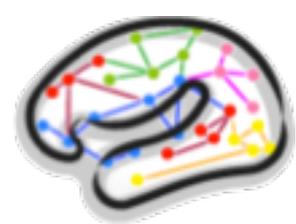
Data point



z-component

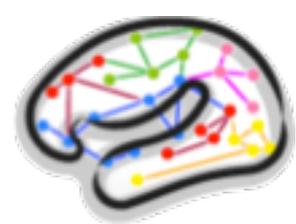
x-component of diffusion gradient



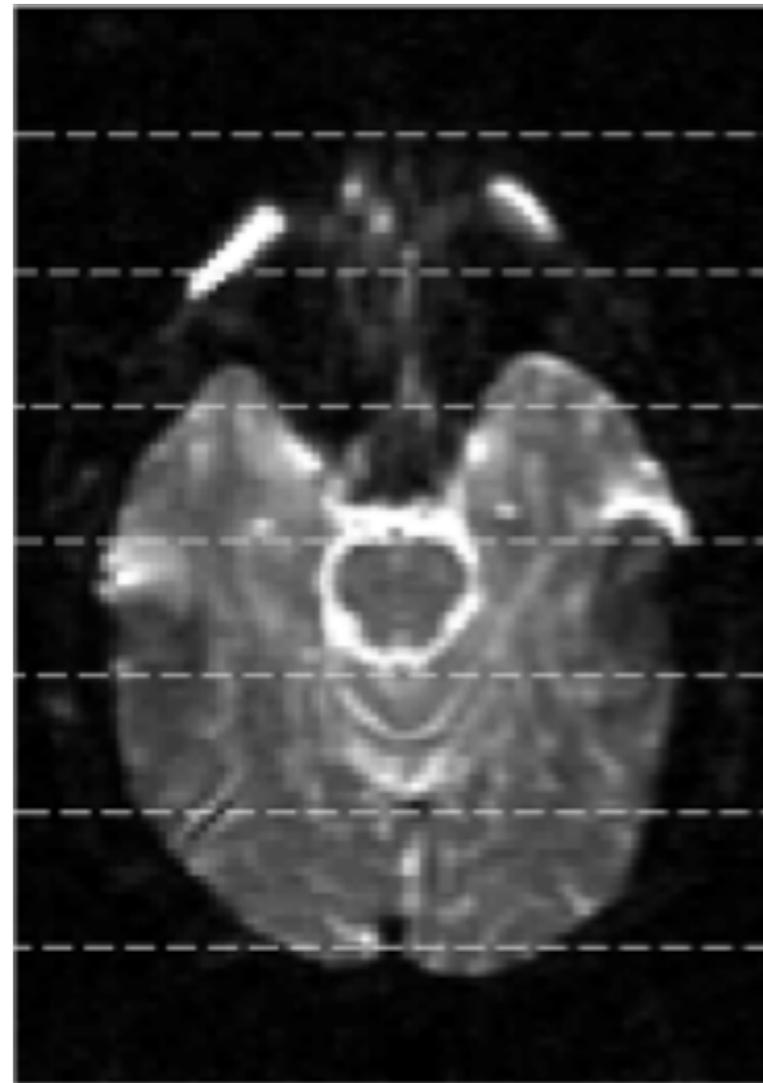
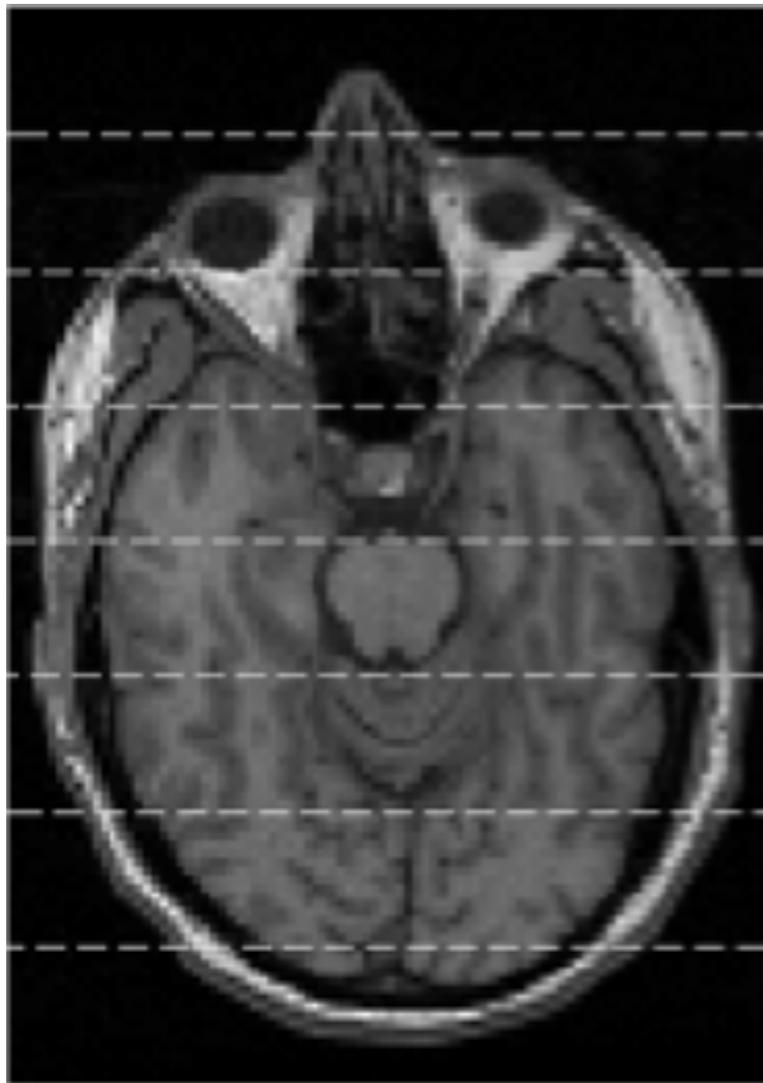


# Outline of the talk

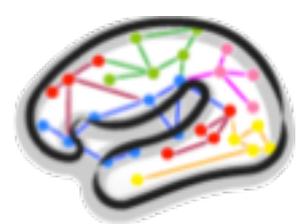
- What is the problem with diffusion data?
- Off-resonance field  $\leftrightarrow$  Distortions
- Where does the off-resonance field come from?
- Worlds shortest course on image registration
- How topup works
- How eddy works
- Outliers
- Practicalities
- Output



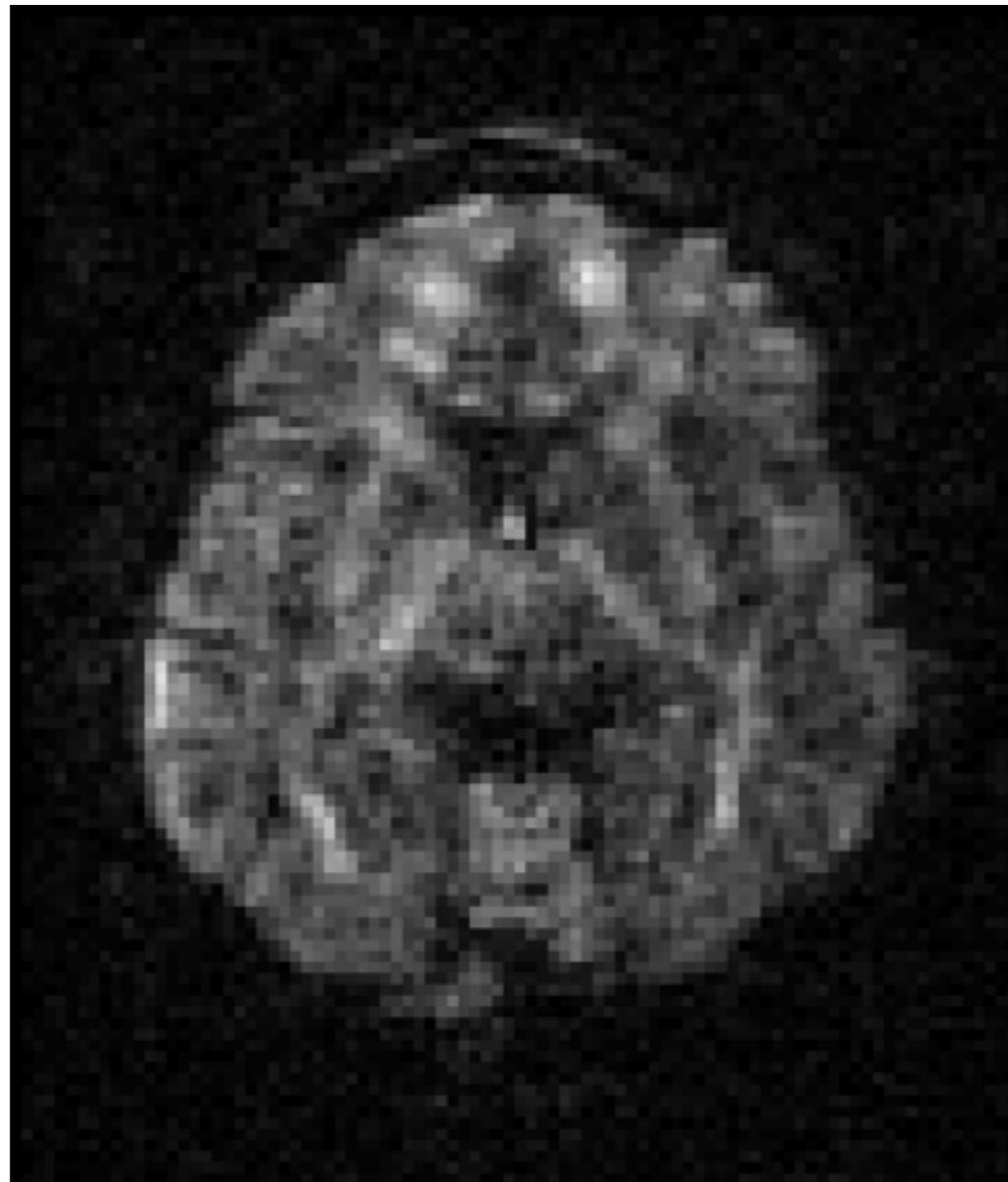
# What is the problem with diffusion data?



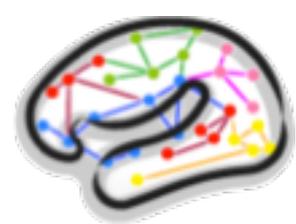
Well, it isn't very anatomically faithful



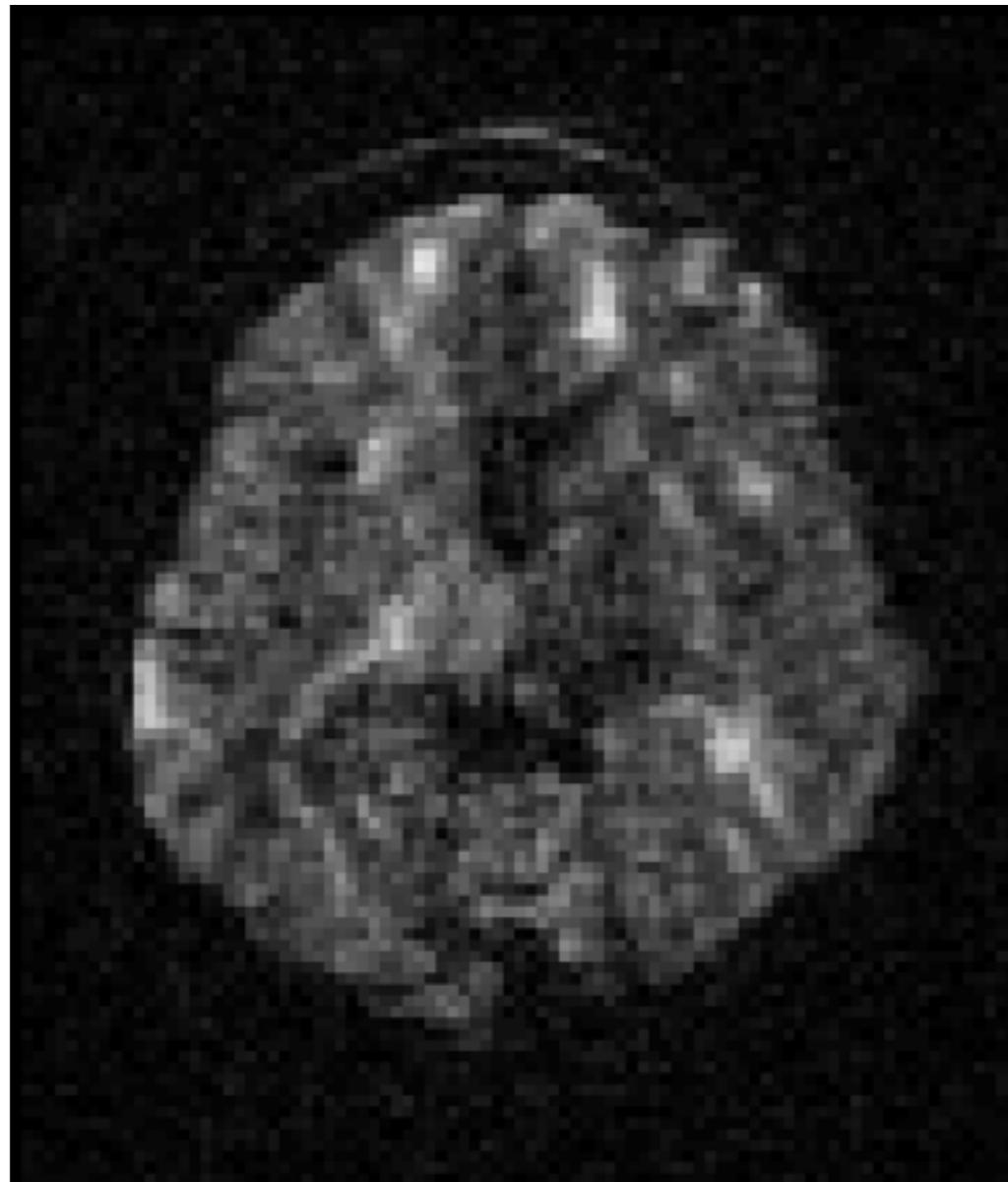
# What is the problem with diffusion data?



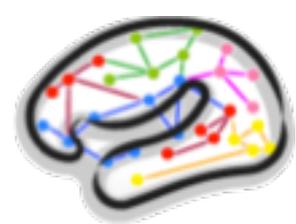
In fact, it isn't even internally consistent



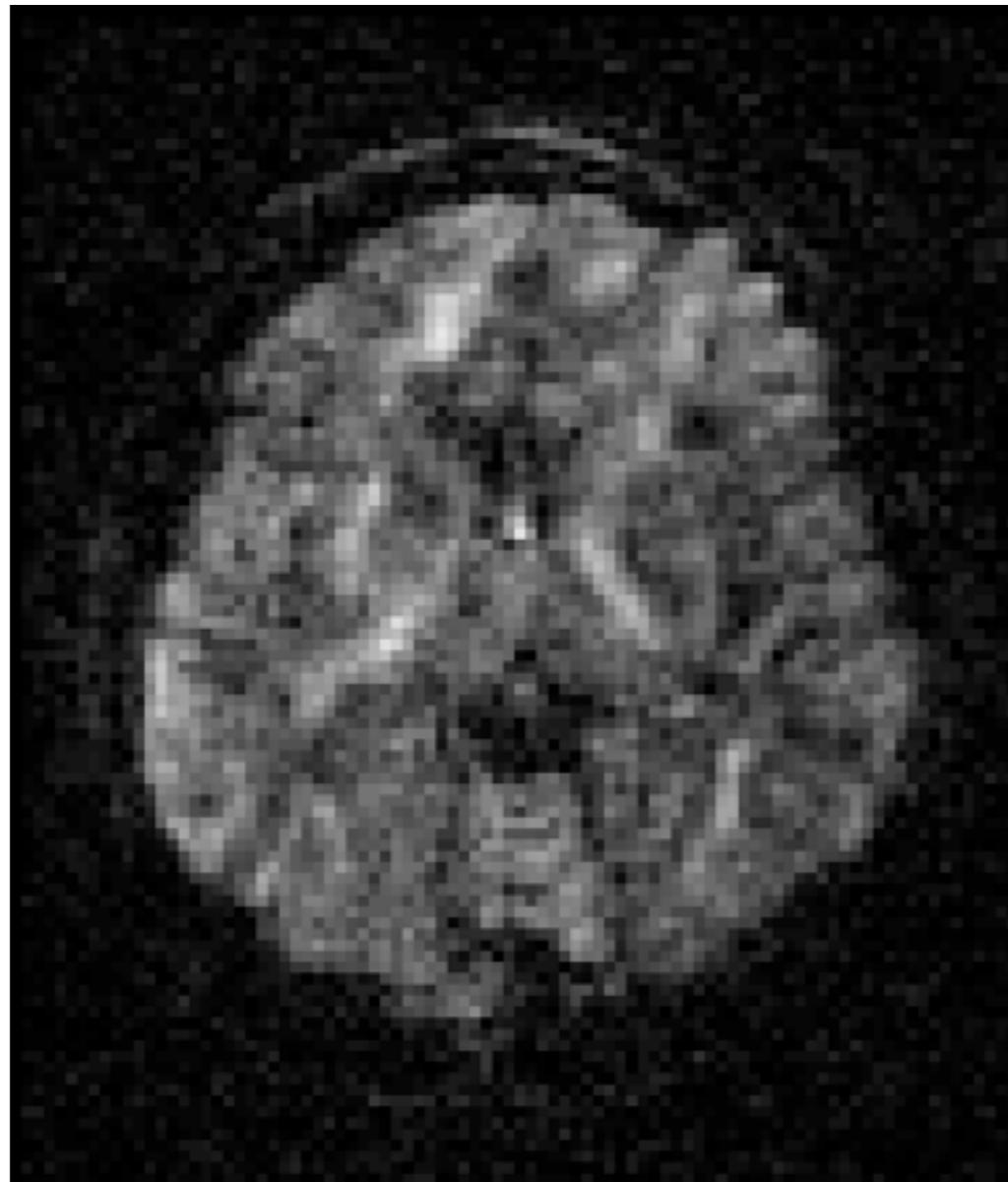
# What is the problem with diffusion data?



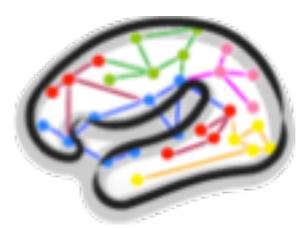
In fact, it isn't even internally consistent



# What is the problem with diffusion data?

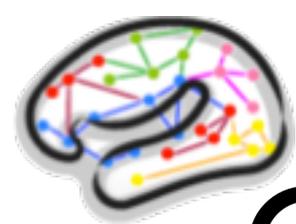


In fact, it isn't even internally consistent



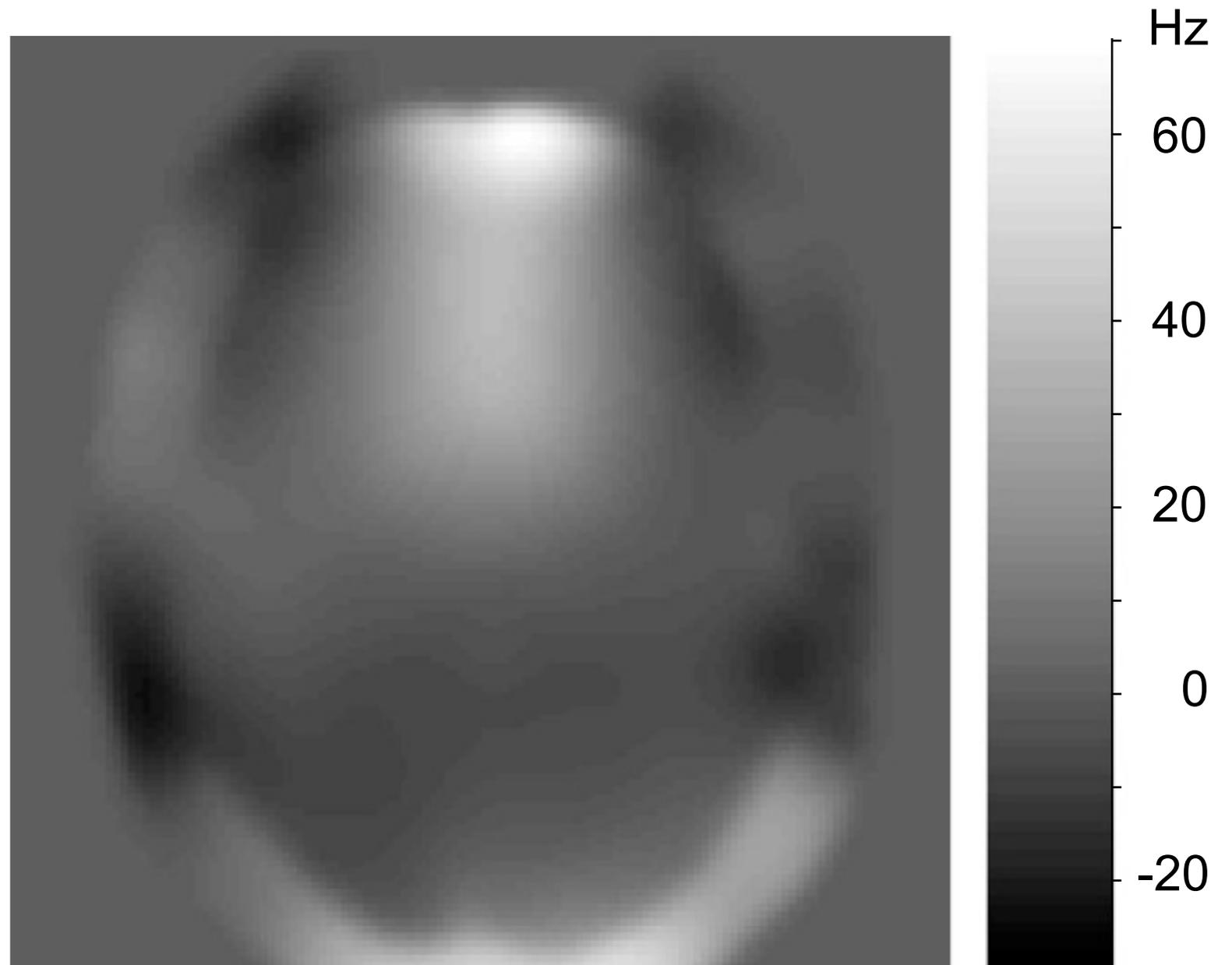
# Outline of the talk

- What is the problem with diffusion data?
- Off-resonance field  $\leftrightarrow$  Distortions
- Where does the off-resonance field come from?
- Worlds shortest course on image registration
- How topup works
- How eddy works
- Outliers
- Practicalities
- Output

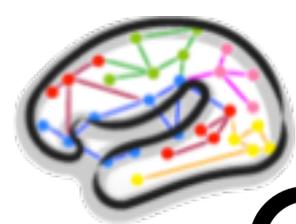


# Off-resonance field $\Rightarrow$ Distortions

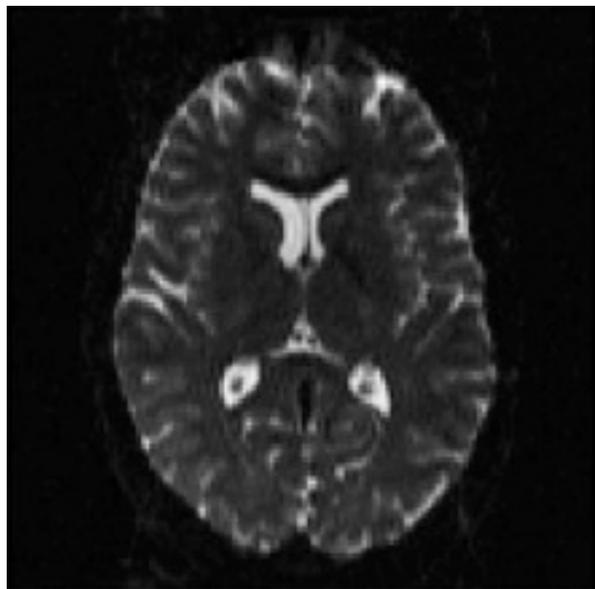
An “off-resonance” field is a map of the difference between what we think the field is and what it really is.



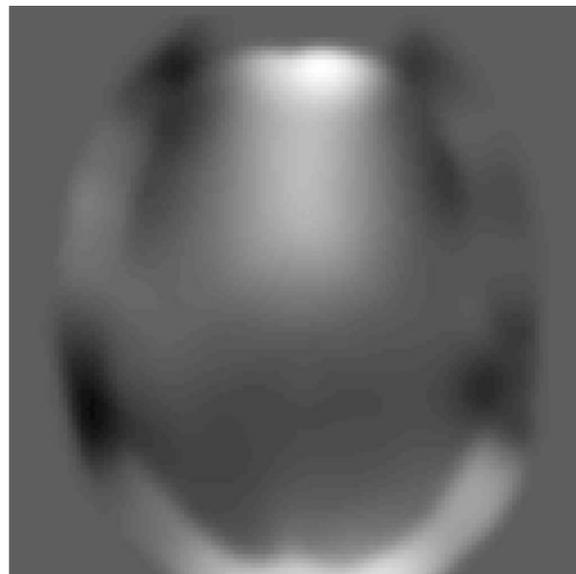
It is all caused by an “off-resonance” field



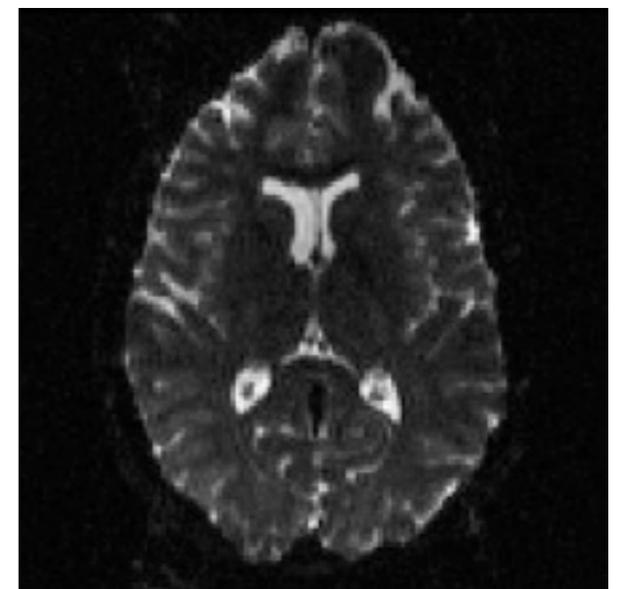
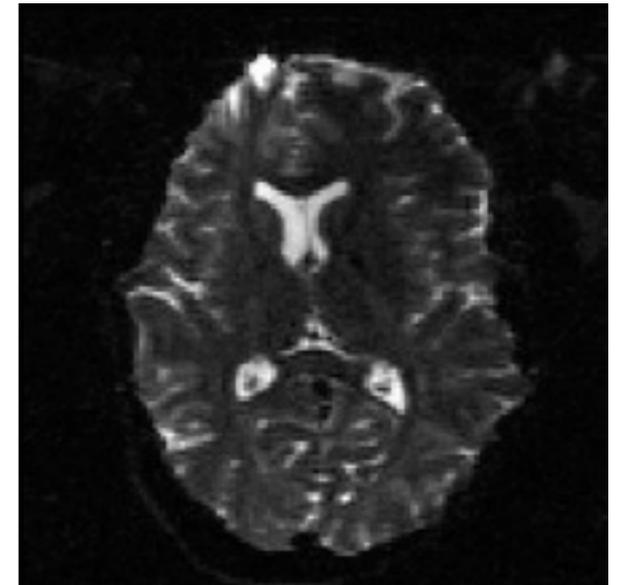
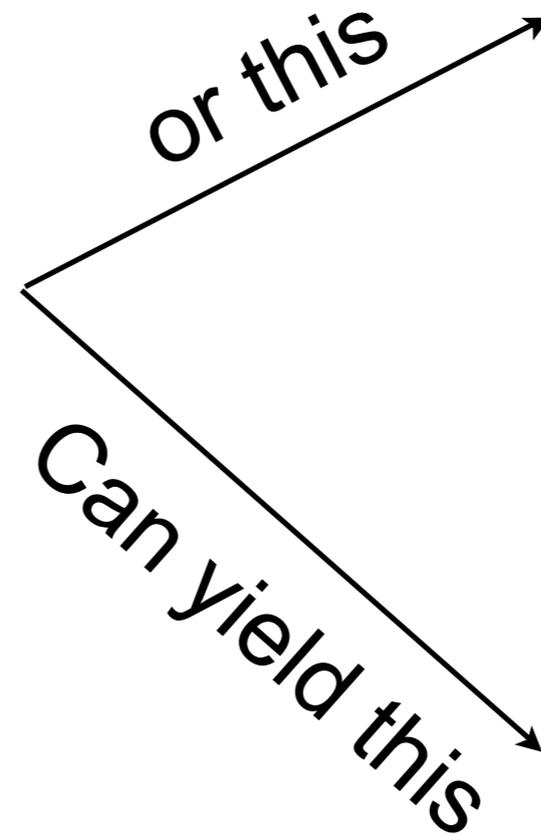
# Off-resonance field $\Rightarrow$ Distortions



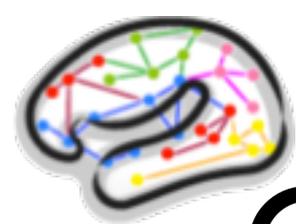
But this object



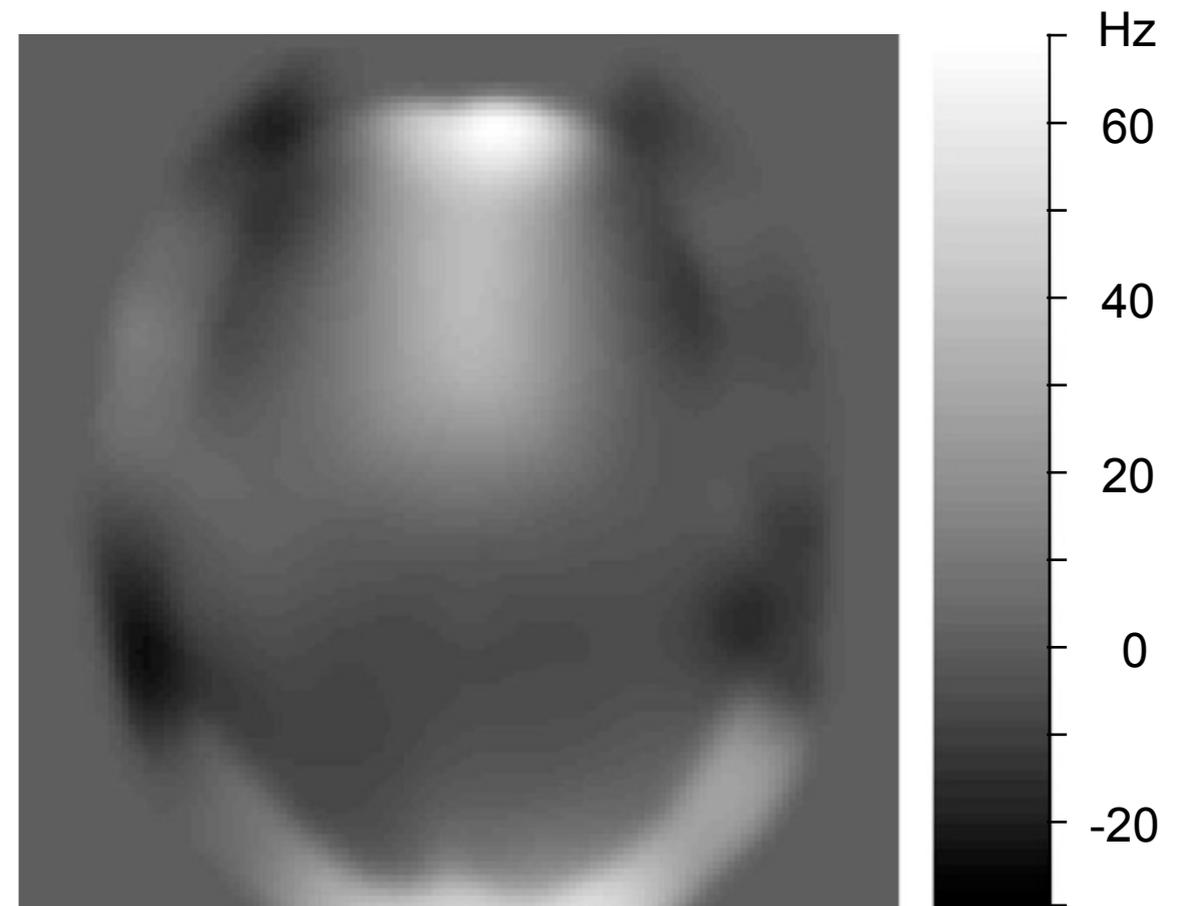
scanned in  
this field



So there is clearly more to this story...

