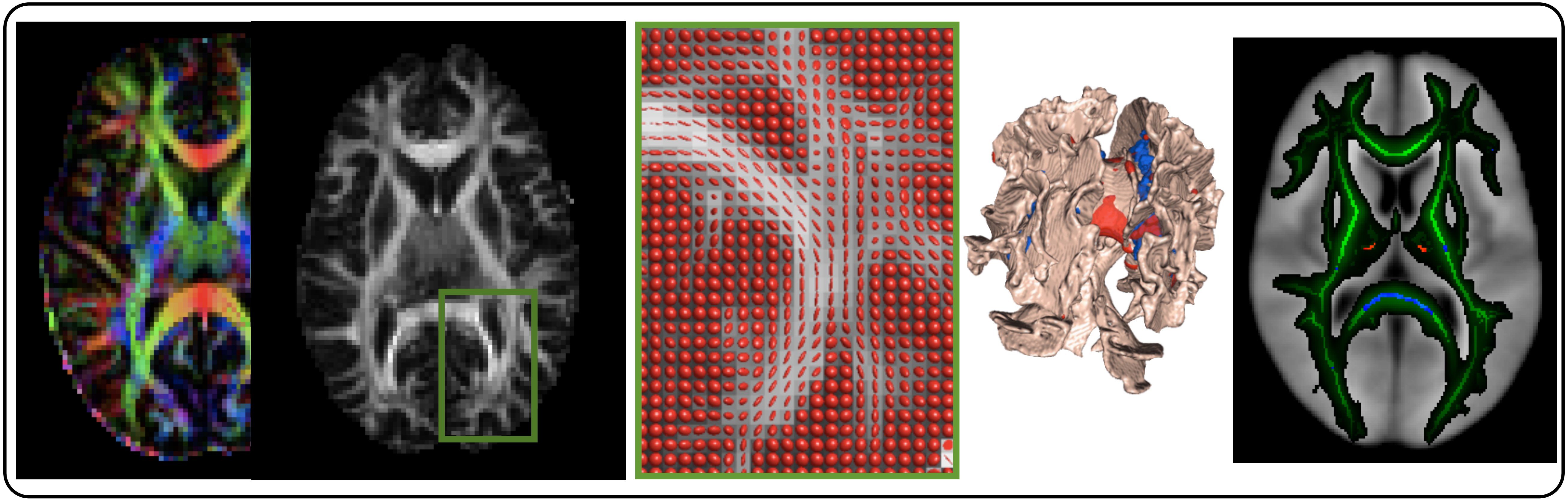
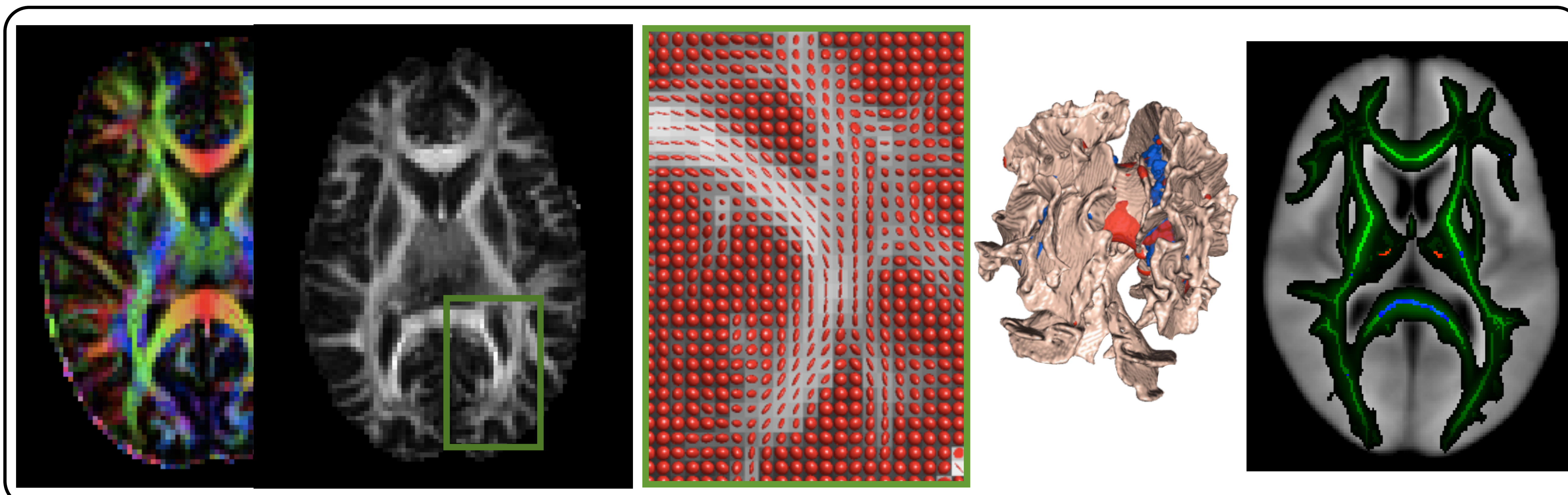
Diffusion MRI Processing and Analysis



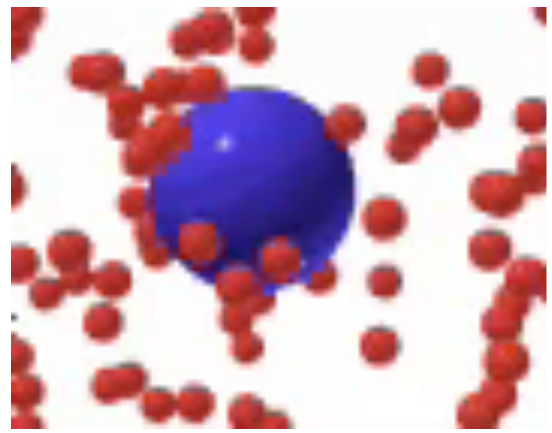
Overview

- What is Diffusion? Diffusion-weighting in MRI
- Diffusion Tensor Model and DTI
- Tract-Based Diffusion analysis (TBSS)
- Distortion Correction for Diffusion MRI



Diffusion - Brownian Motion

Robert Brown (1773-1858)



Molecules are in constant motion at non-zero absolute temperatures (> -273^{o} C)

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:

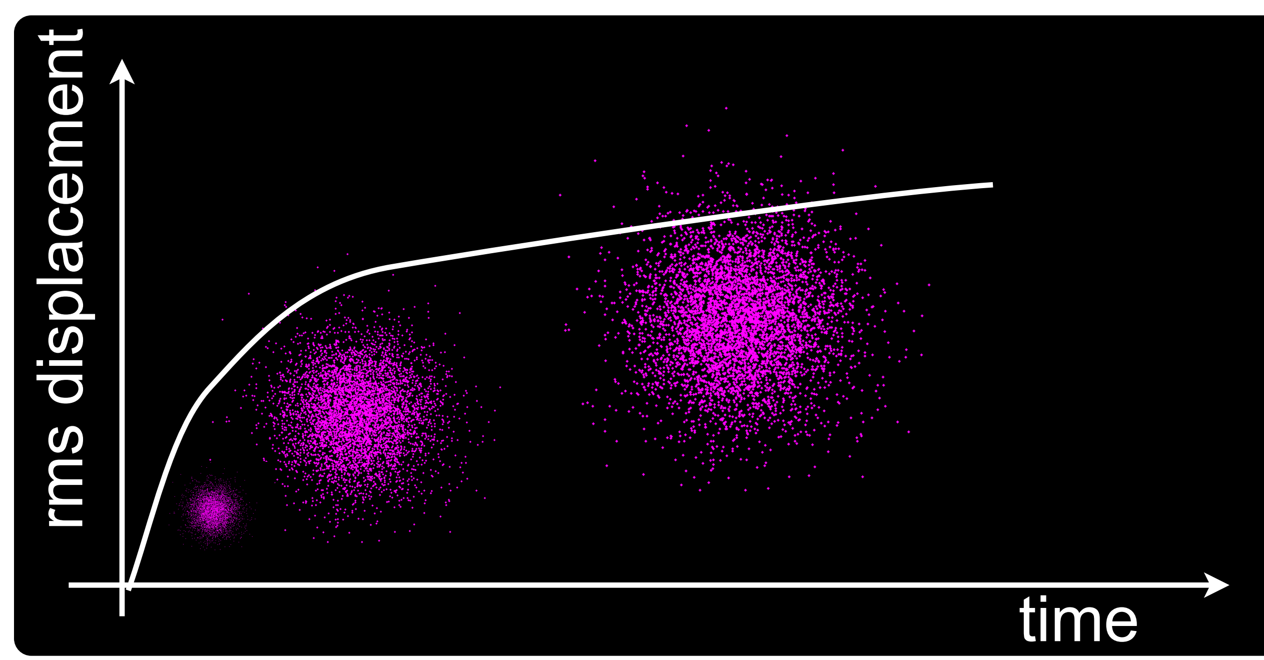
$$<x^2> = 2nDt$$

mean squared displacement

Diffusion coefficient

time

Valid for a homogeneous, barrier-free medium.



Diffusion - Brownian Motion

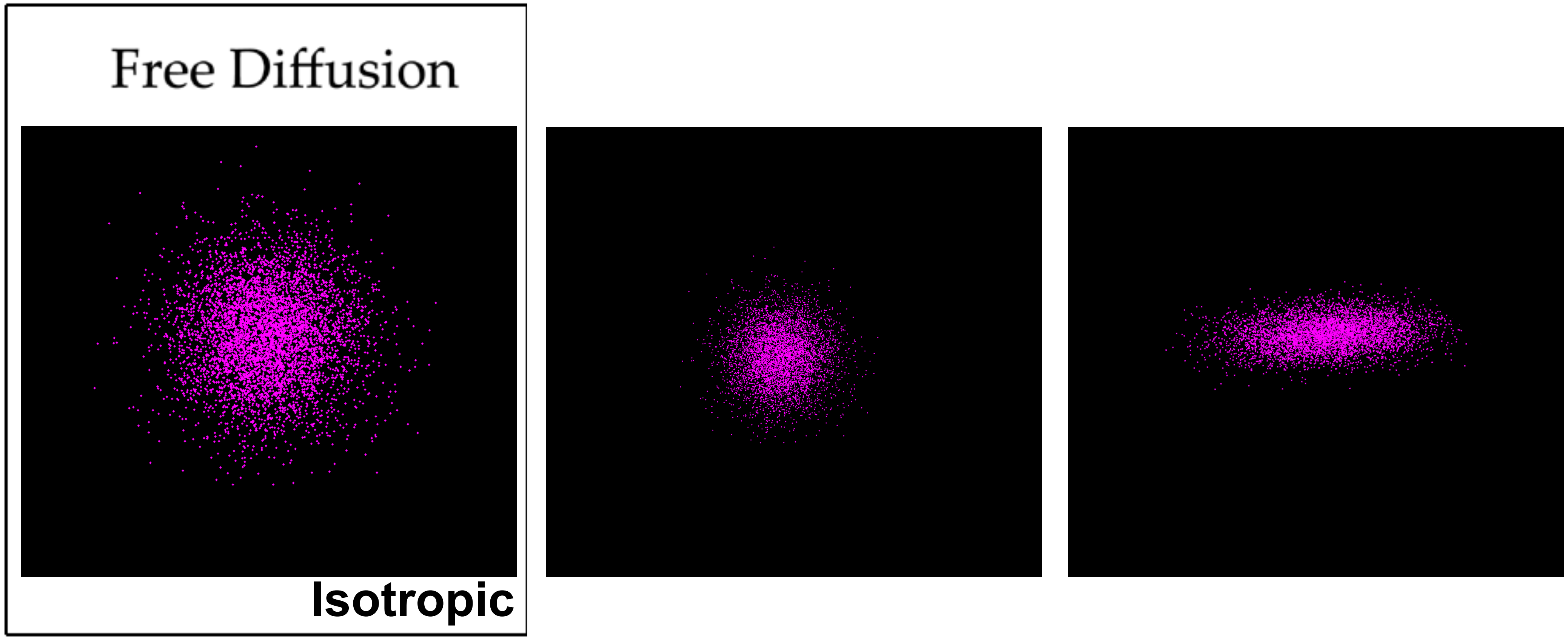
Another way to describe Einstein's equation:

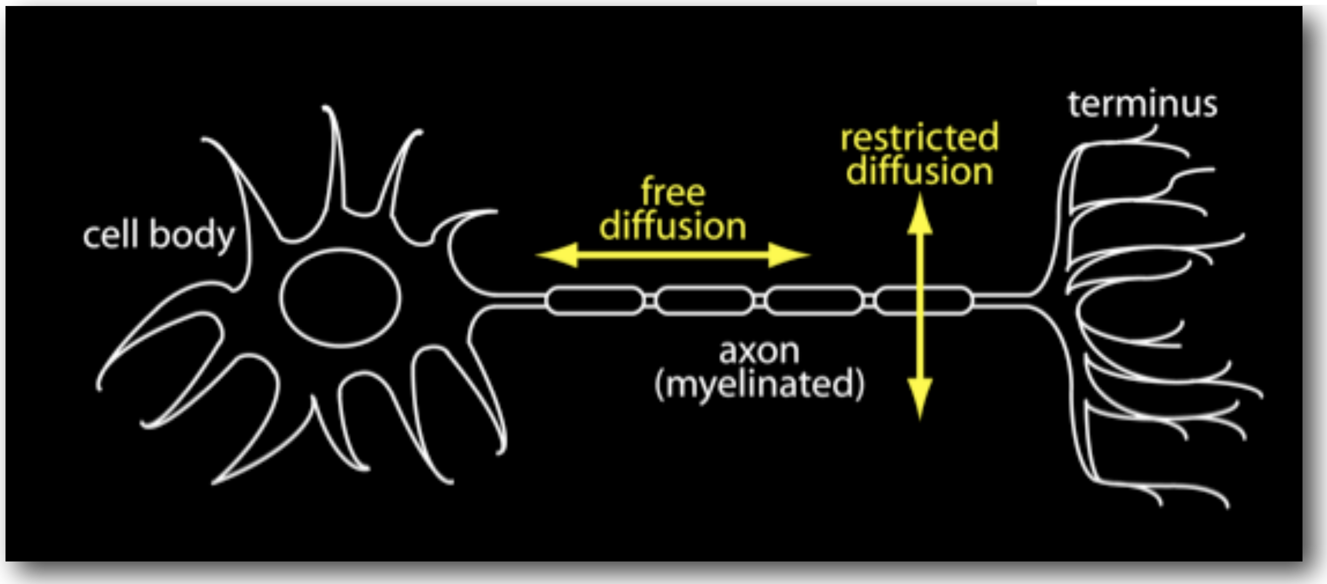
For a barrier-free medium, **diffusion displacements of an ensemble follow a Normal distribution** with N(0, 2tD):

- Zero-mean displacement

- Variance proportional to time and the diffusion coefficient

Water Diffusion in the Brain. Why is it Interesting?

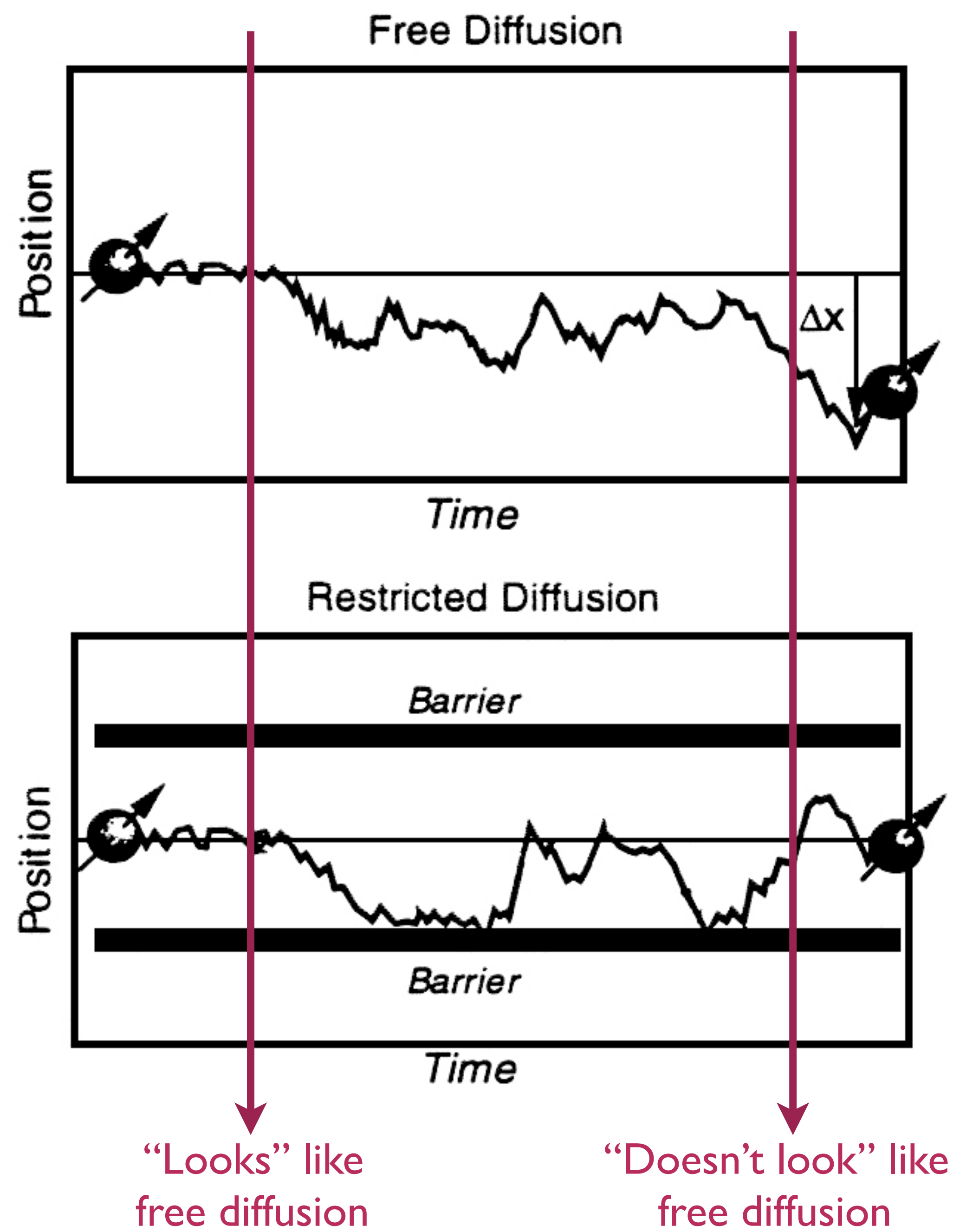




- Diffusion is restricted by tissue boundaries, membranes, etc.
- Marker for tissue microstructure (healthy and pathology)
- Diffusion is **anisotropic** in white matter

[Beaulieu, NMR Biomed, 2002]

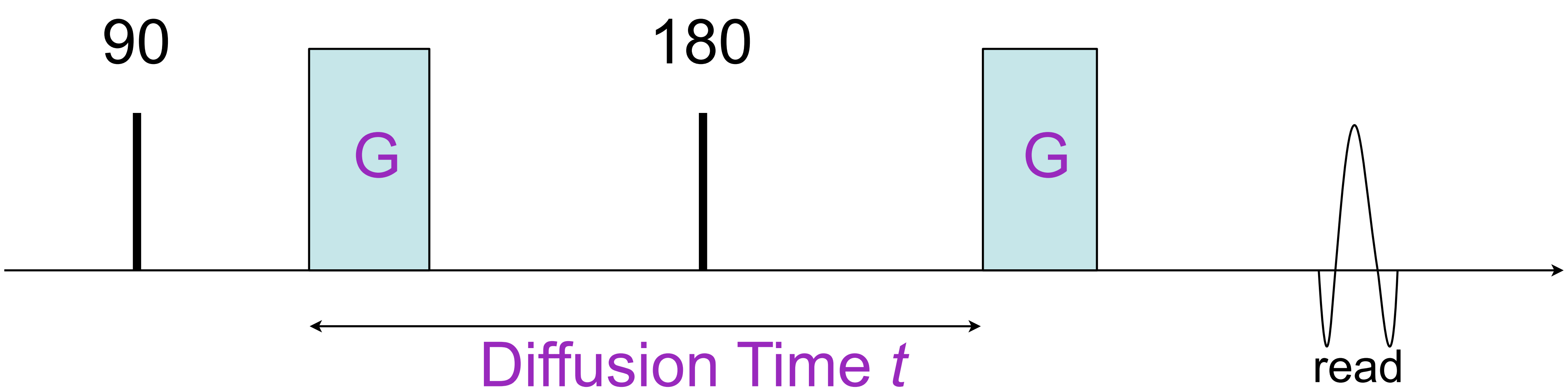
Apparent Diffusion



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

Measuring Diffusion with MRI: Diffusion MRI (dMRI)

Pulsed-Gradient Spin-Echo Sequence:
To achieve diffusion-weighting along a direction **x**, apply strong magnetic field gradients along **x**.



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

[Stejskal & Tanner, 1965]

Measuring Diffusion with MRI: Diffusion MRI (dMRI)

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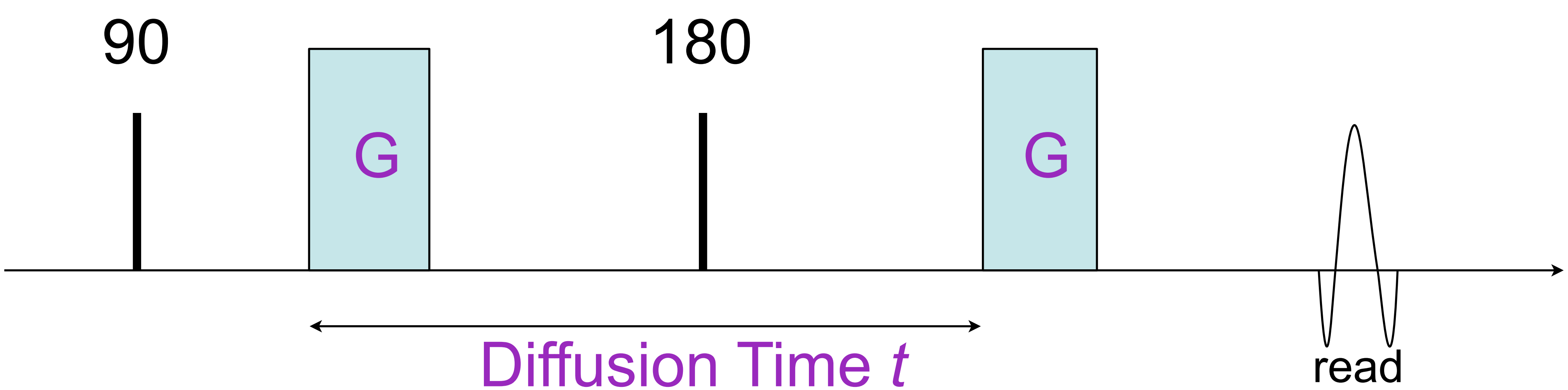


$D \sim 2.4\ \mu m^2/ms$
$t \sim 50ms$

➡ $x = \sqrt{6Dt}\ \sim 27\mu m$

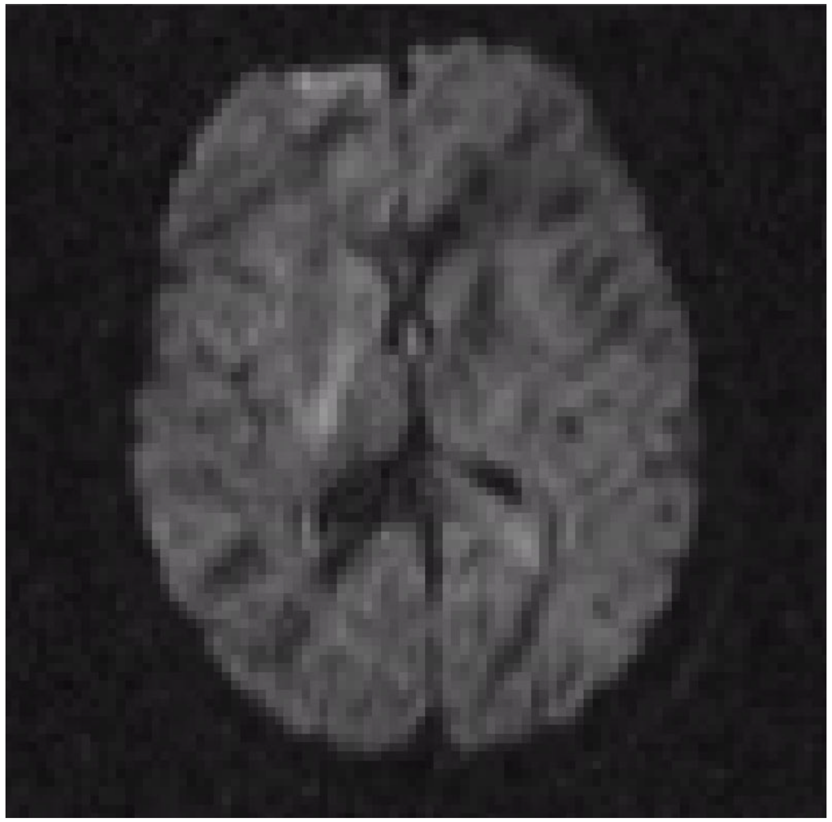
st. deviation of displacements

[Stejskal & Tanner, 1965]

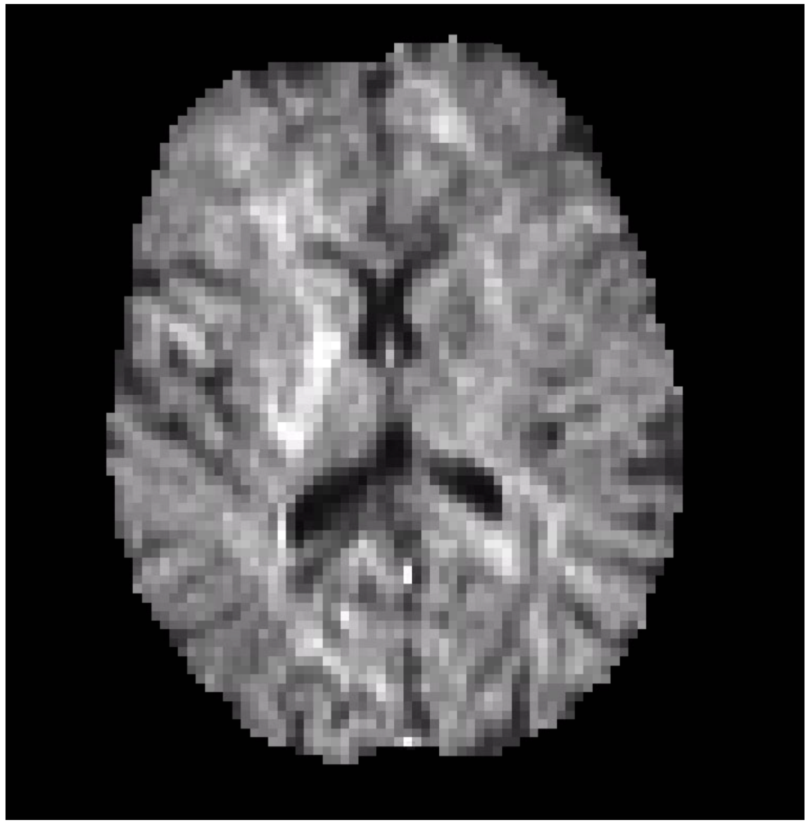
Measuring Diffusion with MRI: Diffusion MRI (dMRI)

T2w Image
No Diffusion-weighting
(G=0)
S_0

Diffusion-weighted
Image
S



Ratio
S/S_0



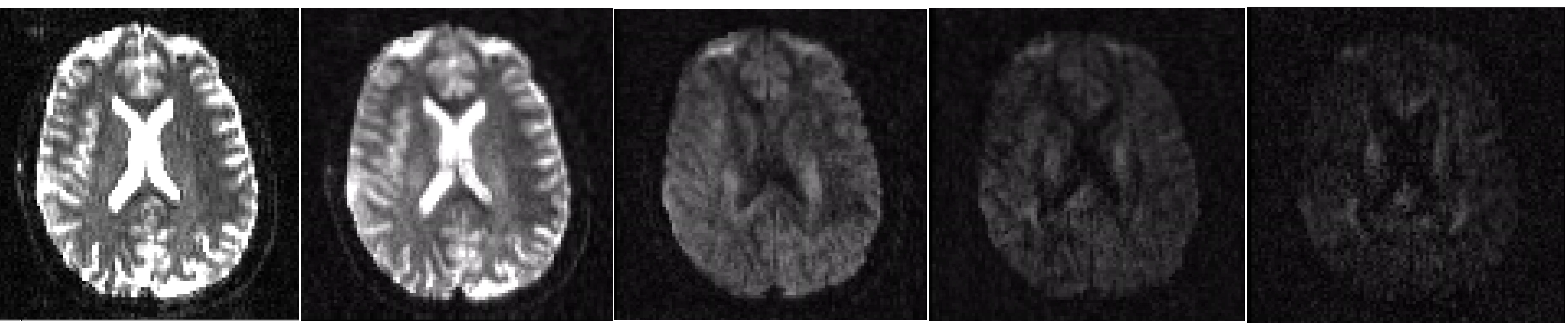
Removes T2w contrast

Measuring Diffusion with MRI:
Diffusion MRI (dMRI)

Diffusion contrast can be modulated by:
A) Diffusion weighting: Gradient **strength,** Diffusion **time**

b value ~ G^2 . DiffTime   (units in s/mm^2)

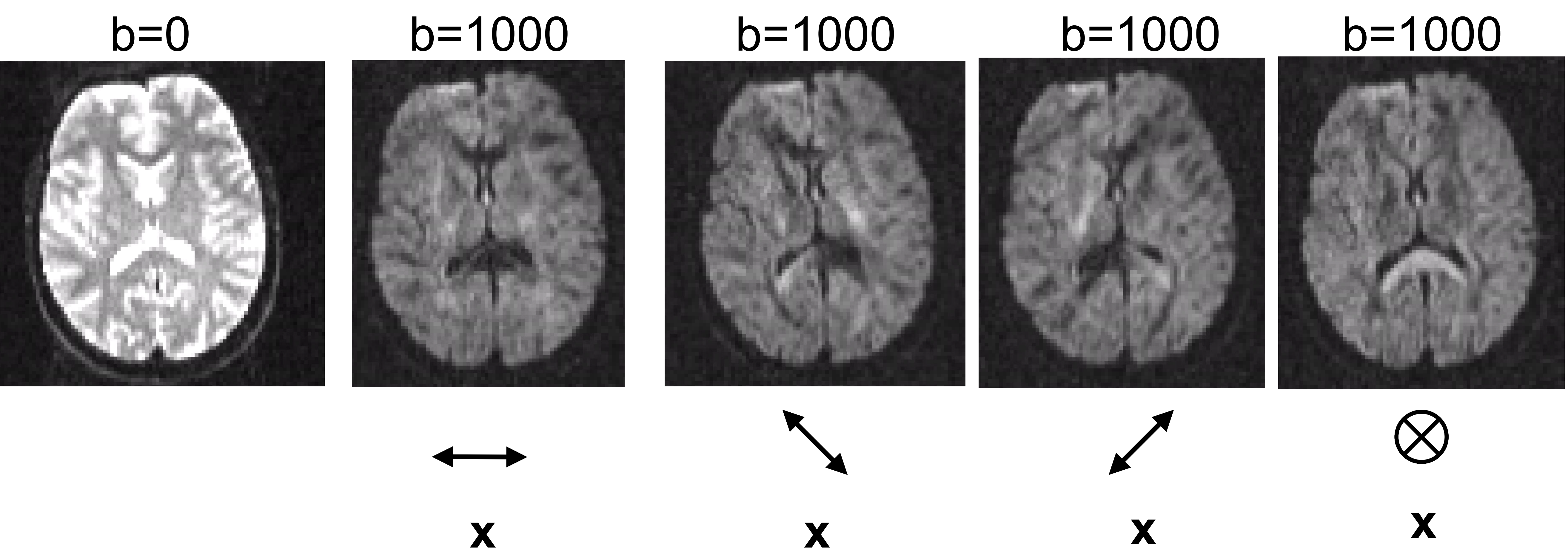
b=0   b=300   b=1000   b=2000   b=3000



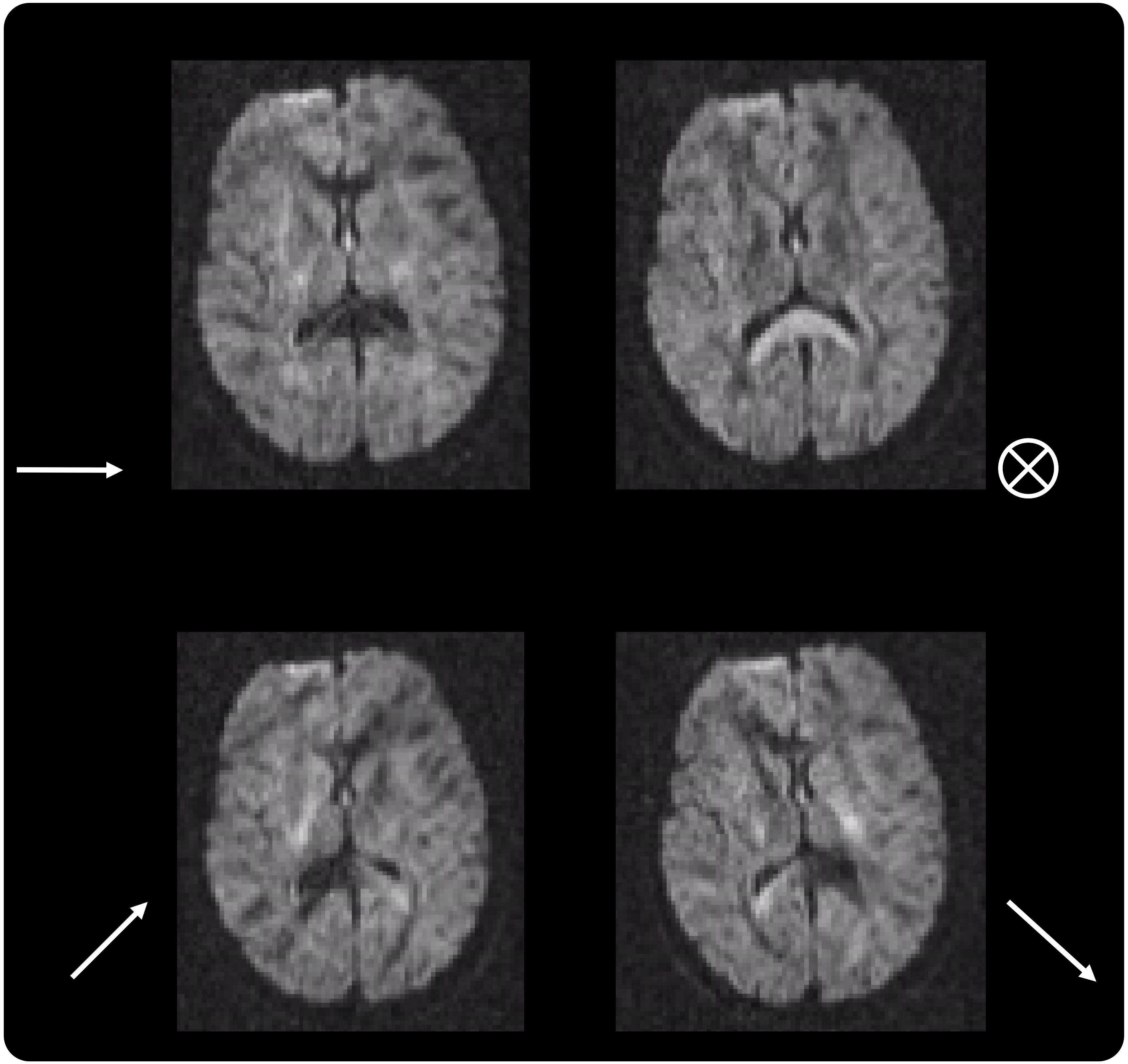
More diffusion contrast with higher b :)
…But less signal left - exponential decay :(

Measuring Diffusion with MRI:
Diffusion MRI (dMRI)

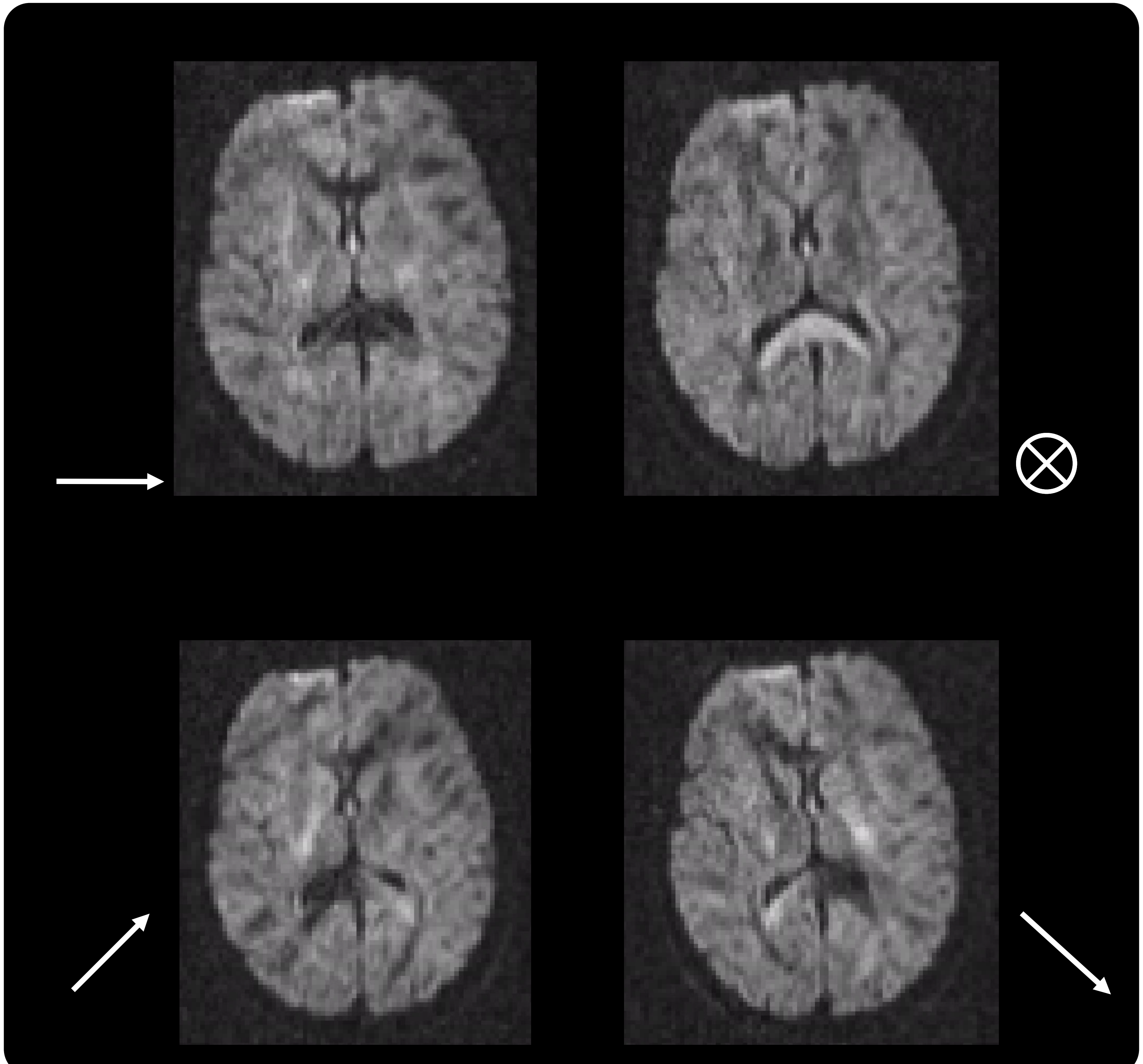
Diffusion contrast can be modulated by:
B) Gradient Direction x



Orientation Contrast in dMRI



Orientation Contrast in dMRI



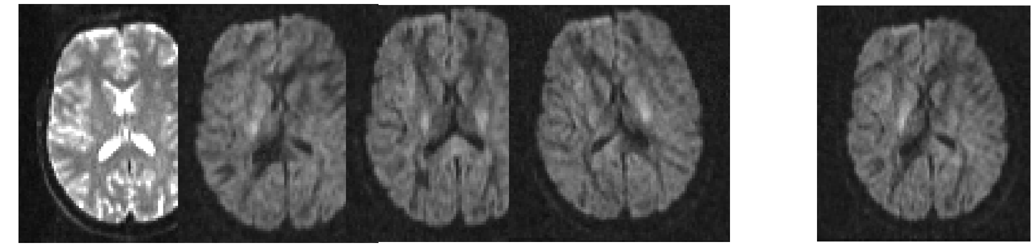
Because diffusion is anisotropic in WM, applying a gradient G along different directions **x**, gives different contrast in WM.

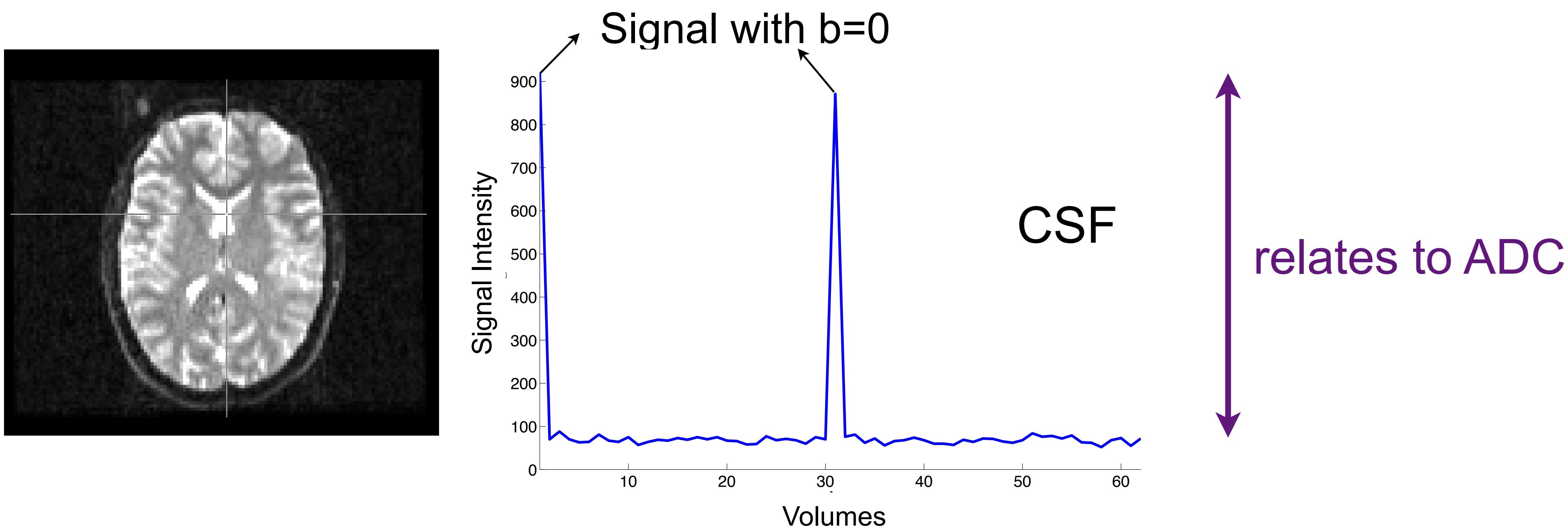
Anisotropic measurements in WM!

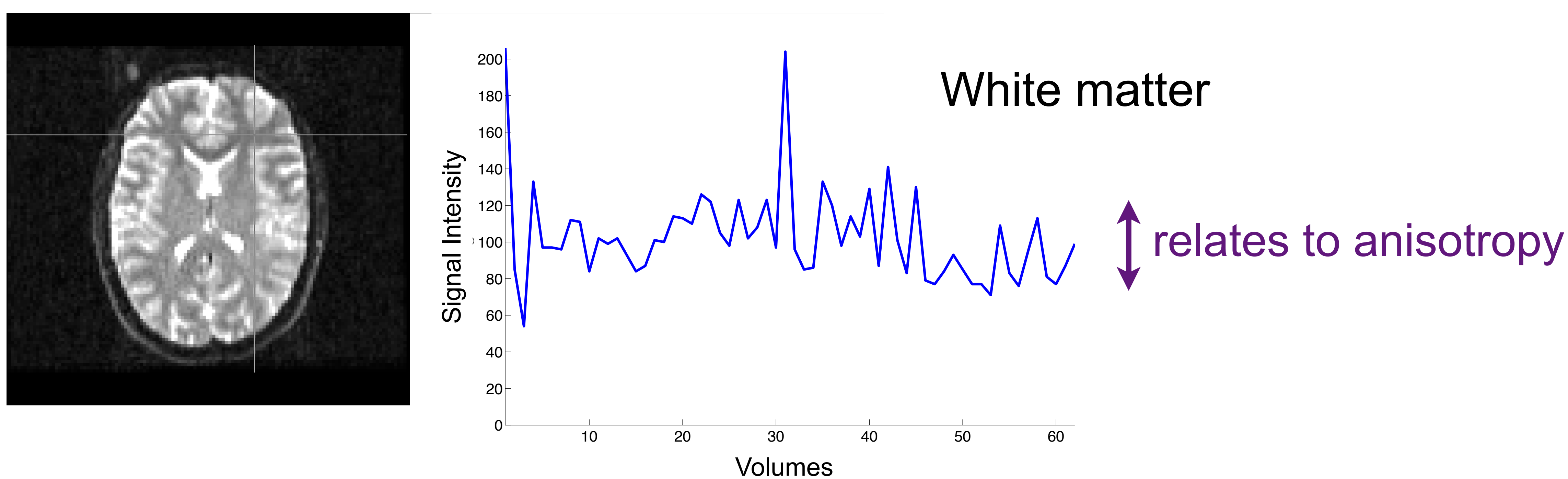
Roughly **Isotropic** in GM and CSF.

A Typical dMRI Protocol

- Normally a few (at least one) b=0 volumes acquired, along with volumes at higher b (~1000 s/mm²).
- Different gradient directions are applied for the high b volumes.







dMRI Summary

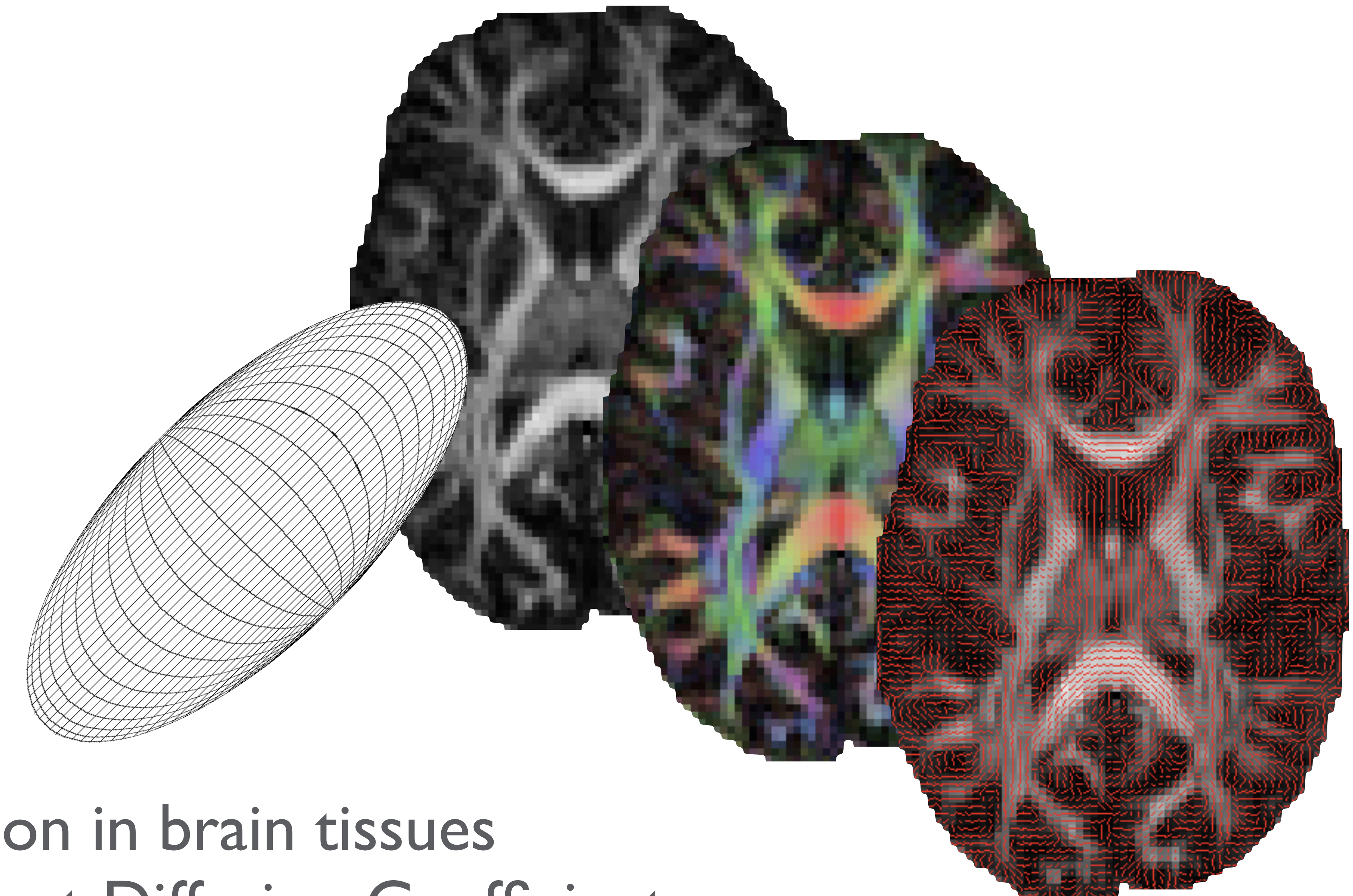
- Images acquired with a Gradient along **x**, have contrast that is sensitive to diffusion of water molecules along **x**.

- 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.

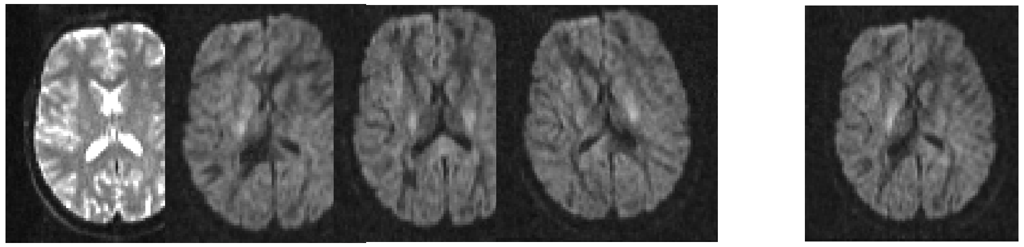
Diffusion Tensor Imaging - basic principles



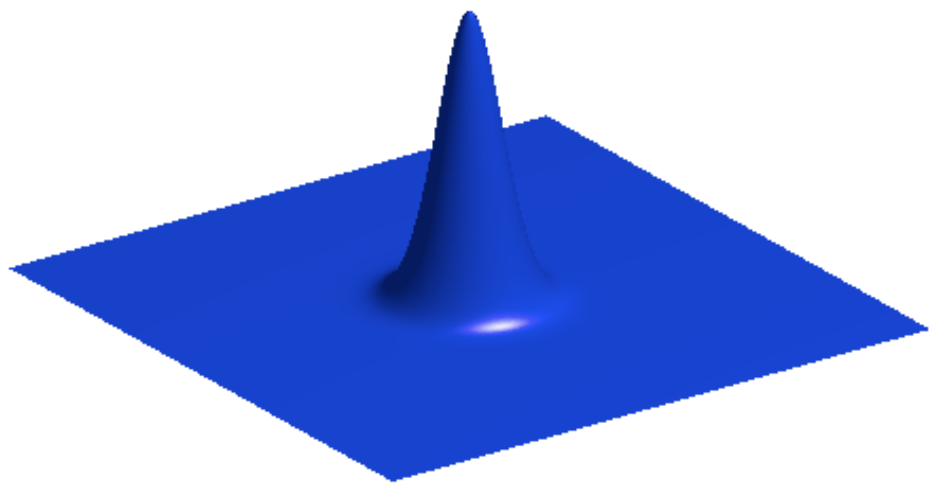
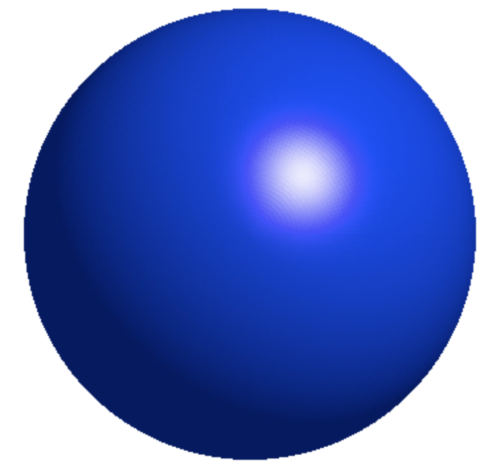
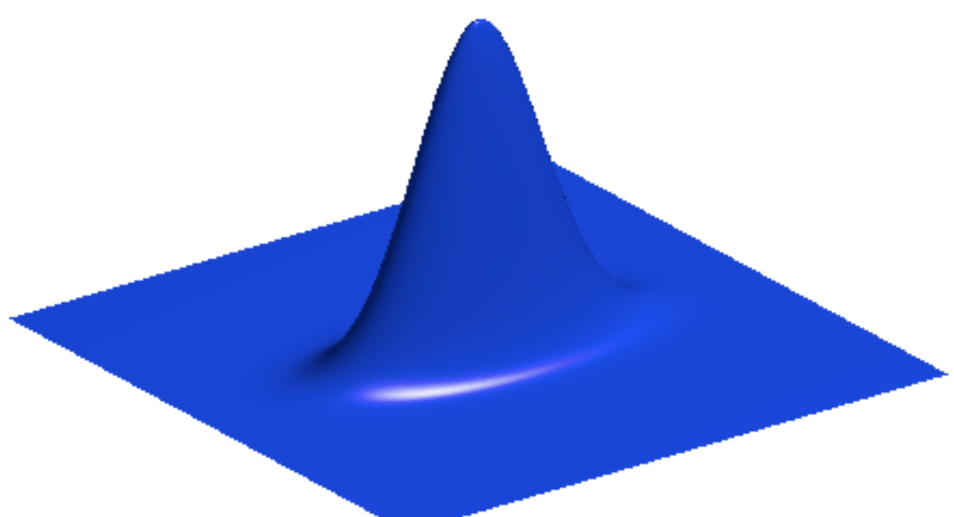
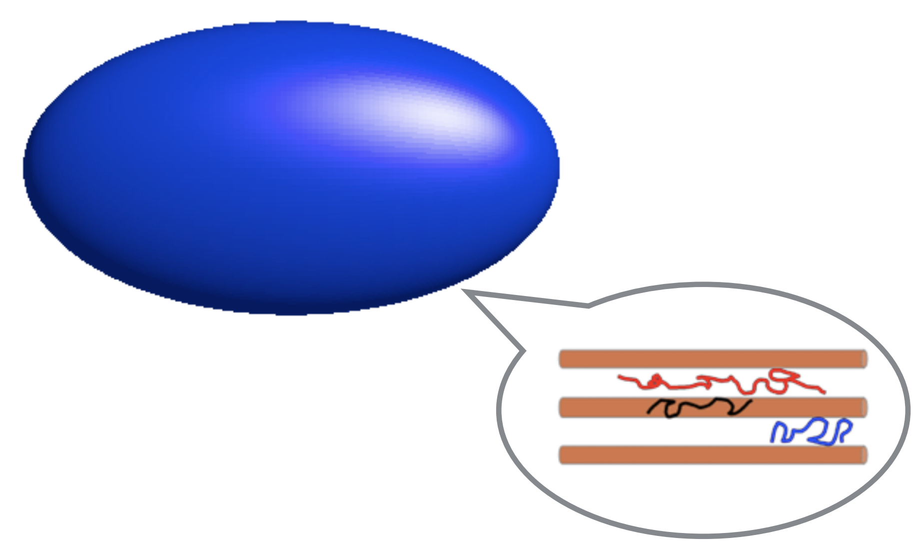
- Diffusion in brain tissues
- Apparent Diffusion Coefficient
- Diffusion Tensor model
- Tensor-derived measures

Diffusion Tensor Imaging (DTI)

- Apply **the diffusion tensor model** to a set of dMRI 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:

b-value for gradient *j* (known)

Unit vector representing the direction of gradient *j* (known)

$$\boxed{S_j = S_0 \exp(-b_j \, \boldsymbol{x}_j^T \, \boldsymbol{D} \, \boldsymbol{x}_j)}$$

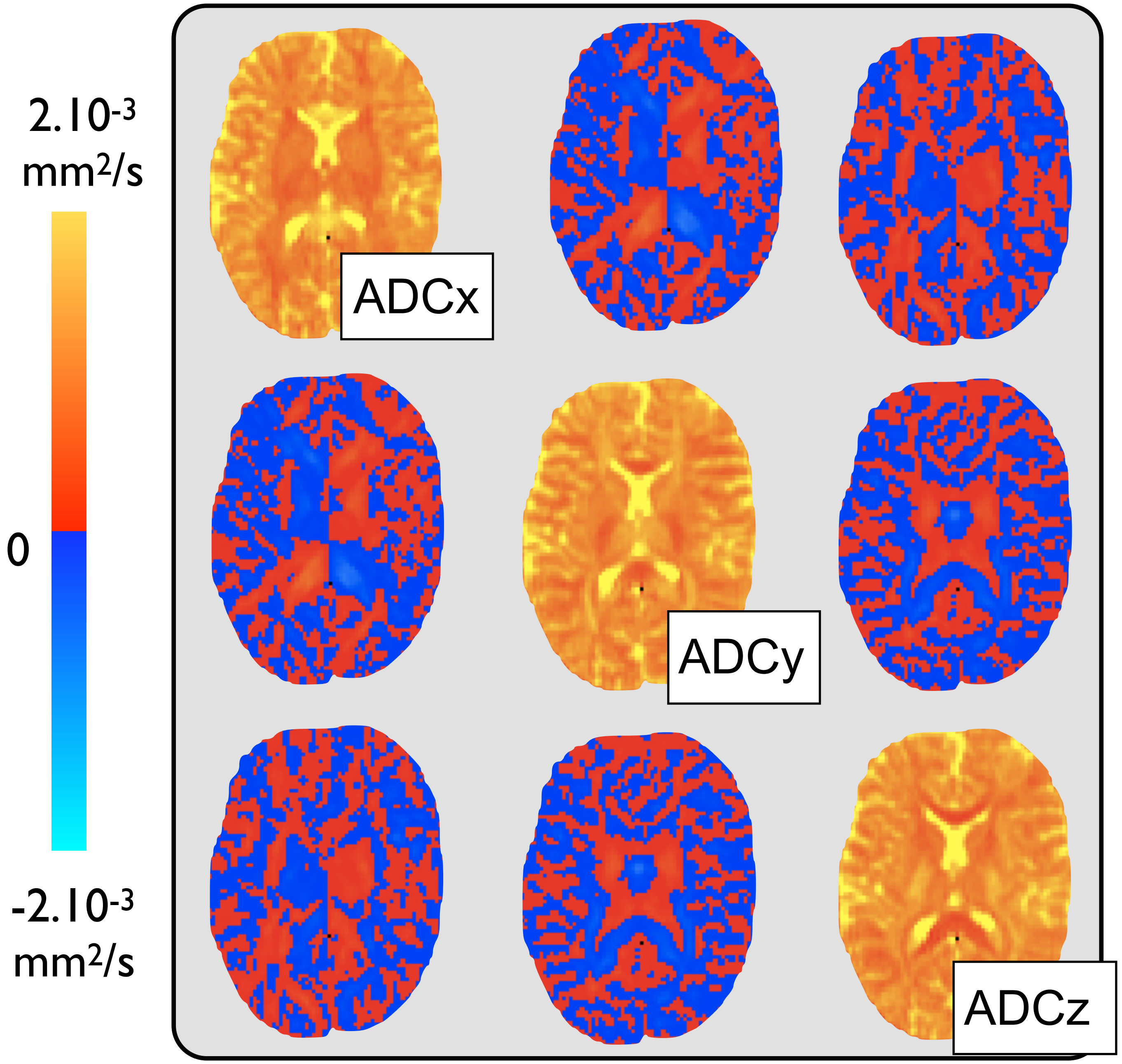
Signal measured after applying a Gradient *j* with direction $\boldsymbol{x}_j$ and b-value b_j (measured)

Signal measured with no diffusion gradient applied

3x3 Diffusion Tensor (unknown)

[Basser, Biophys J,1994], [Basser et al , J Magn Res, 1994]

The Elements of the Diffusion Tensor



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

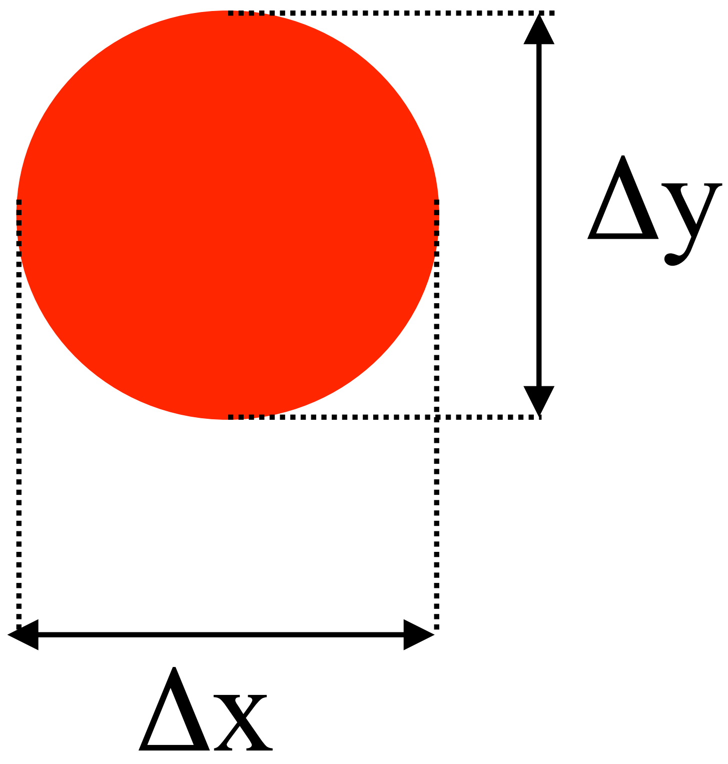
- Tensor is **symmetric** (6 unknowns)

- **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

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

Why do we need a tensor?



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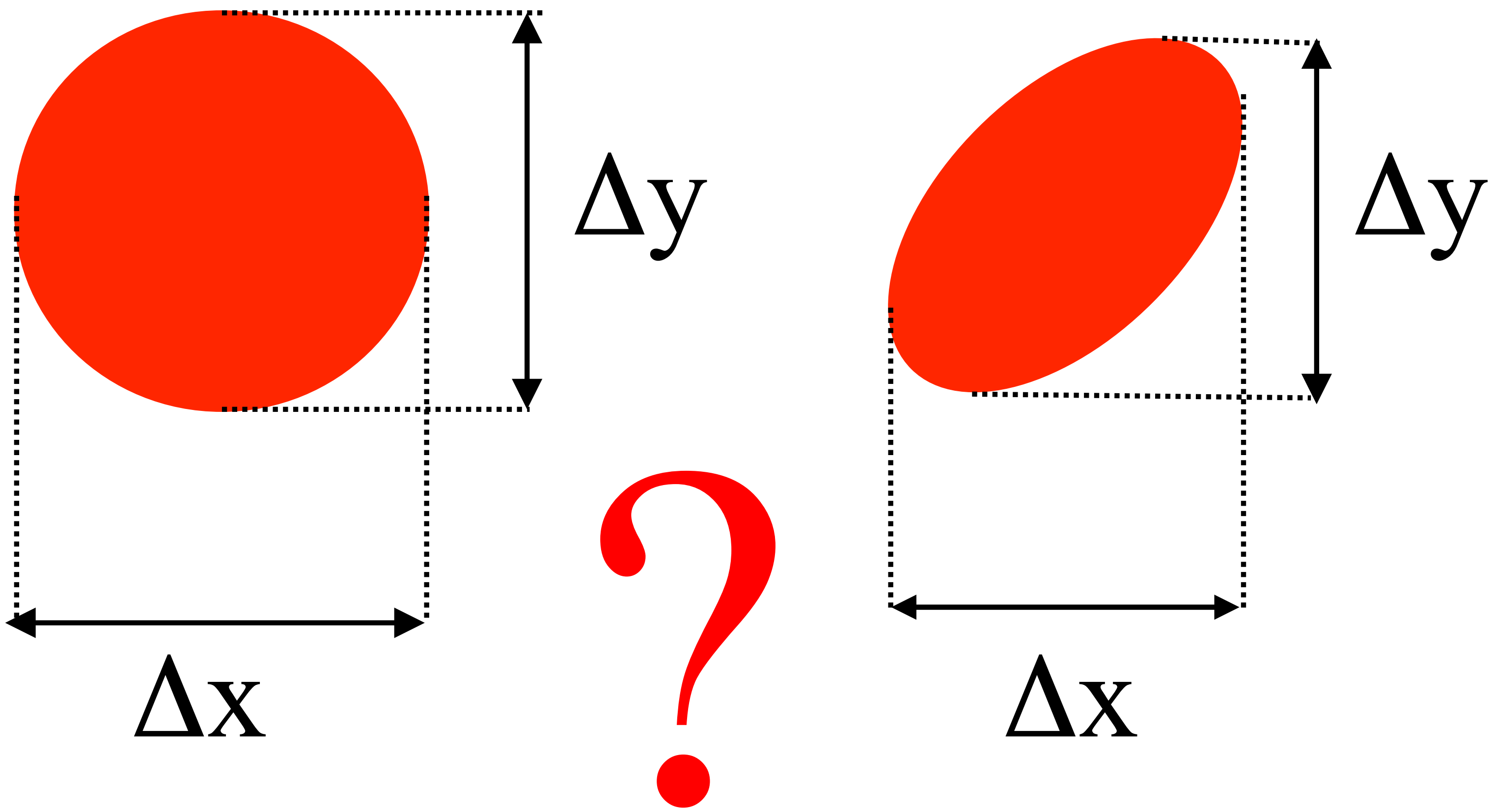

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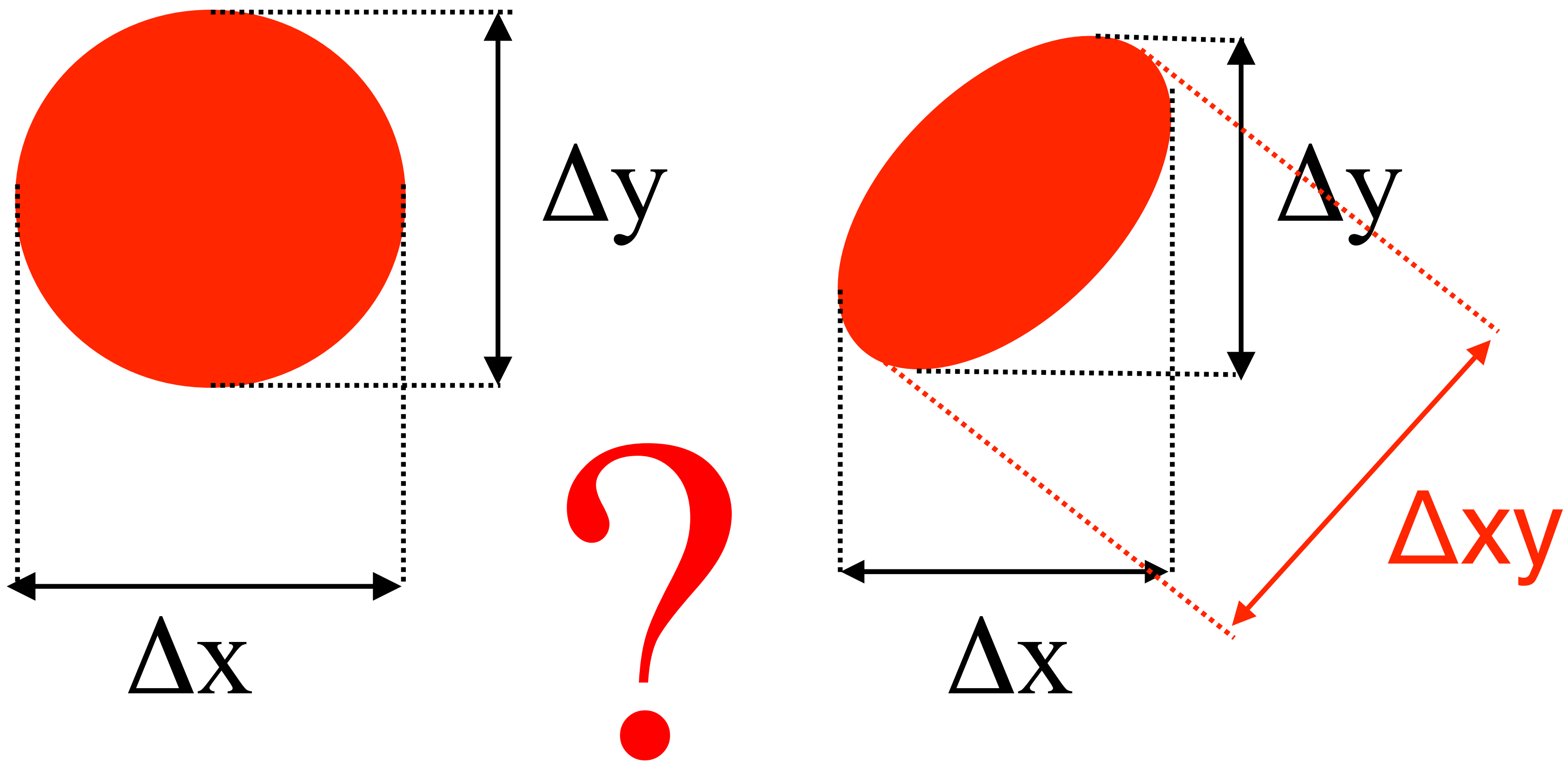
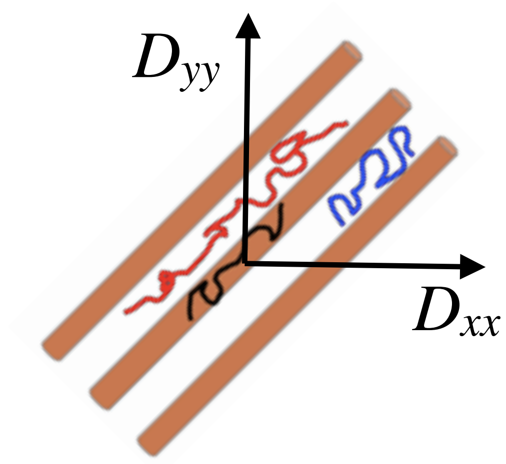


$$\begin{bmatrix} D_x & D_{xy} \\ D_{xy} & D_y \end{bmatrix}$$

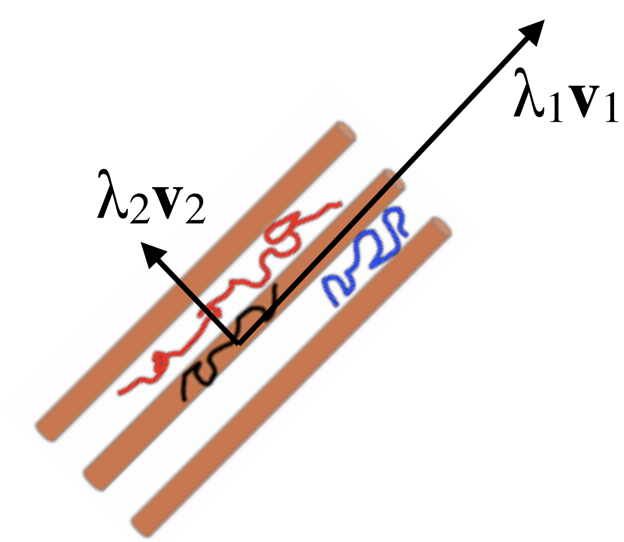
The Diffusion Tensor Eigenspectrum

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



Once 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



$$\mathbf{D} = [\mathbf{v_1}|\mathbf{v_2}|\mathbf{v_3}]^{\mathrm{T}} \begin{bmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{bmatrix} [\mathbf{v_1}|\mathbf{v_2}|\mathbf{v_3}]$$

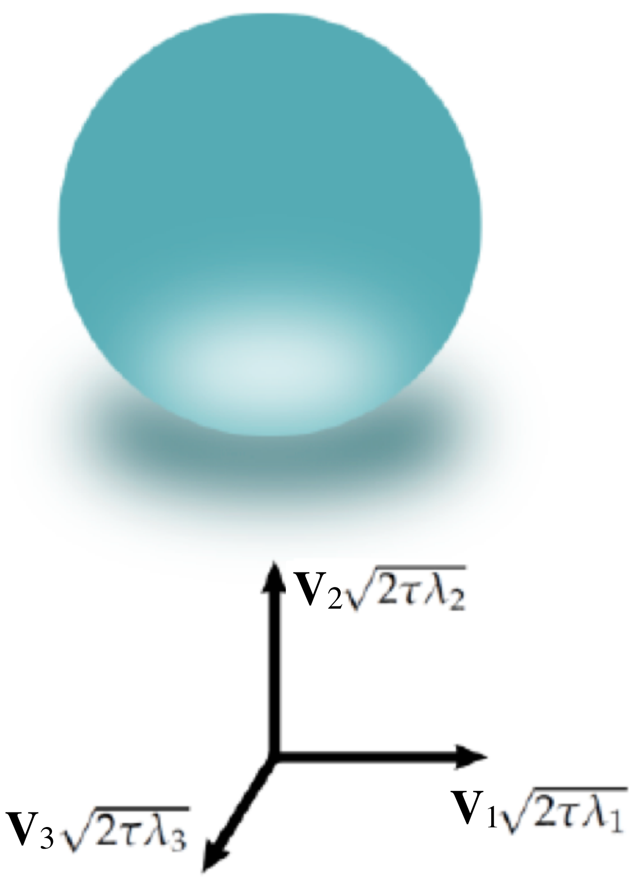
eigenvalues: ADCs along $\mathbf{v}_1,\mathbf{v}_2,\mathbf{v}_3$

