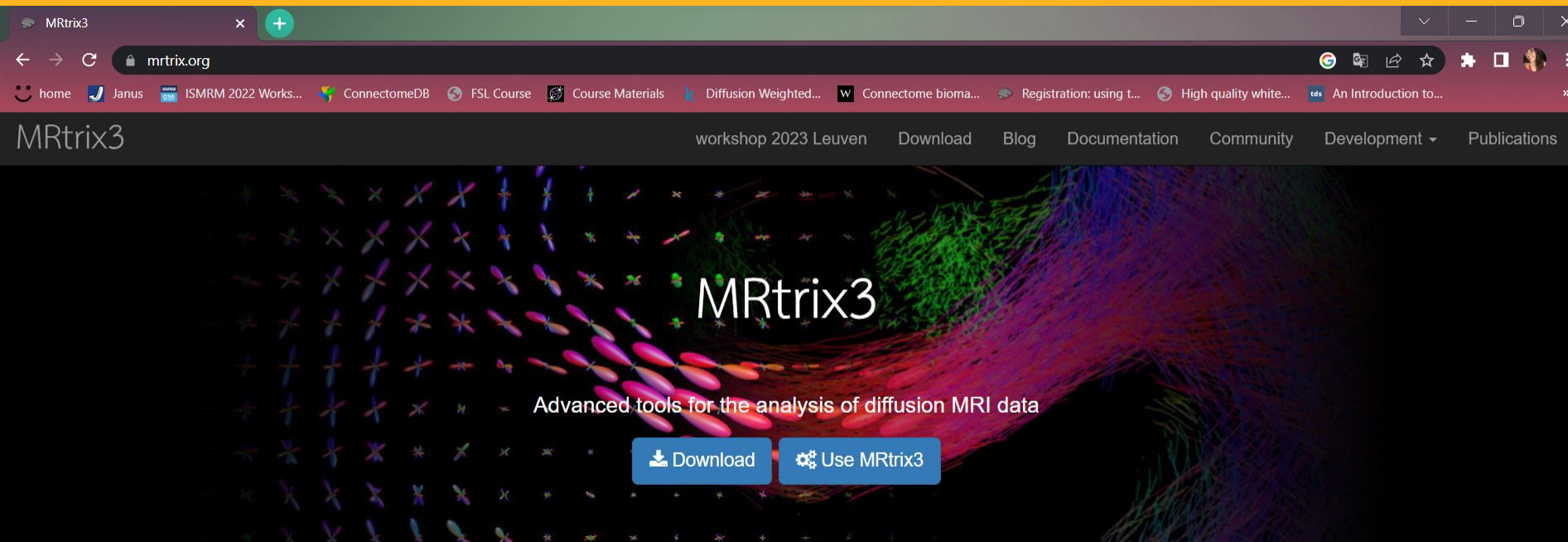


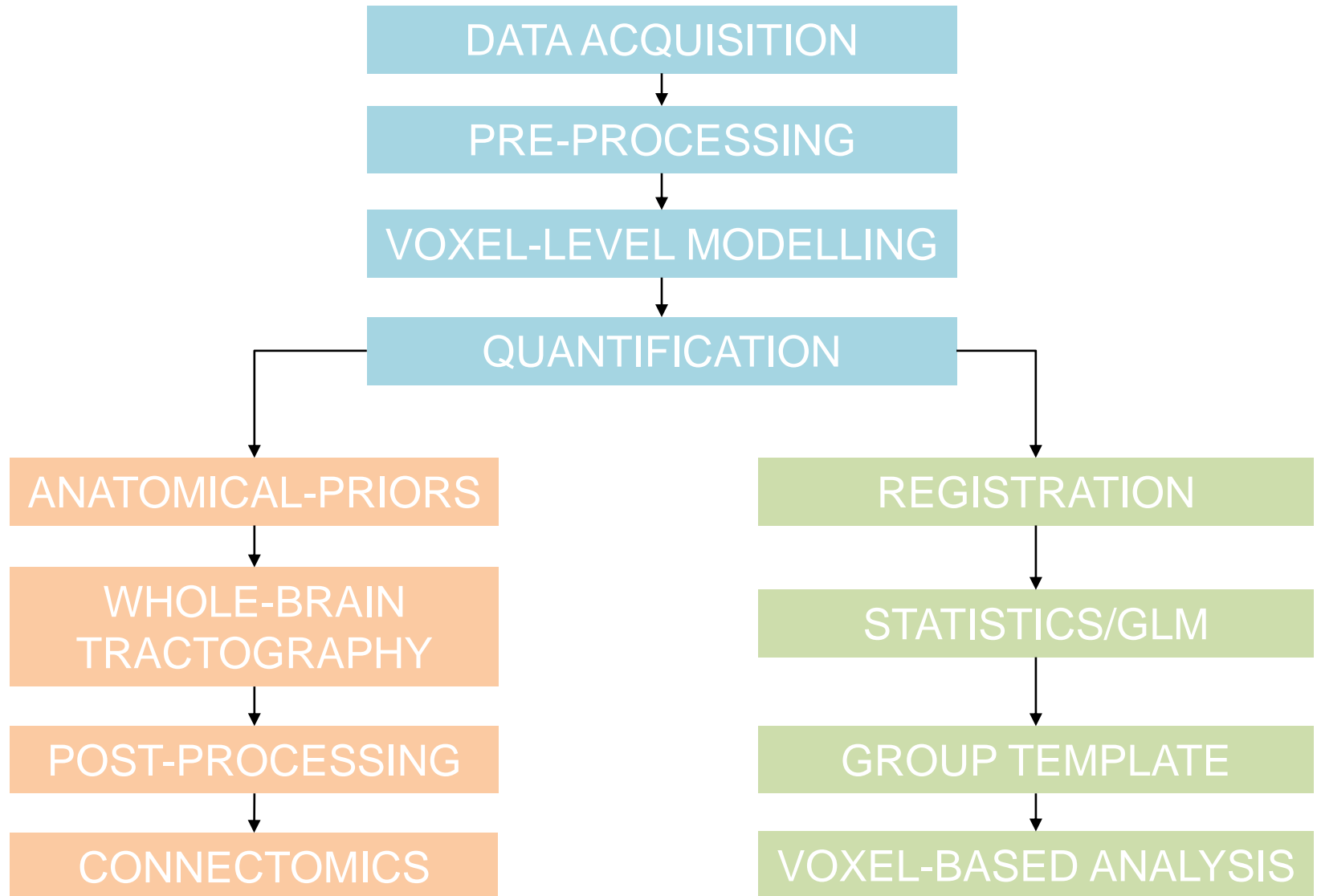
**Hohana G. Konell**

# What is MRtrix3?



MRtrix3 provides a set of tools to perform various types of diffusion MRI analyses, from various forms of tractography through to next-generation group-level analyses. It is designed with consistency, performance, and stability in mind, and is freely available under an open-source license. It is developed and maintained by a team of experts in the field, fostering an active community of users from diverse backgrounds.

# Diffusion analysis



- Tools for image processing, analysis and visualization, with a focus on the analysis of white matter using diffusion-weighted MRI.
- Consistent, well-documented command-line interface
- Consistent handling of data
  - Operations performed in real coordinates where possible
  - handling of multiple image formats
- High performance: C++, multi-threading, OpenGL
- Available on all common modern Operating Systems
- Many commands support the -h or --help option – This displays help page inline
- If in doubt: search online

# How is diffusion MRI data stored?

- A full dMRI data sets consists of – a 4D image – associated DW encoding information
  - Each 3D image is a diffusion weighted image characterized by
    - a diffusion weighting strength or b-value (scalar  $b$ )
    - a diffusion weighting orientation (3D vector  $[x \ y \ z]$ )
- This can be stored in many different ways (.nii, .dcm, .mif)
- Use associated files: bvecs / bvals – MRtrix3 mif/mih: stored in header