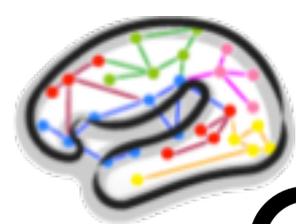


# Off-resonance field $\Rightarrow$ Distortions

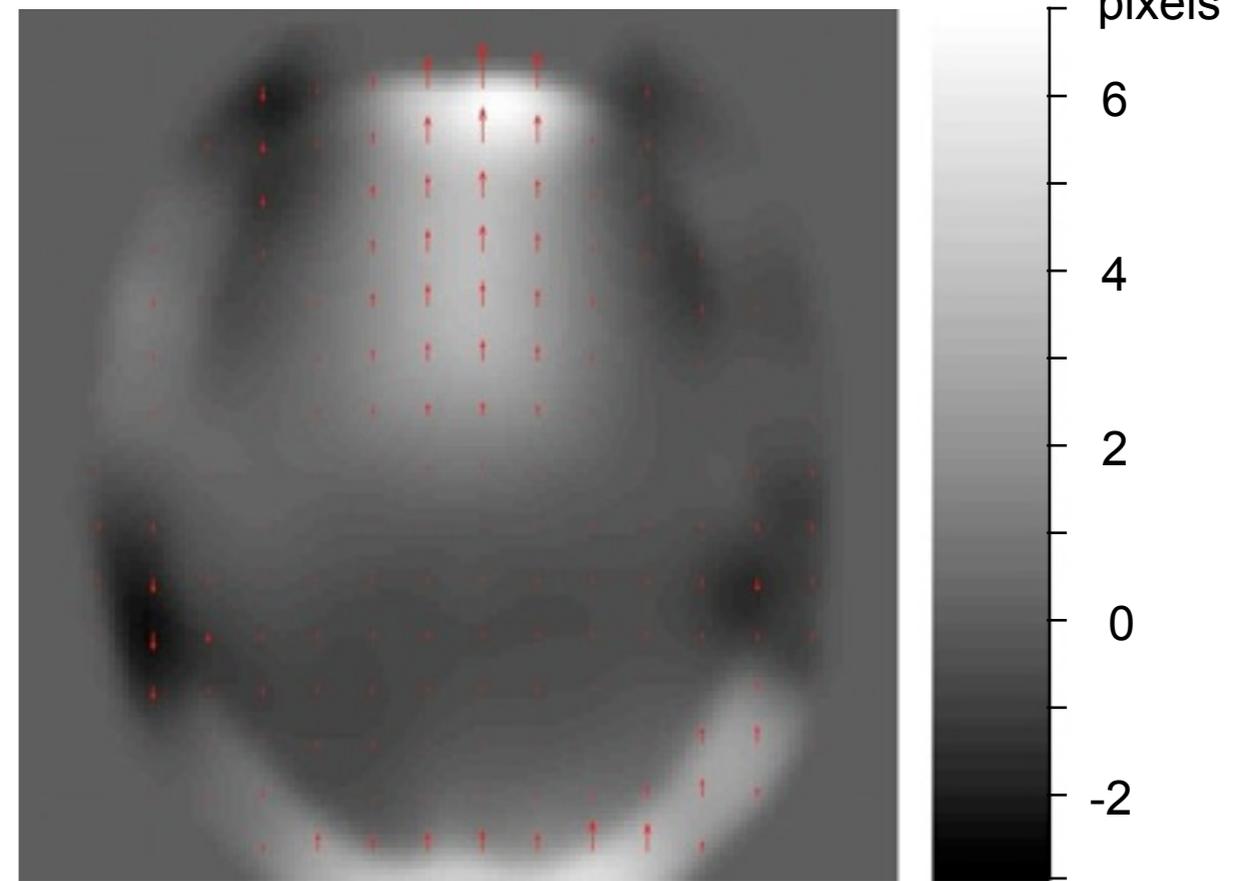
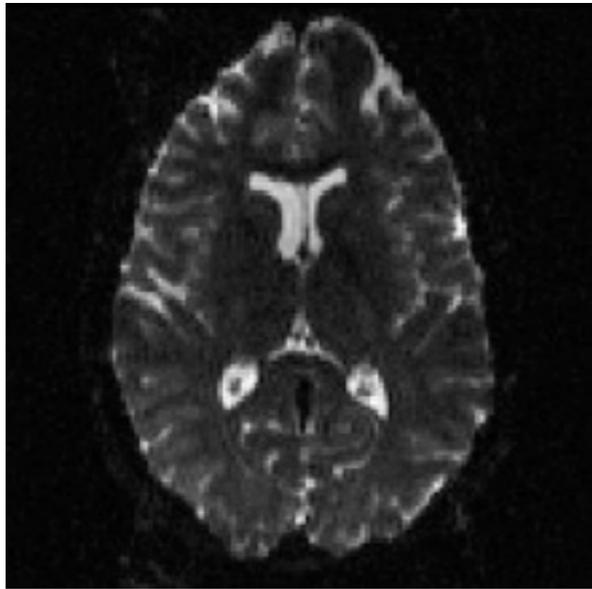


An off-resonance field is effectively a scaled voxel-displacement map.

If we know the imaging parameters we can do the translation.



# Off-resonance field $\Rightarrow$ Distortions

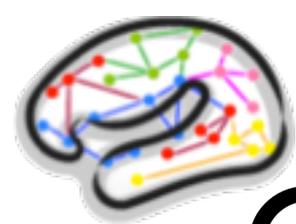


And know what to expect

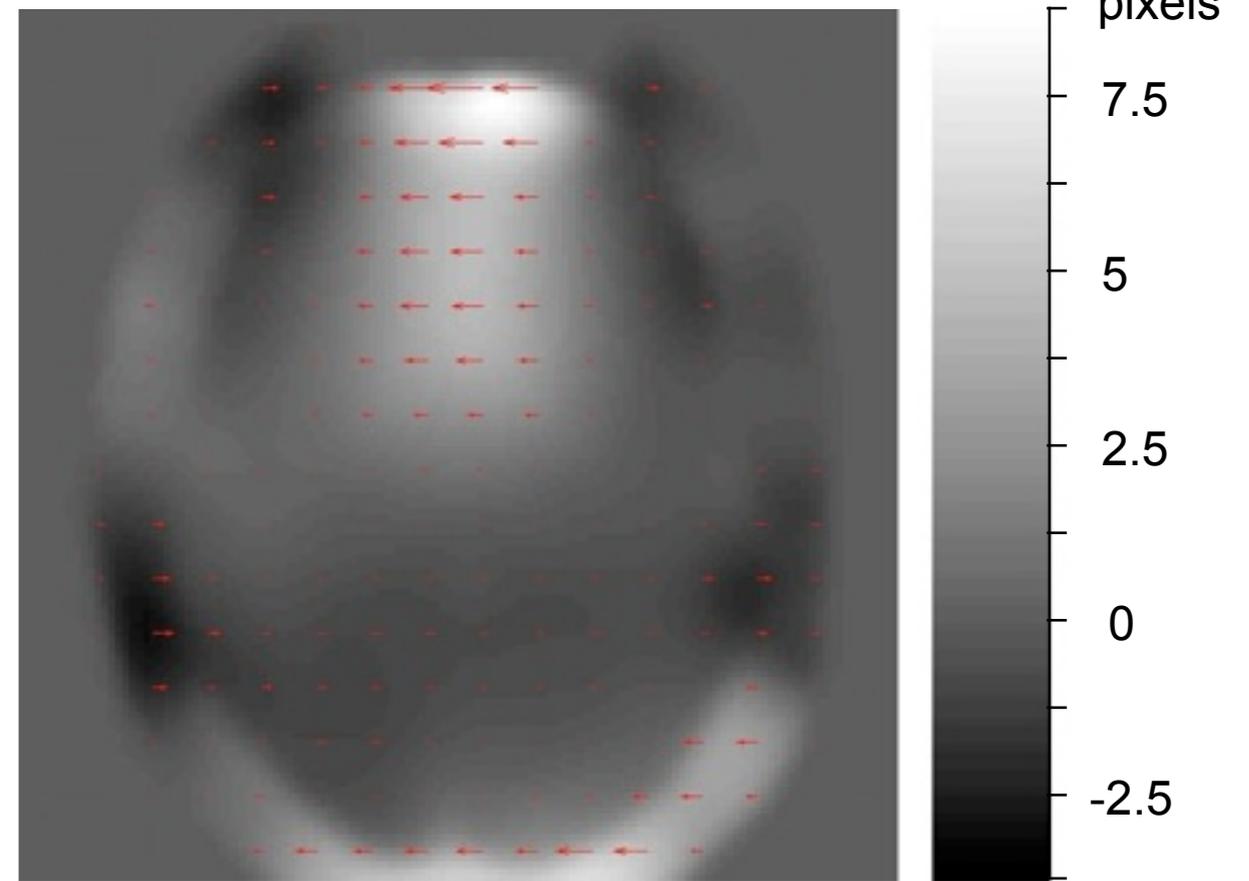
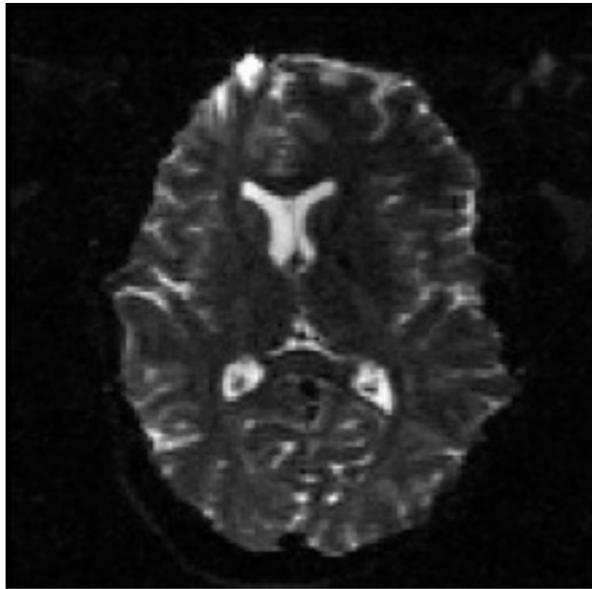
An off-resonance field is effectively a scaled voxel-displacement map.

If we know the imaging parameters we can do the translation.

$$BW/\text{pixel} = 10\text{Hz}, \mathbf{p} = [0 \ 1 \ 0]$$



# Off-resonance field $\Rightarrow$ Distortions

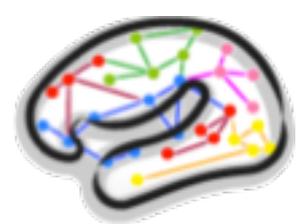


And know what to expect

So, an off-resonance field is effectively a scaled voxel-displacement map.

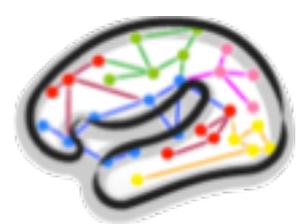
And if we know the imaging parameters we can do the translation.

$$\text{BW/pixel} = 8\text{Hz}, \mathbf{p} = [-1 \ 0 \ 0]$$



# Outline of the talk

- What is the problem with diffusion data?
- Off-resonance field  $\leftrightarrow$  Distortions
- **Where does the off-resonance field come from?**
- Worlds shortest course on image registration
- How topup works
- How eddy works
- Outliers
- Practicalities
- Output



# Where does the off-resonance field come from?

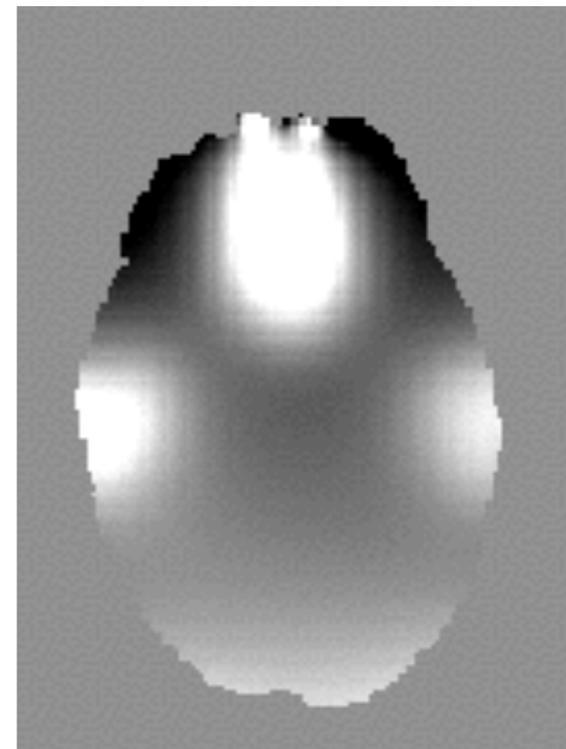
- There are two sources
- The first is the object (head) itself.

(CT of) Human head

$B_0 \odot$

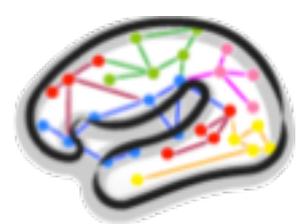


Resulting field



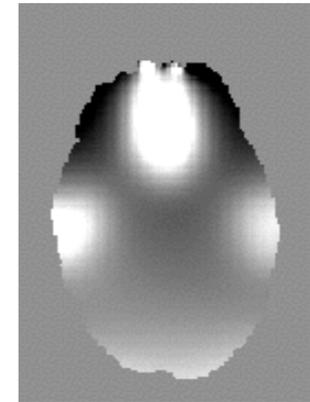
PPMs

Must fulfil  $\begin{cases} \nabla \times \mathbf{H} = 0 \\ \nabla \cdot \mathbf{B} = 0 \end{cases}$  (still)

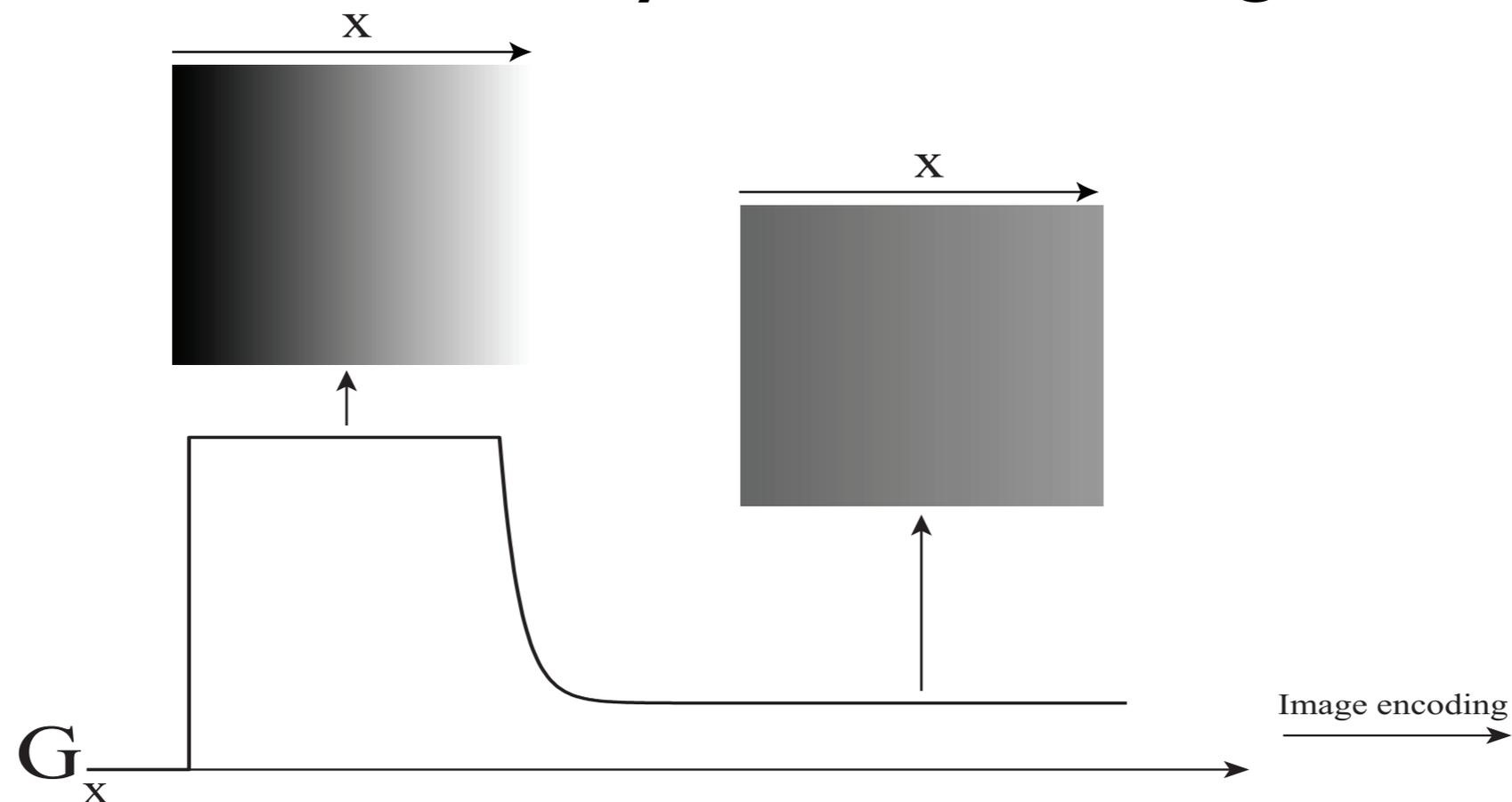


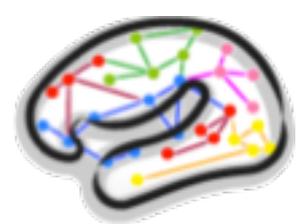
# Where does the off-resonance field come from?

- There are two sources
- The first is the object (head) itself.



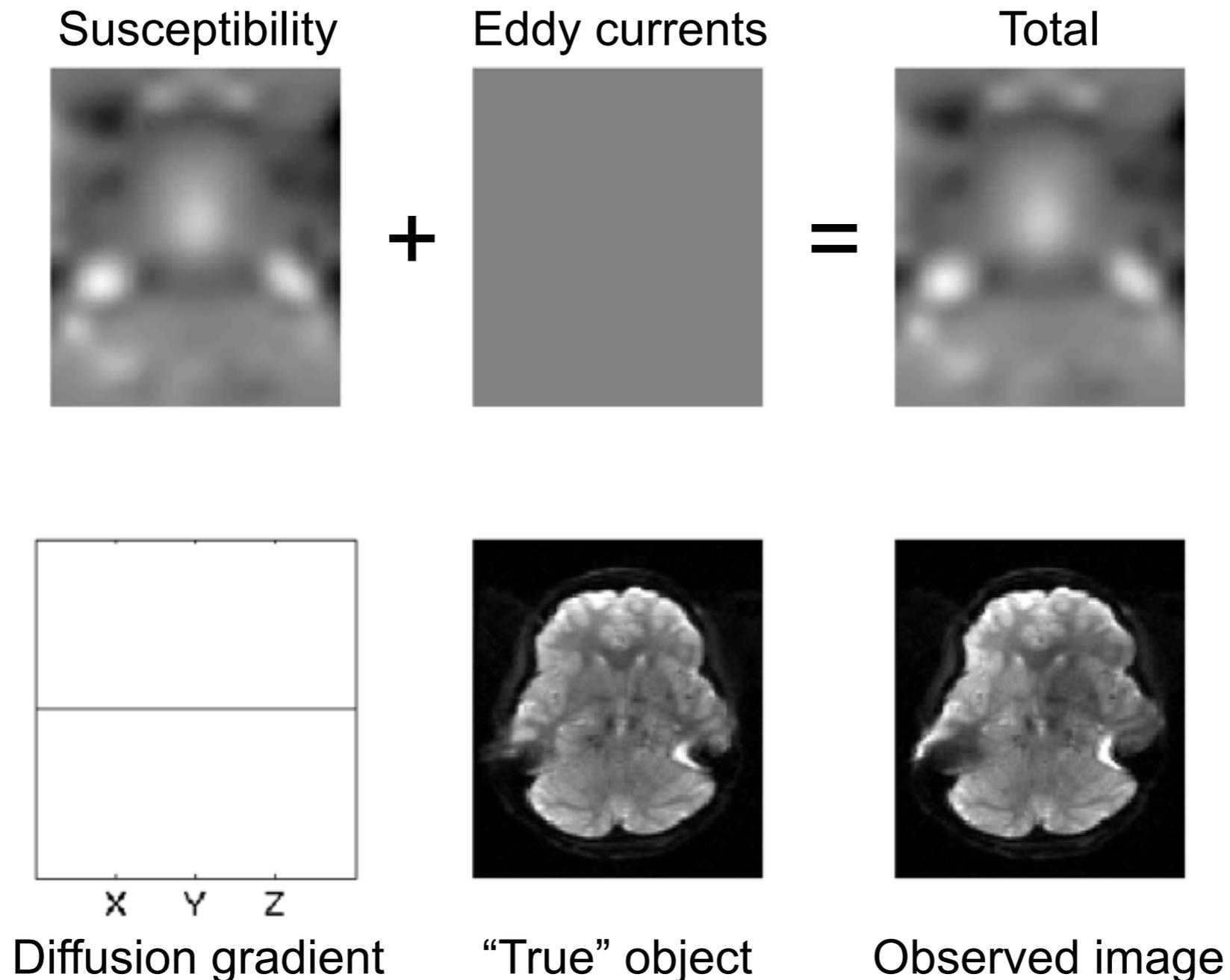
- The second is caused by the diffusion gradient

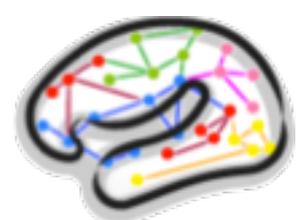




# Where does the off-resonance field come from?

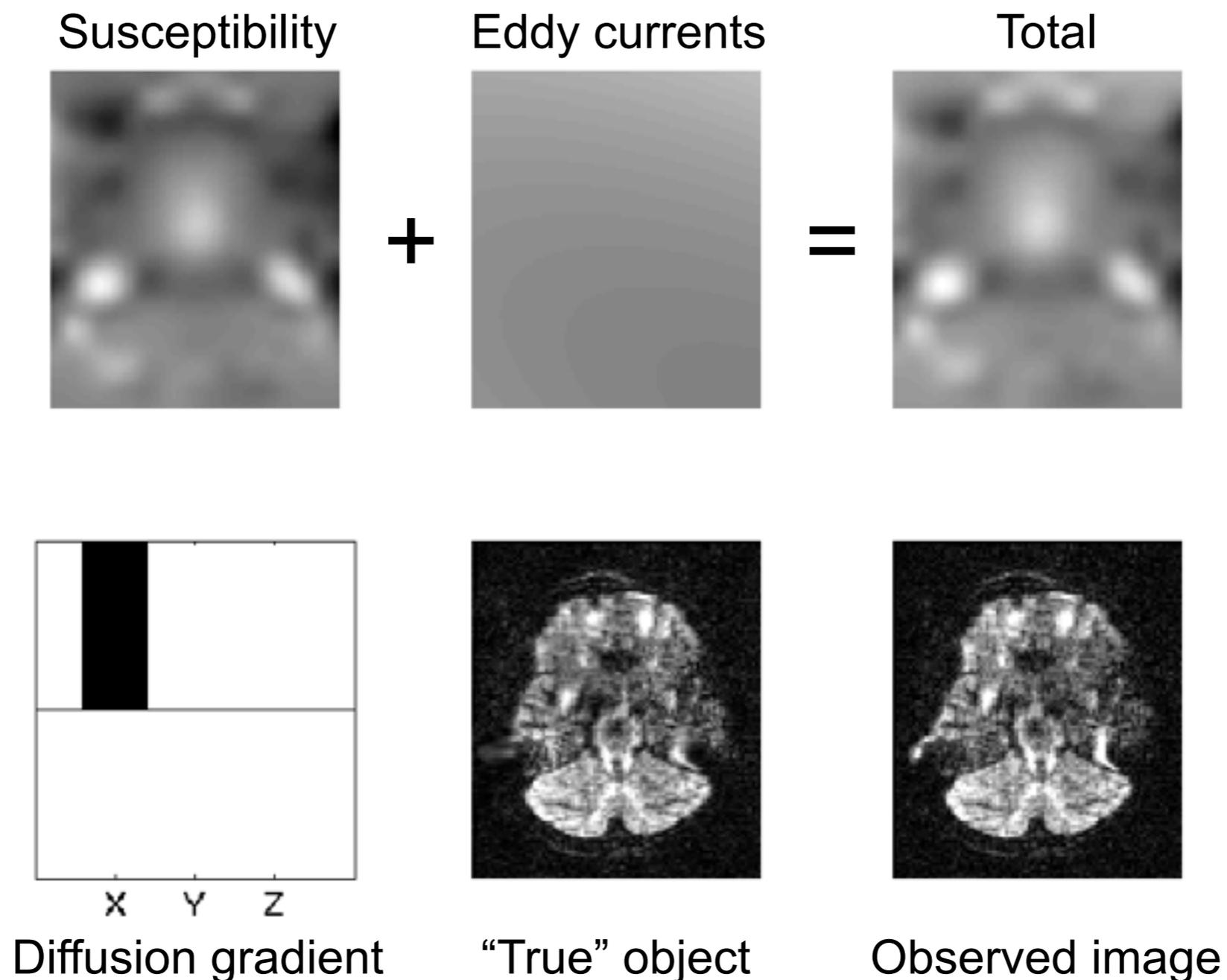
So for any diffusion weighted volume the off-resonance field is the sum of these two contributions

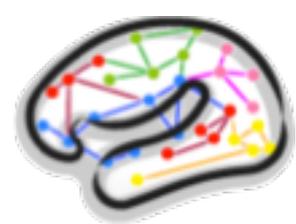




# Where does the off-resonance field come from?

So for any diffusion weighted volume the off-resonance field is the sum of these two contributions

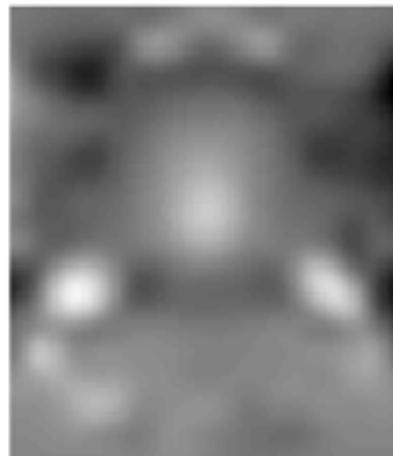




# Where does the off-resonance field come from?

So for any diffusion weighted volume the off-resonance field is the sum of these two contributions

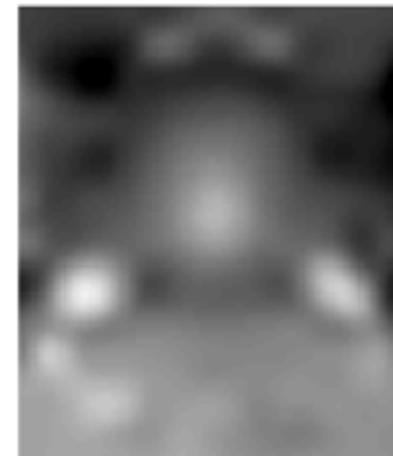
Susceptibility



Eddy currents

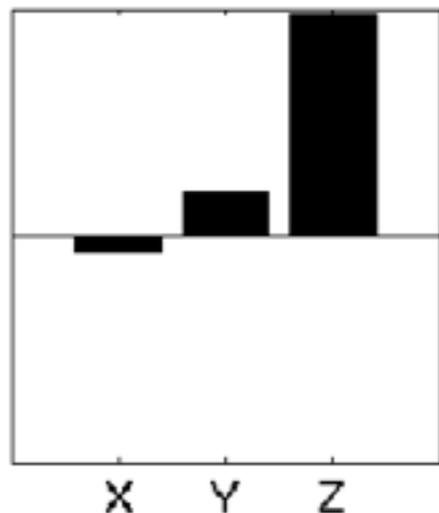


Total

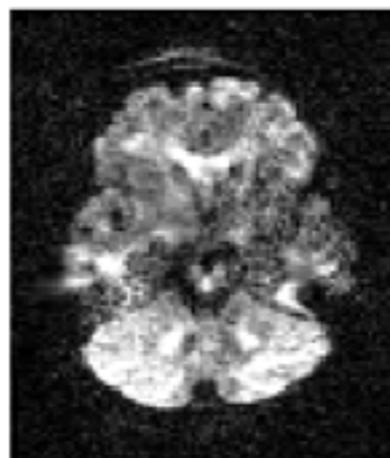


+

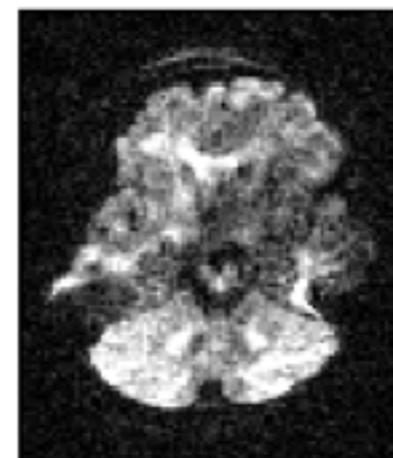
=



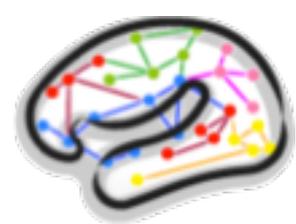
Diffusion gradient



"True" object



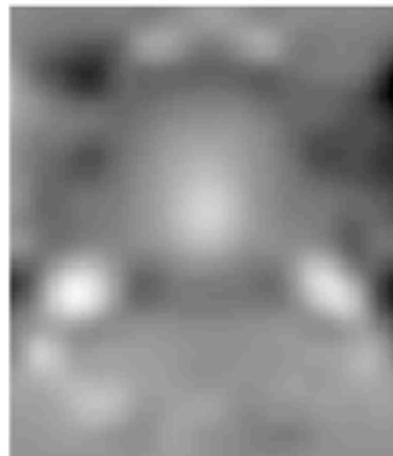
Observed image



# Where does the off-resonance field come from?

So for any diffusion weighted volume the off-resonance field is the sum of these two contributions

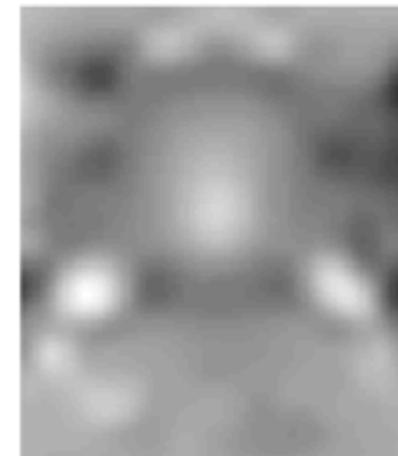
Susceptibility



Eddy currents

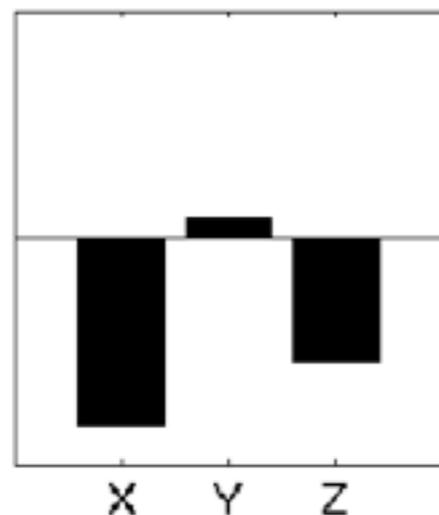


Total

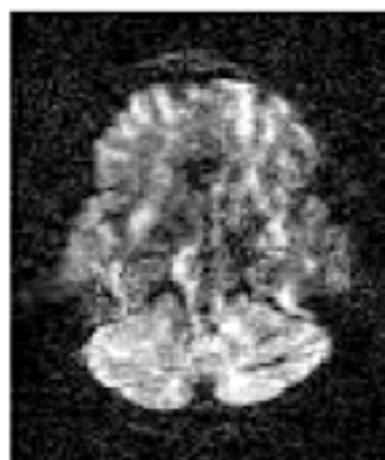


+

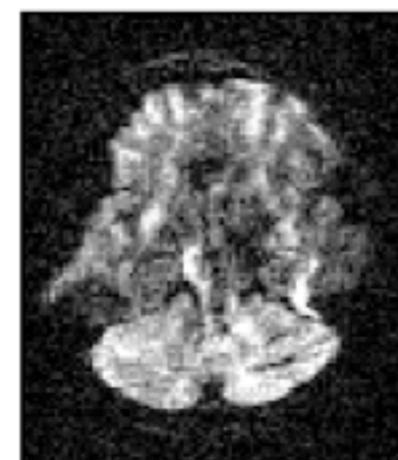
=



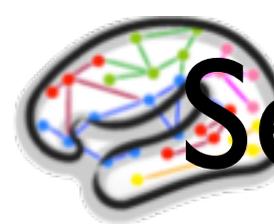
Diffusion gradient



"True" object



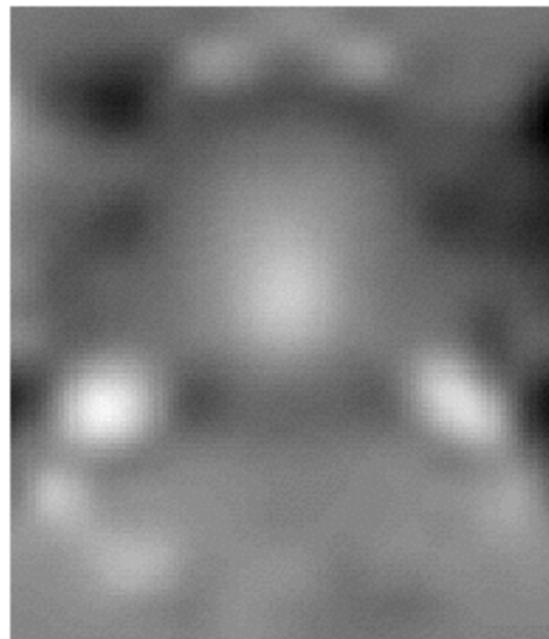
Observed image



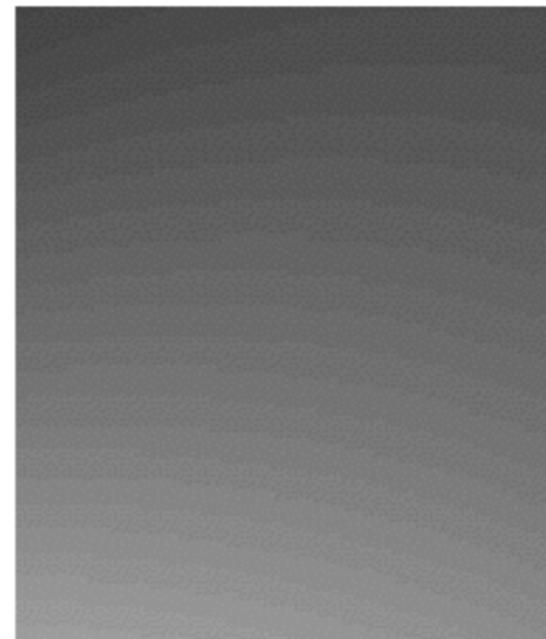
# Separate estimation of susceptibility- and eddy current-fields