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

The Diffusion Tensor Ellipsoid

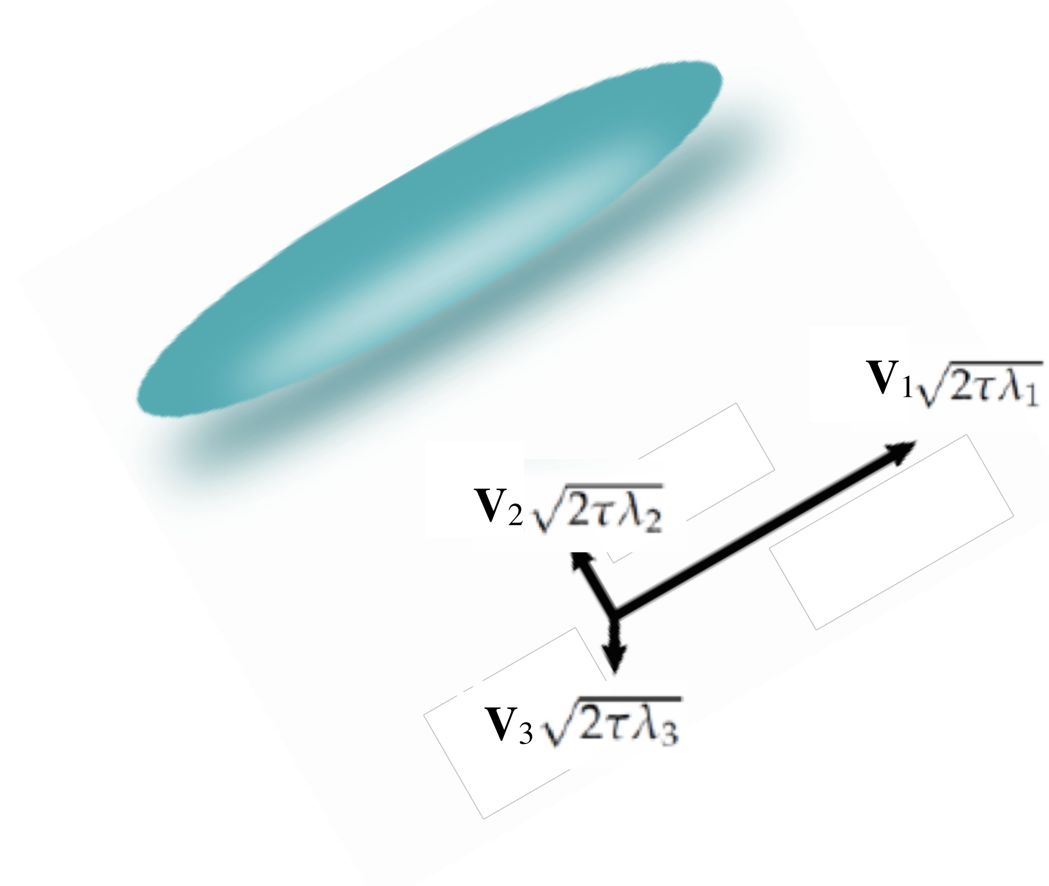
Isotropic voxel

$\lambda_1 \approx \lambda_2 \approx \lambda_3$

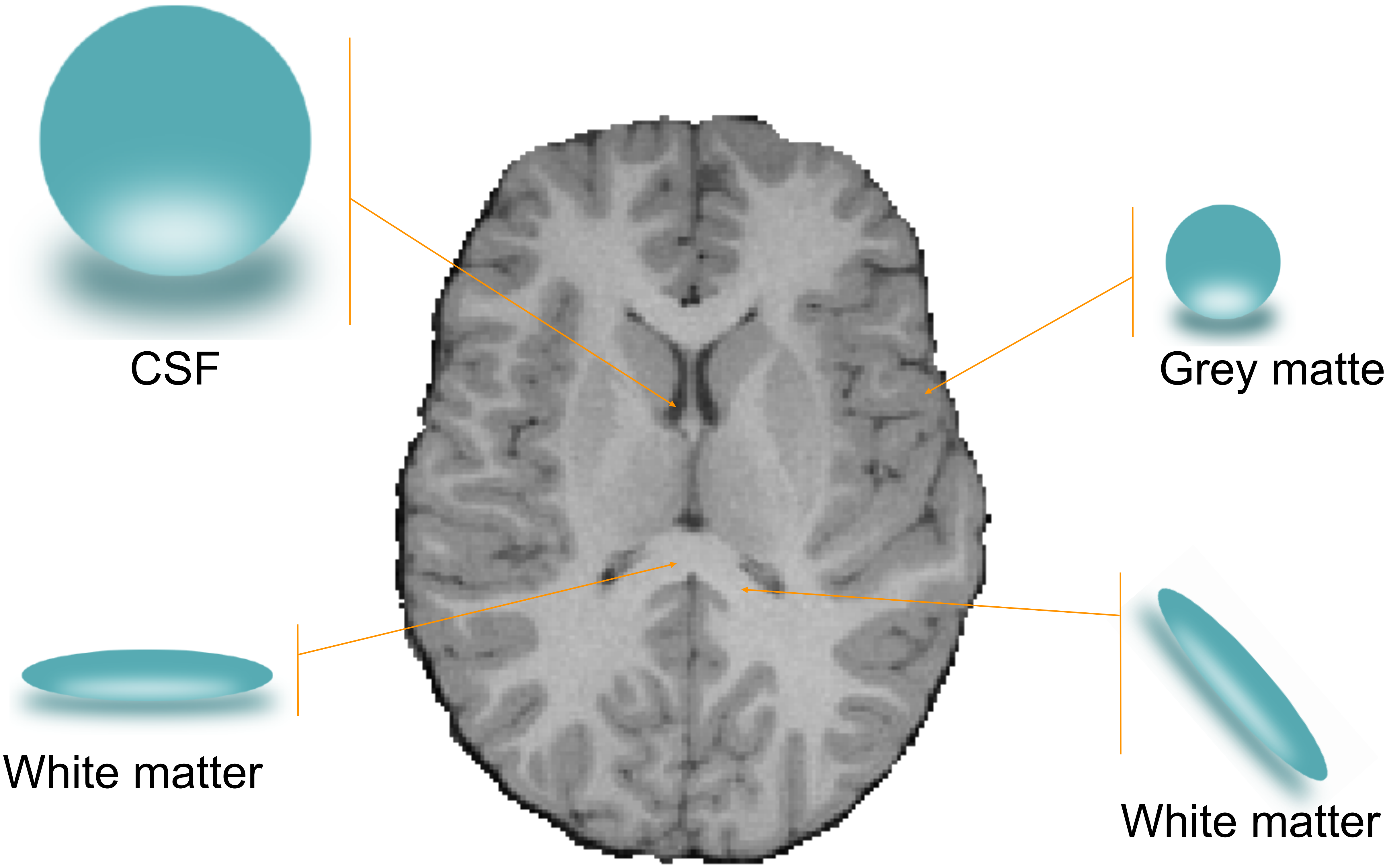


Anisotropic voxel

$\lambda_1 \gg \lambda_2, \lambda_3$



The Diffusion Tensor Ellipsoid



Quantitative Diffusion Maps

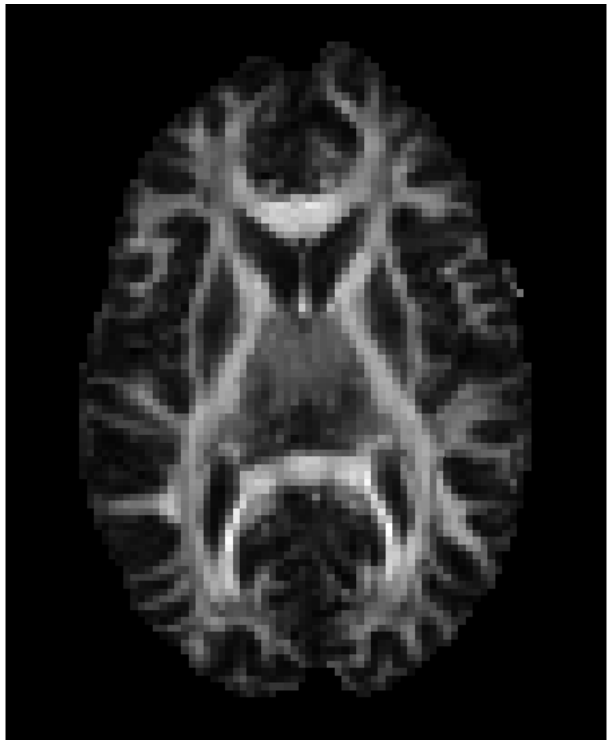
Fractional Anisotropy (FA) ~ Eigenvalues Variance (normalised)
Mean Diffusivity (MD) = Eigenvalues Mean

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

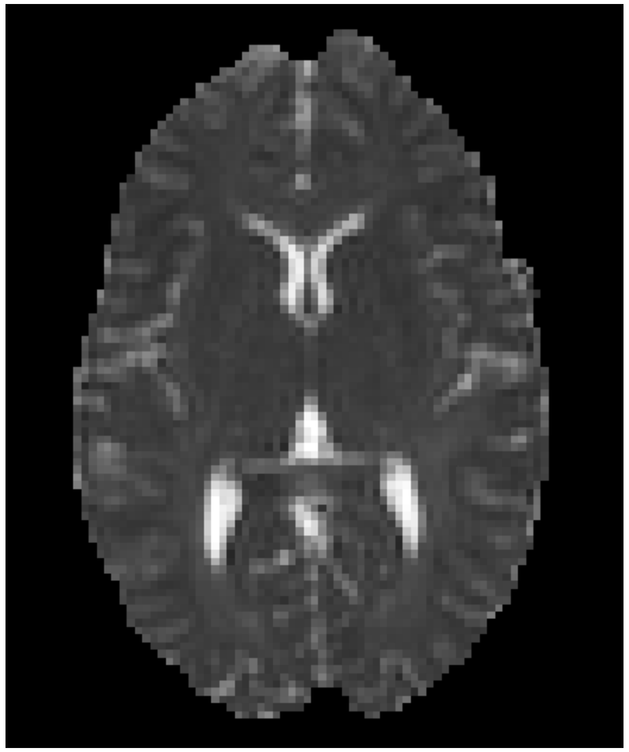
$$MD = \frac{D_{xx} + D_{yy} + D_{zz}}{3} = \frac{\lambda_1 + \lambda_2 + \lambda_3}{3}$$

Quantitative Diffusion Maps

FA

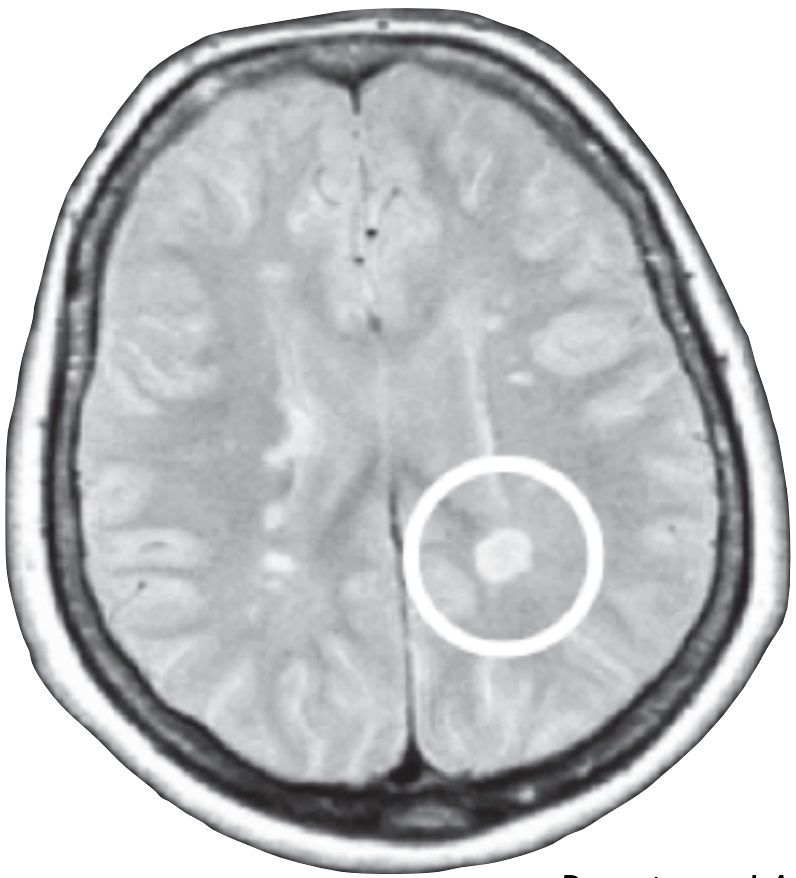


MD

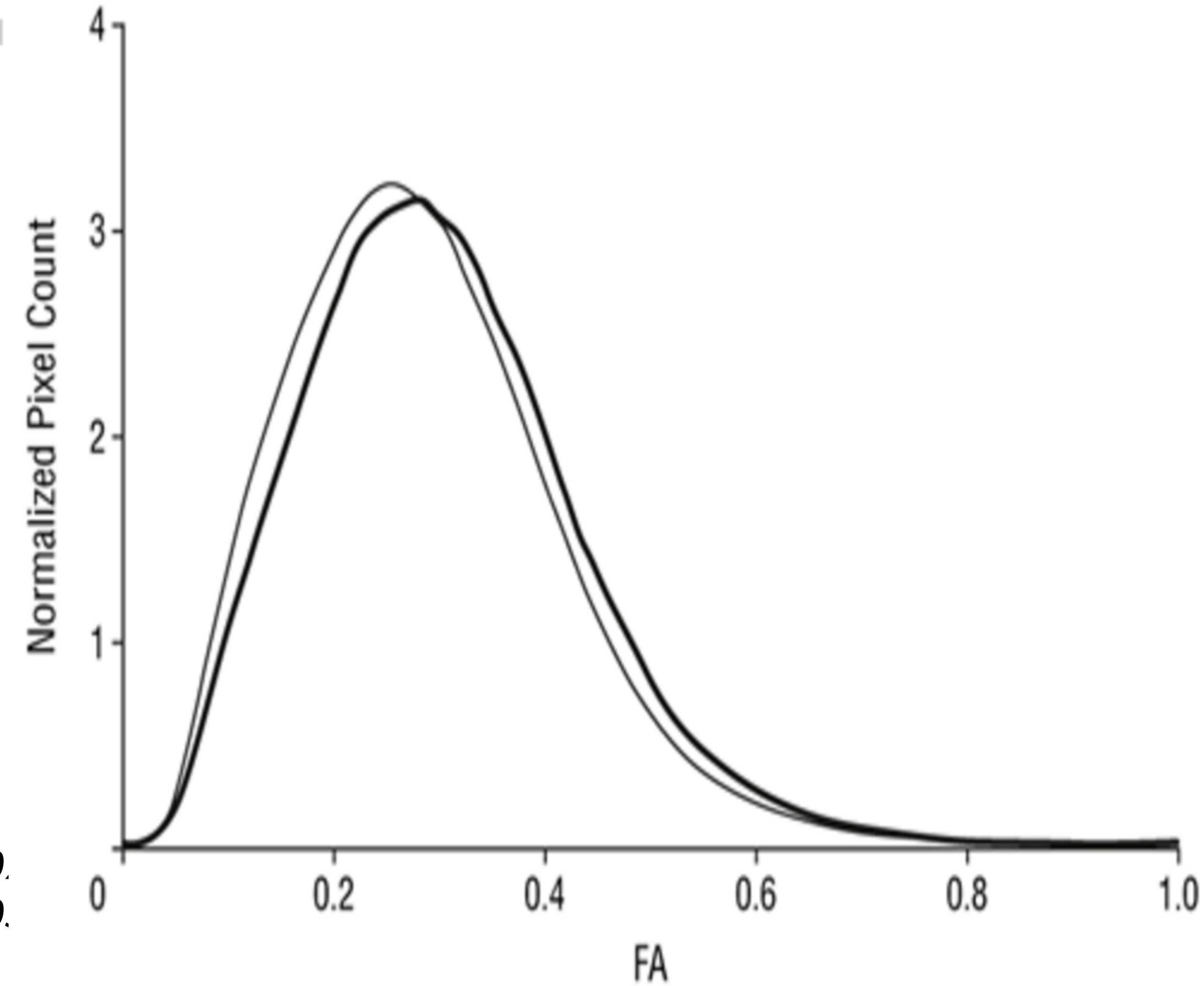


Quantitative Diffusion Maps

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



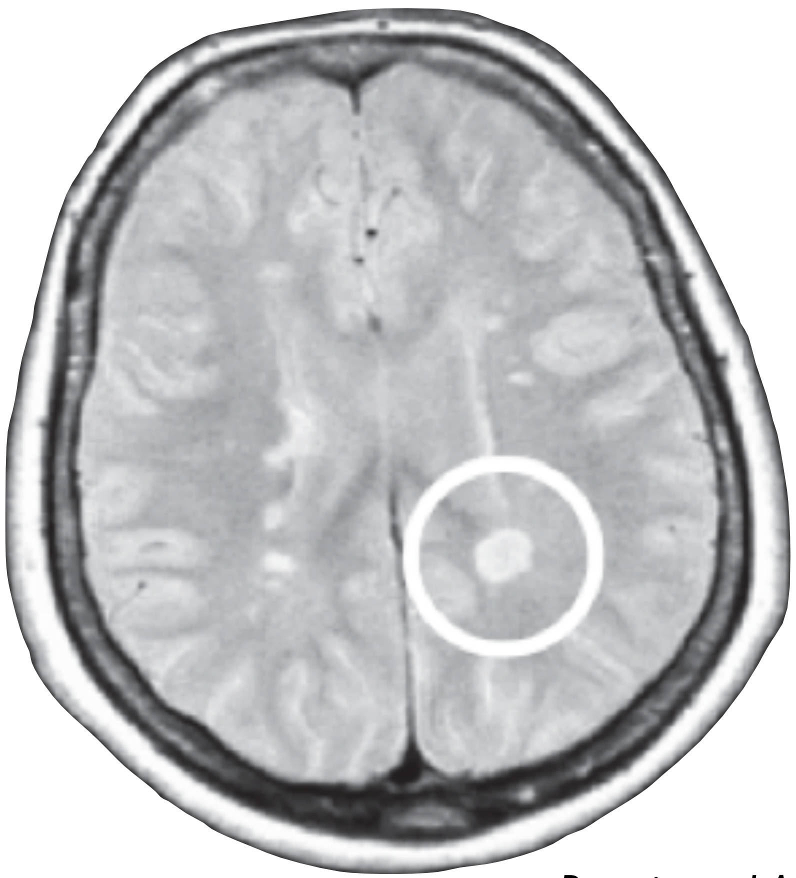
Rovaris et al, Arch Neurol 200.
Gallo et al, Arch Neurol 200.



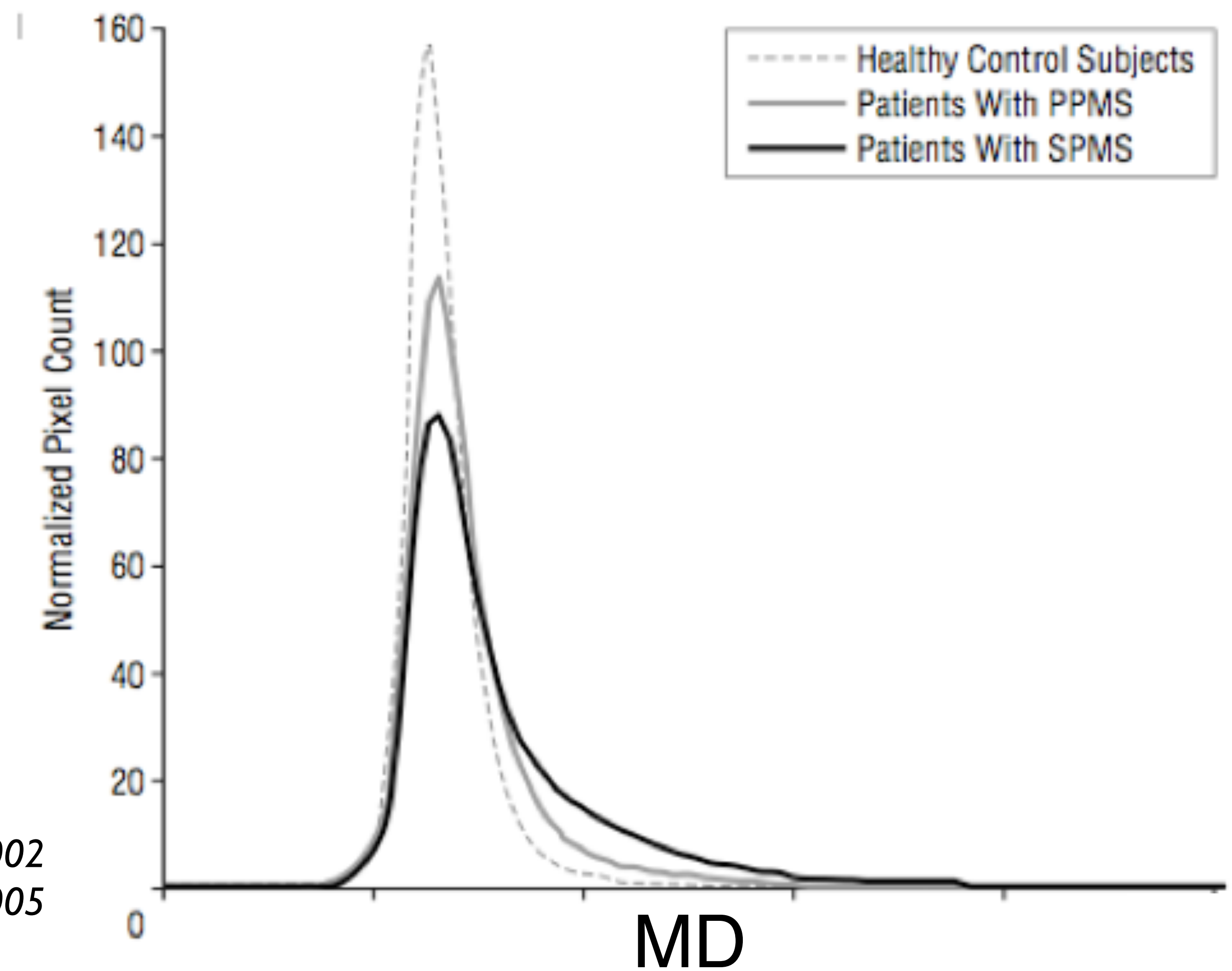
Fractional Anisotropy changes in MS normal appearing white matter

Quantitative Diffusion Maps

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



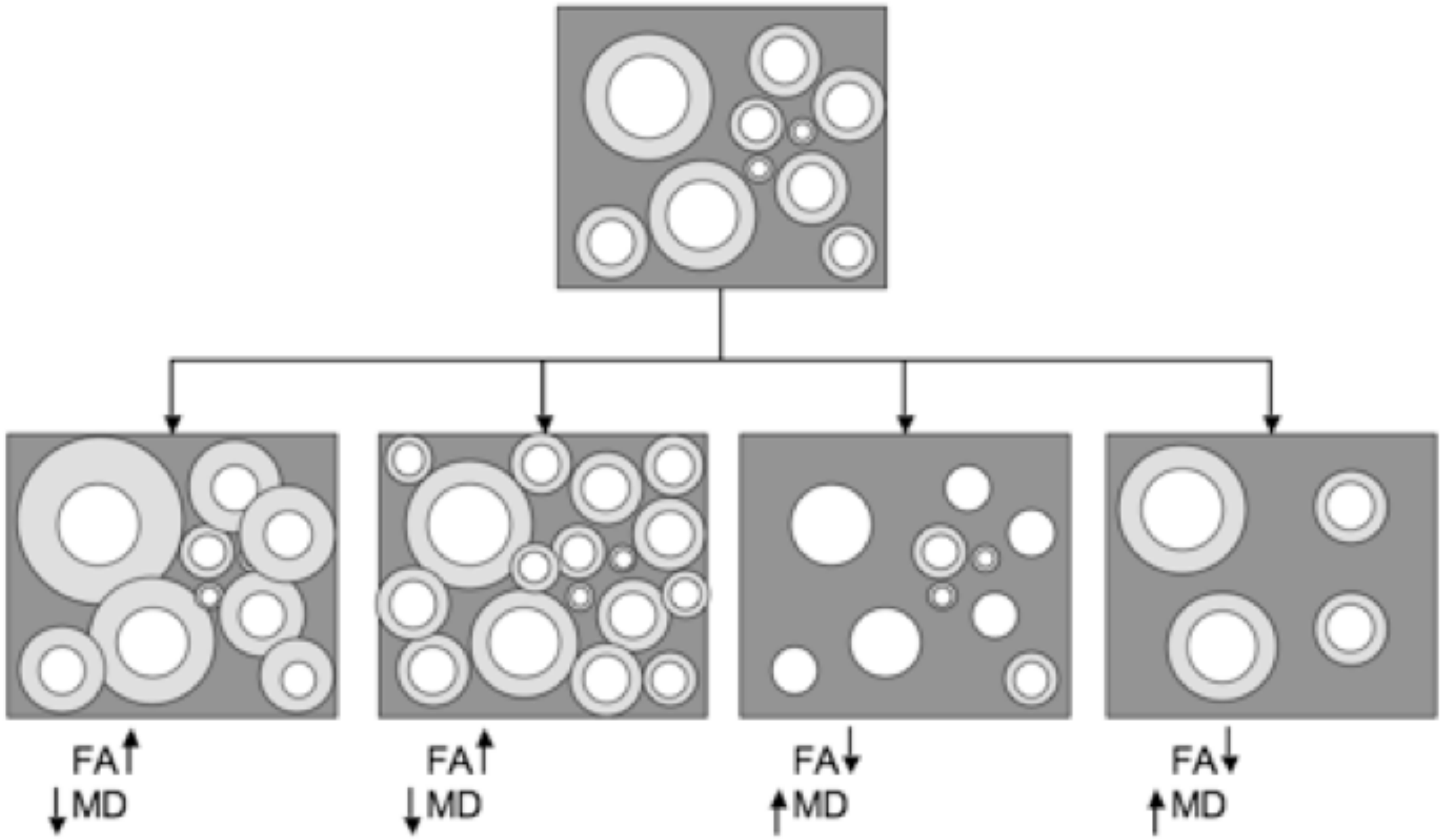
Rovaris et al, Arch Neurol 2002
Gallo et al, Arch Neurol 2005



Fractional Anisotropy changes in MS normal appearing white matter

Quantitative Diffusion Maps

Different scenarios can have same effect on FA, MD



Swelling

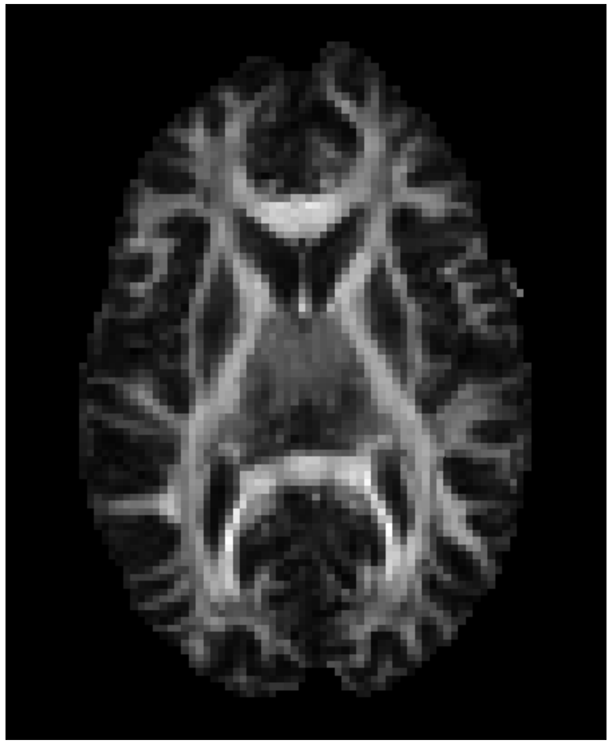
Higher Density

Myelin Loss

Cell Death

Quantitative Diffusion Maps

FA



MD

Longitudinal ADC
(λ_1)

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

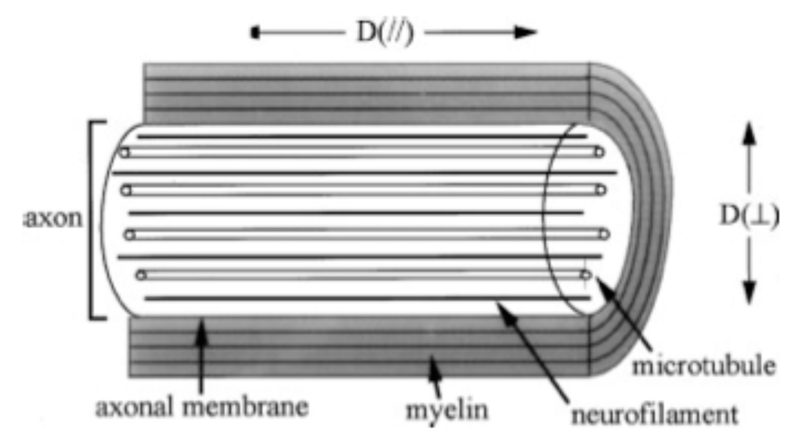
Quantitative Diffusion Maps

FA decrease in WM can be caused:

a) Decrease of longitudinal ADC.
Axonal breakdown?

b) Increase of transverse ADC.
Myelin breakdown?

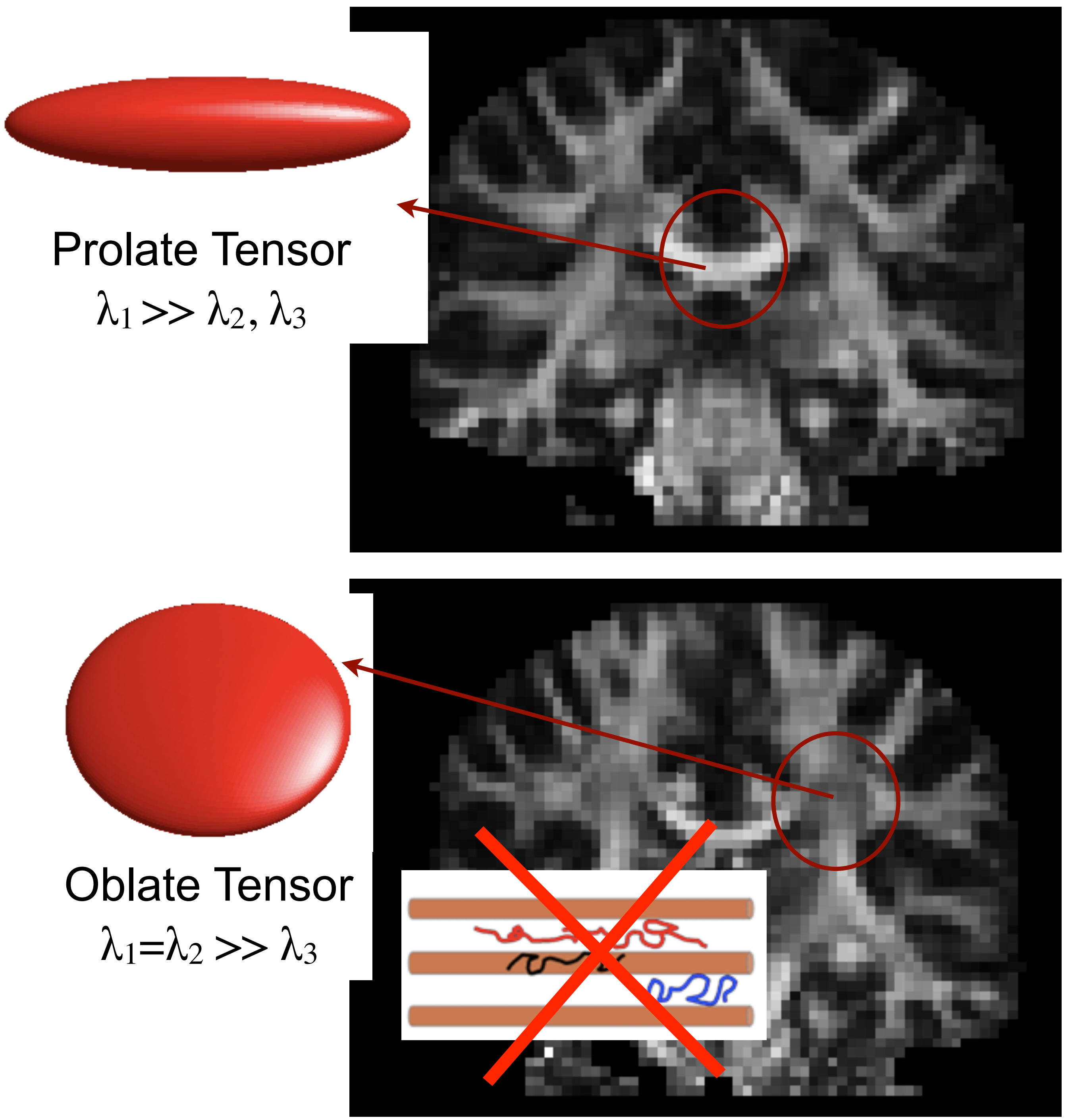
But do not over-interpret your results.
Always keep in mind that the DTI model is an oversimplification of reality



biophysical properties

Tensor and FA in Crossing Regions

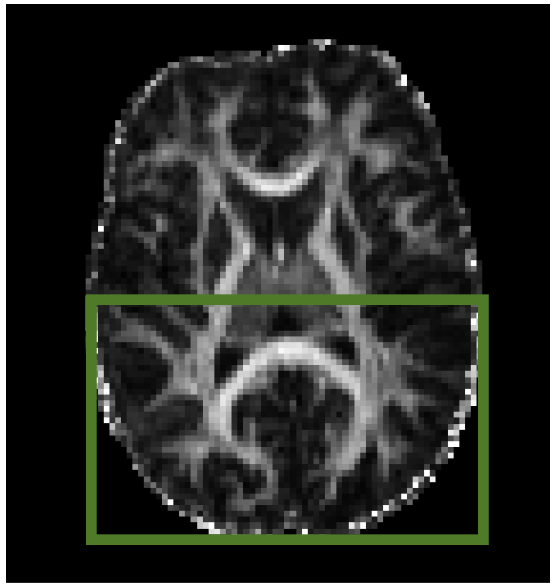
- In voxels containing two crossing bundles, FA is low and the tensor ellipsoid is pancake-shaped (oblate, planar tensor).

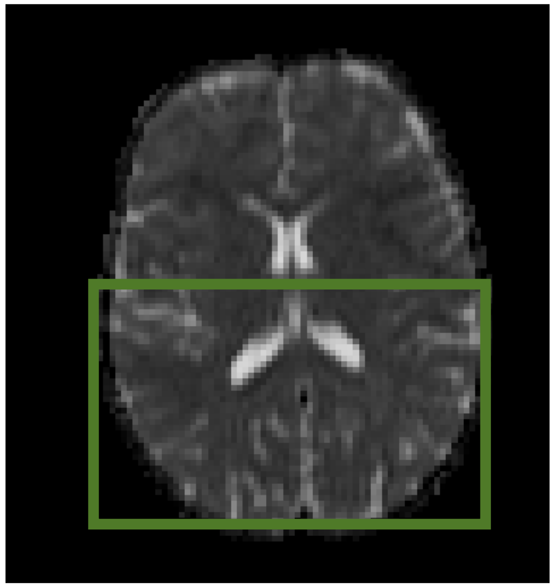


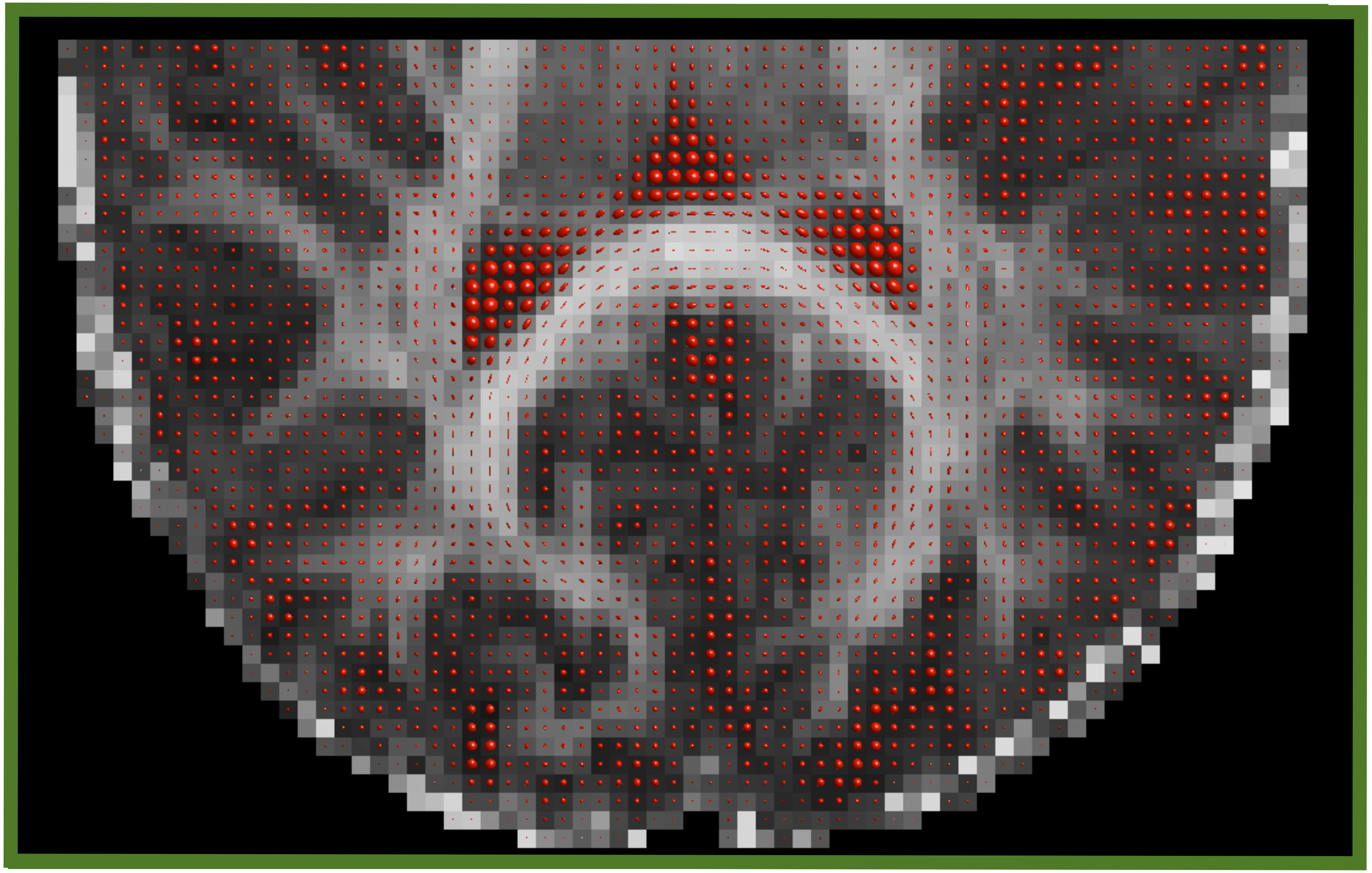
Consequences:

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

Diffusion Tensor Ellipsoids

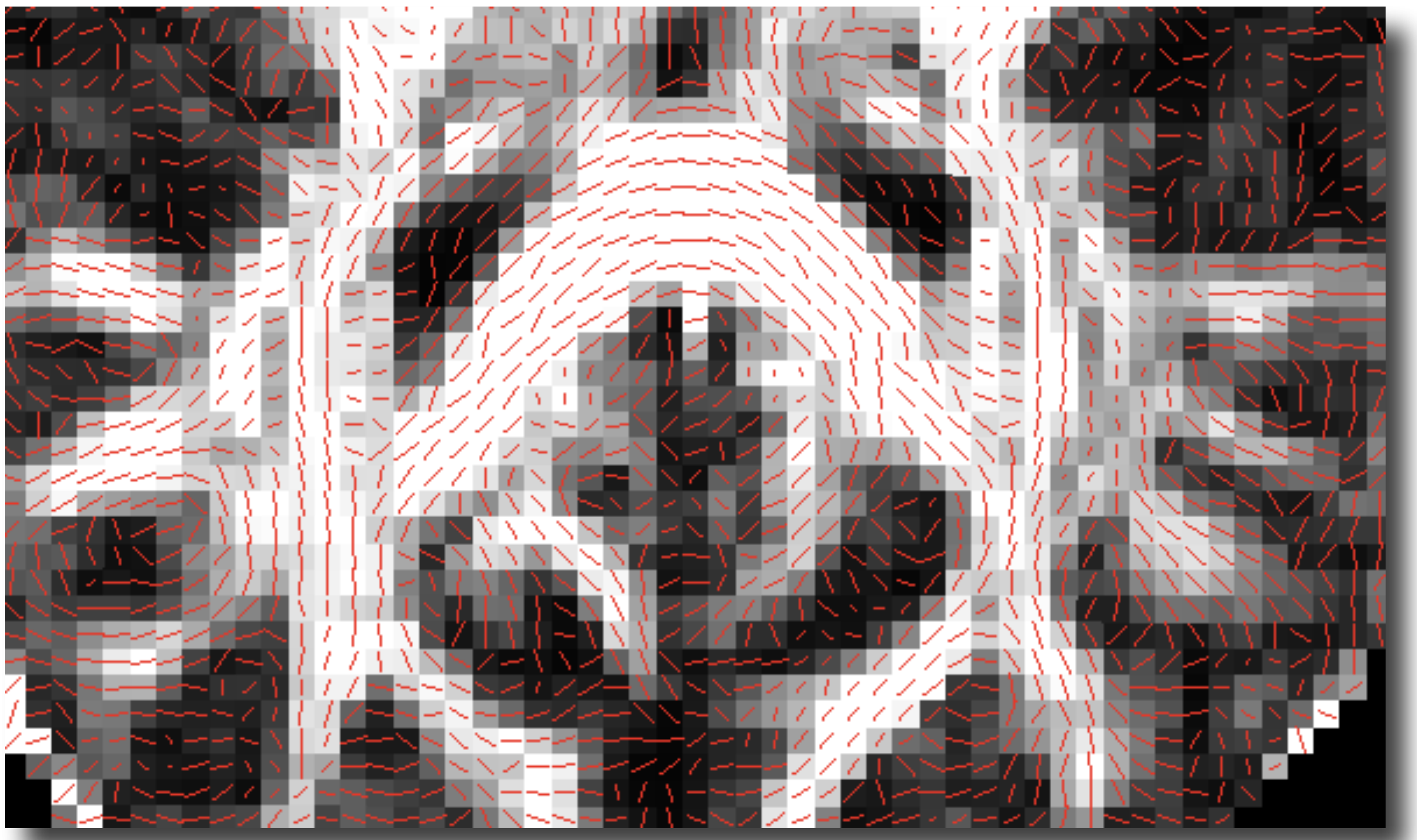




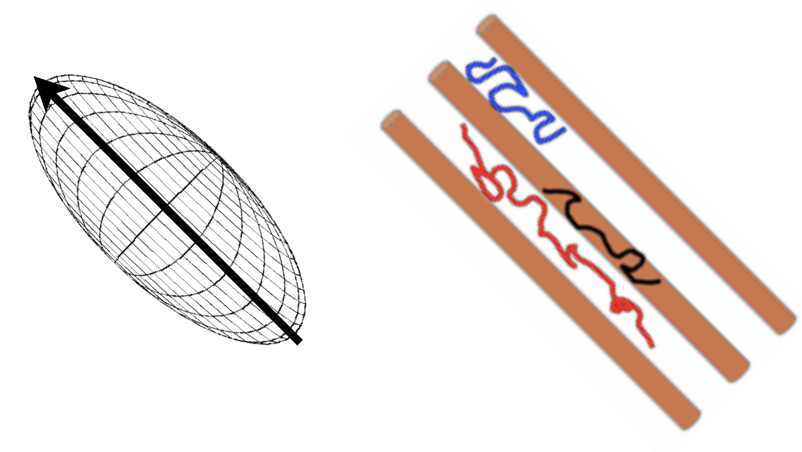


Estimates of Principal Fibre Orientation in WM

$\mathbf{v}_1$ map
Principal Diffusion Direction



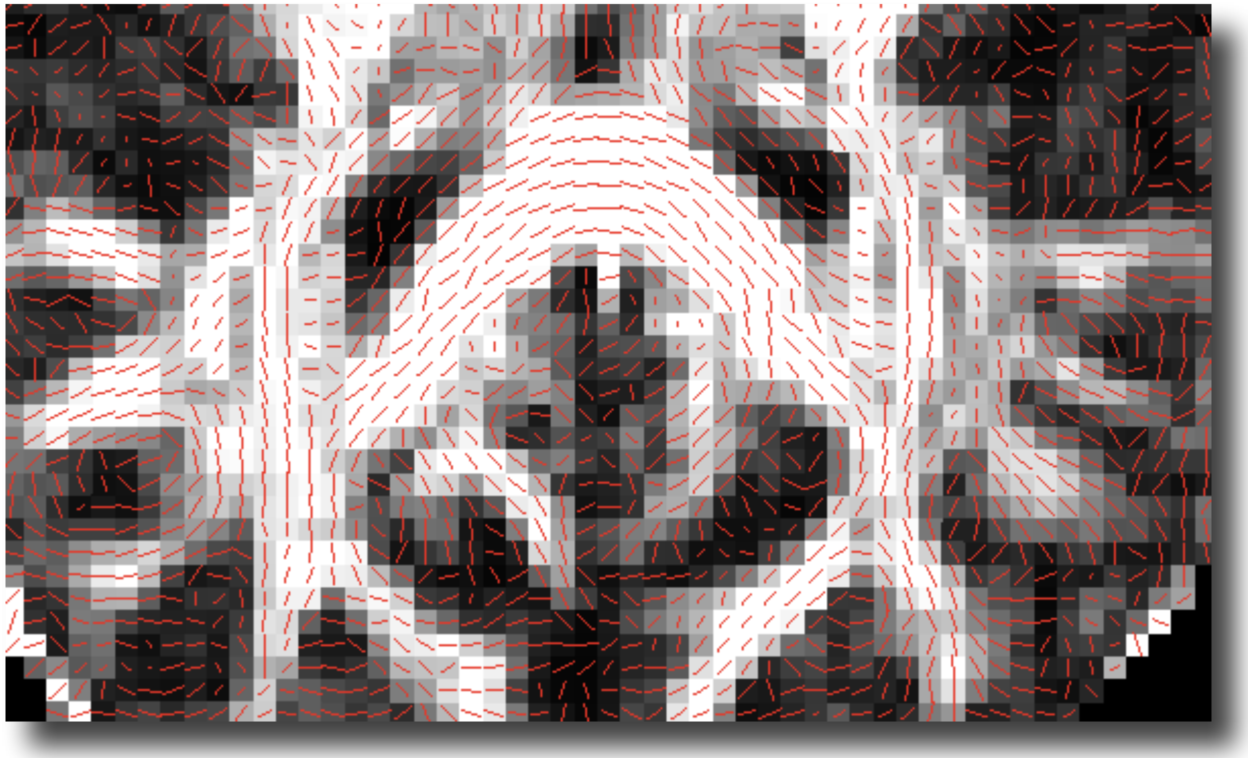
Principal Diffusion Direction

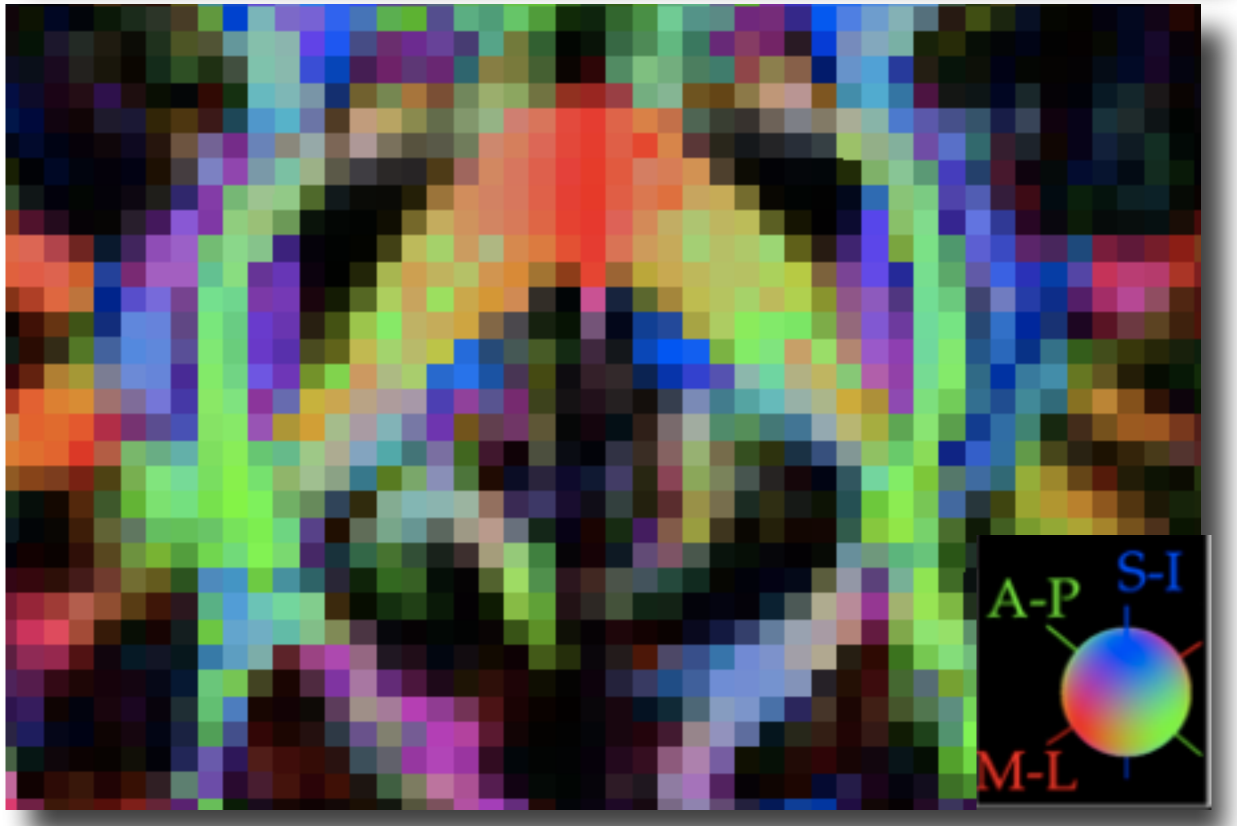


Assumption!!

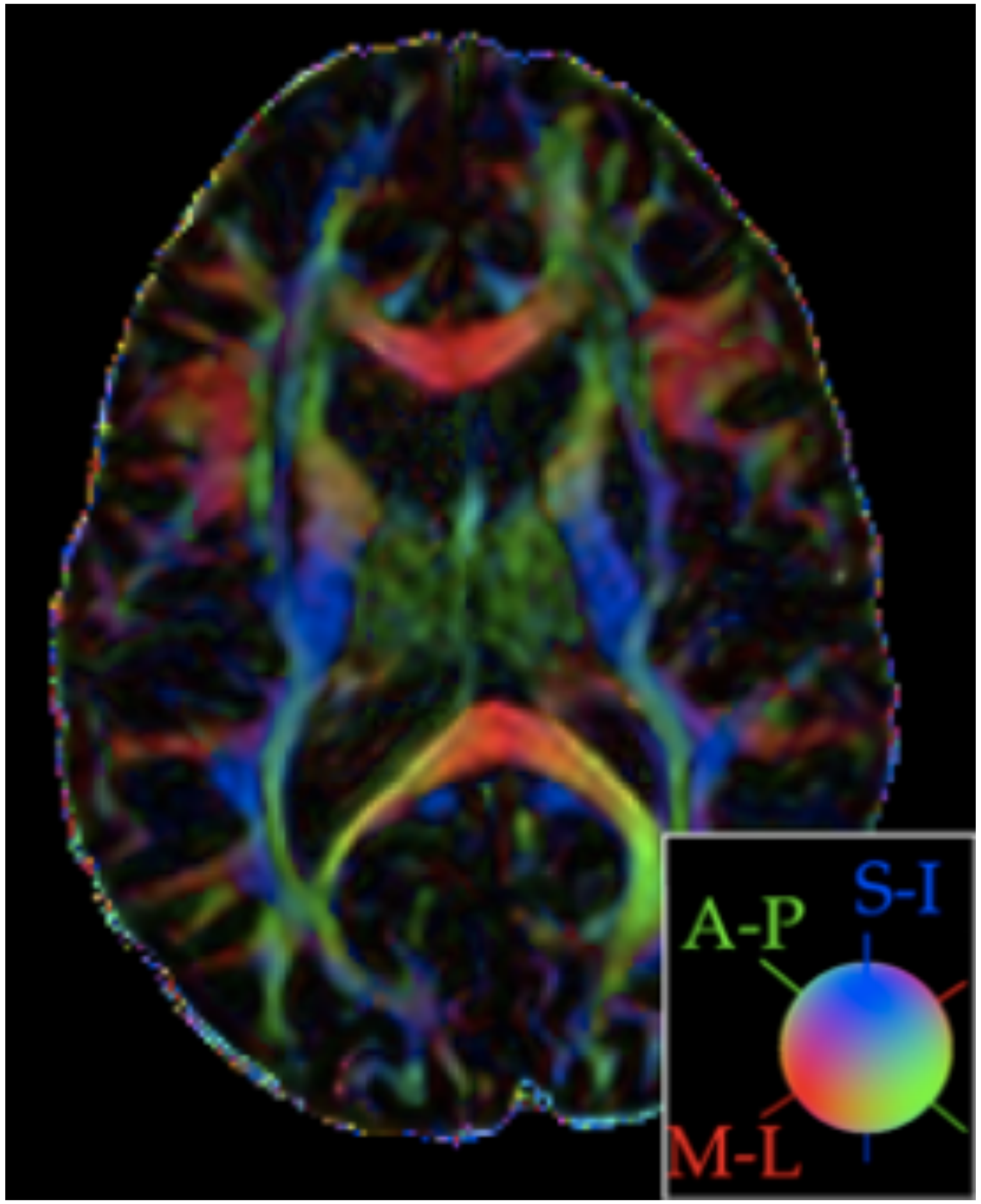
Direction of maximum diffusivity in voxels with anisotropic profile is an **estimate of the major fibre orientation**.

Estimates of Principal Fibre Orientation in WM

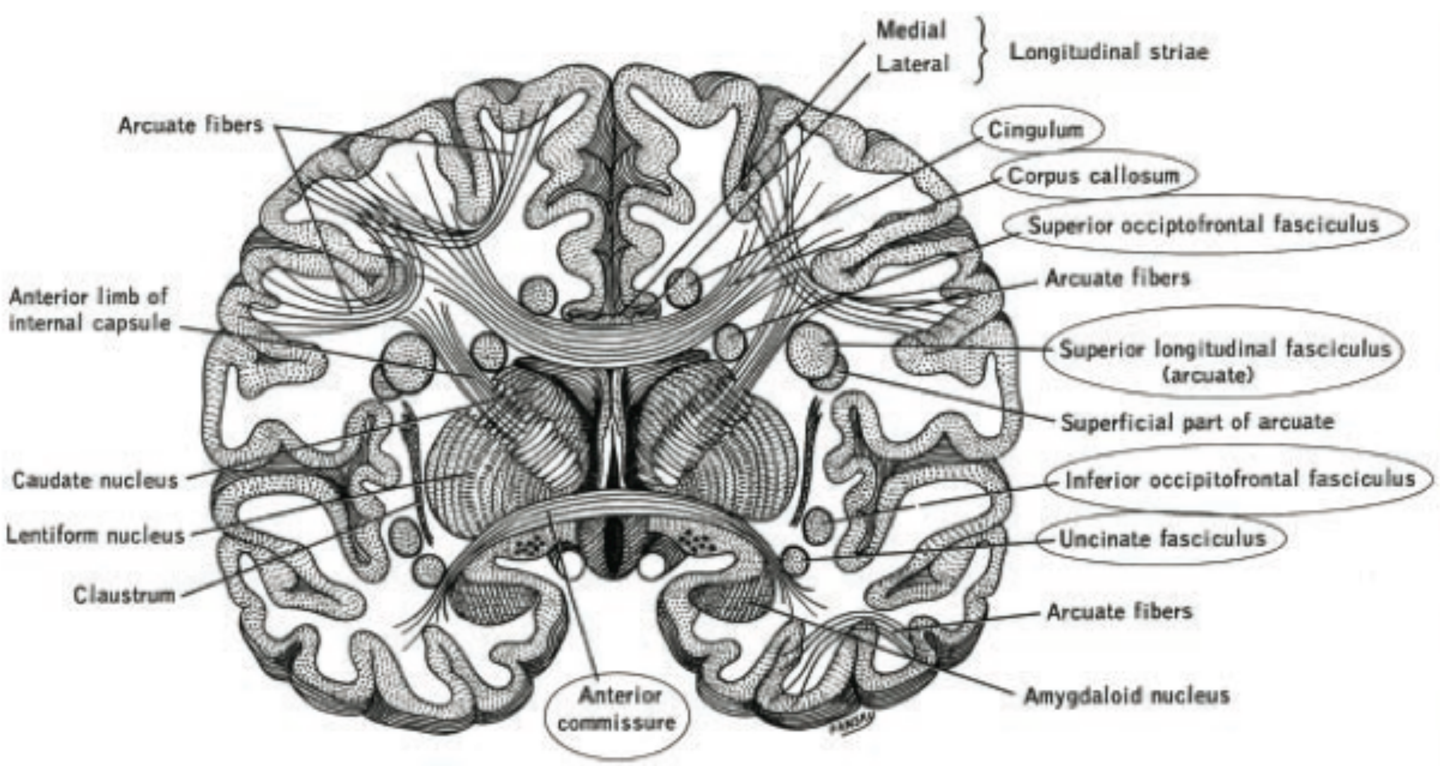


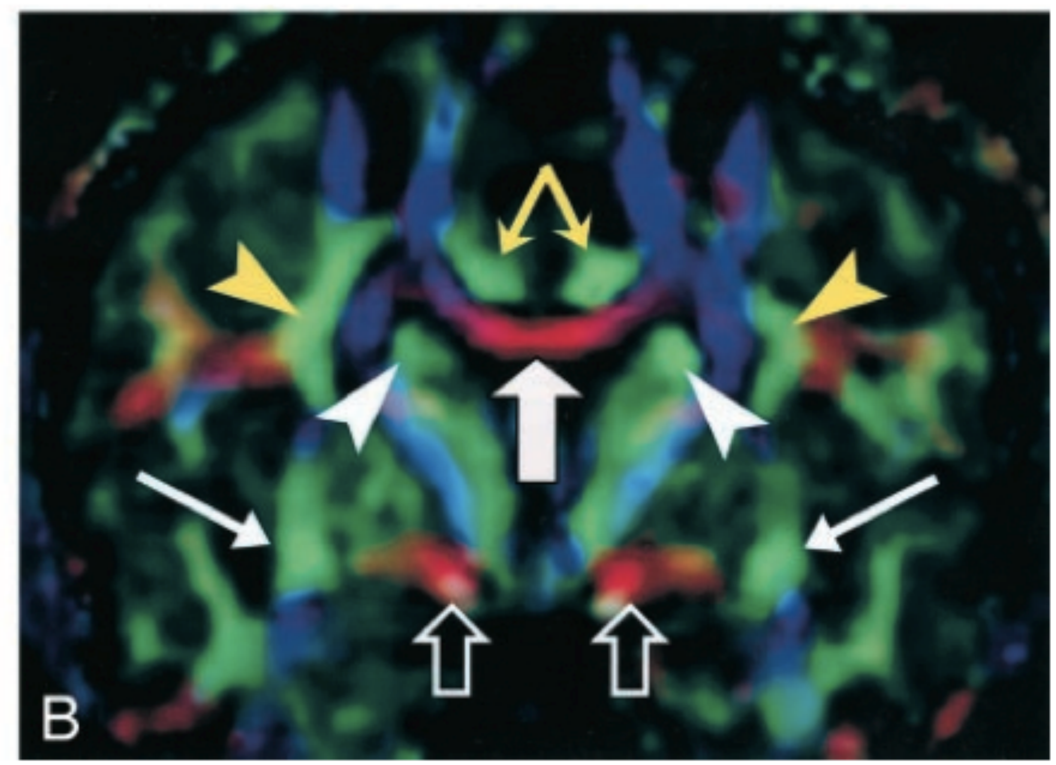


Colour-coded $\mathbf{v_1}$ map

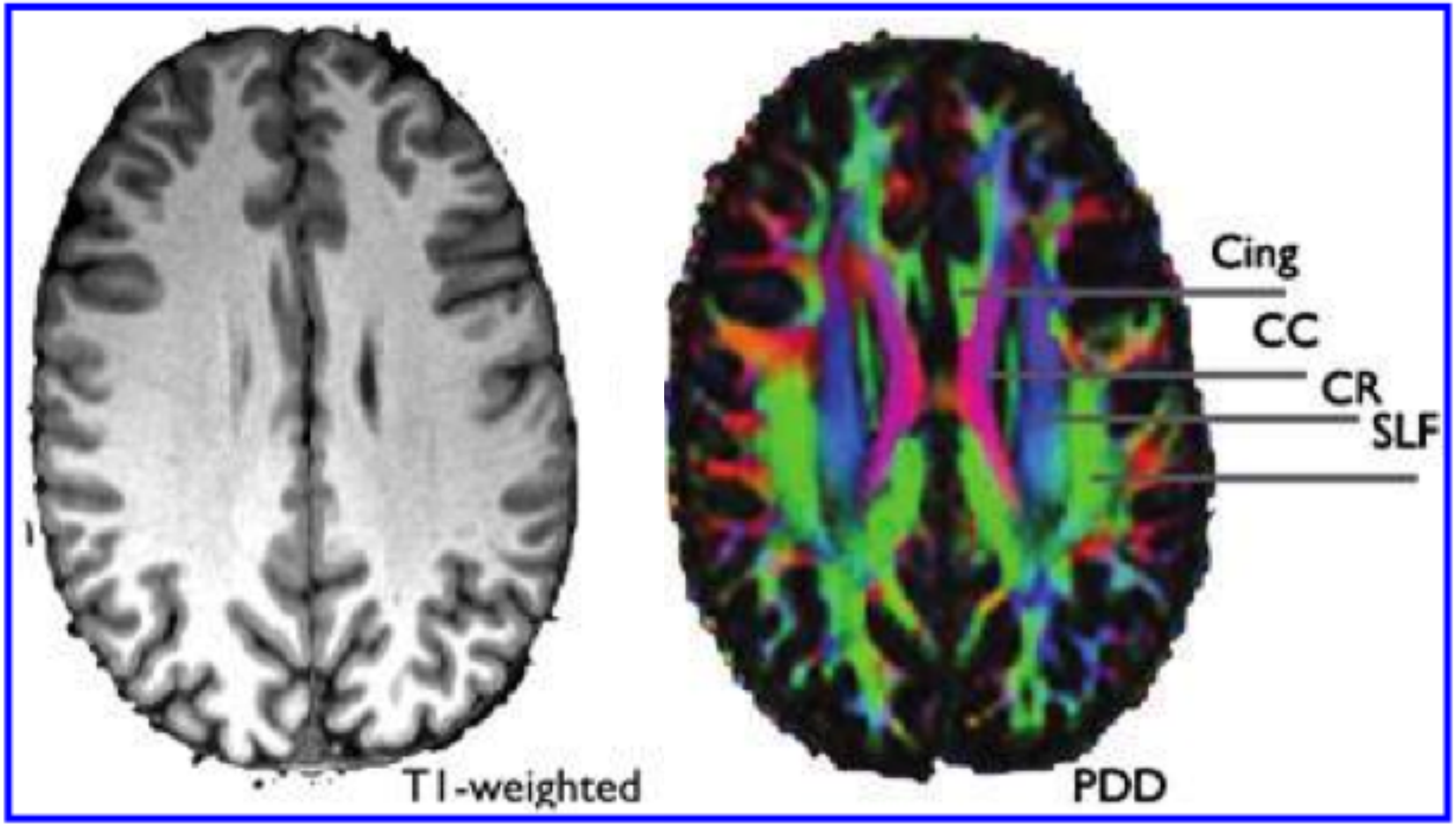


Estimates of Principle Fibre Orientation in WM



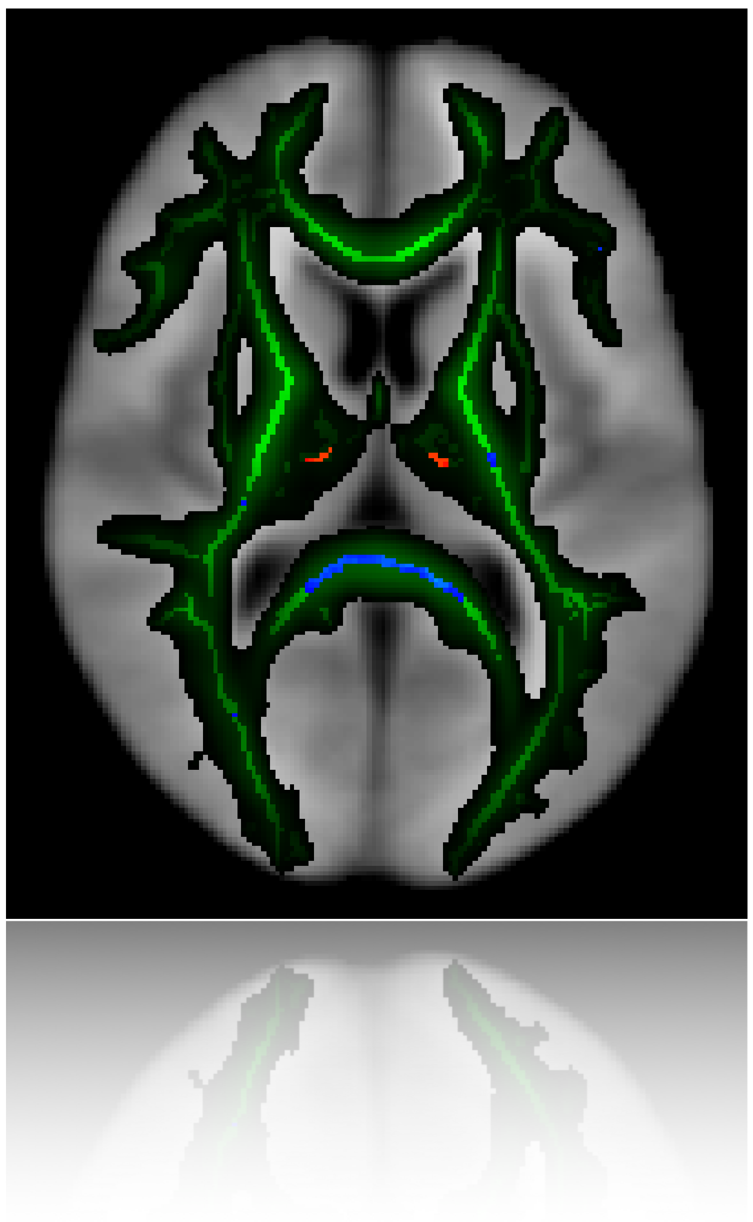


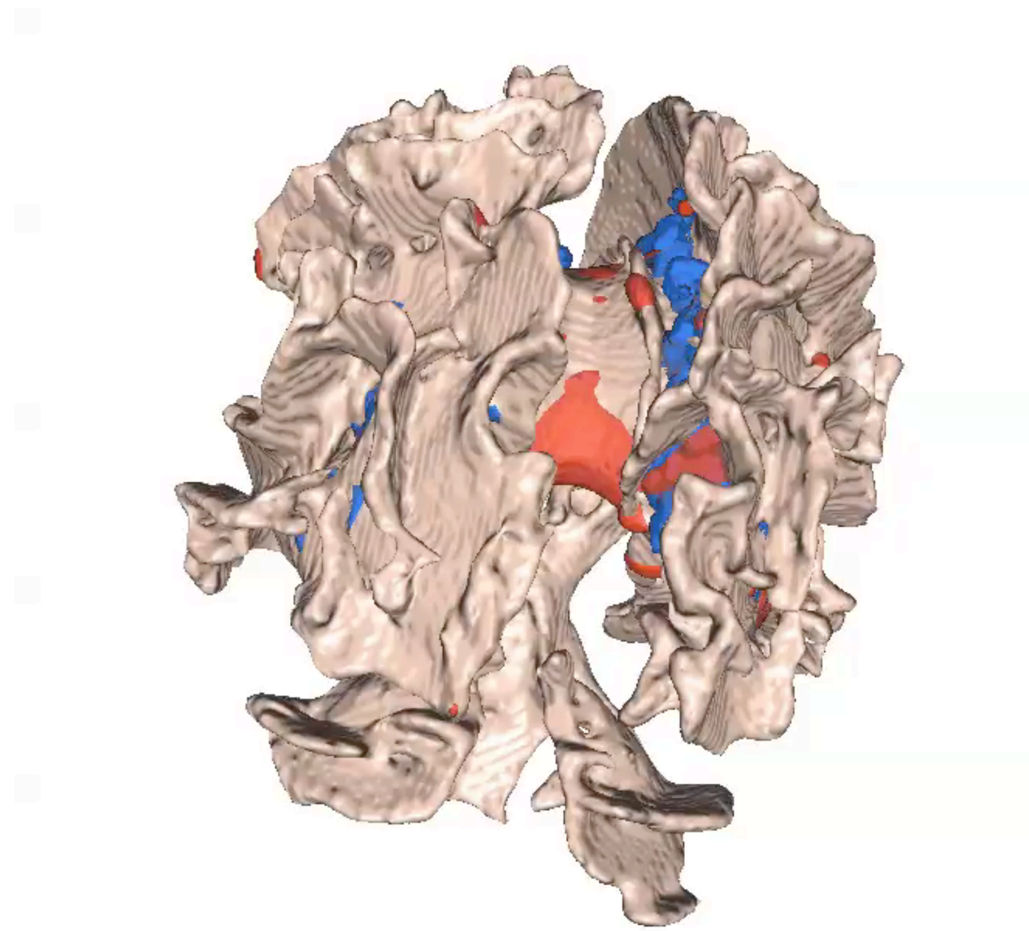
Directional contrast in DTI



TBSS : Tract-Based Spatial Statistics

Robust "voxelwise" cross-subject stats
on diffusion-derived measures



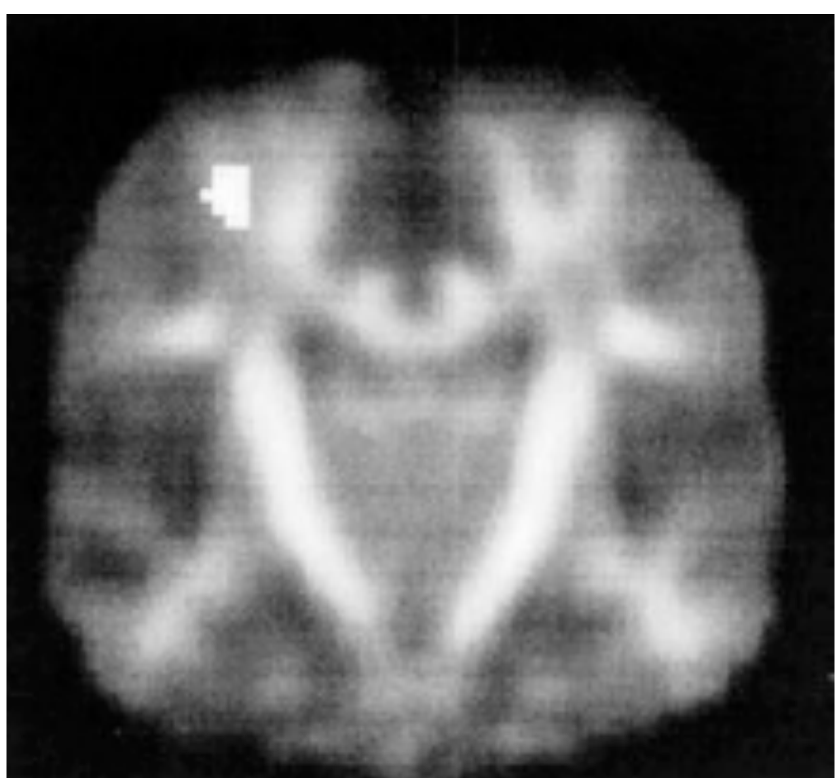


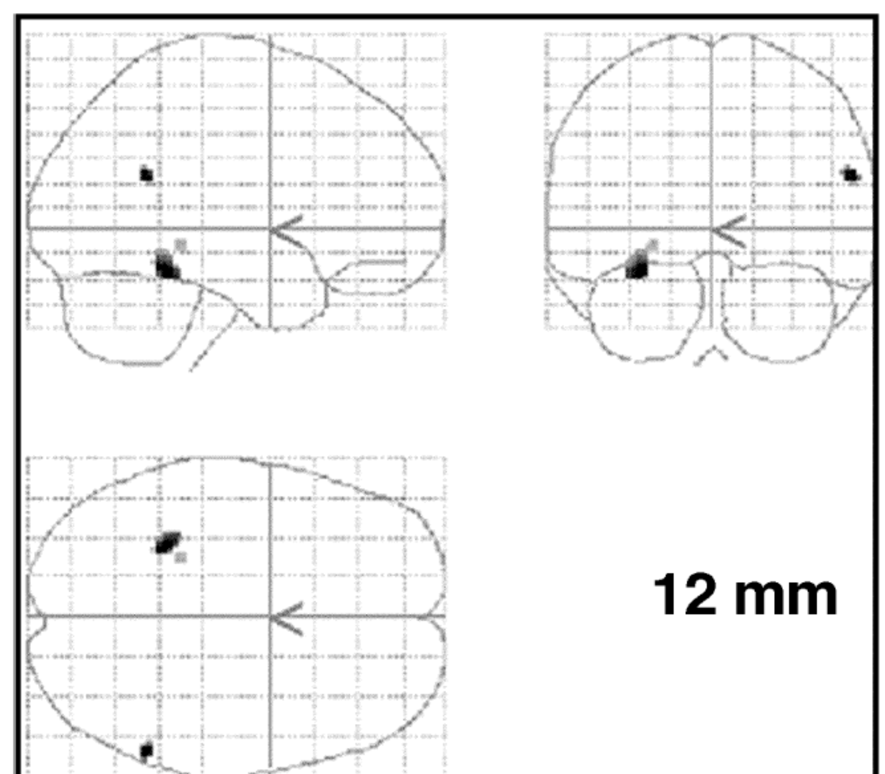
VBM-style Analysis of FA

- VBM [Ashburner 2000, Good 2001]
- Align all subjects' data to standard space
- Segment -> grey matter segmentation
- Smooth GM
- Do voxelwise stats (e.g. controls-patients)