  - It's text: you can read it with a text editor

# How is diffusion MRI data stored?

- bvecs / bvals
  - bvals: a single row of b-values, one per volume
  - bvecs: 3 rows of gradient direction coefficients (gradient directions specified relative to image axes)
  - ‘radiological’ storage convention (as per old Analyze format)
    - LHS coordinate system – transform matrix has negative determinant
  - not ‘radiological’ (default in NIfTI is neurological...):
    - need to invert x-component (first row)

# Image handling in MRtrix3

- All image handling is handled by the MRtrix library – All commands can handle data the same way
- Provides a way to access the data in many different formats:
  - DICOM (single- or multi-frame)
  - NIfTI (versions 1 & 2)
  - MGH / MGZ (FreeSurfer)
  - mif / mih (MRtrix3)
  - ...
- But not all data formats are equivalent!

# Basic and useful commands

mrinfo: querying the image header

- Display relevant header information (dimensions, voxel size, data type, image transform, strides (order of storage), DW encoding, etc.)

mrconvert: convert images

- Allows to: convert between formats, convert between data types, change strides, extract ROI or subset of volumes, reduce dimensionality of image, manipulate header entries.

mrstats: get summary statistics

- Get mean, median, min, max, ... intensity per volume and be supplied with a mask to get statistics within ROI



# Basic and useful commands

mrconcat: concatenate images

- stitch images together along specified axis, create multi-volume image from individual 3D images