So, what we need to estimate is

One of these per  
subject



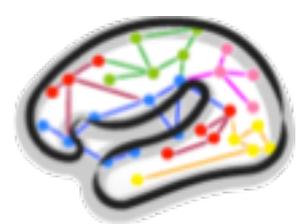
One of these per  
volume



FSL-tools:

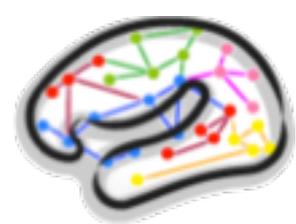
topup

eddy

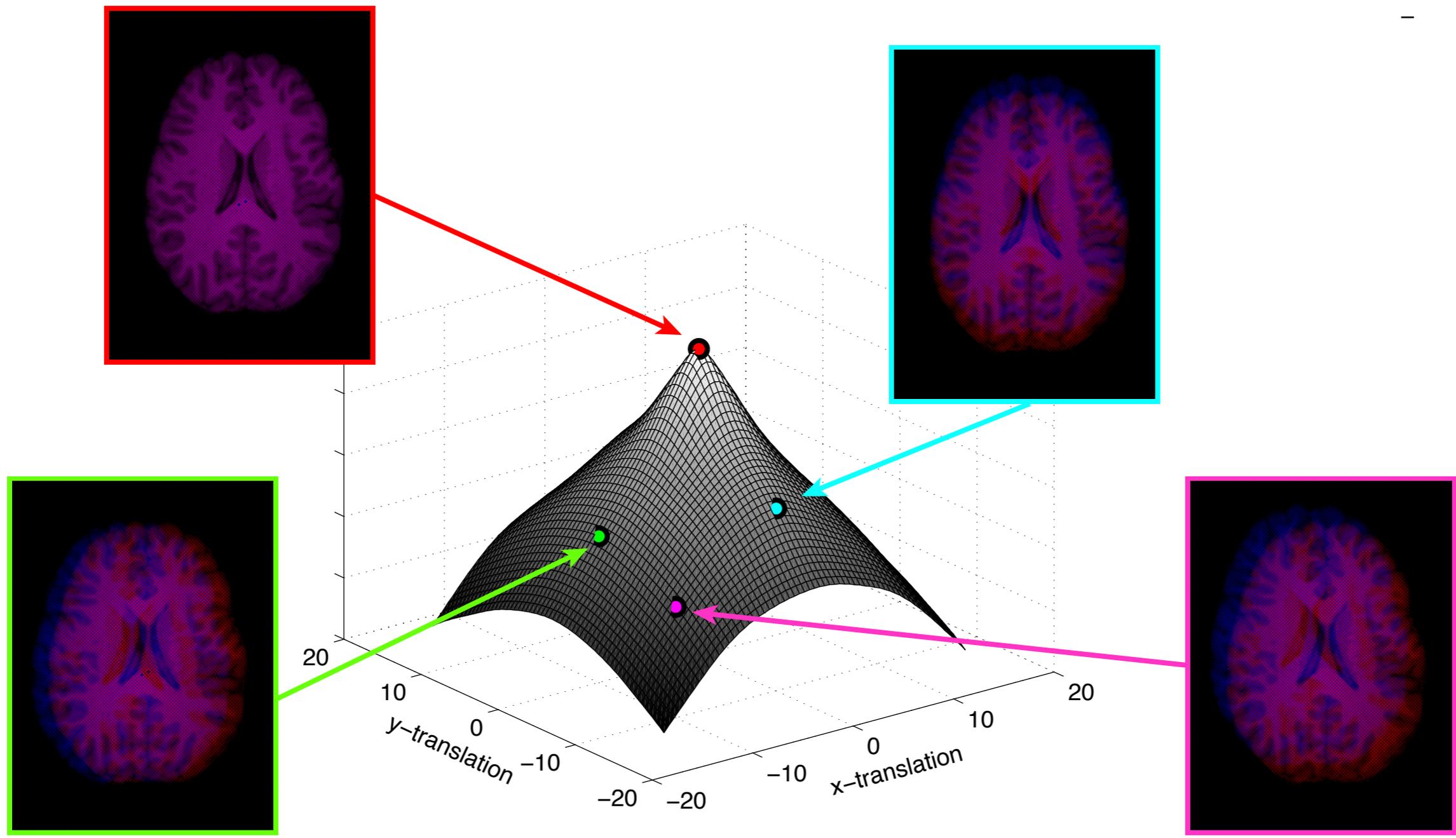


# Outline of the talk

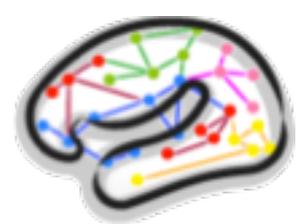
- What is the problem with diffusion data?
- Off-resonance field  $\leftrightarrow$  Distortions
- Where does the off-resonance field come from?
- **Worlds shortest course on image registration**
- How topup works
- How eddy works
- Outliers
- Practicalities
- Output
- Some results



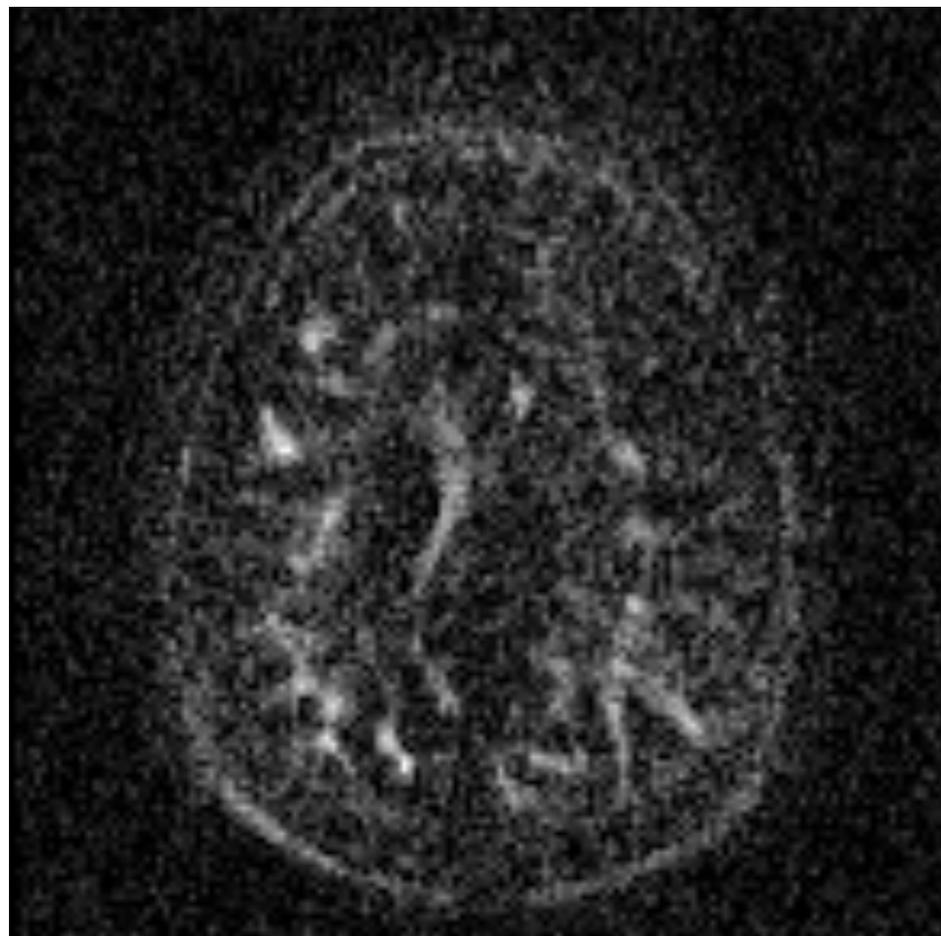
# Worlds shortest course on image registration



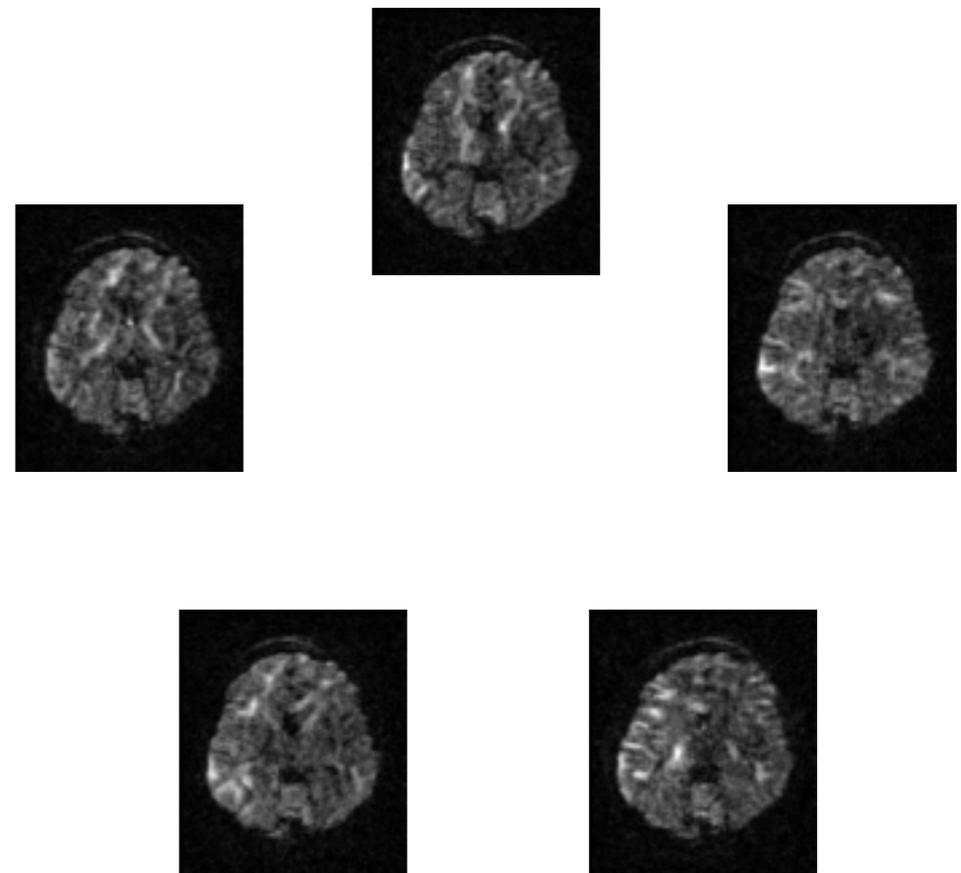
Maximising/minimising an objective/cost-function



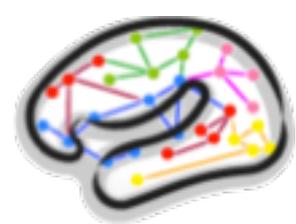
# But it is not easy to register diffusion weighted images



The different diffusion weighted images have different contrast.

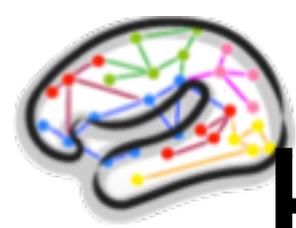


All the images are distorted, only differently. How do we know the truth?

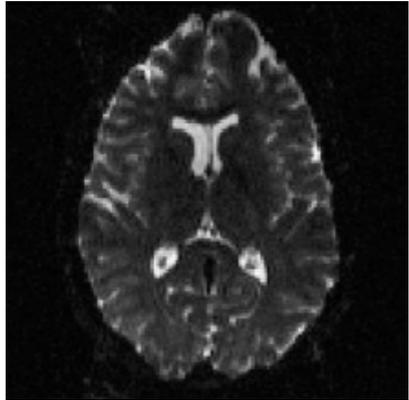


# Outline of the talk

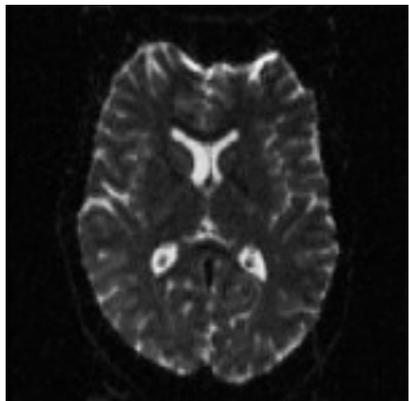
- What is the problem with diffusion data?
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- How eddy works
- Outliers
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# How topup works (very briefly)

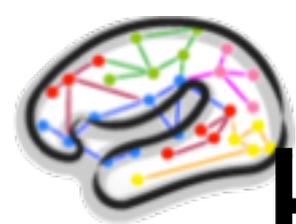


$p=[0 \ 1 \ 0]$

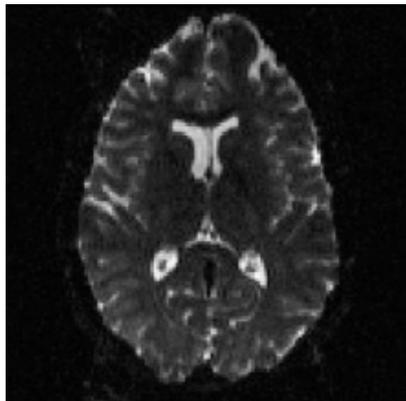


$p=[0 \ -1 \ 0]$

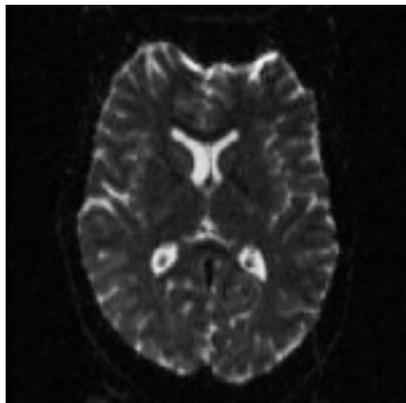
Given two images acquired with different phase-encoding



# How topup works (very briefly)

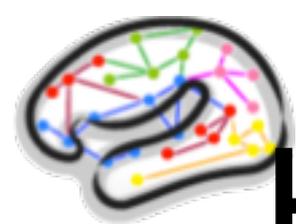


$p=[0 \ 1 \ 0]$

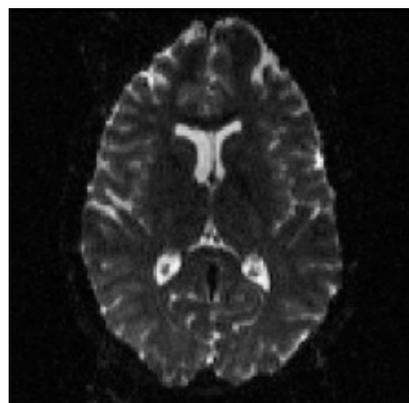


$p=[0 \ -1 \ 0]$

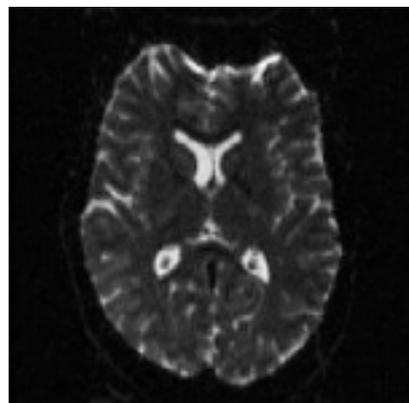
topup “guesses” a field...



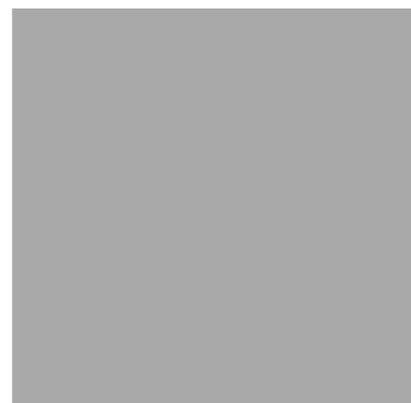
# How topup works (very briefly)



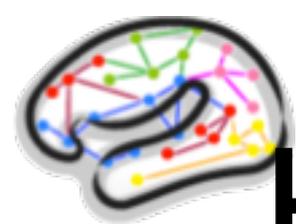
$p=[0 \ 1 \ 0]$



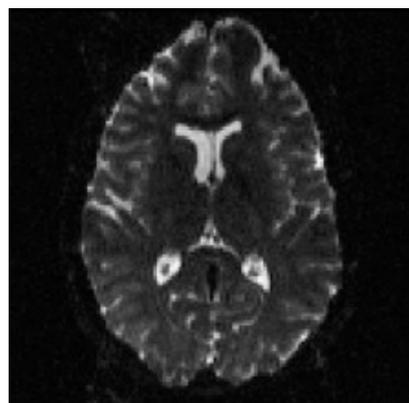
$p=[0 \ -1 \ 0]$



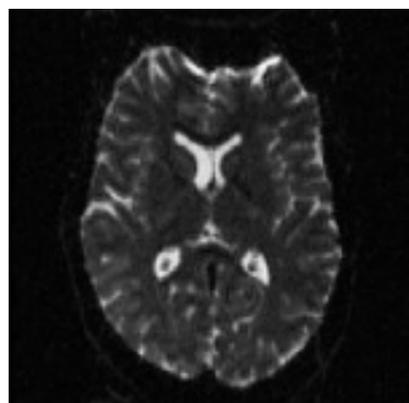
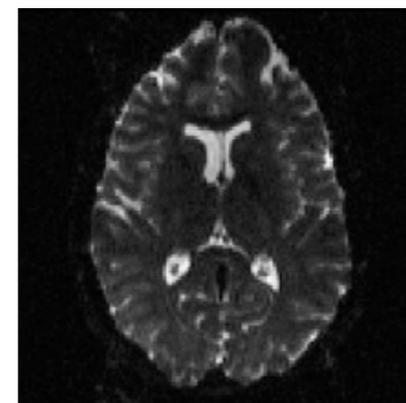
...calculates the displacement maps...



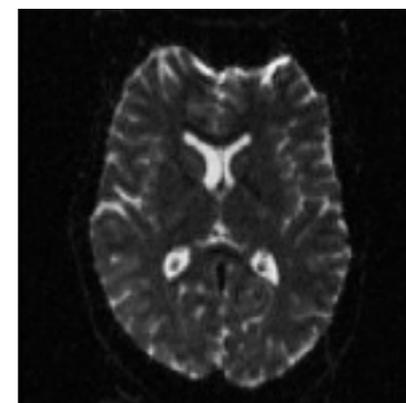
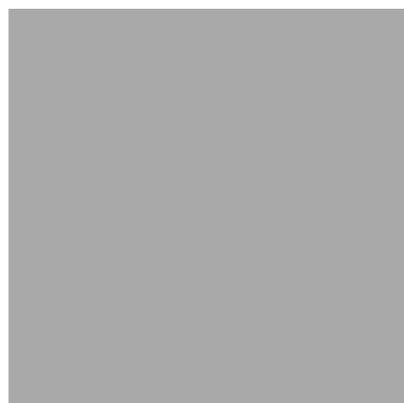
# How topup works (very briefly)



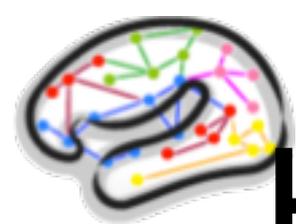
$p=[0 \ 1 \ 0]$



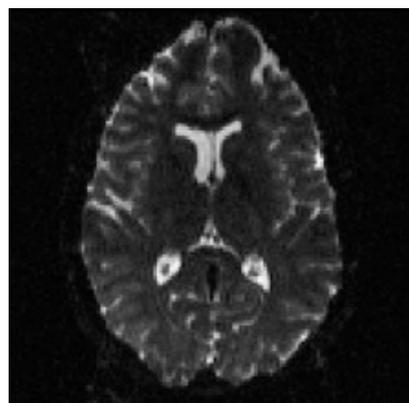
$p=[0 \ -1 \ 0]$



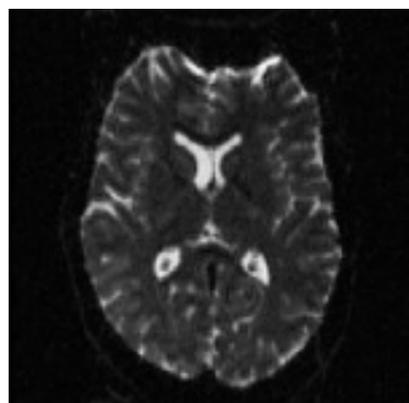
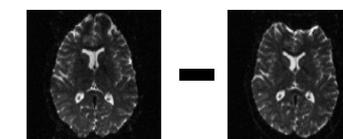
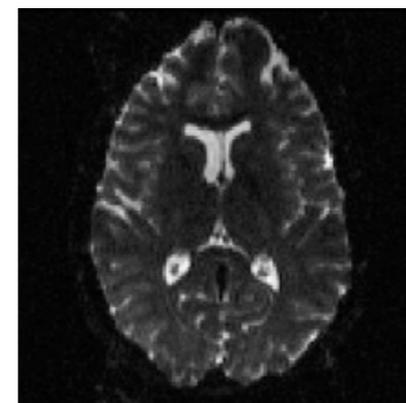
...”corrects” the images...



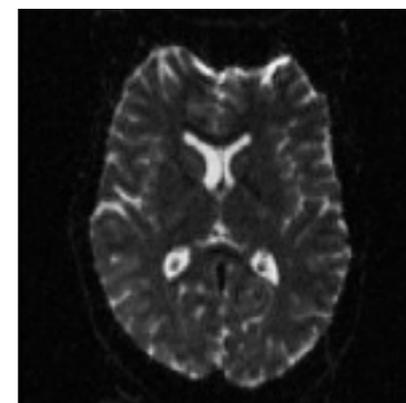
# How topup works (very briefly)



$p=[0 \ 1 \ 0]$



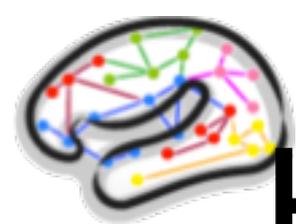
$p=[0 \ -1 \ 0]$



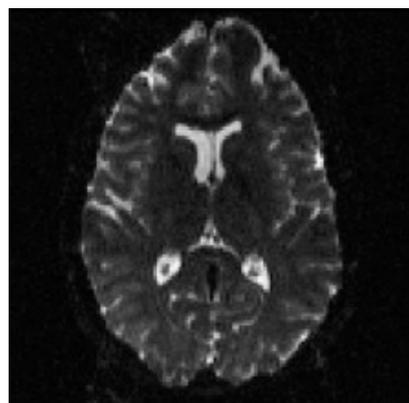
**BAD!**

...and evaluates the results...

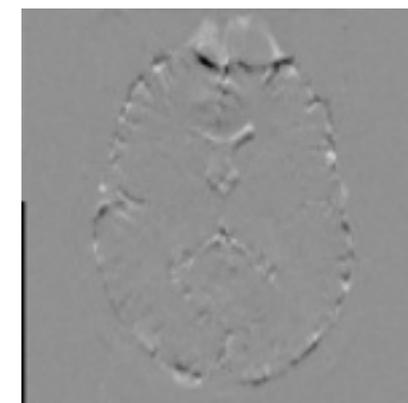
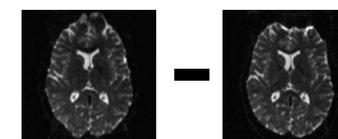
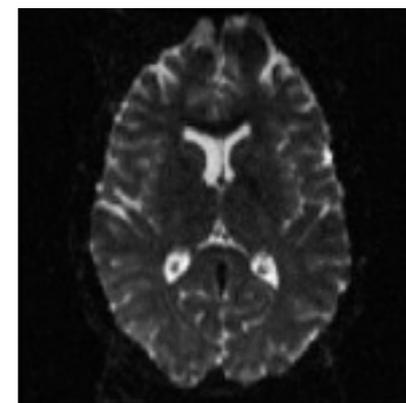
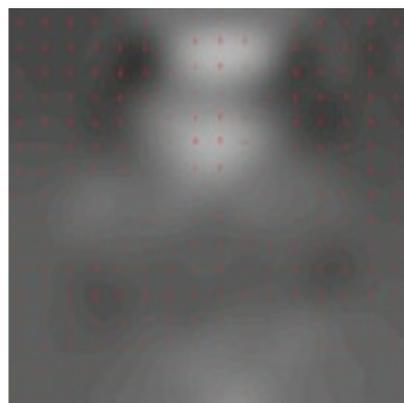
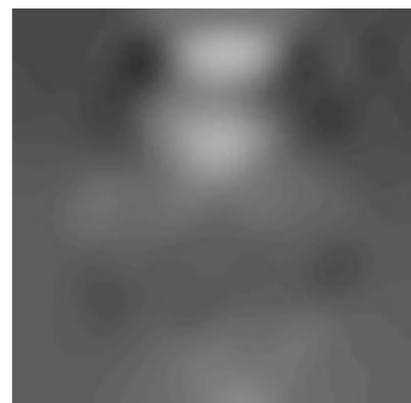
And **this** is the crucial bit.



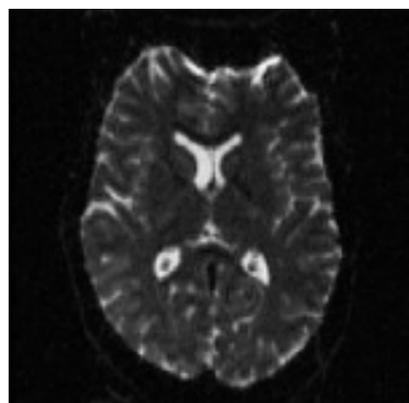
# How topup works (very briefly)



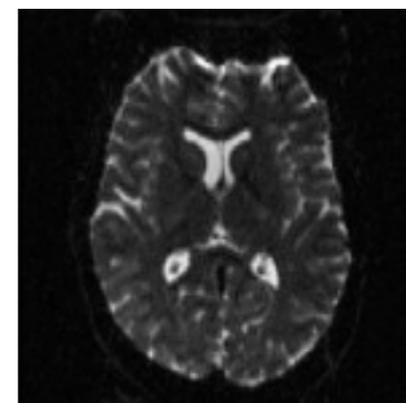
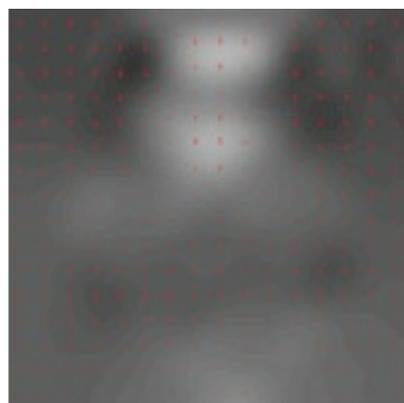
$p=[0 \ 1 \ 0]$



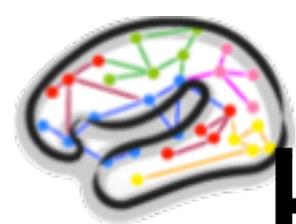
better



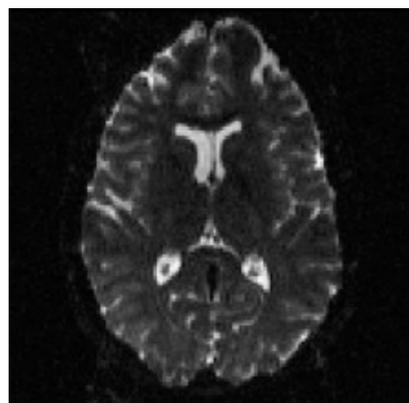
$p=[0 \ -1 \ 0]$



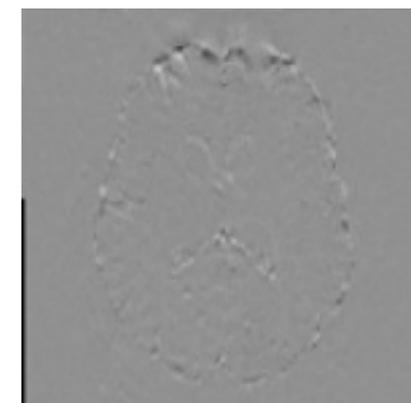
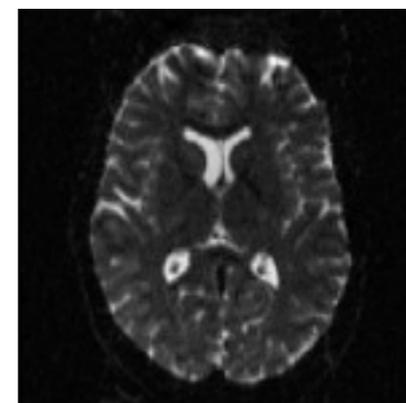
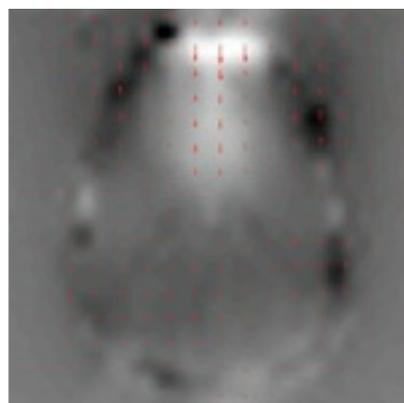
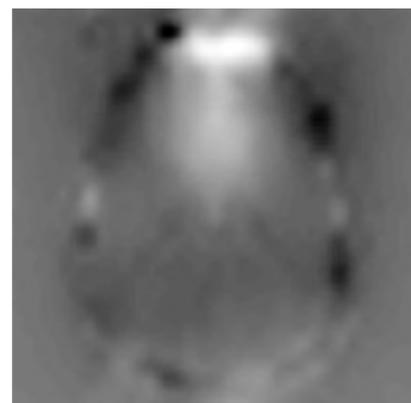
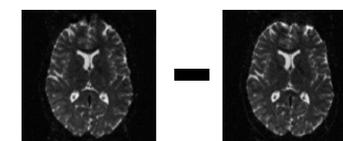
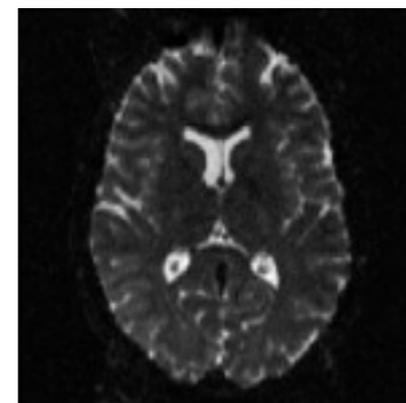
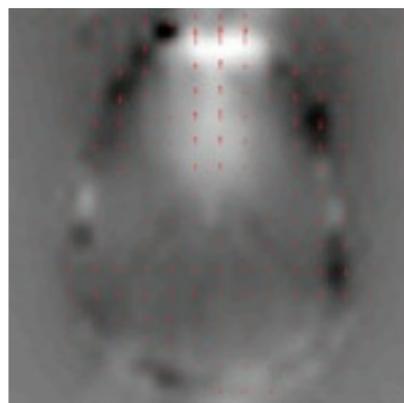
Because topup can then “guess”  
another field



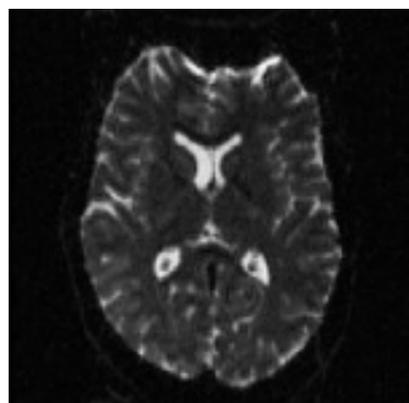
# How topup works (very briefly)



$p=[0 \ 1 \ 0]$

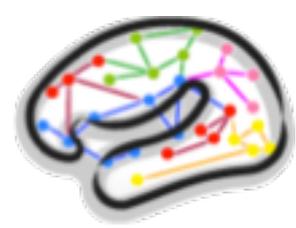


even  
better



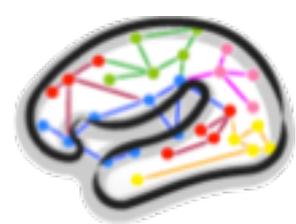
$p=[0 \ -1 \ 0]$

...and another...until it is happy,  
and then it “knows” the field

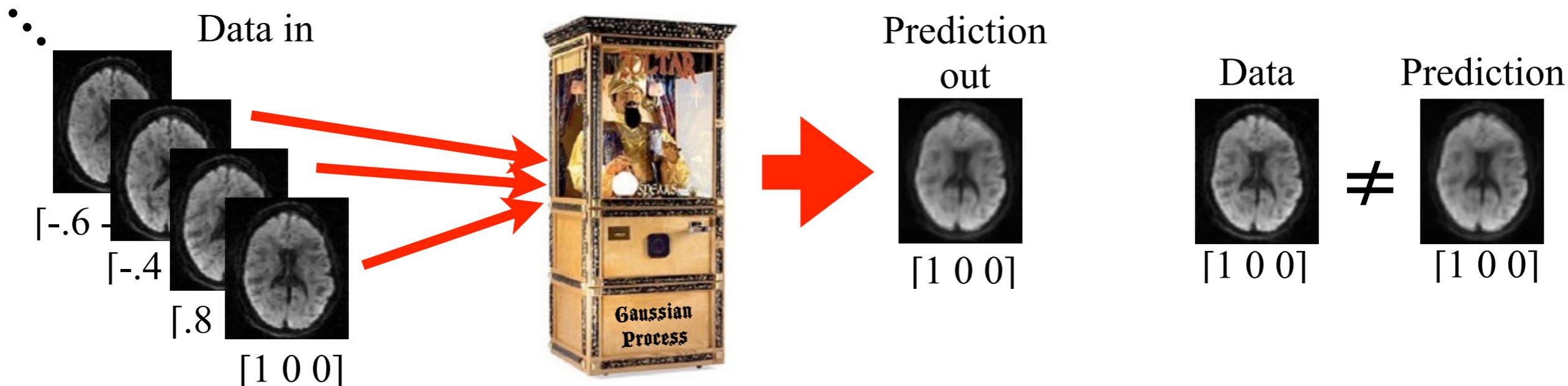


# Outline of the talk

- What is the problem with diffusion data?
- Off-resonance field  $\leftrightarrow$  Distortions
- Where does the off-resonance field come from?
- Worlds shortest course on image registration
- How topup works
- How eddy works
- Outliers
- Practicalities
- Output



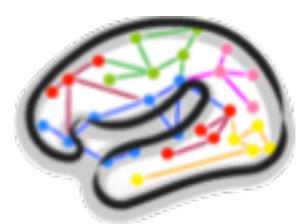
# Zoltar -- The prediction maker



Given some data in, Zoltar will make a prediction what the data “should” be.