- VBM on FA [Rugg-Gunn 2001, Büchel 2004, Simon 2005]
- Like VBM but no segmentation needed

Büchel 2004

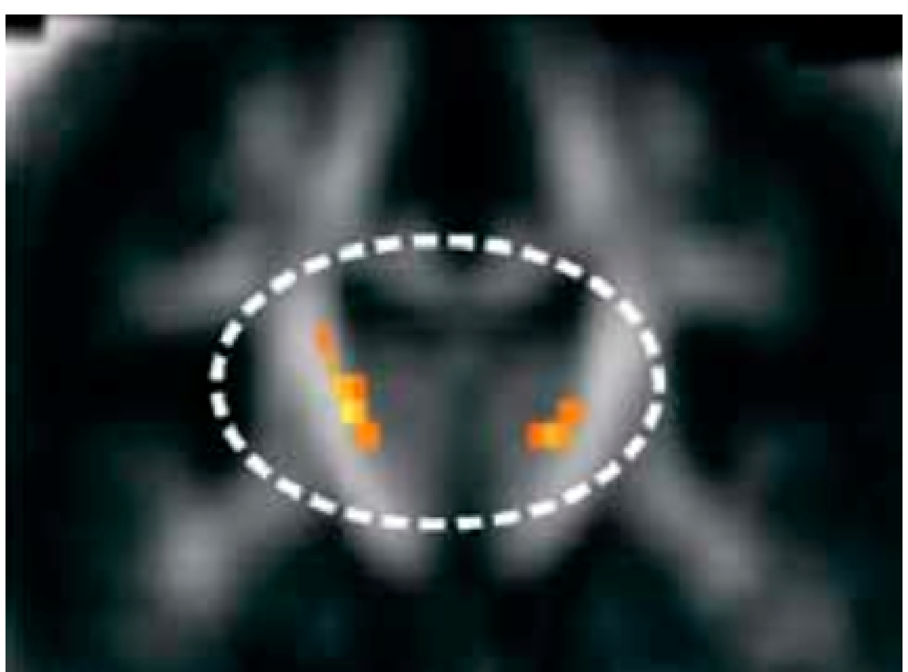
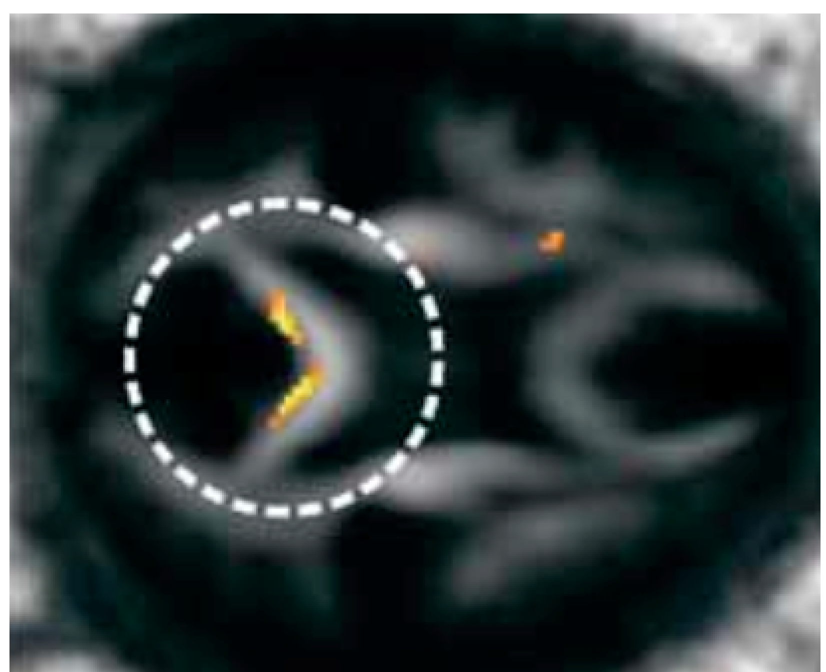
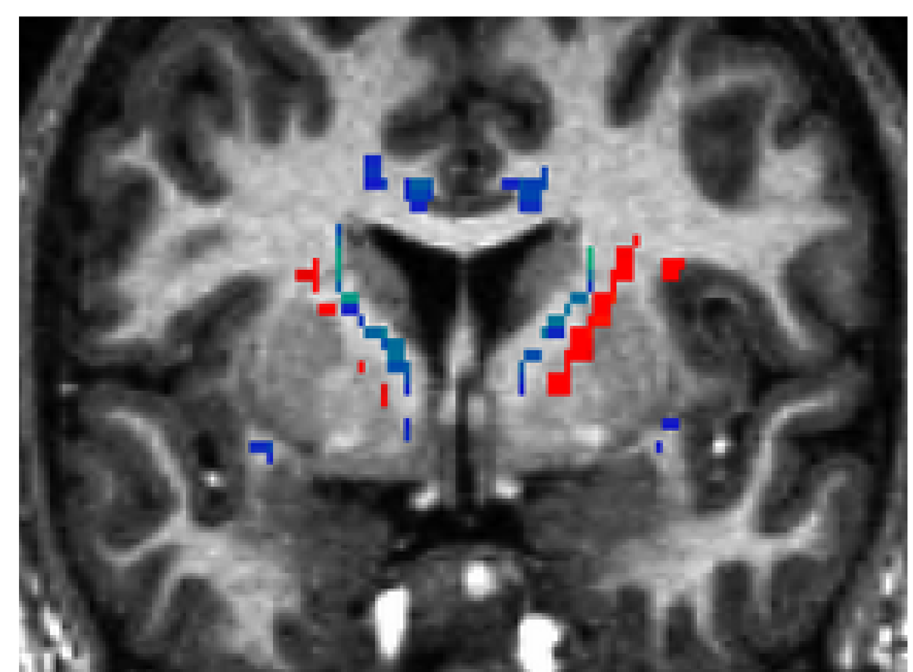




Jones 2005

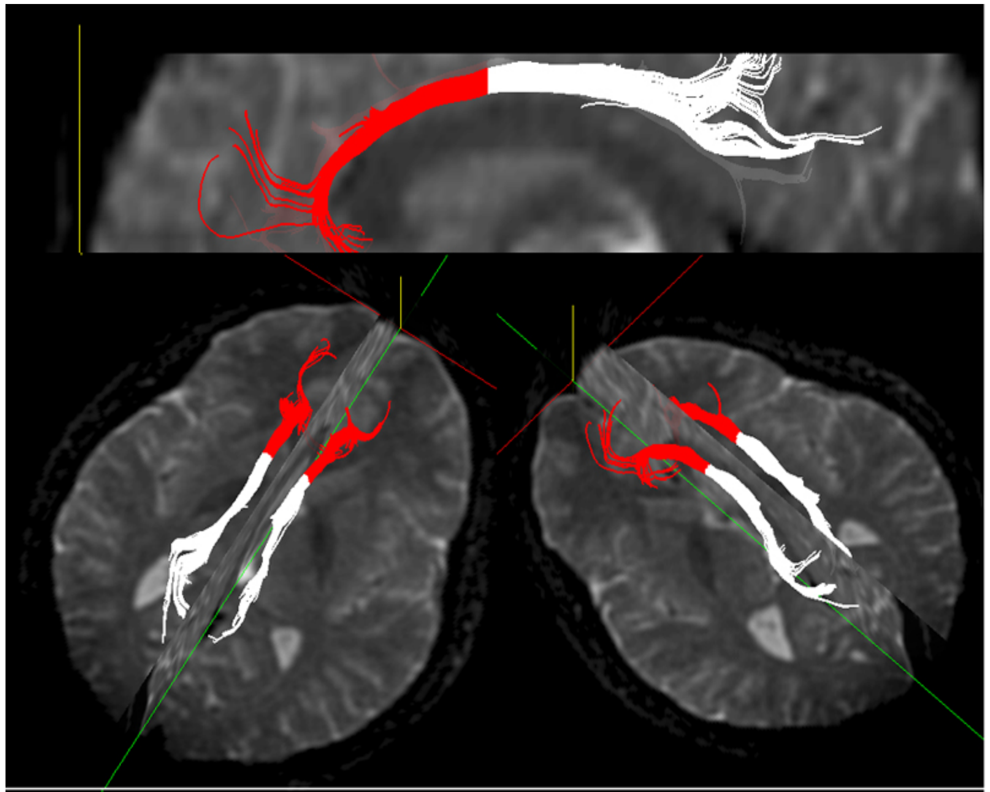
VBM-style Analysis of FA

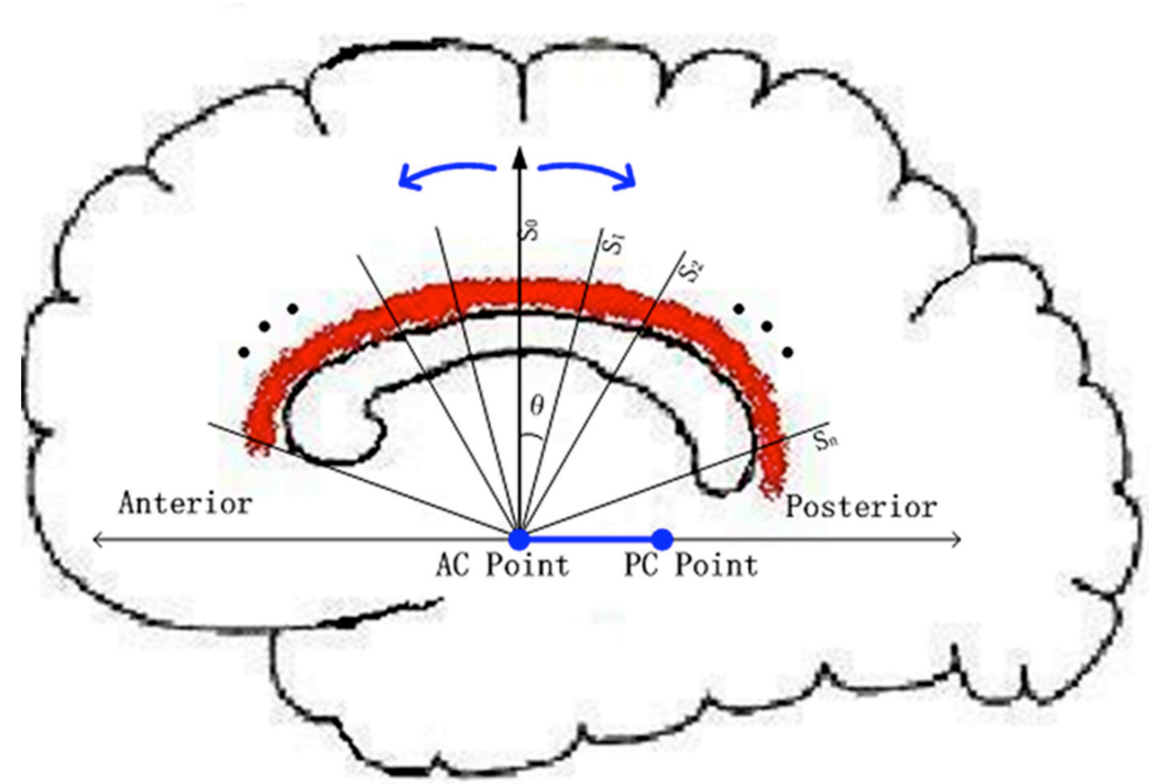
- Strengths
  - Fully automated & quick
  - Investigates whole brain
- Problems [Bookstein 2001, Davatzikos 2004, Jones 2005]
  - Alignment difficult; smallest systematic shifts between groups can be incorrectly interpreted as FA change
  - Needs smoothing to help with registration problems
  - No objective way to choose smoothing extent

Hand-placed voxel/ROI-based FA Comparison

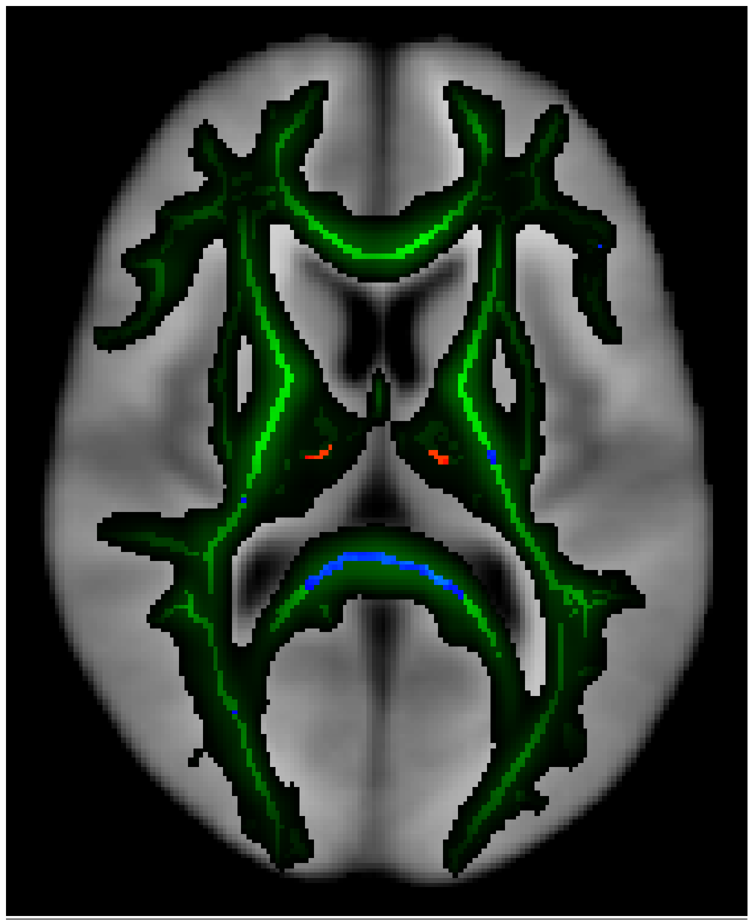
Tractography-Based FA Comparison

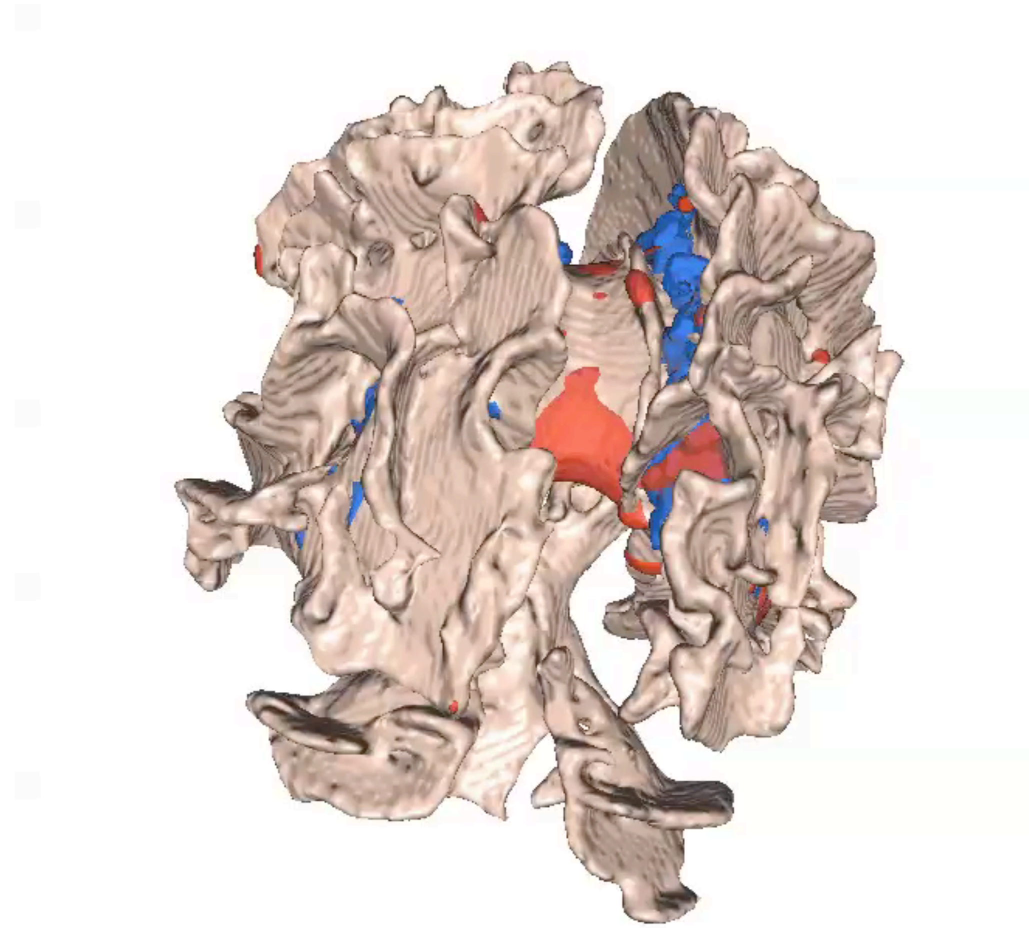




- Method [Gong 2005, Corouge 2006]
  - Define a given tract in all subjects
  - Parameterise FA along tract
  - Compare between subjects
- Strength: correspondence issue hopefully resolved
- Problems
  - Currently requires manual intervention to specify tract
  - Hence doesn't investigate whole brain
  - Projection of FA onto tract needs careful thought

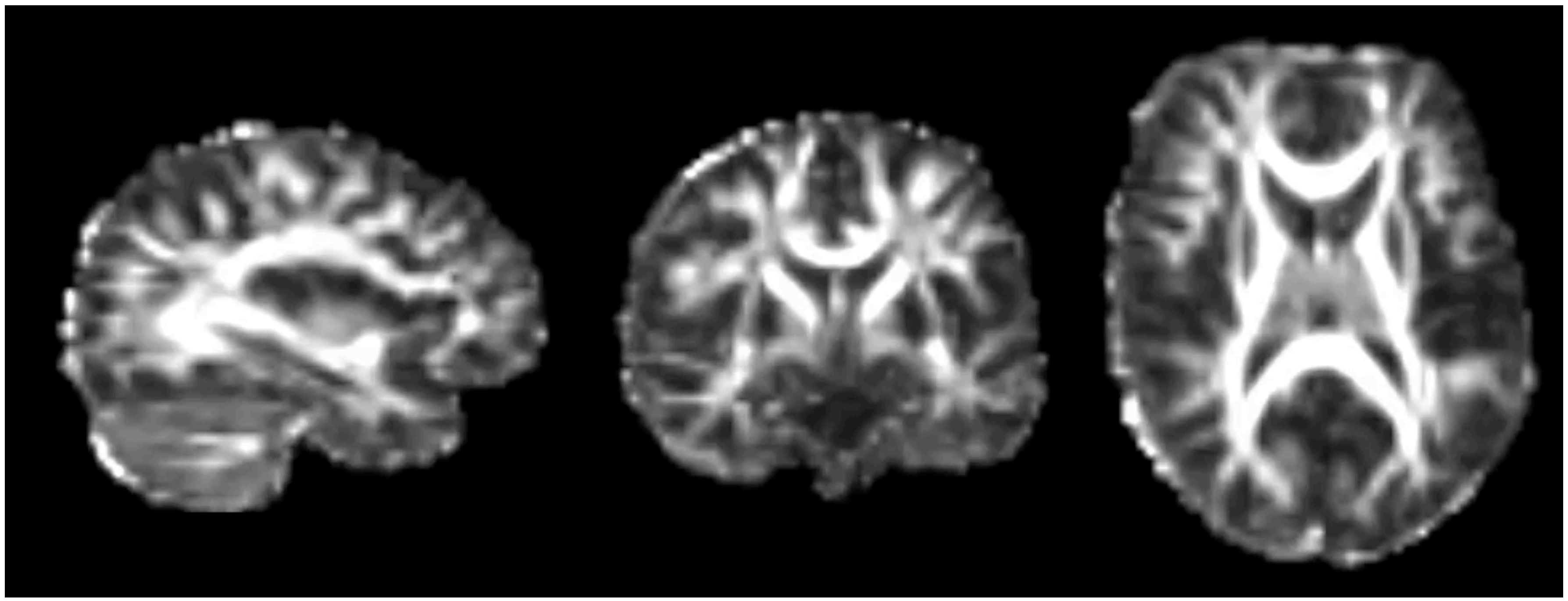
TBSS : Tract-Based Spatial Statistics



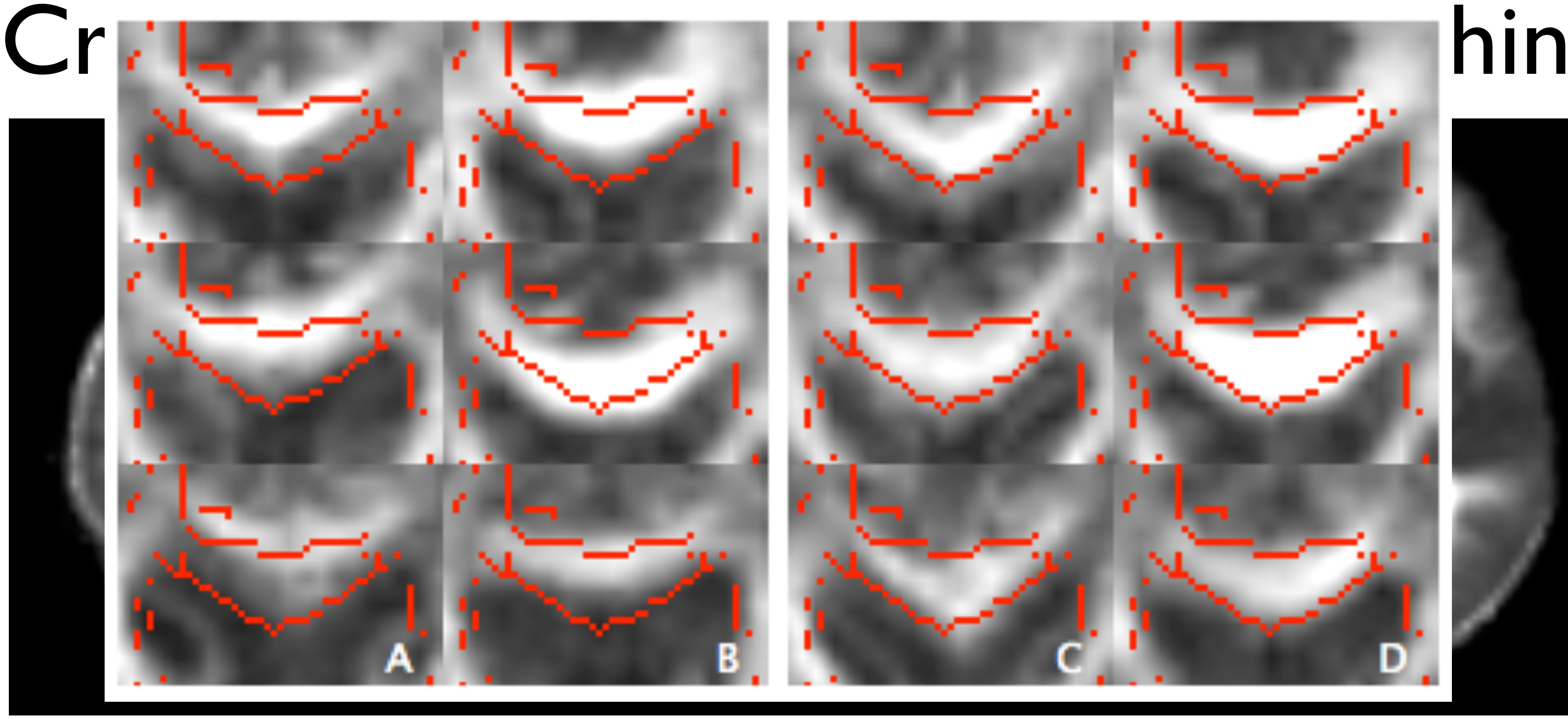


- Need: robust "voxelwise" cross-subject stats on DTI
- Problem: alignment issues confound valid local stats
- TBSS: solve alignment using alignment-invariant features:
- Compare FA taken from tract centres (via skeletonisation)

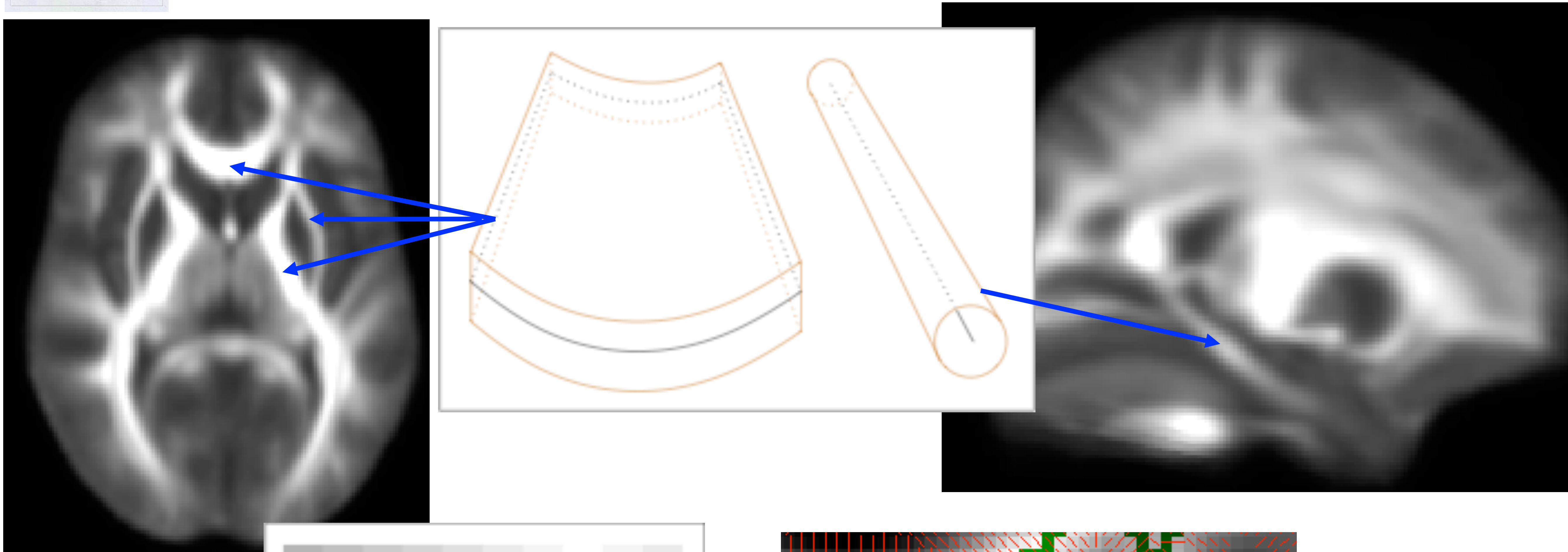
1. Use medium-DoF nonlinear reg to pre-align all subjects' FA
(nonlinear reg: FNIRT)

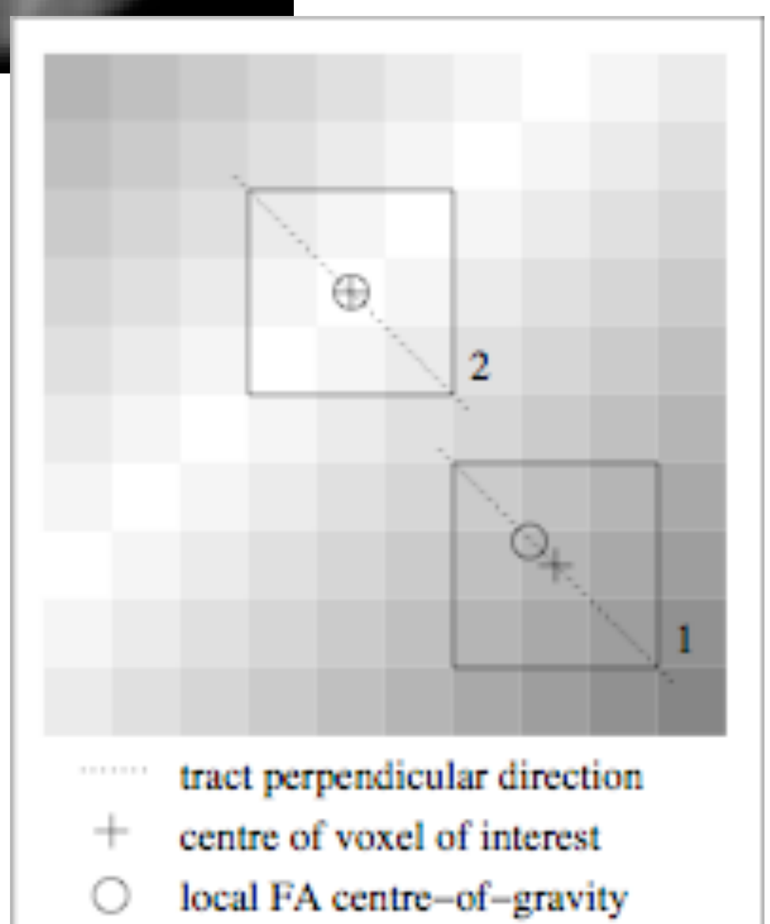


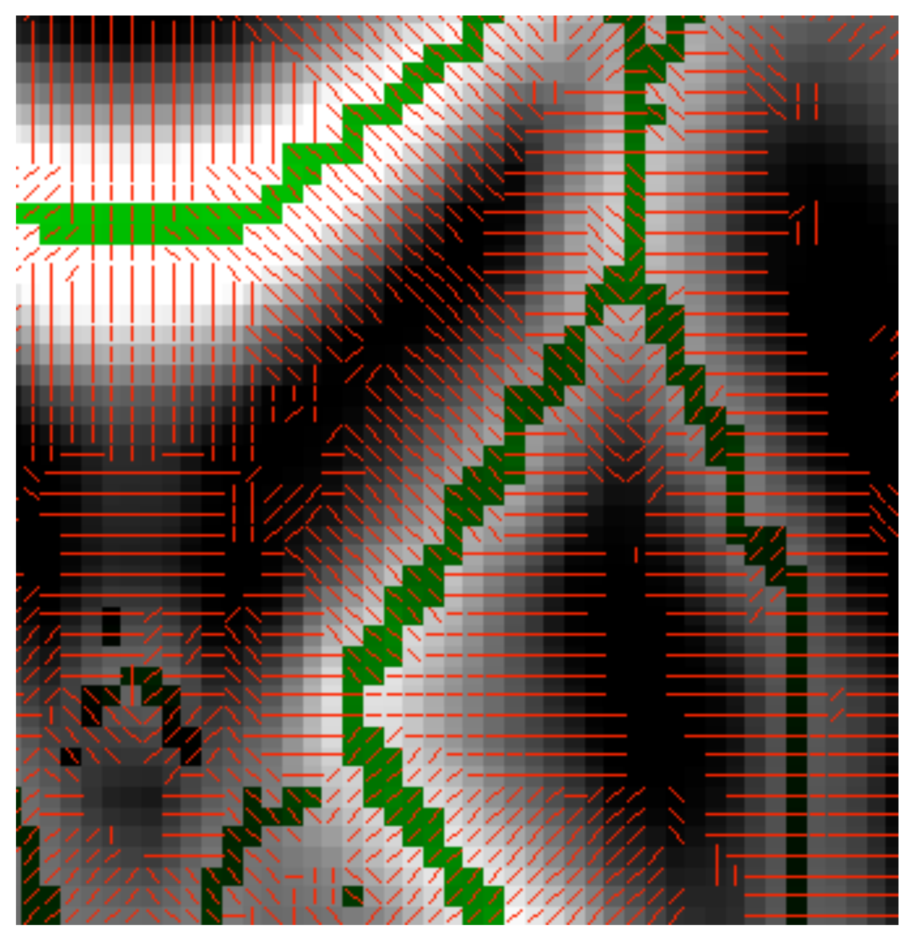
2. Cr hing)



2. "Skeletonise" Mean FA

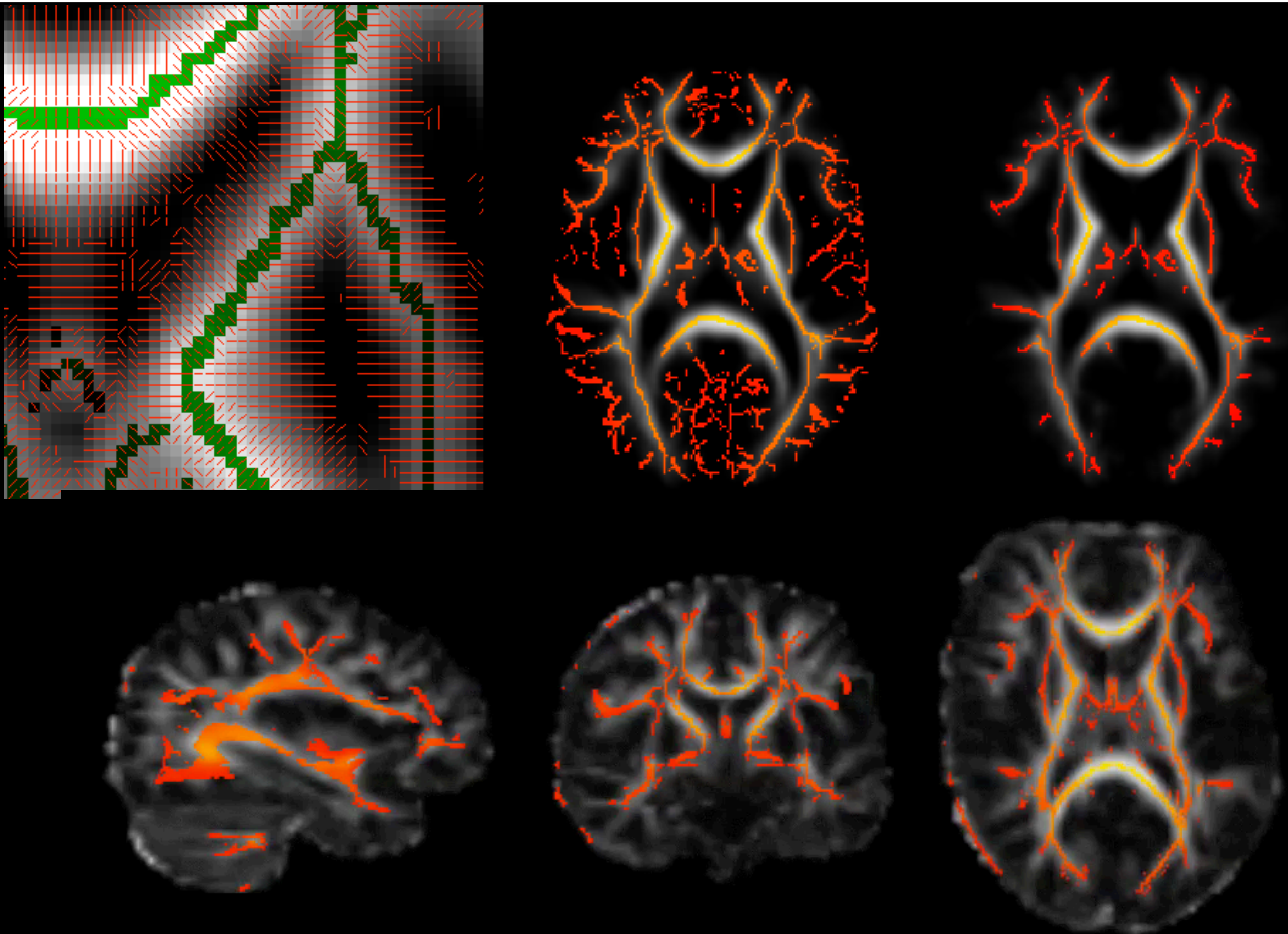






3. Threshold Mean FA Skeleton

giving "objective" tract map



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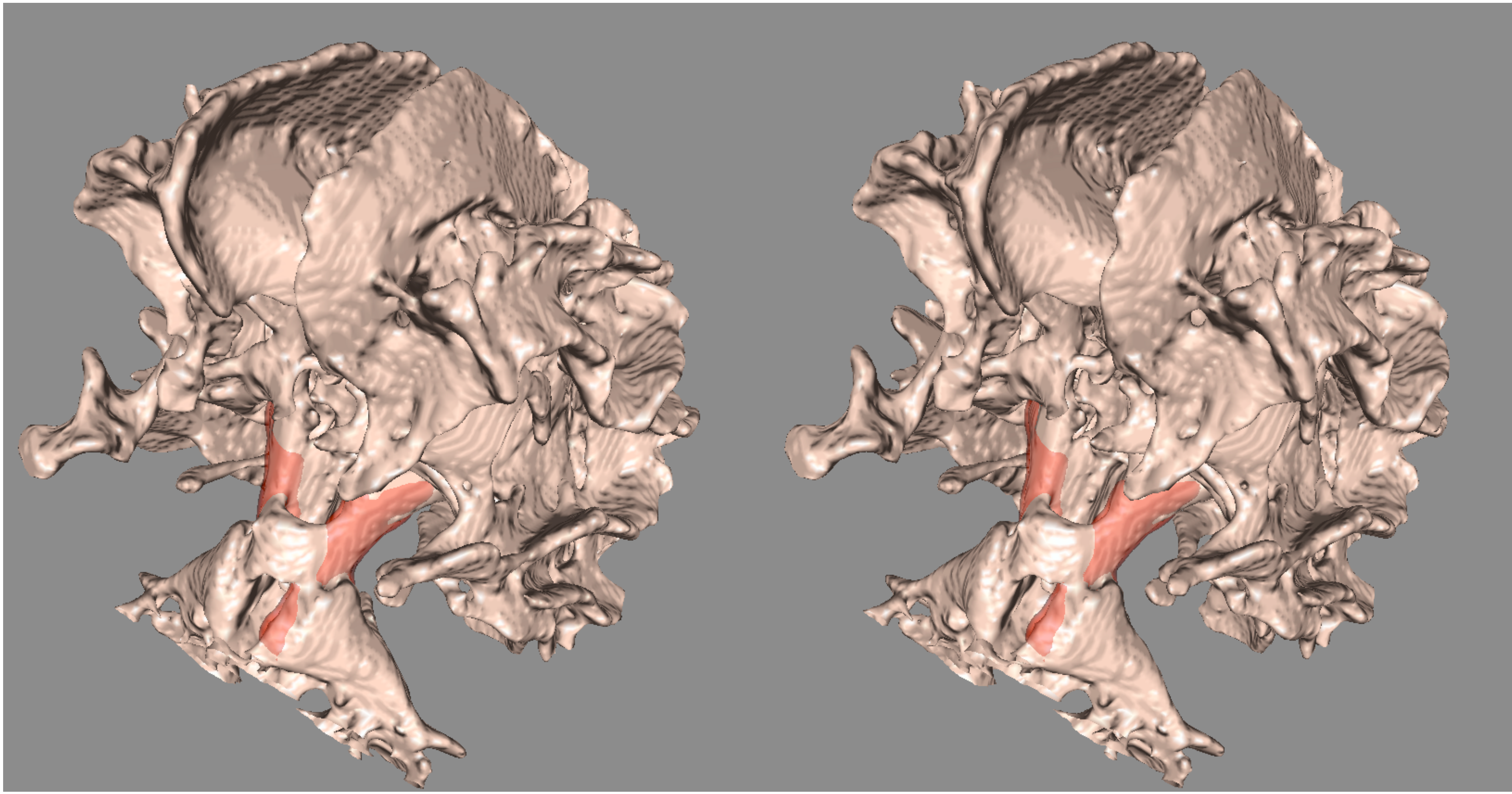

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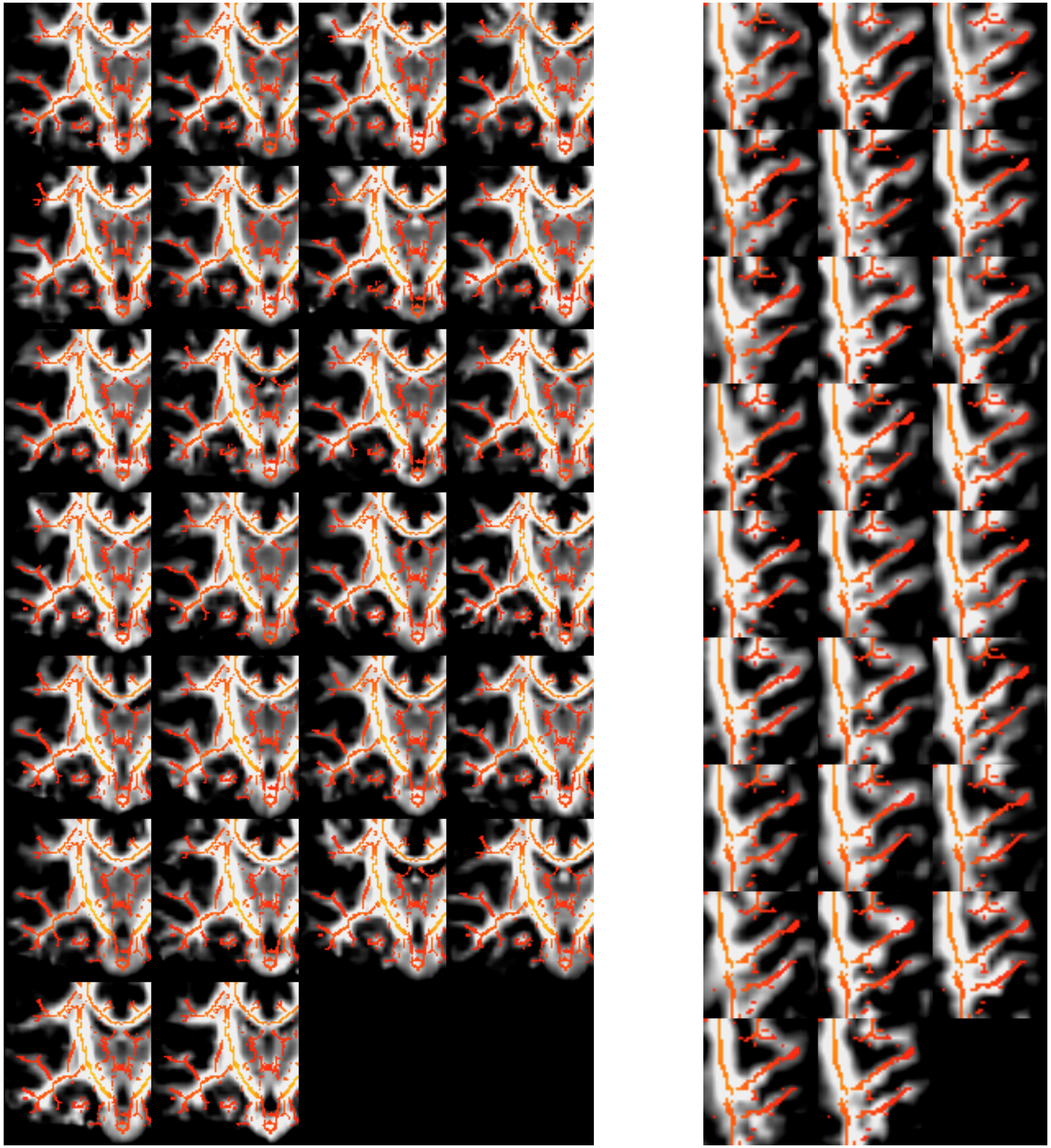
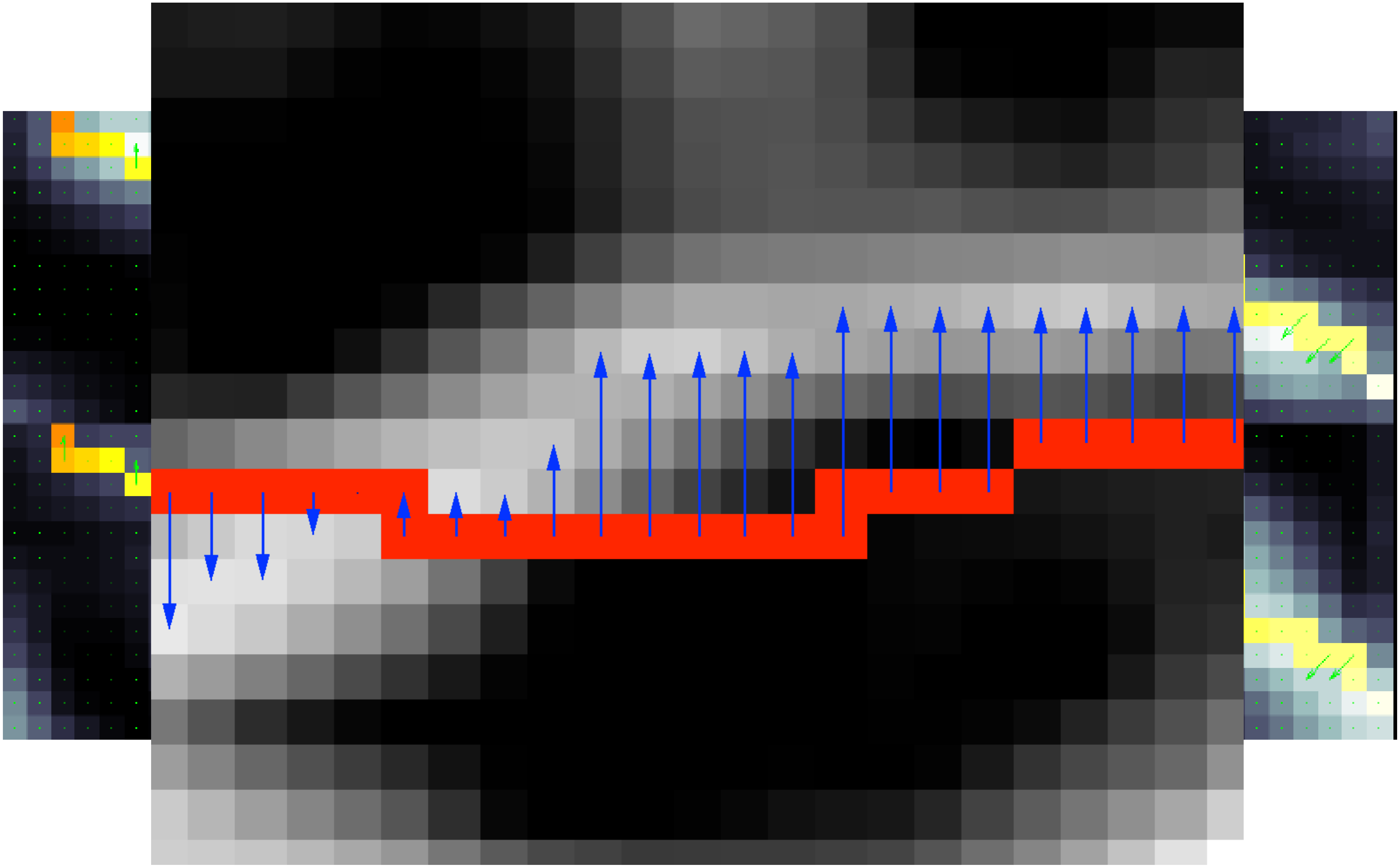
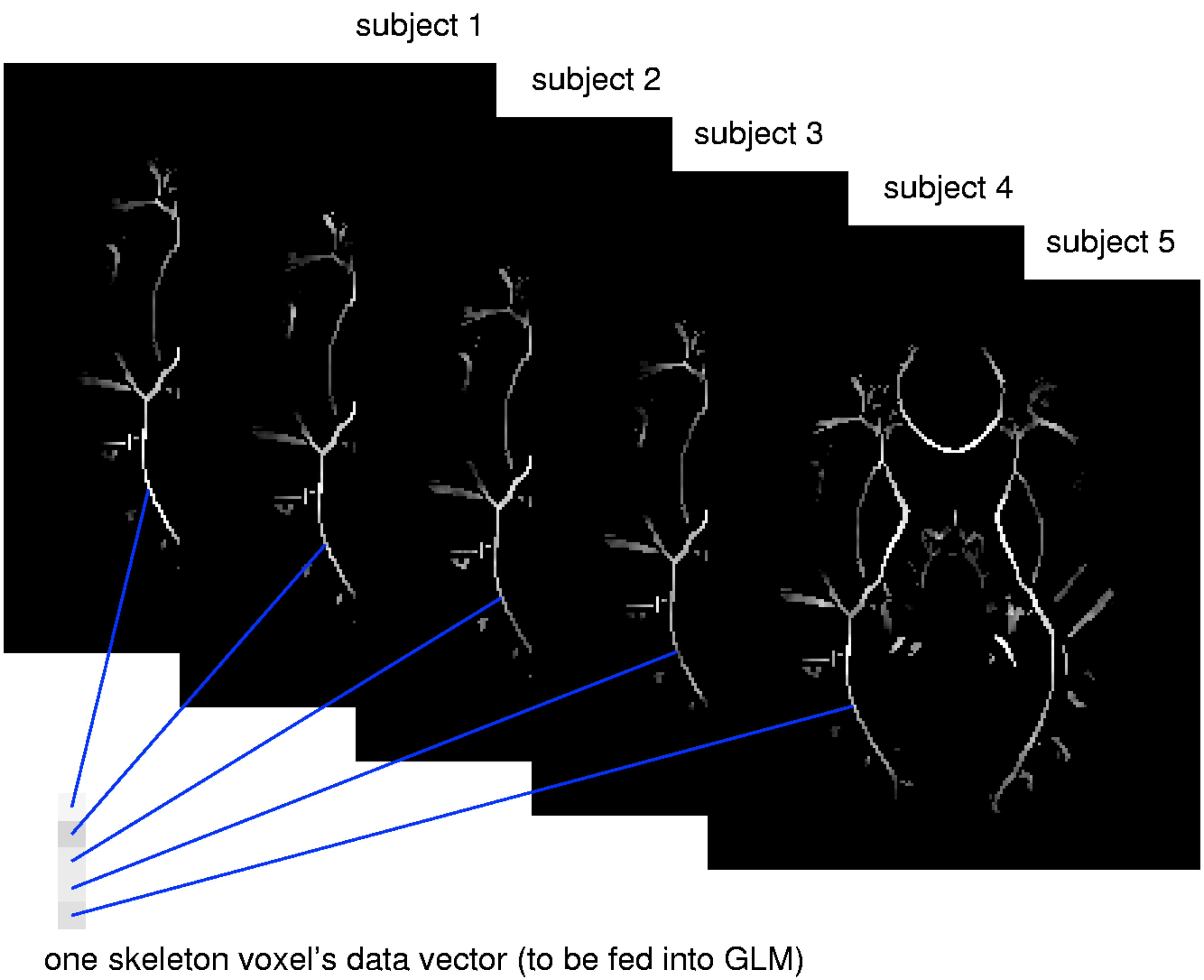
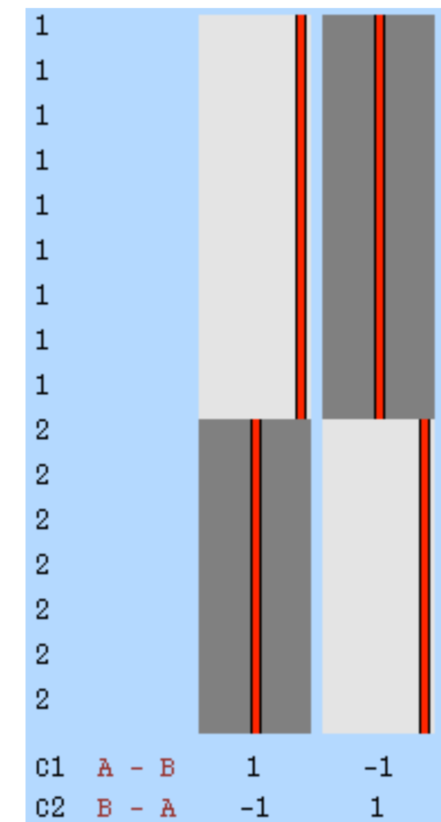


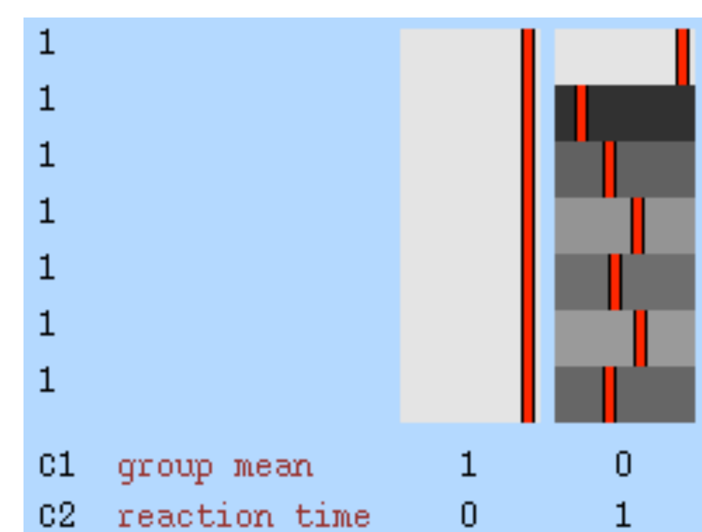
4. For each subject's warped FA, fill each point on the mean-space skeleton with nearest maximum FA value (i.e., from the centre of the subject's nearby tract)



5. Do cross-subject voxelwise stats on skeleton-projected FA and Threshold, (e.g., permutation testing, including multiple comparison correction)

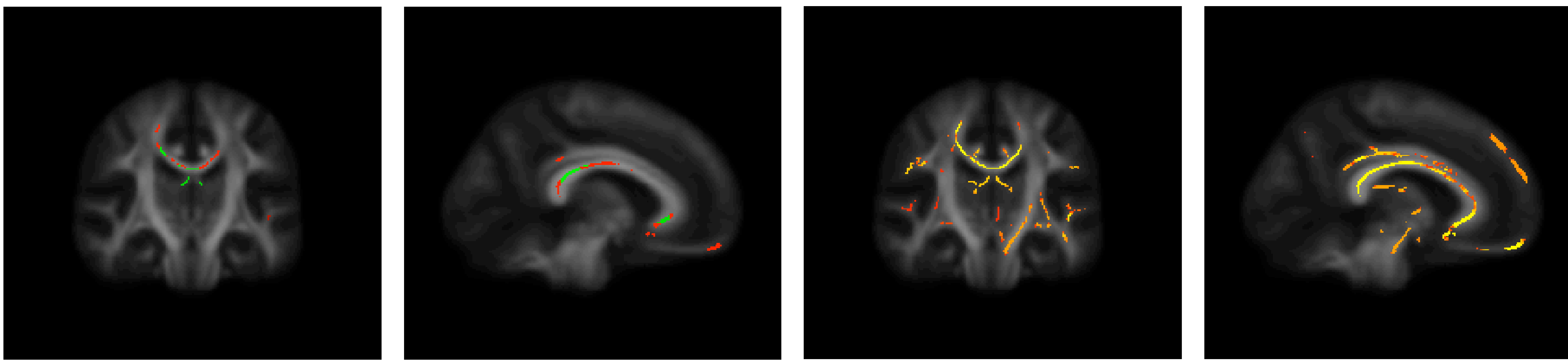


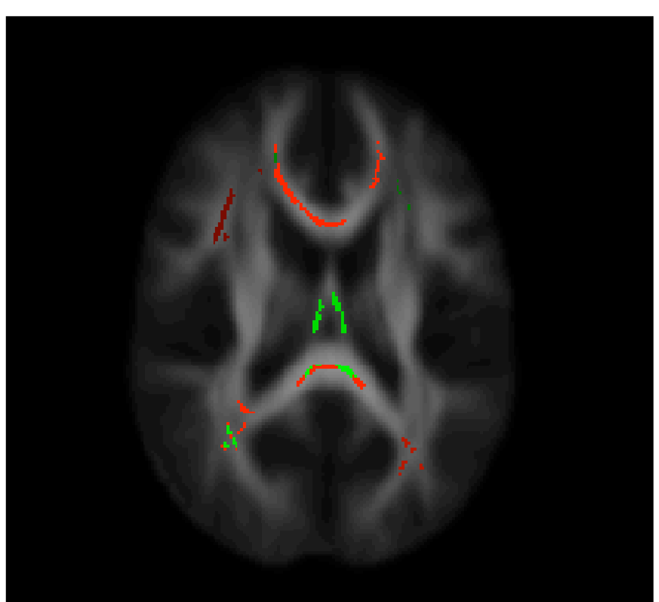




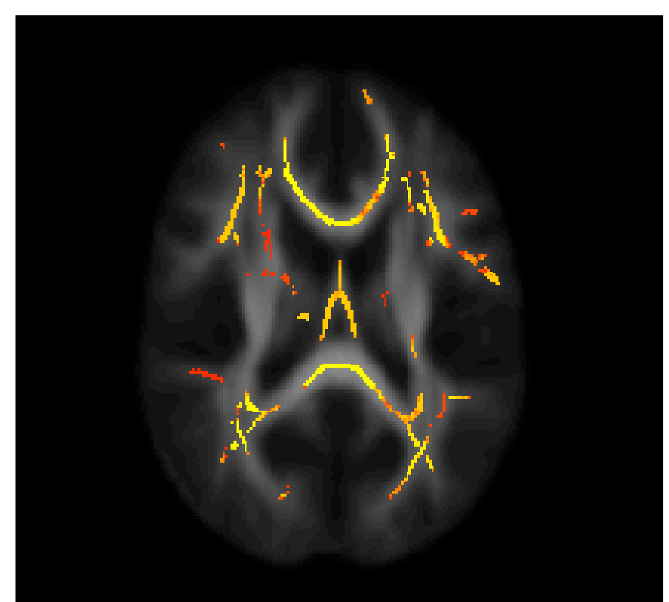
TFCE for TBSS

controls > schizophrenics
p<0.05 corrected for multiple comparisons across space, using randomise





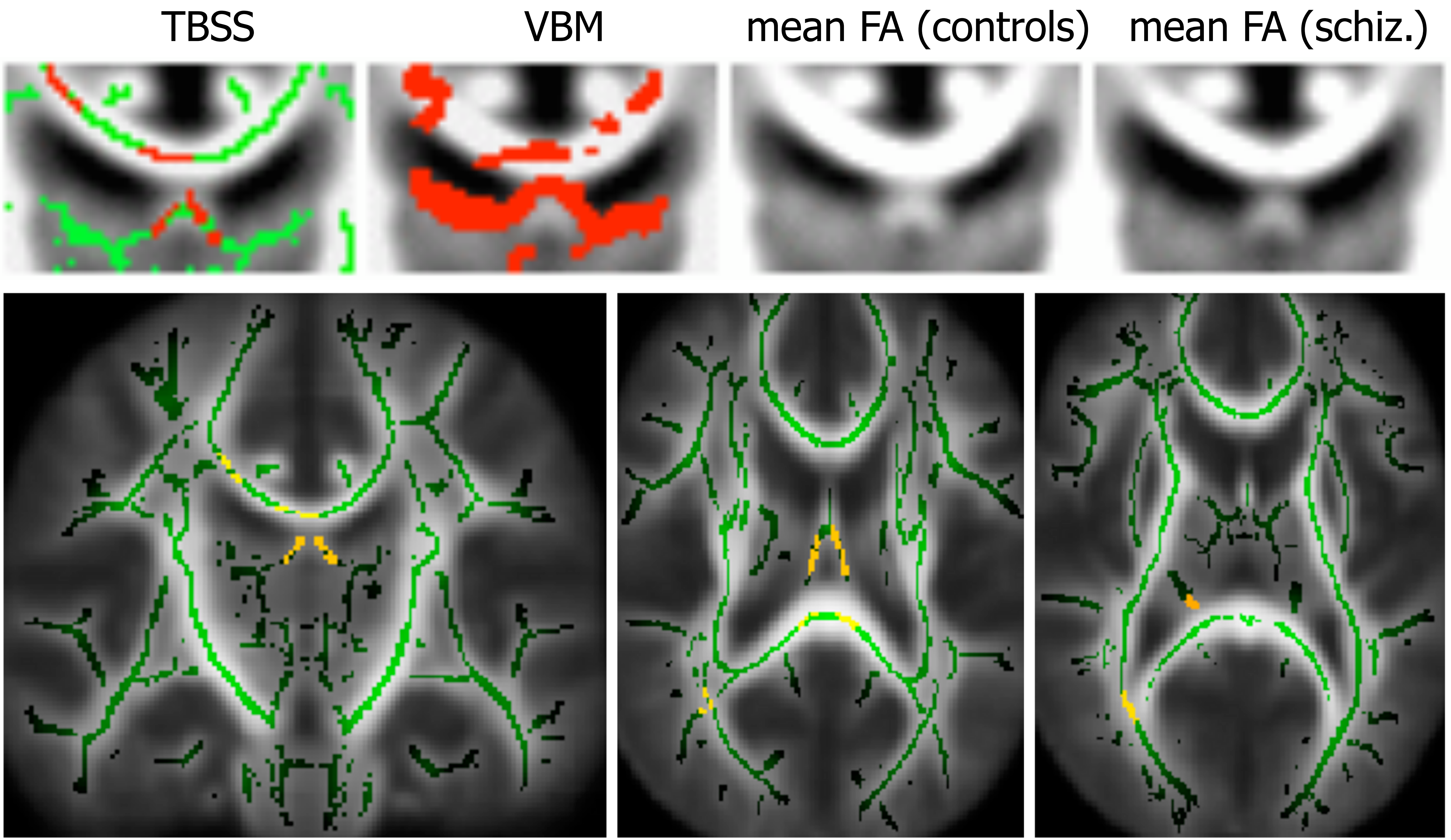
cluster-based:
cluster-forming threshold =
2 or 3



TFCE

Schizophrenia (Mackay)

TBSS & VBM show reduced FA in corpus callosum & fornix
VBM shows spurious result in thalamus due to increased ventricles in schiz.

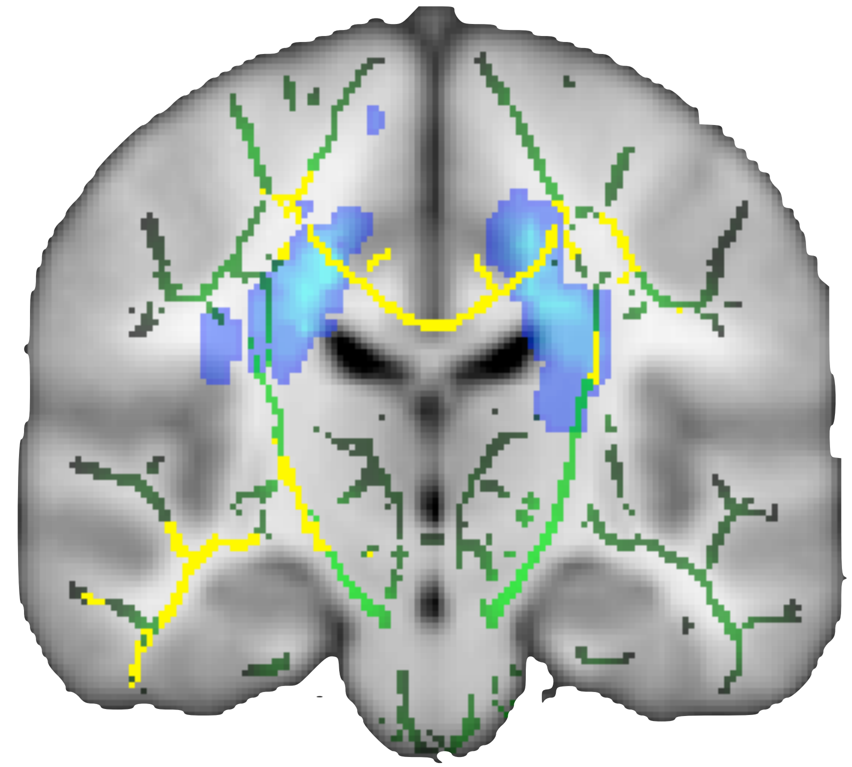


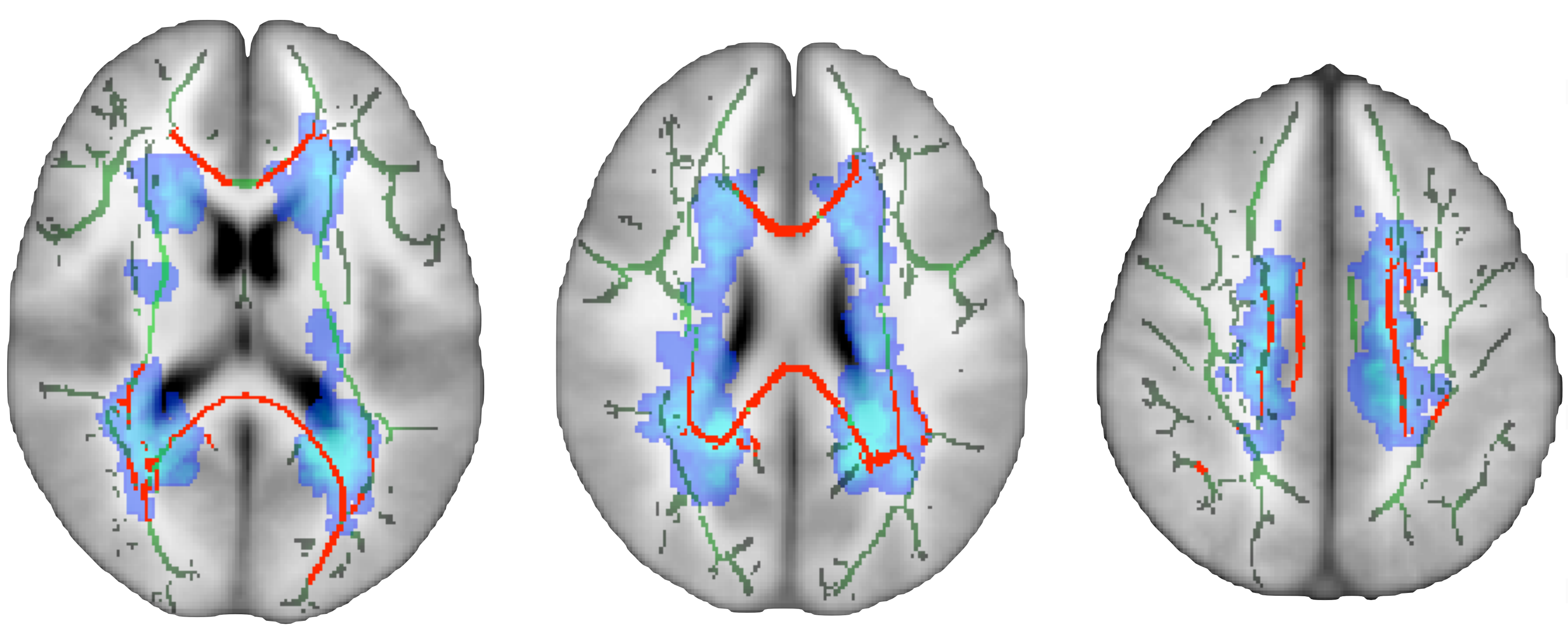
Multiple Sclerosis (Cader, Johansen-Berg & Matthews)

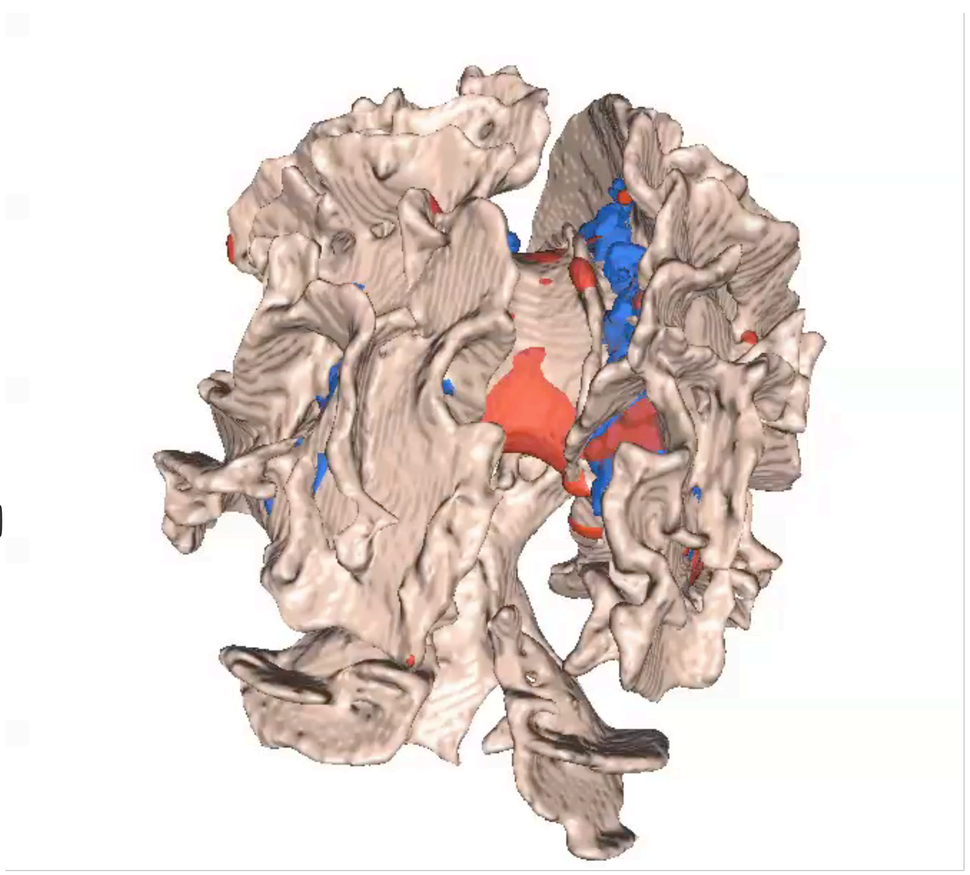
- 15 MS patients

- Yellow = -ve corr. FA vs EDSS

- Blue = group lesion probability (50%)
- Red = -ve corr. FA vs lesion volume
  Note reduced FA away from lesions







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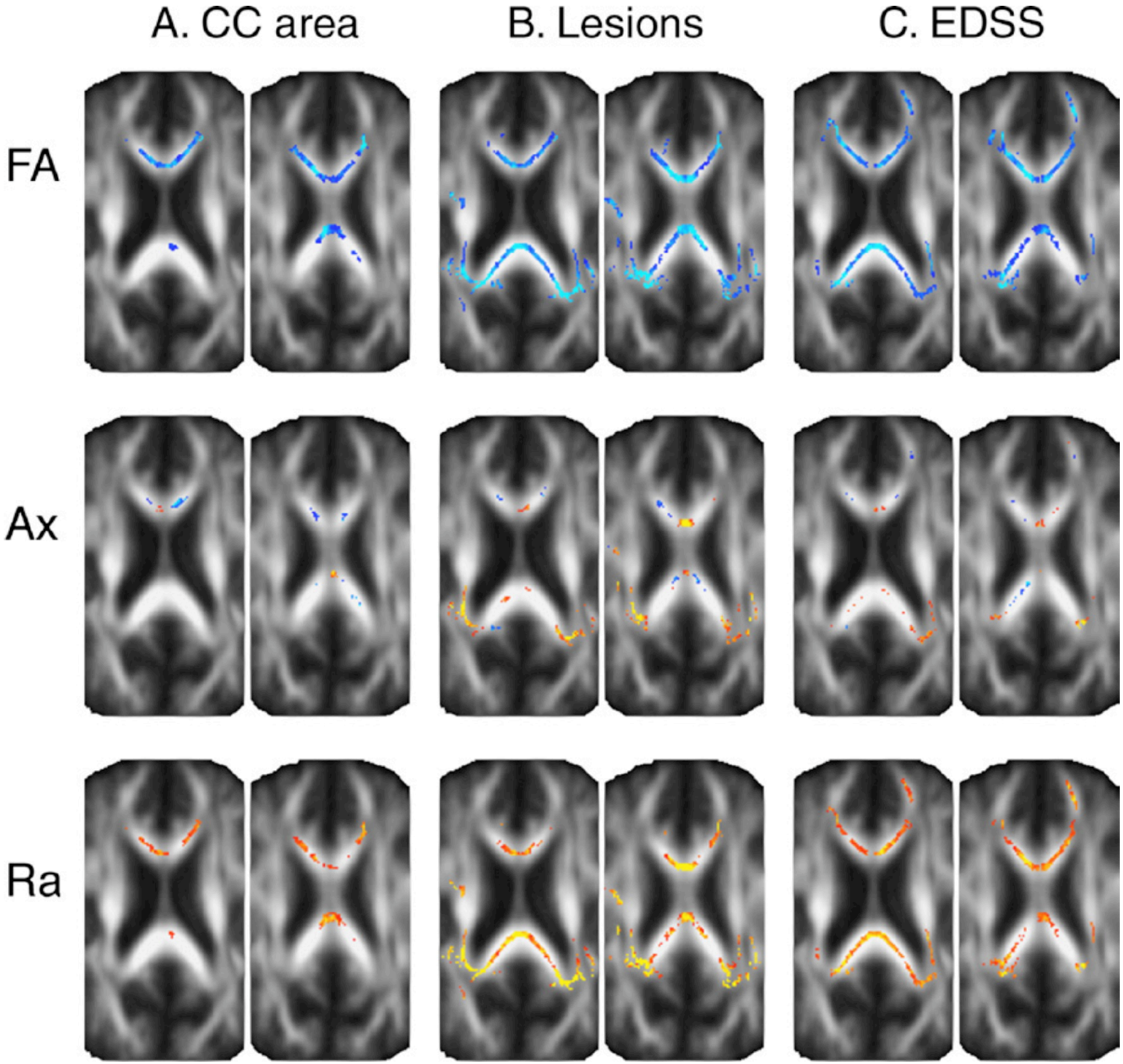
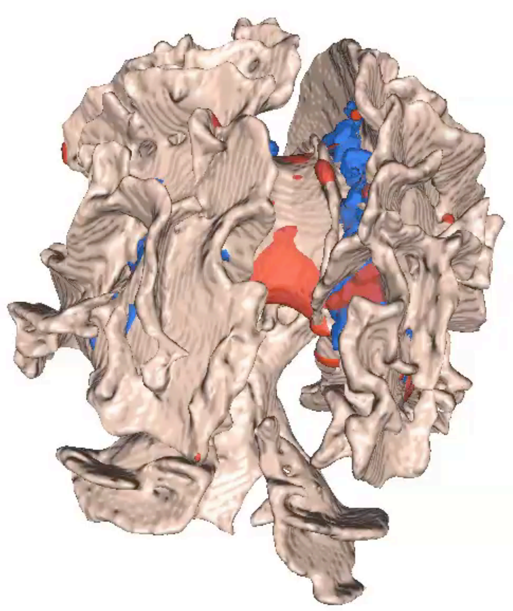


TBSS - Conclusions

- Attempting to solve correspondence/smoothing problems
- Less ambiguity of interpretation / spurious results than VBM
- Easier to test whole brain than ROI / tractography

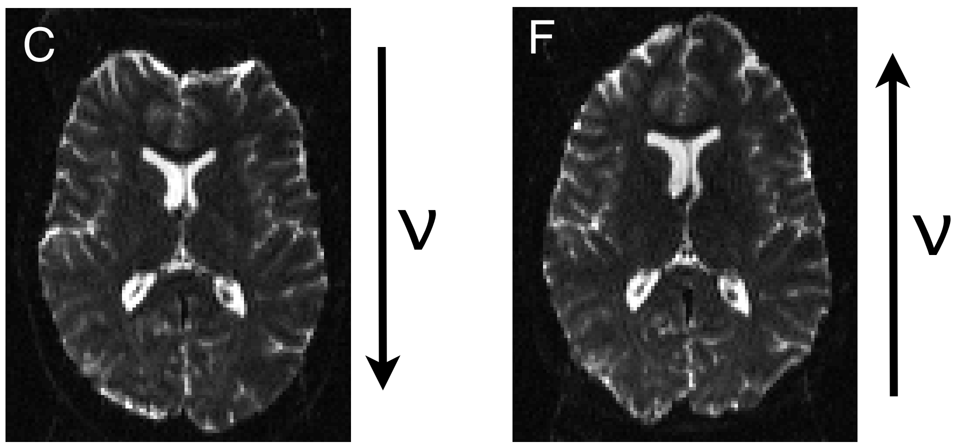
- Limitations & Dangers
    - Interpretation of partial volume tracts still an issue
    - Crossing tracts?