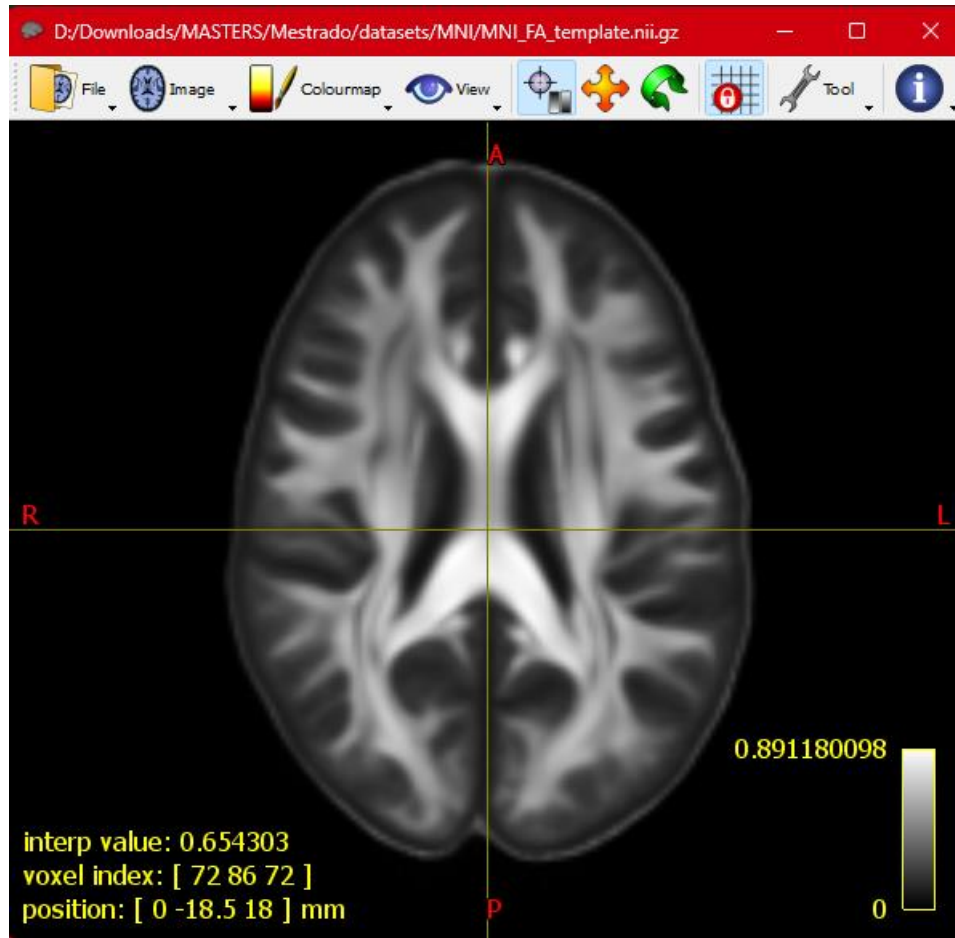
mrcalc: voxel-wise calculations

- Uses a stack-based syntax: operands (images or values) pushed onto stack, operations consume operands and push their result onto stack
- For details, consult help page and/or "introduction to mrcalc" document

mrmath: mean, median, sum, ...

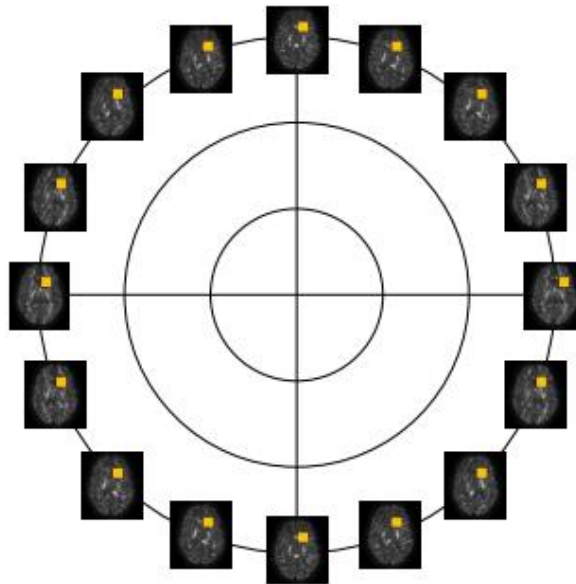
- compute summary statistics: along image axis (e.g. along volumes) and across images

# MRView: the MRtrix3 viewer



- MRView handles all display operations in scanner coordinates
  - bottom left corner shows: voxel intensity, voxel index, position in real space
- Camera view is by default locked to the image axes
  - view can change when switching between images - use 'grid lock' button to toggle

# Diffusion signal



symmetric function on the sphere:

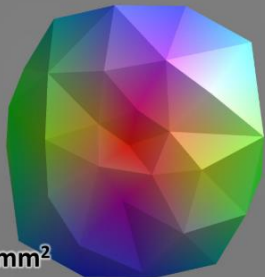


radius  $\sim$  dMRI signal  
in corresponding  
direction

```
$ mrview T1.mif -odf.load_dixel dwi.mif
```



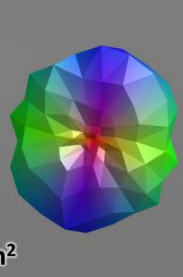
$b = 700 \text{ s/mm}^2$



$b = 1200 \text{ s/mm}^2$



$b = 2800 \text{ s/mm}^2$



# Importing your data

```
$ mrconvert data.nii.gz dwi.mif -fslgrad bvecs.bvec bvals.bval -datatype float32 -  
strides 0,0,0,1
```

```
$ mrinfo dwi.mif
```

# The “standard” preprocessing pipeline

1. DENOISING

2. GIBBS RINGING

3. MOTION AND  
DISTORTION

4. BIAS FIELD

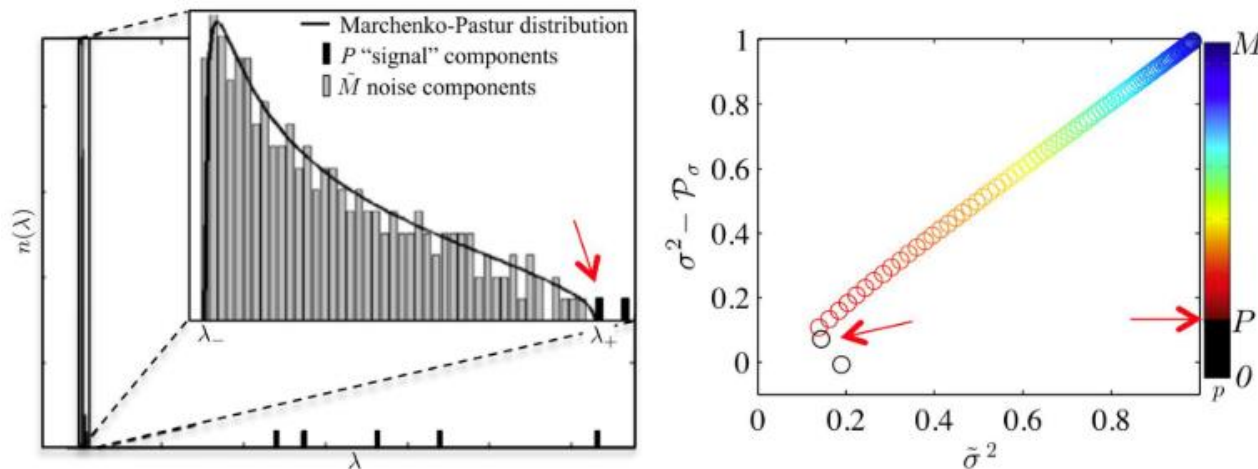
5. BRAIN MASKING

Always check intermediate outputs !!