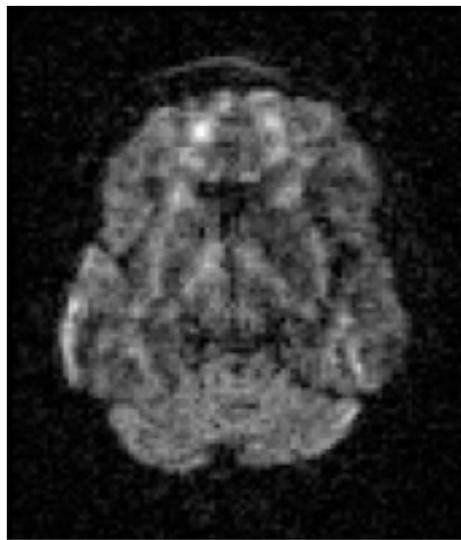
The prediction for a given dwi will not be identical to the “input” for that dwi

I know this sounds crazy, but please trust me on this.  
(Zoltar is actually a Gaussian Process)



# How eddy works: Loading step

Pick the first dwi

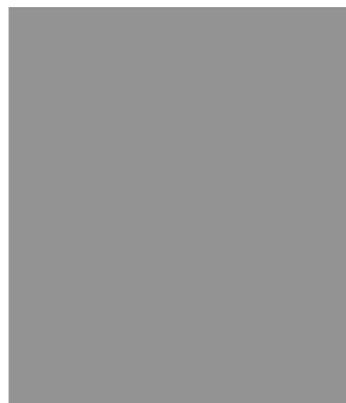


Use current estimates of

Susc



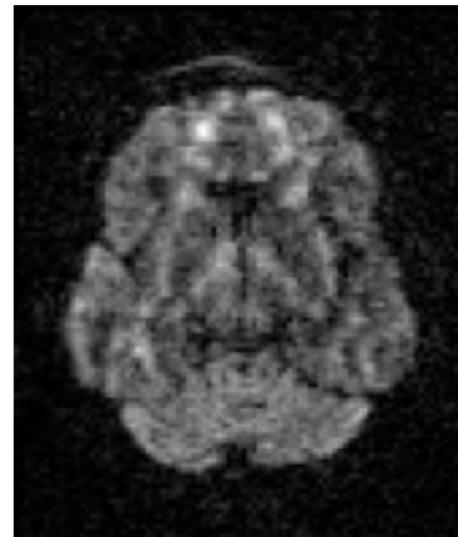
EC



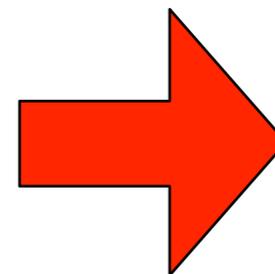
MP

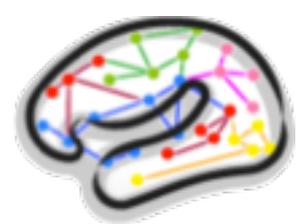
$$\begin{bmatrix} 0 \\ 0 \\ \vdots \\ 0 \end{bmatrix}$$

To correct image



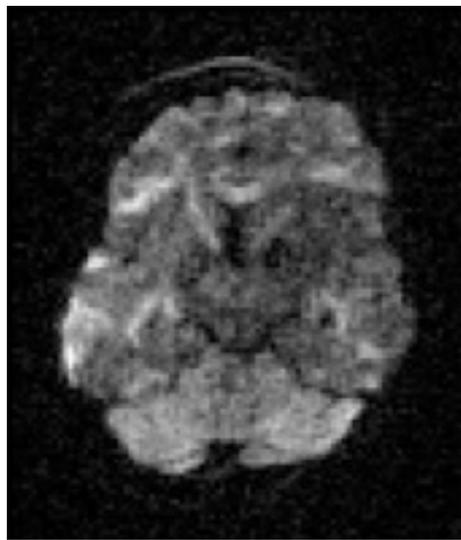
And load into prediction maker





# How eddy works: Loading step

then the 2nd dwi

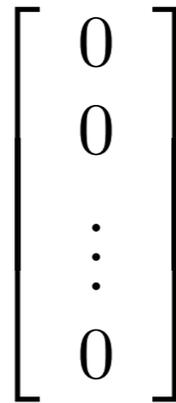


Use current estimates of

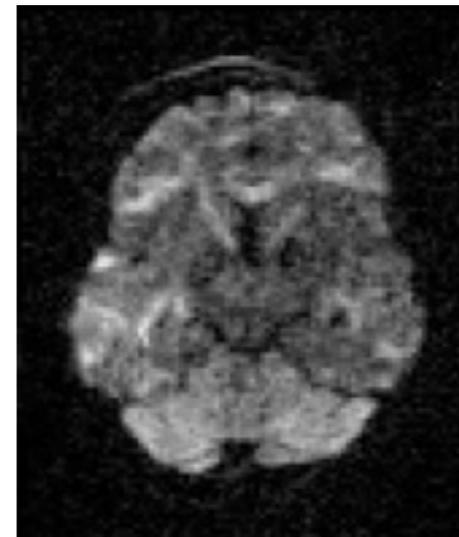
Susc

EC

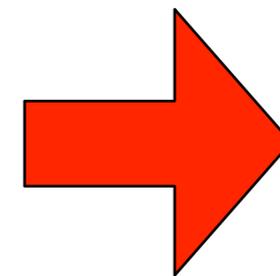
MP



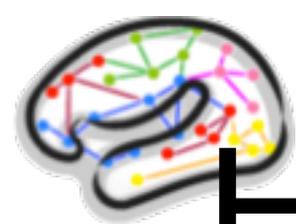
To correct  
2nd image



And load into  
prediction  
maker

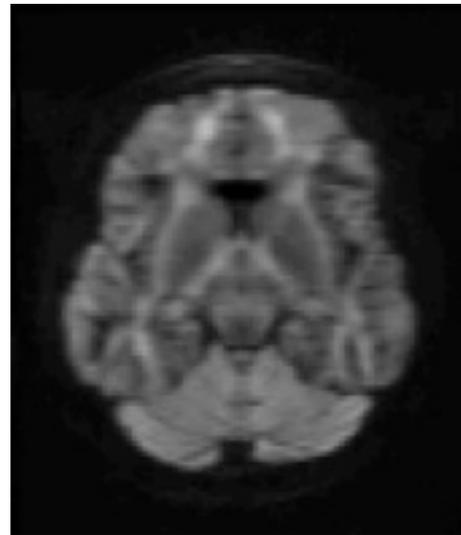
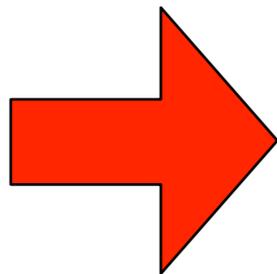


Until we have  
loaded all dwis

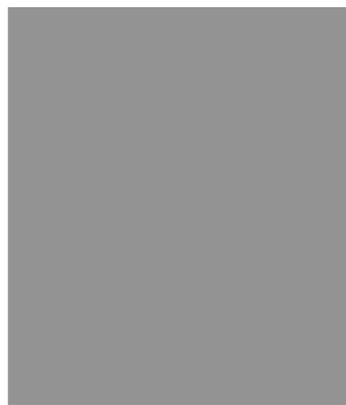


# How eddy works: Estimation step

Draw a prediction  
for first dwi

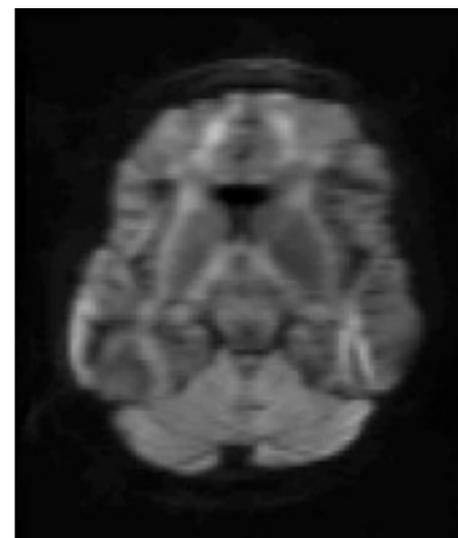


Use current estimates of  
SusC                      EC                      MP

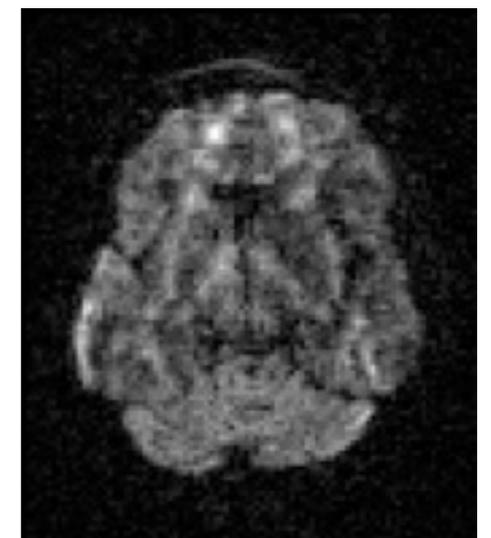


$$\begin{bmatrix} 0 \\ 0 \\ \vdots \\ 0 \end{bmatrix}$$

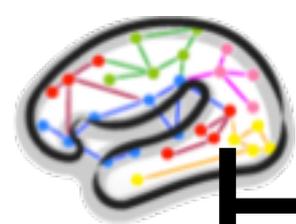
Invert



To get  
prediction in  
“observation  
space”

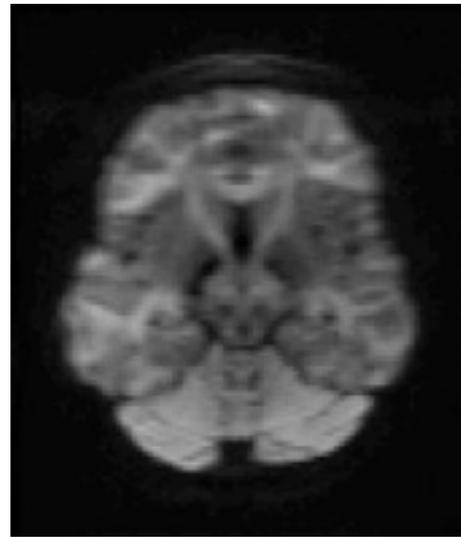
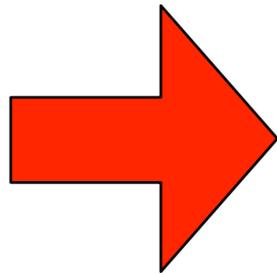


And compare  
to actual  
observation

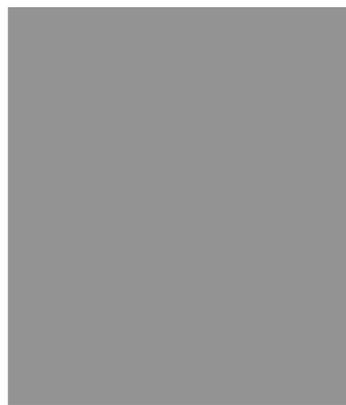


# How eddy works: Estimation step

Draw a prediction  
for 2nd dwi

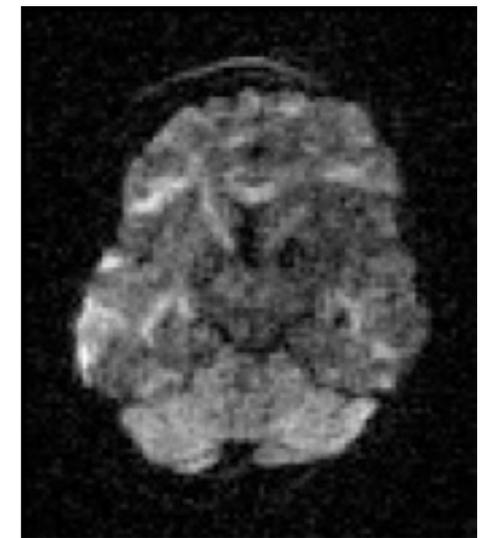
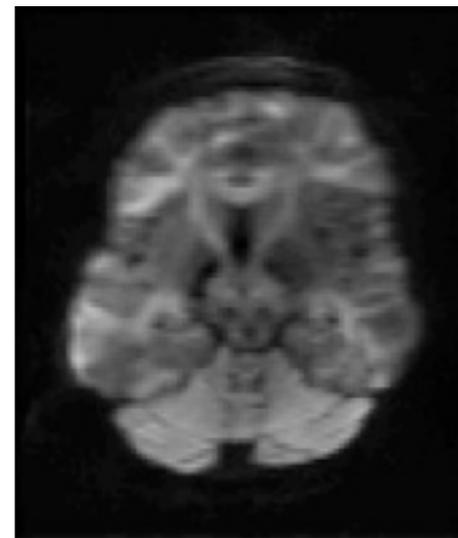


Use current estimates of  
SusC      EC      MP

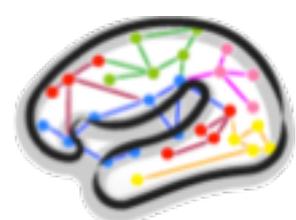


$$\begin{bmatrix} 0 \\ 0 \\ \vdots \\ 0 \end{bmatrix}$$

Invert



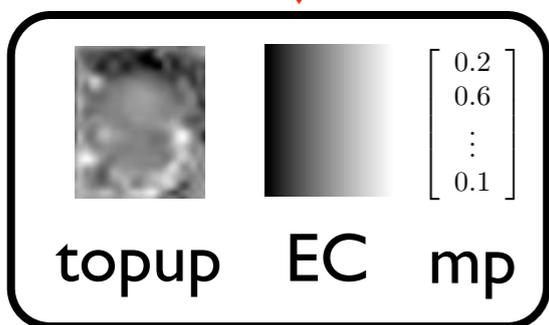
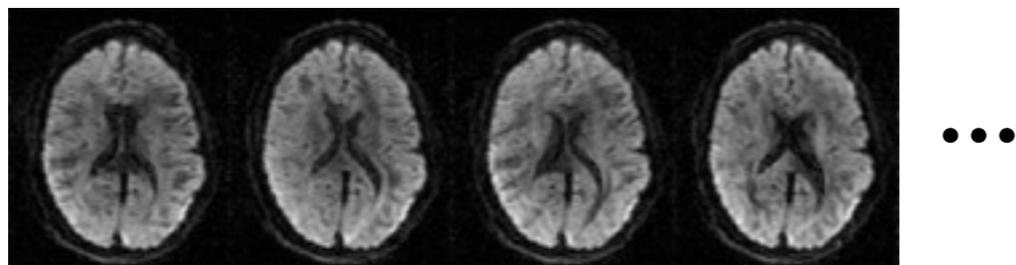
And then we repeat  
the procedure for the  
next dwi ...



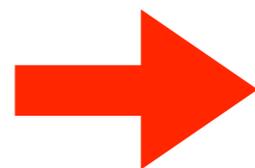
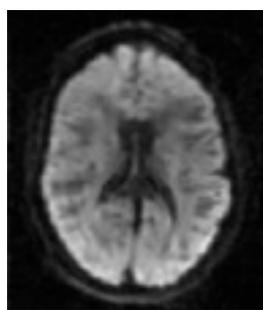
# How eddy works

1. For all scans

$[1\ 0\ 0]$   $[.6\ -.4\ -.7]$   $[.8\ .6\ 0]$   $[-.4\ .9\ 0]$  ...

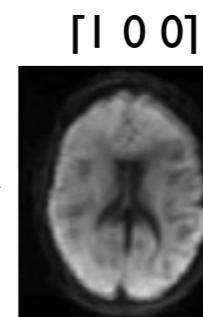
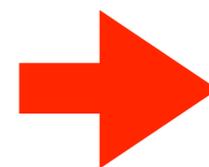


Use susceptibility field and current estimate of EC and movement to “unwarp” scan

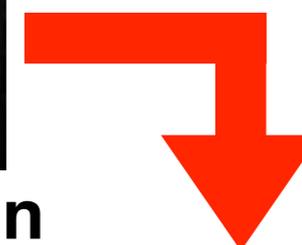


Load into prediction maker

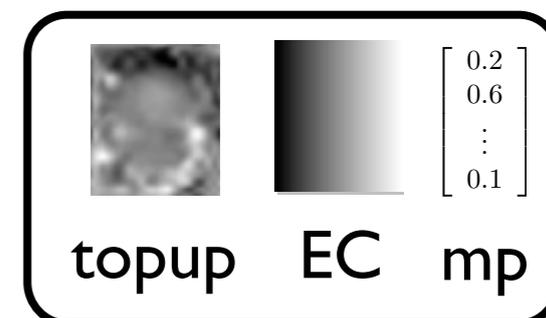
2. For all scans



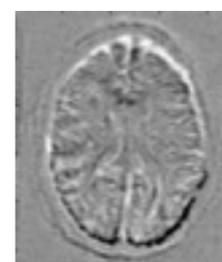
Get prediction



Invert current transform



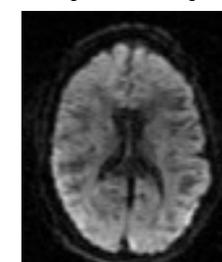
Use difference to update EC and mp



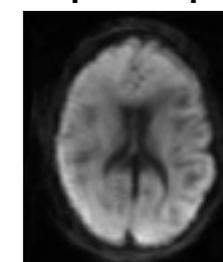
Get prediction in scan space



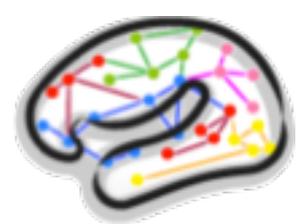
$[1\ 0\ 0]$



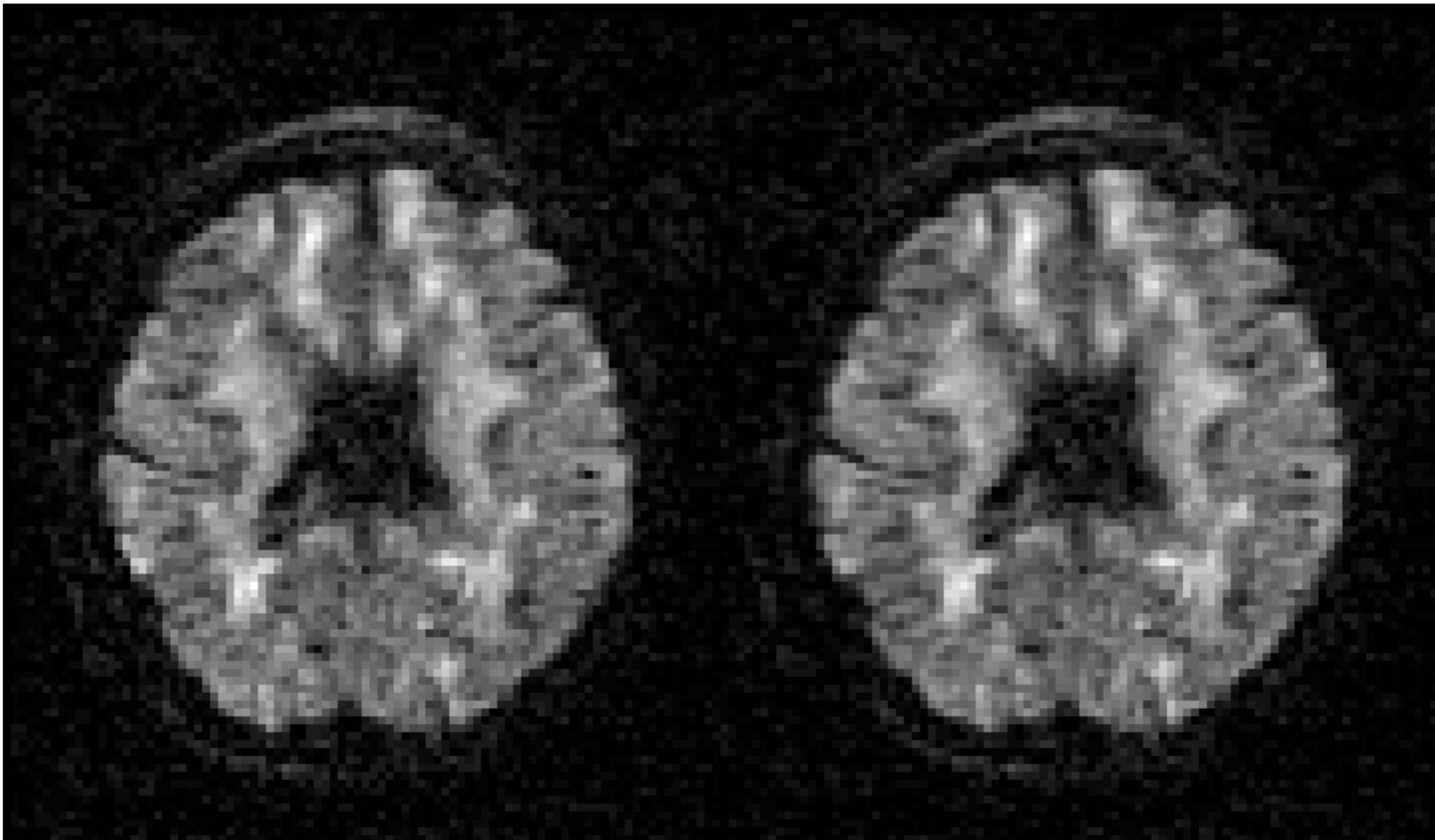
$[1\ 0\ 0]$

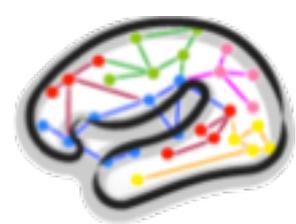


Compare to scan

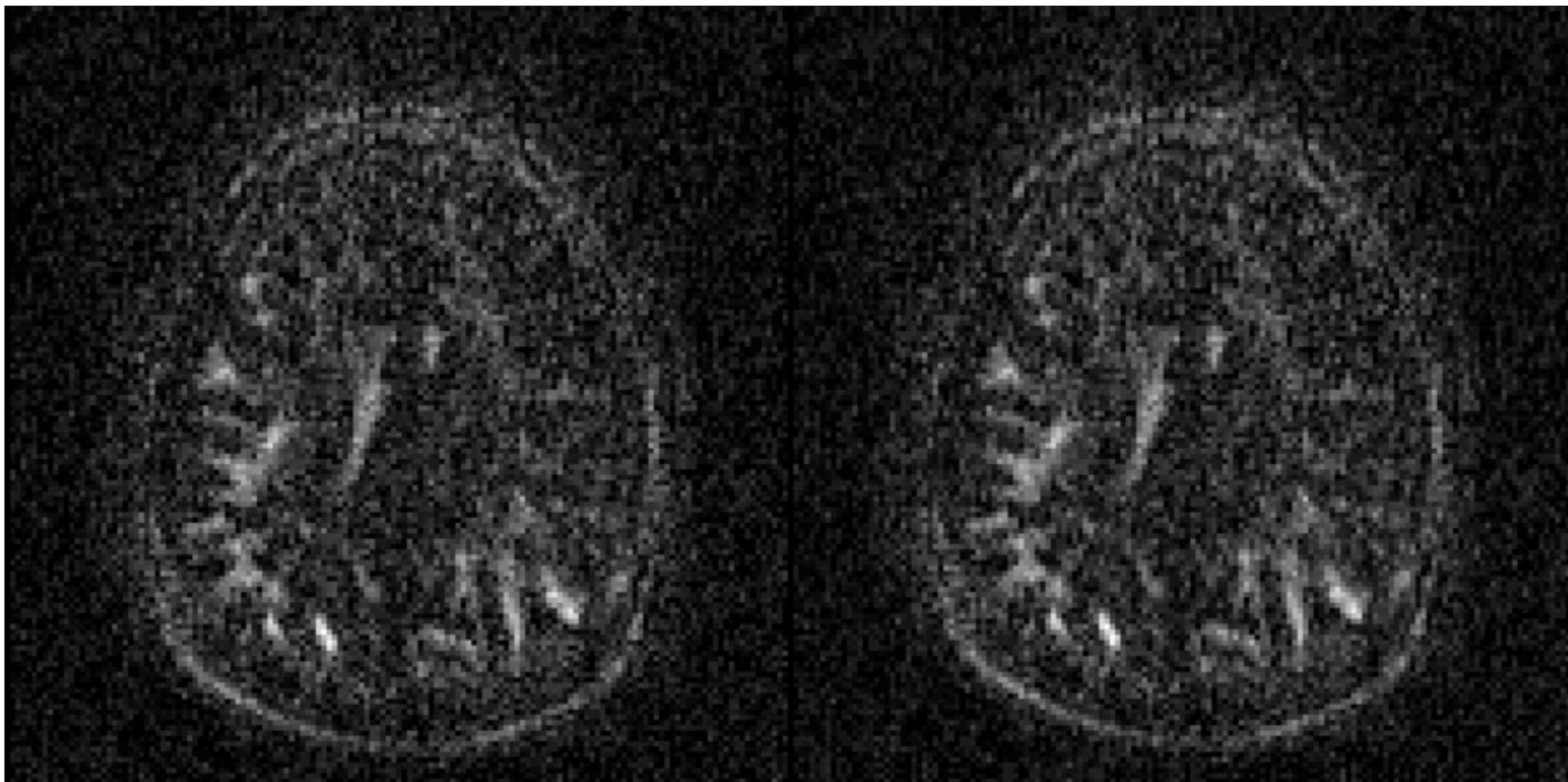


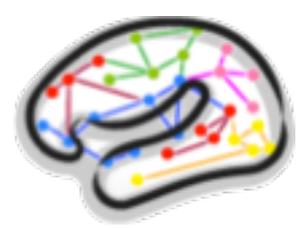
HCP-data, 150 directions,  
 $b=3000$ , blip-left-blip-right



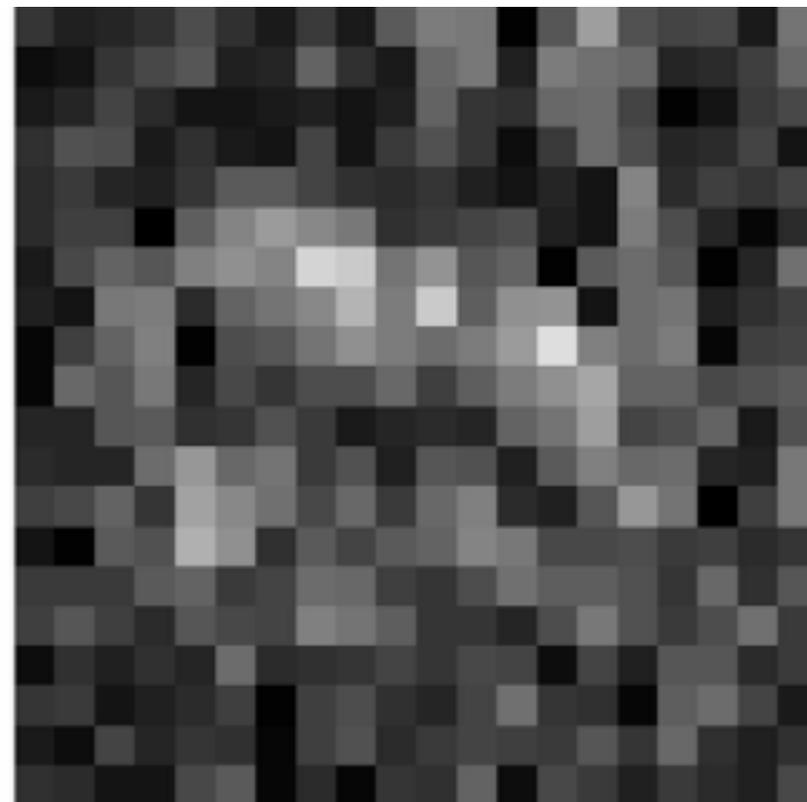
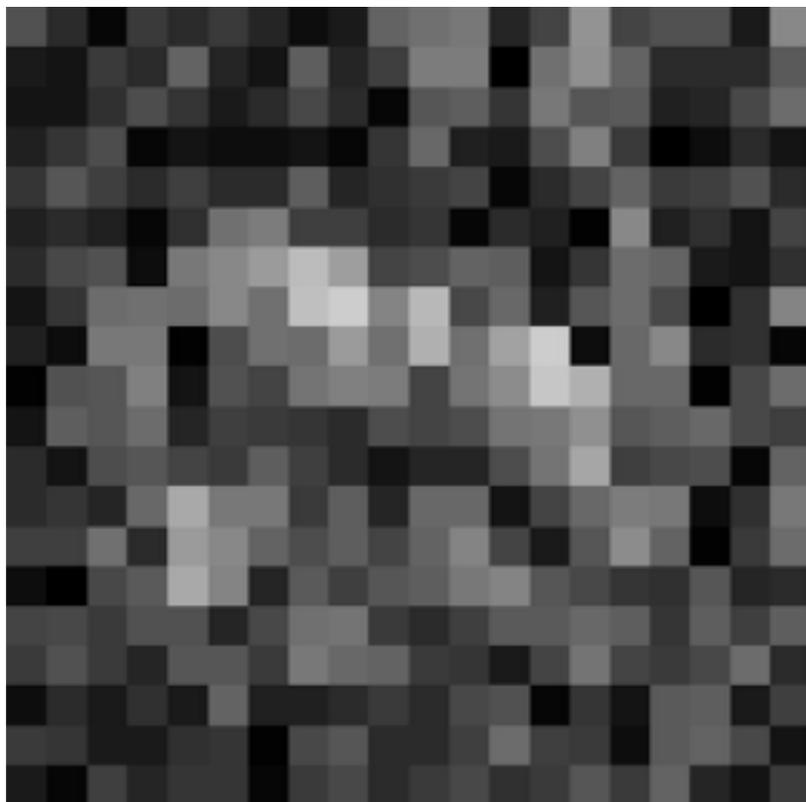
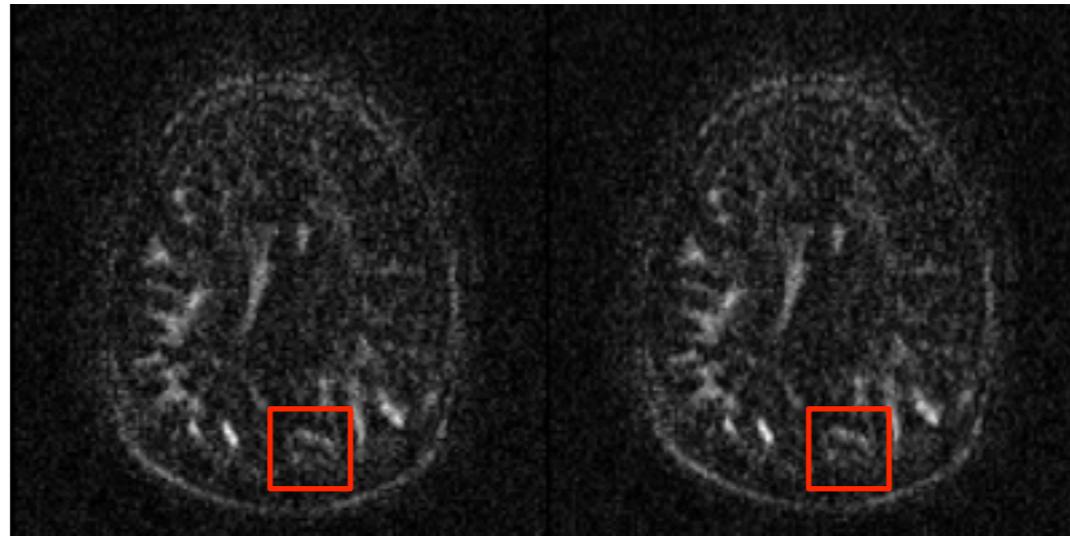


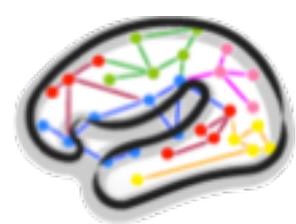
MGH-data, 198 directions,  
 $b=10000!$





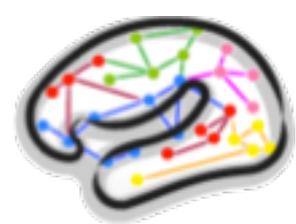
MGH-data, 198 directions,  
 $b=10000!$





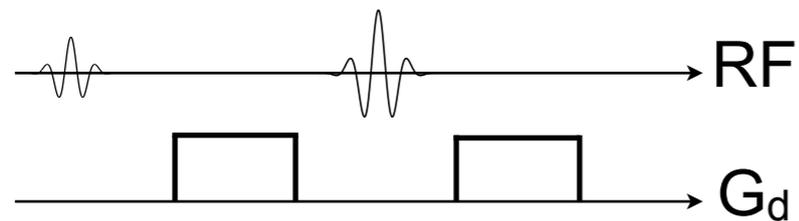
# Outline of the talk

- What is the problem with diffusion data?
- Off-resonance field  $\leftrightarrow$  Distortions
- Where does the off-resonance field come from?
- Worlds shortest course on image registration
- How topup works
- How eddy works
- **Outliers**
- Practicalities
- Output

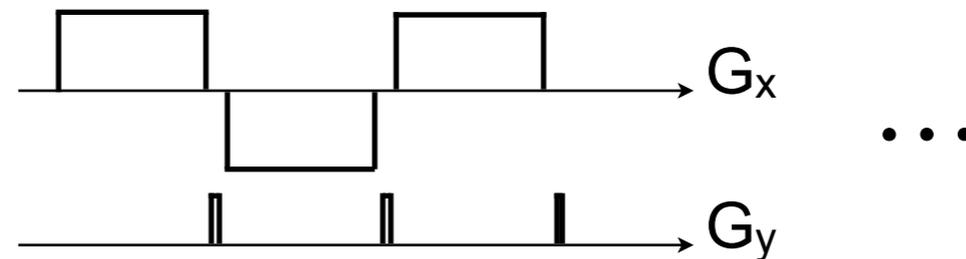


# Movement induced dropout

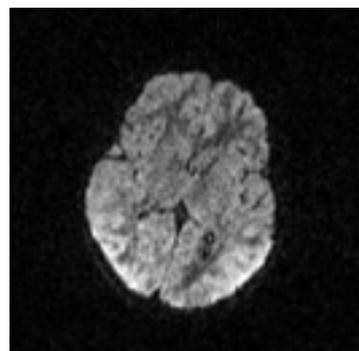
## Diffusion encoding



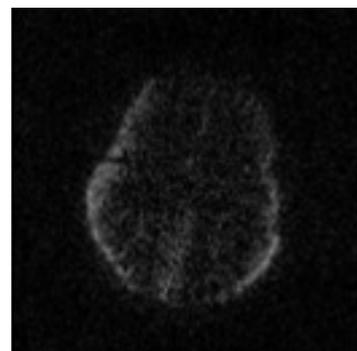
## Image encoding



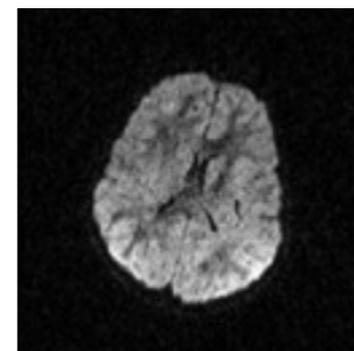
If there is movement during this part...