- Future work
    - Use full tensor (for registration and test statistic)
    - Use other test statistics (MD, PDD, width)
    - Multivariate stats (across voxels and/or different diffusion measures) & discriminant (ICA, SVM)

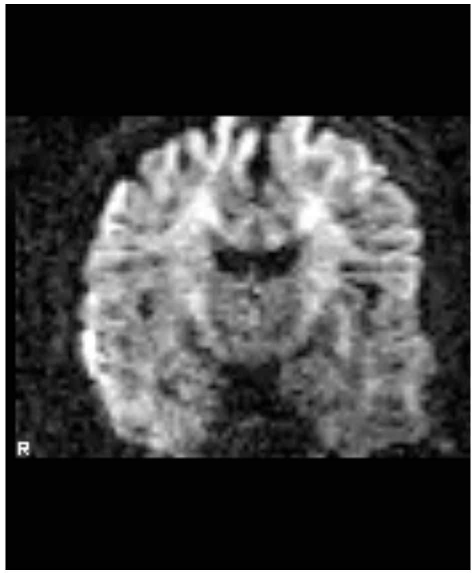


…But what about dMRI distortions?

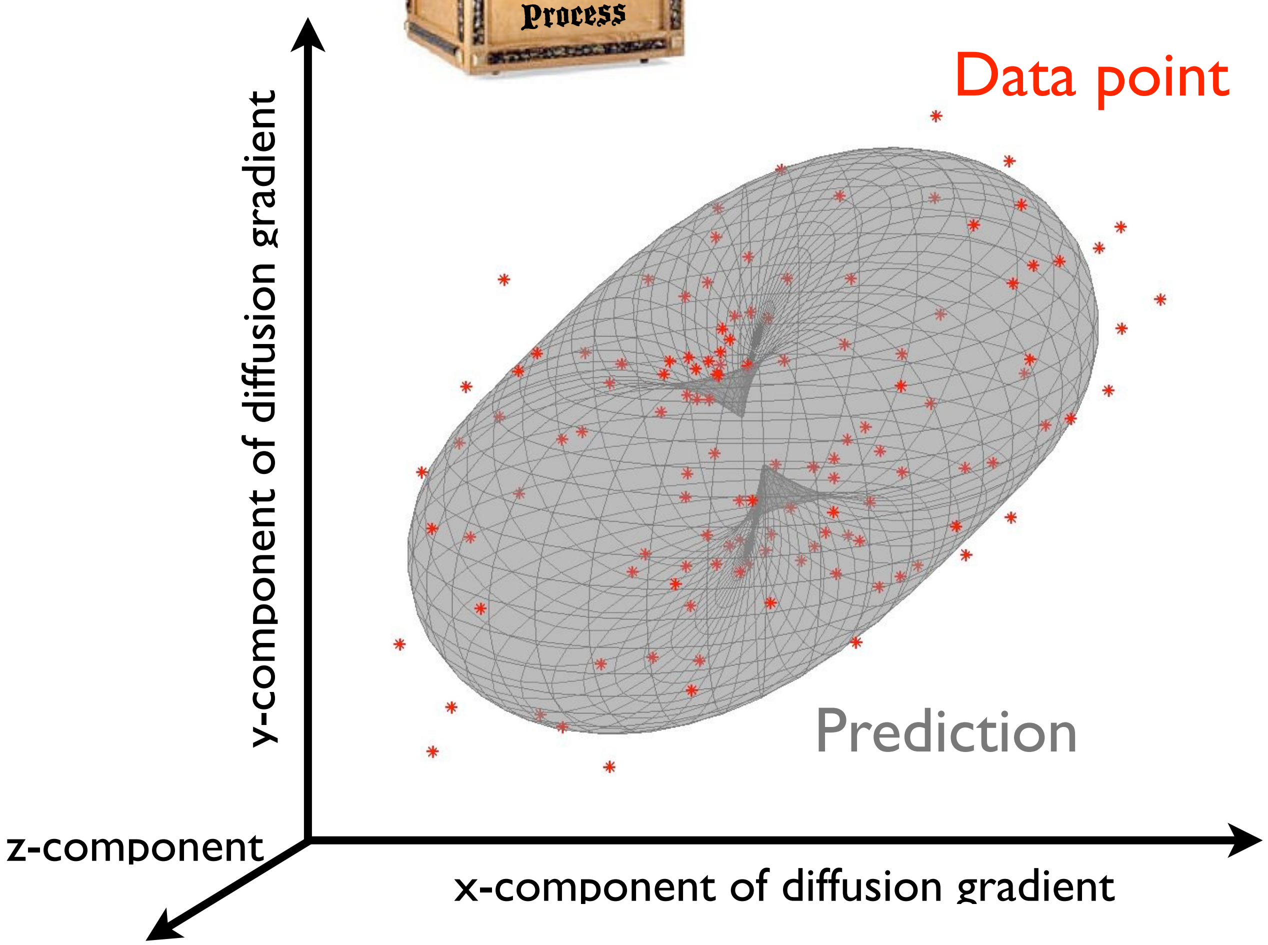
Susceptibility-induced (EPI) Distortions

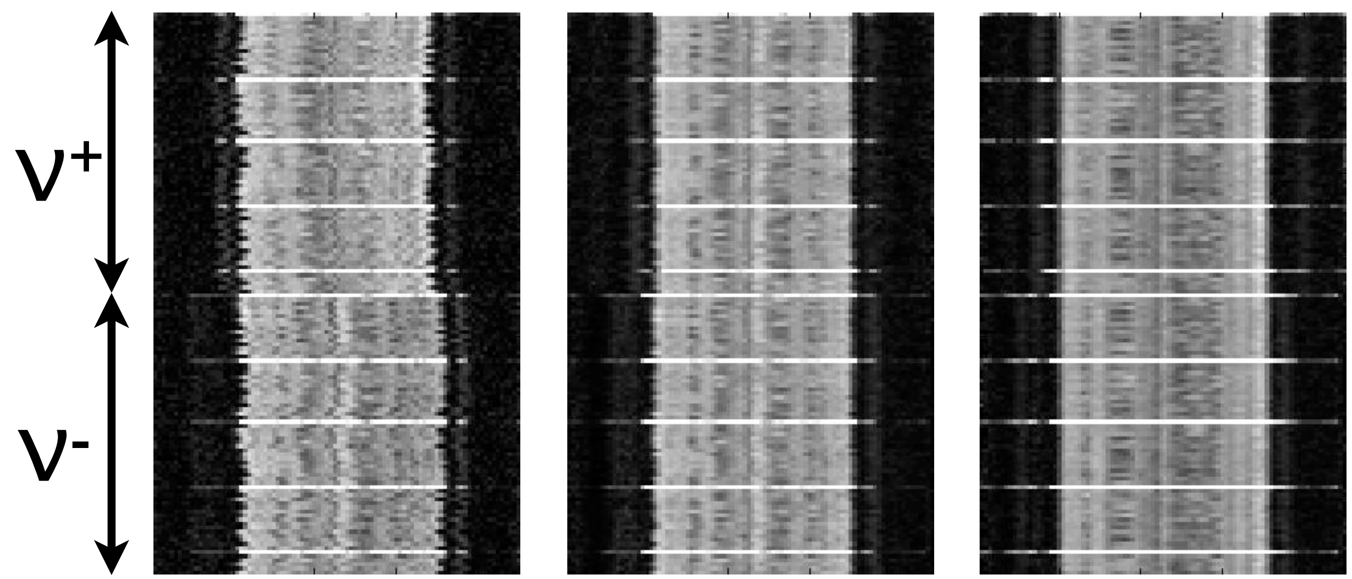


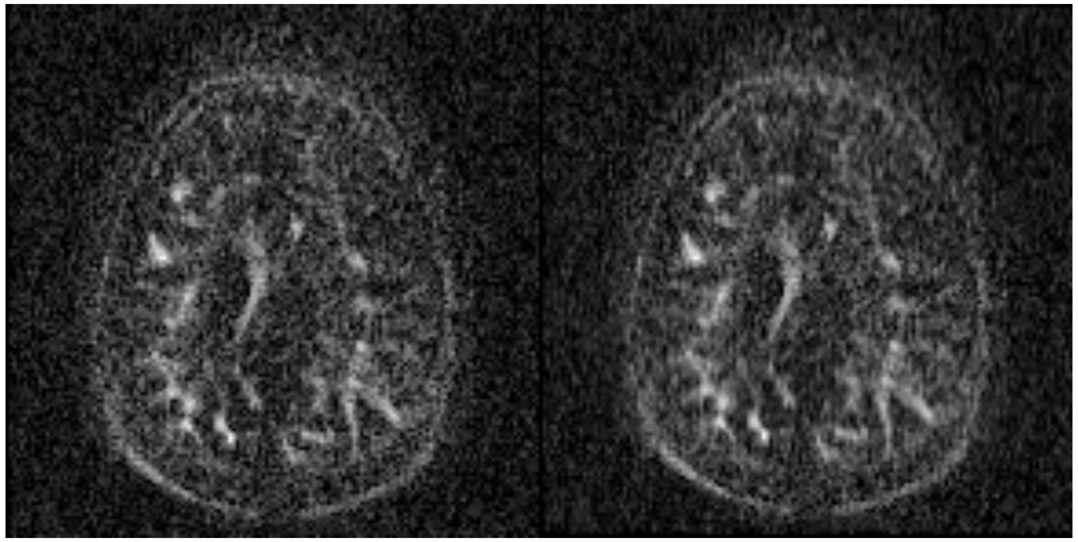
Eddy Current-induced Distortions



eddy and topup - tools for processing of diffusion data







Outline of the talk

- What is the problem with diffusion data?
- Off-resonance field
  - How does it cause distortions?
  - Where does it come from?
- Registering diffusion data
  - How topup works
  - How eddy works
- Practicalities
- Some results
- Quality control
- “New” eddy features

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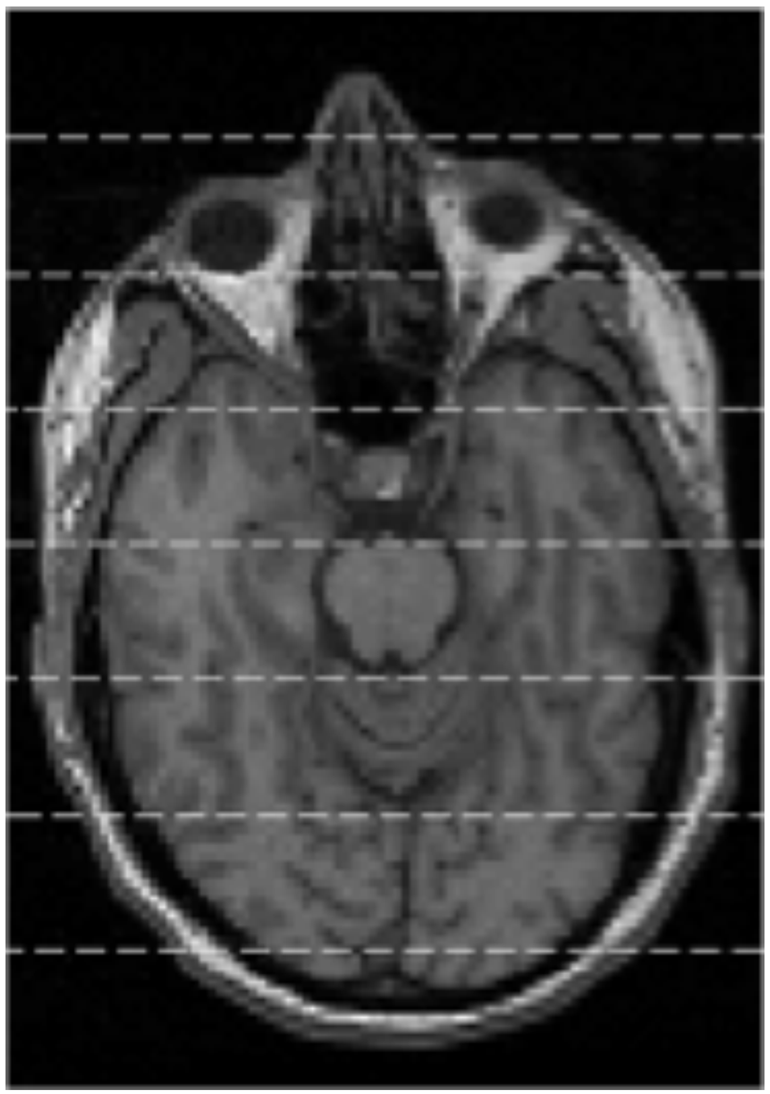
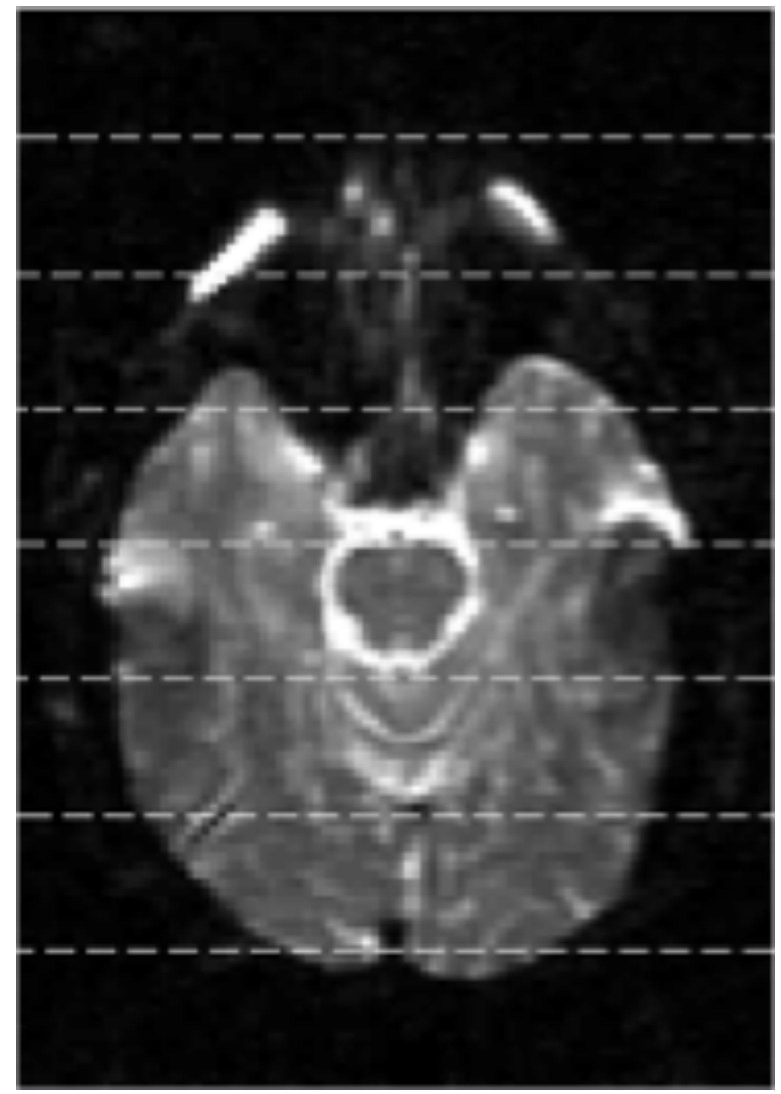
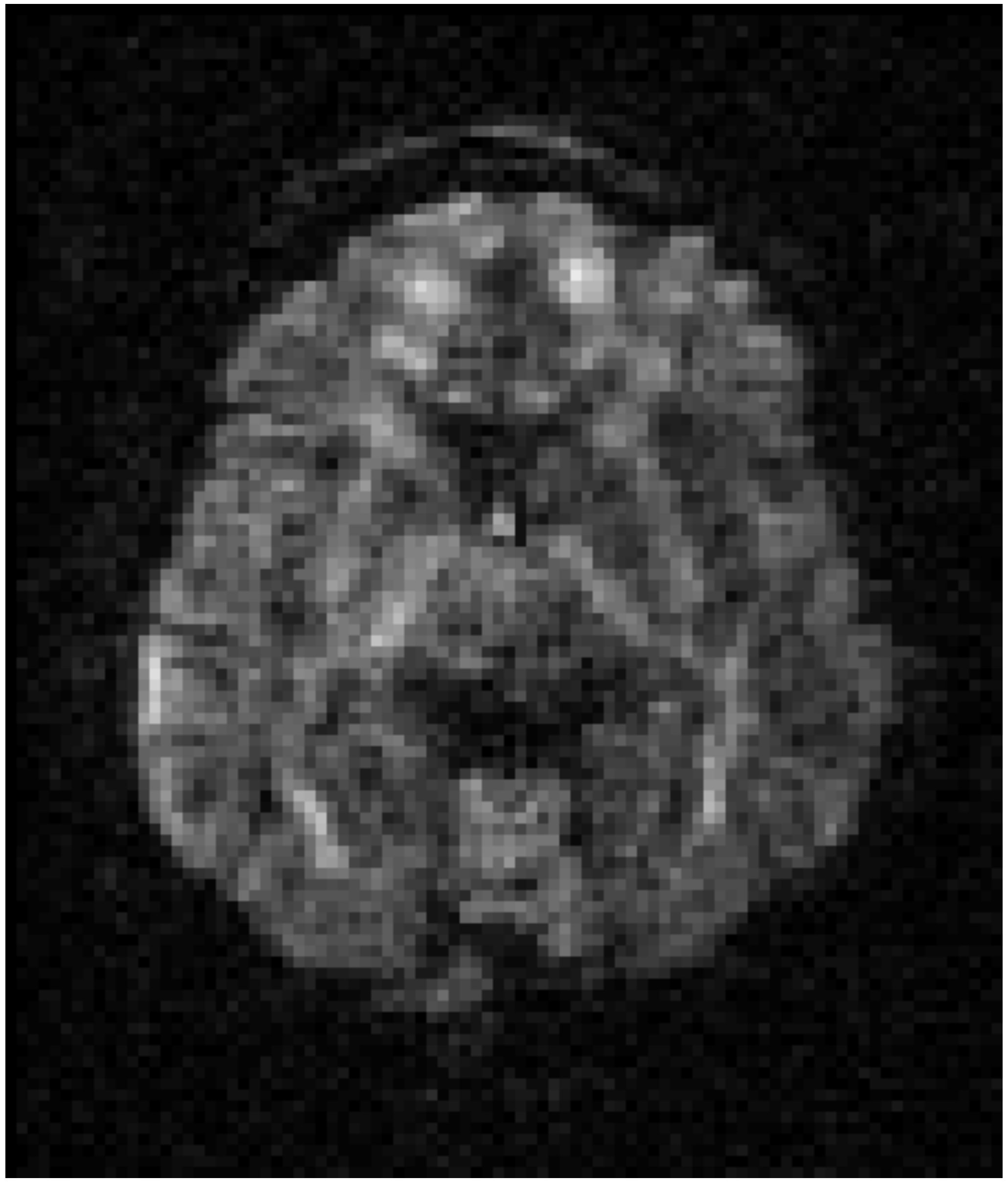
What is the problem with diffusion data?





Well, it isn't very anatomically faithful

What is the problem with diffusion data?



In fact, it isn't even internally consistent

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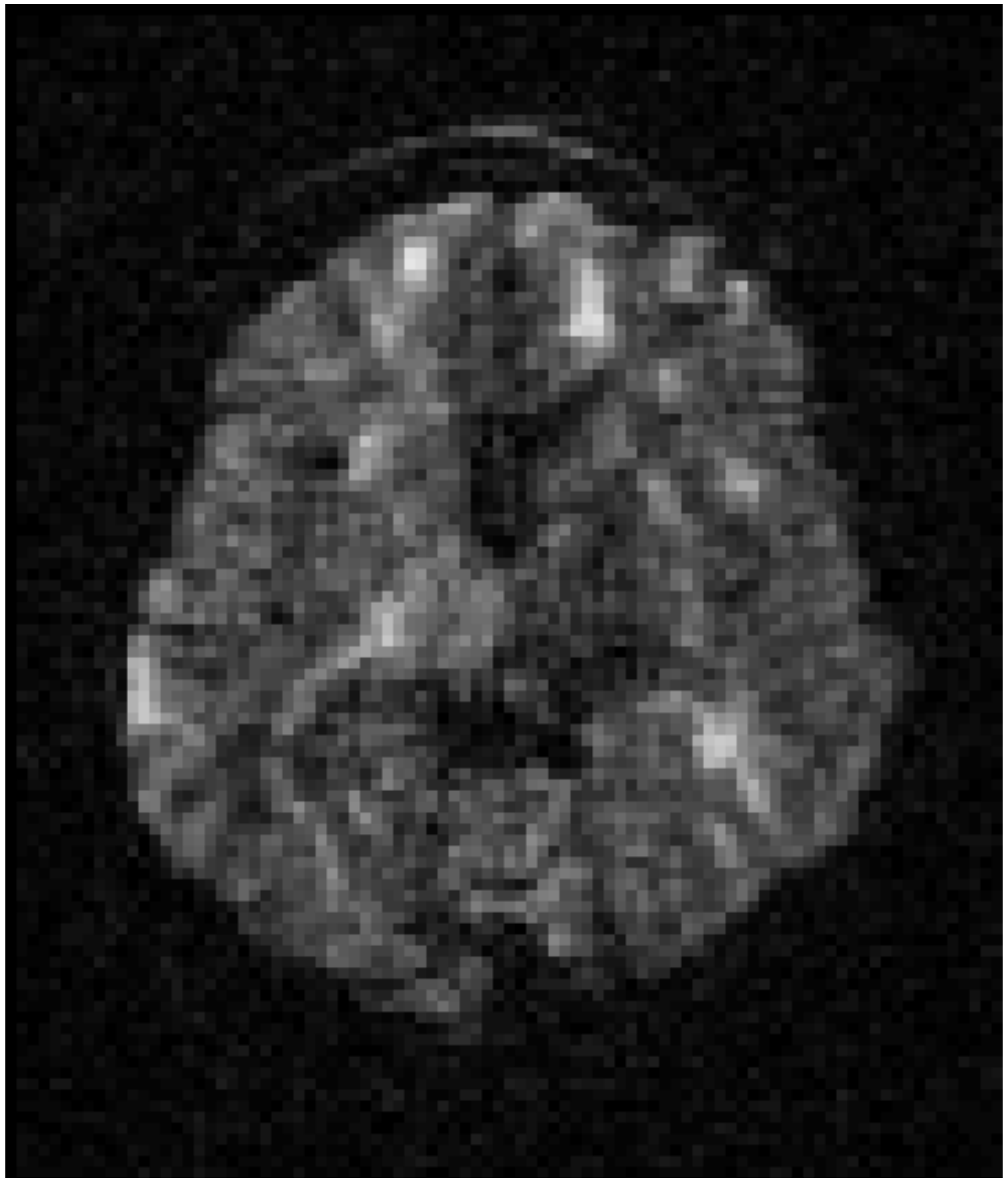

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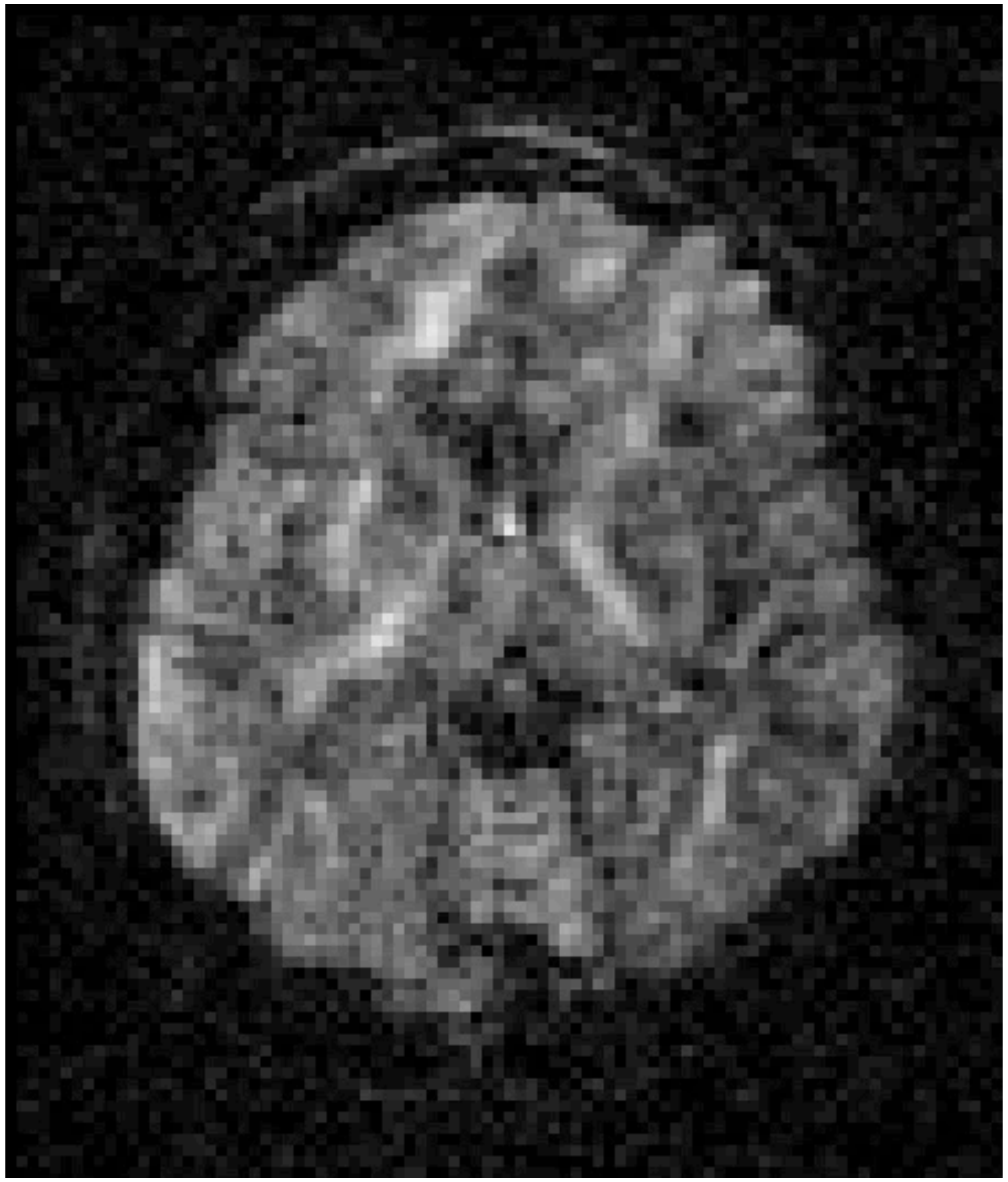

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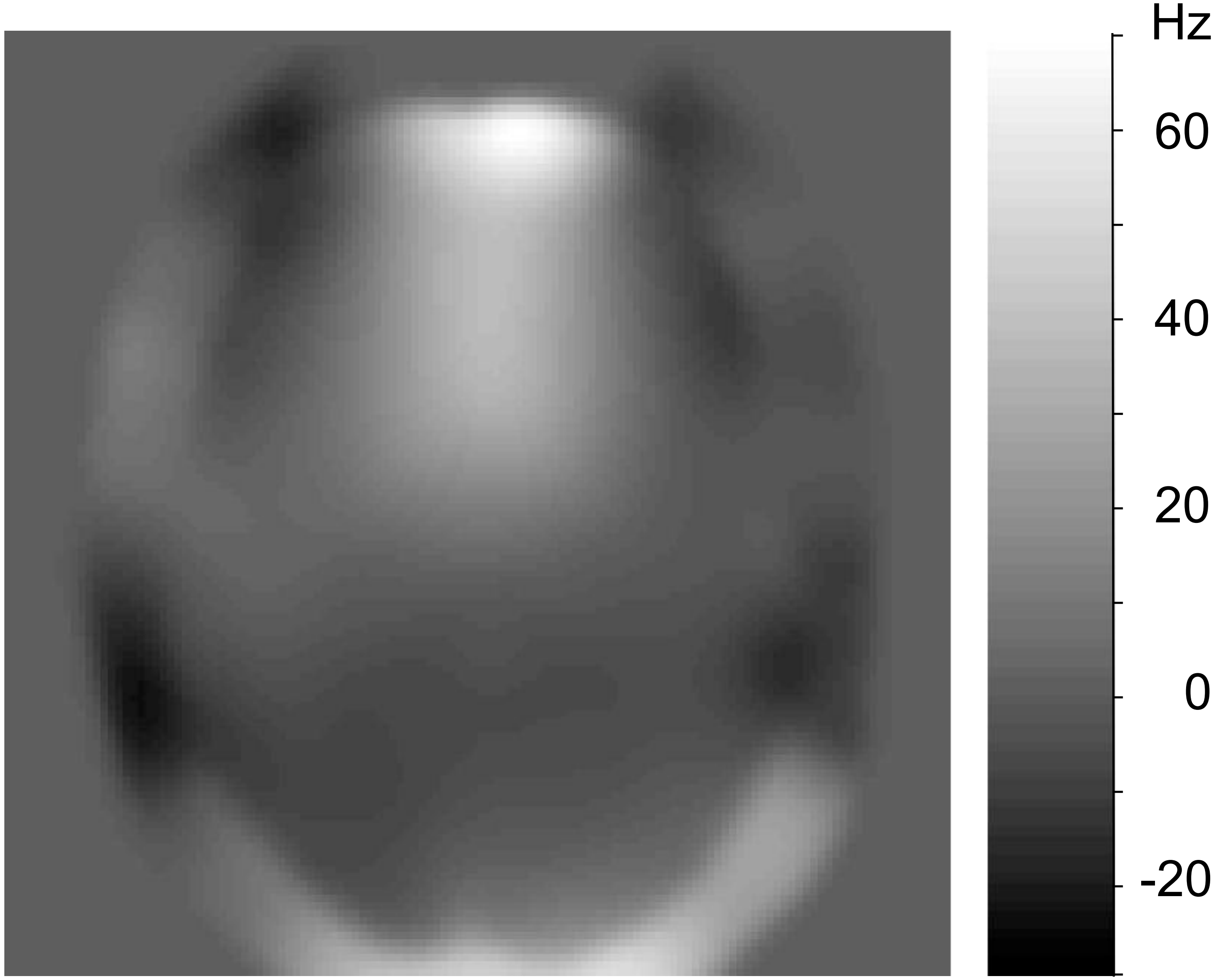
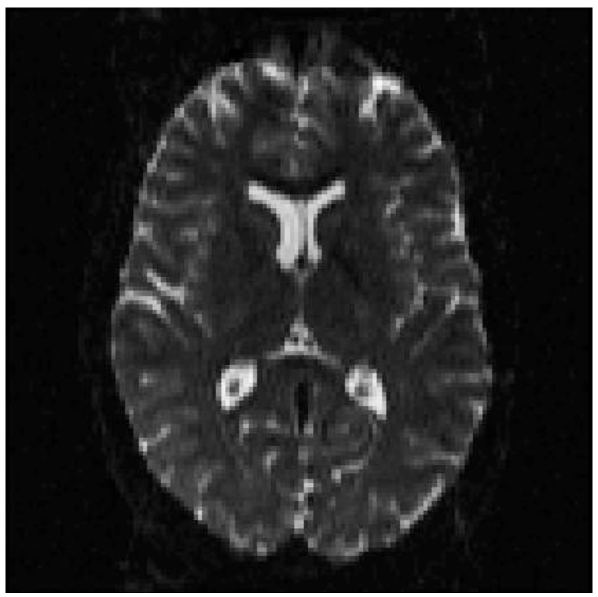
Off-resonance field ⇒ Distortions

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

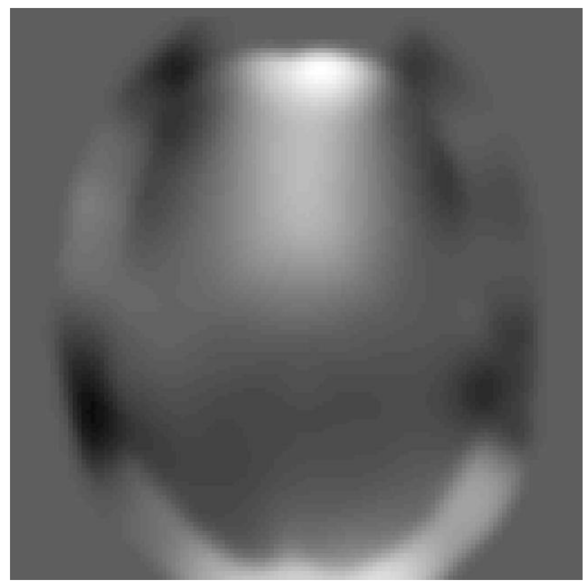


It is all caused by an “off-resonance” field

Off-resonance field ⇒ Distortions

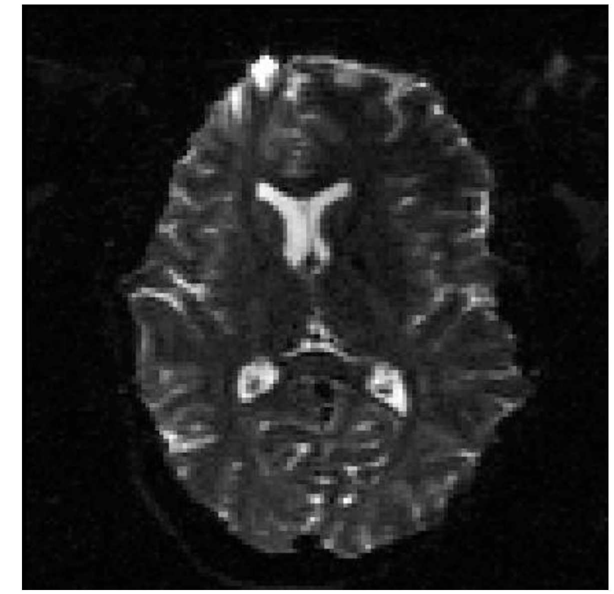


But this object

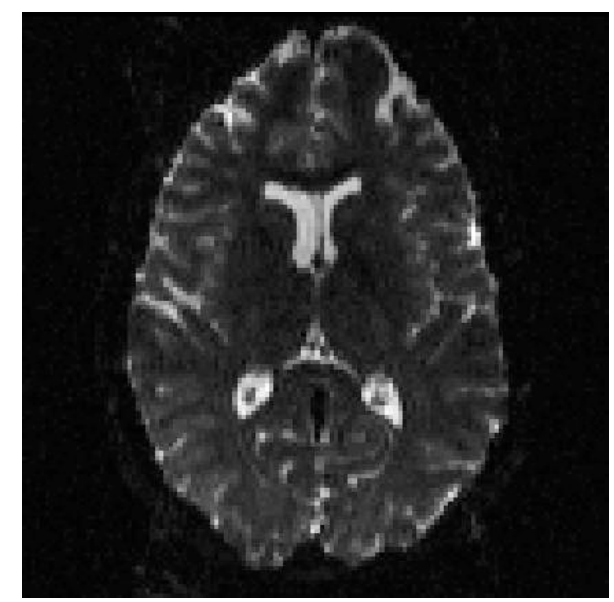


scanned in this field

or this

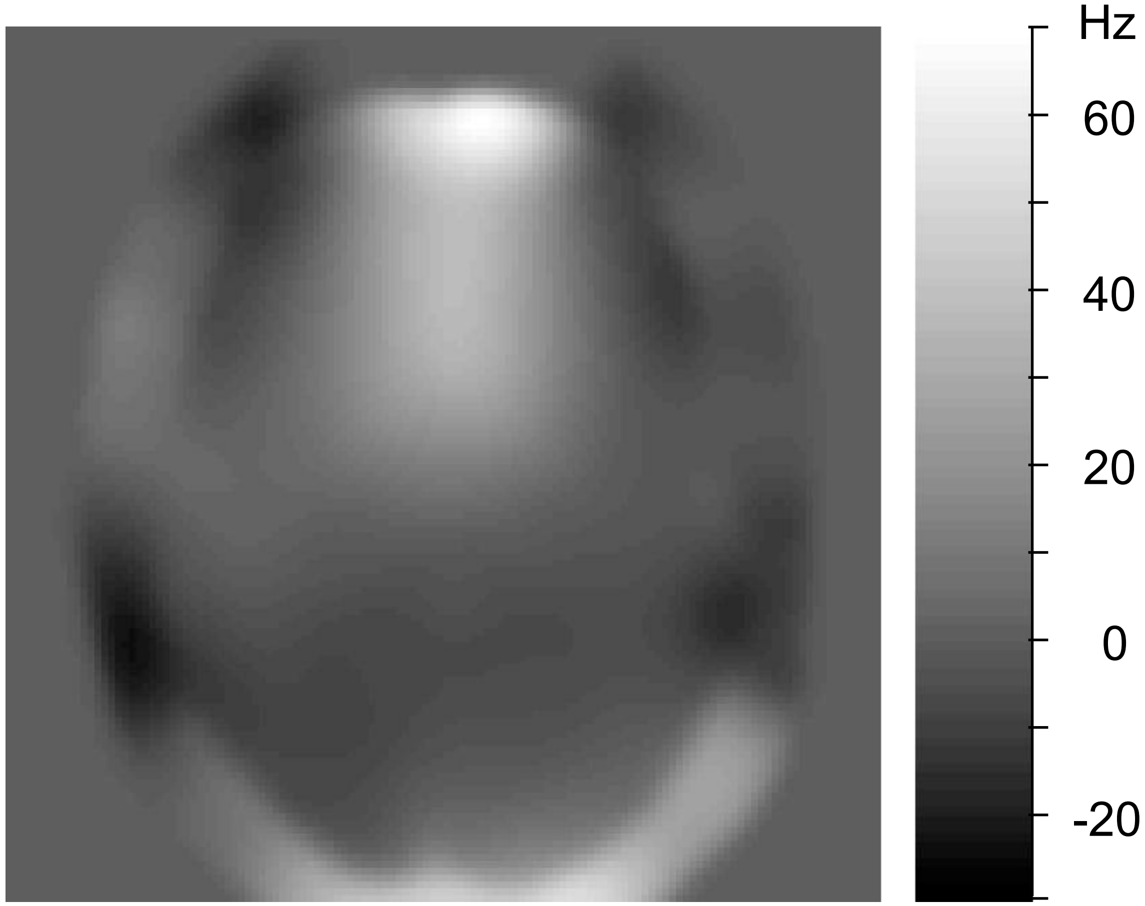


Can yield this



So there is clearly more to this story...

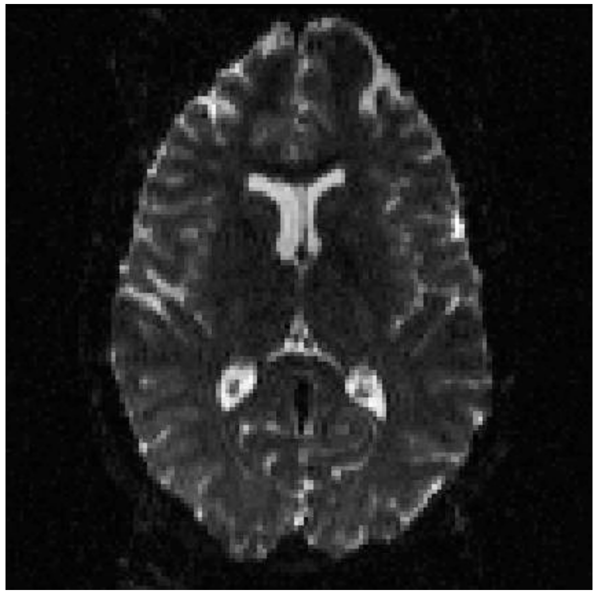
Off-resonance field ⇒ Distortions

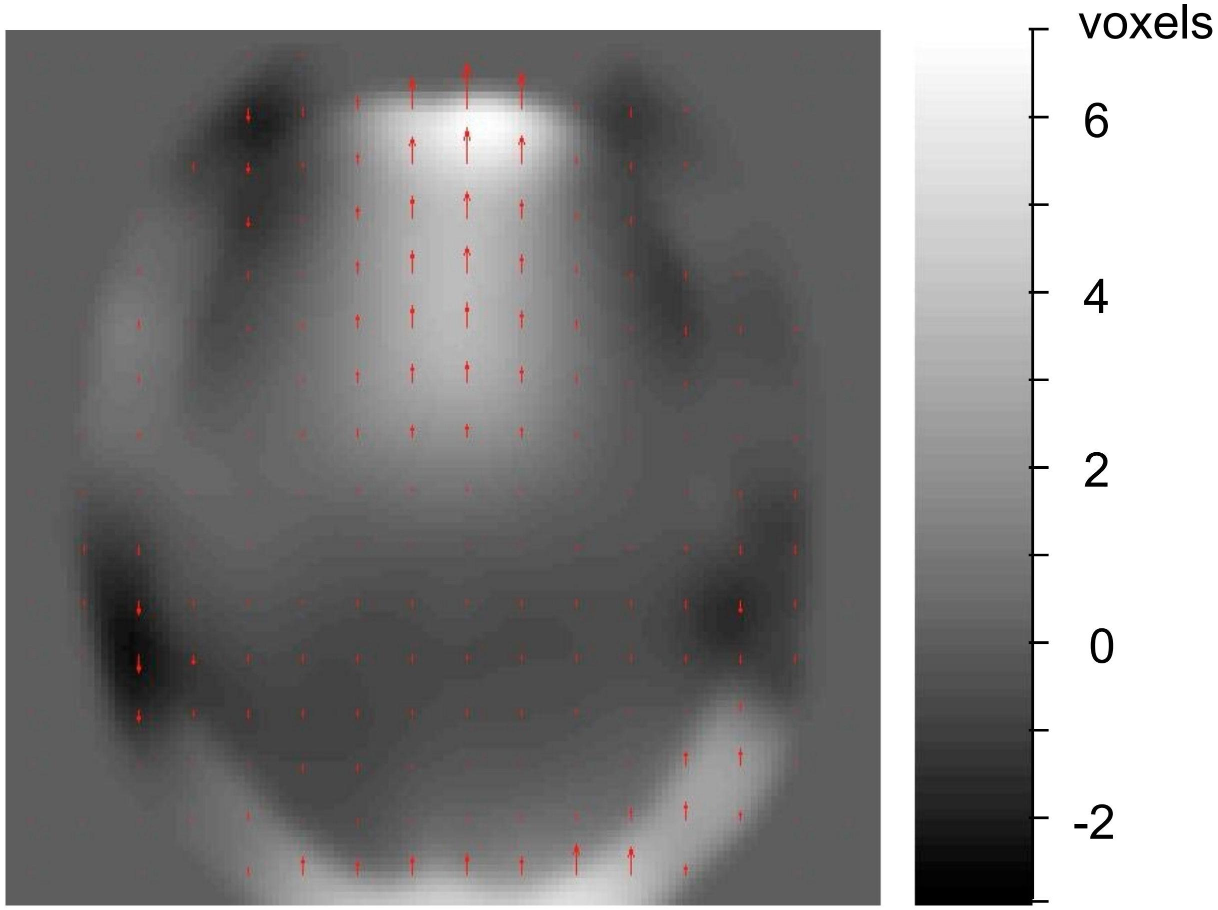


An off-resonance field is effectively a scaled voxel-displacement map.

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

Off-resonance field ⇒ Distortions





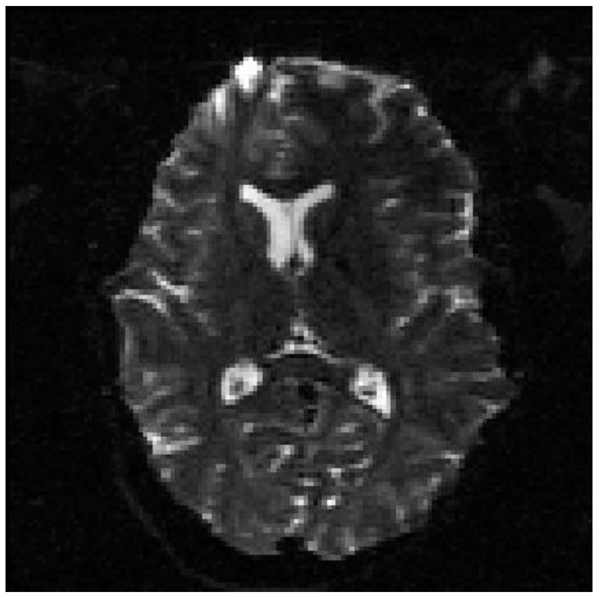
And know what to expect

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

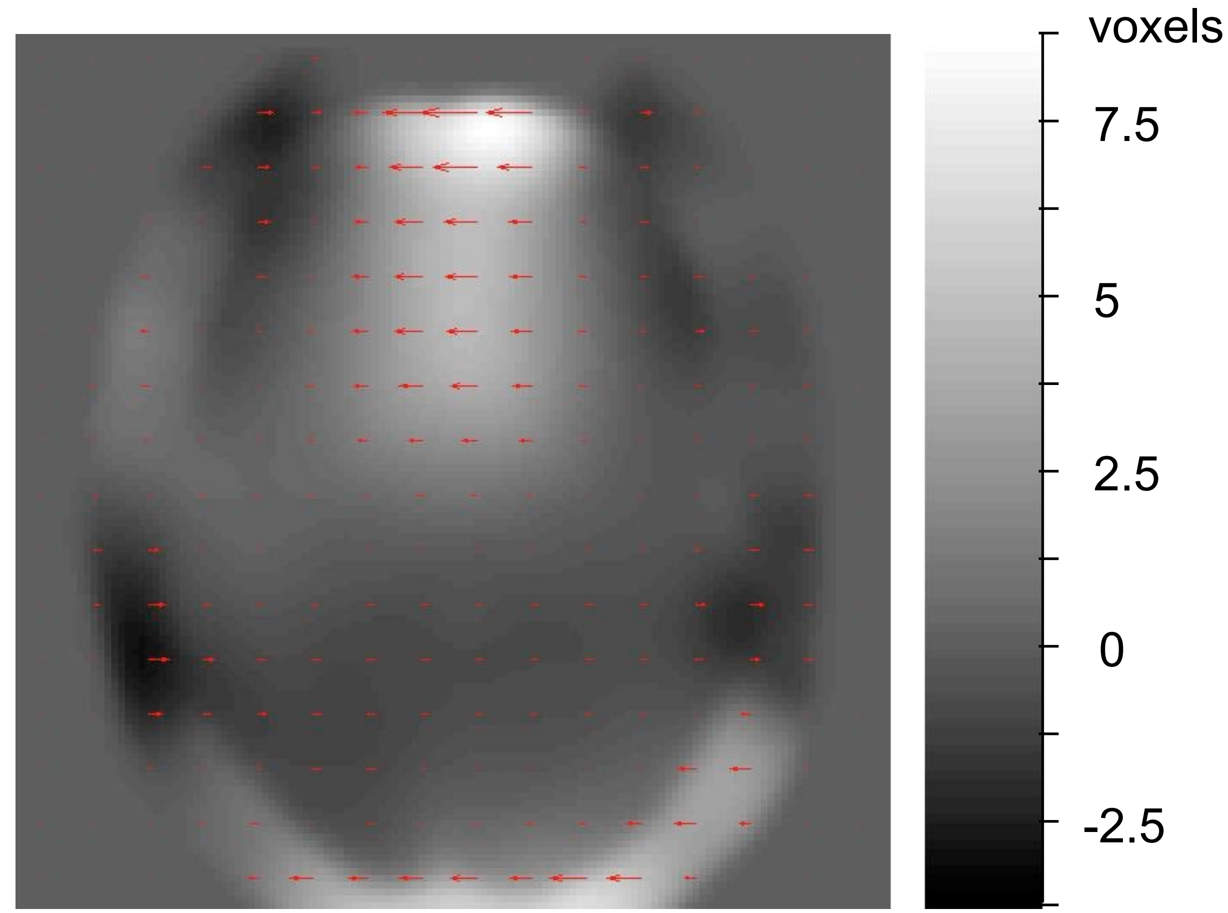
If we know the imaging parameters we can do the translation.

BW/voxel = 10Hz, **p** = [0 1 0]

Off-resonance field ⇒ 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.

BW/voxel = 8Hz, **p** = [-1 0 0]

Outline of the talk

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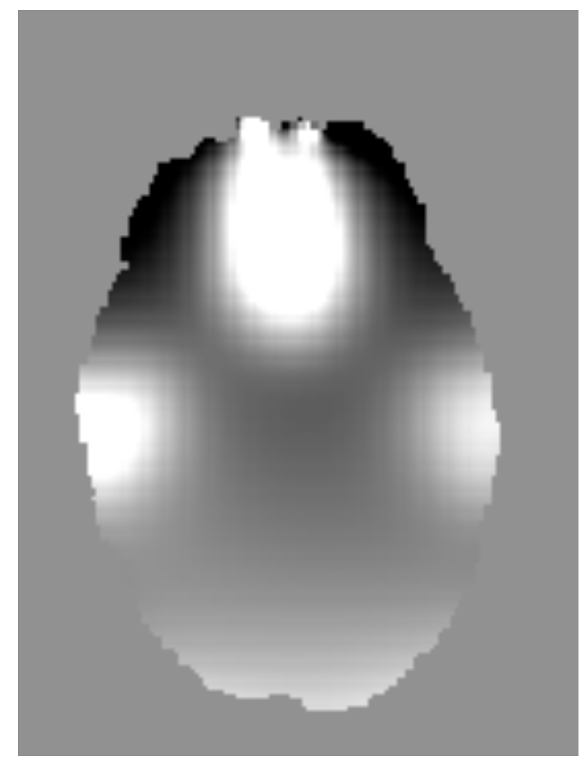
Where does the off-resonance field come from?

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

(CT of) Human head

$B_0 \odot$

Resulting field



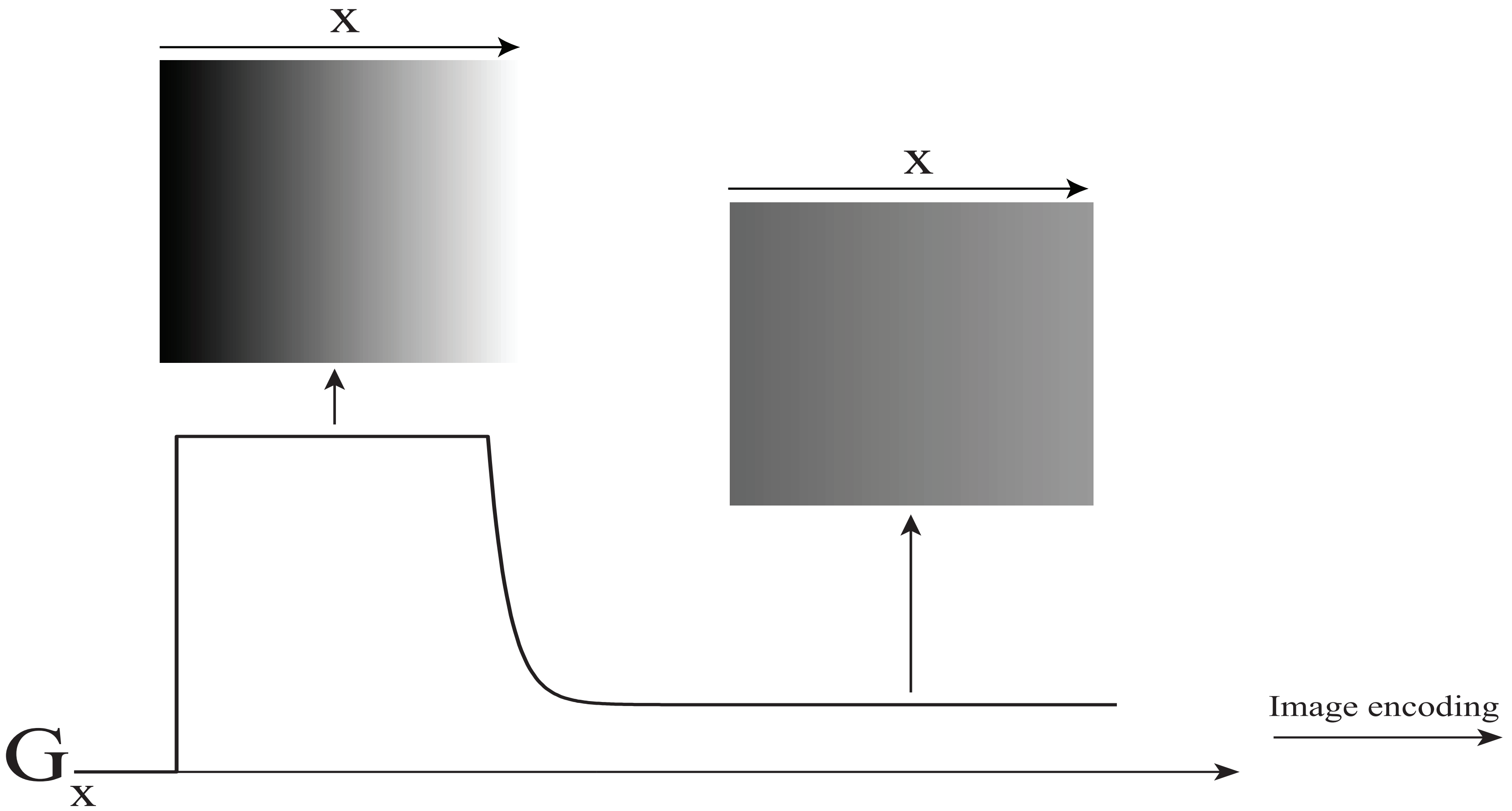
PPMs

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

Where does the off-resonance field come from?

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

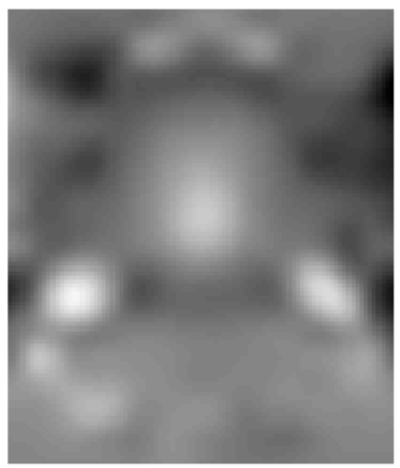
- The second is caused by the diffusion gradient



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

Susceptibility

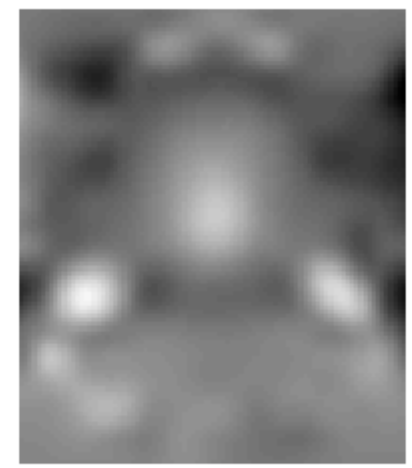


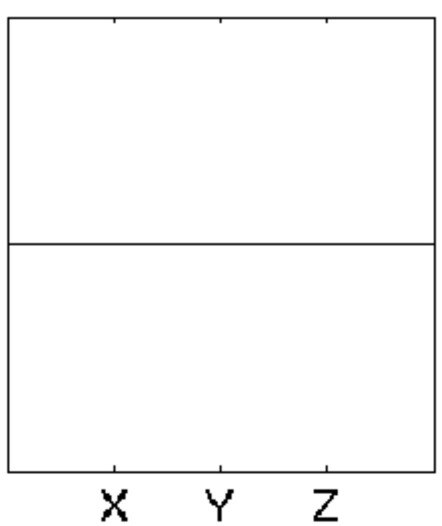
+

Eddy currents

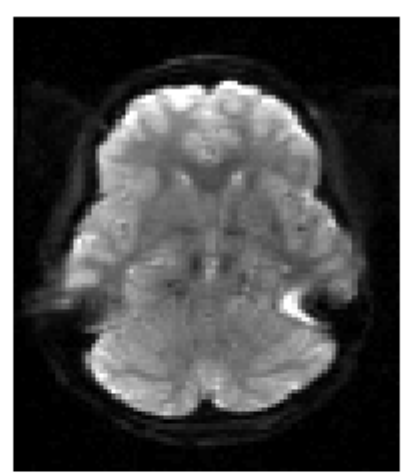
=

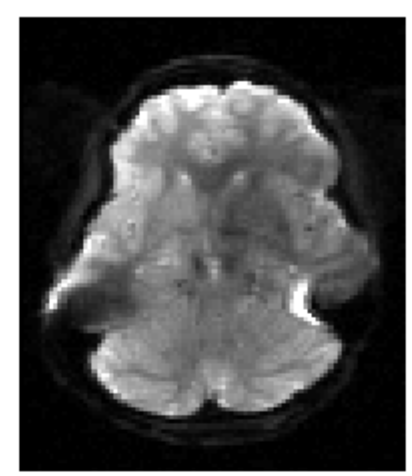
Total





Diffusion gradient

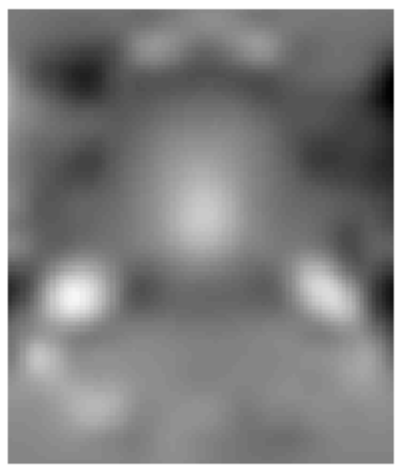

"True" object


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

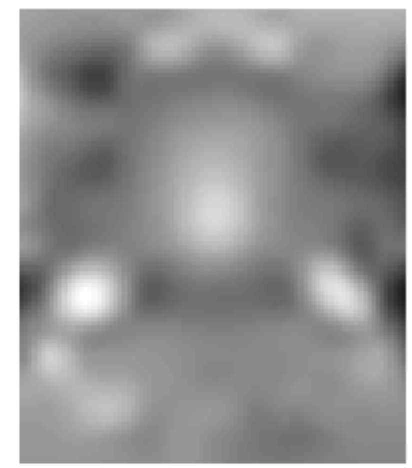


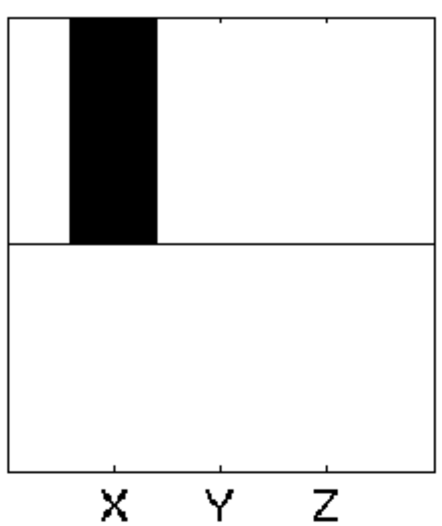
+

Eddy currents

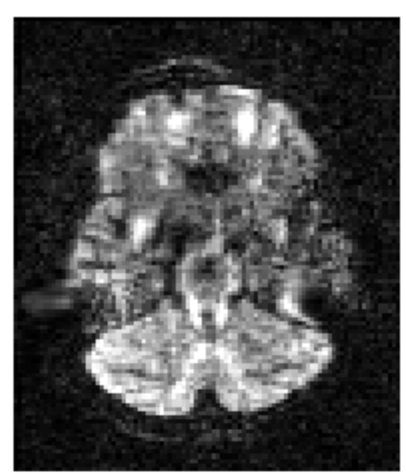
=

Total





Diffusion gradient



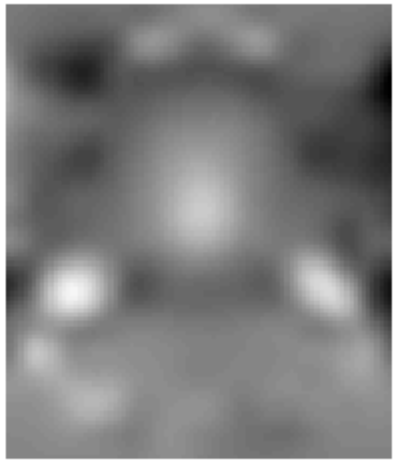
“True” object

Observed image

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

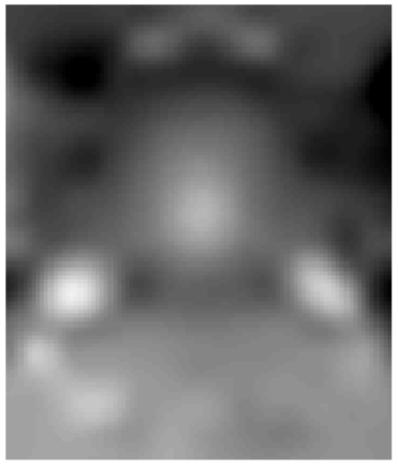


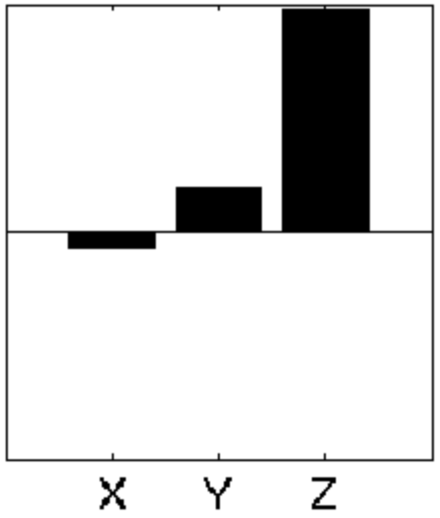
+

Eddy currents

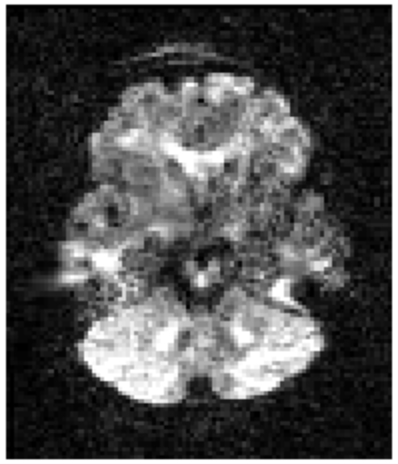
=

Total

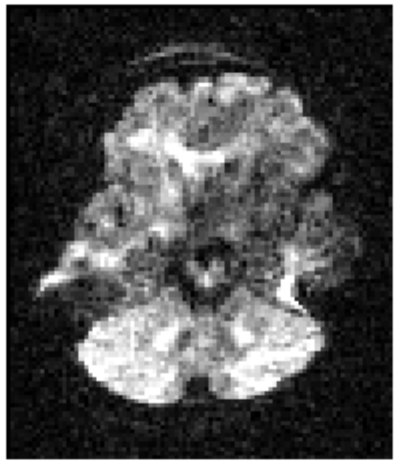




Diffusion gradient



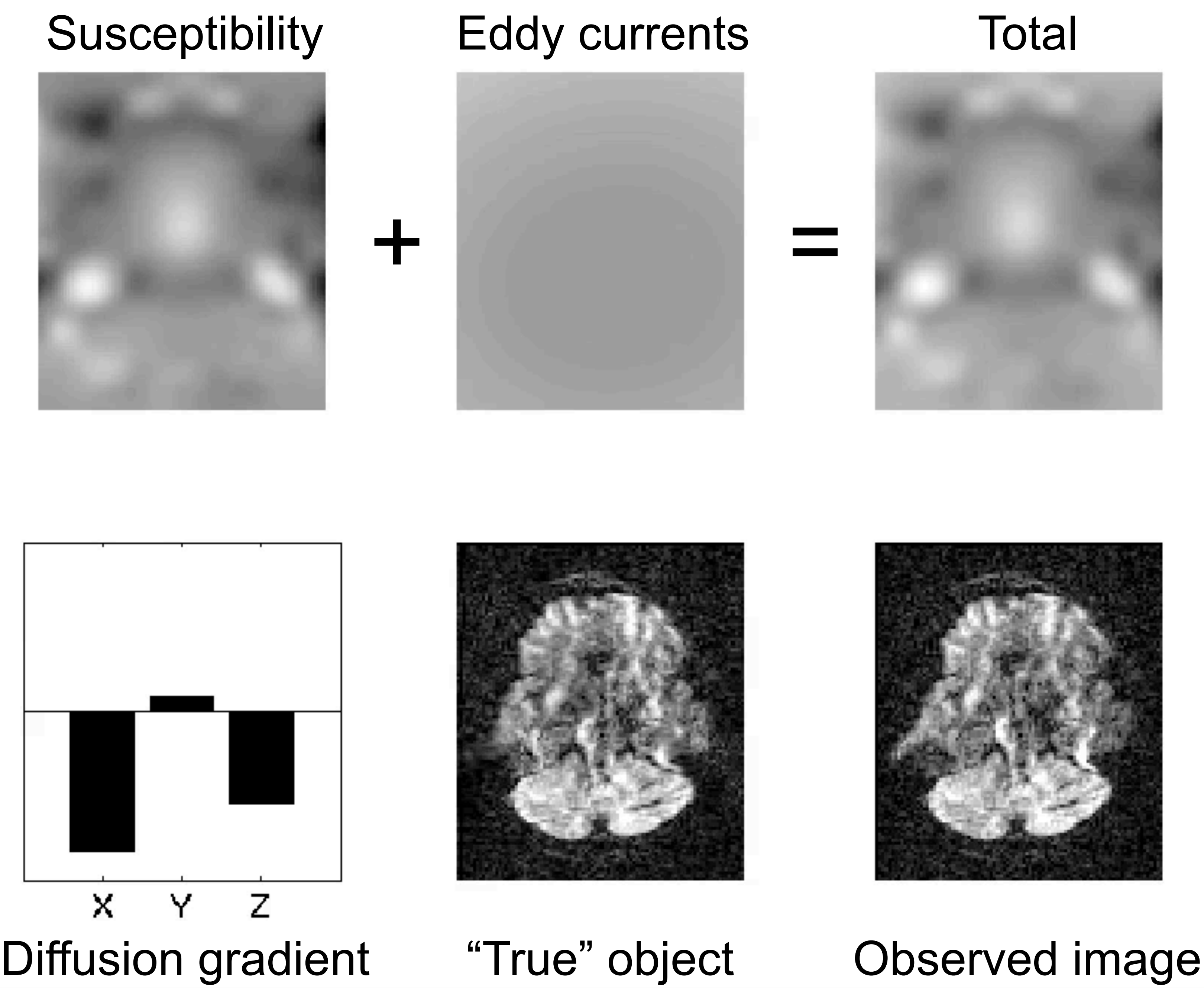
“True” object



Observed image

Where does the off-resonance field come from?