# 1. Denoising

- Main command: `dwidenoise`

*J. Veraart, et al. / NeuroImage 142 (2016) 394–406*



```
$ dwi2mask dwi.mif - | maskfilter - dilate preproc_mask.mif -  
npass 5
```

```
$ dwidenoise dwi.mif denoise.mif -noise noiselevel.mif -  
mask preproc_mask.mif
```

## 2. Gibbs ringing correction

- Main command: mrdegibbs

Kellner et al., MRM, 2016

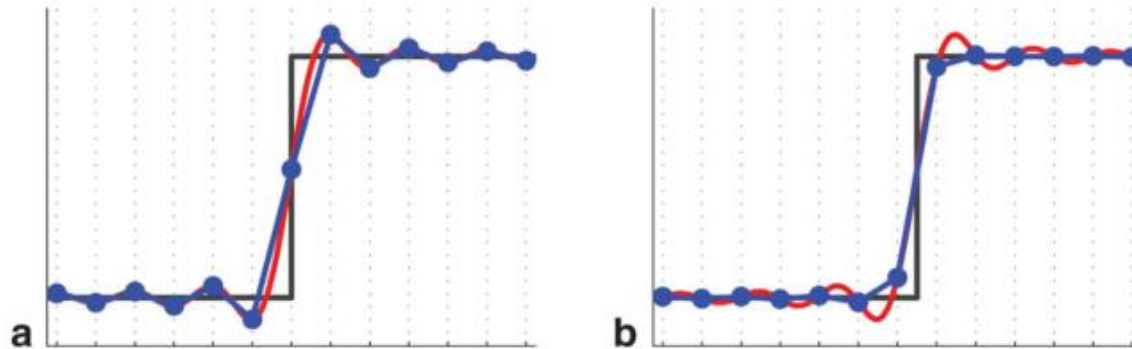


FIG. 1. An image with a single discontinuity (black edge) is reconstructed from truncated k-space data. The resulting image (blue dots) is discrete and exhibits ringing artifacts. The amplitude of the ringing depends on whether the underlying sinc pattern arising from the windowing in k-space (red curve) is sampled at its extrema (a), or at the zero-crossings (b).

\$ mrdegibbs denoise.mif degibbs.mif

# 3. Motion & distortion correction

- Main command: dwifslpreproc

Geometry correction for 3 sources of EPI artefacts:

- Subject motion (rigid translation / rotation in between image volumes)
- Eddy-current induced distortion (low-frequency distortion along phase encoding direction)
- Magnetic field susceptibility induced distortion (distortions along phase encoding direction; strongest at tissue interfaces)

```
$ dwifslpreproc -rpe_none -pe_dir AP degibbs.mif  
geomcorr.mif
```



## 4. B1 bias field correction

- Main command: dwibiascorrect
  - B1 modulation causes intensity modulation
    - Multiplicative bias field
    - Blurring the frequency content
  - Not usually considered an issue in dMRI, since “traditional” DWI analyses normalize to  $b=0$
  - Correction strategy: – FSL fast based on brain segmentation – ANTs N4 (no priors) fits smooth bias field that maximizes frequency content

```
$ dwibiascorrect fsl geomcorr.mif biascorr.mif -bias  
biasfield.mif
```

# 5. Brain masking

- Main command: dwi2mask
  - Brain mask speeds up subsequent analysis
  - MRtrix includes heuristic segmentation script dwi2mask
  - FSL bet can also be useful

```
$ dwi2mask dwi.mif mask.mif
```

# Aligning T1w to DWI

- Multi-modal registration, e.g., using mutual information
- Use FSL flirt

```
$ dwiextract dwi.mif -bzero - | mrmath -axis 3 - mean b0.nii
```

```
$ flirt -dof 6 -cost normmi -in raw/T1w -ref b0 -omat T_fsl.txt
```

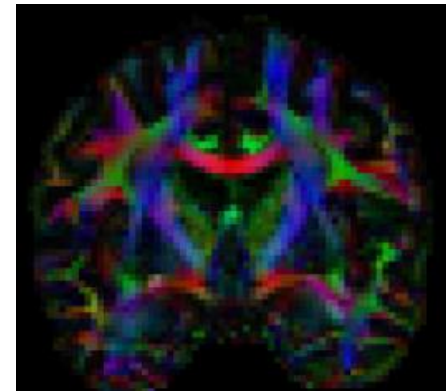
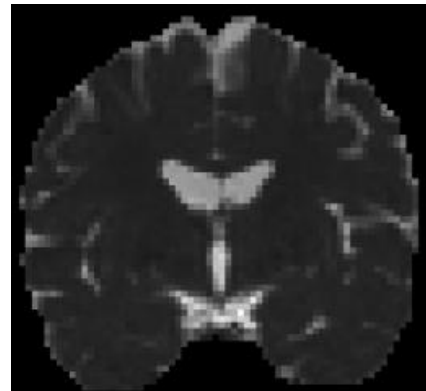
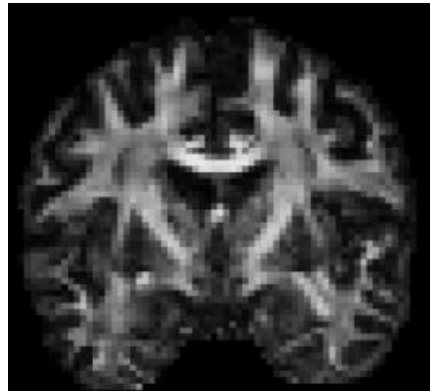
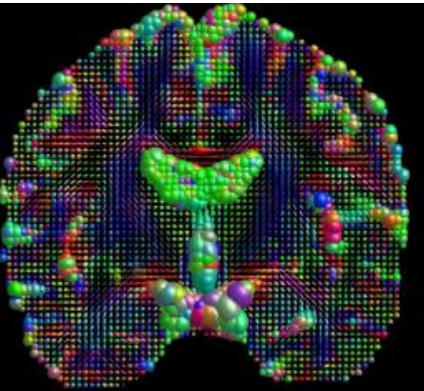
```
$ transformconvert T_fsl.txt raw/T1w.nii.gz b0.nii flirt_import  
T_T1toDWI.txt
```

```
$ mrtransform -linear T_T1toDWI.txt raw/T1w.nii.gz  
T1w.nii.gz
```