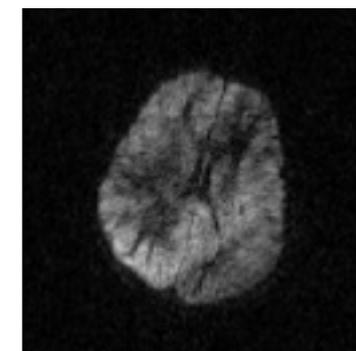
this



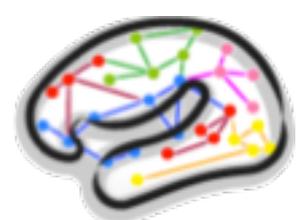
can turn  
to this



or this

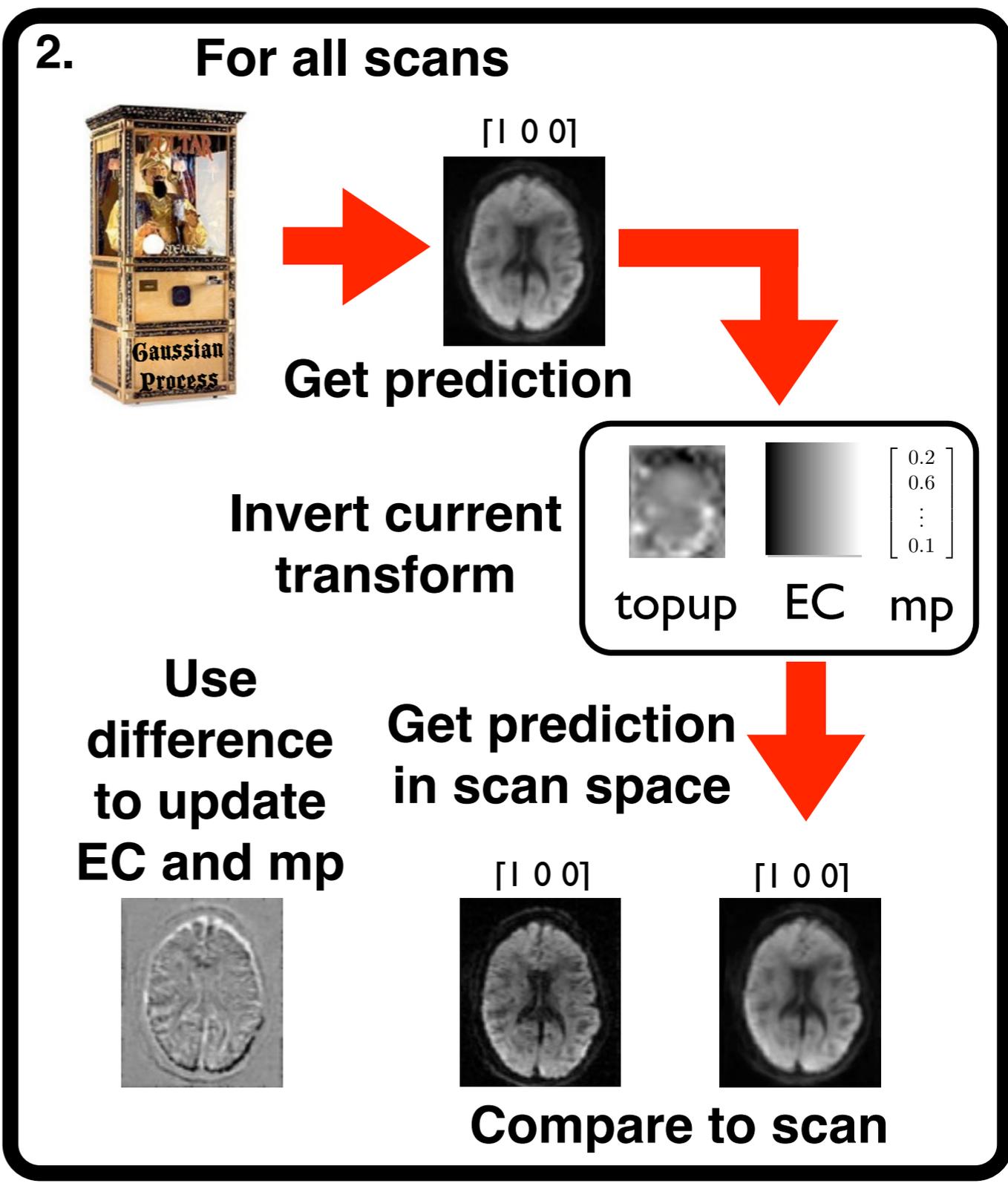
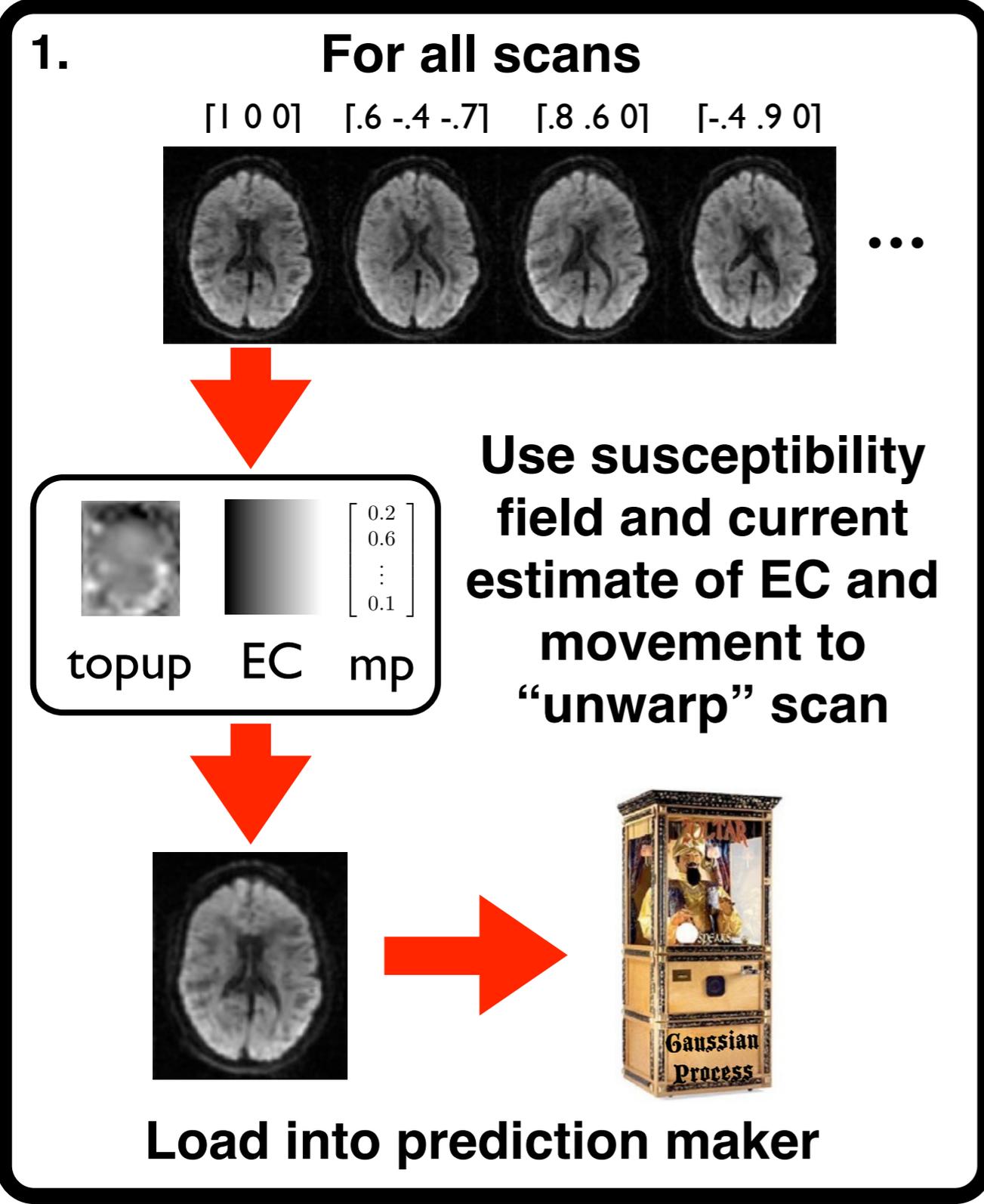


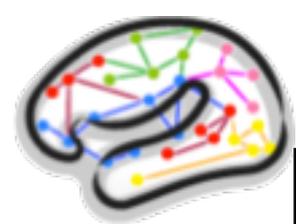
to this



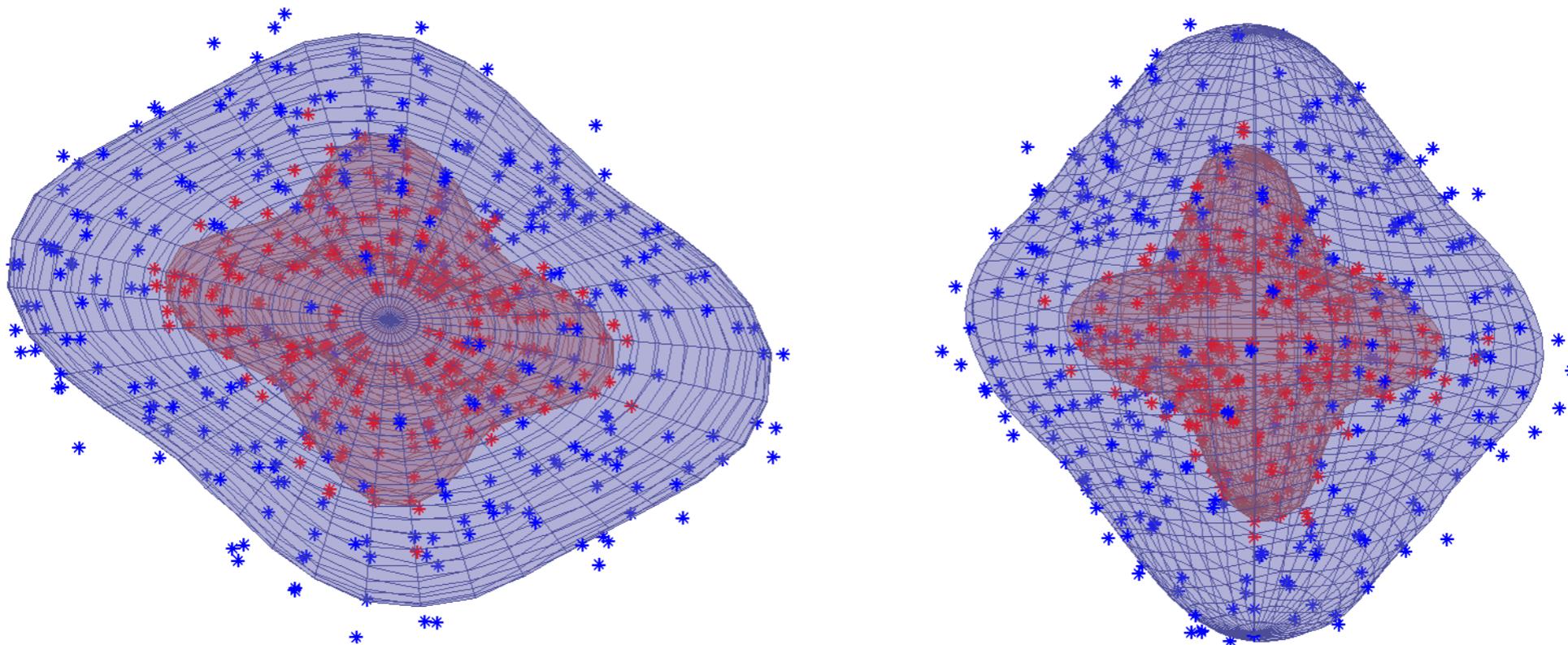
# What can eddy do about it?

## But first a little recap of eddy



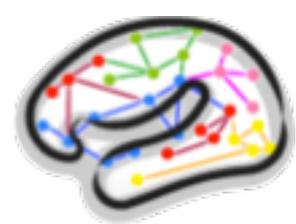


# How are the predictions made?



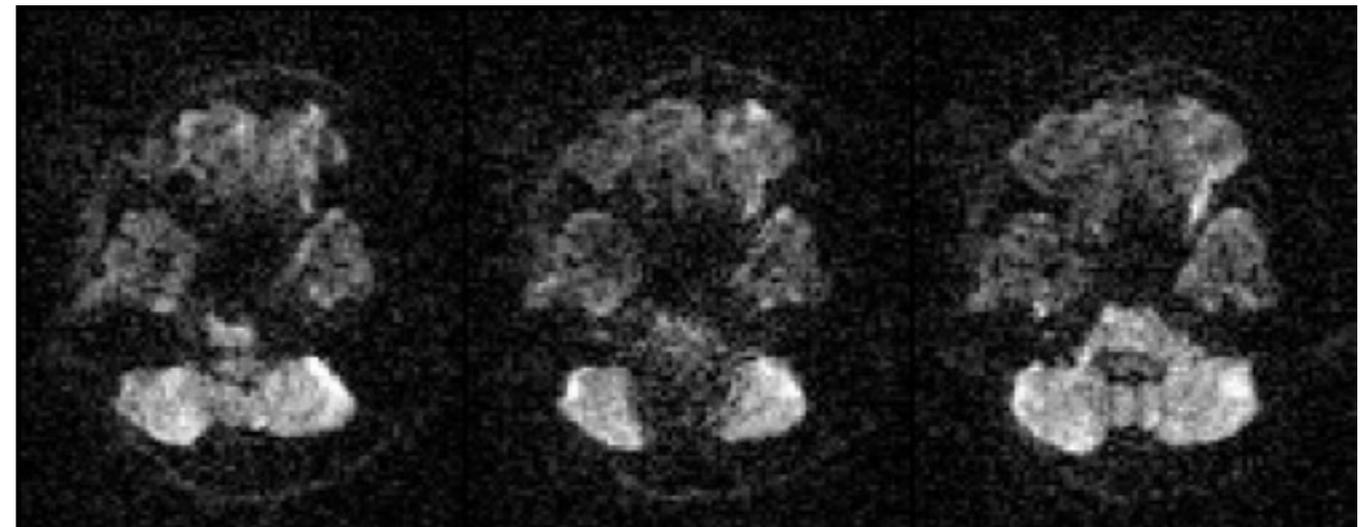
A Gaussian process that simply assumes that the signal varies smoothly as we move in Q-space  
Very few assumptions. Hyperparameters calculated by leave-one-out.

$$\hat{y}_{\mathbf{g}} = K(\mathbf{g}, \mathbf{G}) [K(\mathbf{G}, \mathbf{G}) + \sigma^2 \mathbf{I}]^{-1} \mathbf{y}$$

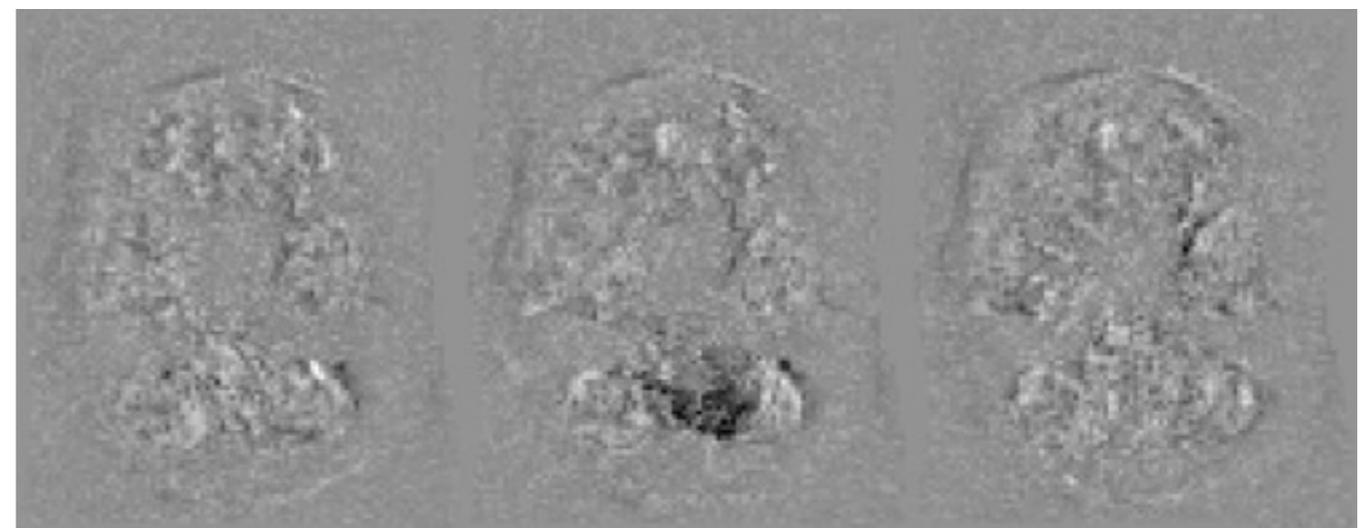


# Outlier detection

Observed data



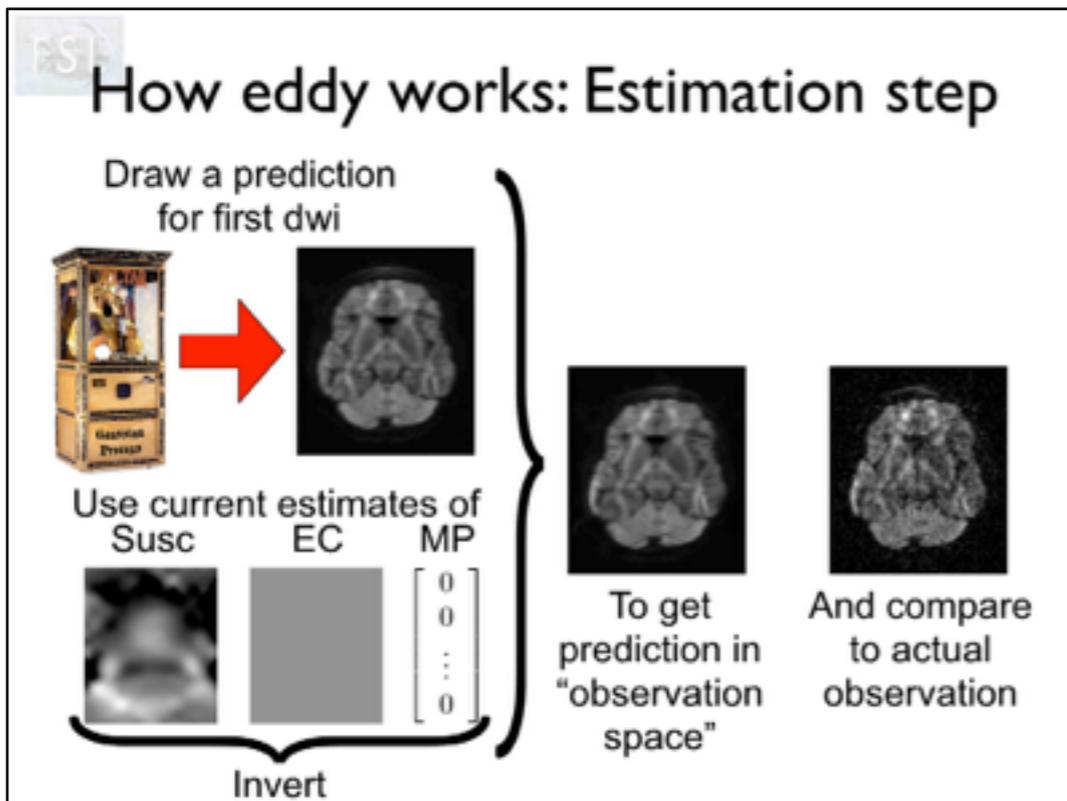
Observed - predicted



$$\bar{x} = 0.084$$

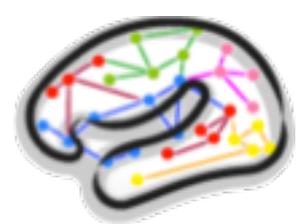
$$\bar{x} = -0.791$$

$$\bar{x} = -0.125$$

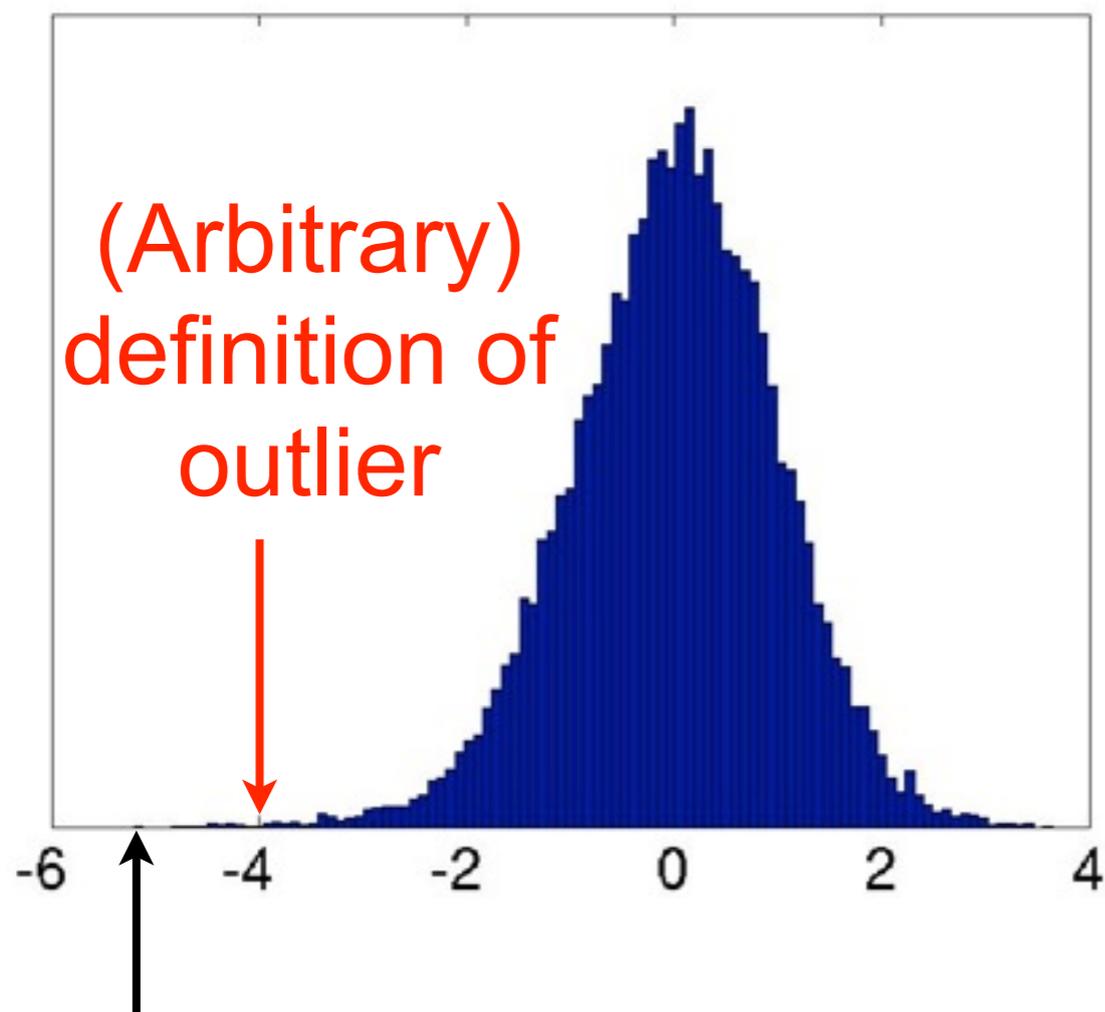


Remember that we do all comparisons in observation space.

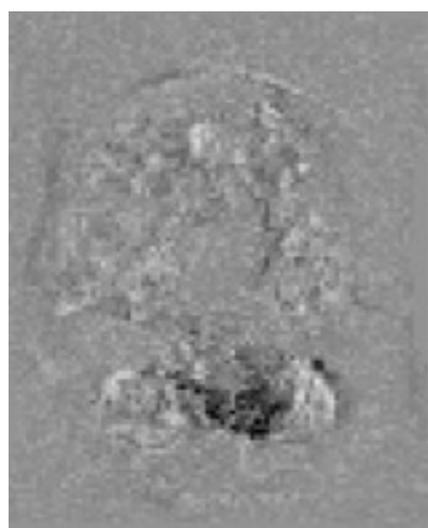
This allows us to calculate the per-slice mean difference between observation and prediction



# Outlier detection

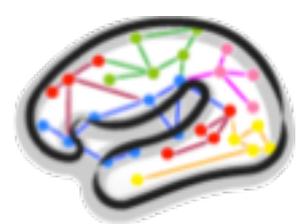


We can calculate the mean difference for every slice in every volume and get an empirical distribution that we can convert to z-scores



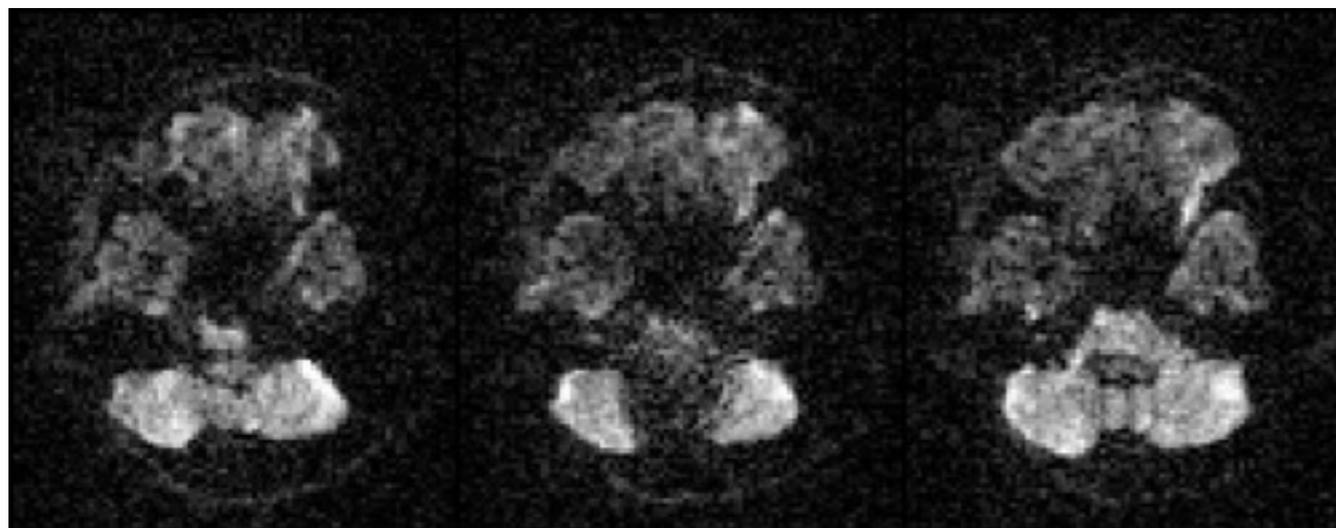
We can define an outlier slice as one with a z-score above an (arbitrary) threshold. We then have a choice of reporting outliers and/or replacing them with their predictions.