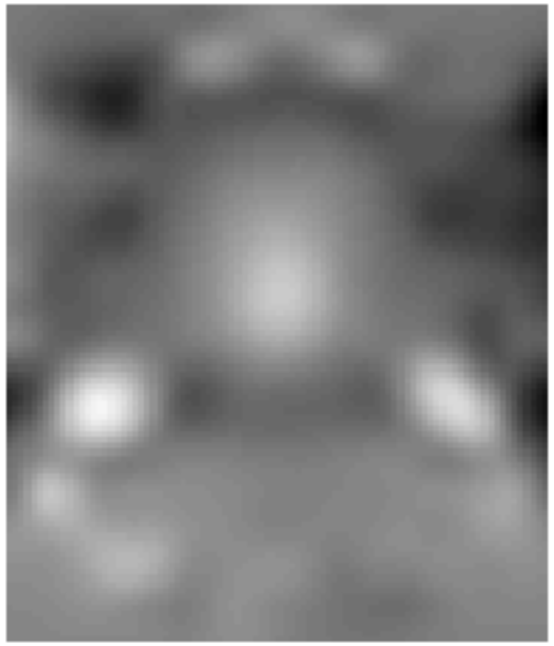
So for any diffusion weighted volume the off-resonance field is the sum of these two contributions



Separate estimation of susceptibility- and eddy current-fields

So, what we need to estimate is

One of these per subject



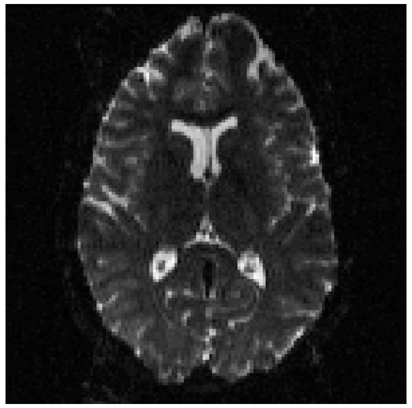
One of these per volume

FSL-tools: topup eddy

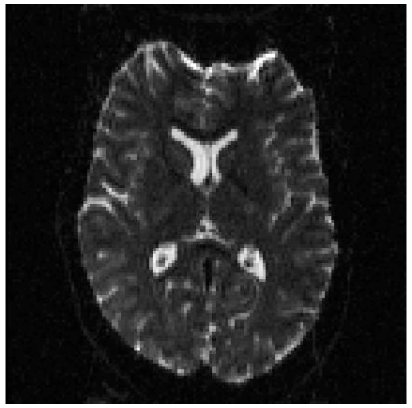
Outline of the talk

- What is the problem with diffusion data?
- Off-resonance field
  - How does it cause distortions?
  - Where does it come from?
- Registering diffusion data
  - How topup works
  - How eddy works
- Practicalities
- Some results
- Quality control
- “New” eddy features

How topup works (very briefly)



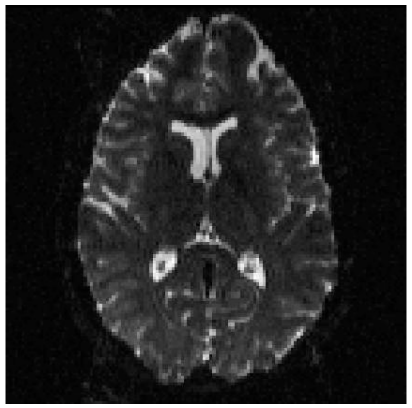
p=[0 1 0]



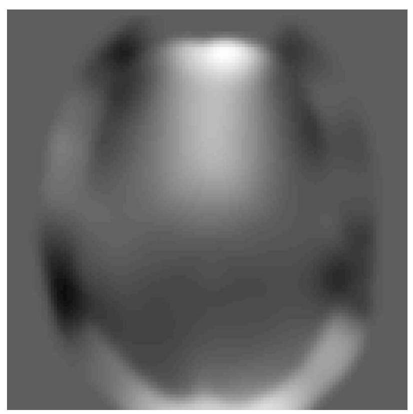
p=[0 -1 0]

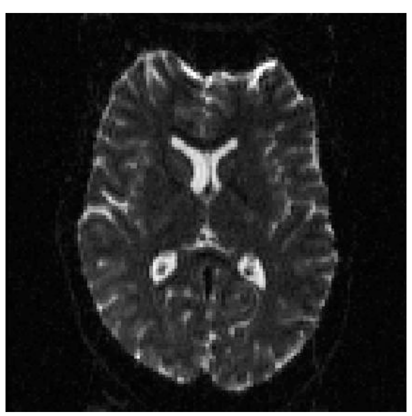
Given two images acquired with different phase-encoding

How topup works (very briefly)



p=[0 1 0]

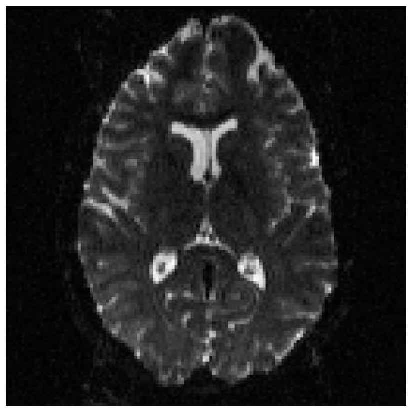




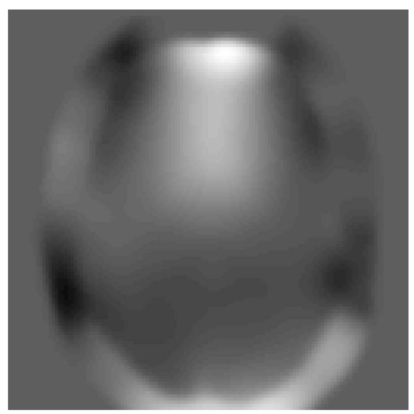
p=[0 -1 0]

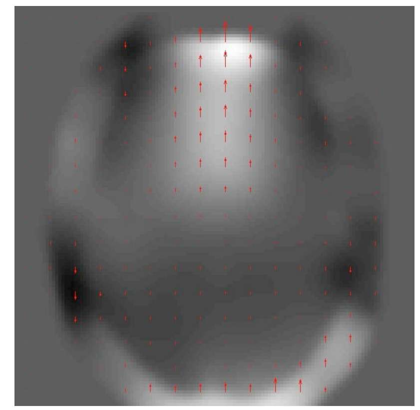
And we know what the off-resonance field is

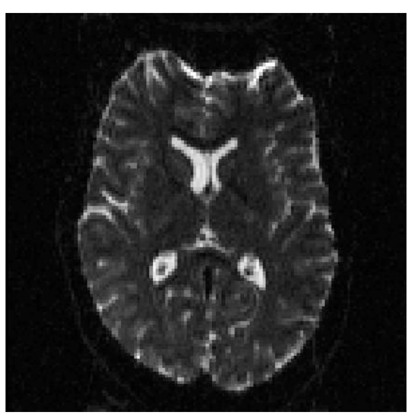
How topup works (very briefly)



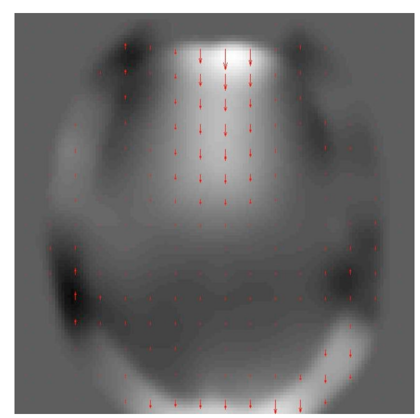
p=[0 1 0]





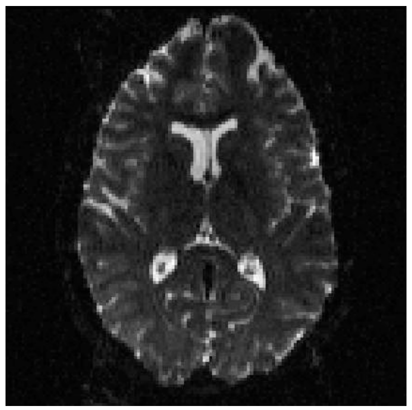


p=[0 -1 0]

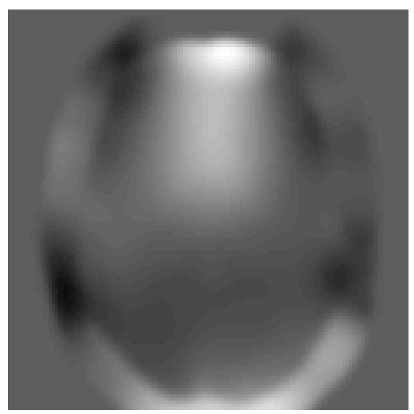


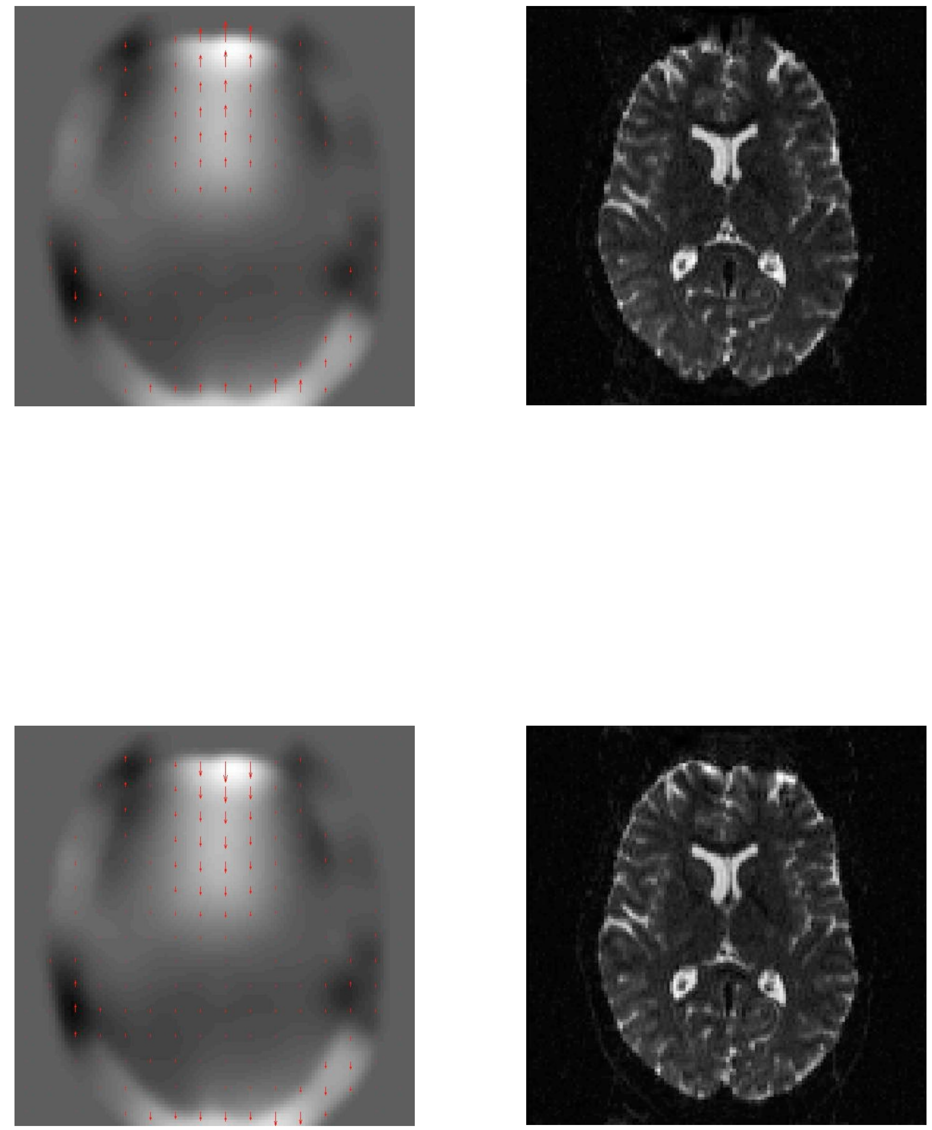
We can combine this with the PE information to get displacement maps

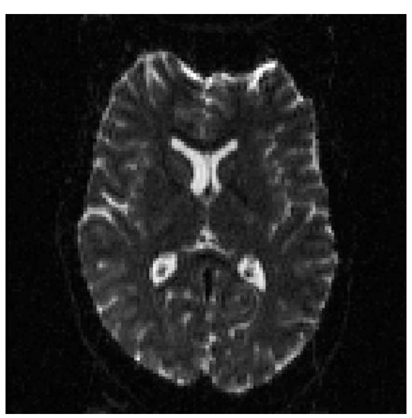
How topup works (very briefly)



p=[0 1 0]



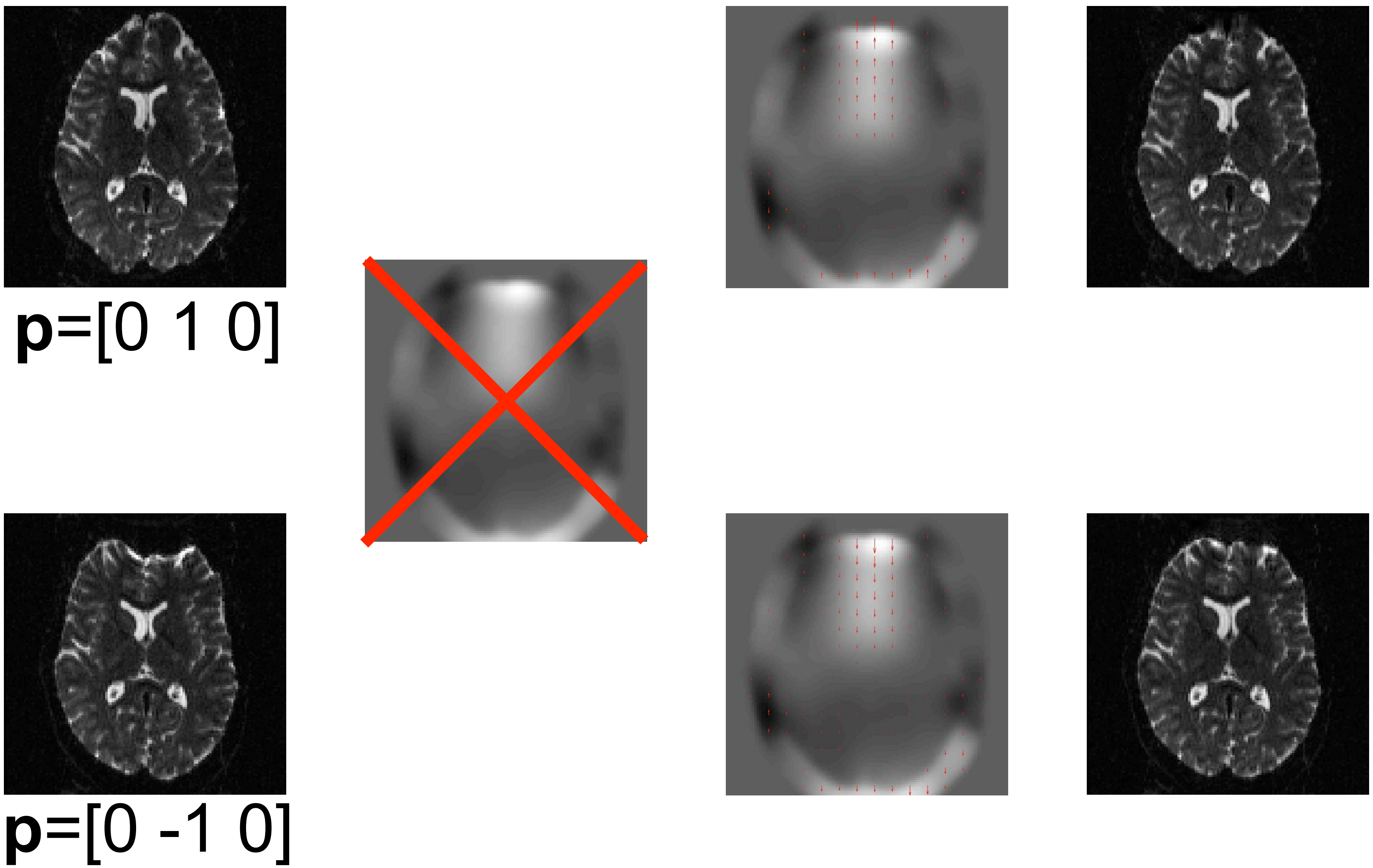




p=[0 -1 0]

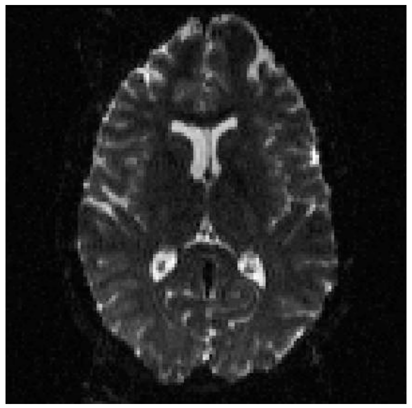
And use that to correct the distortions

How topup works (very briefly)

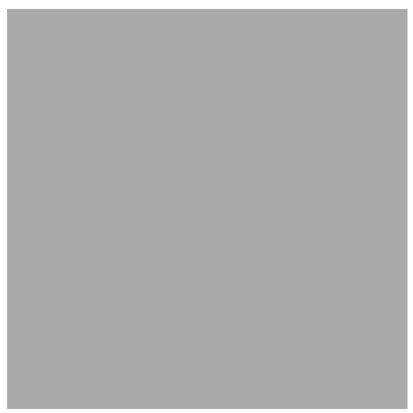


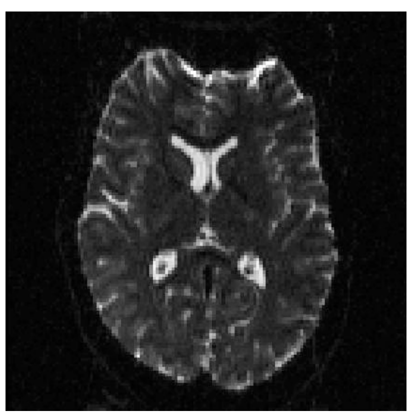
BUT we don’t know the field. That is what we want topup to calculate.

How topup works (very briefly)



p=[0 1 0]

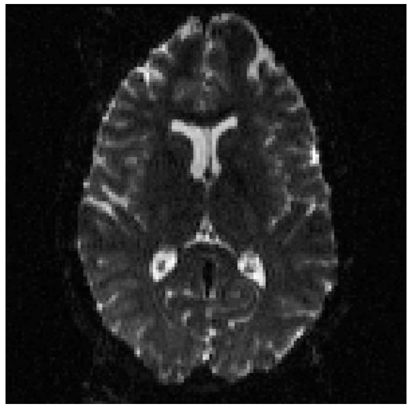




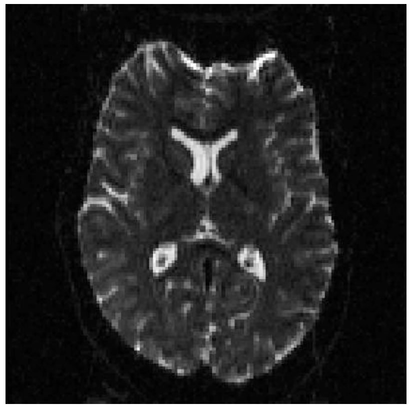
p=[0 -1 0]

topup “guesses” a field...

How topup works (very briefly)



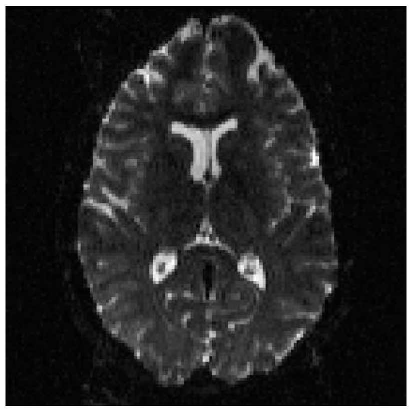
p=[0 1 0]

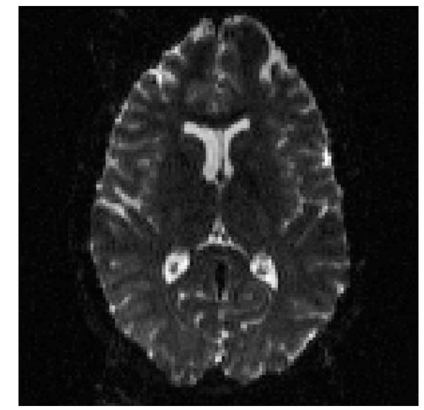


p=[0 -1 0]

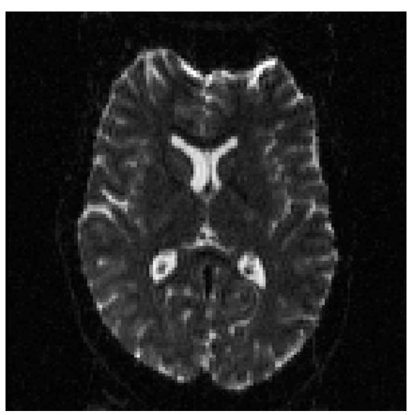
...calculates the displacement maps...

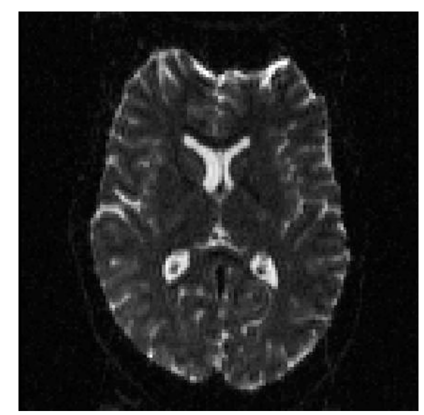
How topup works (very briefly)





p=[0 1 0]

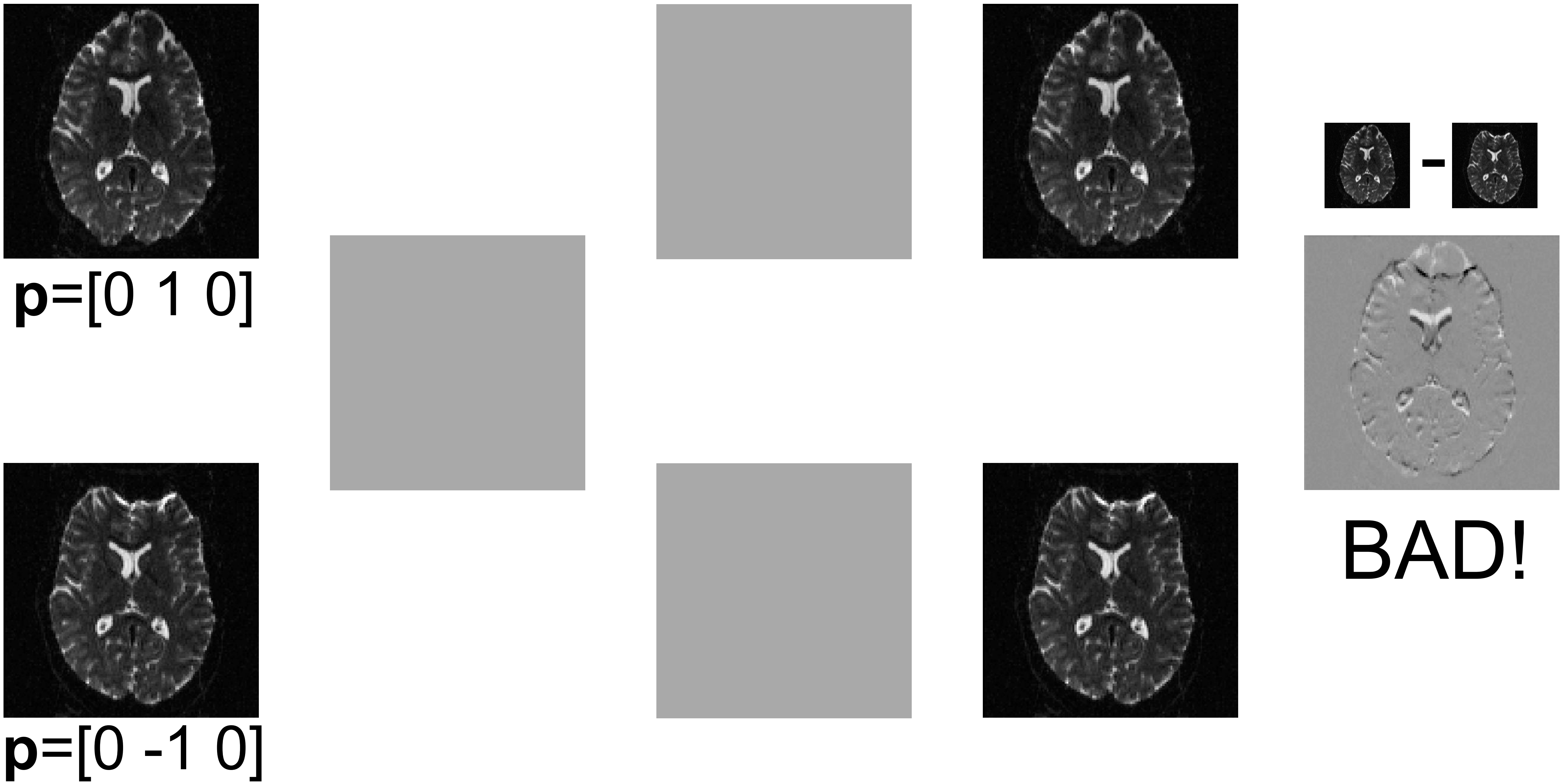




p=[0 -1 0]

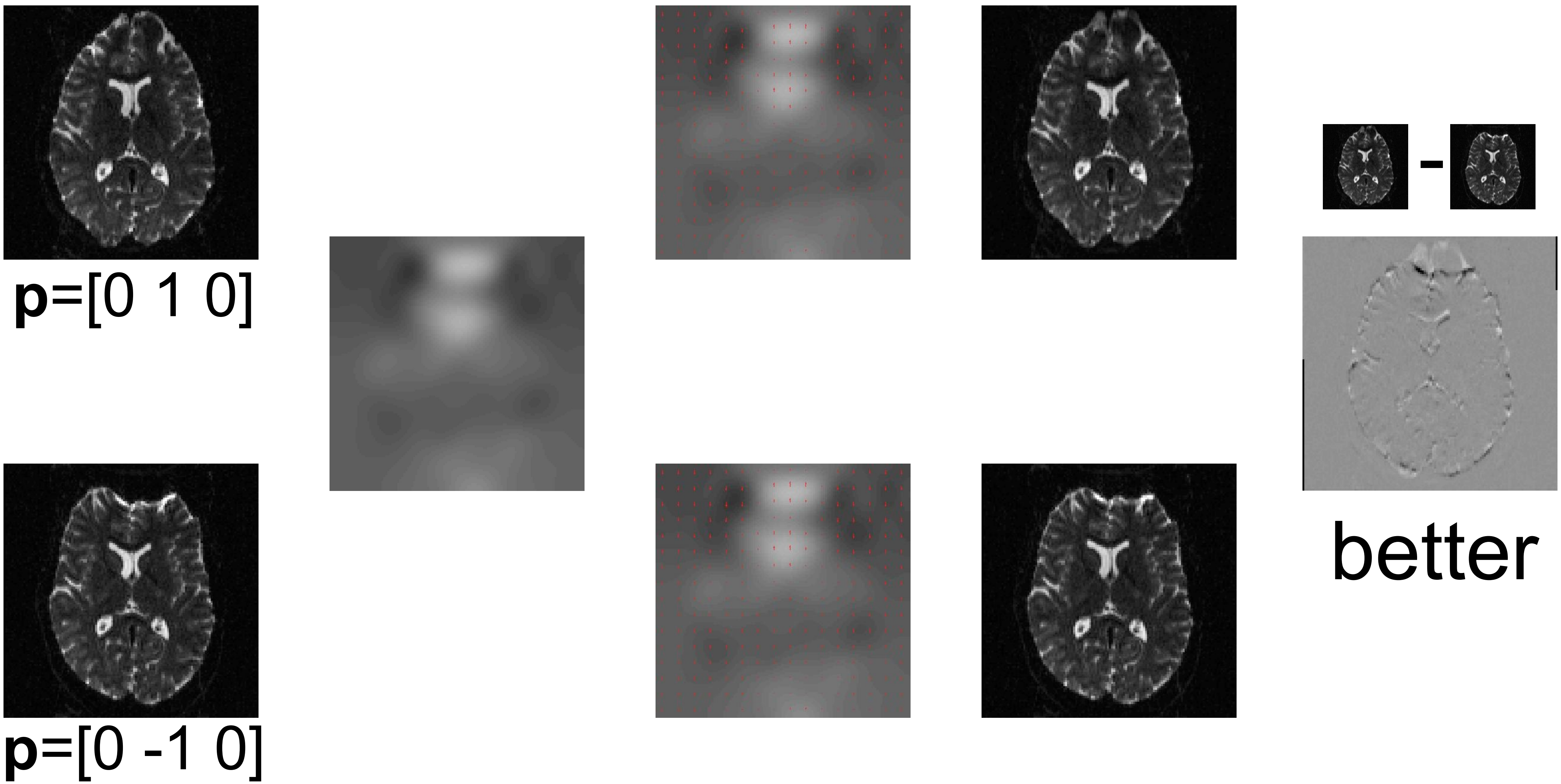
…"corrects" the images…

How topup works (very briefly)



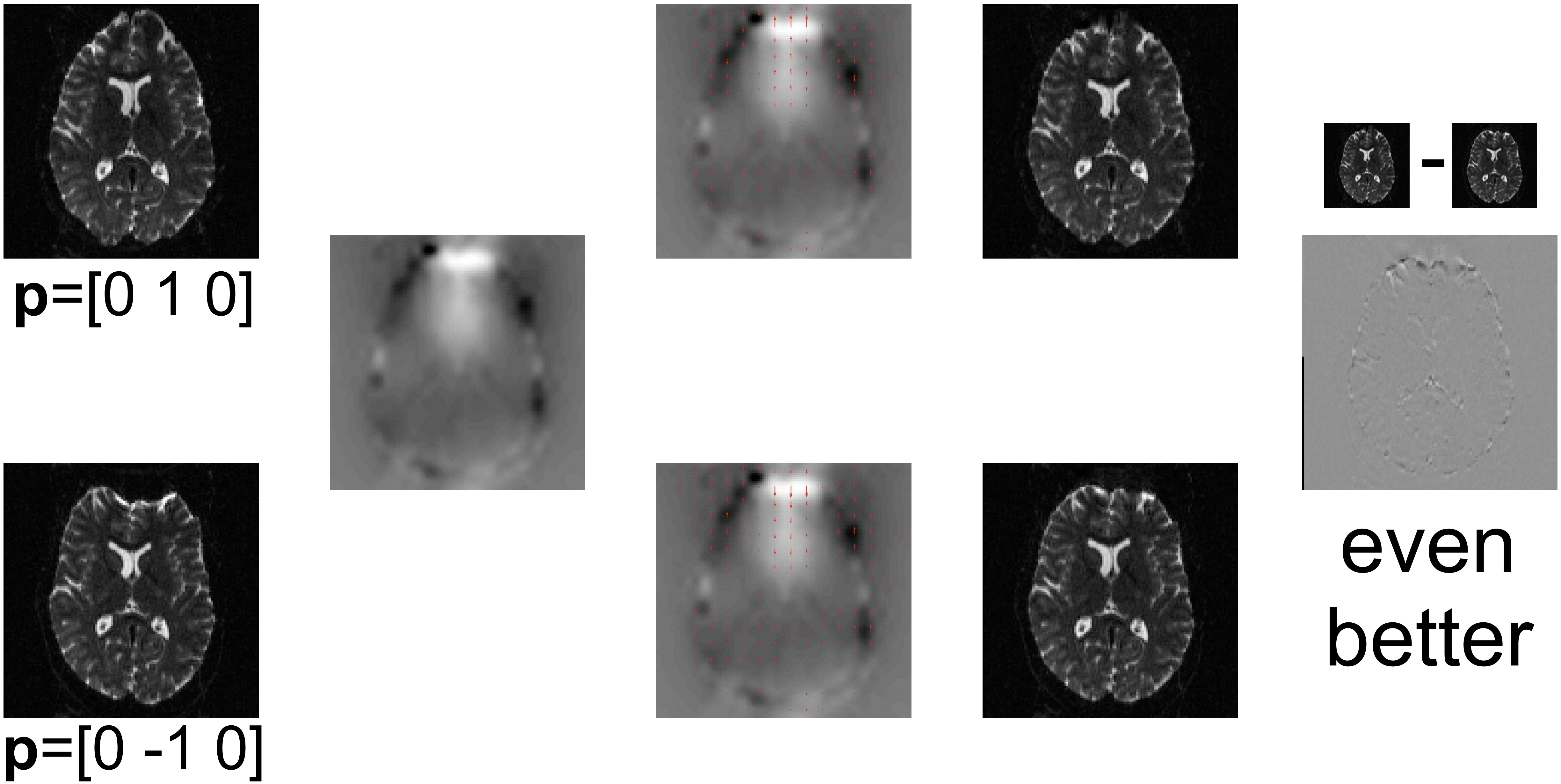
...and evaluates the results...
And **this** is the crucial bit.

How topup works (very briefly)



Because topup can then "guess" another field

How topup works (very briefly)



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

Outline of the talk

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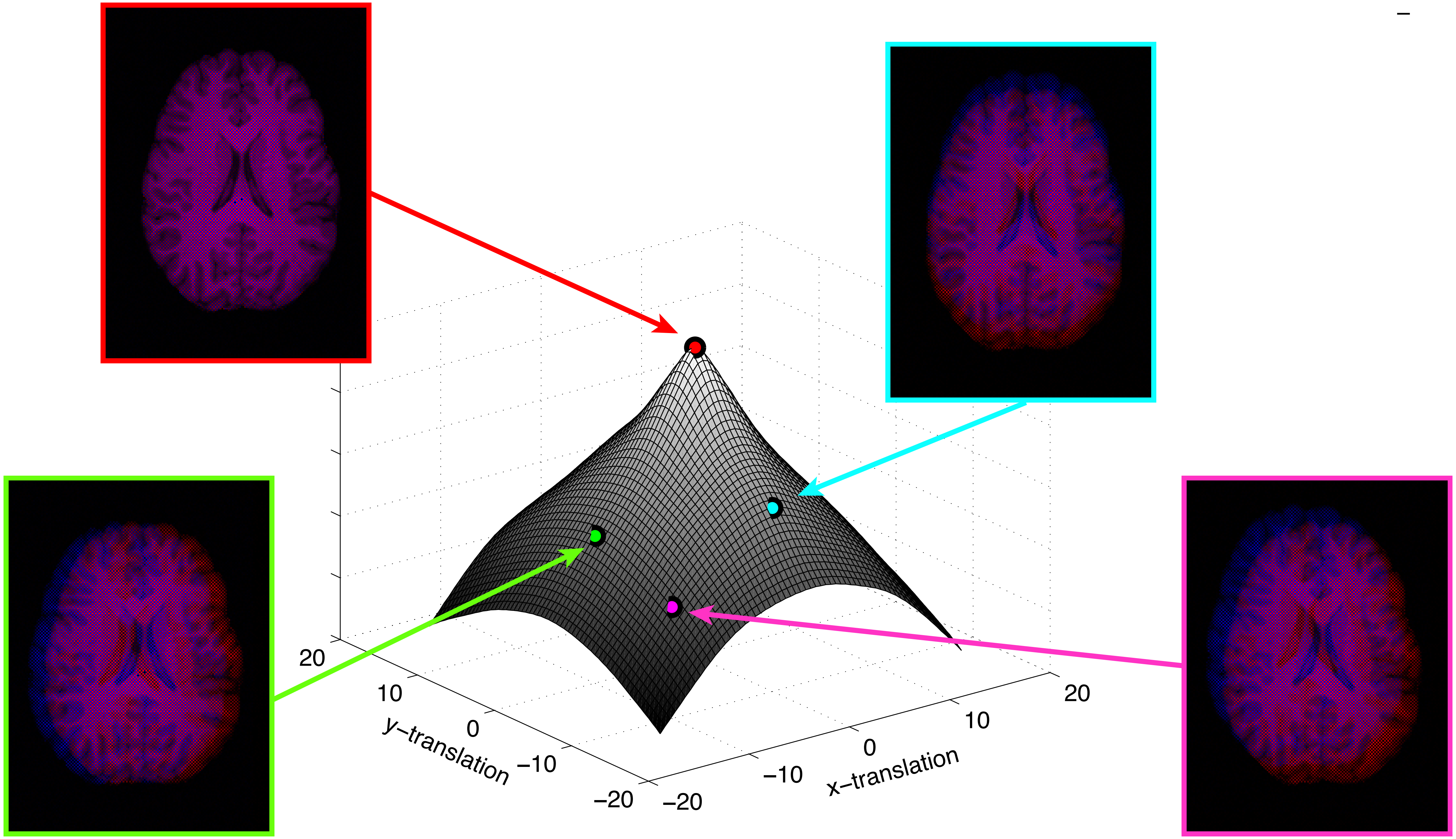
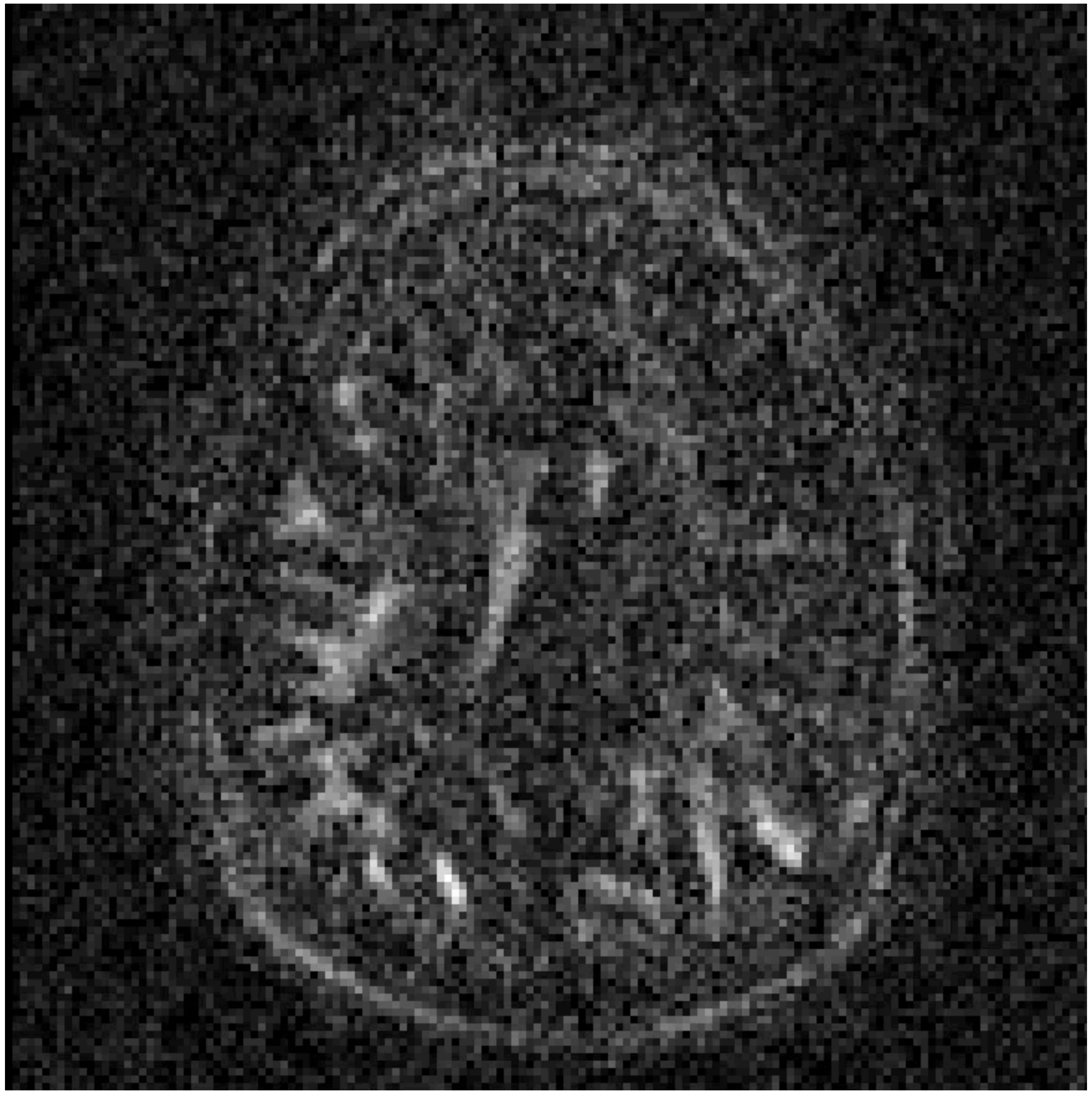
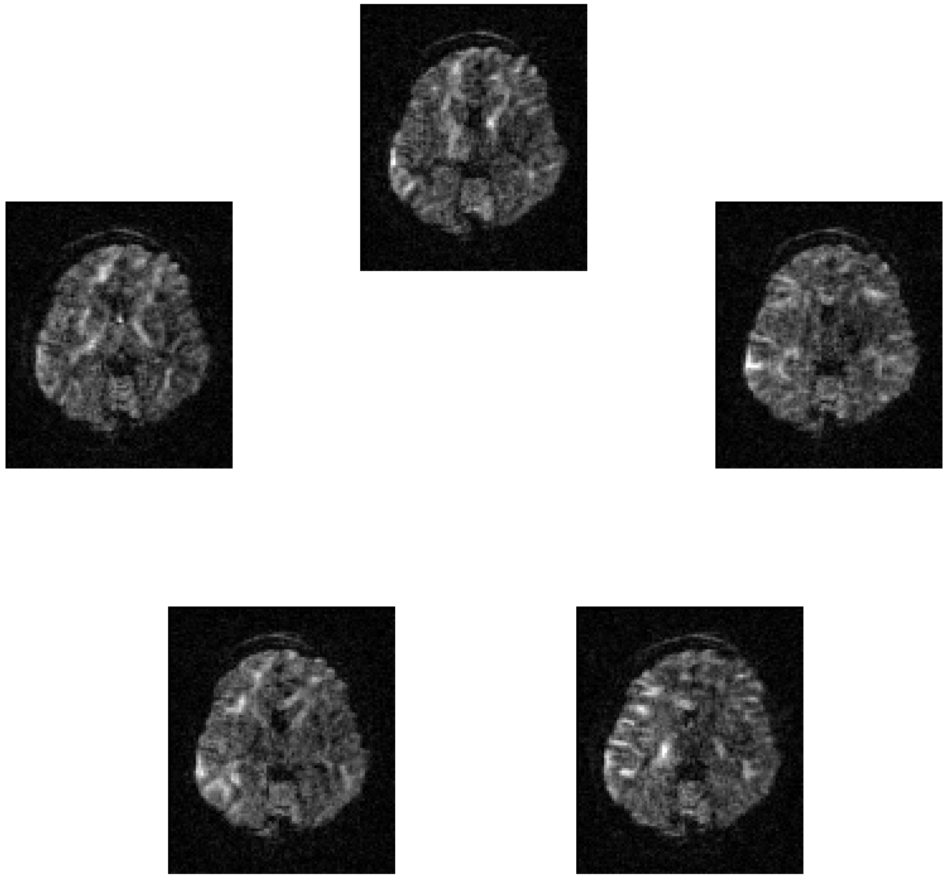
Worlds shortest course on image registration



Maximising/minimising an objective/cost-function

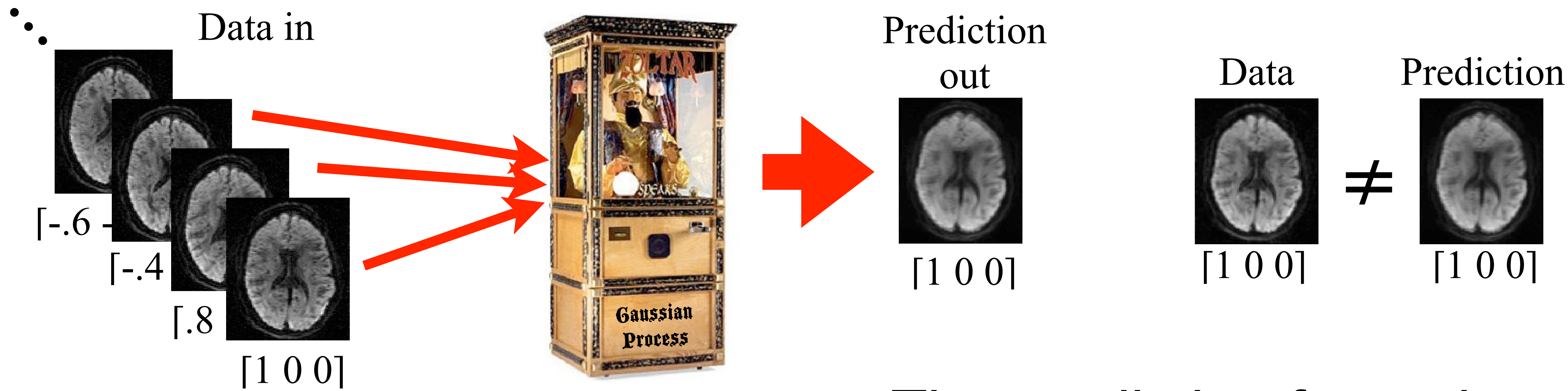
But it is not easy to register diffusion weighted images





- Each image has different distortions -> non-linear registration
- What is the reference image?

Zoltar -- The prediction maker



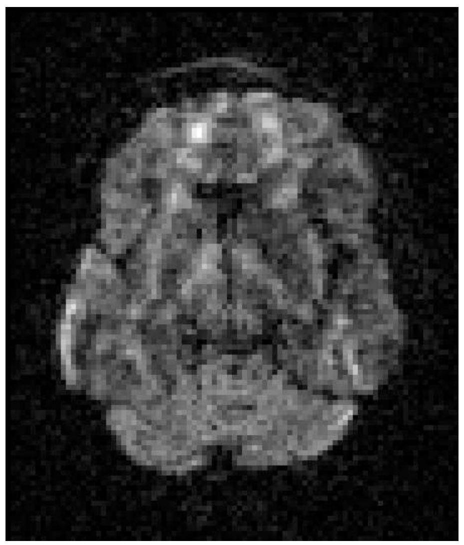
Given some data in, Zoltar will make a prediction what the data "should" be.

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)

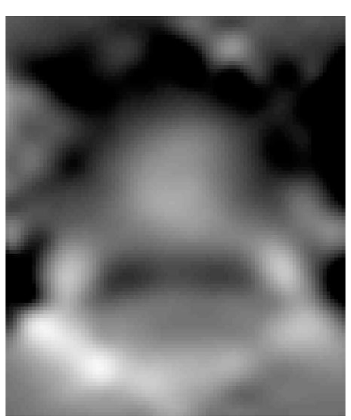
How eddy works: Loading step

Pick the first dwi

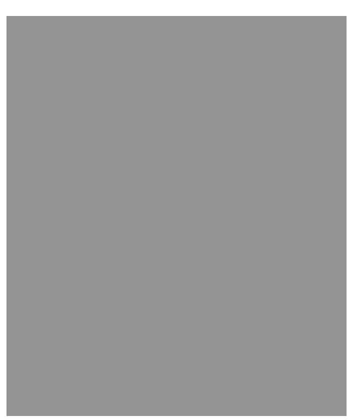


Use current estimates of

Susc



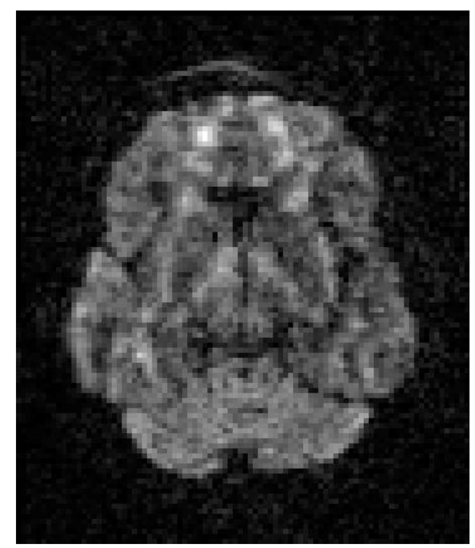
EC



MP

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

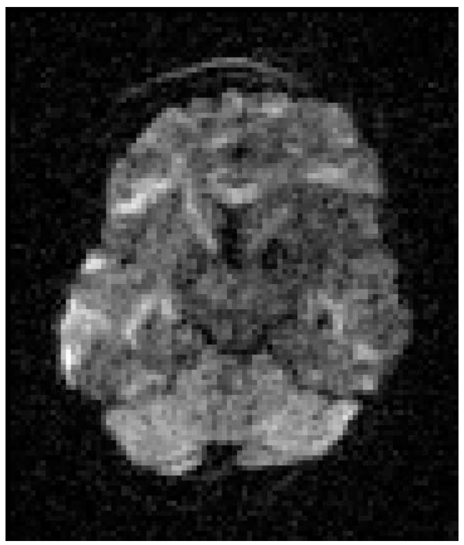
To correct image



And load into prediction maker

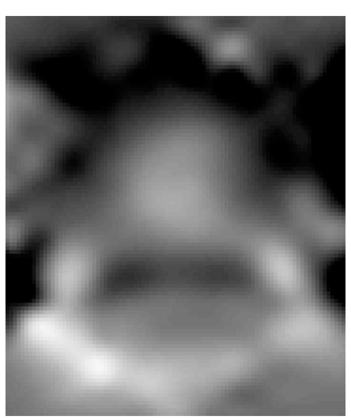
How eddy works: Loading step

then the 2nd dwi

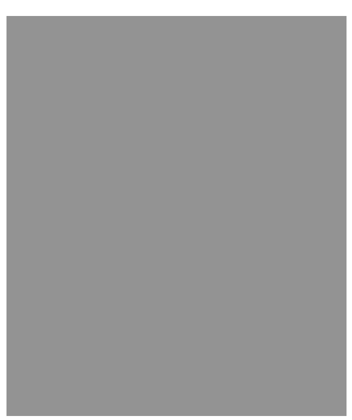


Use current estimates of

Susc



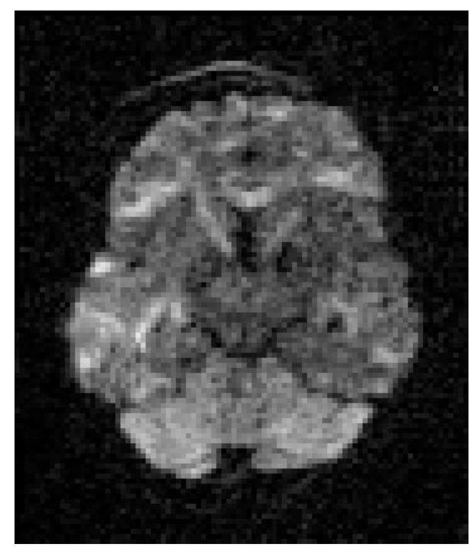
EC



MP

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

To correct 2nd image

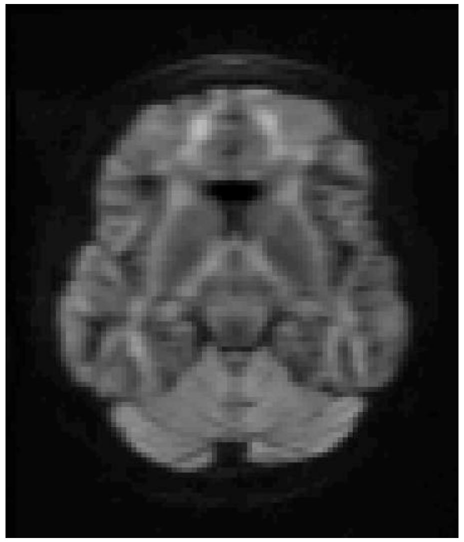


And load into prediction maker

Until we have loaded all dwis

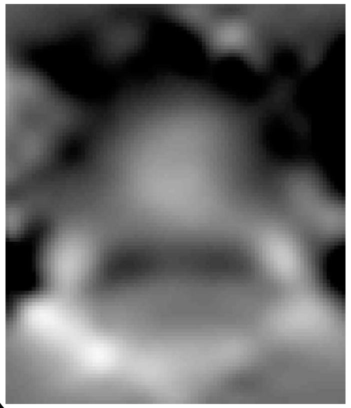
How eddy works: Estimation step

Draw a prediction
for first dwi



Use current estimates of

Susc

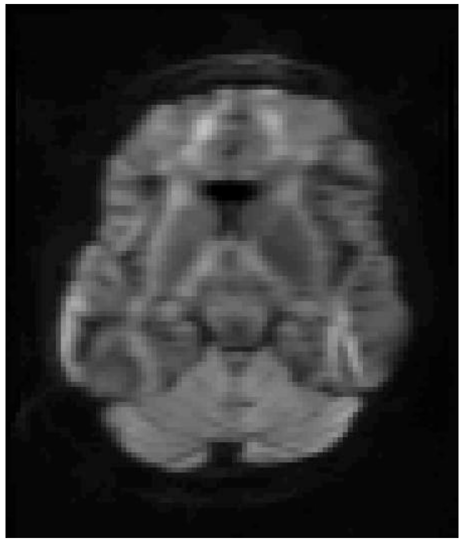


EC

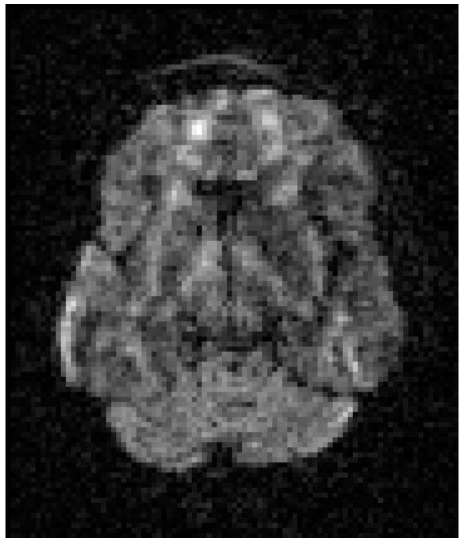
MP

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

Invert



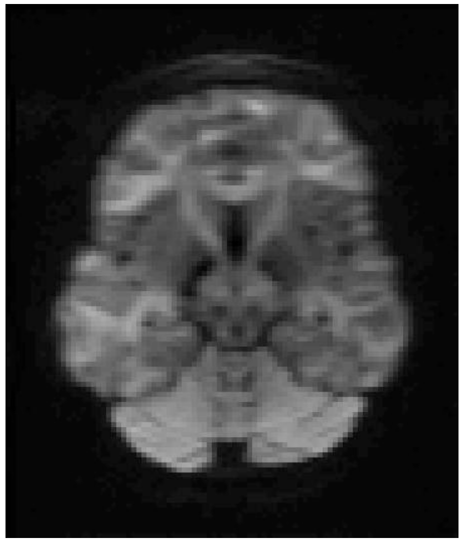
To get prediction in "observation space"



And compare to actual observation

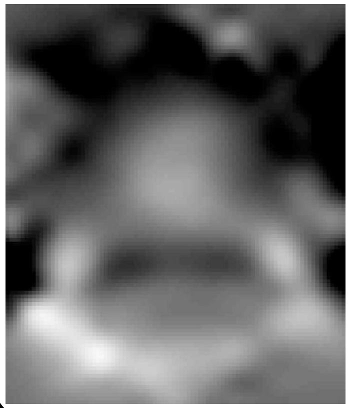
How eddy works: Estimation step

Draw a prediction
for 2nd dwi



Use current estimates of

Susc

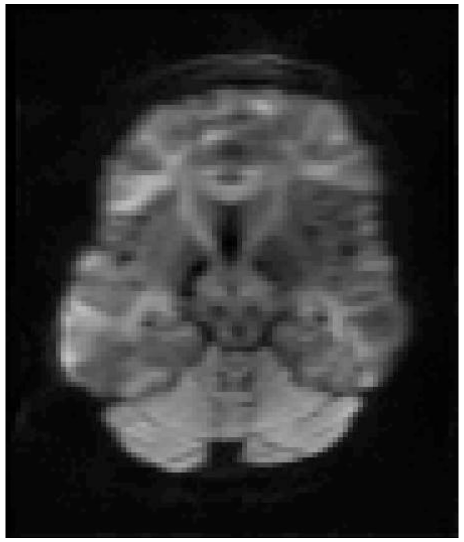


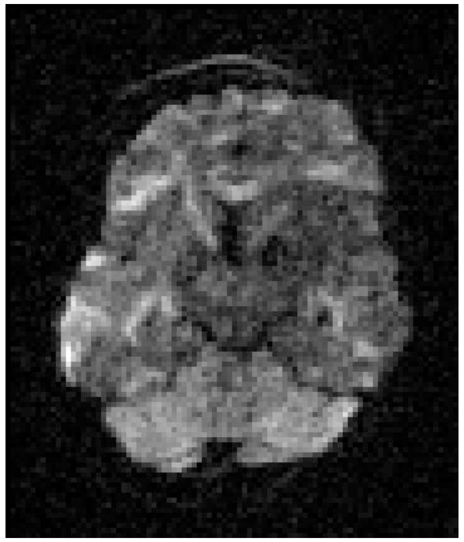
EC

MP

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

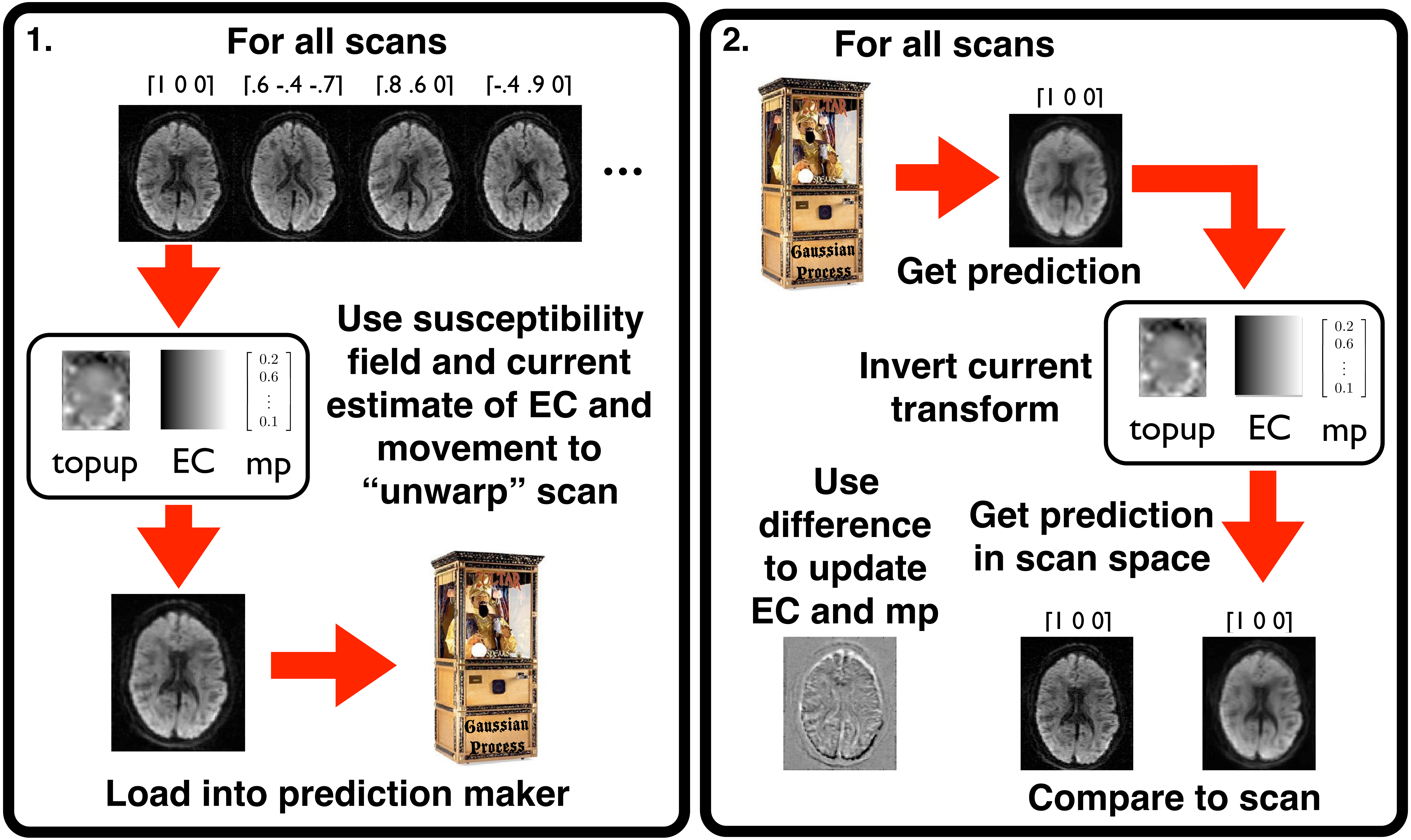
Invert



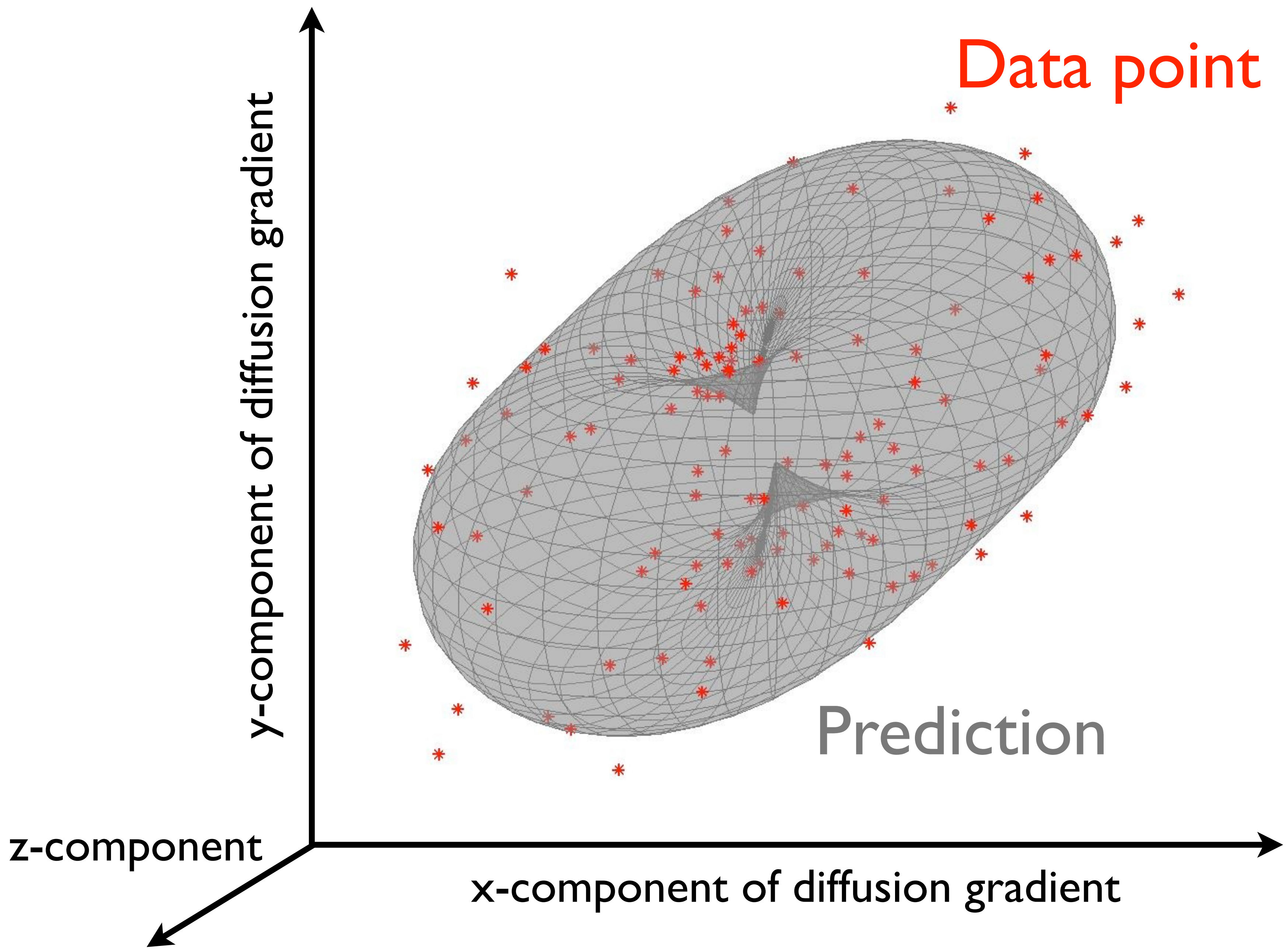


And then we repeat
the procedure for the
next dwi ...

How eddy works



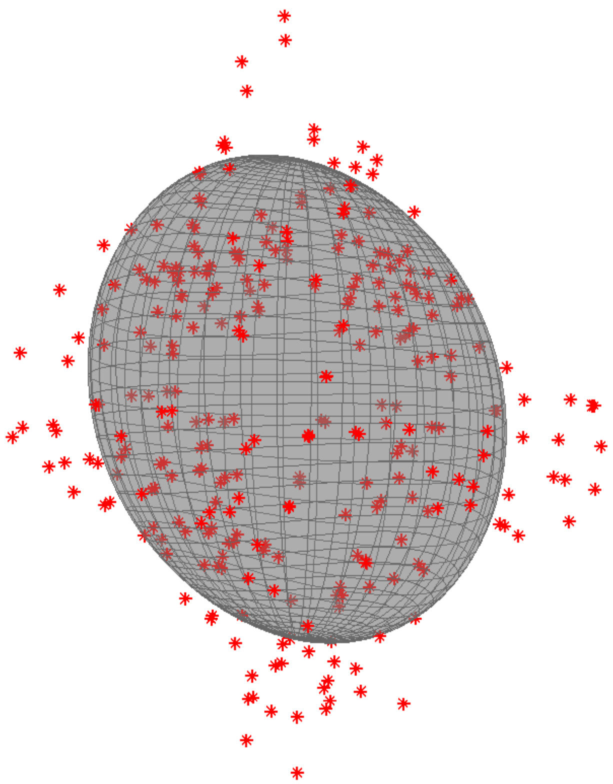
Under the hood of Zoltar



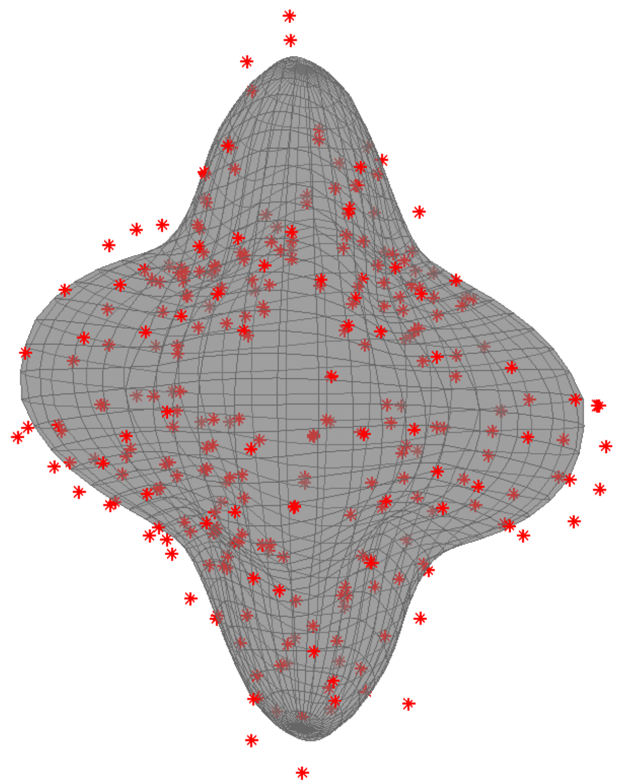
The signal is “modelled” in a data-driven fashion assuming that points close together on the unit sphere have similar signal.

Under the hood of Zoltar

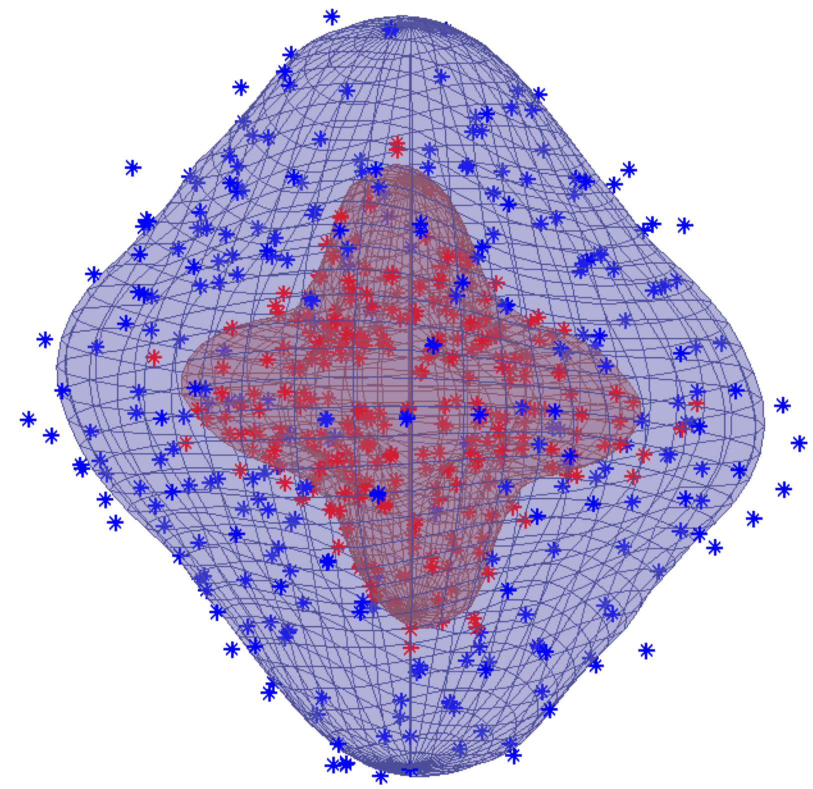
Tensor



Gaussian Process



Multi-shell predictions



The GP can model voxels with complicated anatomy while still being computationally convenient.

Shells with strong signal can help inform predictions in shells with poor signal

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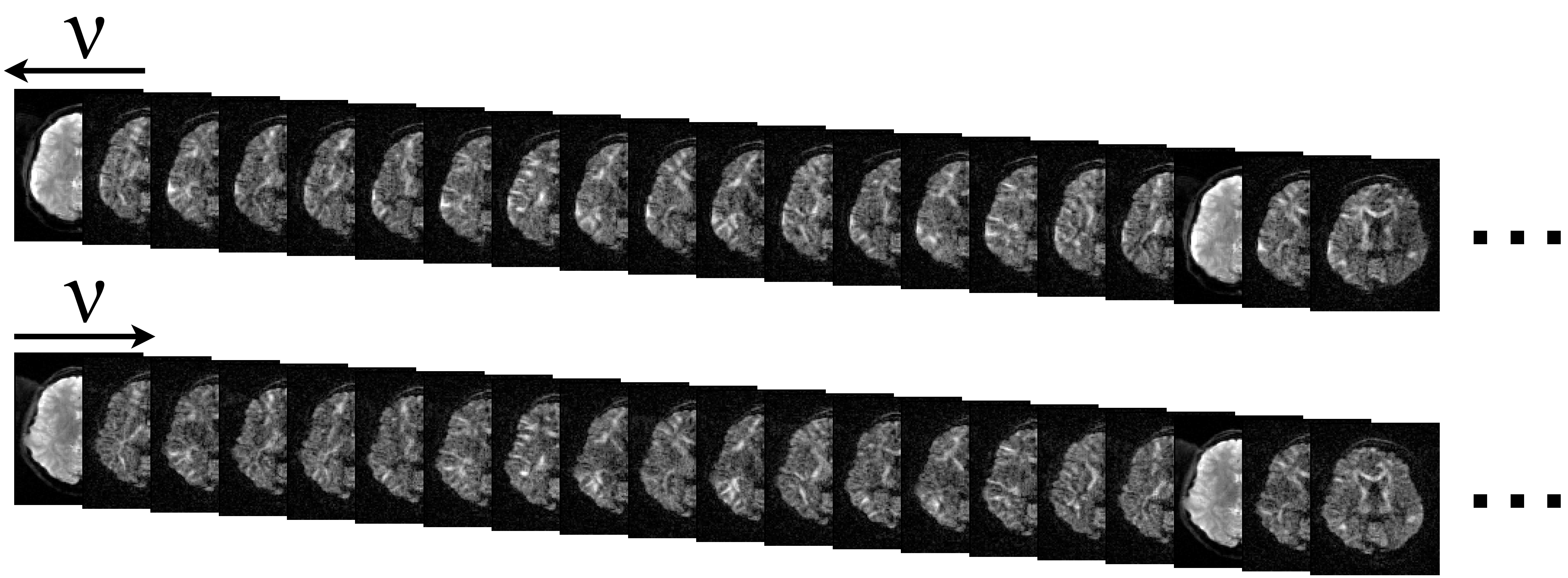
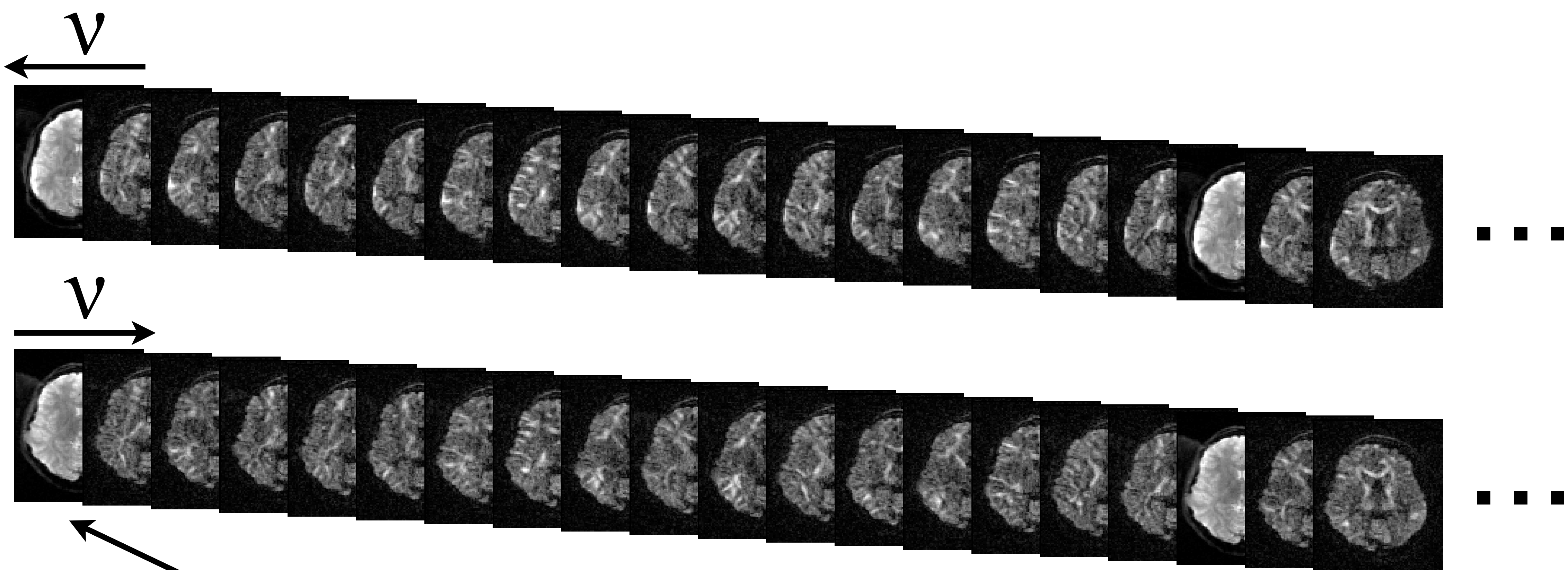
Practicalities



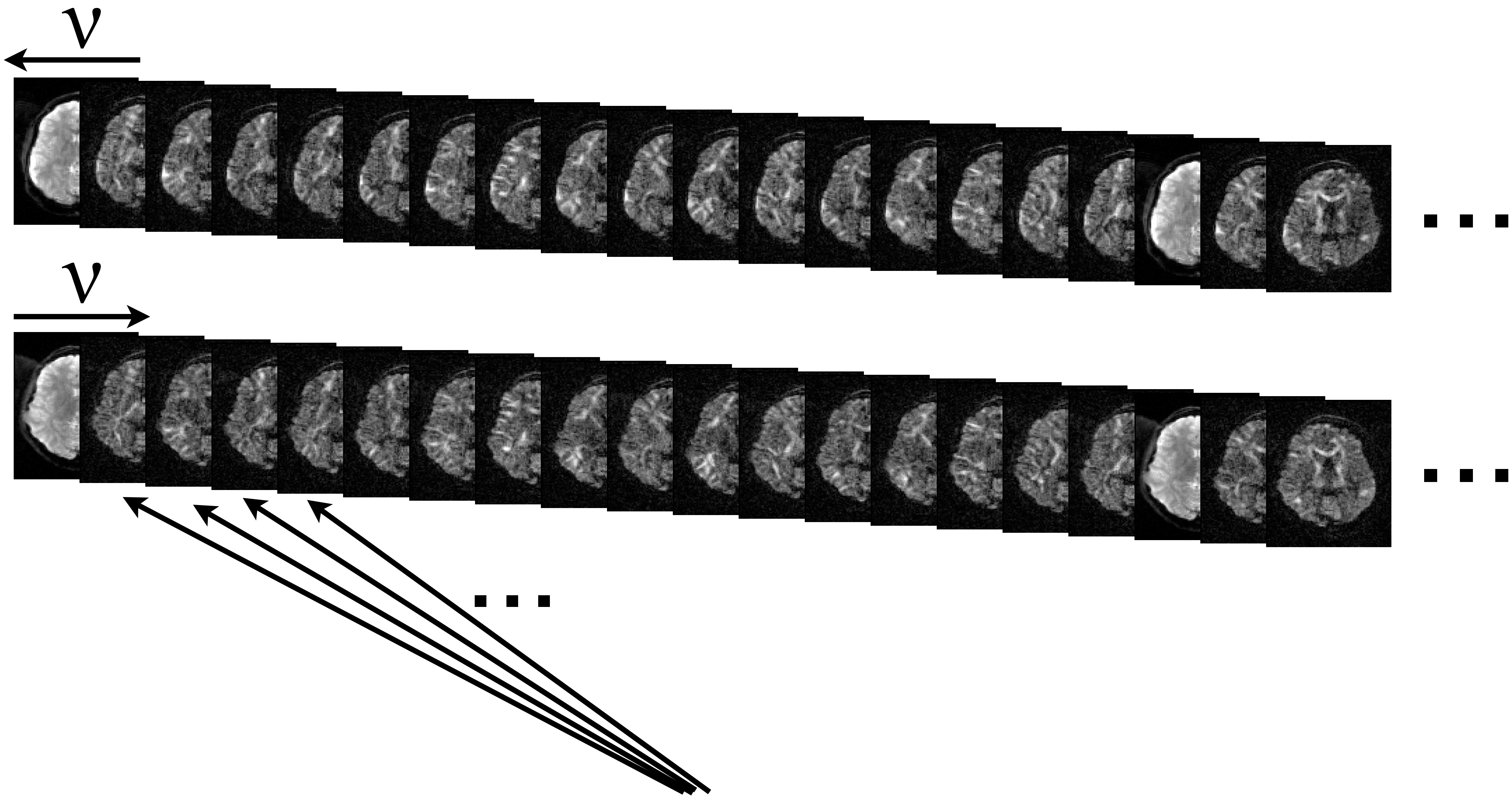
- Our example data consists of:
  - *N* diffusion weighted volumes and *n* *b*=0 volumes
  - *b*=0 volumes interspersed
  - Two repetitions, phase-encode L→R and R→L
  - Same diffusion table for both repetitions

Practicalities



Affected by susceptibility distortions

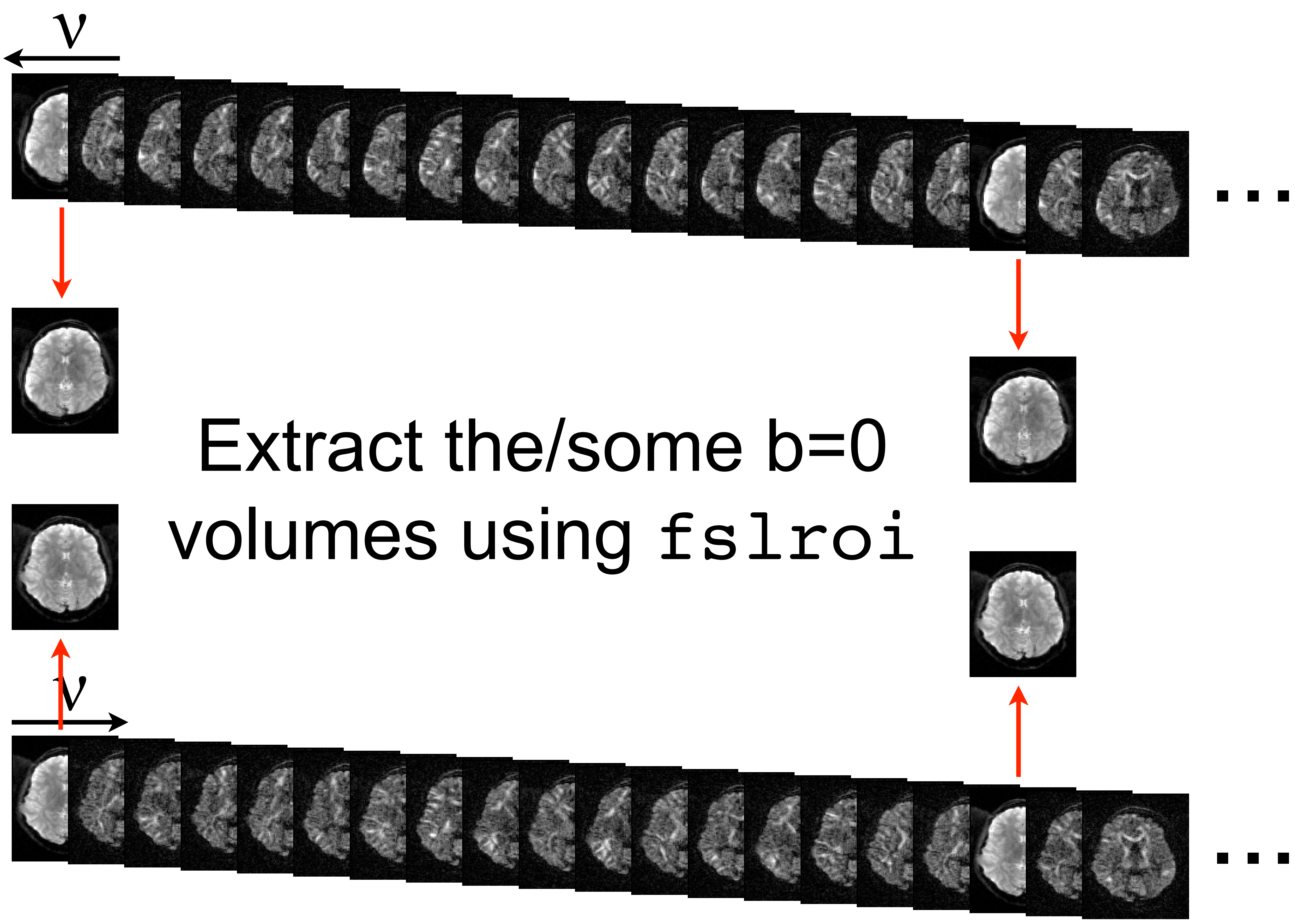
Practicalities



Affected by susceptibility distortions
AND eddy current distortions

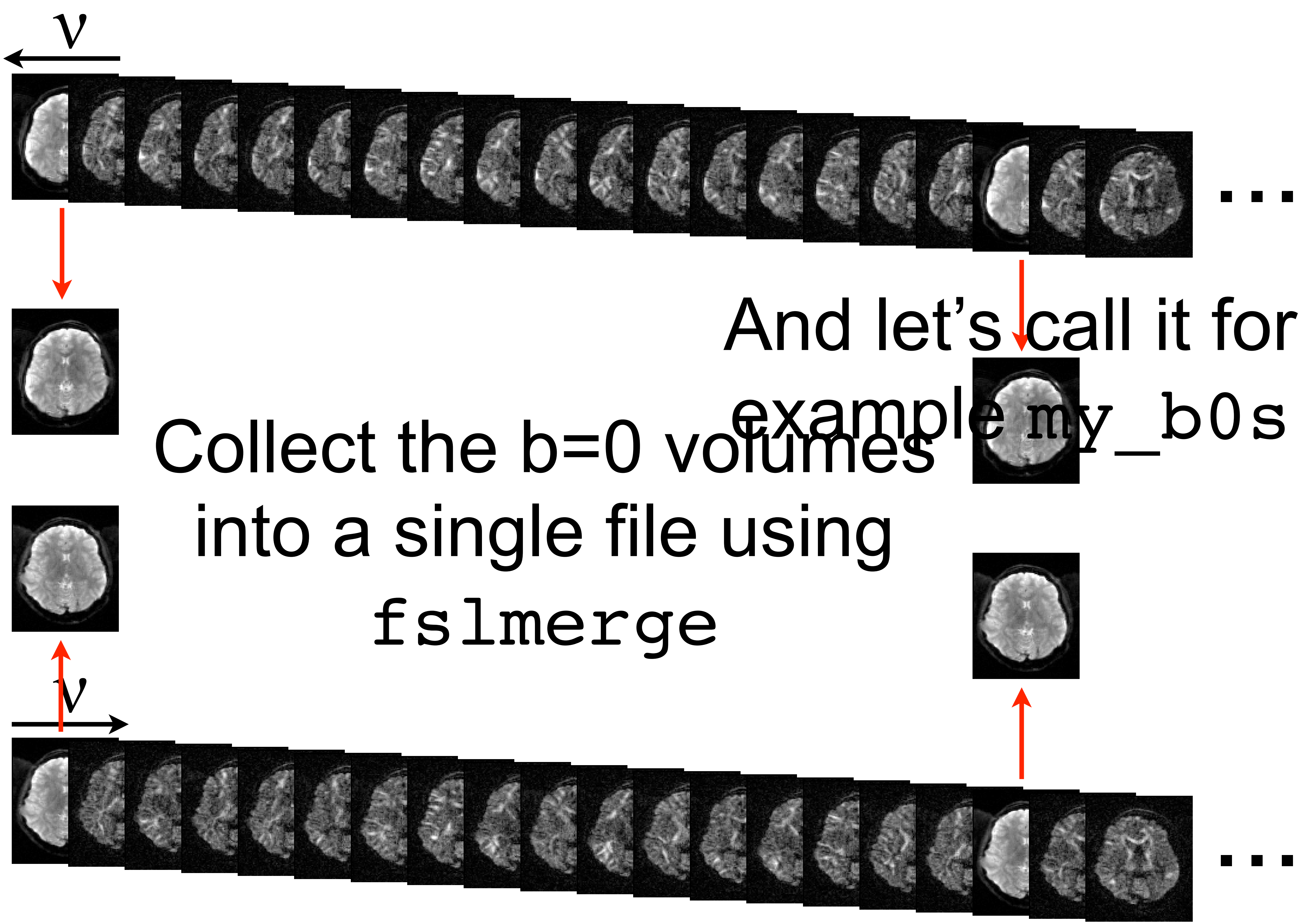
And everything is of course affected by subject movement.