# Voxel level modelling

## Diffusion-Weighted Image:

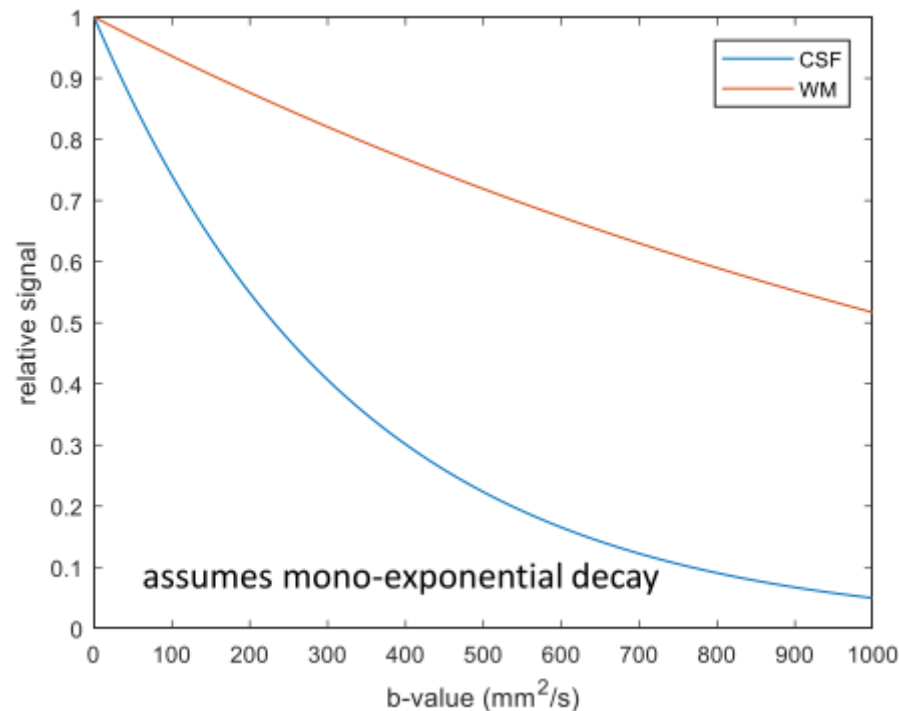
- Contrast is affected by a combination of different factors
  - some intrinsic to the tissue
  - some dependent on the experimental settings
  - measurement by itself only qualitative/relative (not absolute)
- Aim of voxel-level modelling:
  - Extract quantitative (reproducible) metrics about diffusion/tissue from a series of diffusion-weighted images with different experimental settings.



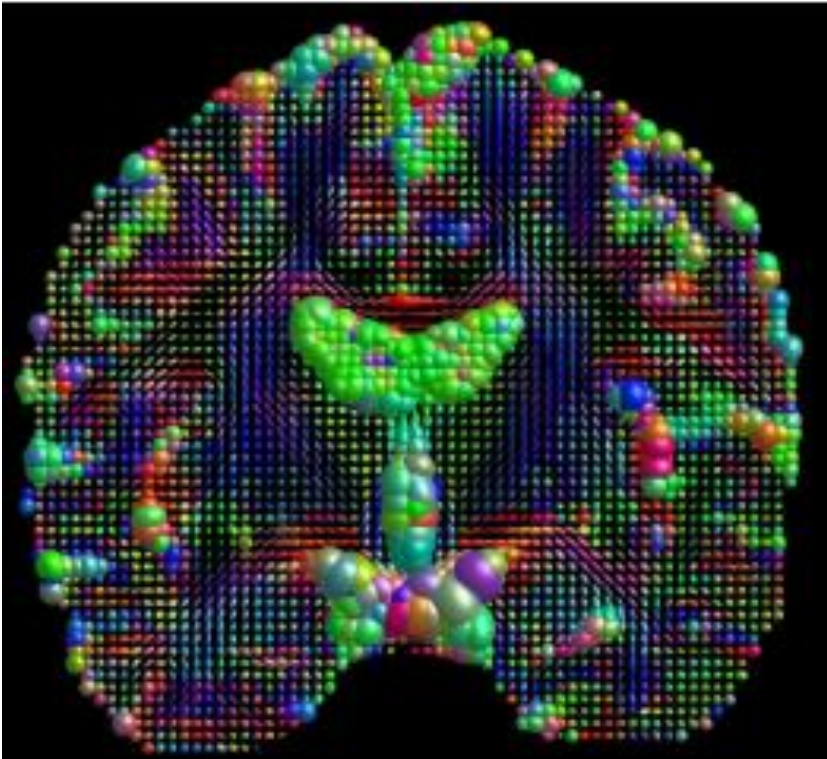
# Apparent diffusion coefficient (ADC)

- If water molecules encounter hindrances along their random walk, their mean squared displacement per unit time (apparent diffusion coefficient) will be lower than when observed in 'free' water.

$$S(b) = S_0 e^{-bD}$$



# Diffusion tensor imaging



diffusion tensor represented as an 'ellipsoid' (isoprobability surface of diffusion PDF)