Worst slice

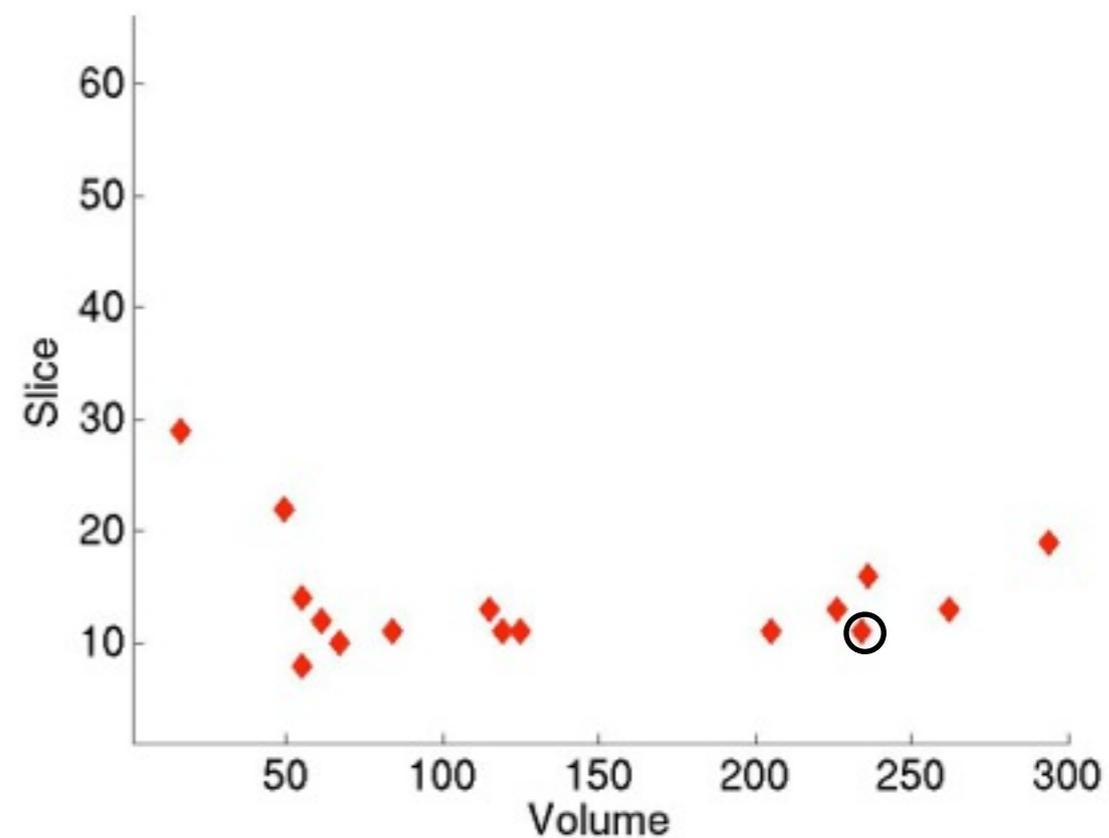
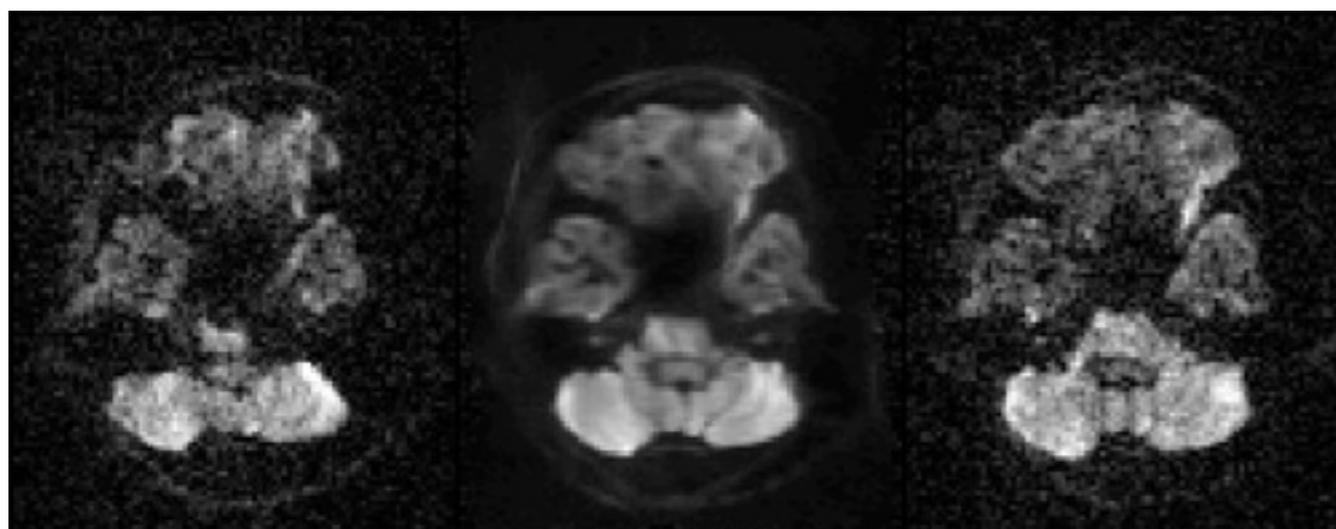


# Outlier detection

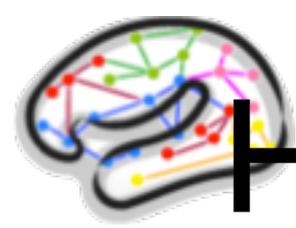
Original data



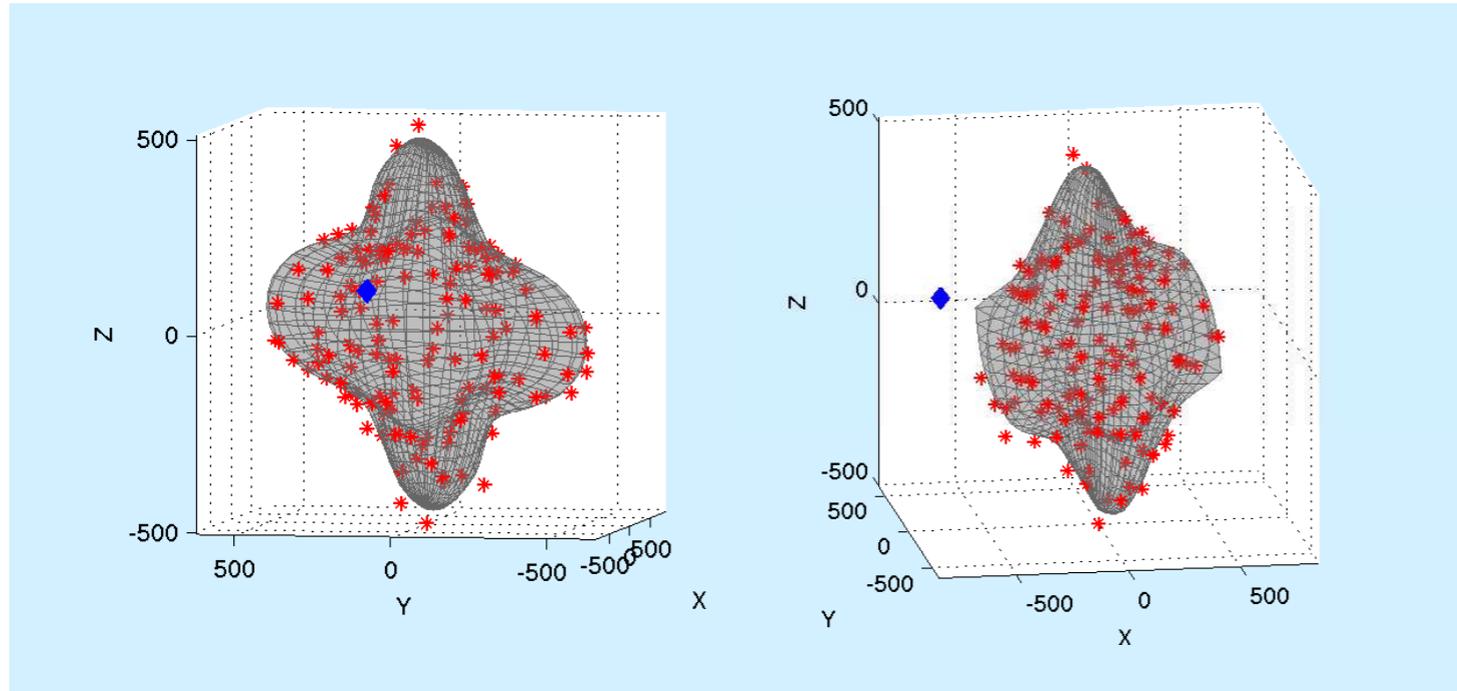
Data after replacement



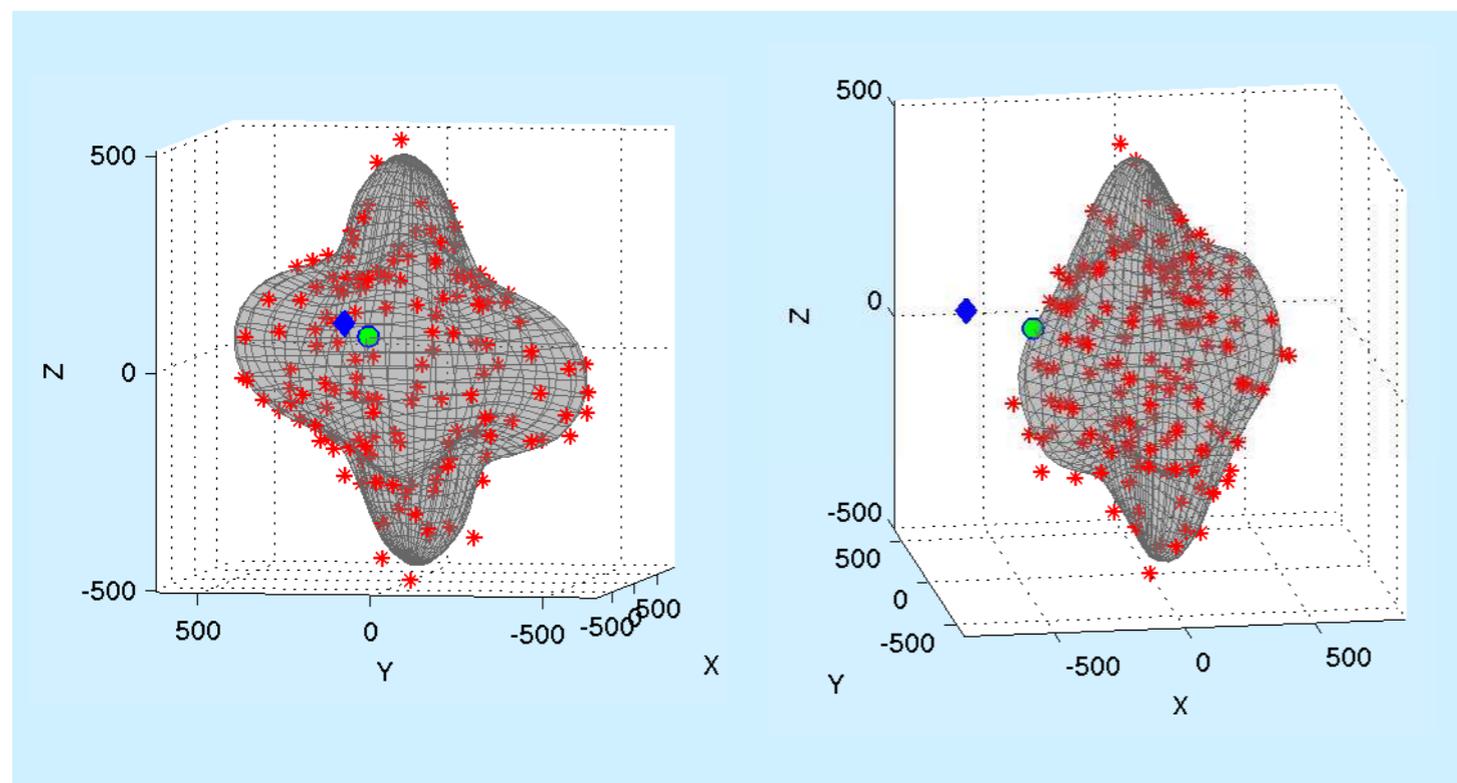
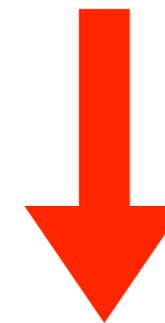
Outliers for a very still volunteer. Outliers mainly in basal slices.



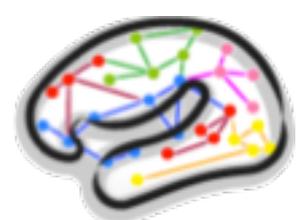
# How to make the “right” prediction



The outlier skews the predictions, but is still recognisable as an outlier



Remove the outlier and recalculate the “model”. The prediction is taken from this new “model”.

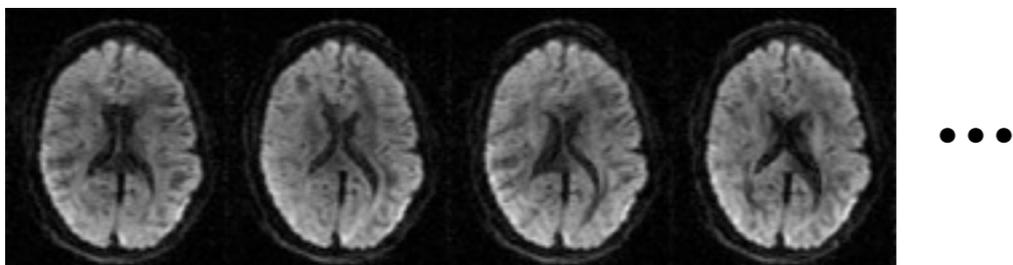


# eddy revisited

1.

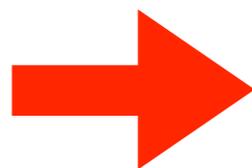
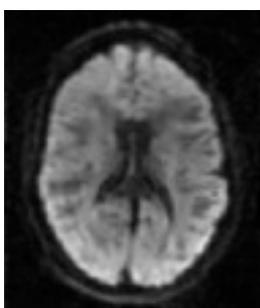
For all scans

$[1\ 0\ 0]$   $[.6\ -.4\ -.7]$   $[.8\ .6\ 0]$   $[-.4\ .9\ 0]$  ...



		$\begin{bmatrix} 0.2 \\ 0.6 \\ \vdots \\ 0.1 \end{bmatrix}$
topup	EC	mp

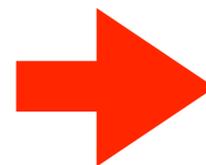
Use susceptibility field and current estimate of EC and movement to “unwarp” scan



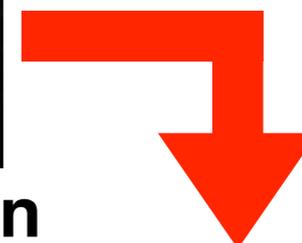
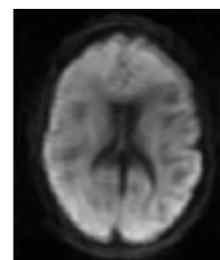
Load into prediction maker

2.

For all scans



$[1\ 0\ 0]$



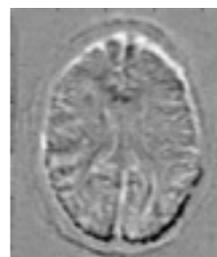
Get prediction

Invert current transform

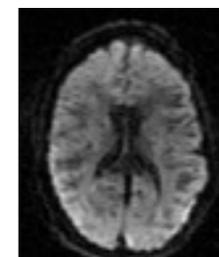
Use difference to update EC, mp and outlier list

		$\begin{bmatrix} 0.2 \\ 0.6 \\ \vdots \\ 0.1 \end{bmatrix}$
topup	EC	mp

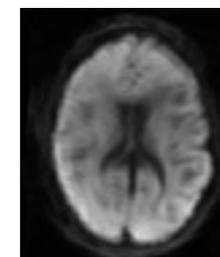
Get prediction in scan space



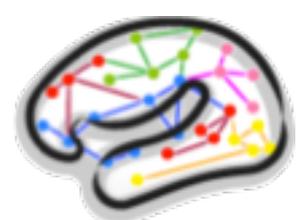
$[1\ 0\ 0]$



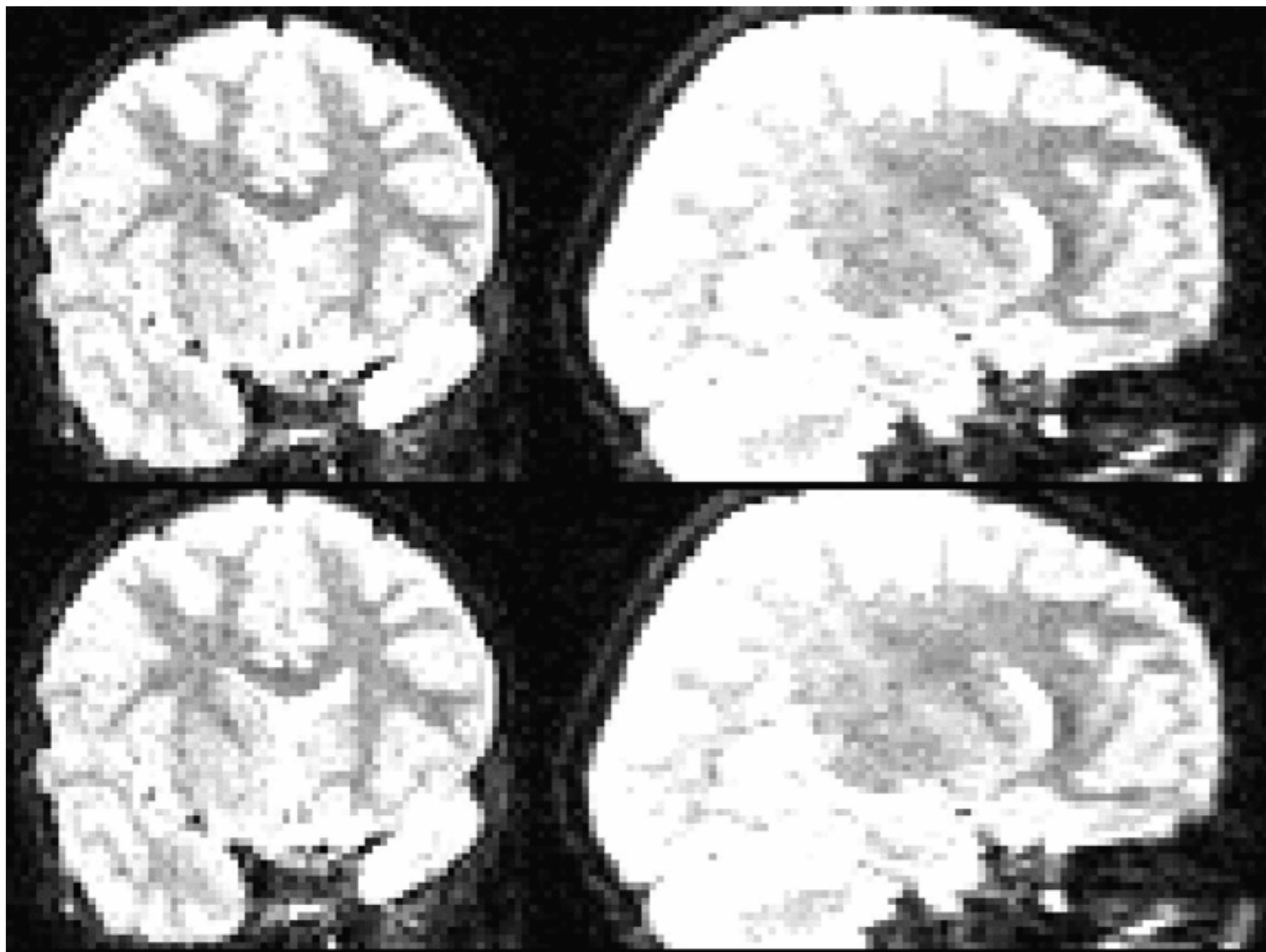
$[1\ 0\ 0]$



Compare to scan

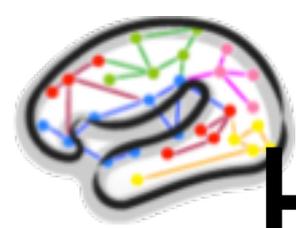


# Norwegian data. 32 directions. Hundreds of children.



Eight year  
old who gets  
tired towards  
the end of  
scanning

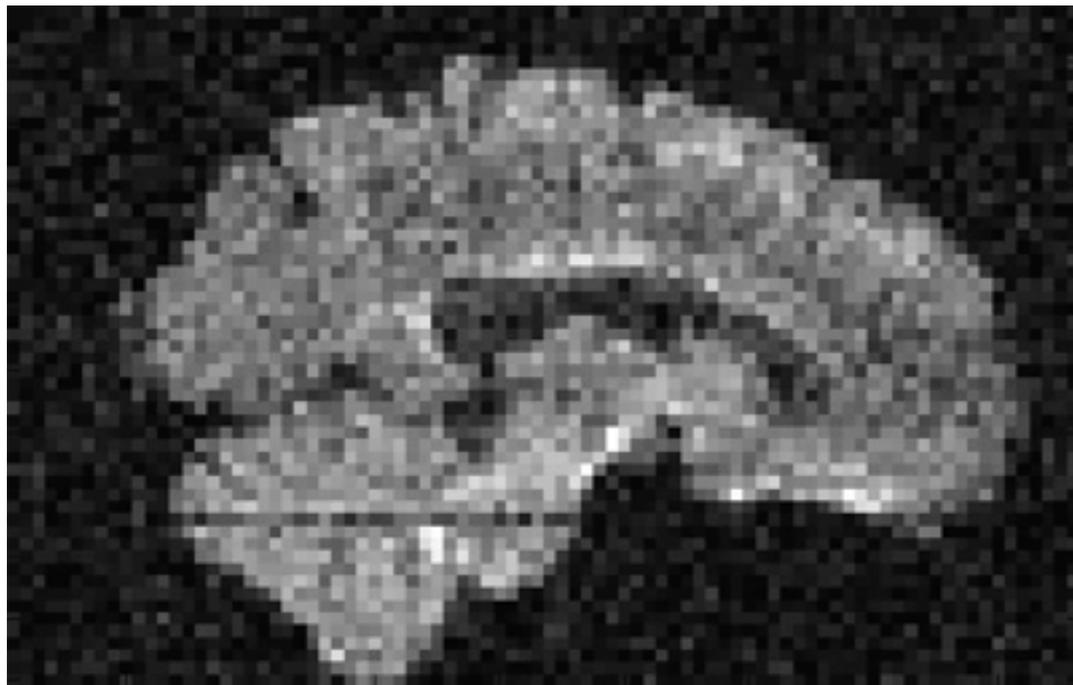
After outlier  
detection  
and  
replacement  
by eddy



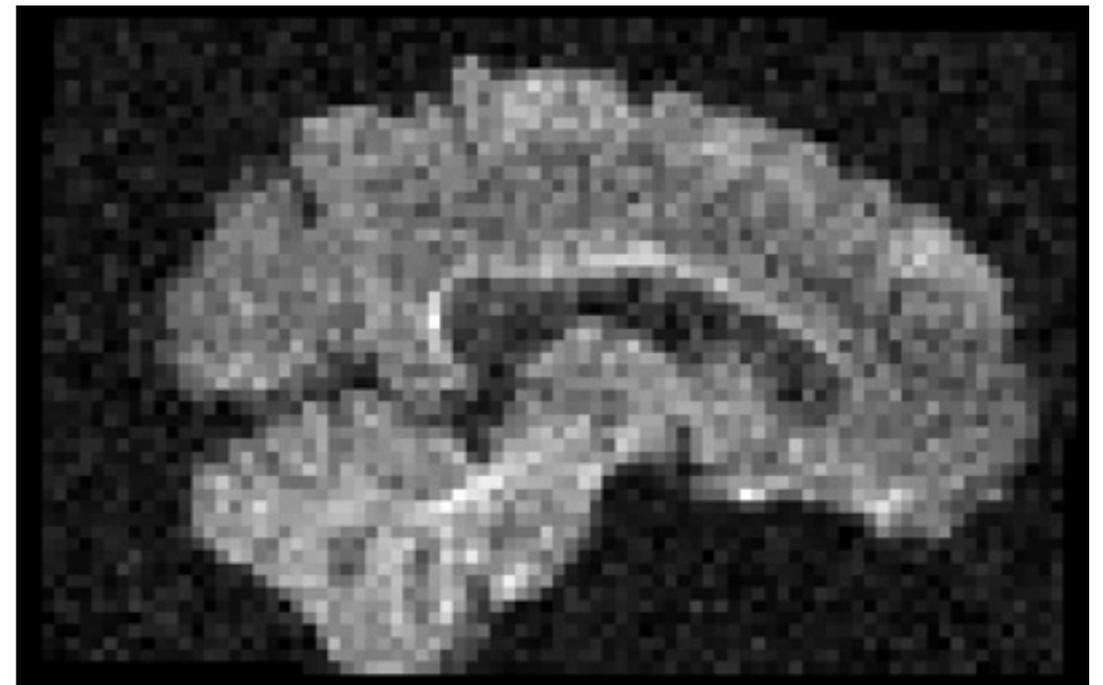
# How accurate are the predictions?

## Simulated data

Simulations courtesy of Mark Graham, UCL.

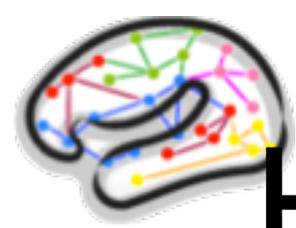


Before

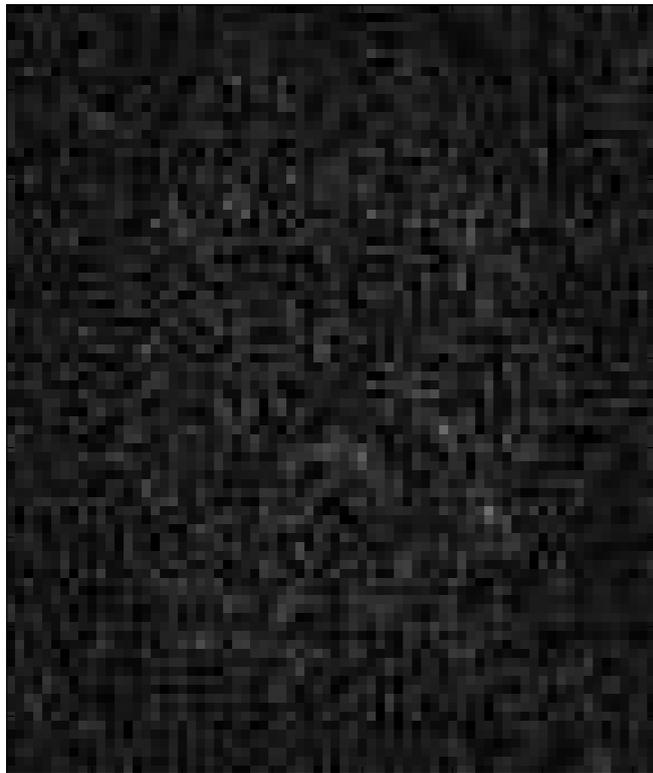


After

Looks good. But is it the “truth”?



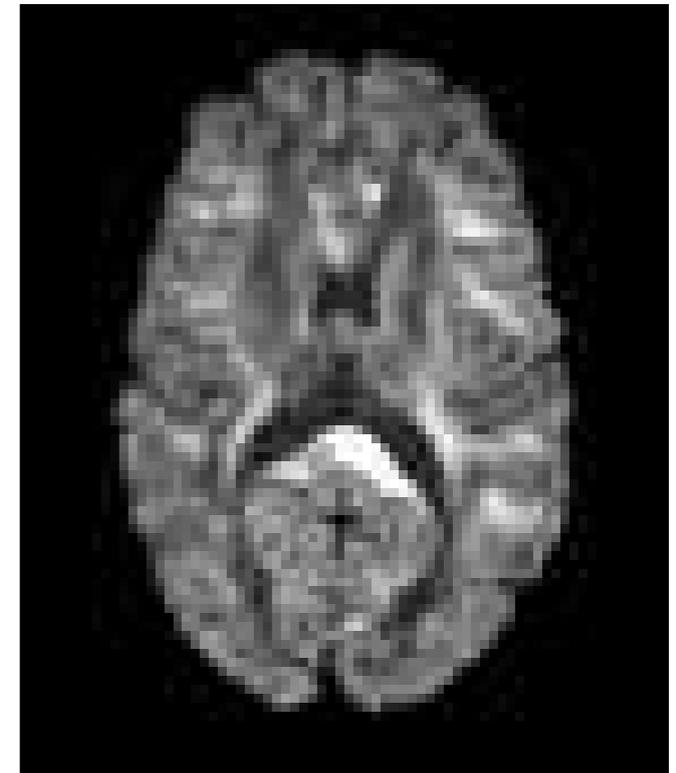
# How accurate are the predictions?



Outlier

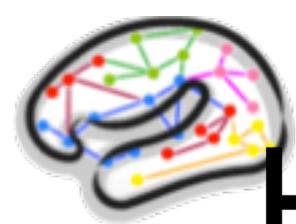


eddy's  
guesstimate

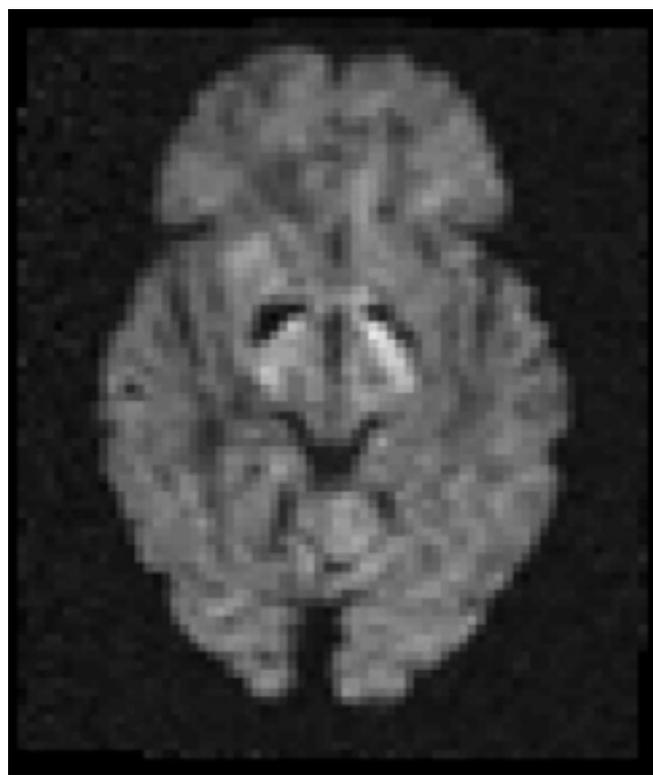


Ground  
truth

With the simulations we know the  
“ground truth”

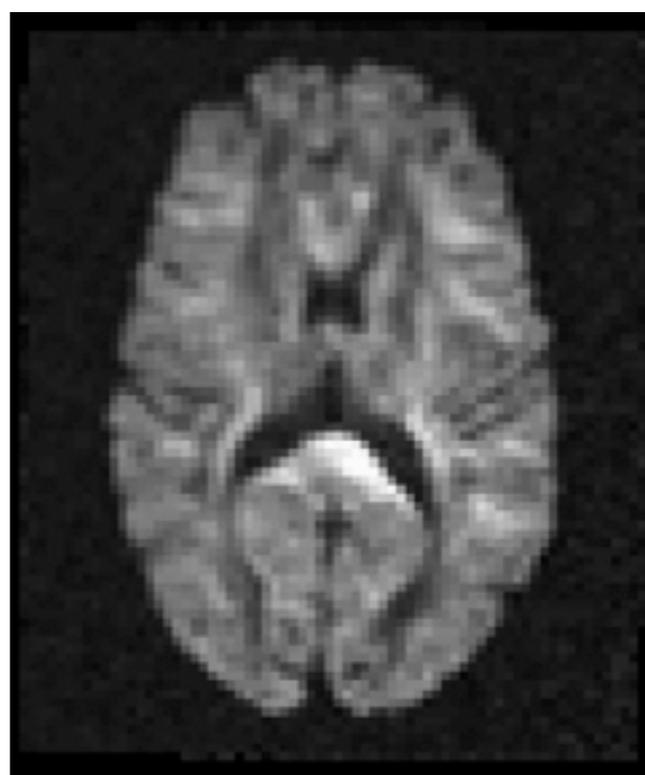


# How accurate are the predictions?



Slice 21

$g=[.5 \ .8 \ .4]$



Slice 28

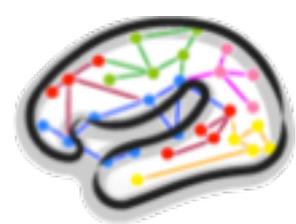
$g=[-.3 \ -.7 \ -.7]$



Slice 42

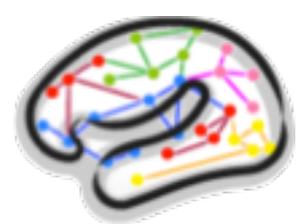
$g=[.3 \ -.7 \ .6]$

And some other slices/directions

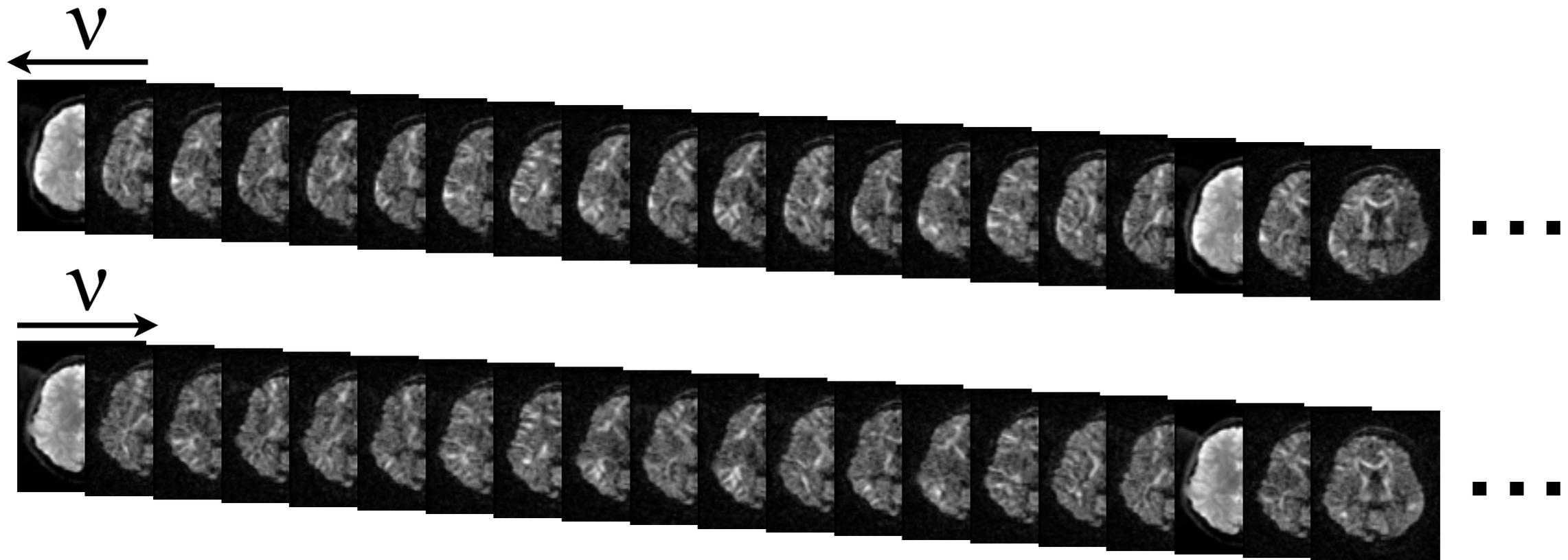


# Outline of the talk

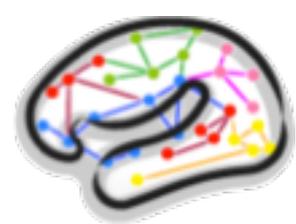
- What is the problem with diffusion data?
- Off-resonance field  $\leftrightarrow$  Distortions
- Where does the off-resonance field come from?
- Worlds shortest course on image registration
- How topup works
- How eddy works
- Outliers
- **Practicalities**
- Output



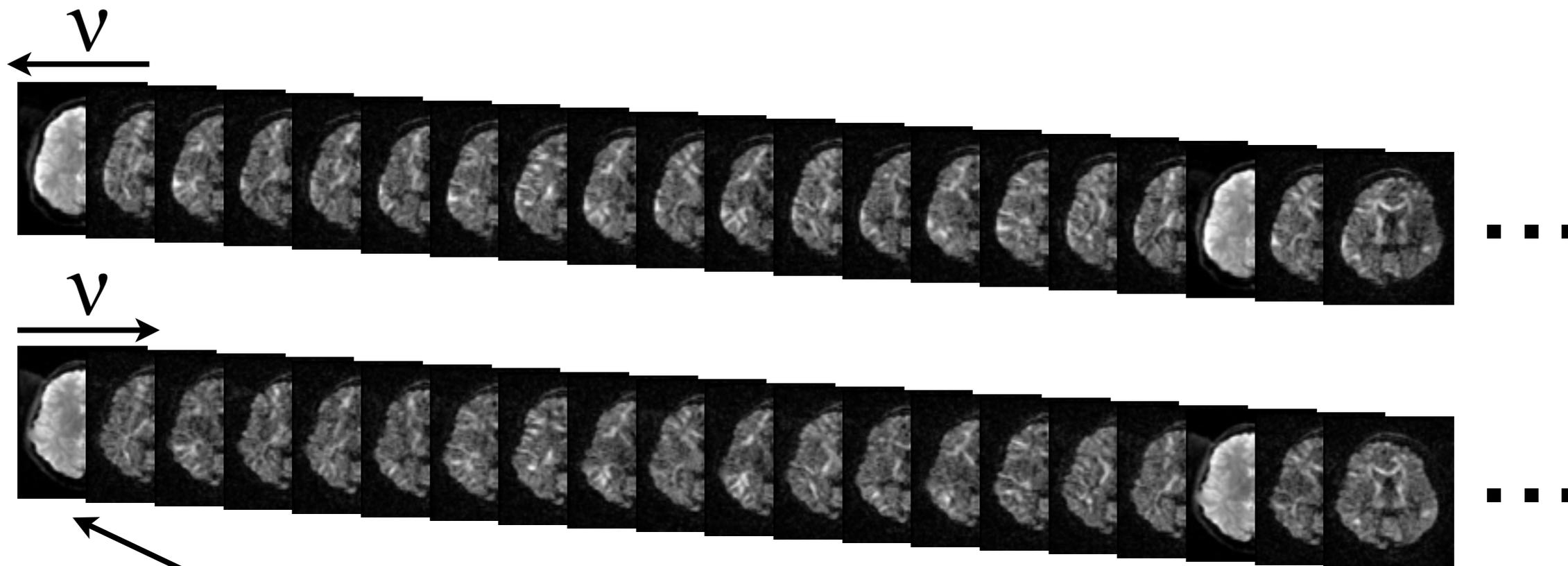
# Practicalities



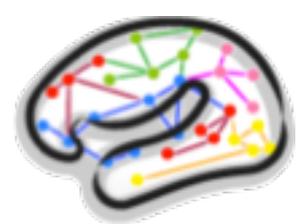
- Our example data consists of:
  - $N$  diffusion weighted volumes and  $n$   $b=0$  volumes
  - $b=0$  volumes interspersed
  - Two repetitions, phase-encode  $L \rightarrow R$  and  $R \rightarrow L$
  - Same diffusion table for both repetitions