So, let's start with susceptibility



Extract the/some b=0 volumes using `fslroi`

So, let's start with susceptibility

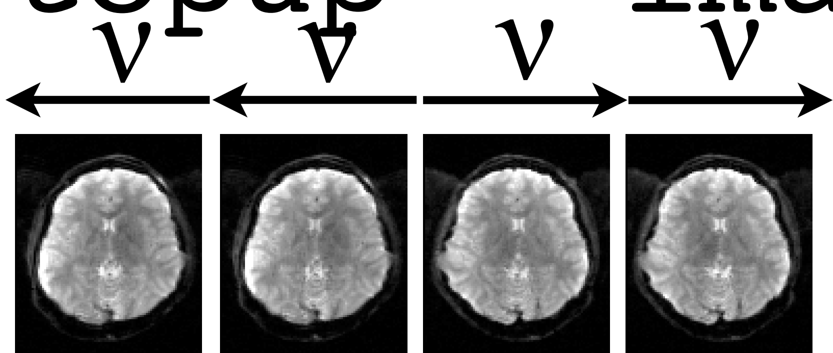


Collect the b=0 volumes into a single file using `fslmerge`

And let's call it for example `my_b0s`

And the tool for that is `topup`

`topup --imain=my_b0s`



`my_b0s`

But we also need to inform topup about the acquisition parameters

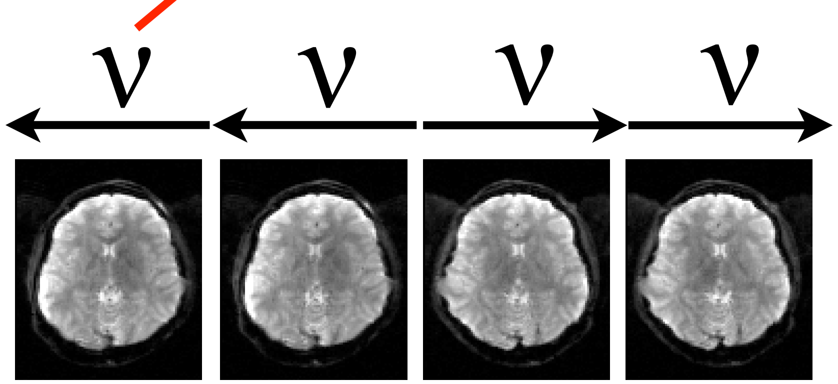
And the tool for that is `topup`

```
topup --imain=my_b0s
```

Means PE in x-direction, L→R

```
-1 0 0 0.051
```

Total readout time (in seconds)



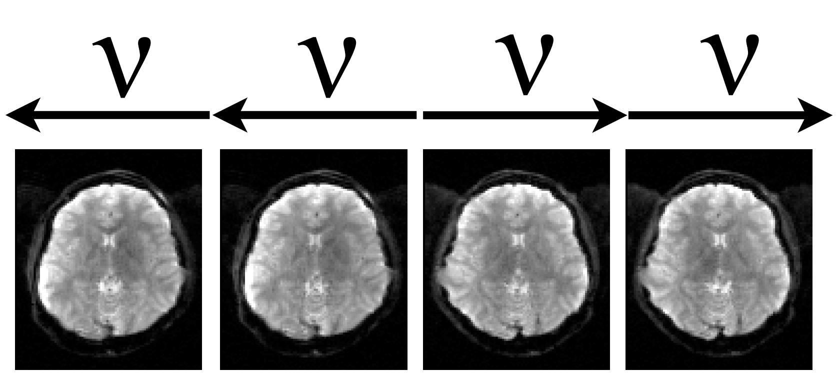
my_b0s

And the tool for that is `topup`

```
topup --imain=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`

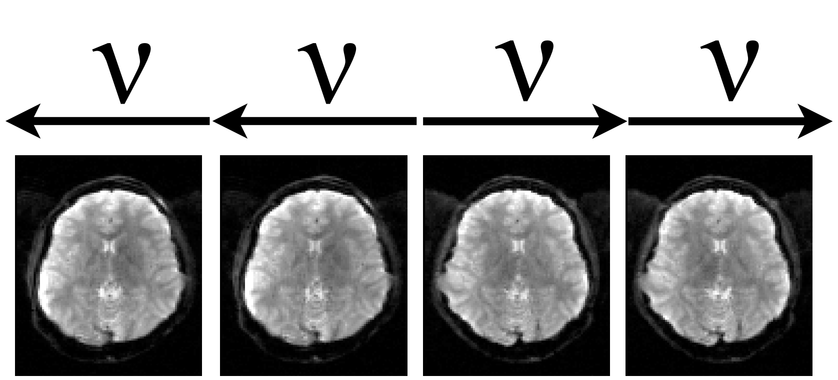


my_b0s

And the tool for that is `topup`

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

And then some technical details



`my_b0s`

```
-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`

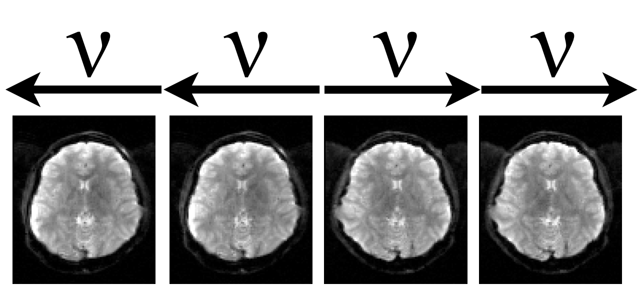
And finally we need to tell it where to put the results

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

my_topup_movpar.txt

```
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
```

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



my_b0s

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

acqparams.txt

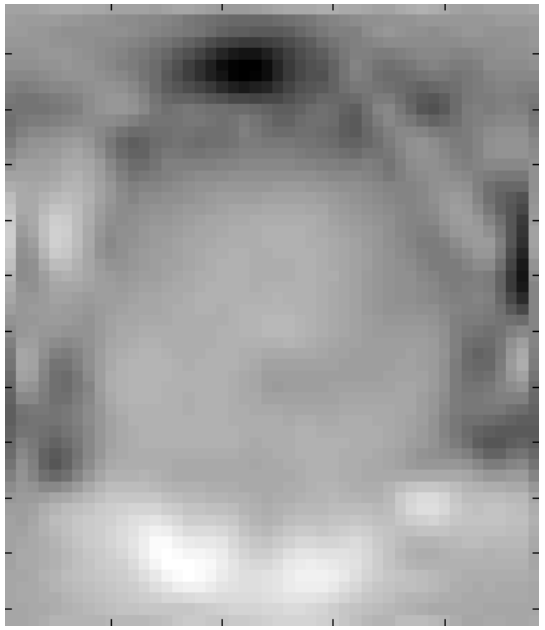
b02b0.cnf

And the tool for that is `topup`

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

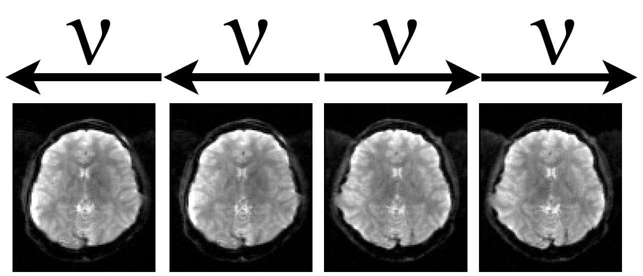
`topup --imain=my_b0s --datain=acqparams.txt --config=b02b0.cnf` **`--out=my_topup`**

`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
```



`my_b0s`

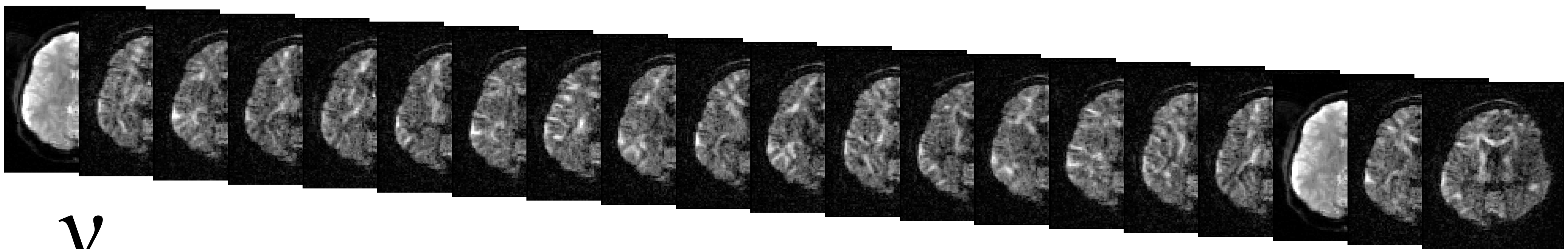
```
-1 0 0 0.051
-1 0 0 0.051
1 0 0 0.051
1 0 0 0.051
```

`acqparams.txt`

`b02b0.cnf`

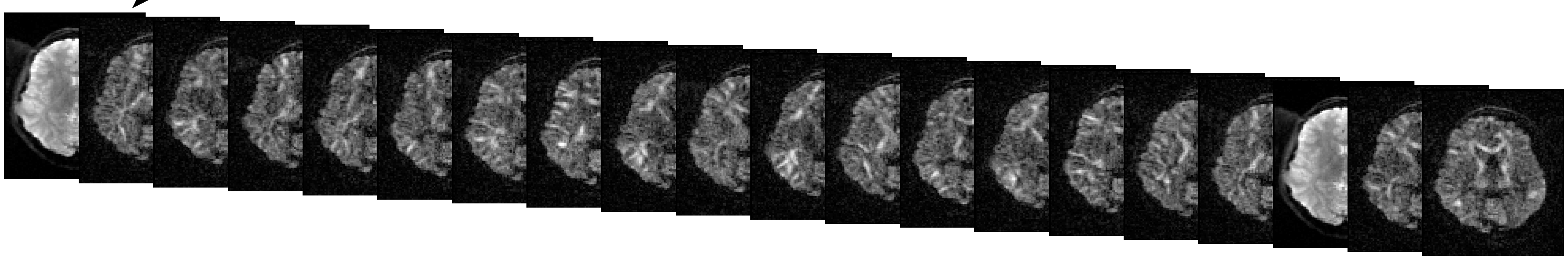
Back to the full data-set

ν



...

ν



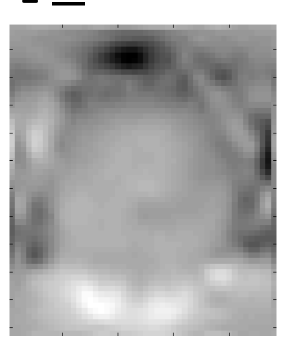
...

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

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

acqparams.txt

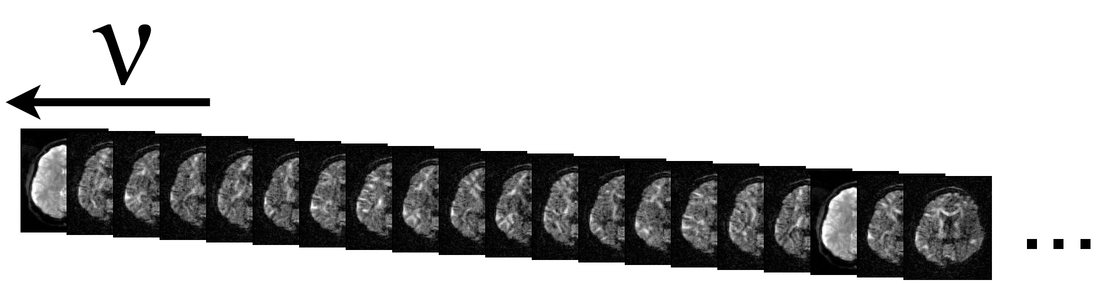
my_topup_fieldcoef.nii

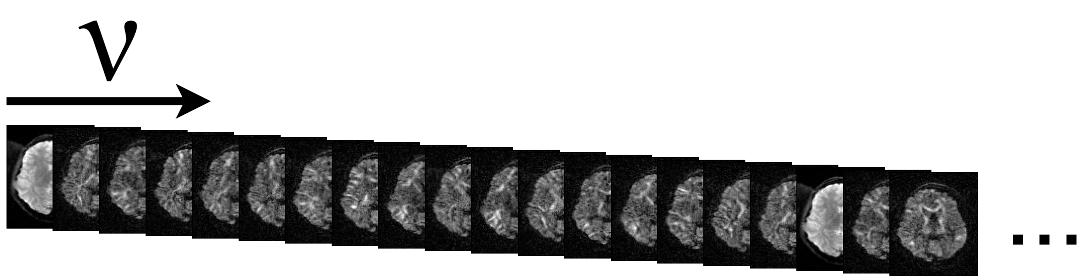


```
0 0 0 0 0 0
0.72 -0.02 -0.07 0.002 0.000 0.002
0 -0.11 -0.33 0.002 0.013 -0.004
-0.70 -0.12 -0.43 0.002 0.014 -0.004
```

my_topup_movpar.txt

Collect all data in one file

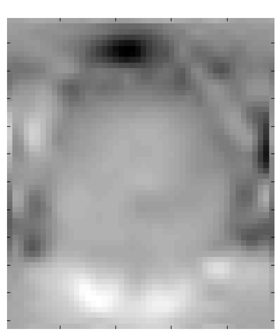




LR_RL

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

my_topup_fieldcoef.nii



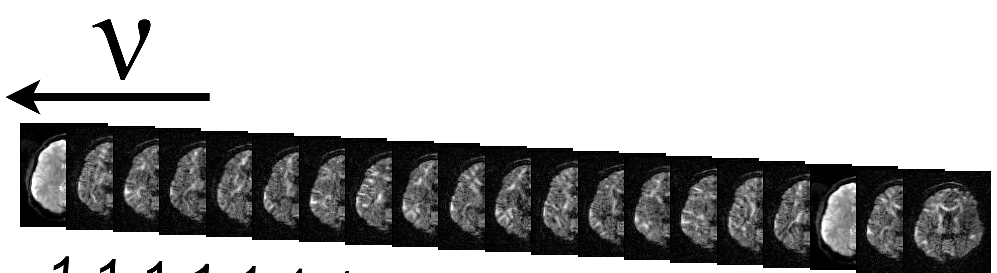
```
-1 0 0 0.051
-1 0 0 0.051
1 0 0 0.051
1 0 0 0.051
```

acqparams.txt

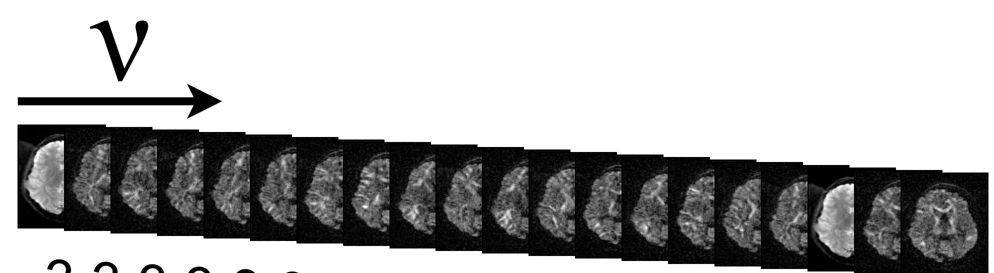
```
0 0 0 0 0 0
0.72 -0.02 -0.07 0.002 0.000 0.002
0 -0.11 -0.33 0.002 0.013 -0.004
-0.70 -0.12 -0.43 0.002 0.014 -0.004
```

my_topup_movpar.txt

Inform eddy of acquisition parameters



…



… `LR_RL`

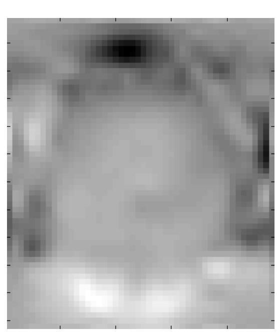
1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 2 2 2 … 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 4 4 4 … `indx.txt`

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

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

`acqparams.txt`

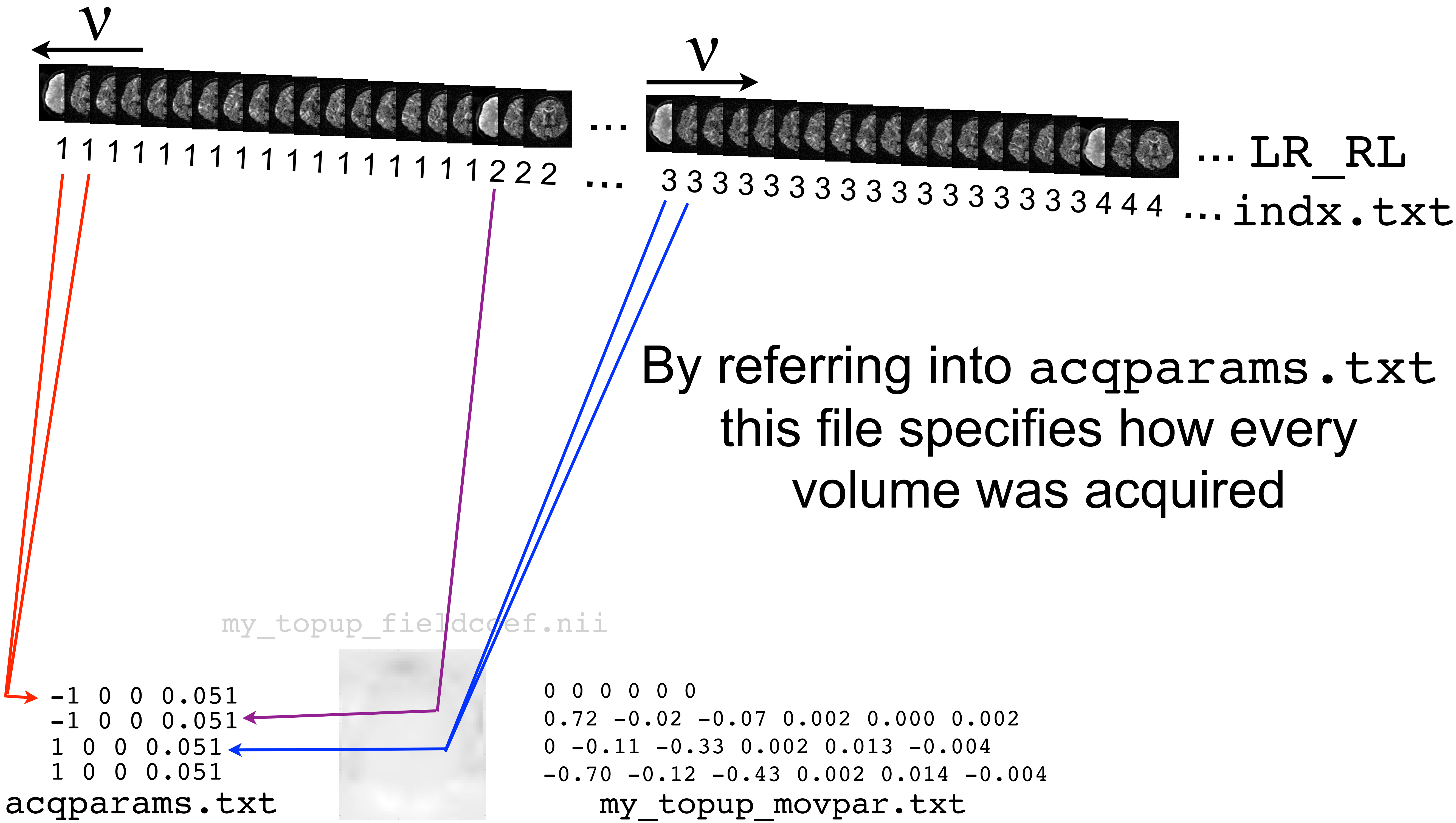
`my_topup_fieldcoef.nii`



```
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`

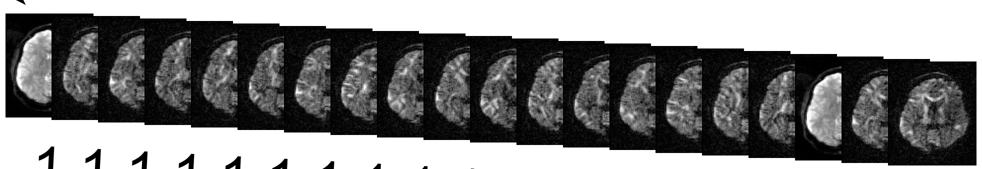
Inform eddy of acquisition parameters



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

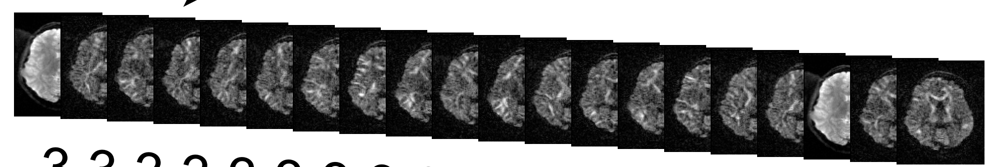
Inform eddy of acquisition parameters

ν



1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 2 2 2 ...

ν



... LR_RL

3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 4 4 4 ... indx.txt

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

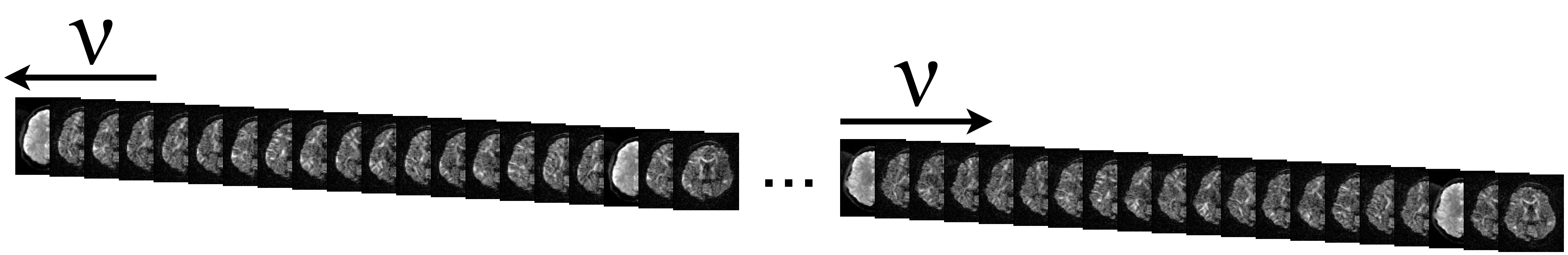

```
-1 0 0 0.051
-1 0 0 0.051
1 0 0 0.051
1 0 0 0.051
```

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



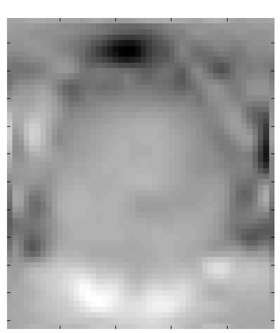
0 1000 1000 1000 ... `bvals`

↑ ↗ ↘ ... `bvecs`

text-files

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`

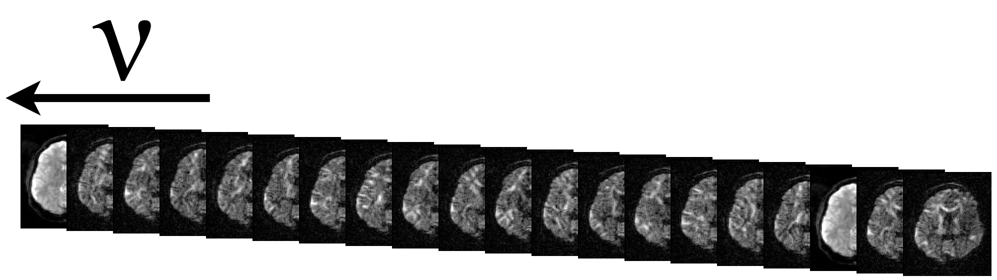


```
-1 0 0 0.051
-1 0 0 0.051
1 0 0 0.051
1 0 0 0.051
```
`acqparams.txt`

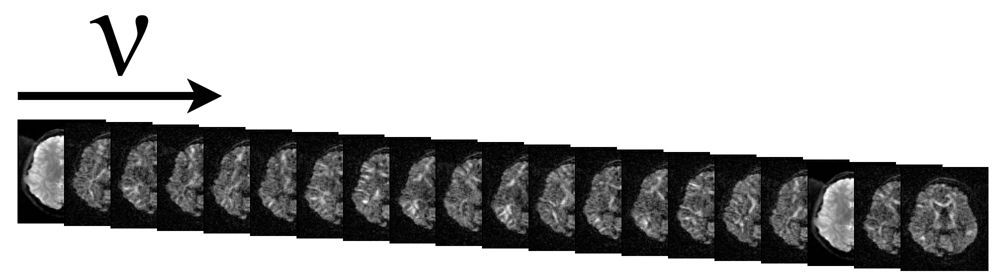
```
0 0 0 0 0 0
0.72 -0.02 -0.07 0.002 0.000 0.002
0 -0.11 -0.33 0.002 0.013 -0.004
-0.70 -0.12 -0.43 0.002 0.014 -0.004
```
`my_topup_movpar.txt`

```
1111...
```
`indx.txt`

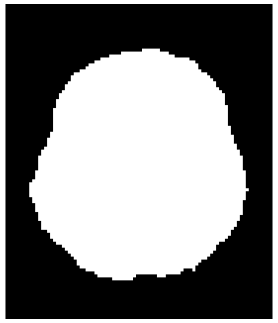
And where the brain is



…



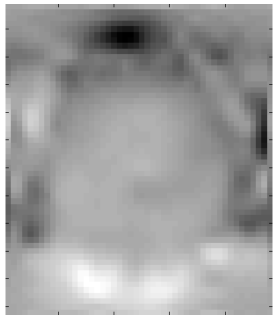
… LR_RL



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

1111...

indx.txt

0 1000 1000 1000 …

bvals

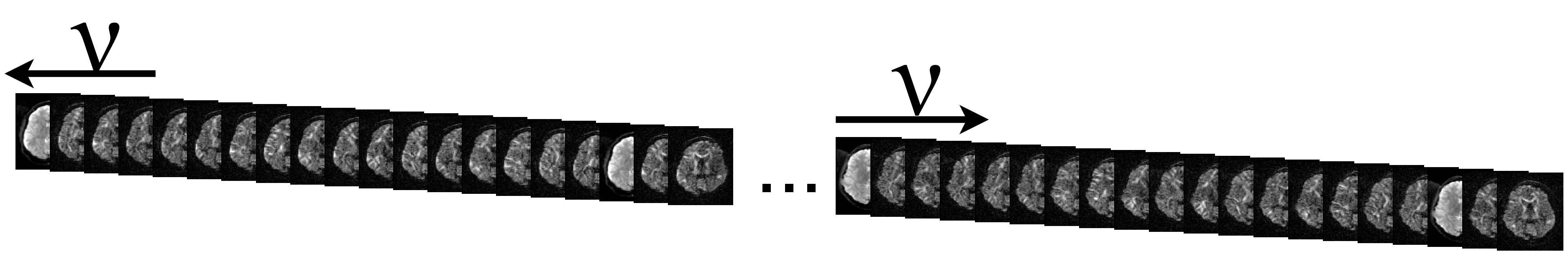
↑ ↗ ↘ …

bvecs

And now we can run eddy

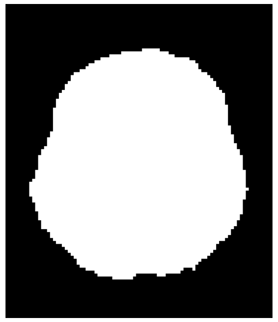
```
eddy --imain=LR_RL --acqp=acqparams.txt
--index=indx.txt --bvecs=bvecs
--bvals=bvals --mask=brain_mask
--topup=my_topup --out=my_eddy
```

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

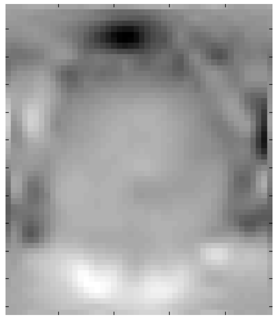


... LR_RL

brain_mask.nii



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

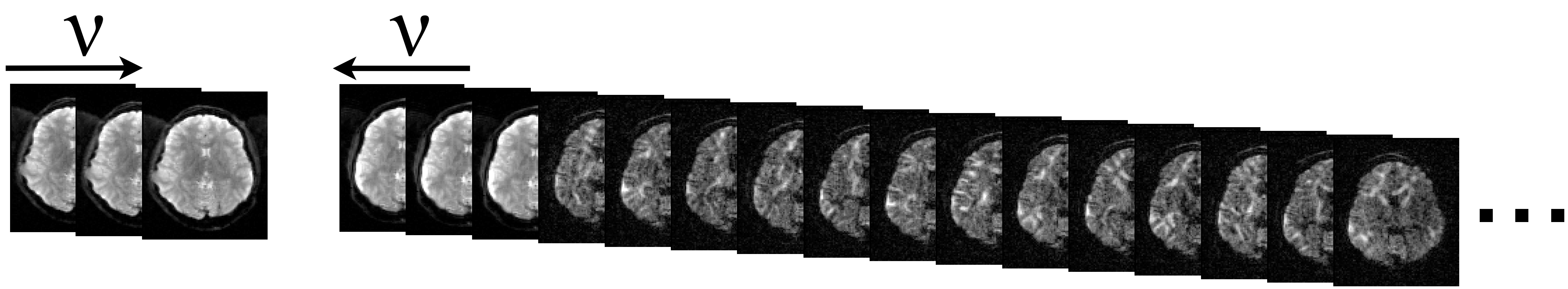
0 1000 1000 1000 ...

bvals

↑ ↗ ↘ ...

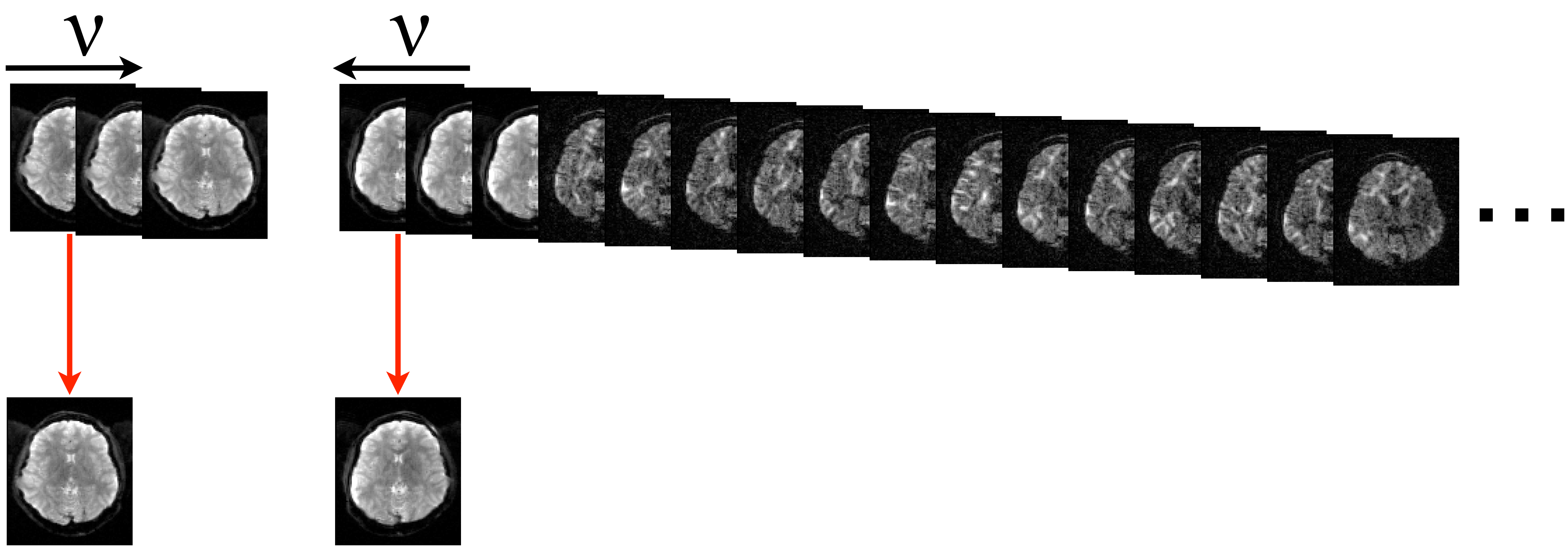
bvecs

A simpler (and perhaps more realistic) example



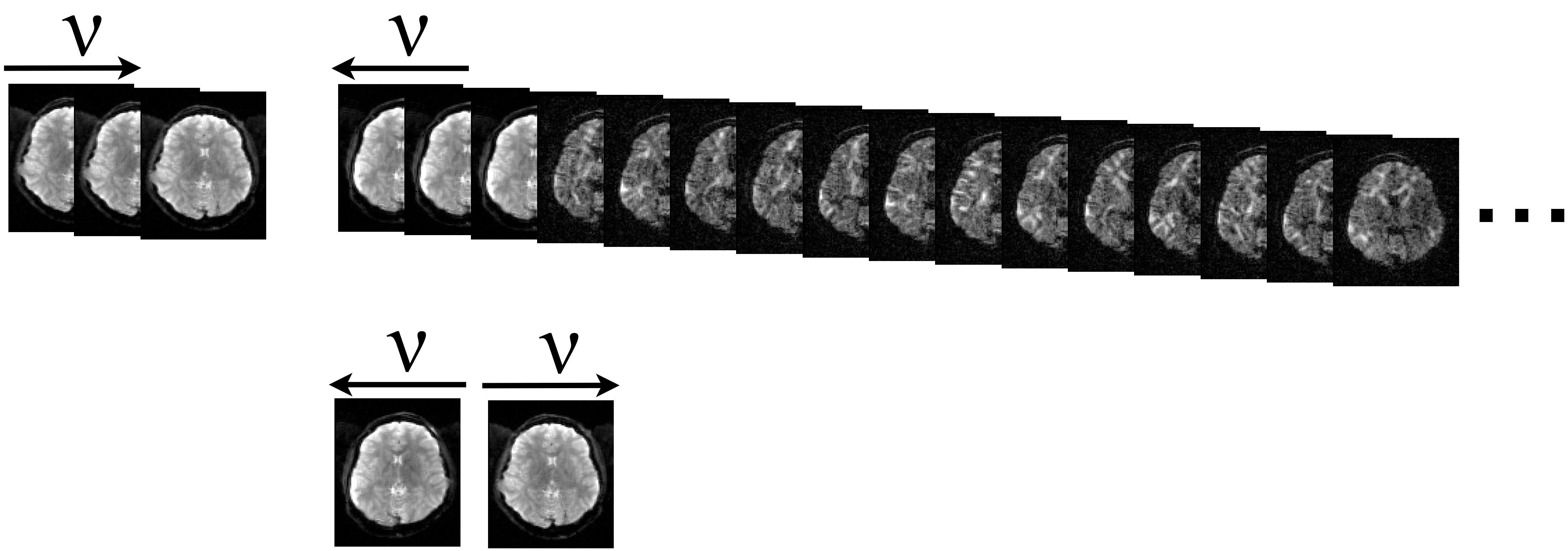
- Data consists of:
  - *N* diffusion weighted volumes and *n* *b*=0 volumes
  - *b*=0 volumes interspersed, but 2–3 are up front.
  - 2–3 b=0 volumes with opposing PE acquired just before the acquisition of the diffusion data set.

A simpler (and perhaps more realistic) example



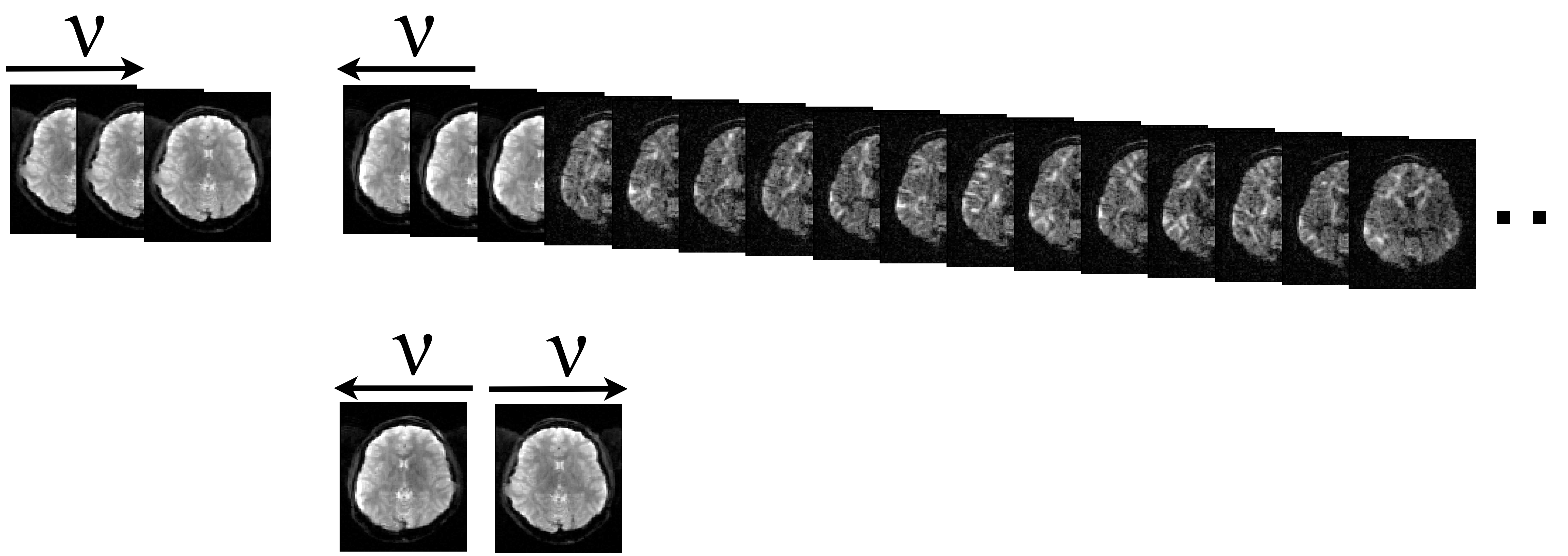
Extract one “good” *b*=0 volume for each PE-direction using `fslroi`

A simpler (and perhaps more realistic) example



Collect them into one 4D file using `fslmerge`

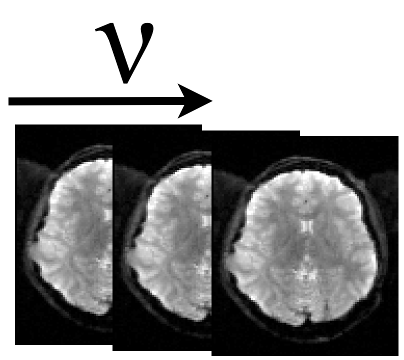
A simpler (and perhaps more realistic) example

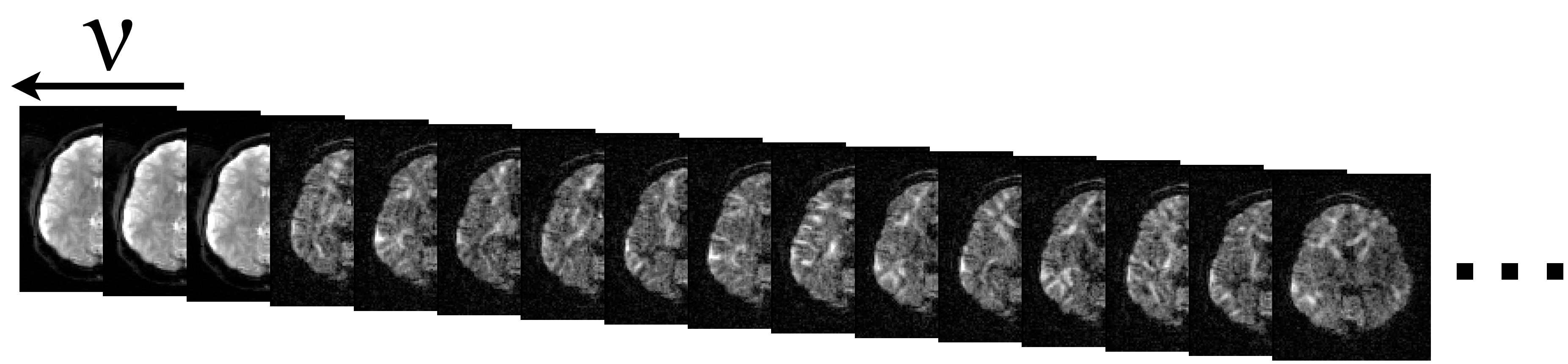


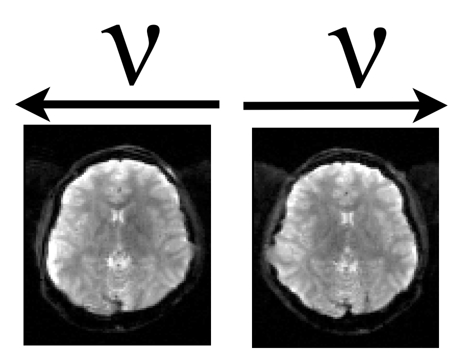

```
-1 0 0 0.051
1 0 0 0.051
```

Create text file `acqparams.txt`

A simpler (and perhaps more realistic) example





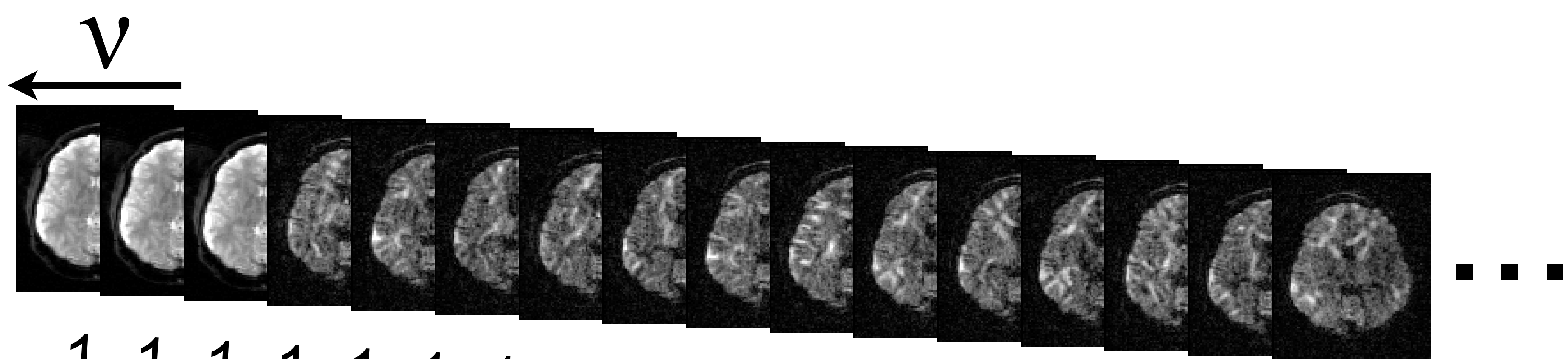



```
-1 0 0 0.051
1 0 0 0.051
```

And run `topup`

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

A simpler (and perhaps more realistic) example

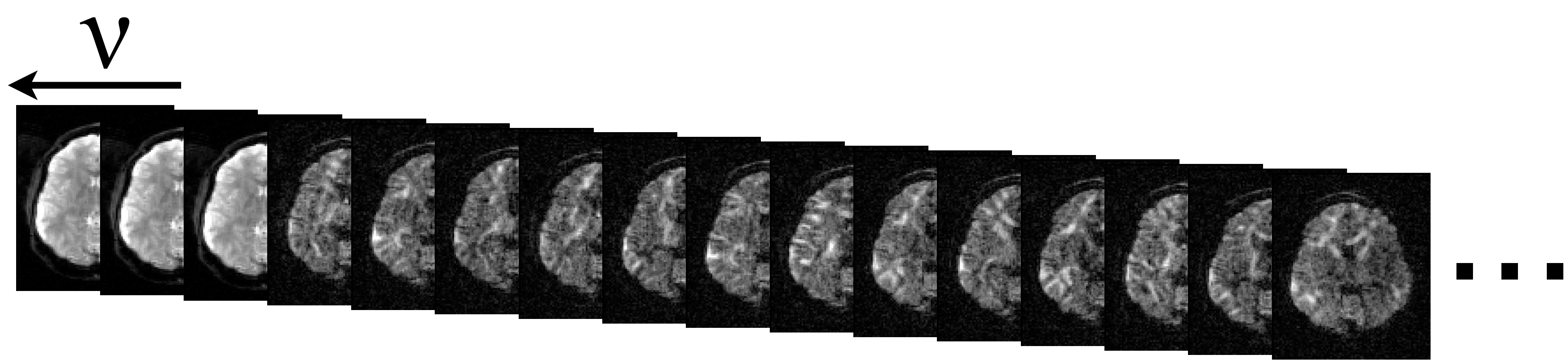


1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 ...

... `indx.txt` is now very simple

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

A simpler (and perhaps more realistic) example



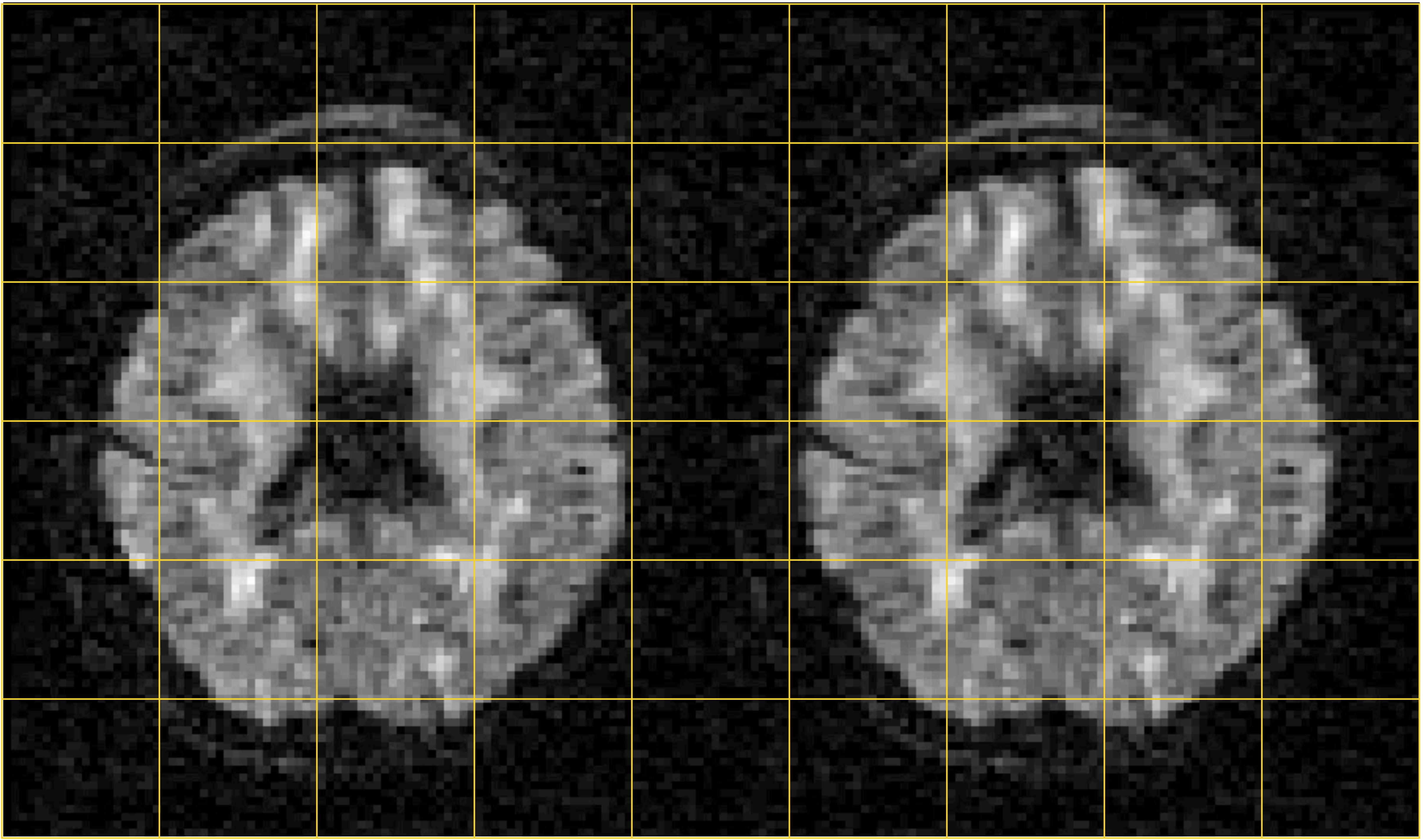

```
eddy --imain=LR_RL --acqp=acqparams.txt
--index=indx.txt --bvecs=bvecs
--bvals=bvals --mask=brain_mask
--topup=my_topup --out=my_eddy
```

And the `eddy` command is the same as before (N.B. you need to create `brain_mask.nii.gz` in the same way as before)

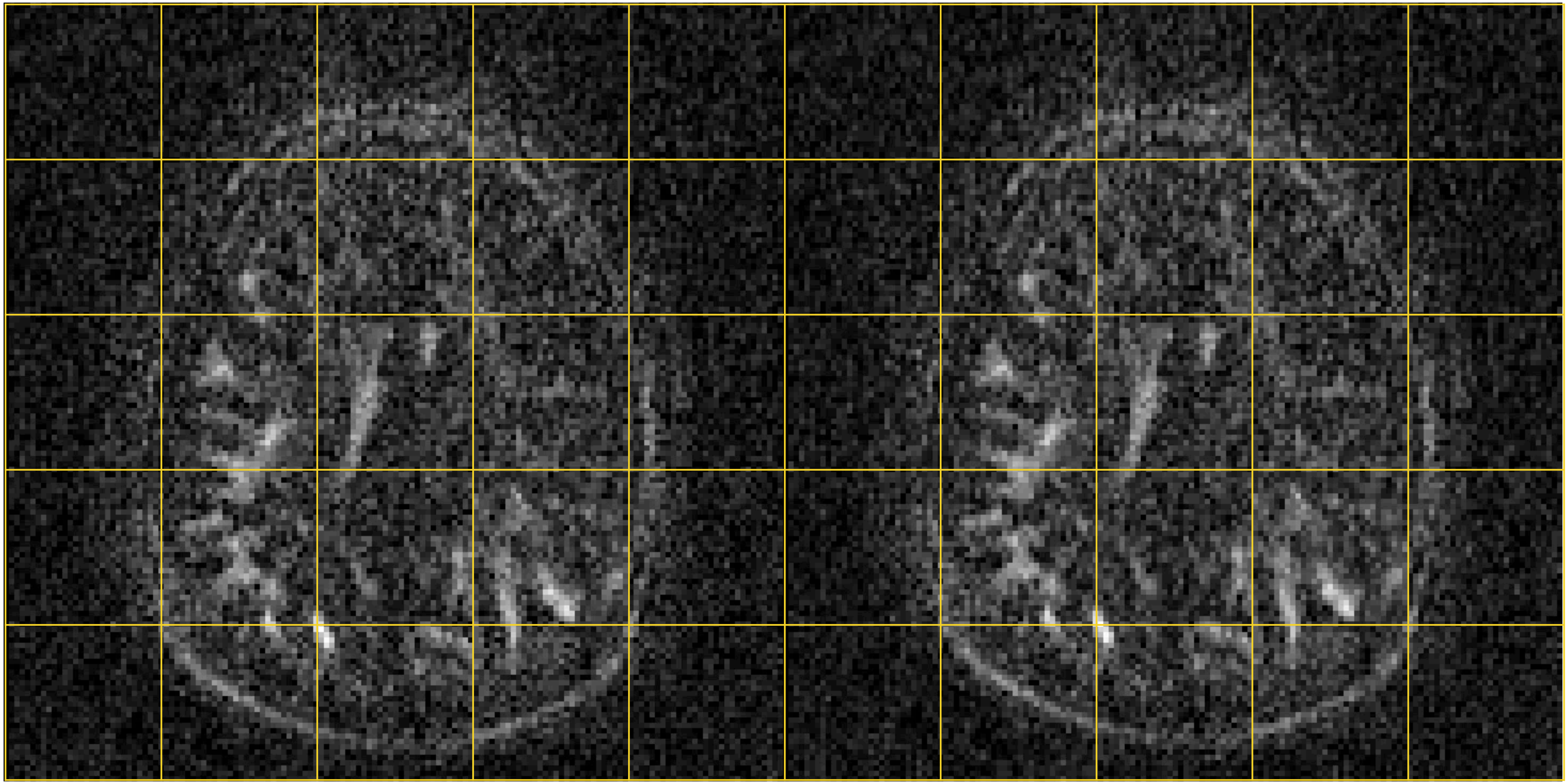
Outline of the talk

- What is the problem with diffusion data?
- Off-resonance field
  - How does it cause distortions?
  - Where does it come from?
- Registering diffusion data
  - How topup works
  - How eddy works
- Practicalities
- Some results
- Quality control
- "New" eddy features

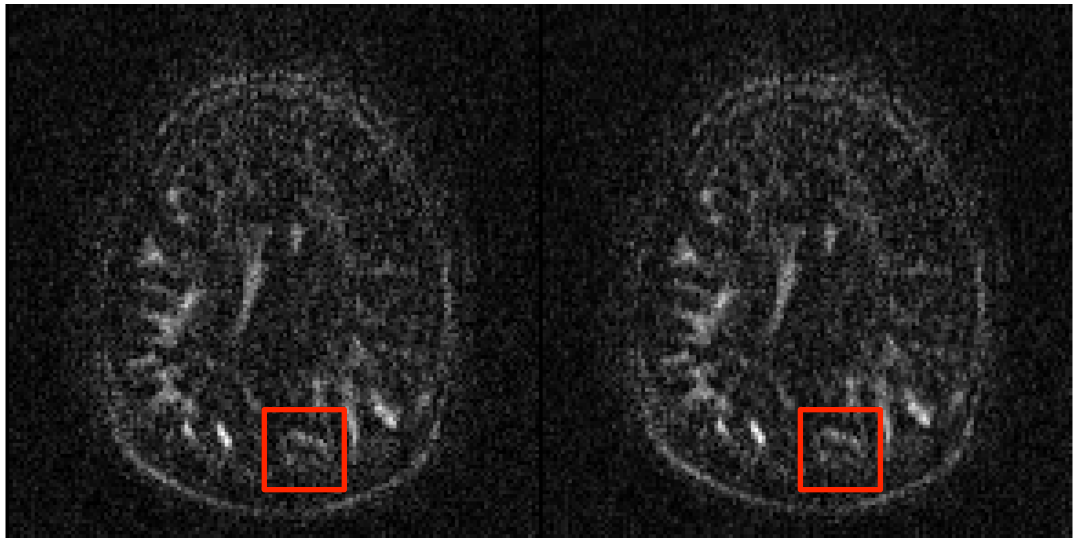
HCP-data, 150 directions, b=3000, blip-up-blip-down

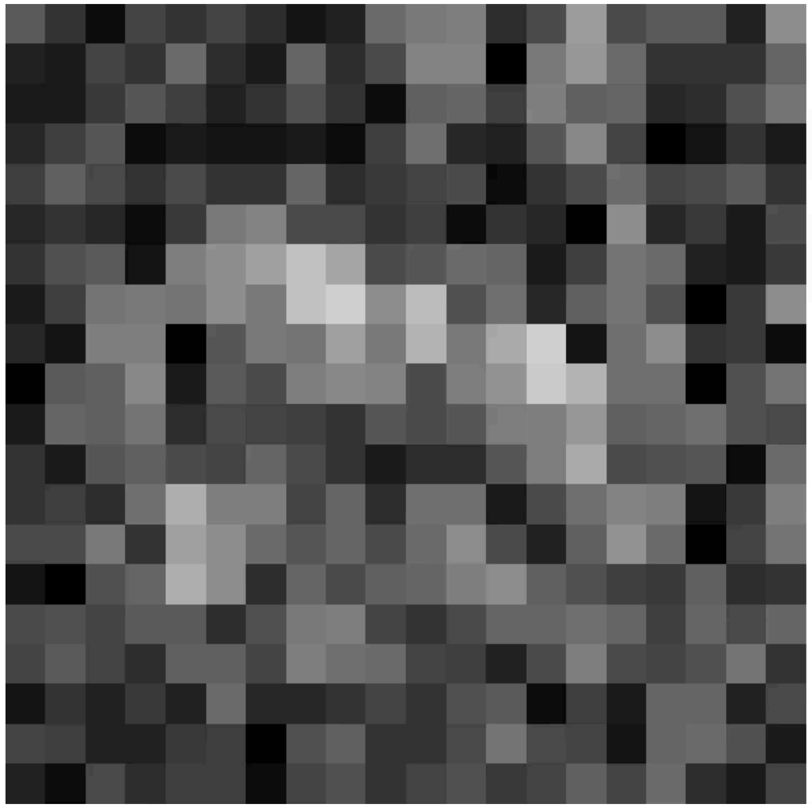


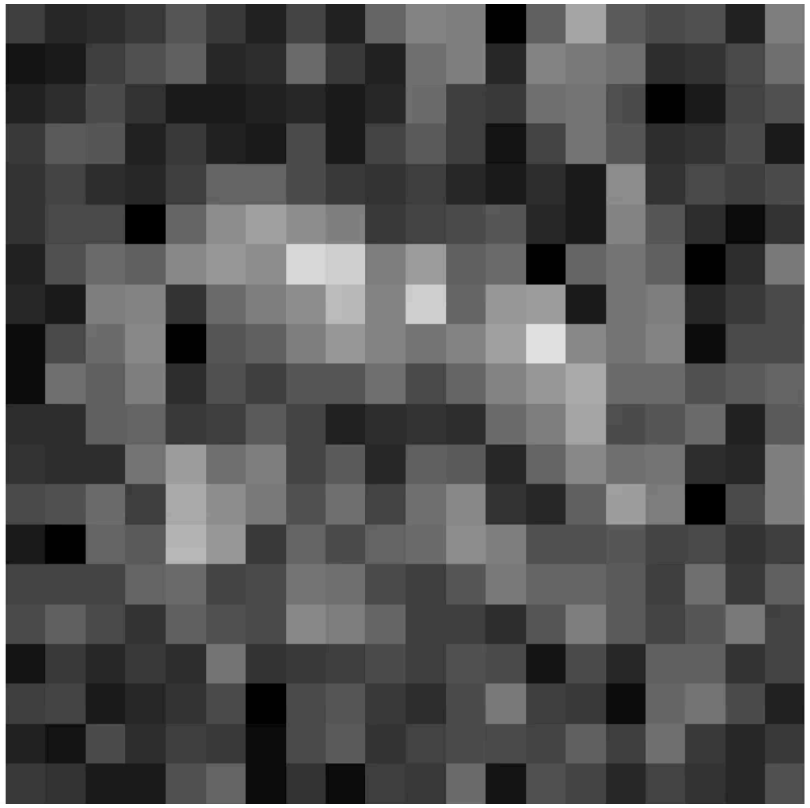
MGH-data, 198 directions, b=10000!



MGH-data, 198 directions, b=10000!