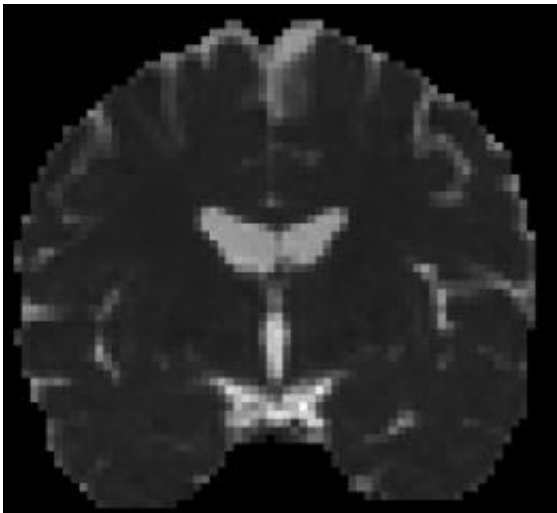
```
$ dwi2tensor -mask mask.mif dwi.mif tensor.mif
```

# Diffusion metrics



fractional anisotropy (FA)

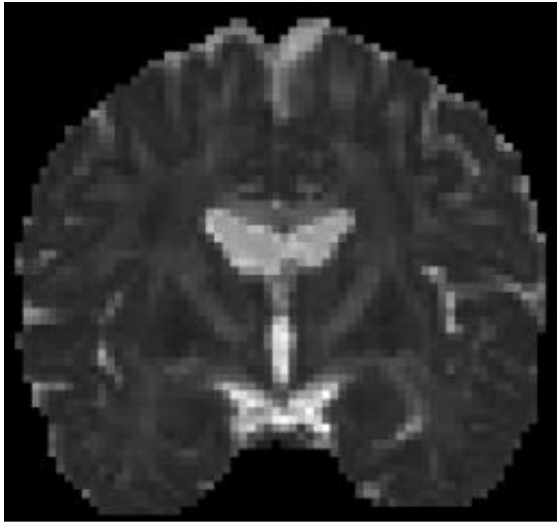
```
$tensor2metric tensor.mif -fa fa.mif
```



apparent diffusion coefficient (ADC)  
mean diffusivity (MD)

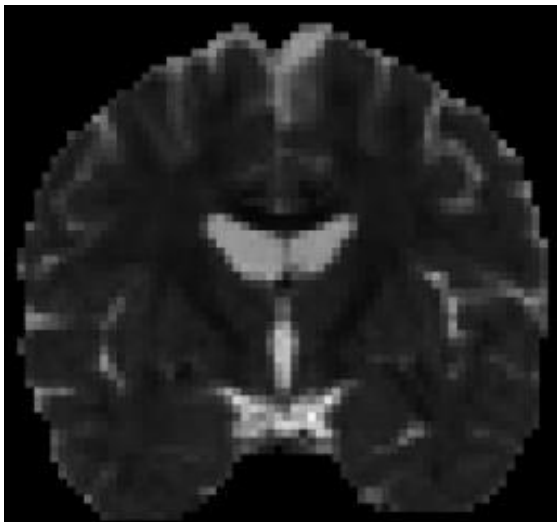
```
$tensor2metric tensor.mif -adc md.mif
```

# Diffusion metrics



axial diffusivity (AD)

```
$tensor2metric tensor.mif -ad ad.mif
```

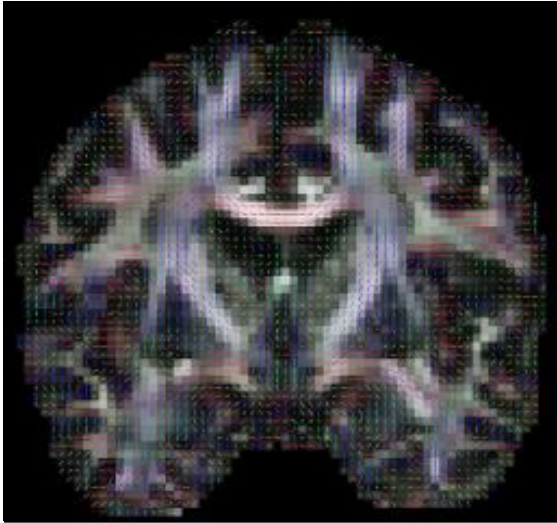


radial diffusivity (RD)

```
$tensor2metric tensor.mif -rd rd.mif
```

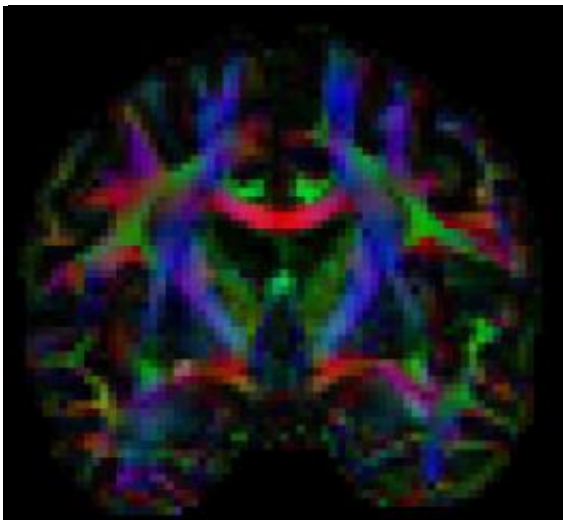


# Diffusion metrics



principal diffusion vector (PDV)