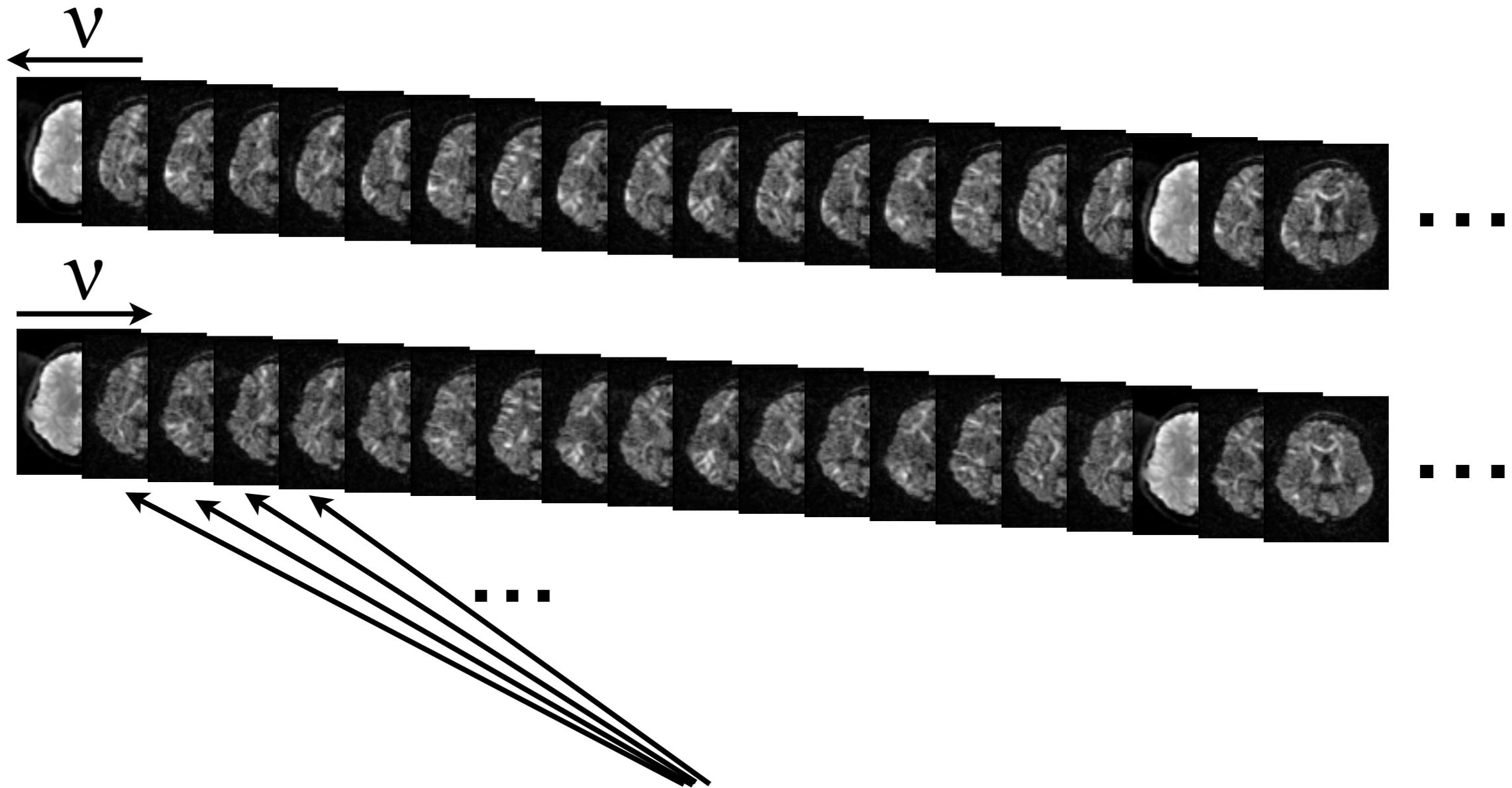
# Practicalities



Affected by susceptibility distortions

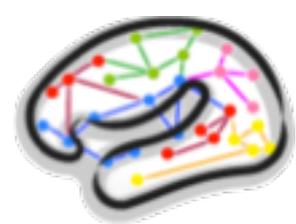


# Practicalities

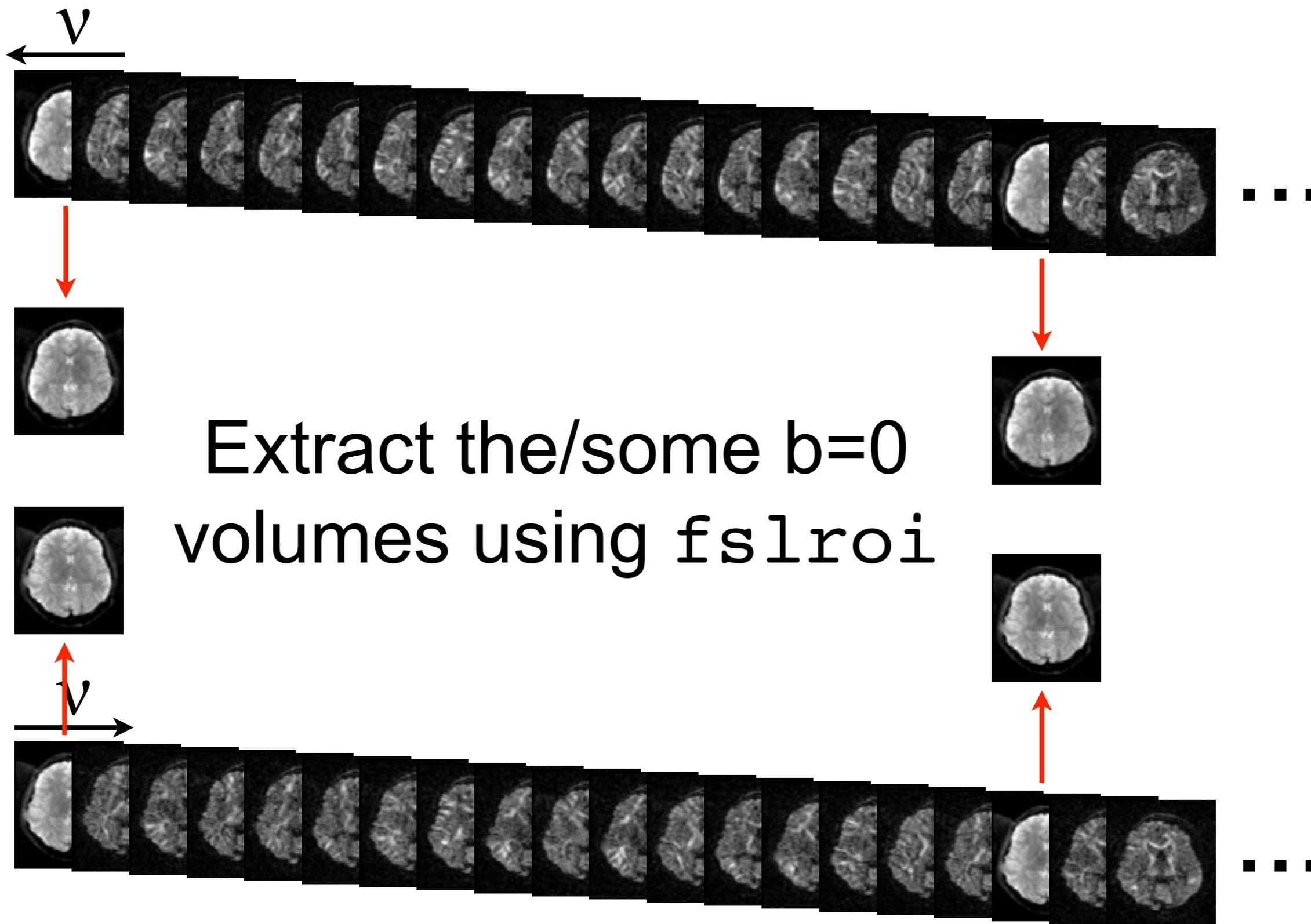


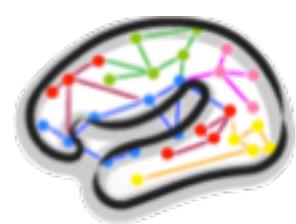
Affected by susceptibility distortions  
AND eddy current distortions

And everything is of course affected by subject  
movement.

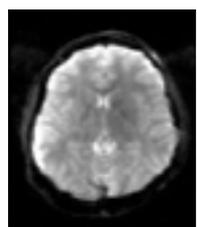
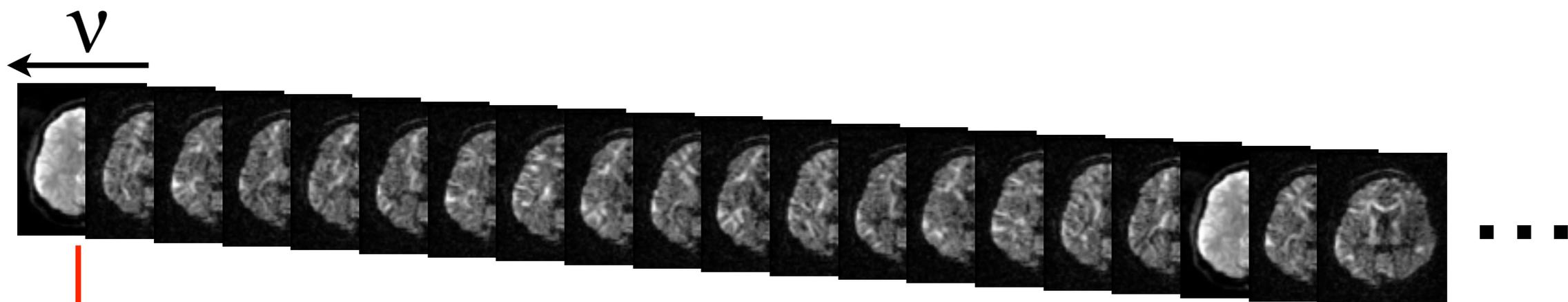


# So, let's start with susceptibility



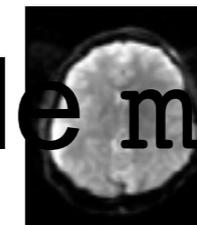


# So, let's start with susceptibility



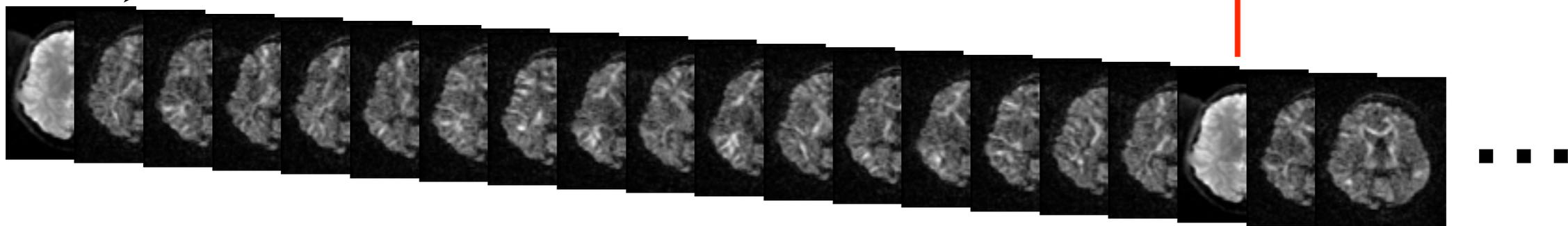
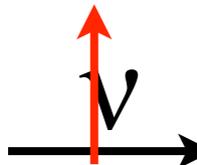
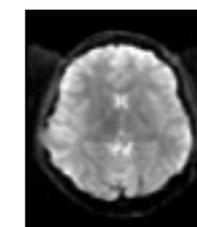
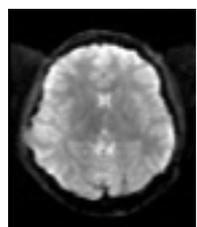
And let's call it for

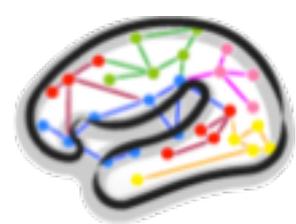
example `my_b0s`  
Collect the  $b=0$  volumes



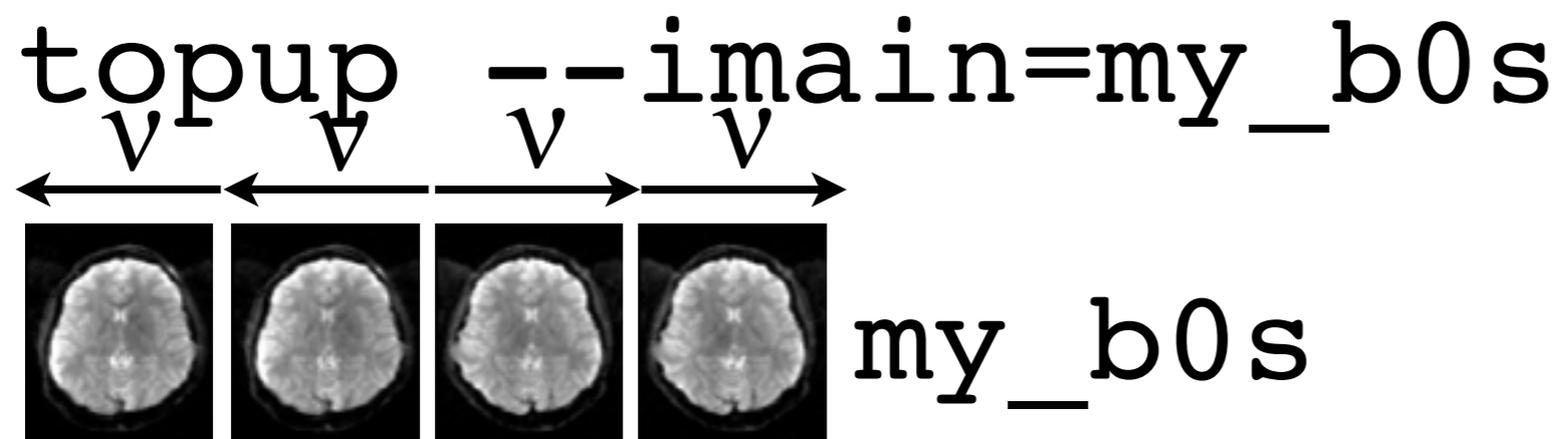
into a single file using

`fs1merge`

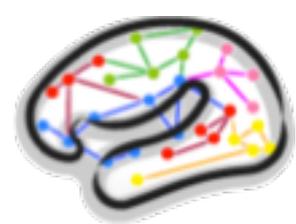




# And the tool for that is topup



But we also need to inform topup about the acquisition parameters



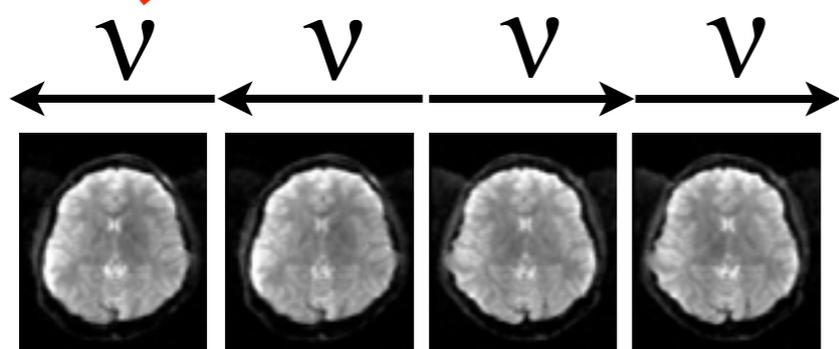
# And the tool for that is topup

```
topup --iain=my_b0s
```

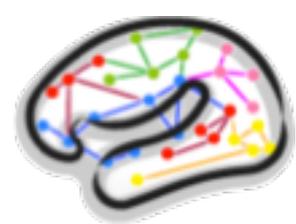
Means PE in x-direction, L→R

-1 0 0 0.051

Total readout time  
(in seconds)



my\_b0s

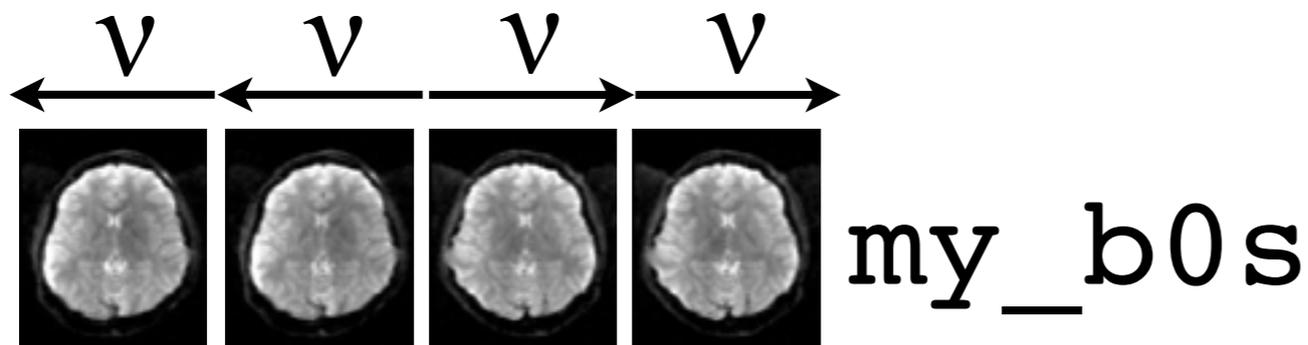


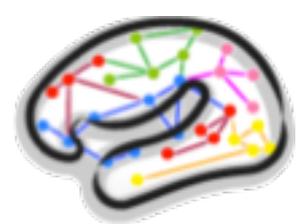
# And the tool for that is topup

```
topup --iain=my_b0s --datain=acqparams.txt
```

```
-1 0 0 0.051  
-1 0 0 0.051  
1 0 0 0.051  
1 0 0 0.051
```

Text file that we can  
call for example  
acqparams.txt



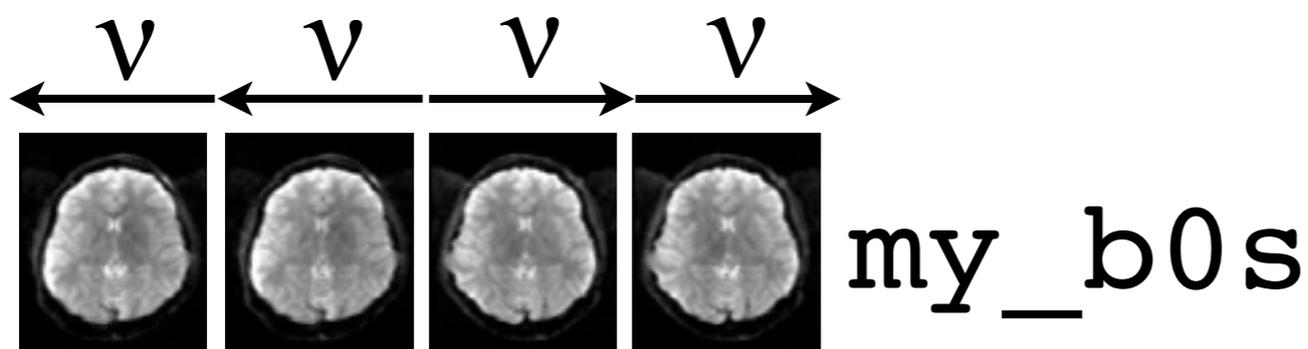


# And the tool for that is topup

```
topup --iain=my_b0s --datain=acqparams.txt --config=b02b0.cnf
```

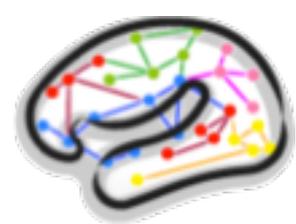


And then some technical details



```
-1 0 0 0.051  
-1 0 0 0.051  
1 0 0 0.051  
1 0 0 0.051
```

acqparams.txt



# And the tool for that is topup

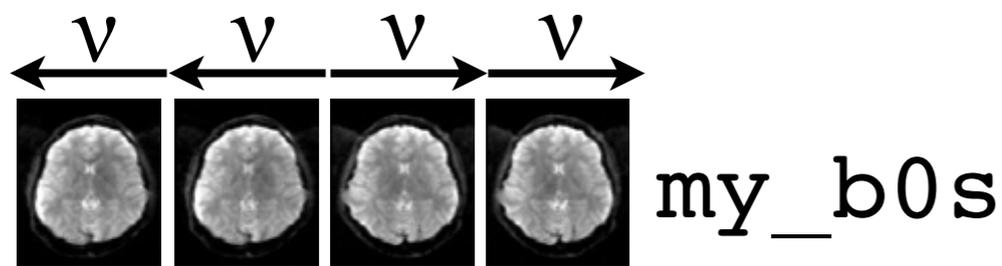
And finally we need to tell it where to put the results

```
topup --imain=my_b0s --datain=acqparams.txt --config=b02b0.cnf --out=my_topup
```

my\_topup\_movpar.txt

Tells position of 2nd b=0 scan relative the first

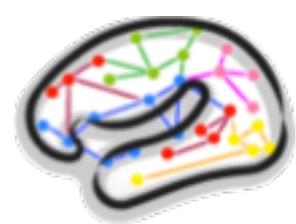
```
0 0 0 0 0 0
0.72 -0.02 -0.07 0.002 0.000 0.002
0 -0.11 -0.33 0.002 0.013 -0.004
-0.70 -0.12 -0.43 0.002 0.014 -0.004
```



```
-1 0 0 0.051
-1 0 0 0.051
1 0 0 0.051
1 0 0 0.051
```

b02b0.cnf

acqparams.txt

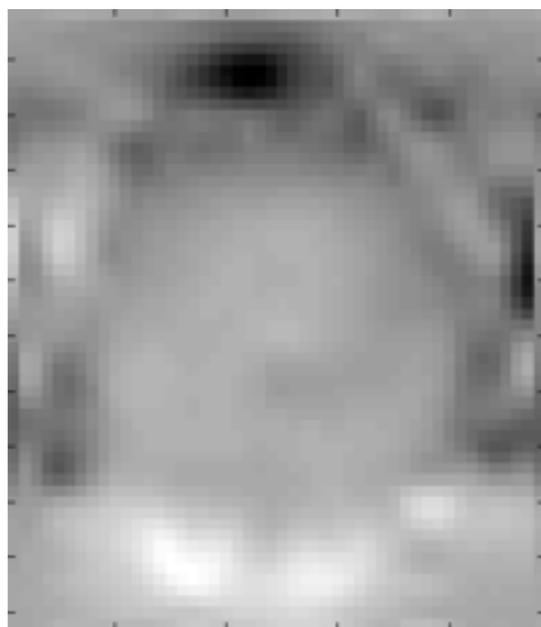


# And the tool for that is topup

And finally we need to tell it where to put the results

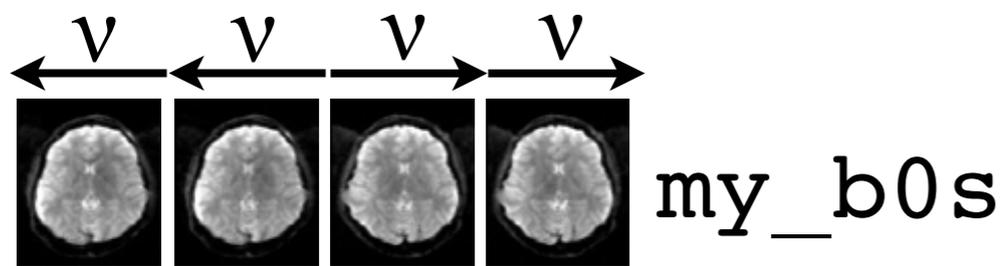
```
topup --imain=my_b0s --datain=acqparams.txt --config=b02b0.cnf --out=my_topup
```

my\_topup\_fieldcoef.nii



my\_topup\_movpar.txt

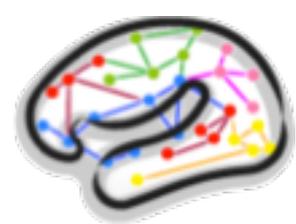
```
0 0 0 0 0 0
0.72 -0.02 -0.07 0.002 0.000 0.002
0 -0.11 -0.33 0.002 0.013 -0.004
-0.70 -0.12 -0.43 0.002 0.014 -0.004
```



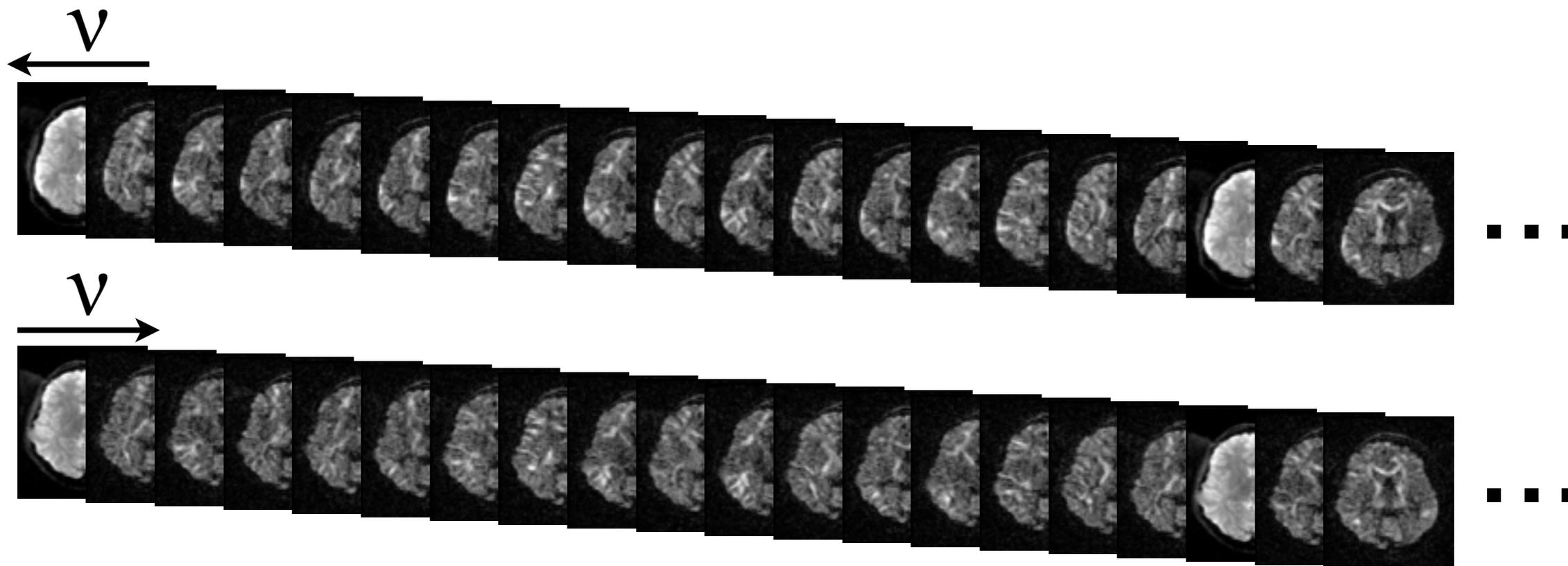
```
-1 0 0 0.051
-1 0 0 0.051
1 0 0 0.051
1 0 0 0.051
```

acqparams.txt

b02b0.cnf



# Back to the full data-set

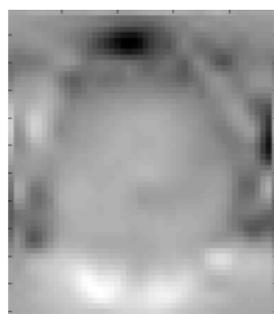


Now we want to correct the eddy current-distortions and subject movement in the whole data set.

my\_topup\_fieldcoef.nii

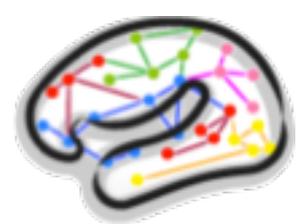
```
-1 0 0 0.051  
-1 0 0 0.051  
1 0 0 0.051  
1 0 0 0.051
```

acqparams.txt

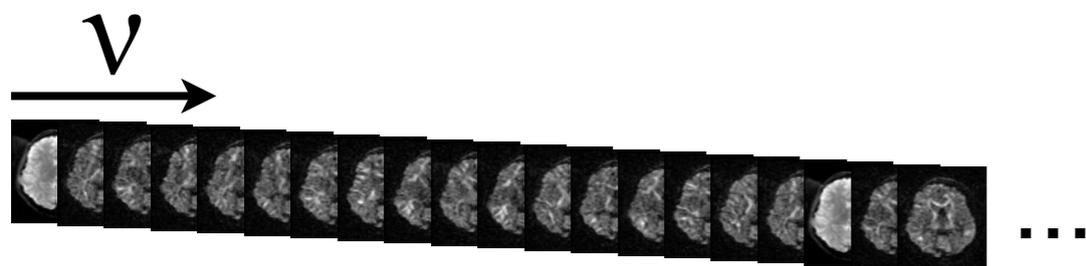
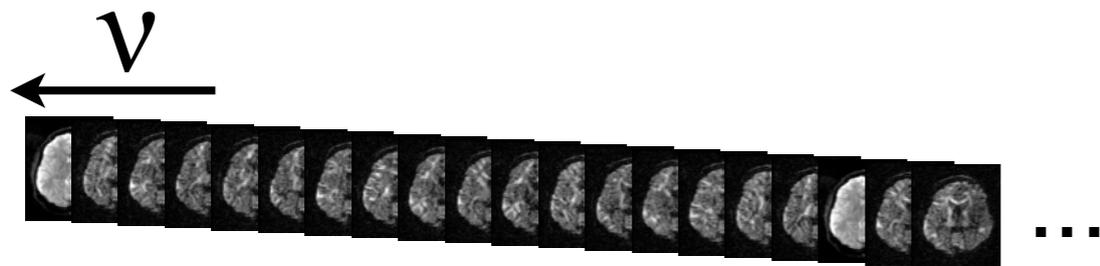


```
0 0 0 0 0 0  
0.72 -0.02 -0.07 0.002 0.000 0.002  
0 -0.11 -0.33 0.002 0.013 -0.004  
-0.70 -0.12 -0.43 0.002 0.014 -0.004
```

my\_topup\_movpar.txt



# Collect all data in one file



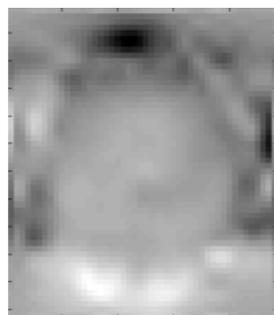
LR\_RL

The first thing we do is to collect all data in a single file using `fs1merge` and call it for example `LR_RL`

`my_topup_fieldcoef.nii`

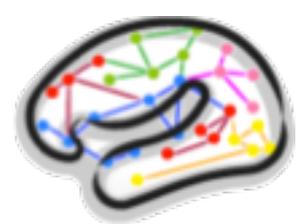
```
-1 0 0 0.051  
-1 0 0 0.051  
1 0 0 0.051  
1 0 0 0.051
```

`acqparams.txt`

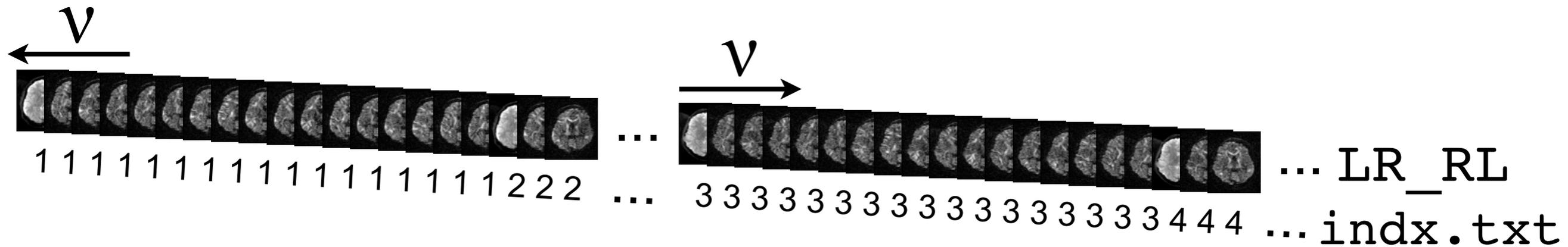


```
0 0 0 0 0 0  
0.72 -0.02 -0.07 0.002 0.000 0.002  
0 -0.11 -0.33 0.002 0.013 -0.004  
-0.70 -0.12 -0.43 0.002 0.014 -0.004
```

`my_topup_movpar.txt`



# Inform eddy of acquisition parameters

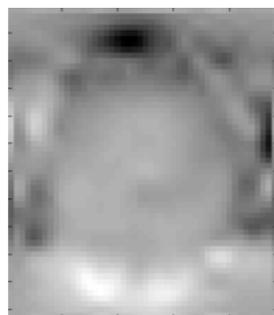


Then we make a text file with one index for each volume, and call it for example `indx.txt`