Outline of the talk

- What is the problem with diffusion data?
- Off-resonance field
  - How does it cause distortions?
  - Where does it come from?
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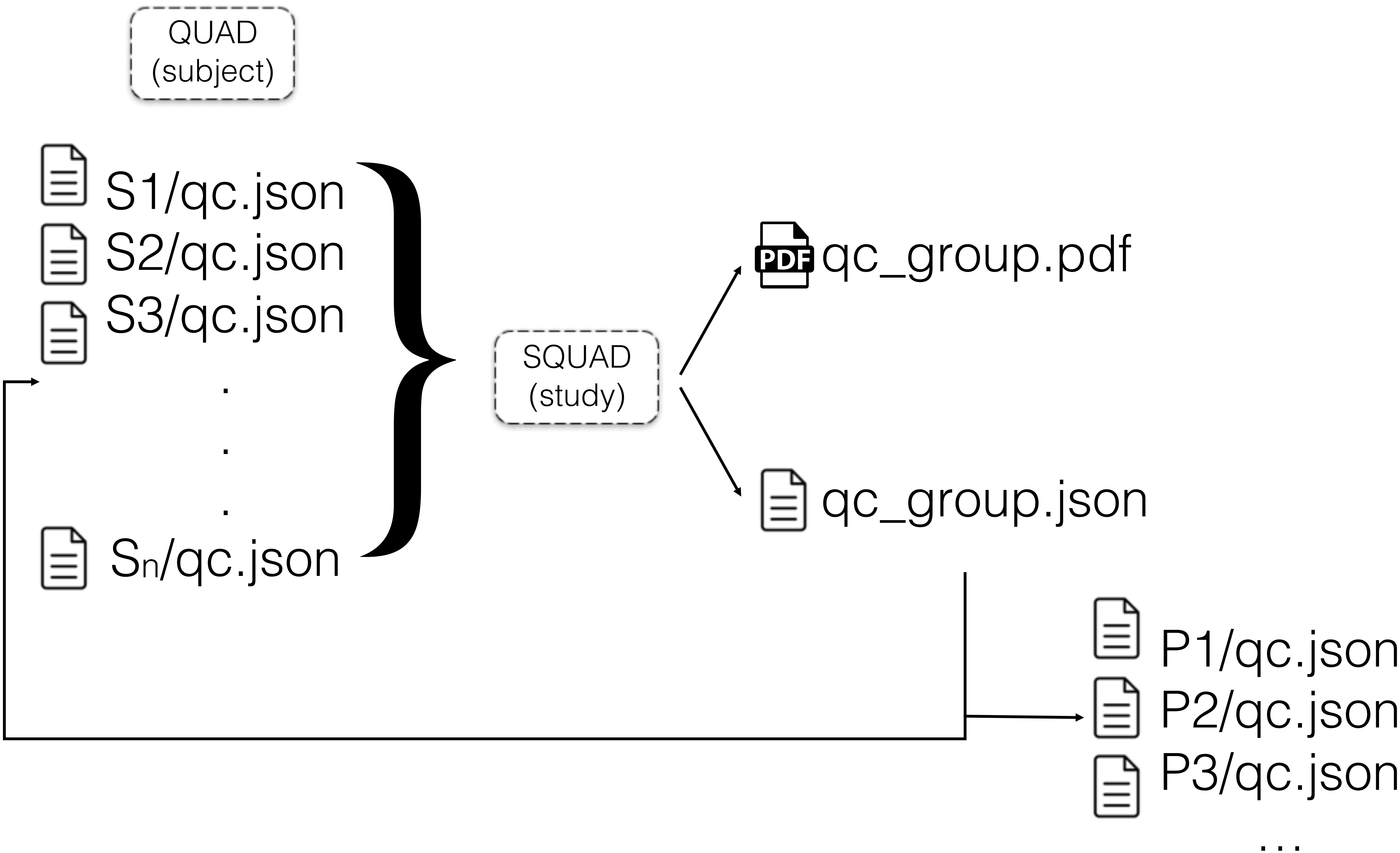
  - How topup works
  - How eddy works
- Practicalities
- Some results
- Quality control
- “New” eddy features

EDDY QC: data quality summary



EDDY QC: single-subject reports

Biobank subject A

Volume-to-volume motion

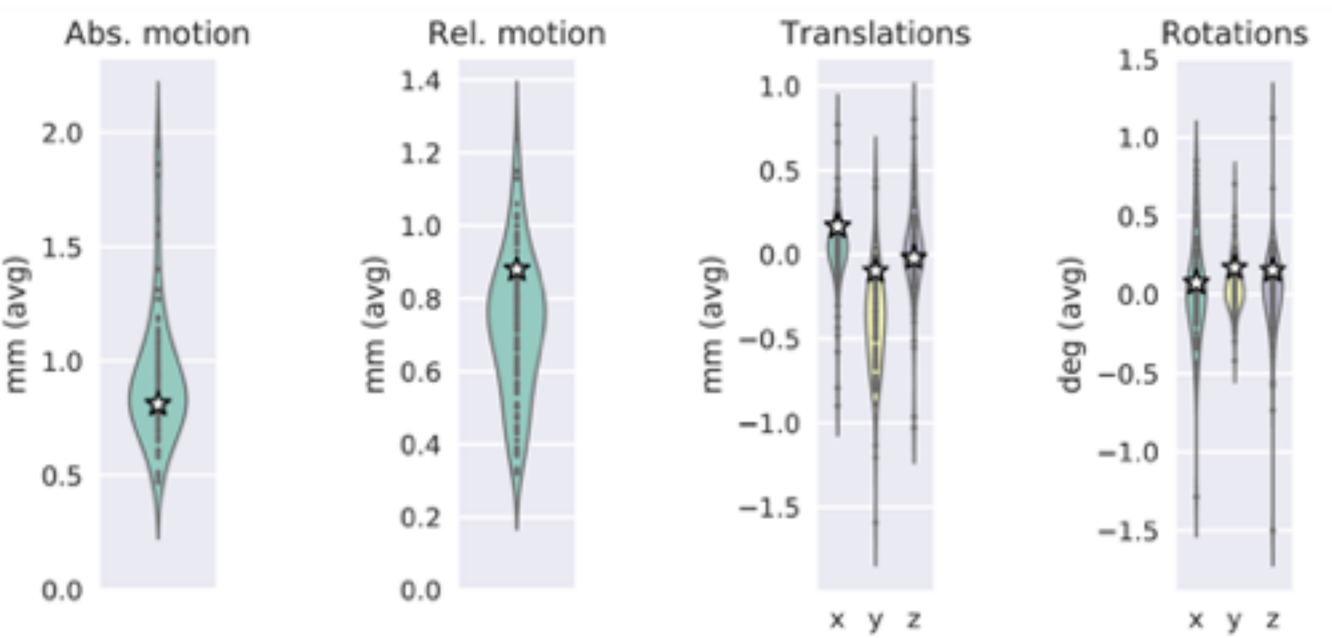
Average abs. motion (mm)	0.81
Average rel. motion (mm)	0.88
Average x translation (mm)	0.17
Average y translation (mm)	-0.10
Average z translation (mm)	-0.02
Average x rotation (deg)	0.07
Average y rotation (deg)	0.17
Average z rotation (deg)	0.15

Within-volume motion

Avg std x translation (mm)	0.02
Avg std y translation (mm)	0.11
Avg std z translation (mm)	0.04
Avg std x rotation (deg)	0.05
Avg std y rotation (deg)	0.05
Avg std z rotation (deg)	0.06

Outliers

Total outliers (%)	0.11
Outliers (b=1000 s/mm^2)	0.22
Outliers (b=2000 s/mm^2)	0.00
Outliers (PE dir=[0. 1. 0.])	0.00
Outliers (PE dir=[0. -1. 0.])	0.11



Biobank subject B

Volume-to-volume motion

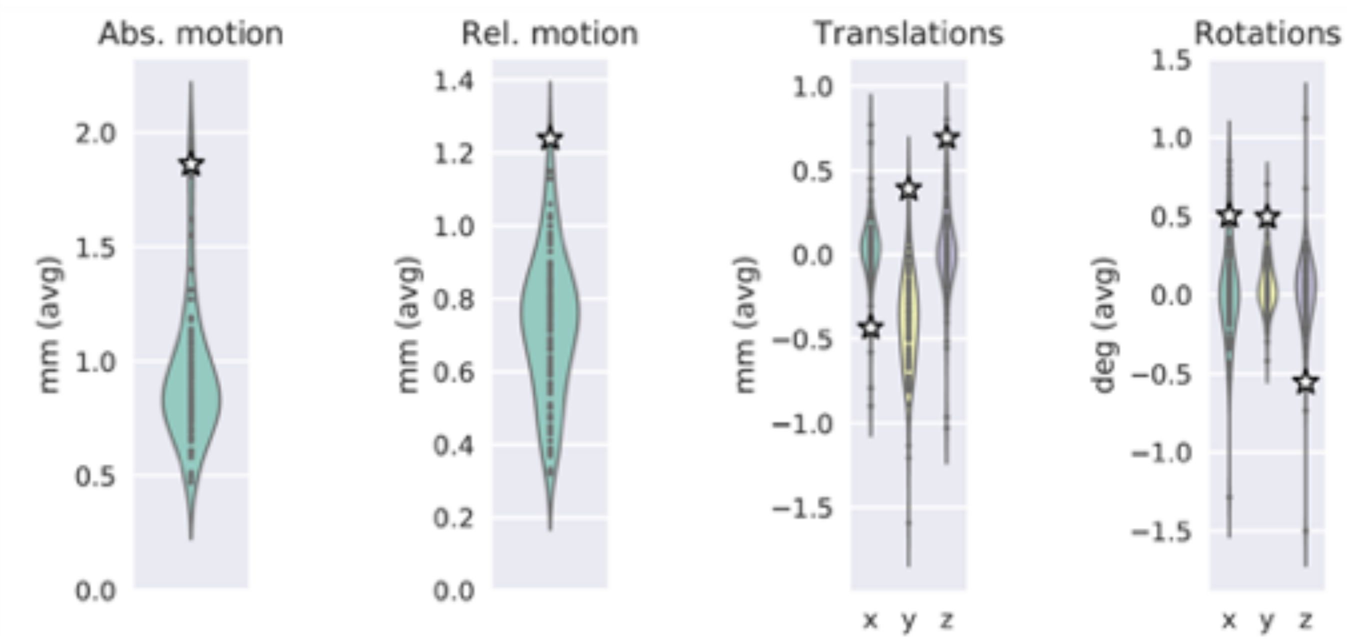
Average abs. motion (mm)	1.86
Average rel. motion (mm)	1.24
Average x translation (mm)	-0.43
Average y translation (mm)	0.39
Average z translation (mm)	0.69
Average x rotation (deg)	0.50
Average y rotation (deg)	0.49
Average z rotation (deg)	-0.55

Within-volume motion

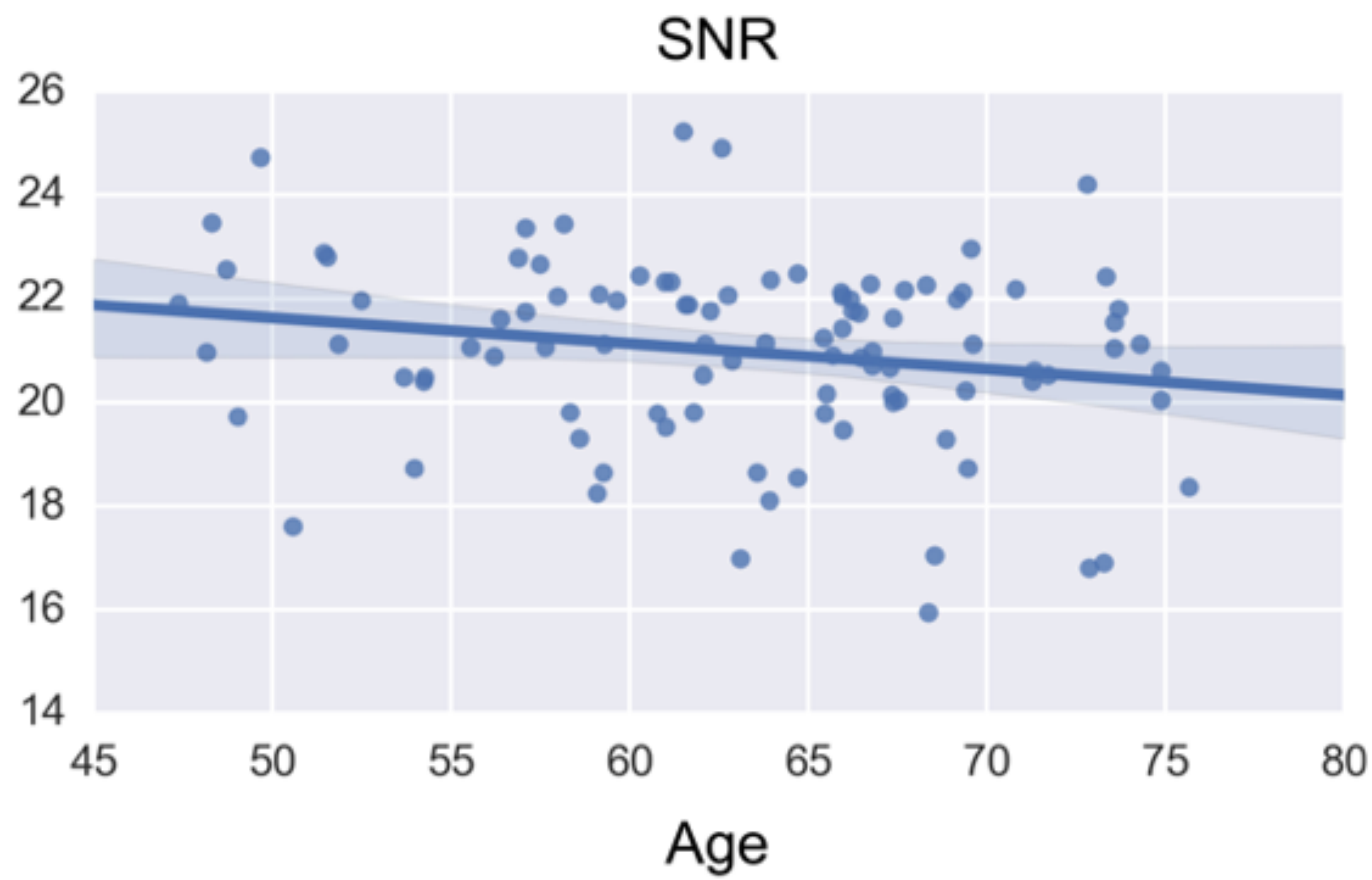
Avg std x translation (mm)	0.08
Avg std y translation (mm)	0.22
Avg std z translation (mm)	0.13
Avg std x rotation (deg)	0.15
Avg std y rotation (deg)	0.09
Avg std z rotation (deg)	0.11

Outliers

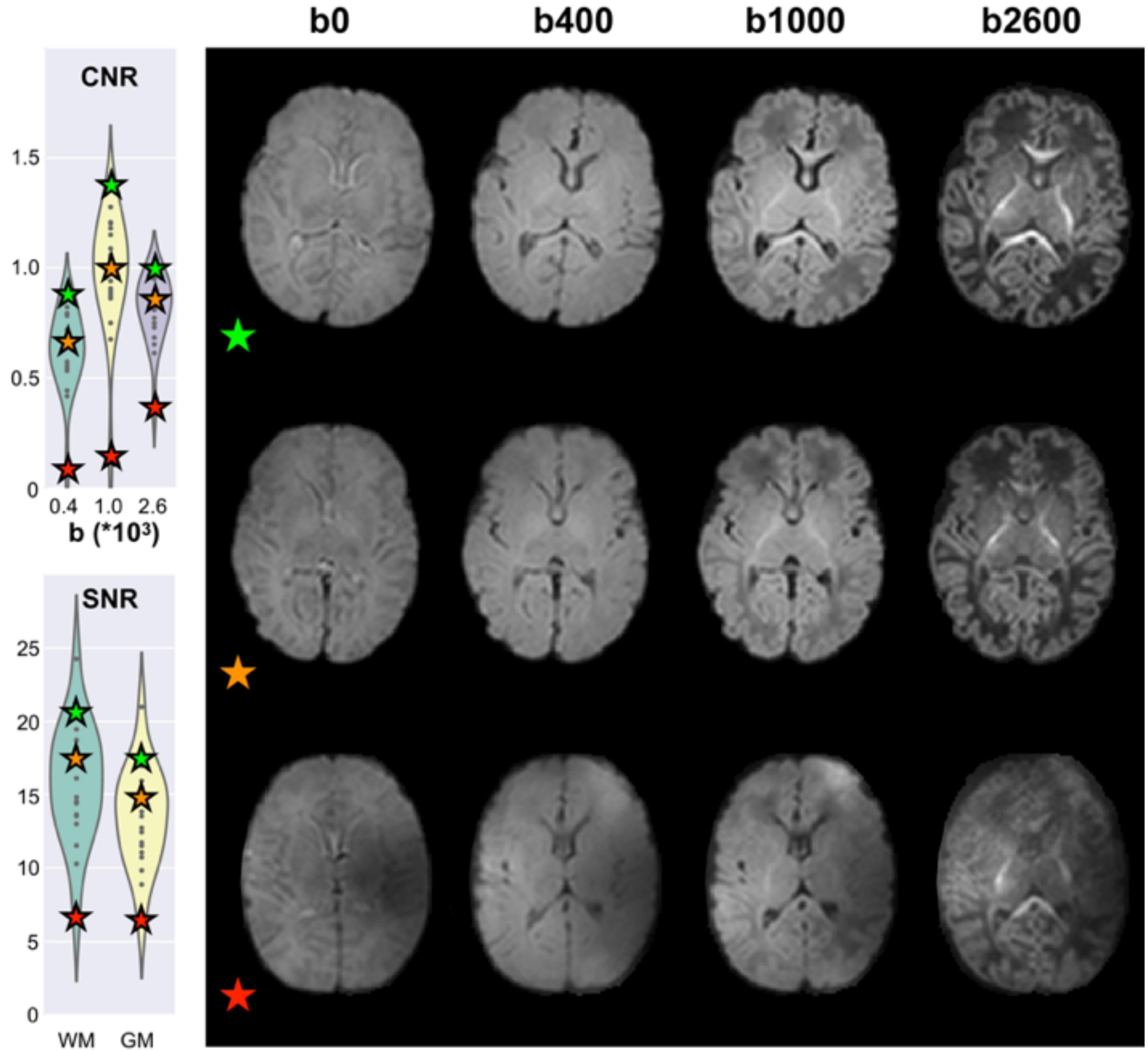
Total outliers (%)	2.86
Outliers (b=1000 s/mm^2)	4.69
Outliers (b=2000 s/mm^2)	1.13
Outliers (PE dir=[0. 1. 0.])	2.55
Outliers (PE dir=[0. -1. 0.])	2.66



EDDY QC: group report



Data quality illustration



Outline of the talk

- What is the problem with diffusion data?
- Off-resonance field
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  - Movement-induced dropout
  - Intra-volume motion
  - Susceptibility-by-movement

Movement induced dropout

Diffusion encoding

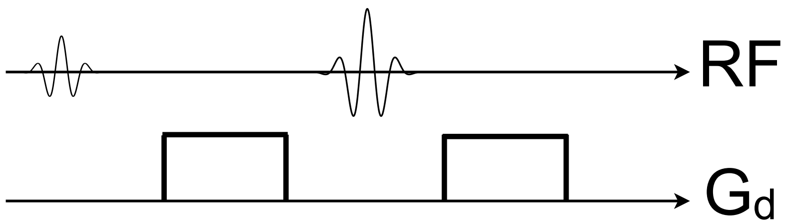
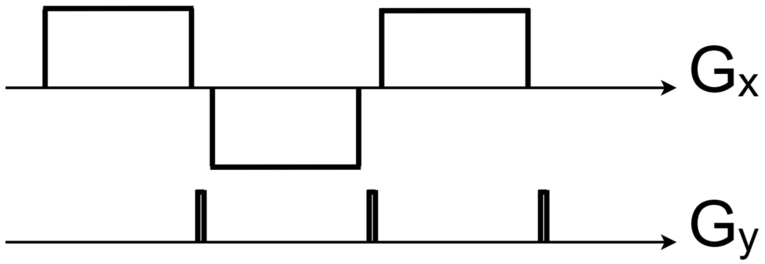
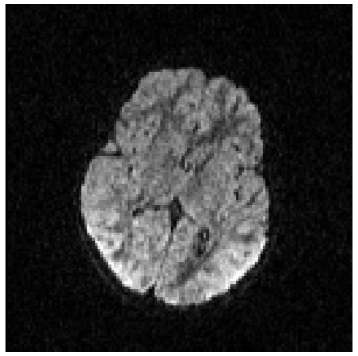


Image encoding

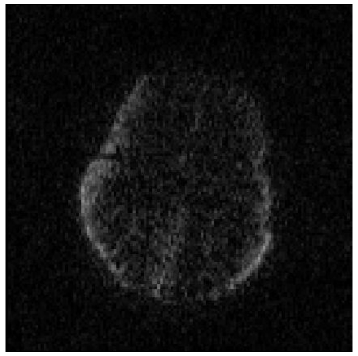


...

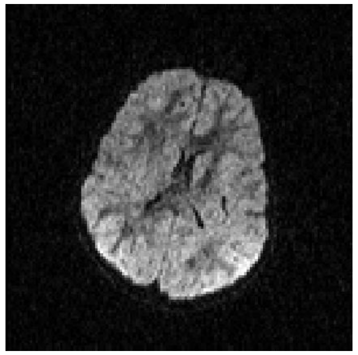
If there is movement during this part...



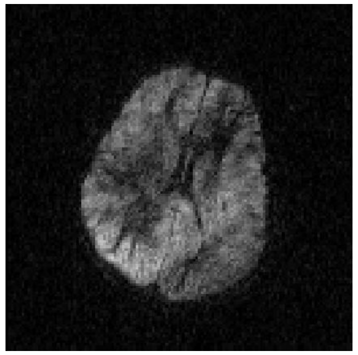
this



can turn to this

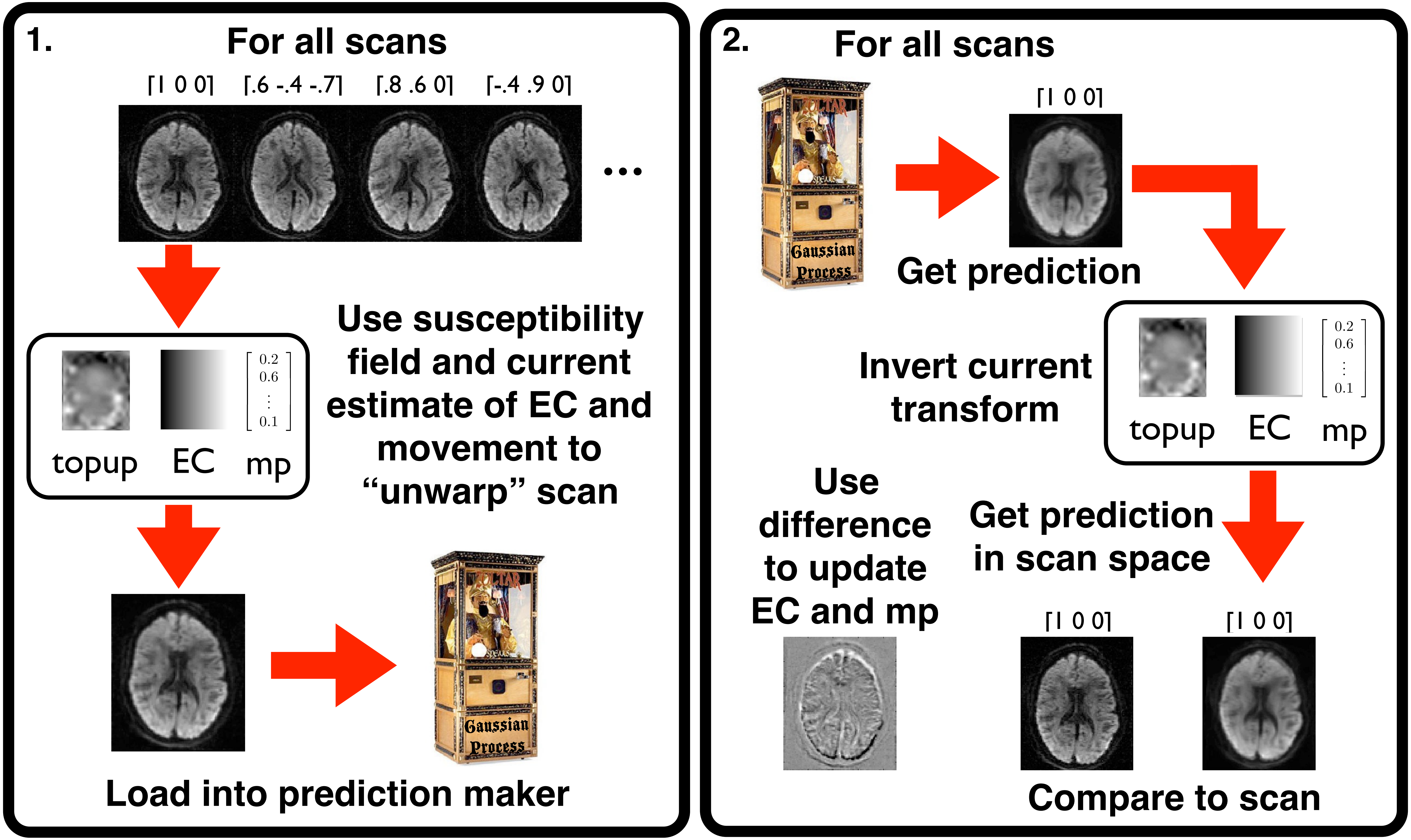


or this

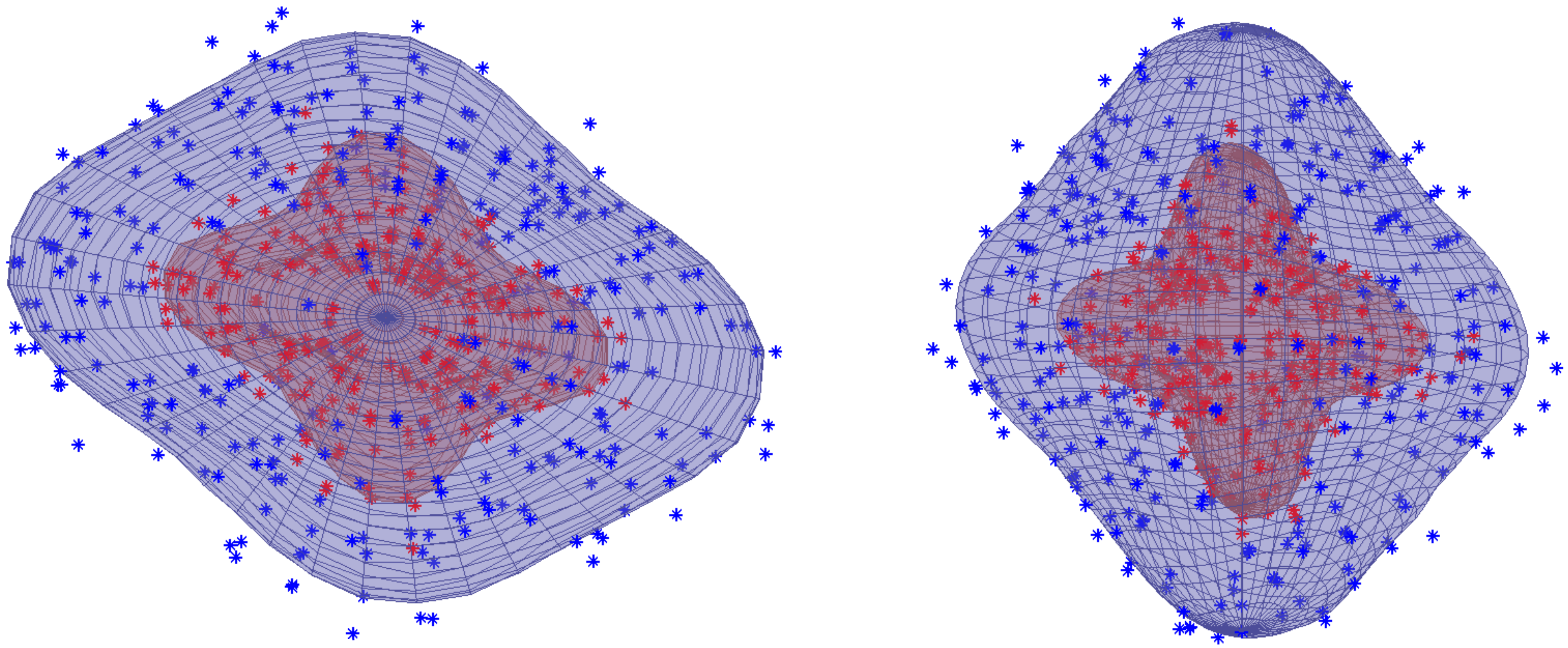


to this

What can eddy do about it?
But first a little recap of eddy



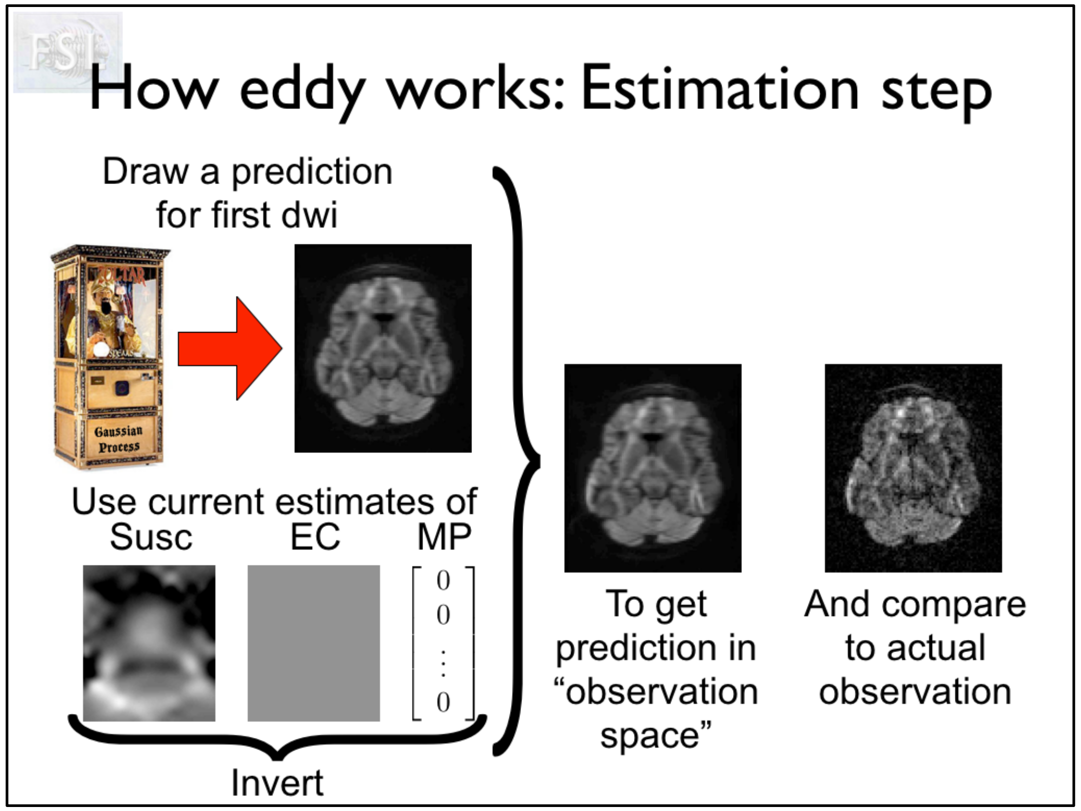
How are the predictions made?



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.

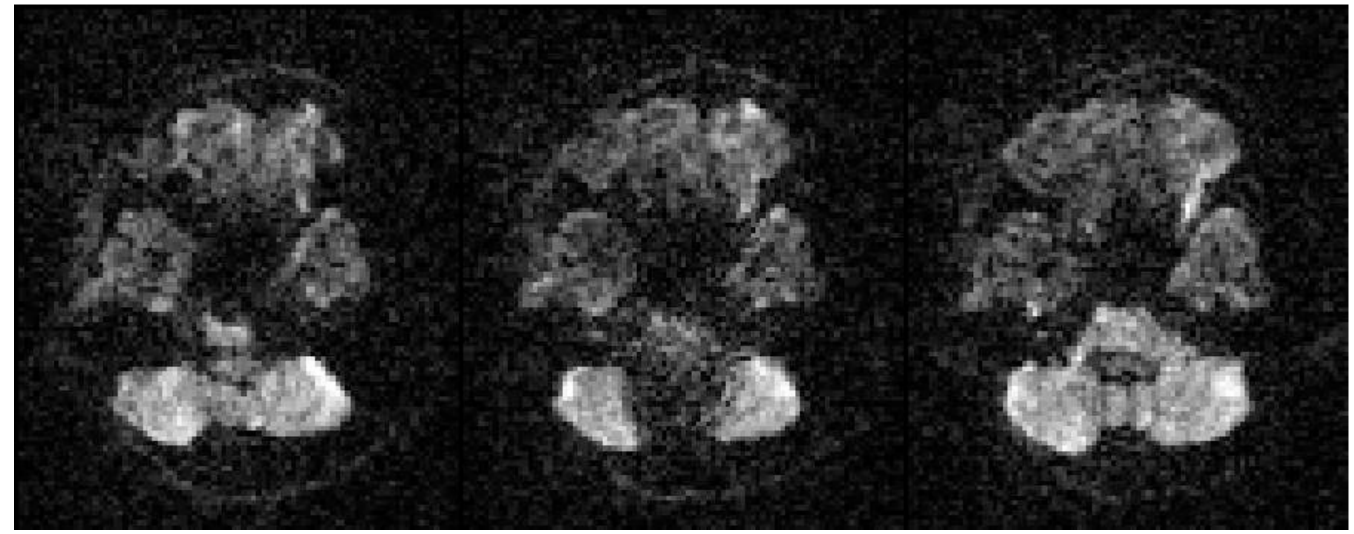
$$\hat{y}_{\mathbf{g}} = K(\mathbf{g}, \mathbf{G}) \left[K(\mathbf{G}, \mathbf{G}) + \sigma^2 \mathbf{I} \right]^{-1} \mathbf{y}$$

Outlier detection

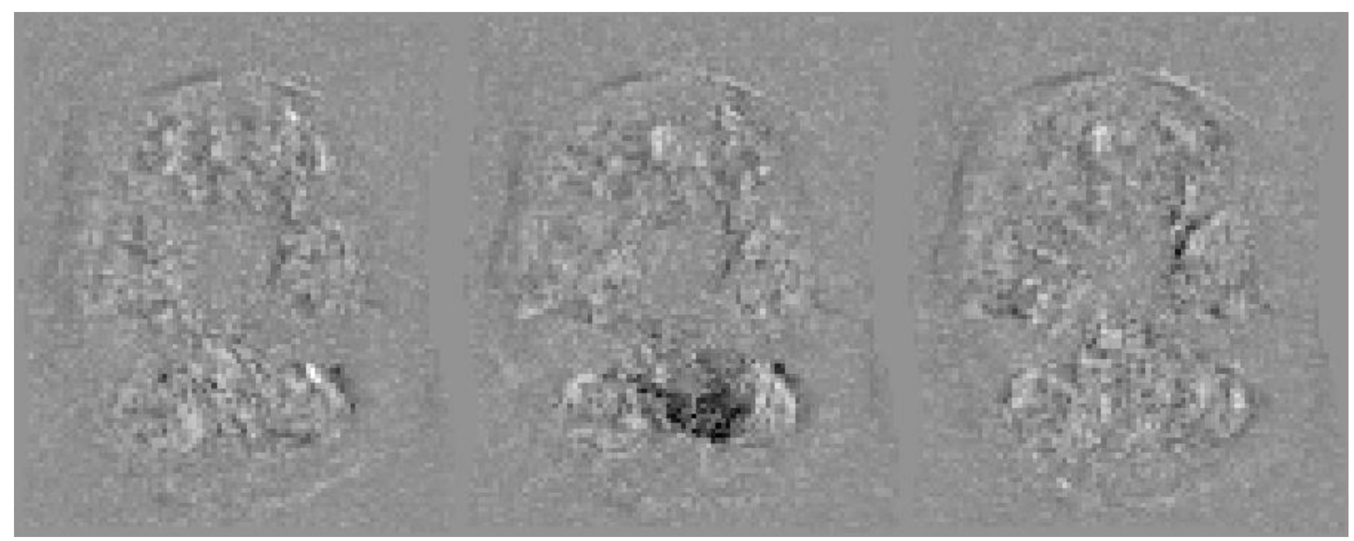


Remember that we do all comparisons in observation space.

Observed data



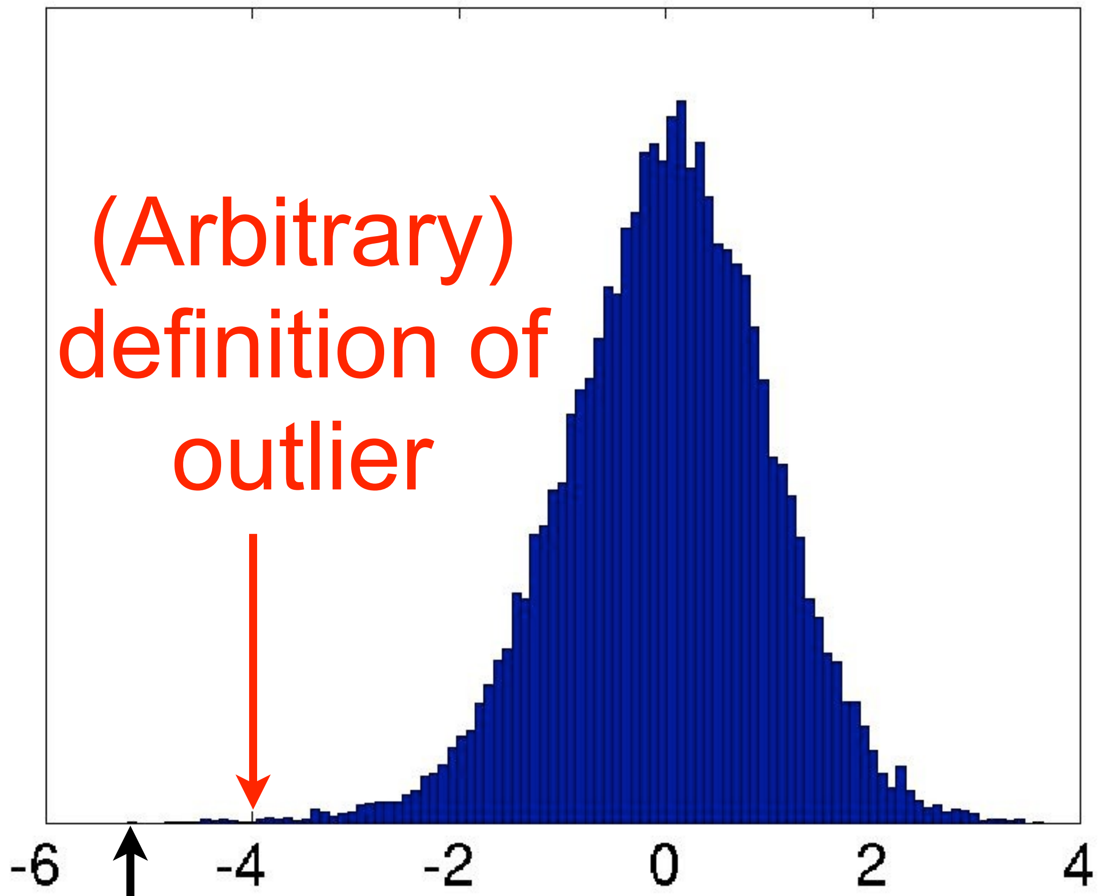
Observed - predicted



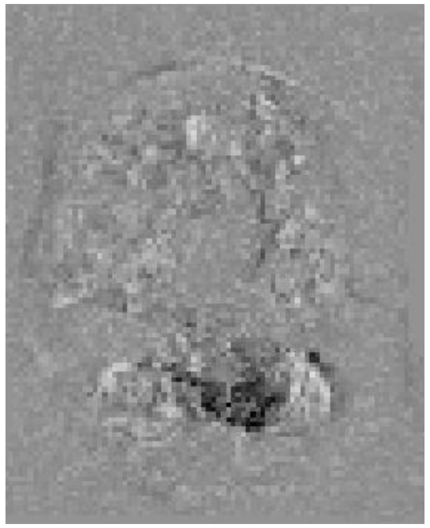
$\overline{x} = 0.084$ $\overline{x} = -0.791$ $\overline{x} = -0.125$

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

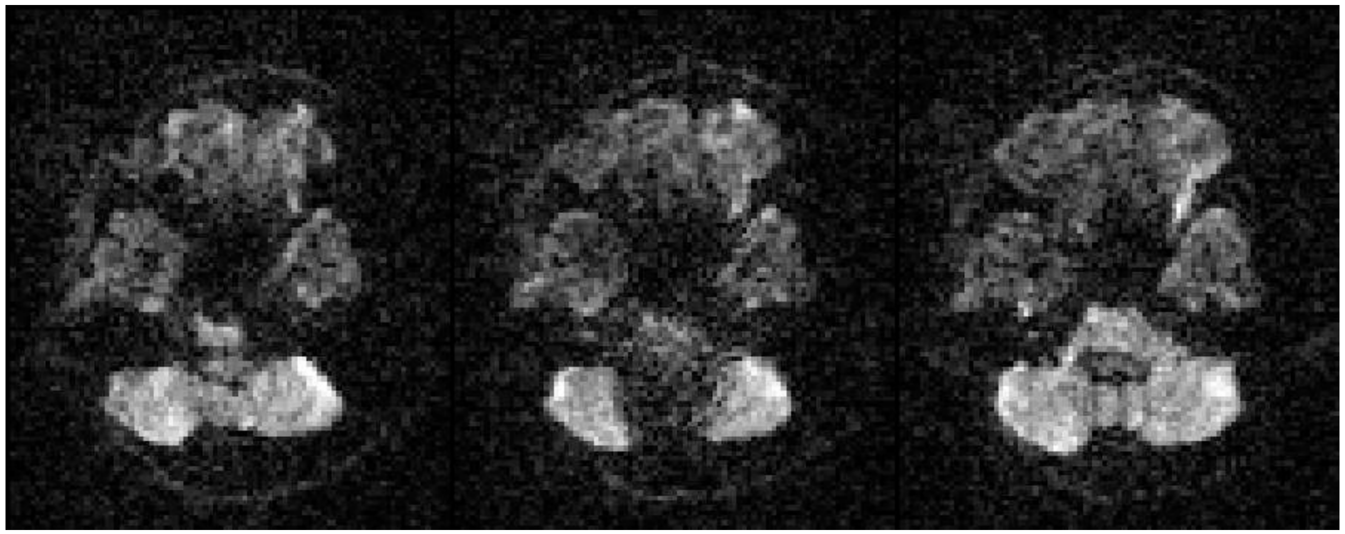


Worst slice

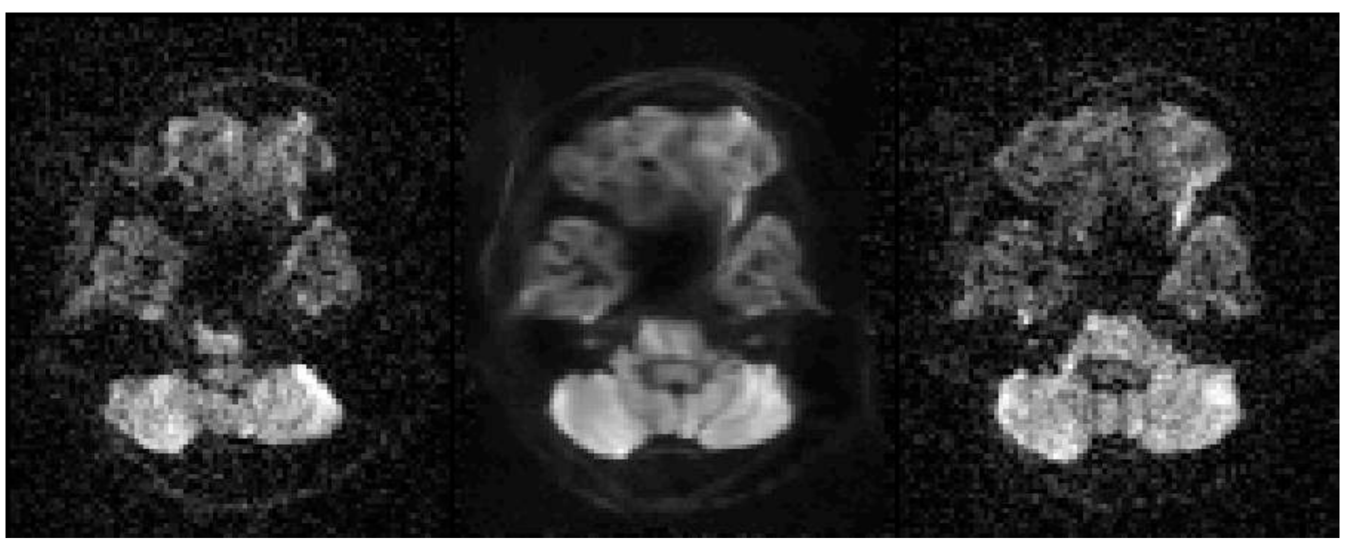
We can define an outlier slice as one with a z-score above an (arbitrary) threshold. We then have a choice of reporting outliers and/or replacing them with their predictions.

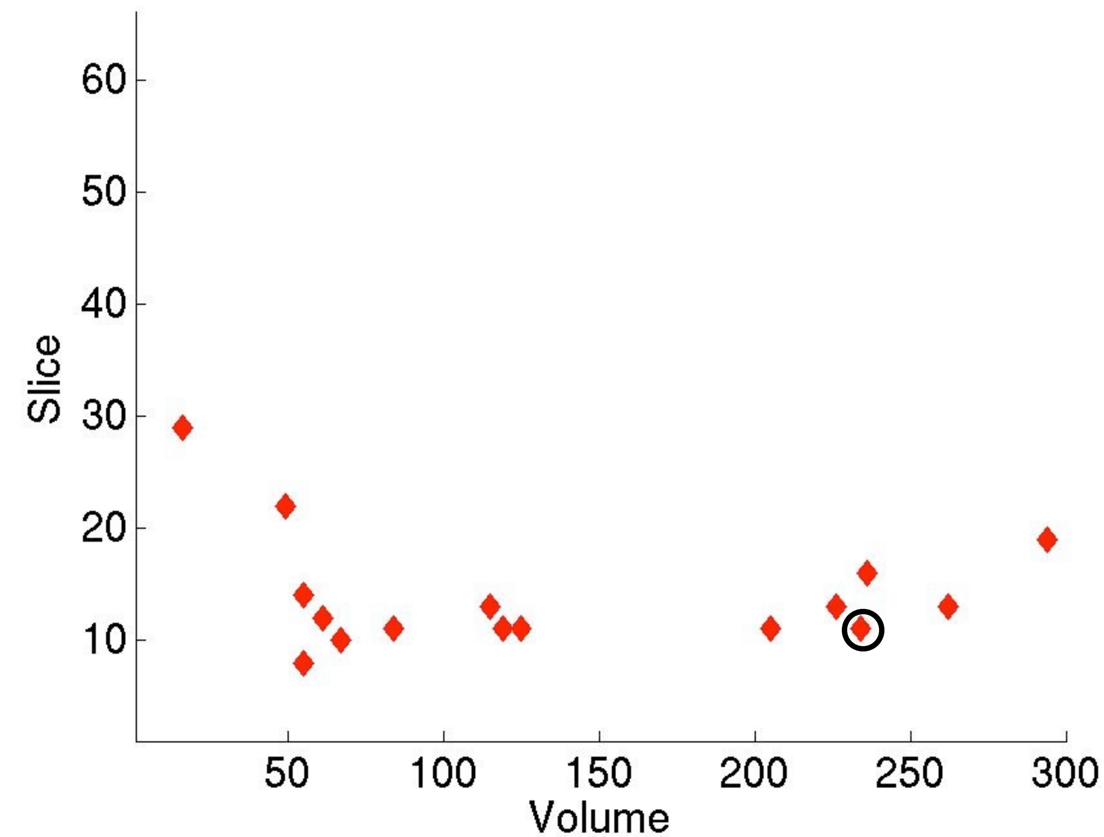
Outlier detection

Original data



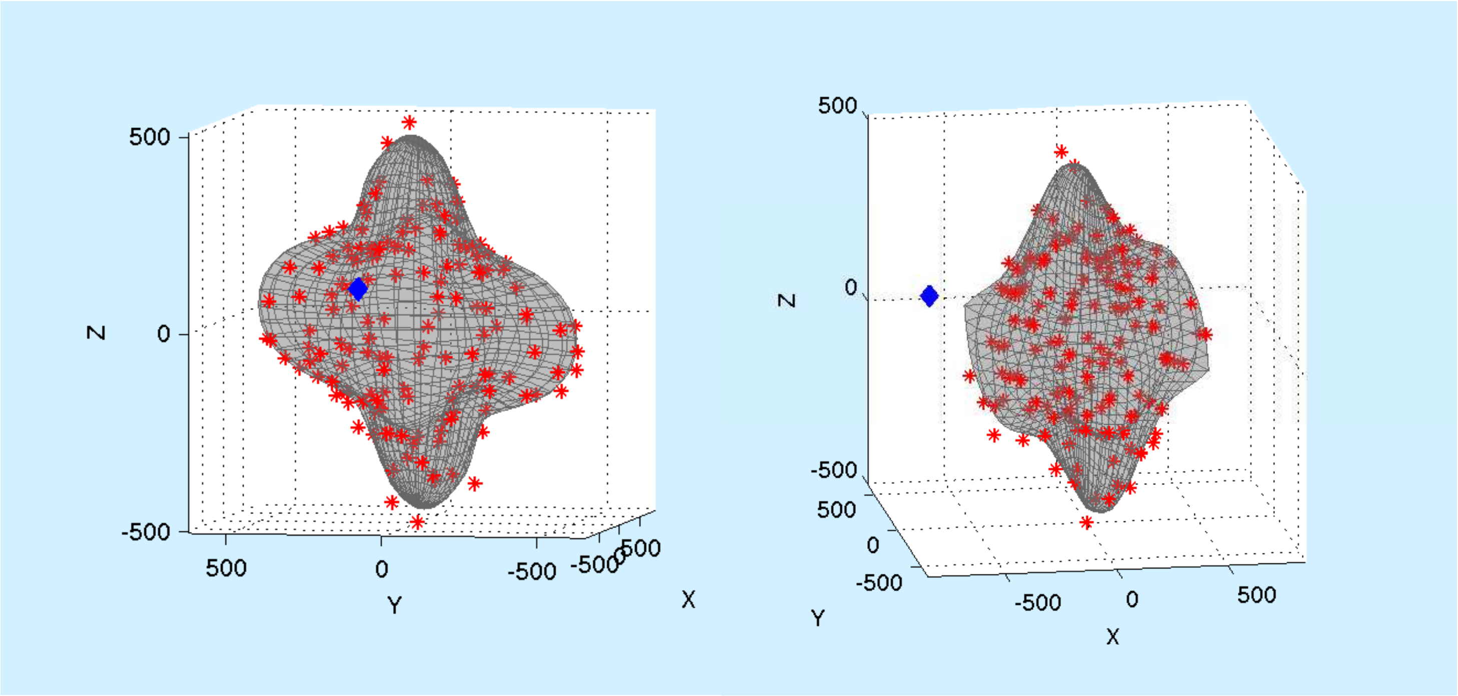
Data after replacement



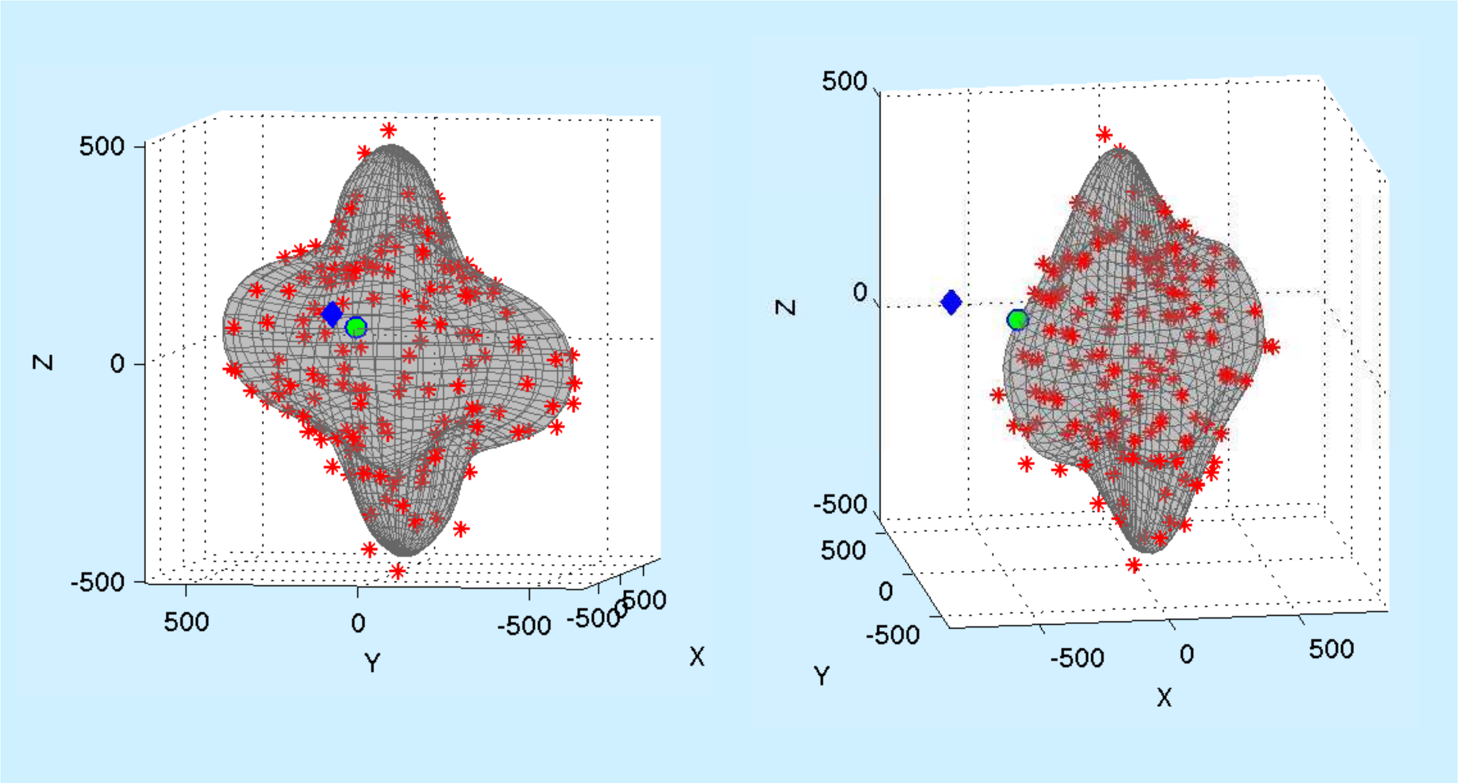


Outliers for a very still volunteer. Outliers mainly in basal slices.

How to make the “right” prediction

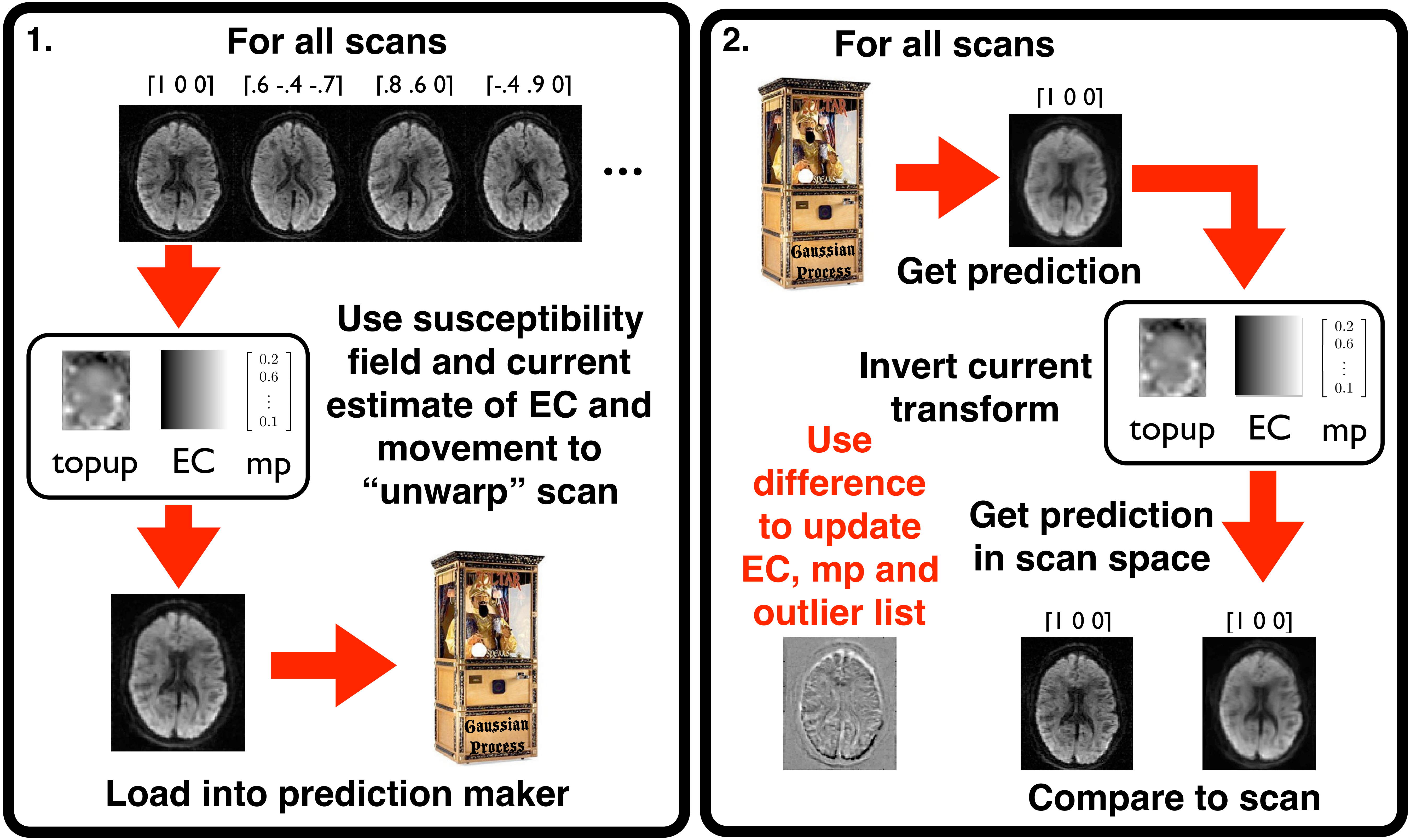


The outlier skews the predictions, but is still recognisable as an outlier

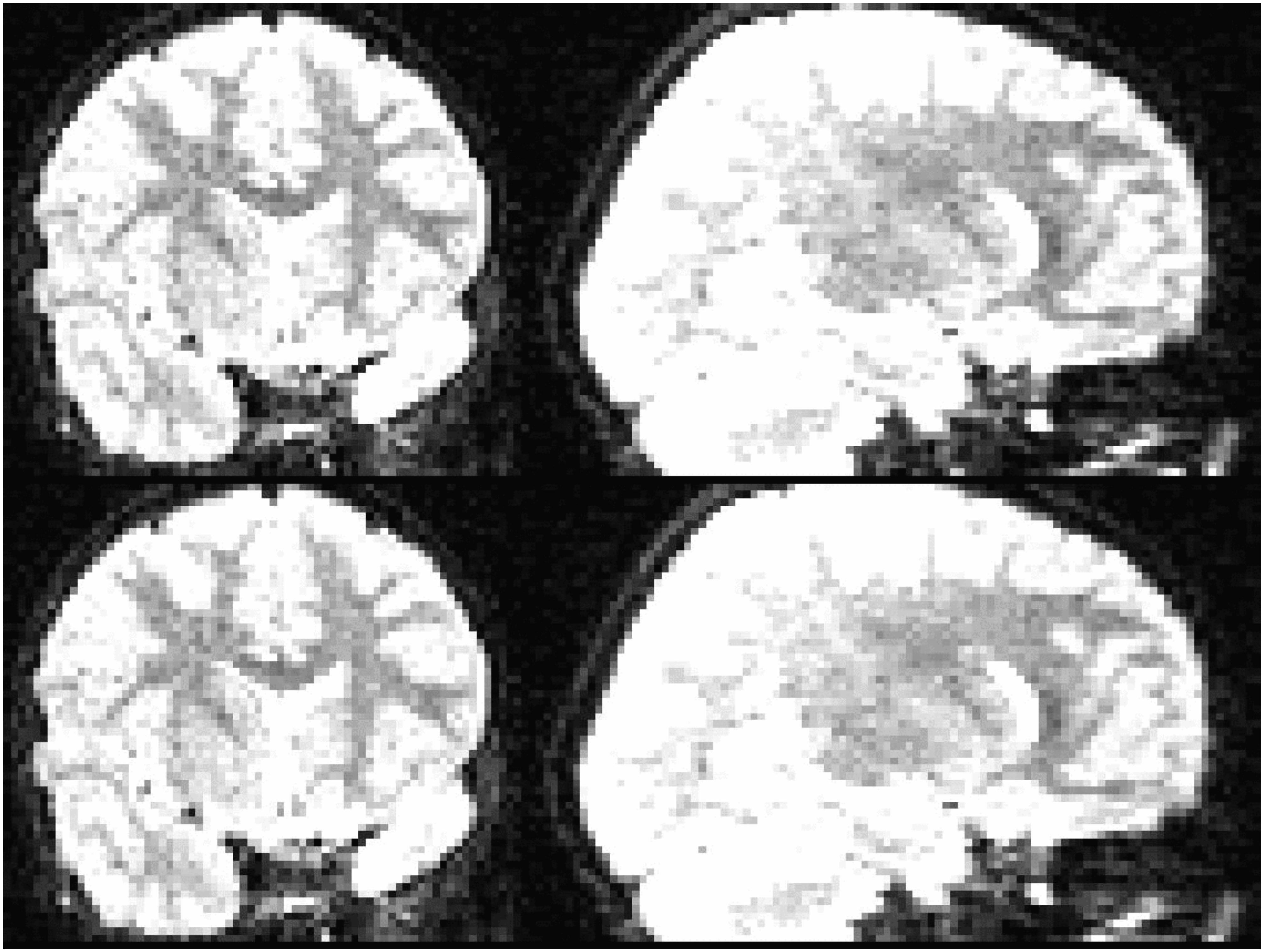


Remove the outlier and recalculate the “model”. The prediction is taken from this new “model”.

eddy revisited



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

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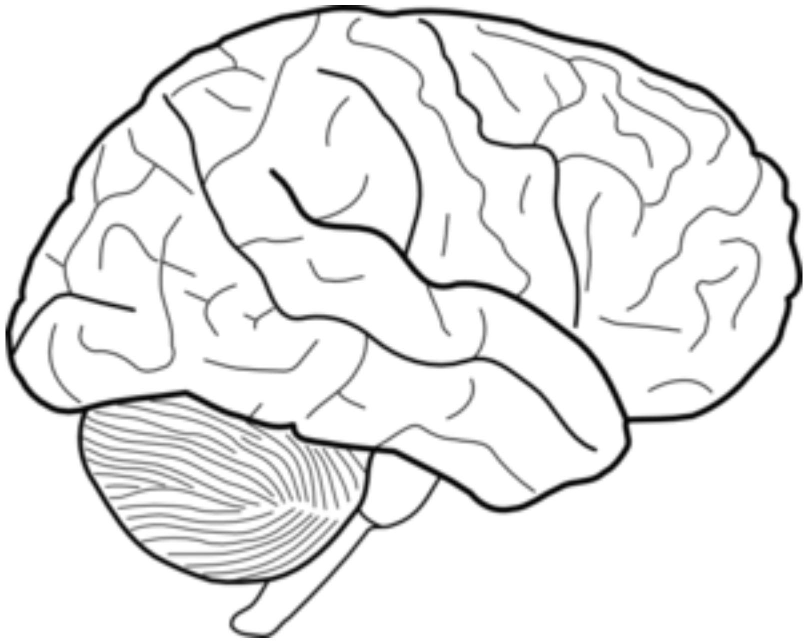
  - Intra-volume motion
  - Susceptibility-by-movement

Intra-volume movement

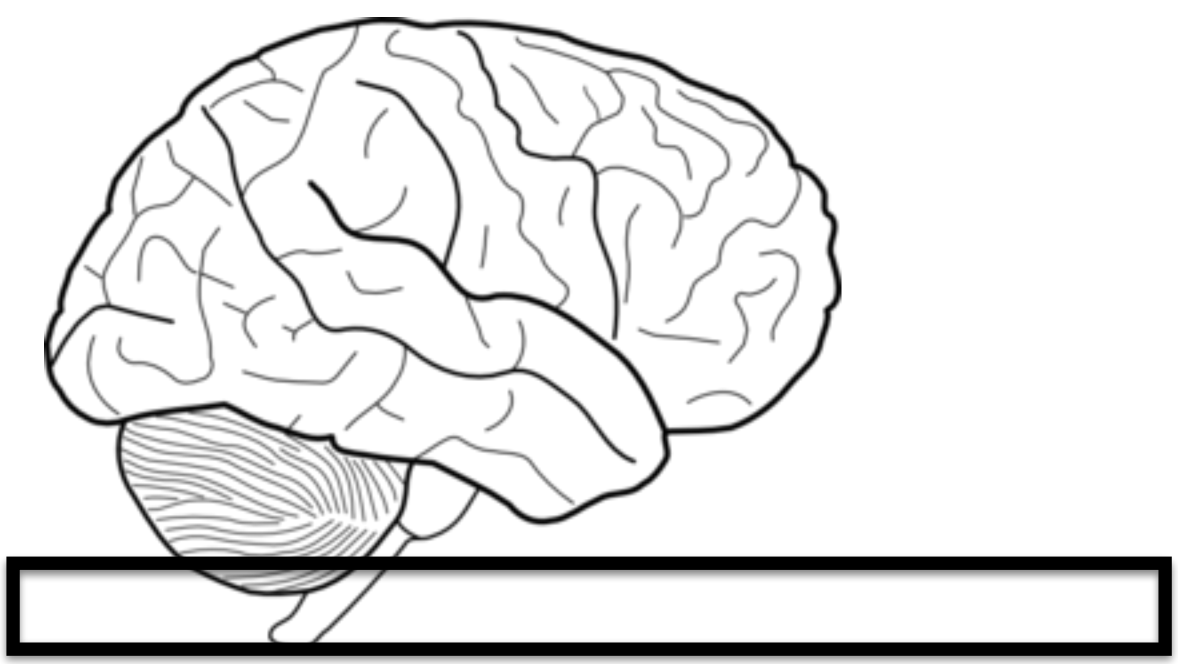
One of the (possibly naive) assumptions of most movement correction is that any movement is instantaneous and occurs between the acquisition of consecutive volumes.



This is the brain we set out to image

Intra-volume movement

One of the (possibly naive) assumptions of most movement correction is that any movement is instantaneous and occurs between the acquisition of consecutive volumes.



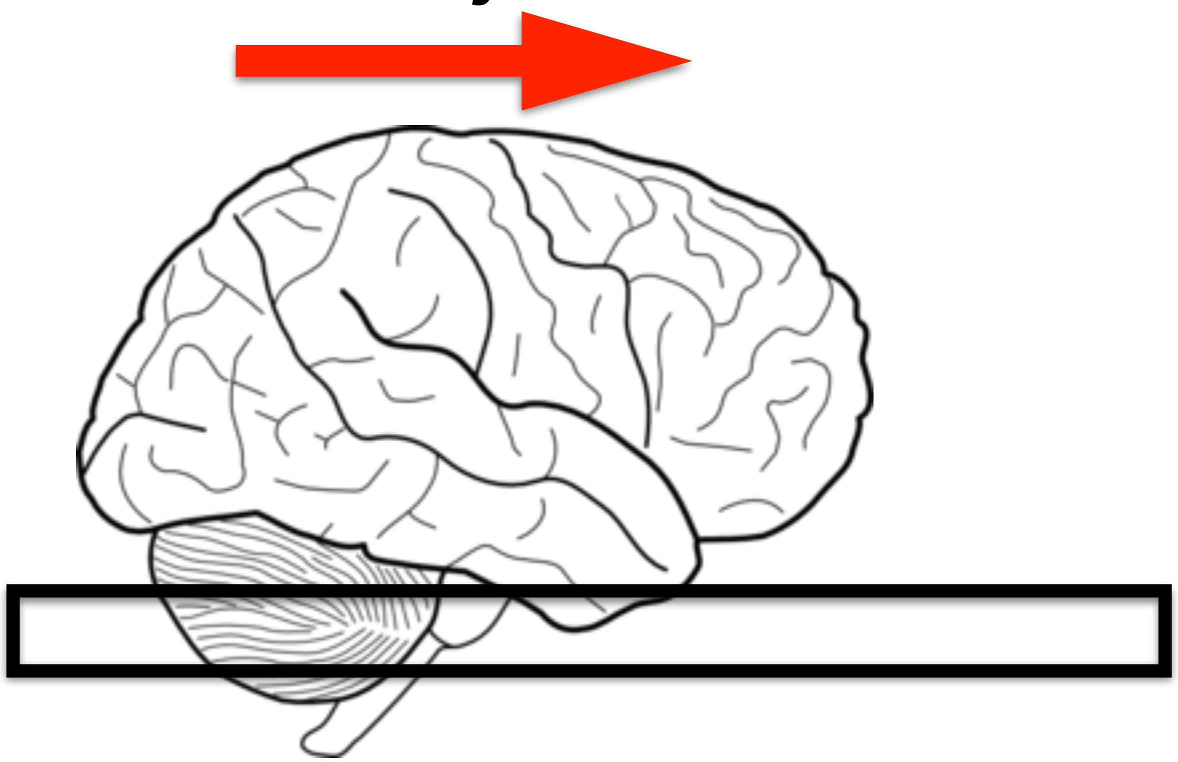
This is the brain we set out to image

And here we have acquired the first slice

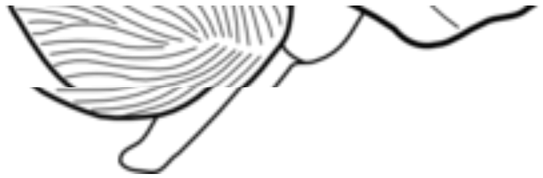
Intra-volume movement

One of the (possibly naive) assumptions of most movement correction is that any movement is instantaneous and occurs between the acquisition of consecutive volumes.

But the subject moves



This is the brain we set out to image

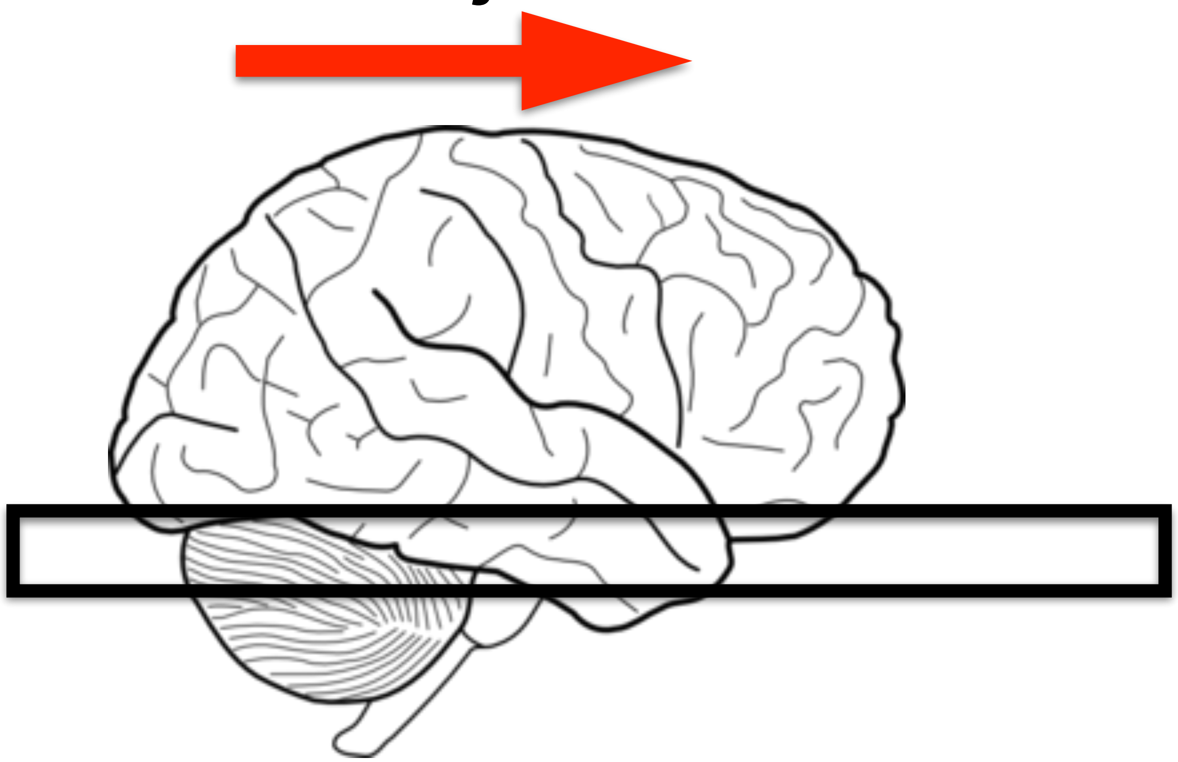


So the brain is offset in the second slice

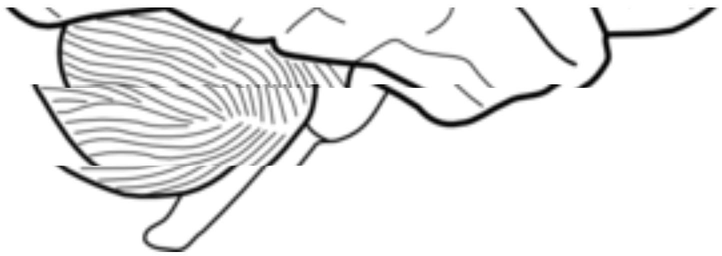
Intra-volume movement

One of the (possibly naive) assumptions of most movement correction is that any movement is instantaneous and occurs between the acquisition of consecutive volumes.

But the subject moves



This is the brain we set out to image

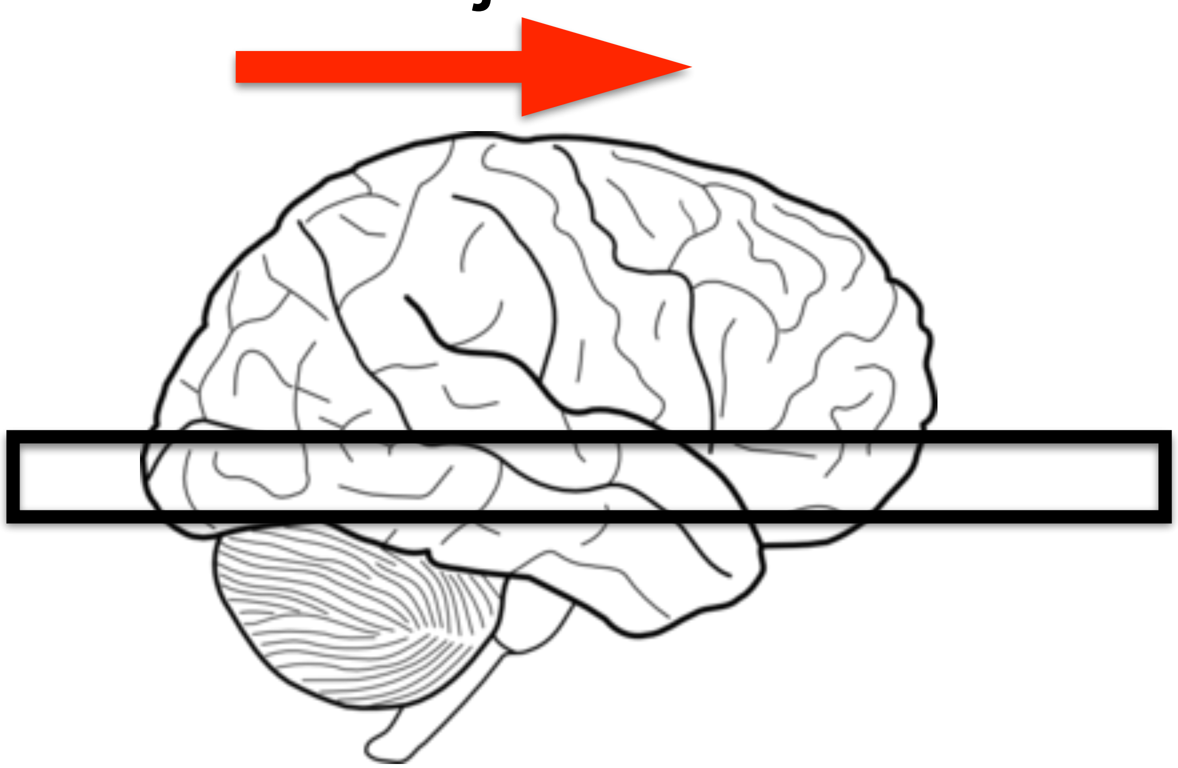


And even more so in the third slice

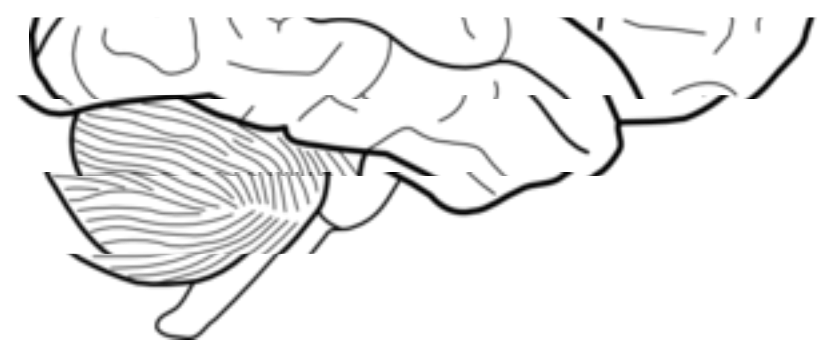
Intra-volume movement

One of the (possibly naive) assumptions of most movement correction is that any movement is instantaneous and occurs between the acquisition of consecutive volumes.

But the subject moves



This is the brain we set out to image

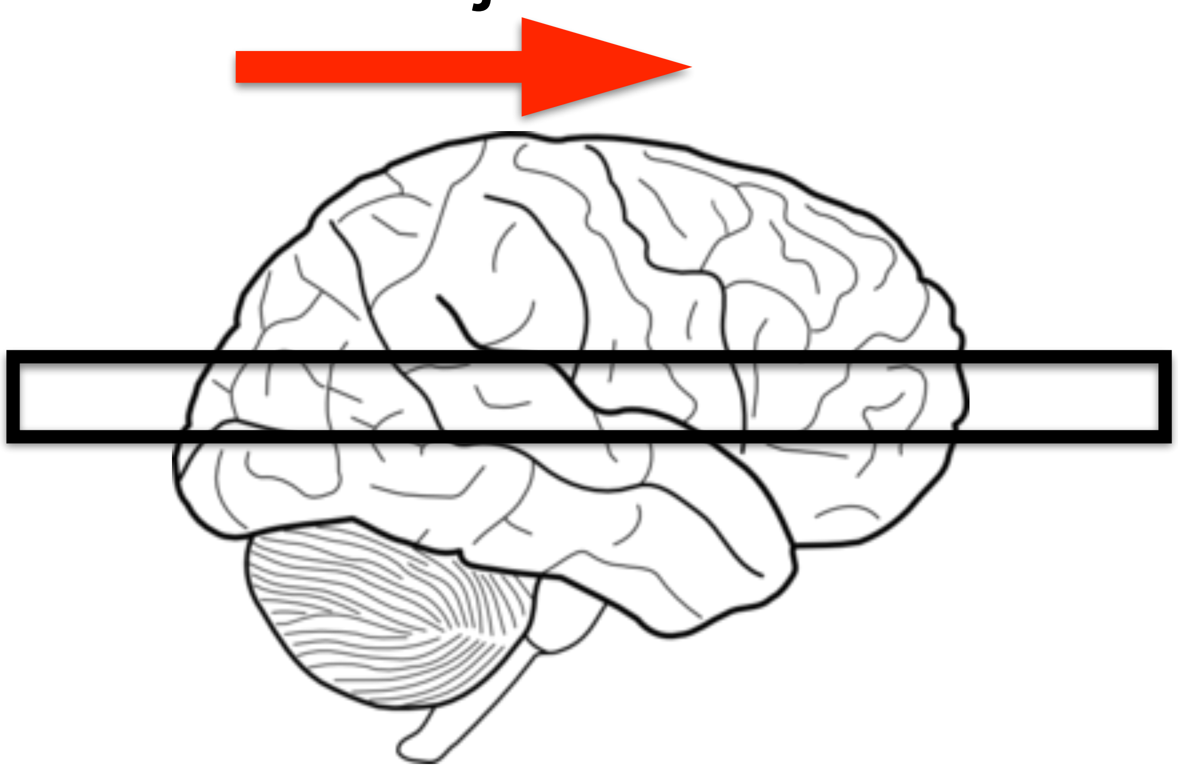


And more …

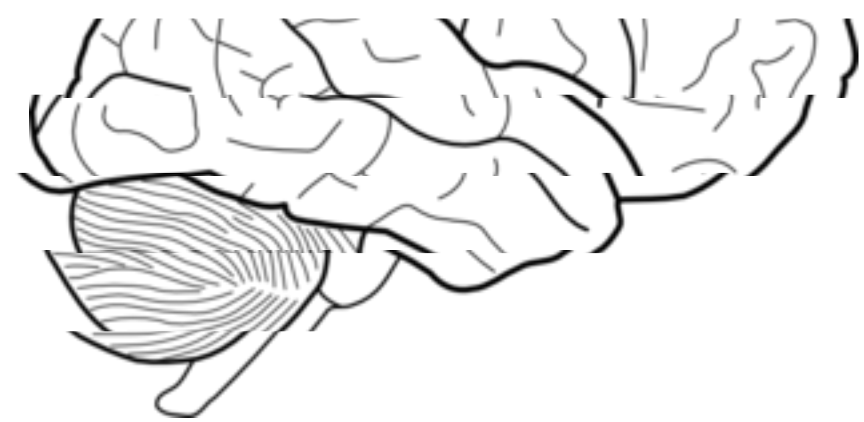
Intra-volume movement

One of the (possibly naive) assumptions of most movement correction is that any movement is instantaneous and occurs between the acquisition of consecutive volumes.