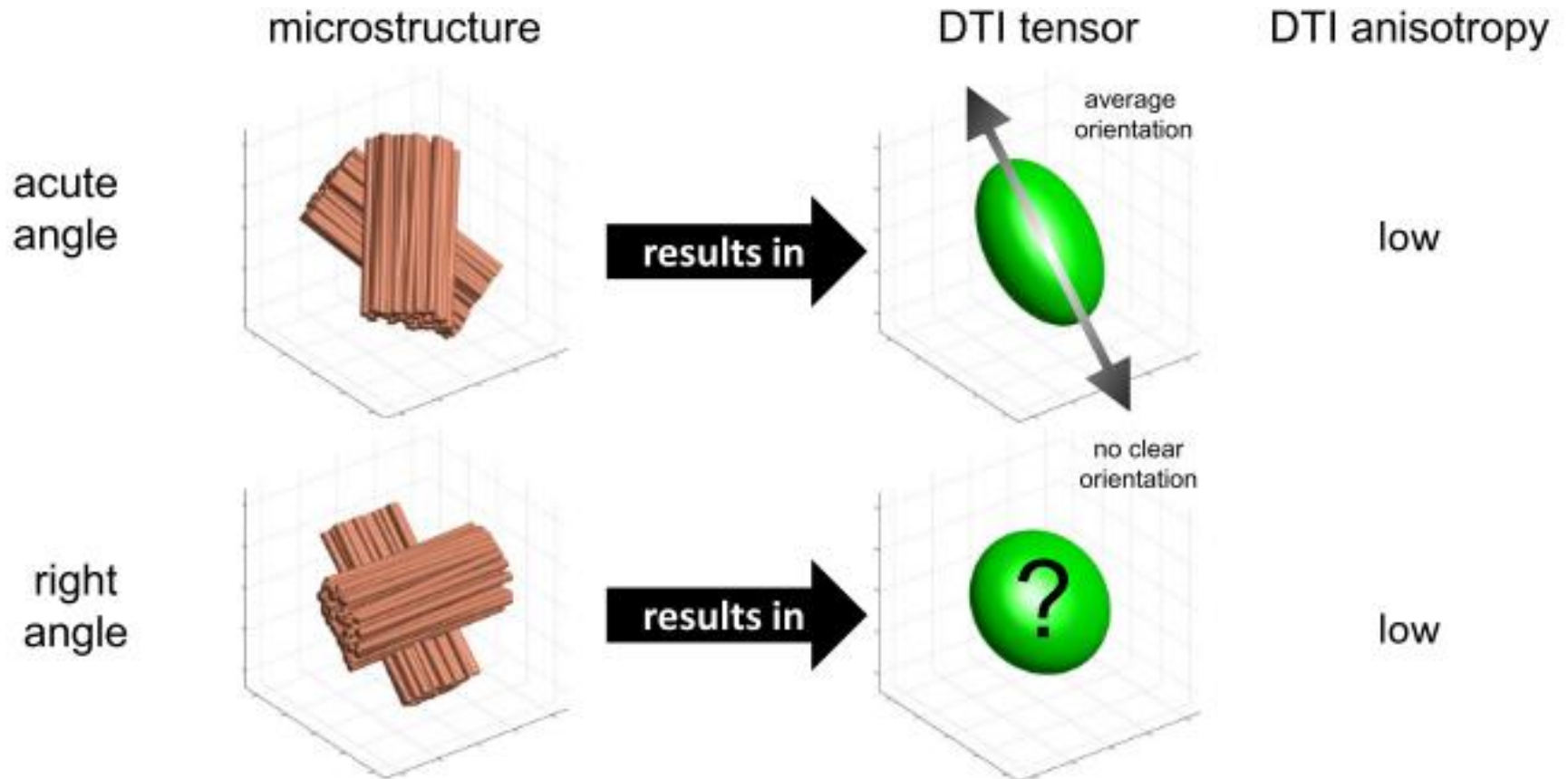
```
$tensor2metric dt.mif -vector dt_ev.mif
```



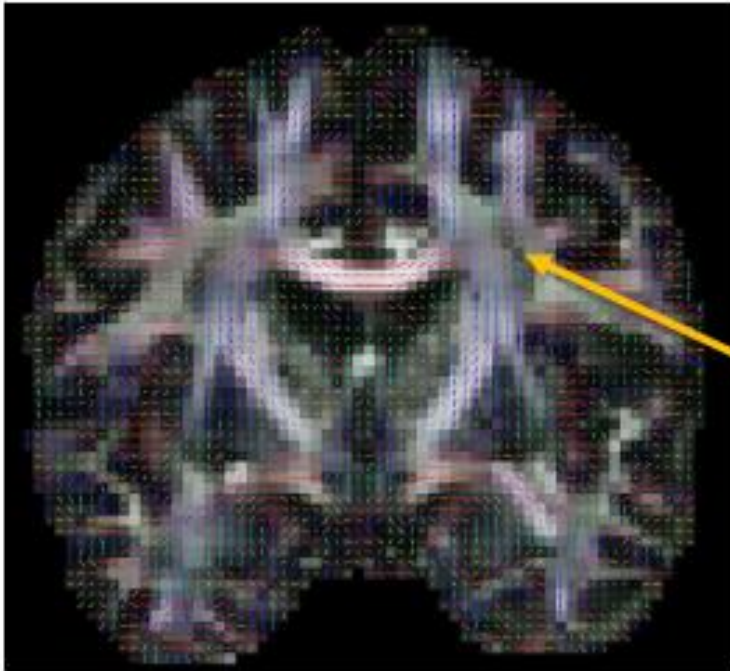
directionally encoded color (DEC) FA

```
$tensor2metric dt.mif -vector dt_ev.mif
```