`my_topup_fieldcoef.nii`

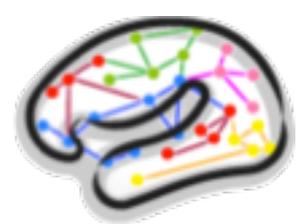
```
-1 0 0 0.051  
-1 0 0 0.051  
1 0 0 0.051  
1 0 0 0.051
```

`acqparams.txt`

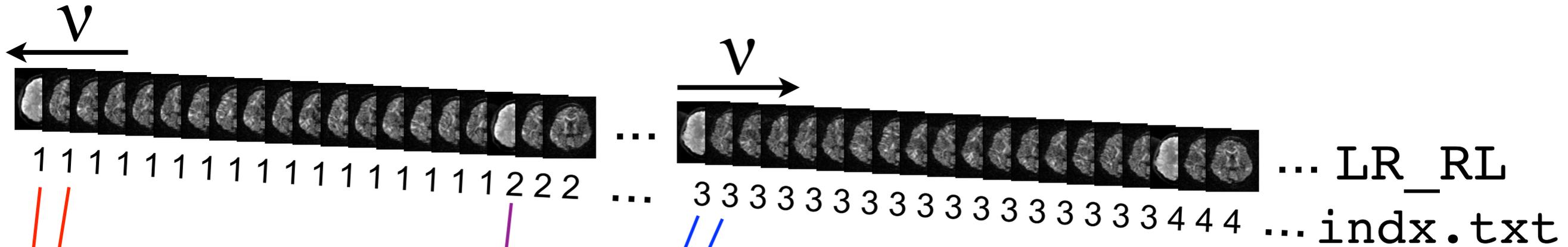


```
0 0 0 0 0 0  
0.72 -0.02 -0.07 0.002 0.000 0.002  
0 -0.11 -0.33 0.002 0.013 -0.004  
-0.70 -0.12 -0.43 0.002 0.014 -0.004
```

`my_topup_movpar.txt`

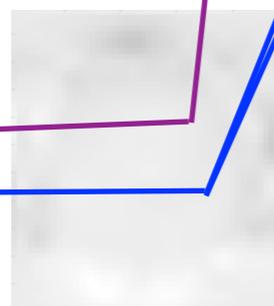


# Inform eddy of acquisition parameters



By referring into `acqparams.txt` this file specifies how every volume was acquired

`my_topup_fieldcoef.nii`



```

-1 0 0 0.051
-1 0 0 0.051
 1 0 0 0.051
 1 0 0 0.051

```

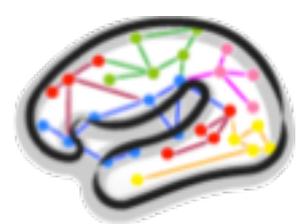
`acqparams.txt`

```

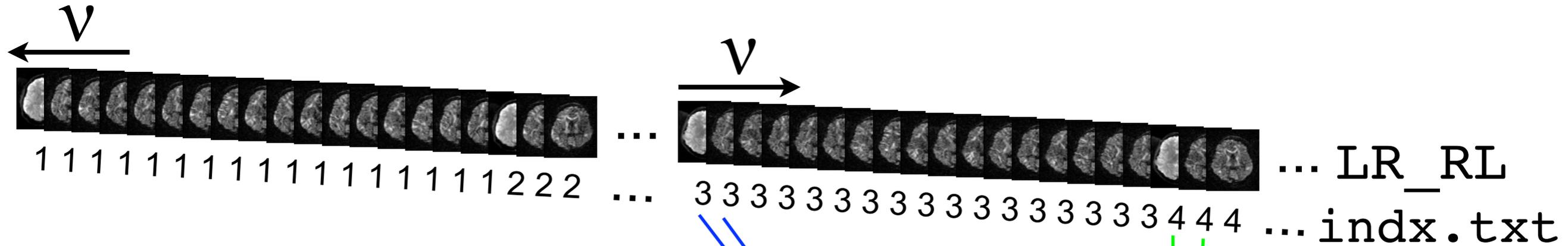
0 0 0 0 0 0
0.72 -0.02 -0.07 0.002 0.000 0.002
0 -0.11 -0.33 0.002 0.013 -0.004
-0.70 -0.12 -0.43 0.002 0.014 -0.004

```

`my_topup_movpar.txt`



# Inform eddy of acquisition parameters



And by referring into  
`my_topup_movpar.txt` it  
 gives a starting guess for the  
 relative subject position for each  
 volume

`my_topup_fieldcoef.nii`

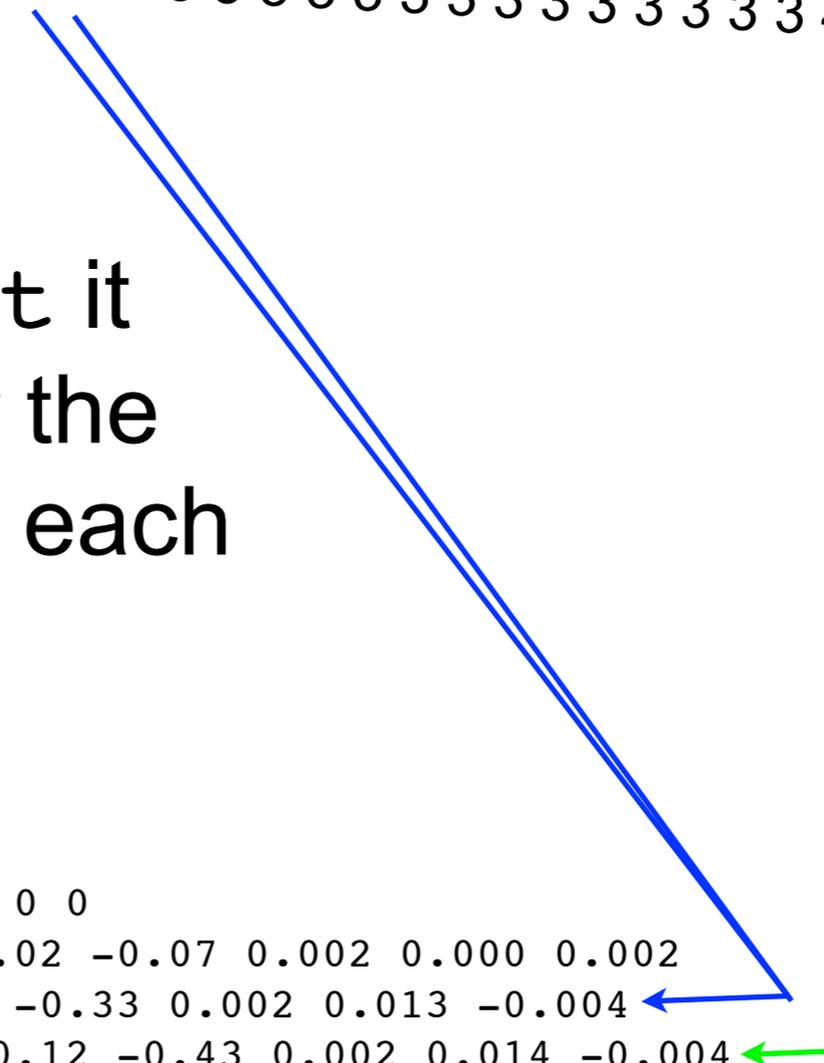
```
-1 0 0 0.051
-1 0 0 0.051
 1 0 0 0.051
 1 0 0 0.051
```

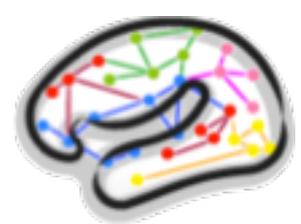
`acqparams.txt`



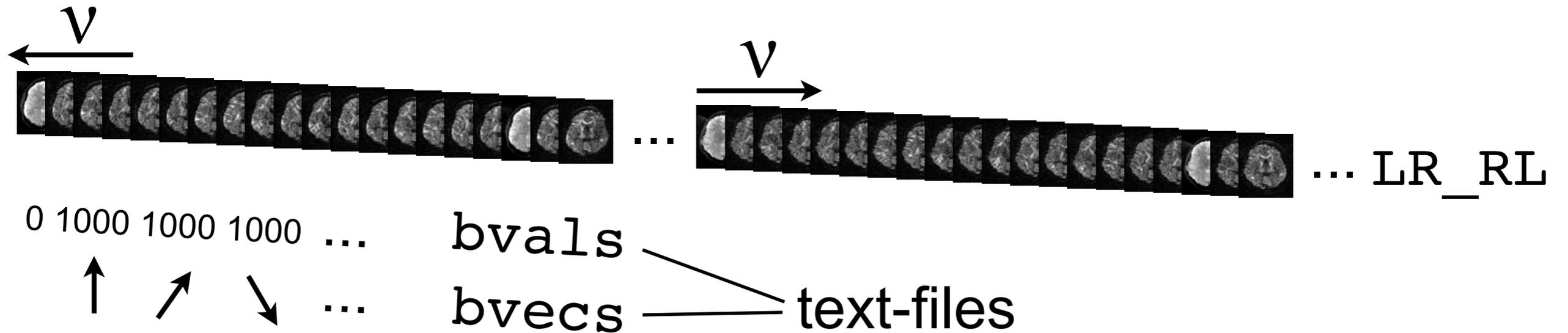
```
0 0 0 0 0 0
0.72 -0.02 -0.07 0.002 0.000 0.002
0 -0.11 -0.33 0.002 0.013 -0.004
-0.70 -0.12 -0.43 0.002 0.014 -0.004
```

`my_topup_movpar.txt`





# And of diffusion parameters

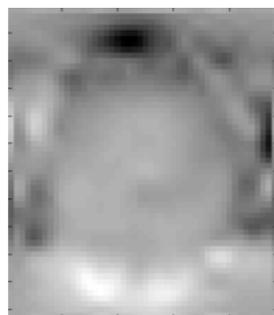


And we also need to know the b-value and b-vector for each volume (same as for `dtifit` or `bedpost`).

`my_topup_fieldcoef.nii`

```
-1 0 0 0.051
-1 0 0 0.051
 1 0 0 0.051
 1 0 0 0.051
```

`acqparams.txt`

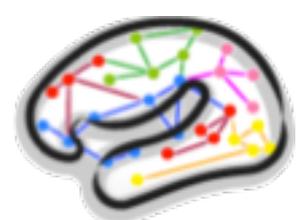


```
0 0 0 0 0 0
0.72 -0.02 -0.07 0.002 0.000 0.002
0 -0.11 -0.33 0.002 0.013 -0.004
-0.70 -0.12 -0.43 0.002 0.014 -0.004
```

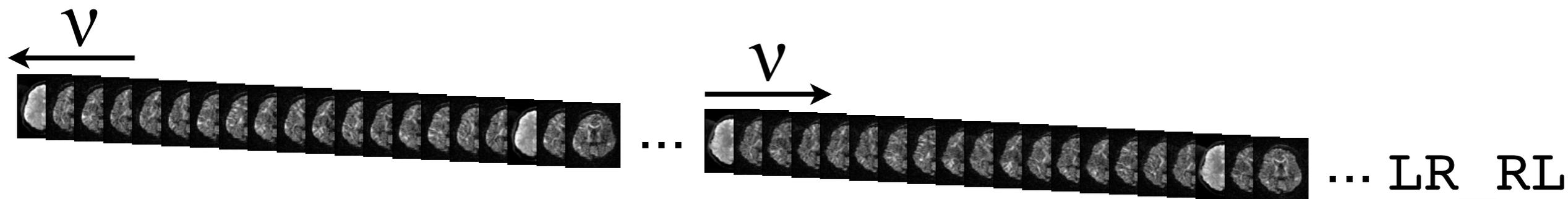
`my_topup_movpar.txt`

1111...

`indx.txt`



# And where the brain is



brain\_mask.nii

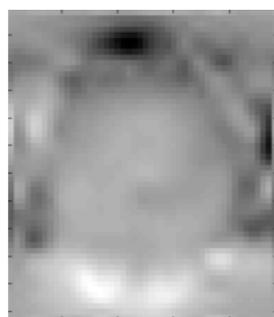
And finally a binary mask that tells eddy which voxels are brain. Also the same that is used for dtifit/bedpost.

my\_topup\_fieldcoef.nii

```

-1 0 0 0.051
-1 0 0 0.051
 1 0 0 0.051
 1 0 0 0.051
acqparams.txt

```



```

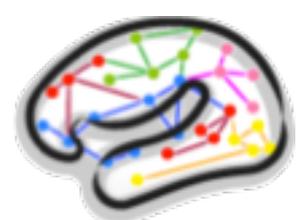
0 0 0 0 0 0
0.72 -0.02 -0.07 0.002 0.000 0.002
0 -0.11 -0.33 0.002 0.013 -0.004
-0.70 -0.12 -0.43 0.002 0.014 -0.004
my_topup_movpar.txt

```

```

0 1000 1000 1000 ...
bvals
1111...
↑ ↗ ↘ ...
bvecs

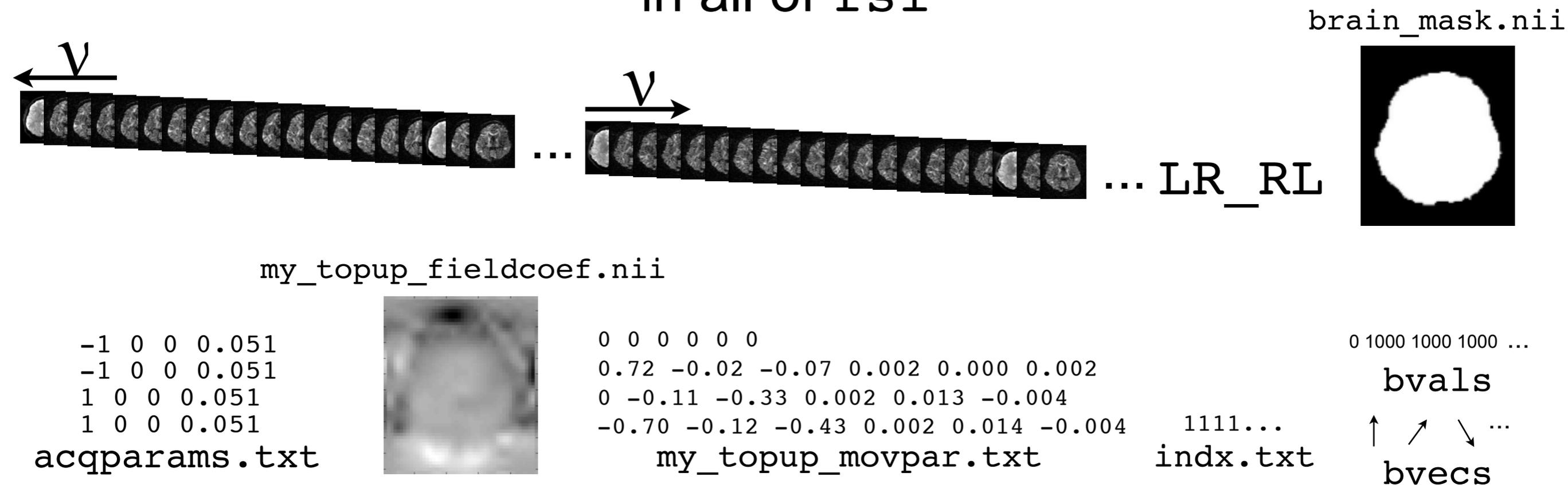
```

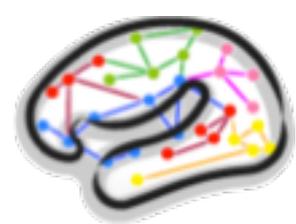


# And now we can run eddy

```
eddy --i=LR_RL --acqp=acqparams.txt
--index=indx.txt --bvecs=bvecs
--bvals=bvals --mask=brain_mask
--topup=my_topup --out=my_eddy
```

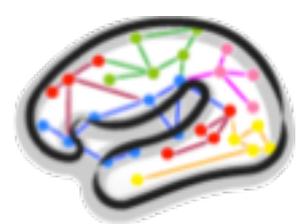
And now we are ready for the most horrible command line  
in all of `fs1`





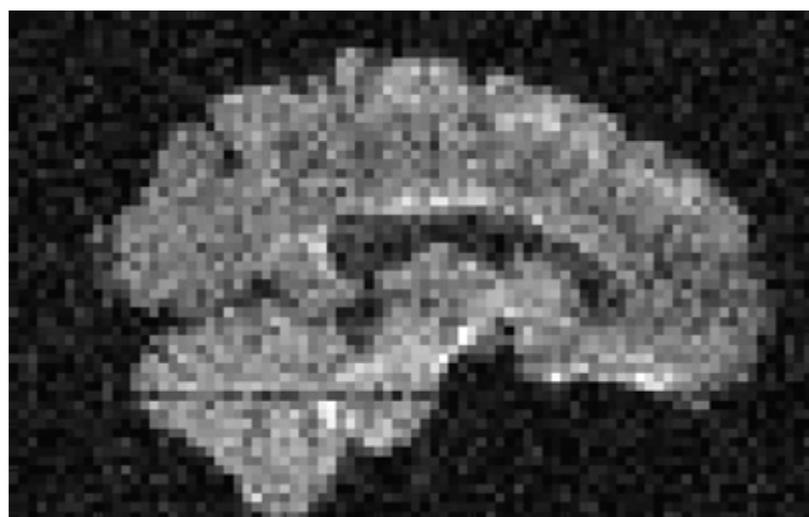
# Outline of the talk

- What is the problem with diffusion data?
- Off-resonance field  $\leftrightarrow$  Distortions
- Where does the off-resonance field come from?
- Worlds shortest course on image registration
- How topup works
- How eddy works
- Outliers
- Practicalities
- **Output**

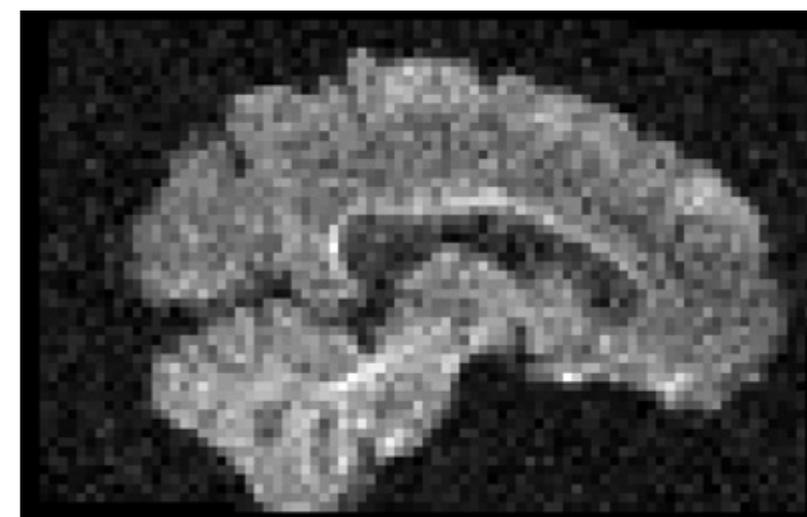


# Output

```
eddy --i=LR_RL...bla bla... --out=my_eddy
```

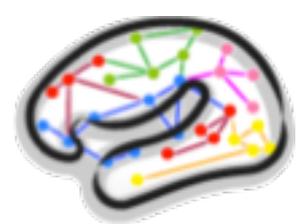


LR\_RL.nii.gz



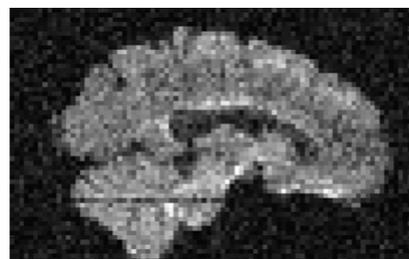
my\_eddy.nii.gz

This is the “main” output,  
and chances are you will  
never need anything else.

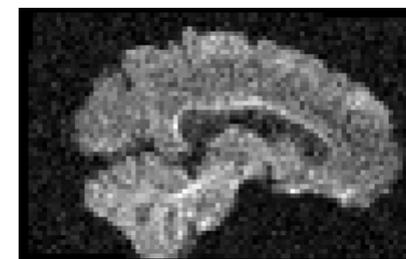


# Output

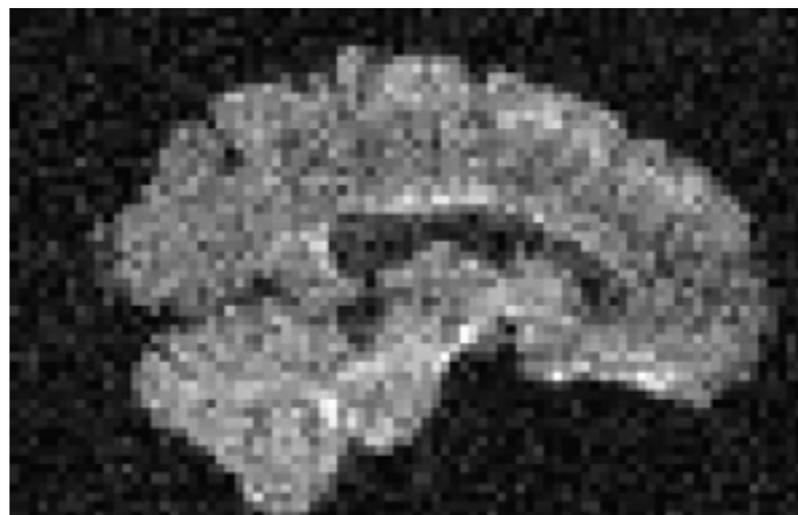
```
eddy --i=LR_RL...bla bla... --o=my_eddy
```



LR\_RL.nii.gz

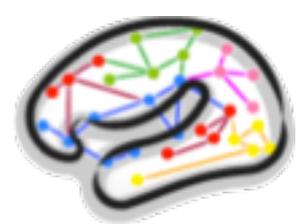


my\_eddy.nii.gz



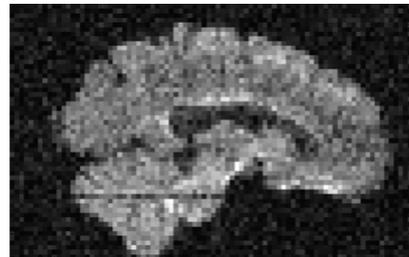
my\_eddy.eddy\_outlier\_free\_data.nii.gz

This has been corrected **only** for outliers.  
Distortions and movements have **not** been corrected.  
Unlikely to be of interest.

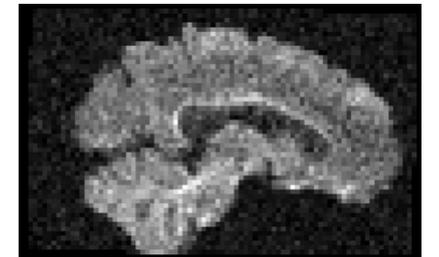


# Output

```
eddy --i=LR_RL.nii.gz --o=my_eddy.nii.gz
```



LR\_RL.nii.gz

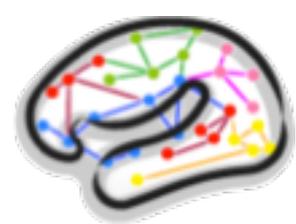


my\_eddy.nii.gz

```
0 0 0 0 0 ...  
0.114 -0.014 -0.126 -0.003 0.004 ...  
0.190 0.050 -0.131 -0.003 0.006 ...  
0.177 0.112 -0.184 -0.002 0.009 ...  
.  
.  
.
```

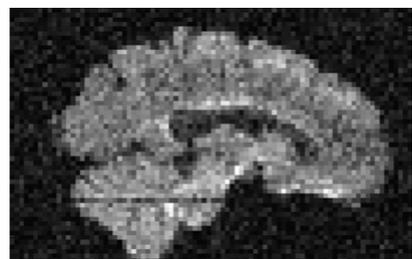
my\_eddy.eddy\_parameters

This is a text-file with the estimated movement and EC parameters.  
Unlikely to be of interest.

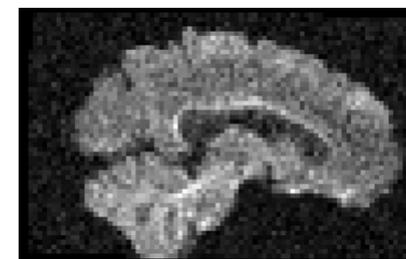


# Output

```
eddy --i=LR_RL...bla bla... --out=my_eddy
```



LR\_RL.nii.gz

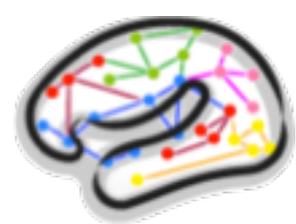


my\_eddy.nii.gz

Cumulative	Relative preceding volume
0	0
0.299	0.299
0.401	0.148
0.491	0.136
.	.
.	.
.	.

my\_eddy.eddy\_movement\_rms

This is a text-file with the cumulative and “delta” movement RMS for each volume.  
Useful for QC and for excluding volumes/subjects.

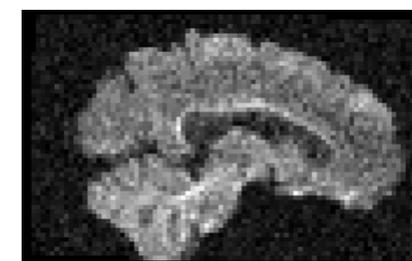


# Output

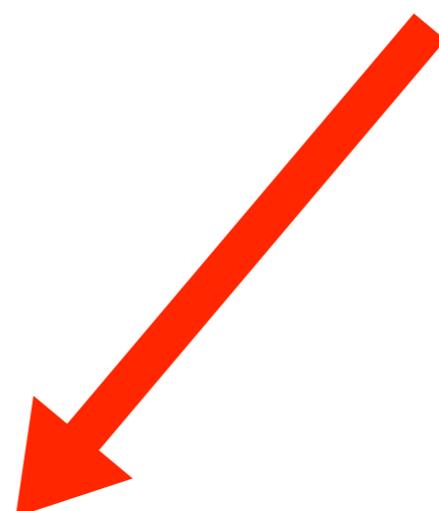
```
eddy --i=LR_RL...bla bla... --o=my_eddy
```



LR\_RL.nii.gz



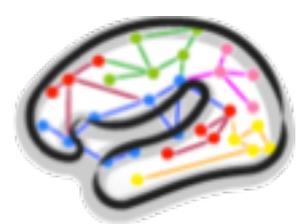
my\_eddy.nii.gz



	Slice...					
Volume...	0	0	-0.089	1.080	-0.002	...
	0	0	0.812	1.563	1.090	...
	0	0	0.107	0.606	0.207	...
	0	0	-0.975	-0.620	-0.467	...
	.	.	.	.	.	.

my\_eddy.eddy\_outlier\_n\_stdev\_map

This is a text-file with one value per slice and volume. It specifies how many standard deviations away from the prediction it is. Useful for QC and for excluding volumes/subjects.



# Output

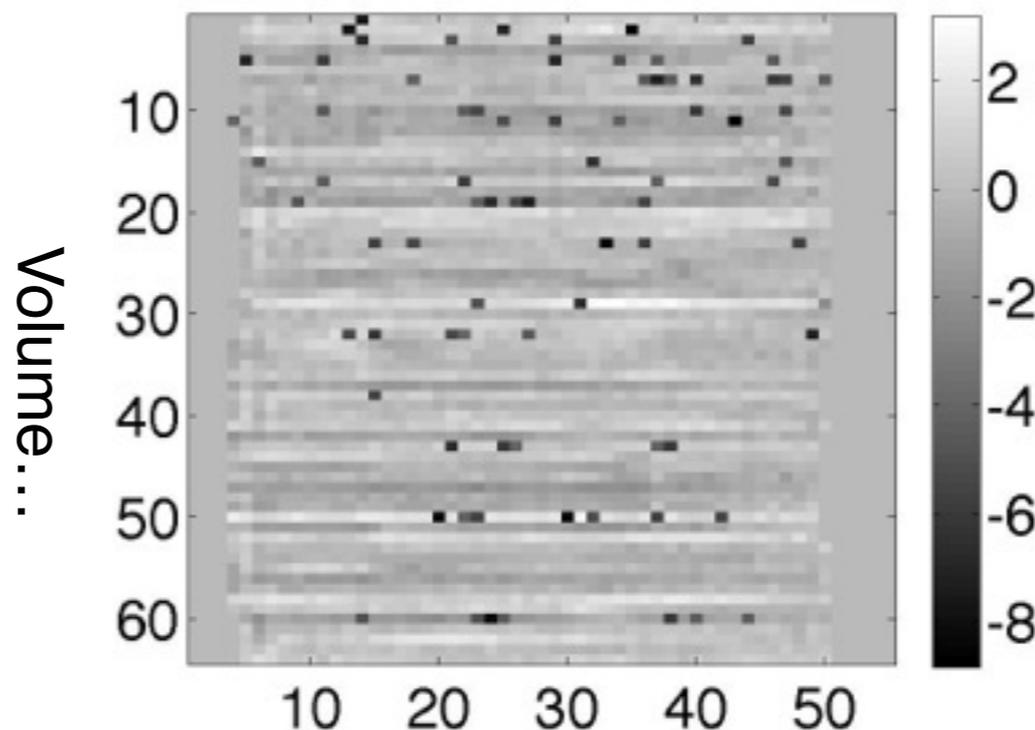
```
eddy --i=LR_RL...bla bla... --out=my_eddy
```



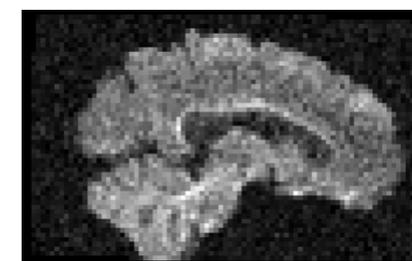
LR\_RL.nii.gz



Slice...

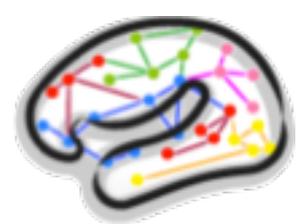


my\_eddy.eddy\_outlier\_n\_stdev\_map



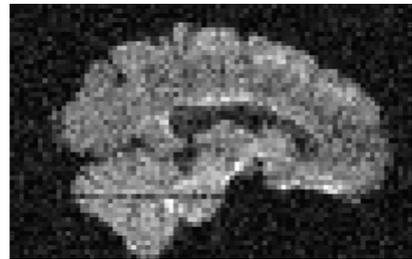
my\_eddy.nii.gz

This is a text-file with one value per slice and volume. It specifies how many standard deviations away from the prediction it is. Useful for QC and for excluding volumes/subjects.

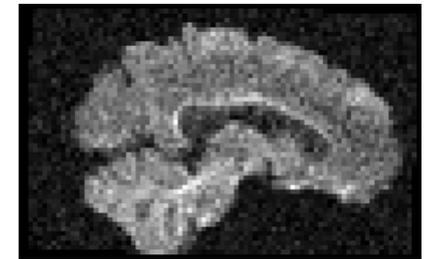


# Output

```
eddy --i=LR_RL.nii.gz --o=my_eddy.nii.gz
```



LR\_RL.nii.gz

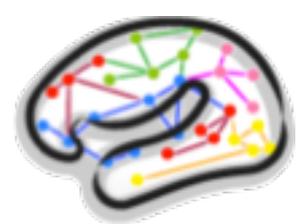


my\_eddy.nii.gz

	Slice...						
Volume...	0	0	0	0	0	...	
	0	0	0	0	0	...	
	0	0	0	0	0	...	
	0	0	0	0	0	...	
.	.	.	.	.	.	.	
.	.	.	.	.	.	.	

my\_eddy.eddy\_outlier\_map

This is a text-file with one value per slice and volume. A “one” signifies an outlier, a “zero” signifies an OK slice. Useful for QC and for excluding volumes/subjects.



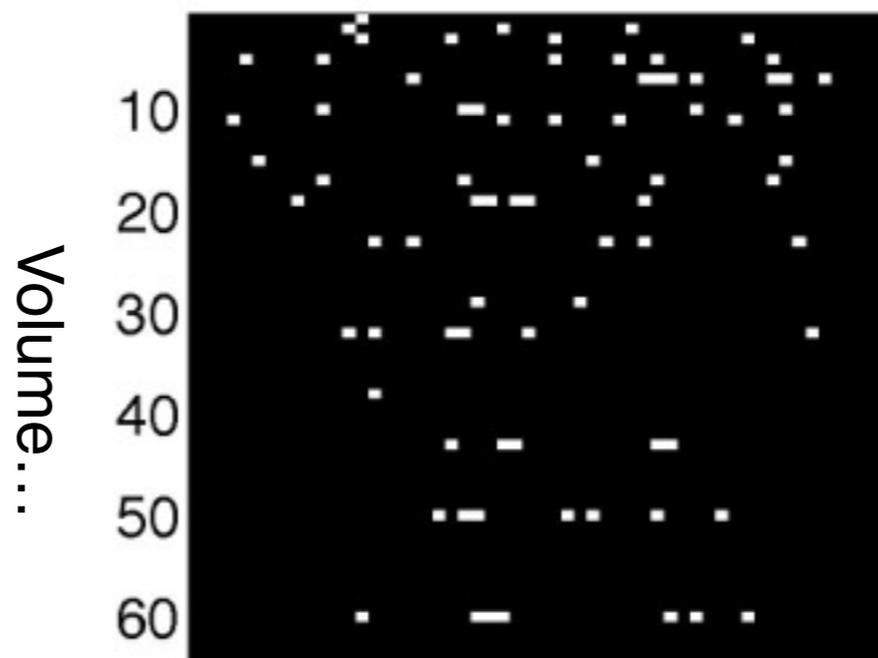
# Output

```
eddy --iain=LR_RL ...bla bla... --out=my_eddy
```



LR\_RL.nii.gz

Slice...



my\_eddy.eddy\_outlier\_map



my\_eddy.nii.gz

This is a text-file with one value per slice and volume. A “one” signifies an outlier, a “zero” signifies an OK slice. Useful for QC and for excluding volumes/subjects.