But the subject moves



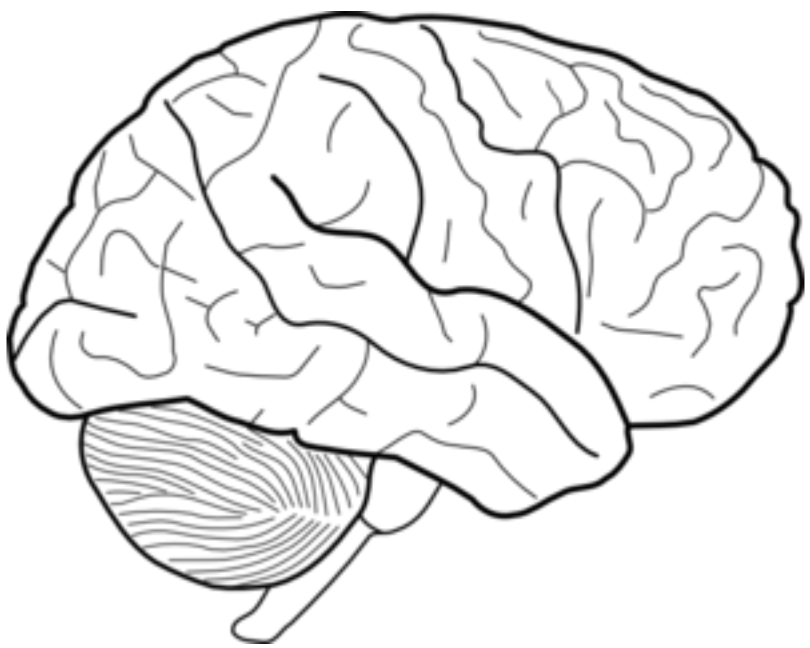
This is the brain we set out to image



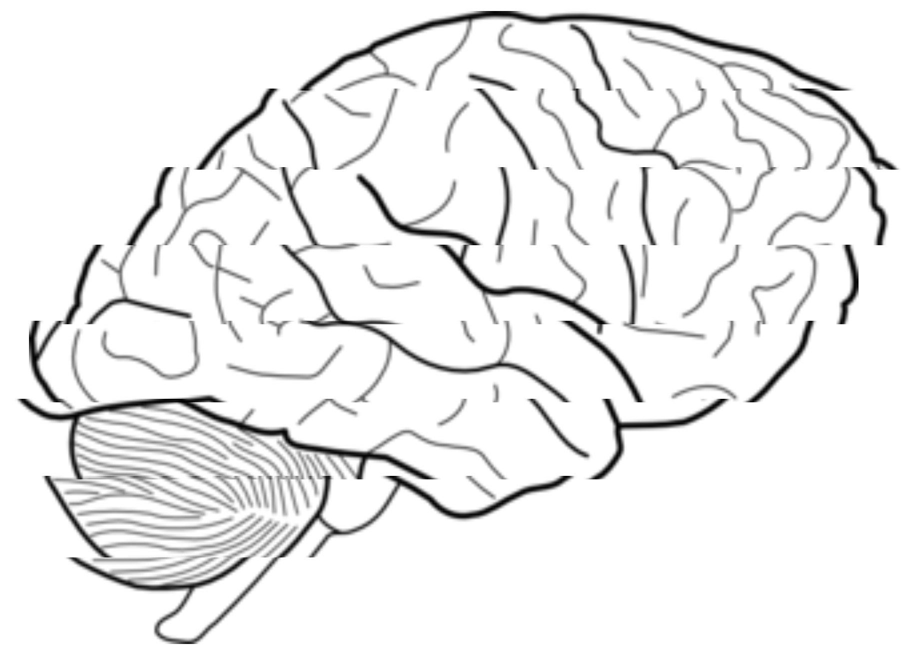
… and more …

Intra-volume movement

One of the (possibly naive) assumptions of most movement correction is that any movement is instantaneous and occurs between the acquisition of consecutive volumes.



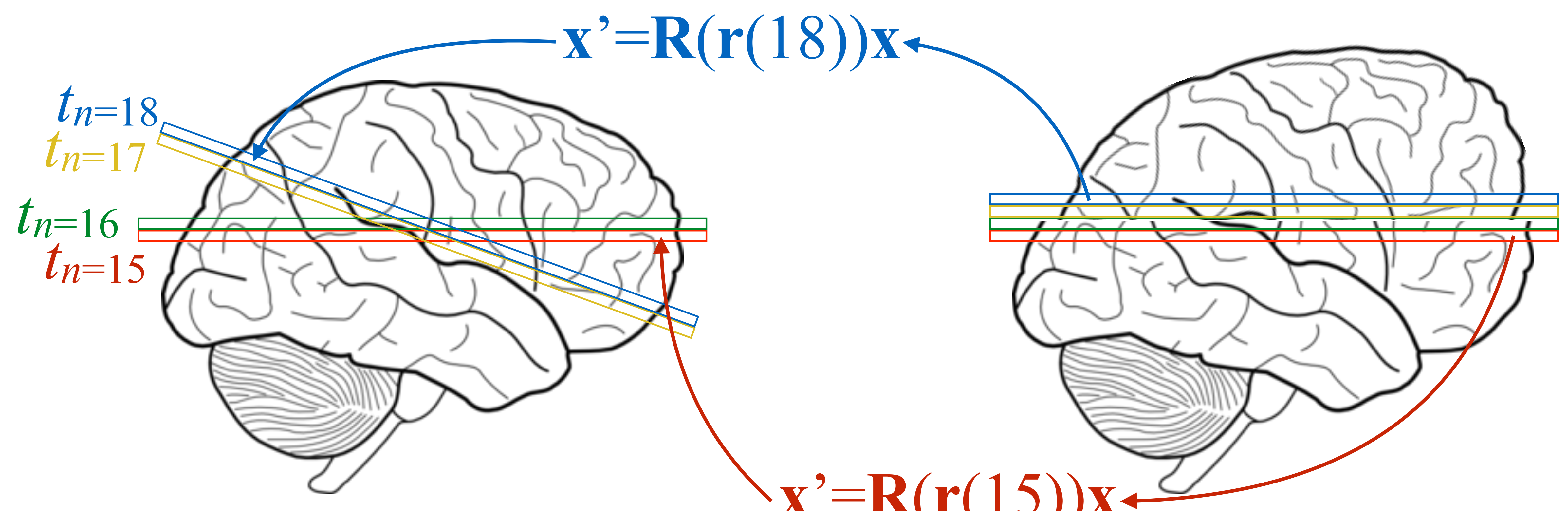
This is the brain we set out to image



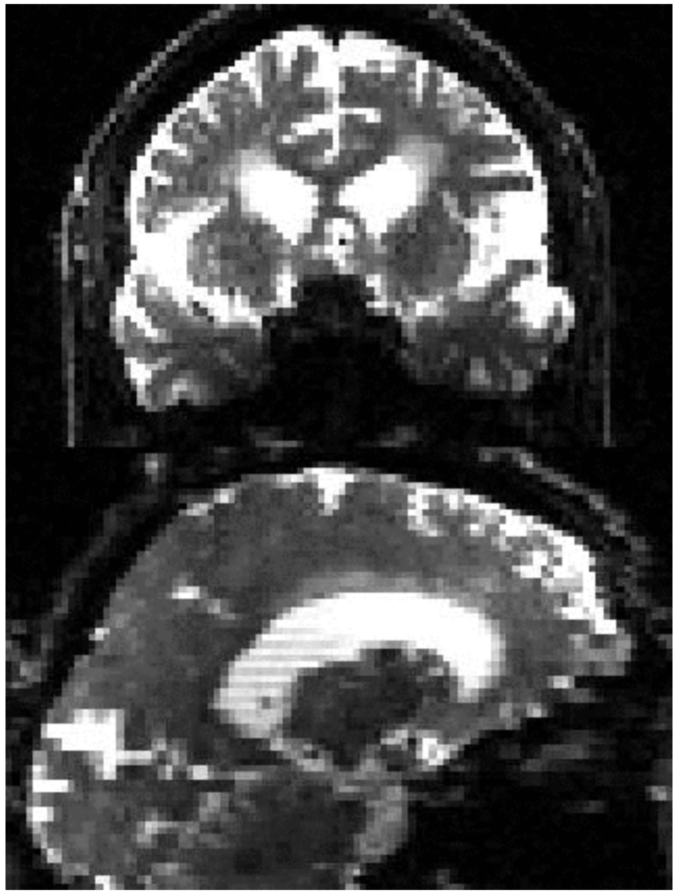
etc.

Intra-volume movement

- This is known as the “slice-to-vol” problem or the “intra-volume movement” problem.
- The new version of `eddy` addresses this problem.
- It estimates the slice wise movement through the same Gaussian Process based forward model.



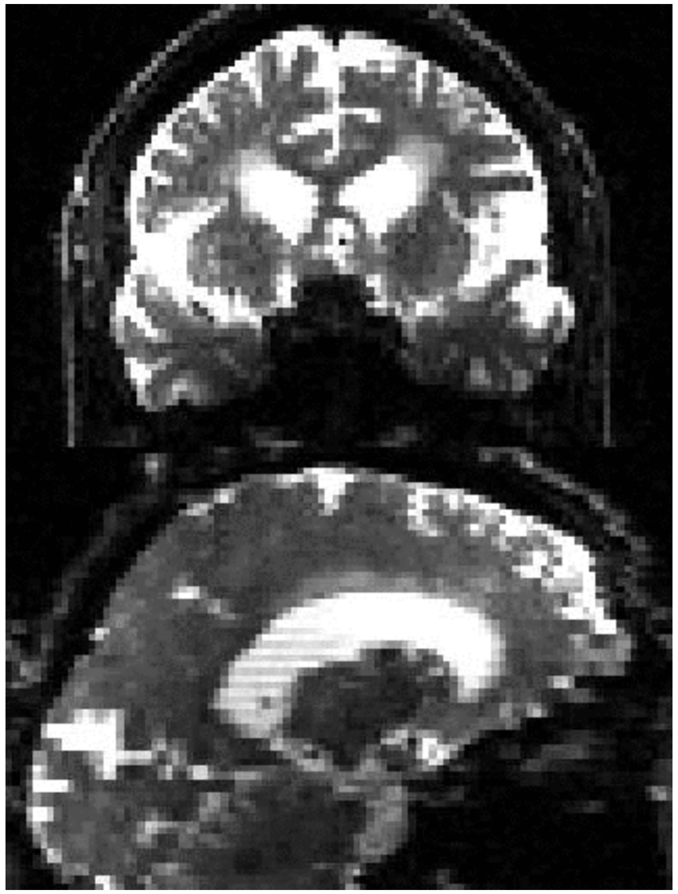
Intra-volume movement



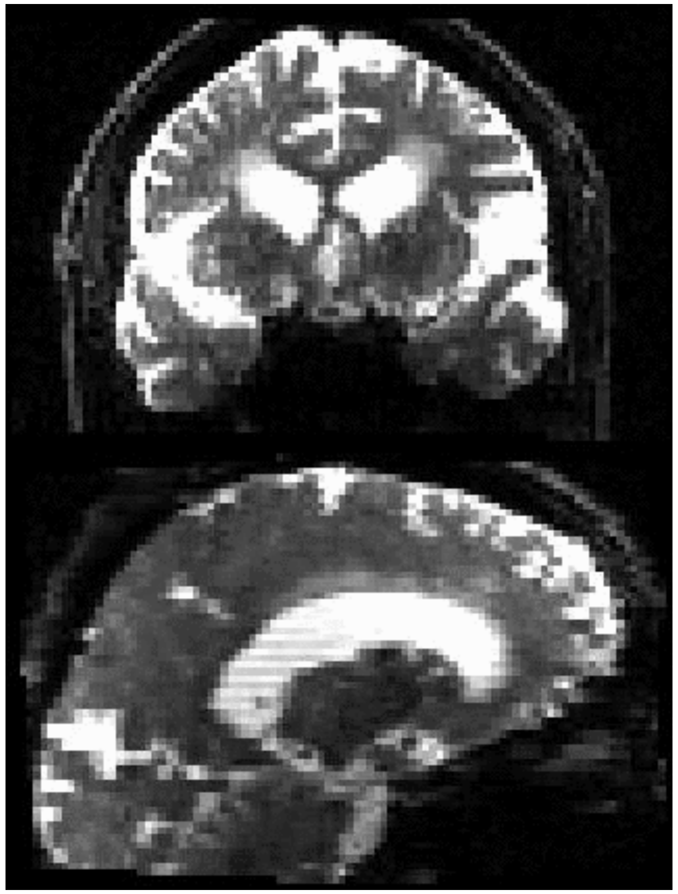
Original data

Problematic elderly subject. Lots of movement induced signal loss and intravolume movement

Intra-volume movement



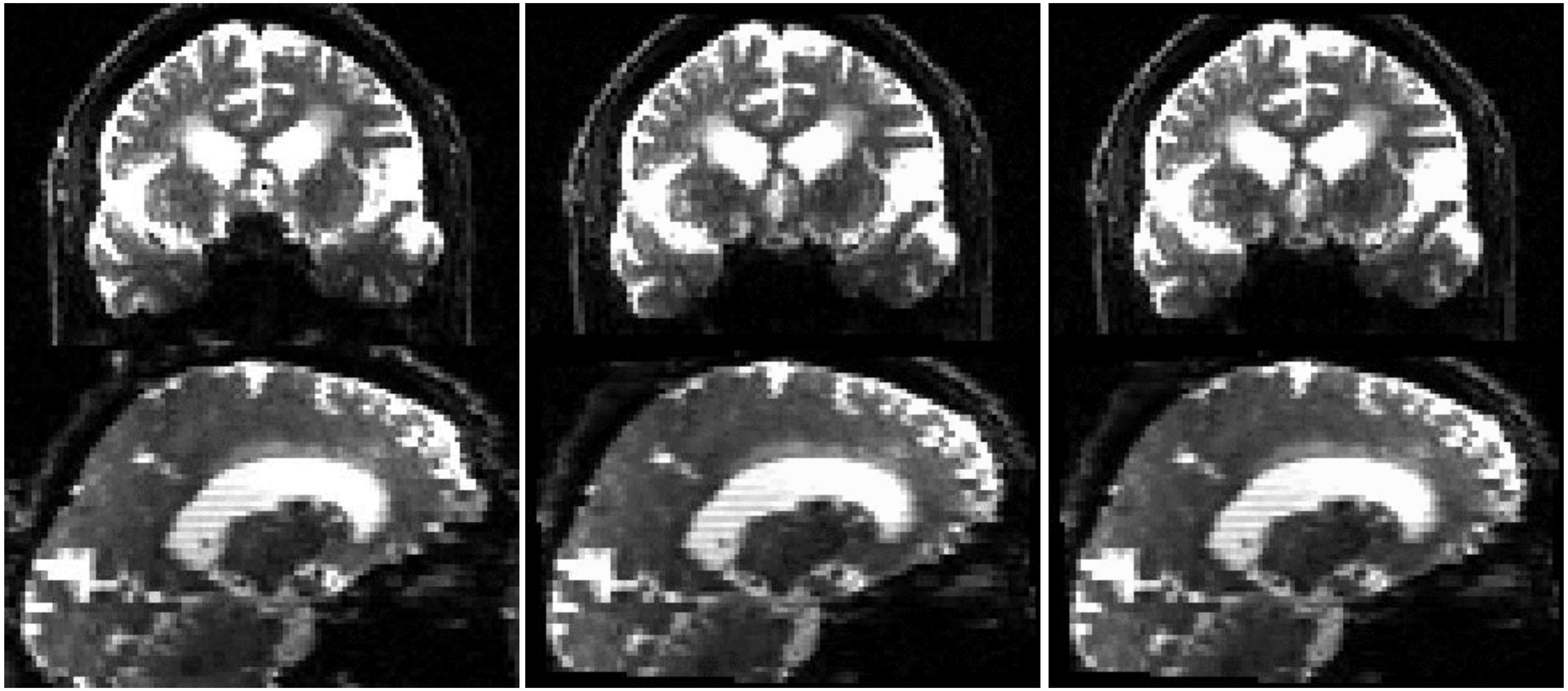
Original data



After correction without outlier correction

Problematic elderly subject. Lots of movement induced signal loss and intravolume movement

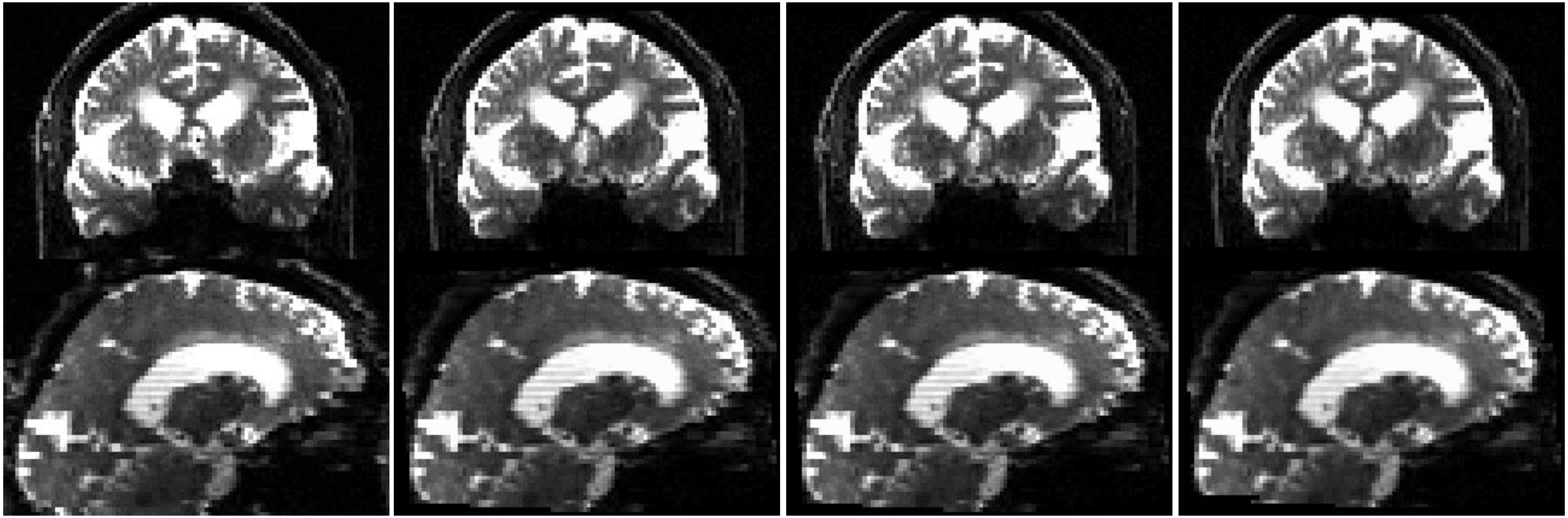
Intra-volume movement



Original data | After correction without outlier correction | After correction with outlier replacement

Problematic elderly subject. Lots of movement induced signal loss and intravolume movement

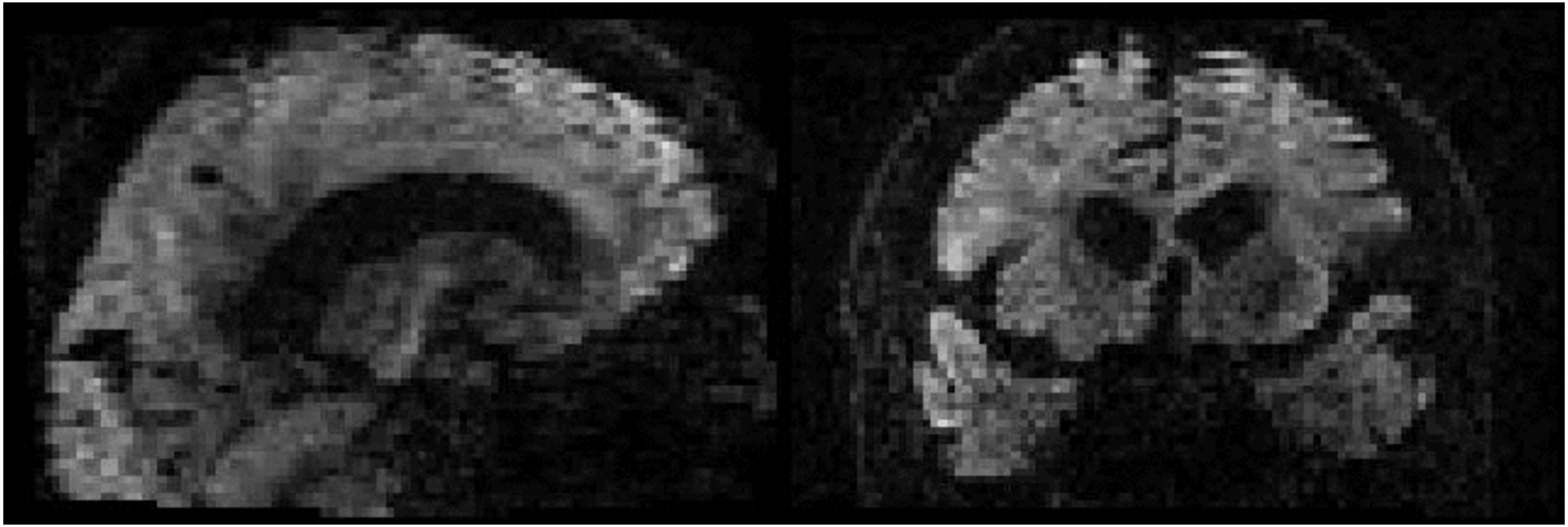
Intra-volume movement



Original data	After correction without outlier correction	After correction with outlier replacement	After intravolume movement correction.

Problematic elderly subject. Lots of movement induced signal loss and intravolume movement

Intra-volume movement



Highlighting the difference between just OLR and OLR combined with S2V correction

Problematic elderly subject. Lots of movement induced signal loss and intravolume movement

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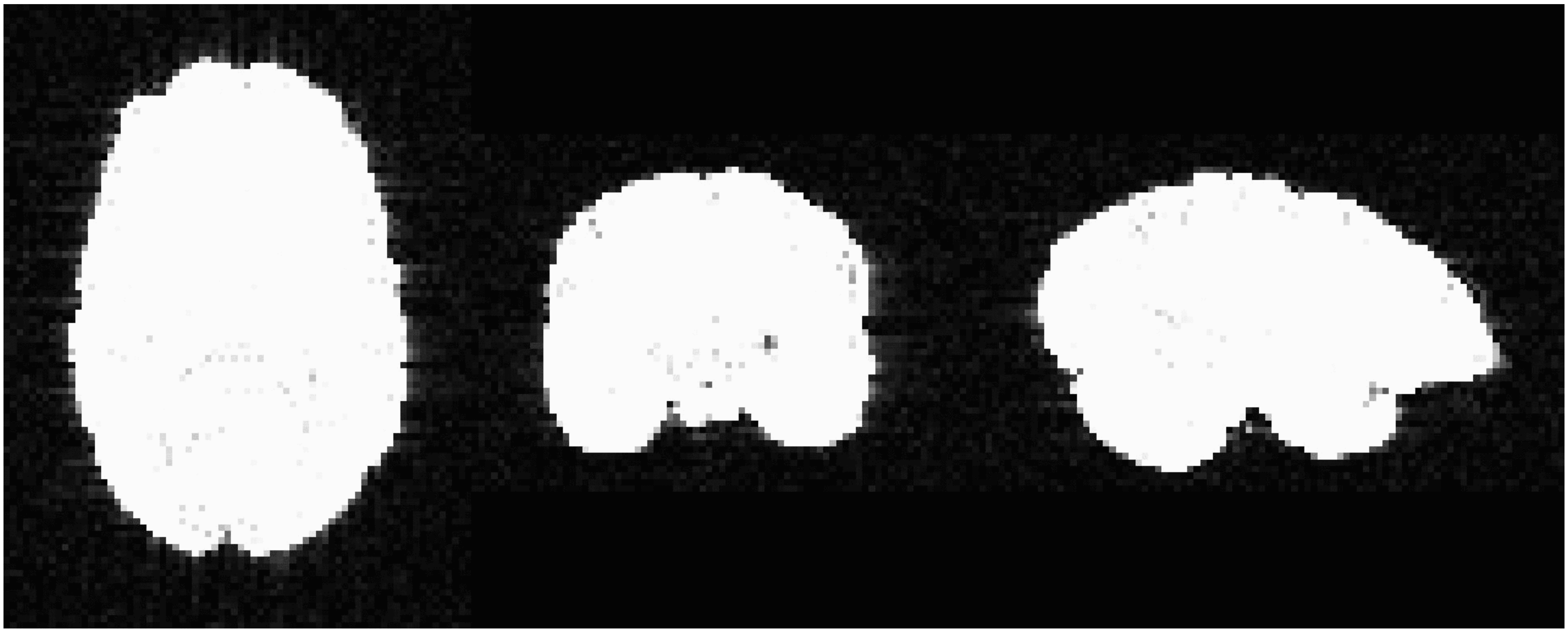
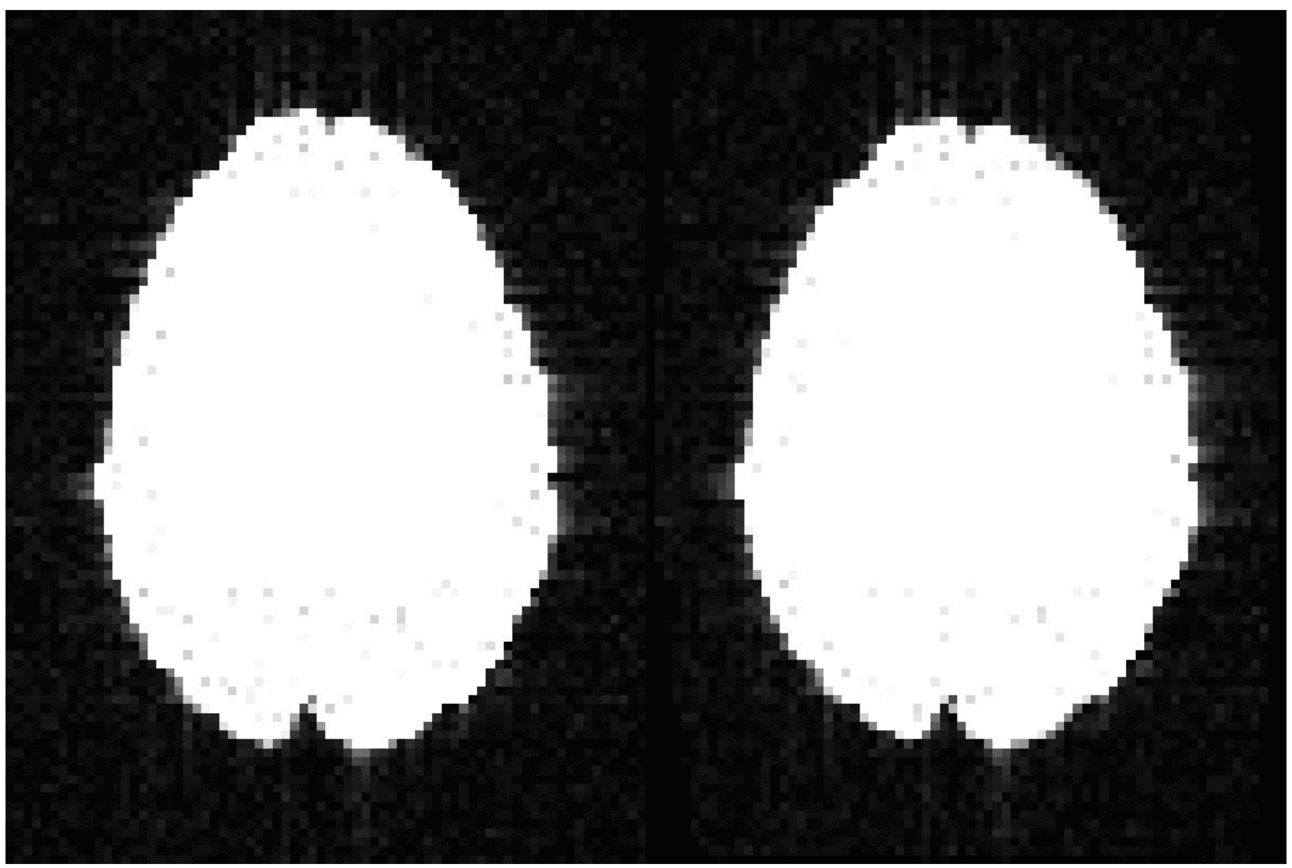
  - Susceptibility-by-movement

Some data with lots of movement



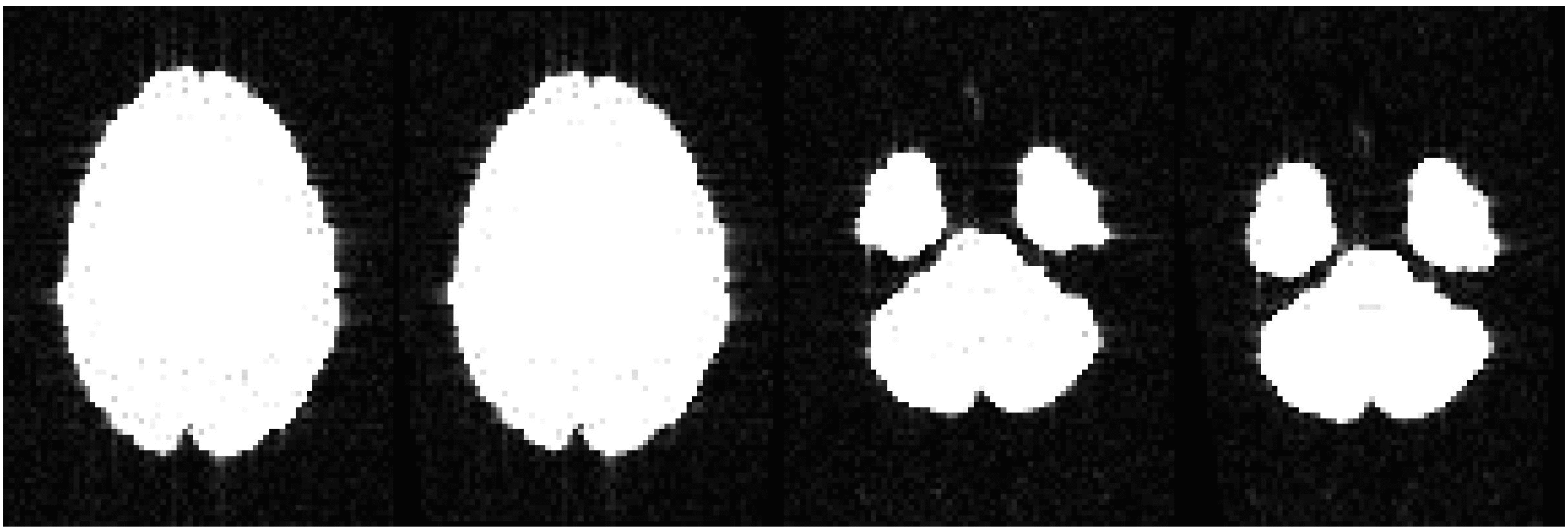
Some data with lots of movement, aligned with eddy

Before After



Some data with lots of movement, aligned with eddy

Before	After	Before	After



Why is that then?

Motion-induced Magnetic Field Changes Inside the Brain

Jiaen Liu[1], Jacco de Zwart[1], Peter van Gelderen[1], and Jeff Duyn[1]

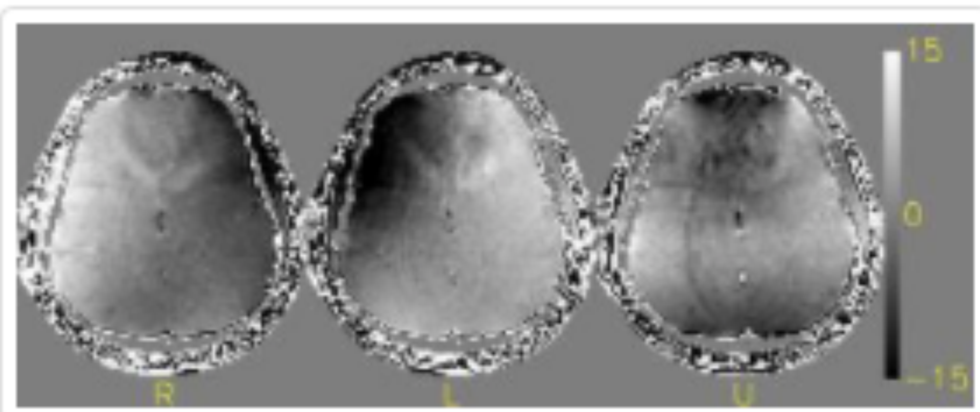


Fig. 1 Changes of field maps in four different positions relative to the field map in the reference position obtained under the "phantom shim" setting. The unit of the field maps is Hz.

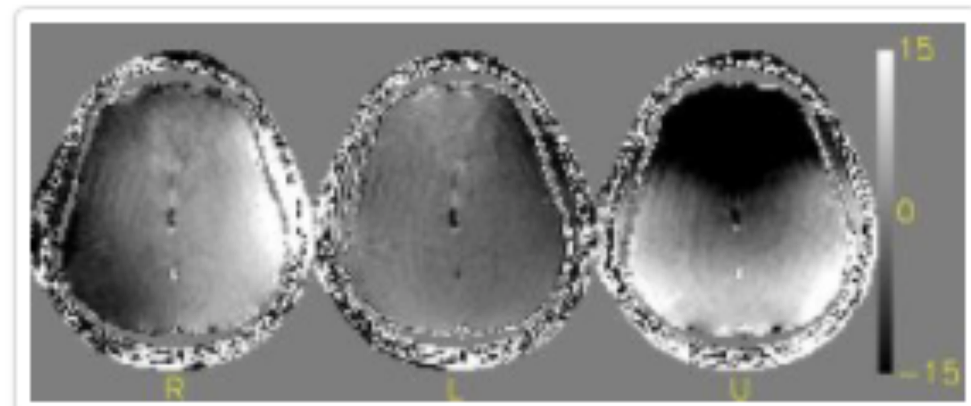


Fig. 2 Changes of field maps in four different positions relative to the field map in the reference position obtained under the "subject shim" setting. The unit of the field maps is Hz.

ISMRM Honolulu

In case you think that was exaggerated

Problematic HCP subject.

Why is that then?

Richard Bowtell

Will field shifts due to head rotation compromise motion correction?

Aleksandra Sulikowska[1], Samuel Wharton[1], Paul M Glover[1], and Penny A Gowland[1]
[1]*Sir Peter Mansfield Magnetic Resonance Centre, University of Nottingham, Nottingham, Nottinghamshire, United Kingdom*

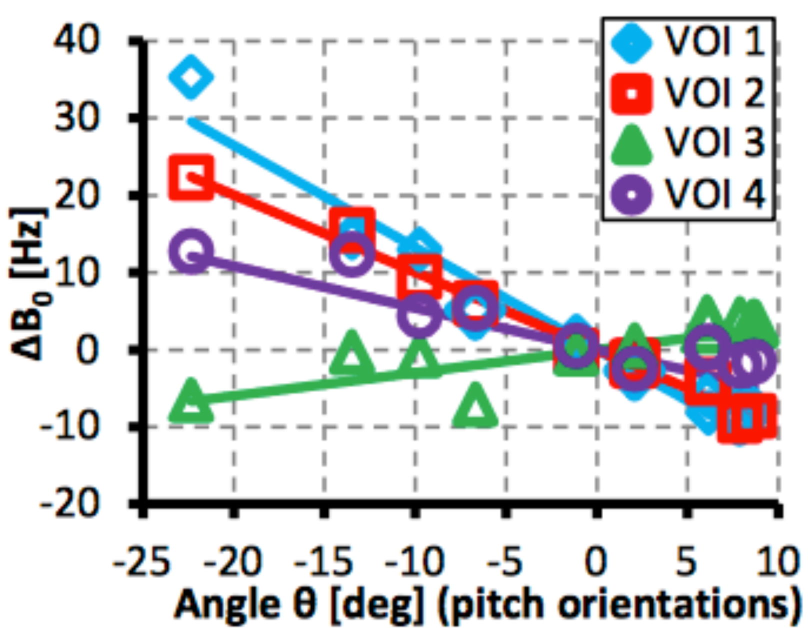


***Fig. 3.** Figure showing mean field shift in the VOIs during **pitch** rotations.*

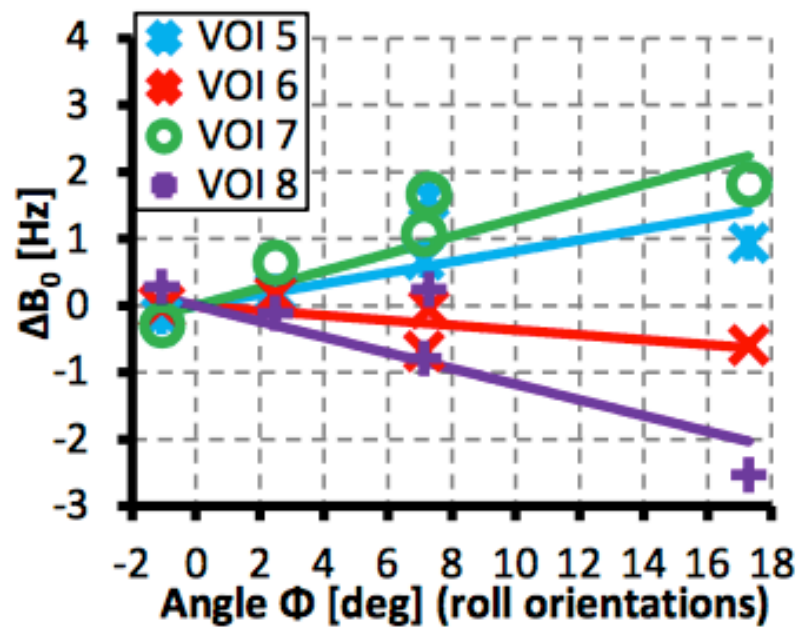


***Fig. 4.** Figure showing mean field shift in the VOIs during **roll** rotations.*

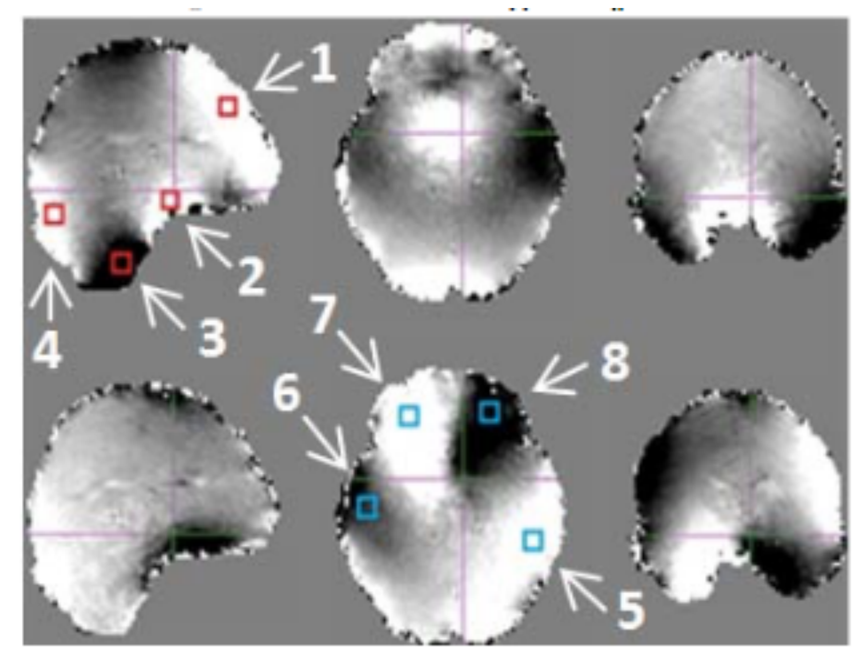
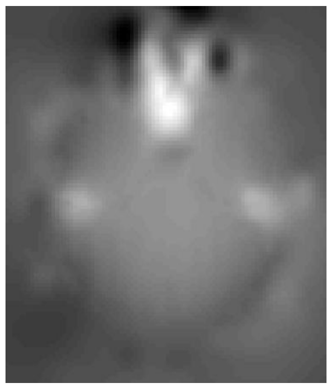
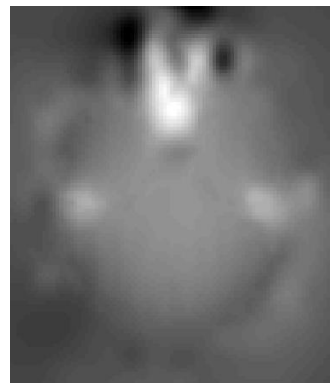
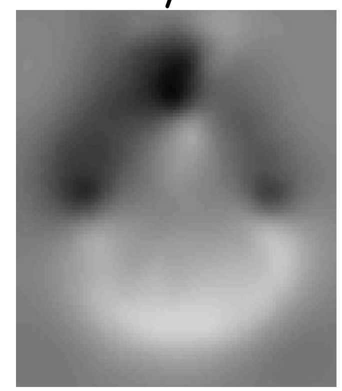
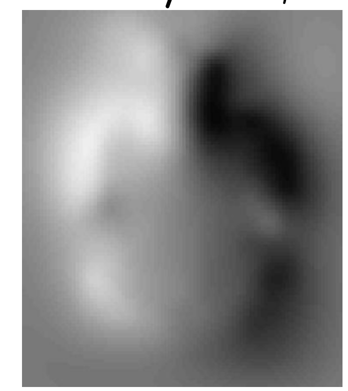
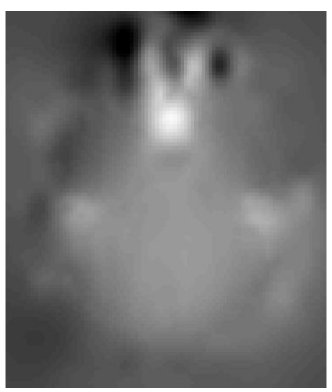
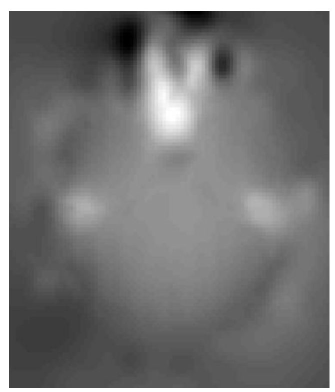
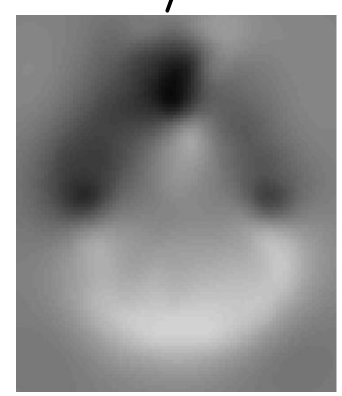
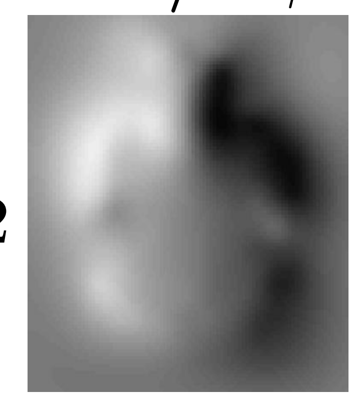


***Fig. 2.** B_0 field difference maps for 2 head orientations, **TOP:** pitch **θ=7.87 deg**, **BOTTOM:** roll **Φ=7.13 deg**. Squares indicate VOIs (**red**: volumes 1-4; **blue**: volumes 5-8). Grey scale= -5 Hz to 5 Hz.*

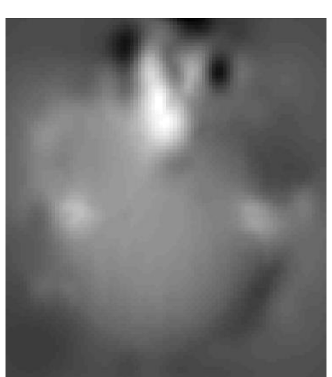
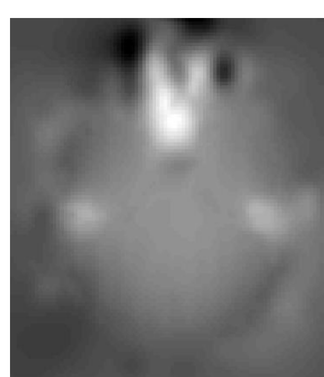
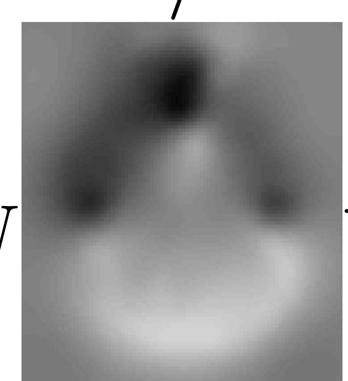
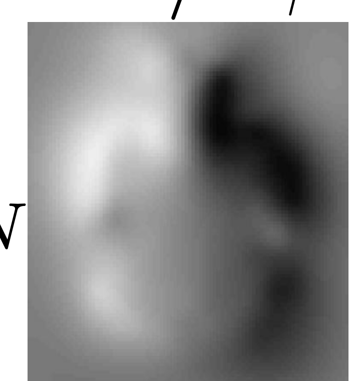
ISMRM Milan

So, maybe we can use a low order Taylor expansion

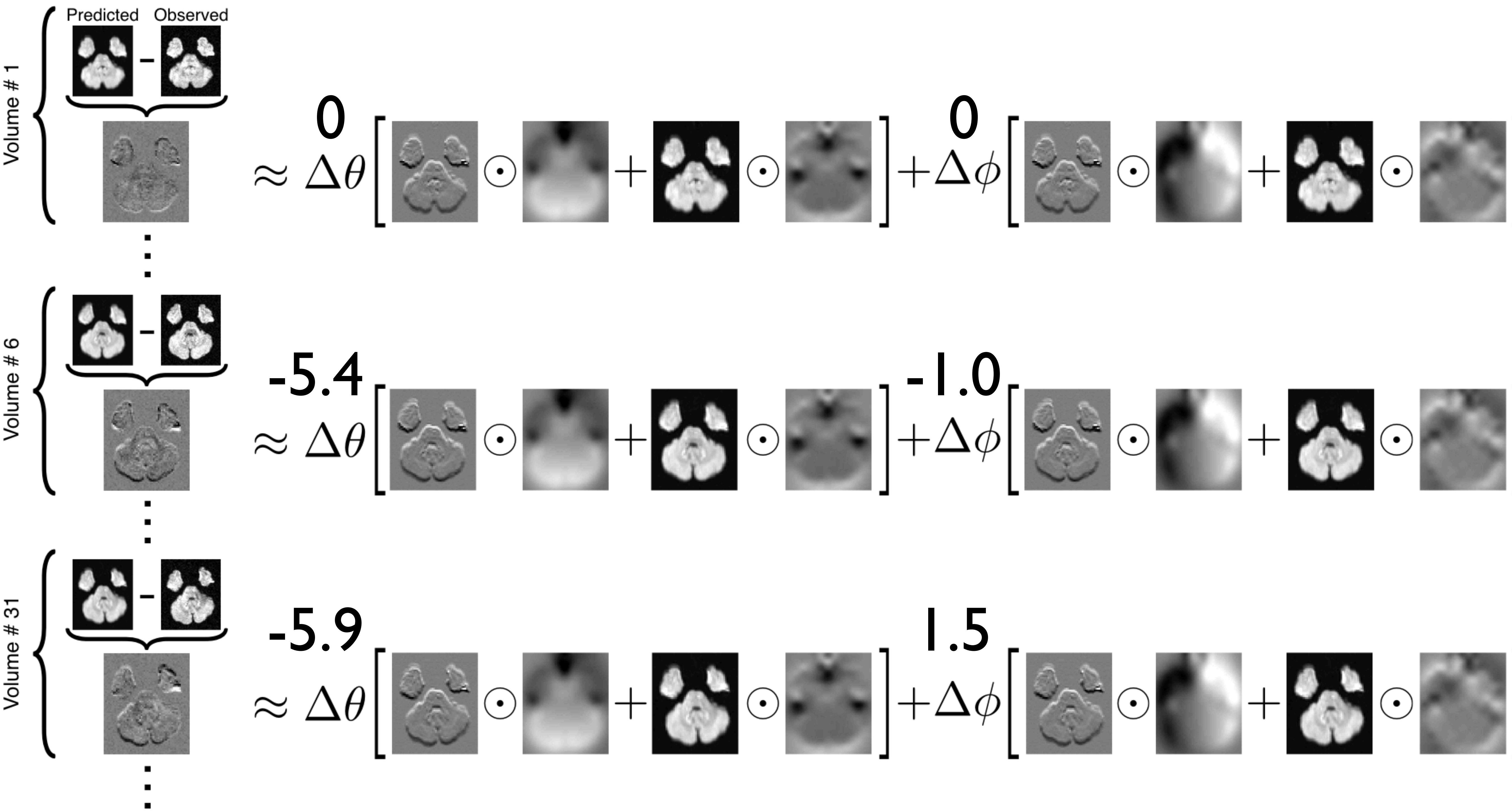
ω_1  $\approx$ ω_0  $+\Delta\theta_1$ $\partial\omega/\partial\theta$  $+\Delta\phi_1$ $\partial\omega/\partial\phi$ 

ω_2  $\approx$ ω_0  $+\Delta\theta_2$ $\partial\omega/\partial\theta$  $+\Delta\phi_2$ $\partial\omega/\partial\phi$ 

$\vdots \quad \vdots \quad \vdots \quad \vdots$

ω_N  $\approx$ ω_0  $+\Delta\theta_N$ $\partial\omega/\partial\theta$  $+\Delta\phi_N$ $\partial\omega/\partial\phi$ 

We need a forward model for the observed changes



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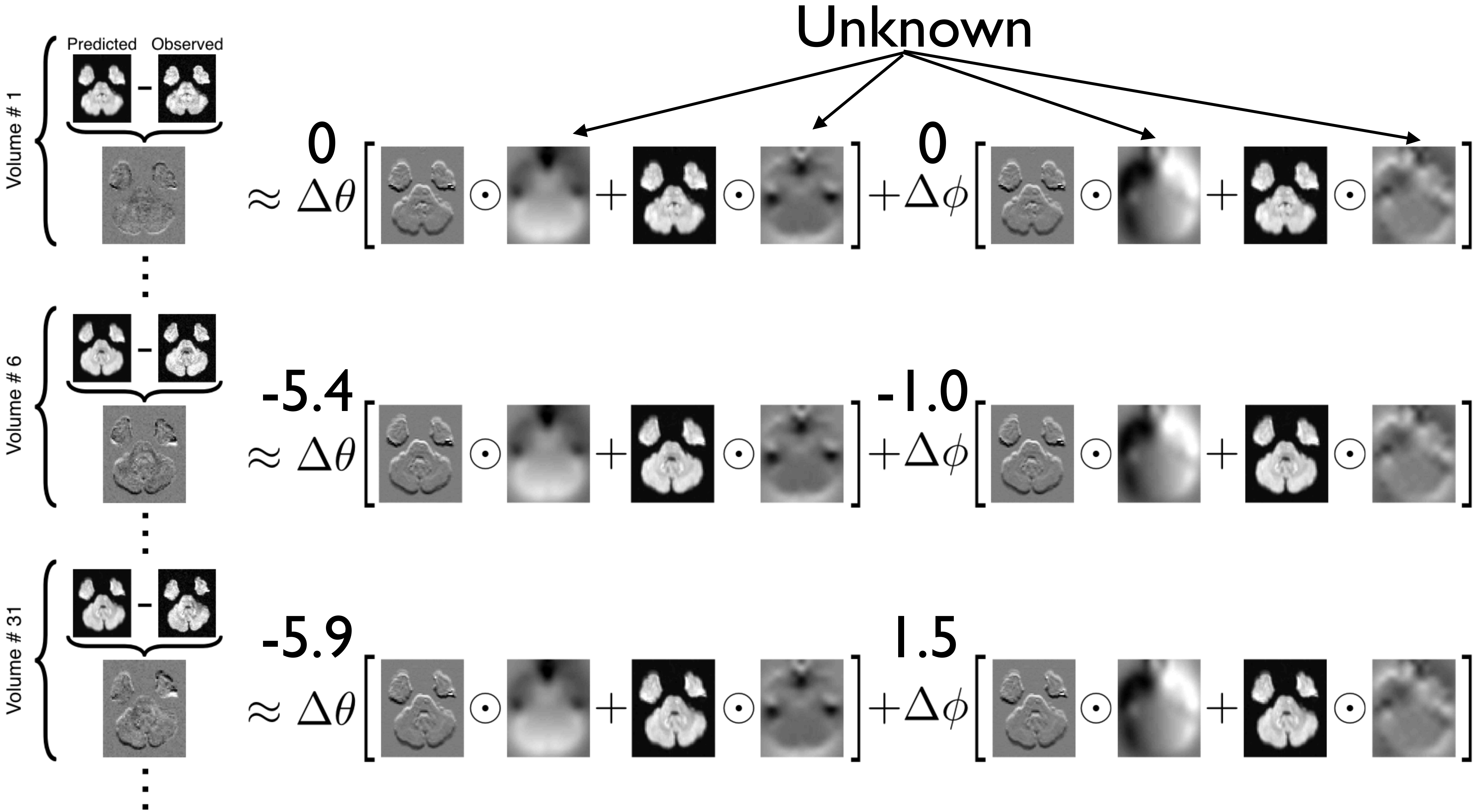
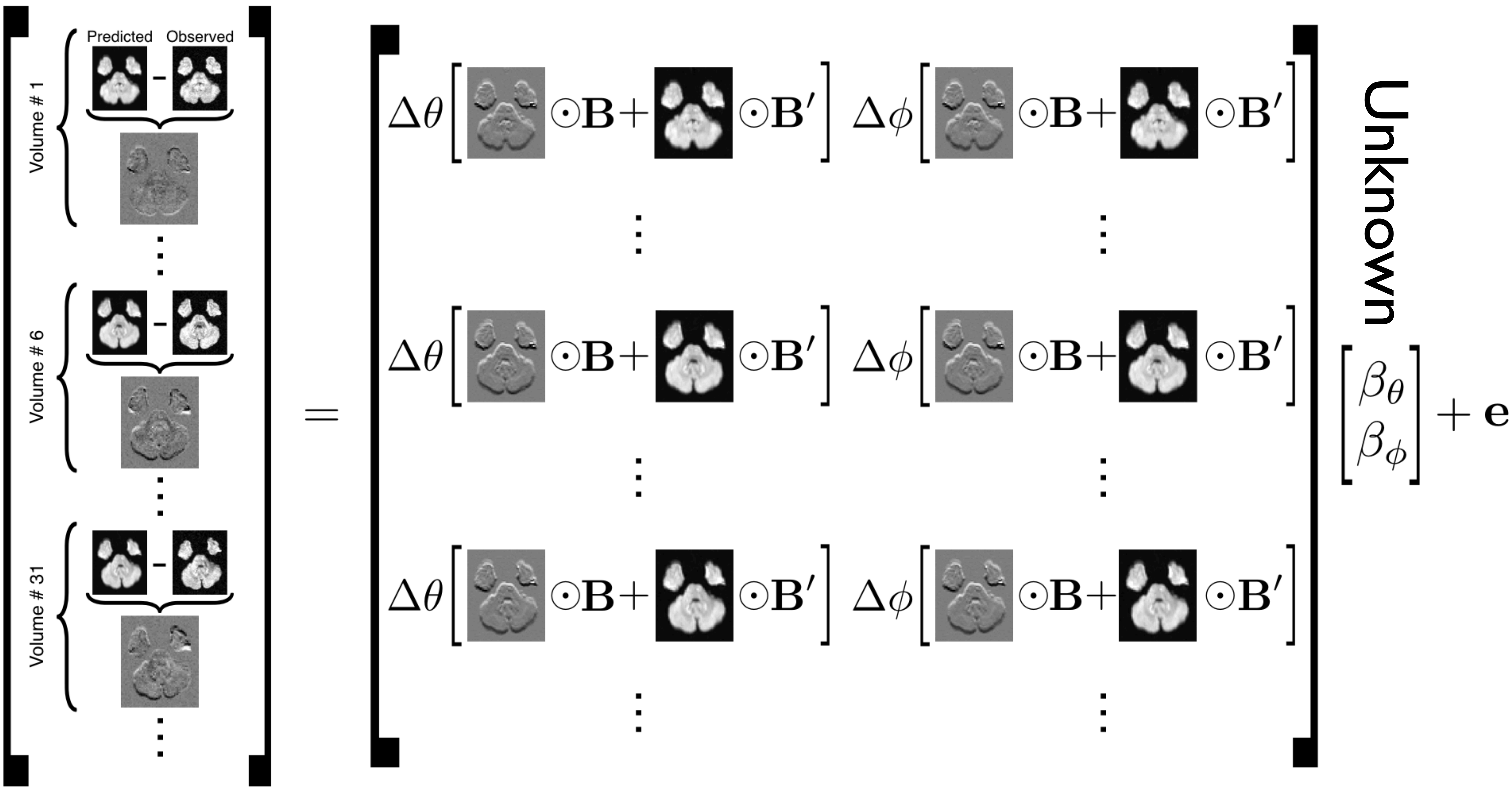


And then to invert that model to find the unknowns



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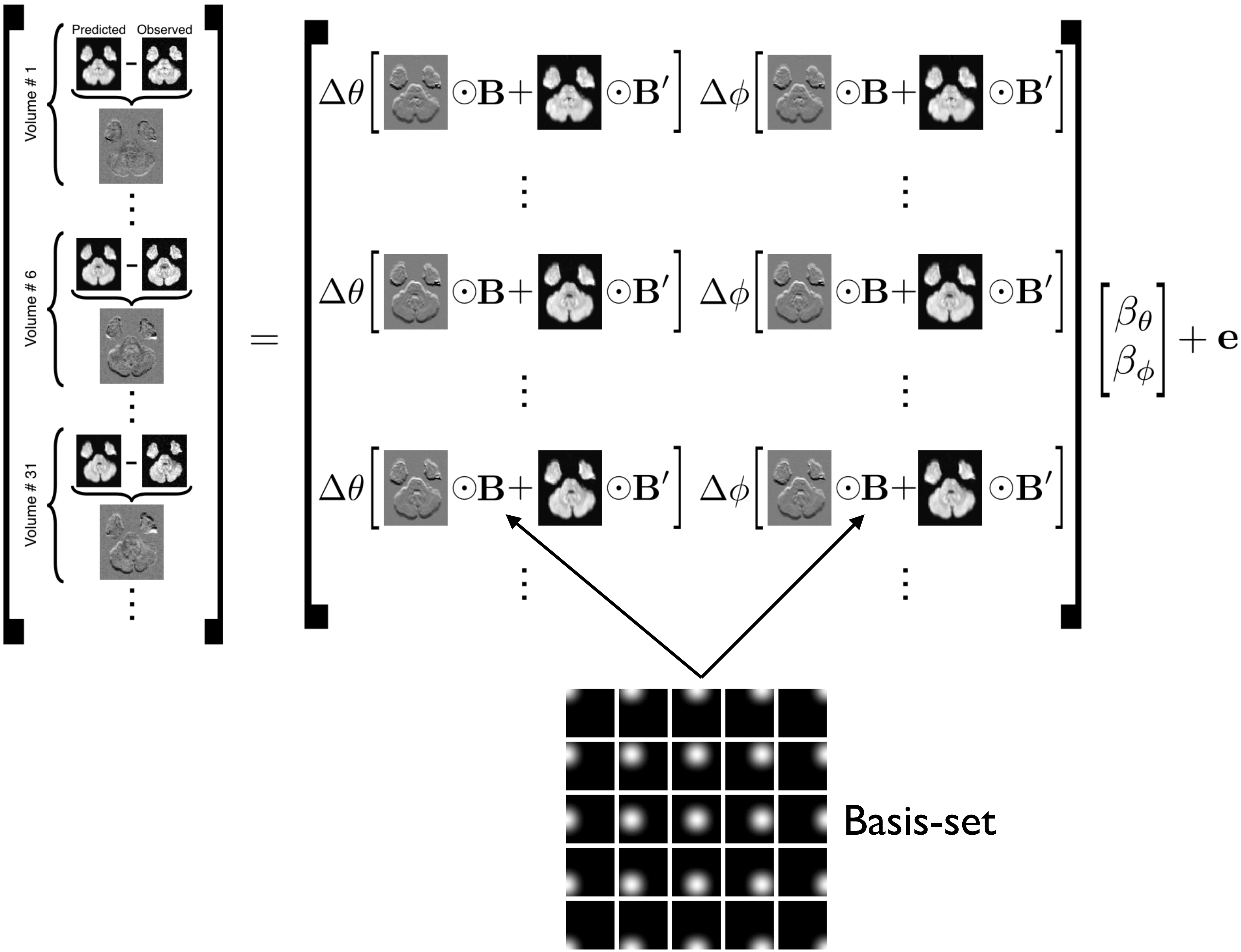

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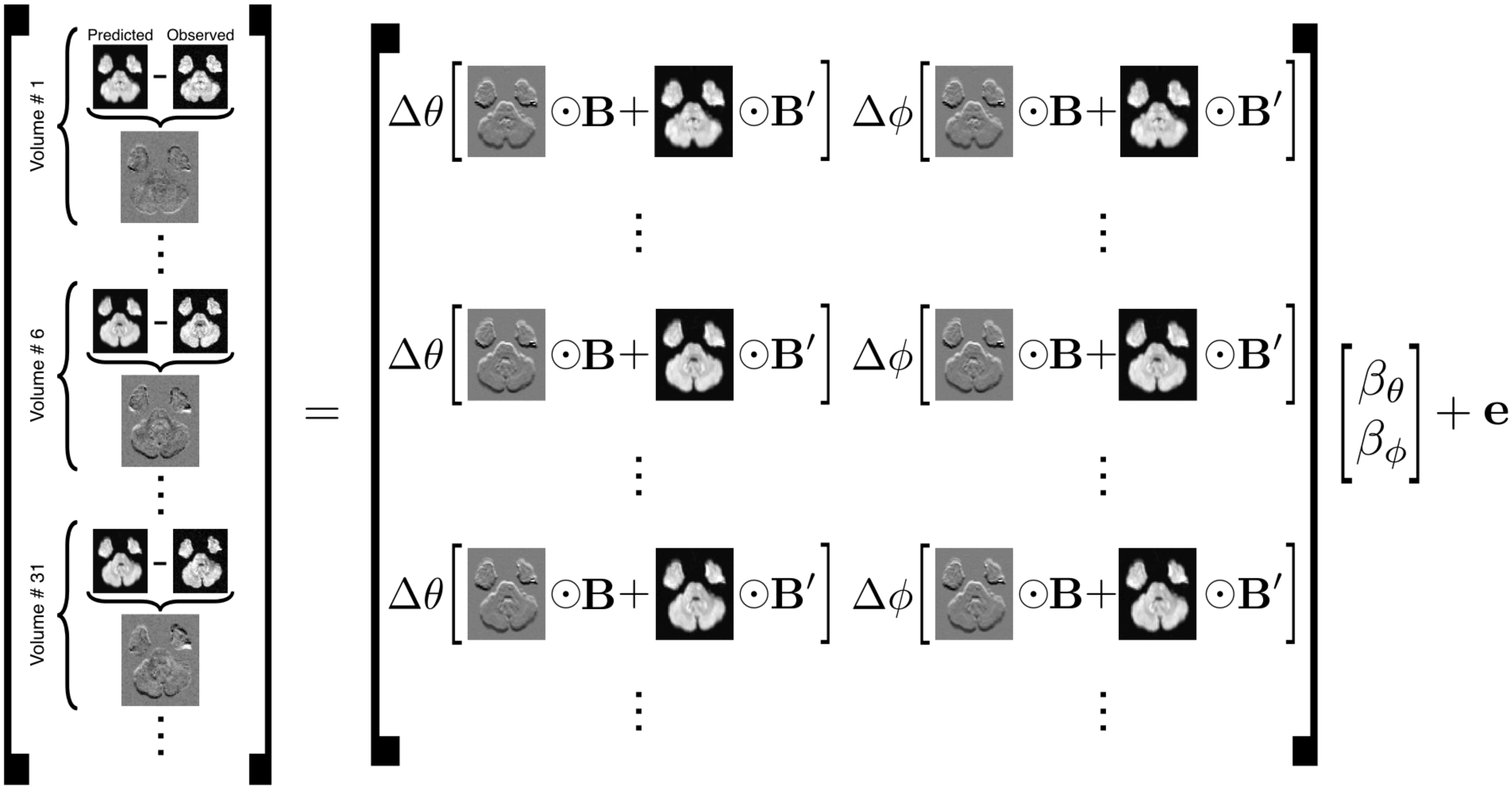
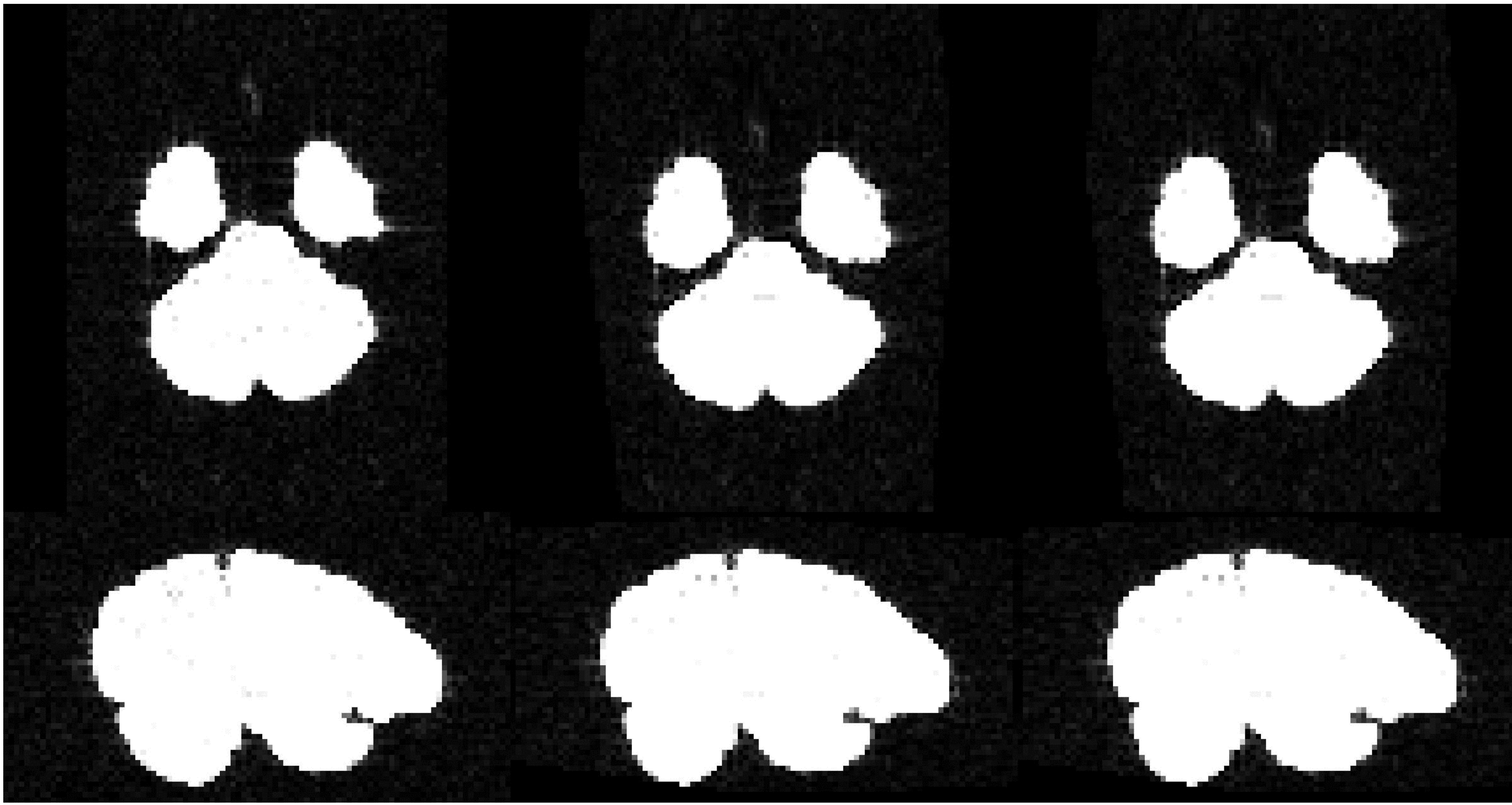


$$\mathbf{y} = \mathbf{X} \mathbf{b} + \mathbf{e}$$

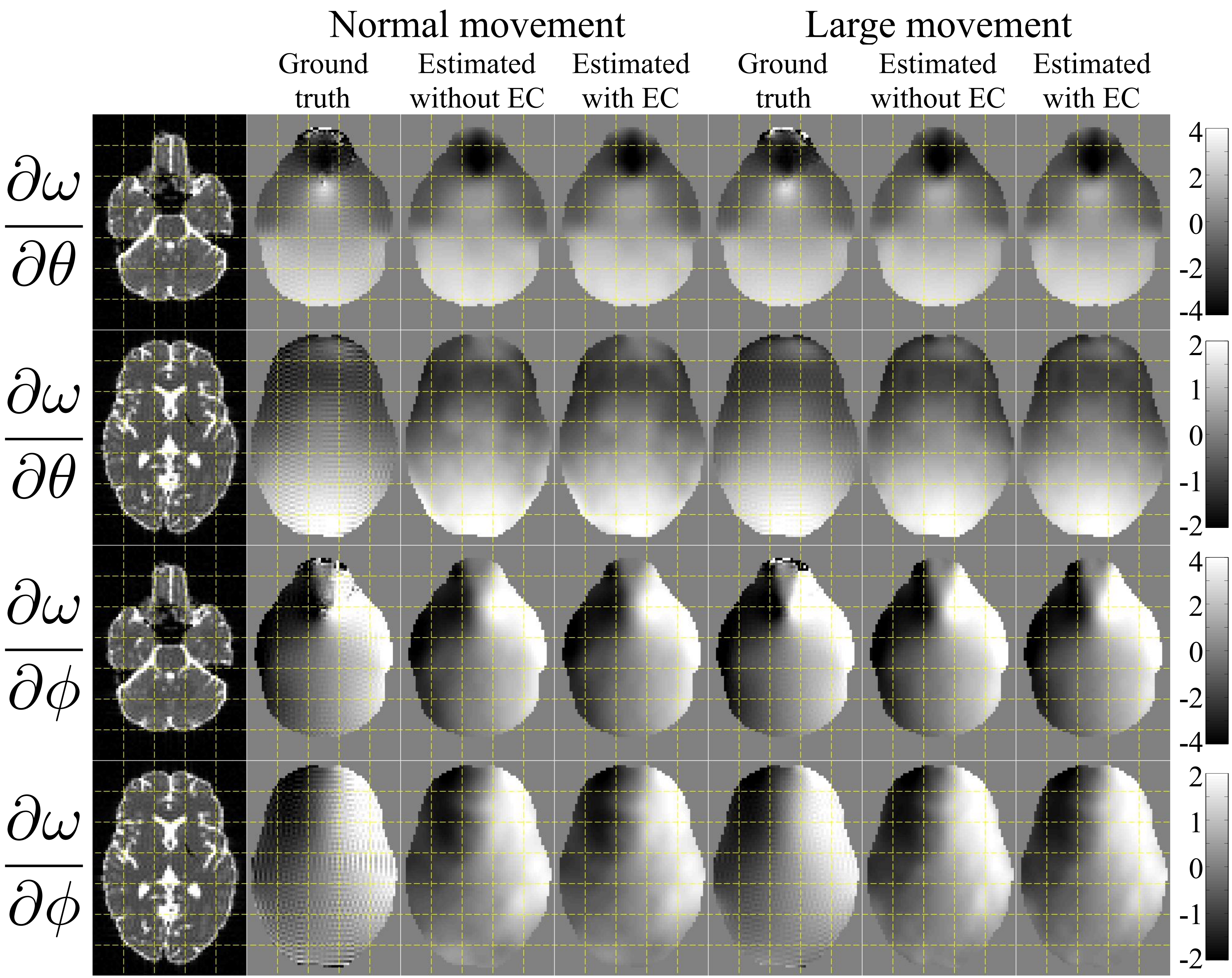
$$\hat{\mathbf{b}}^{(k+1)} = \hat{\mathbf{b}}^{(k)} + \left(\mathbf{X}^T\mathbf{X}\right)^{-1}\mathbf{X}^T\mathbf{y}$$

And now things look a lot better

Before After With Susc-by-move



And this is what the estimated derivative fields look like



And the problematic HCP subject