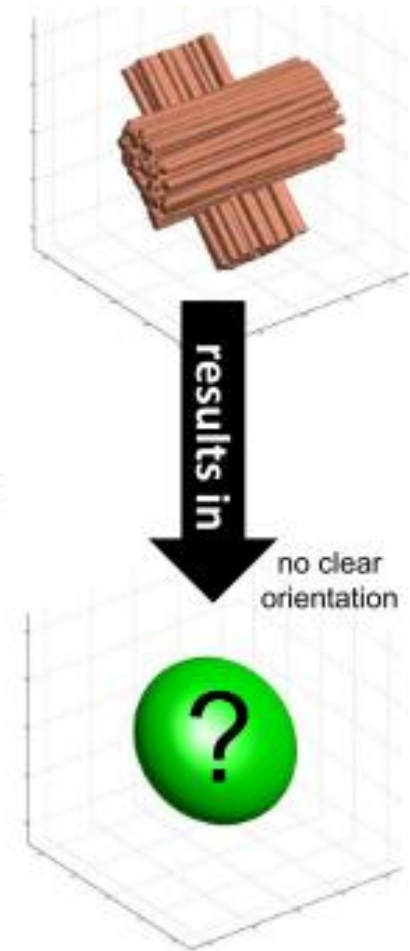
# Crossing fiber problem



# Crossing fiber problem



Causes drop in FA



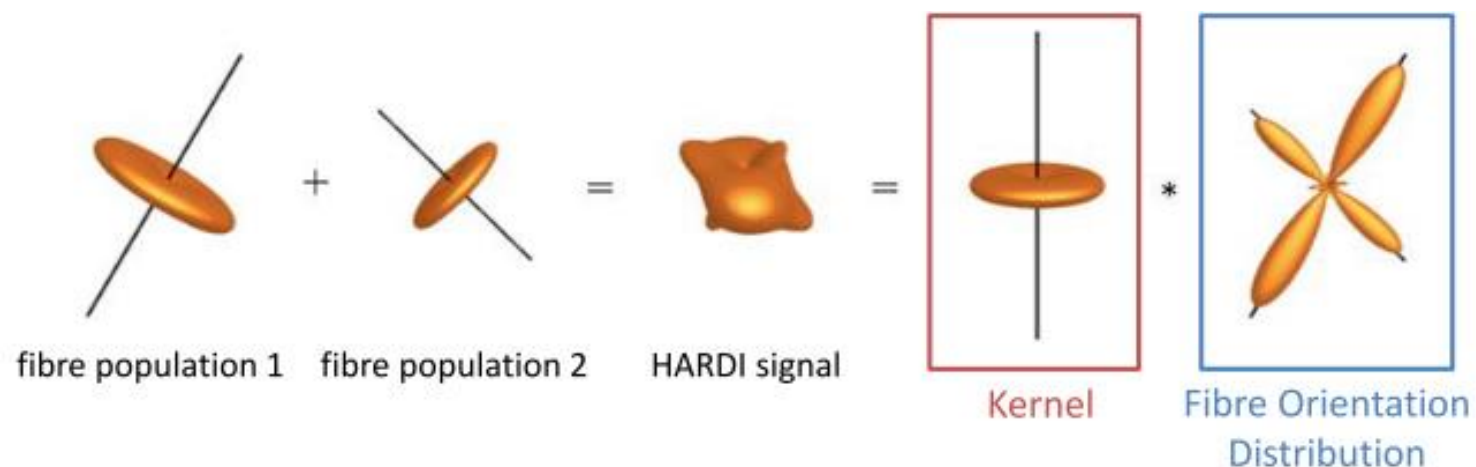
# How can we model crossing fibers?

Let's build a forward model first:

- Assume that WM fibers along a single axis have a fixed and equal contribution to the dMRI signal (response function or kernel)
- Assume no exchange between fiber compartments, such that the signal is the sum of the kernels of all fiber populations

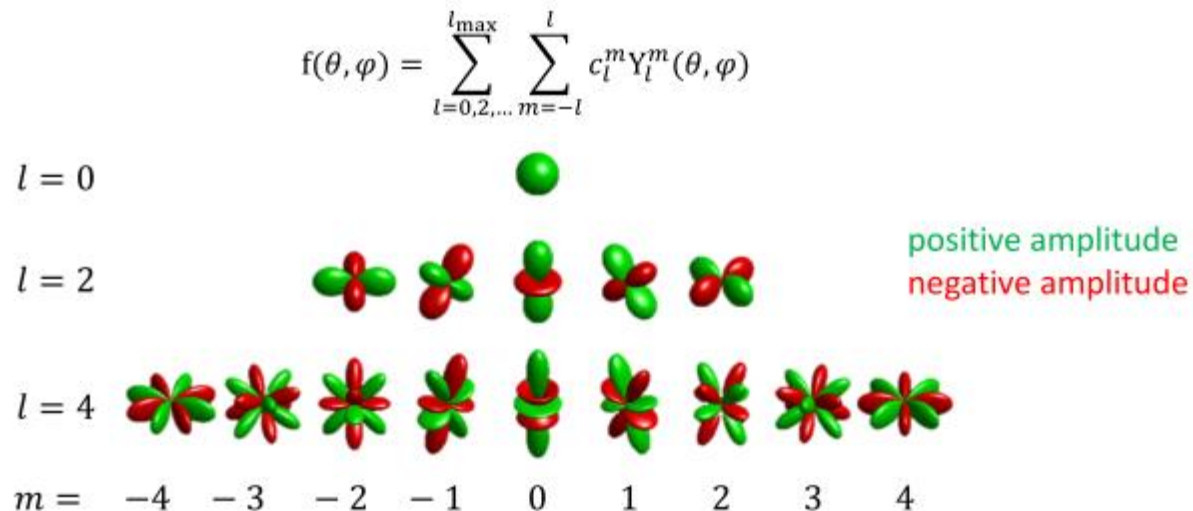
General form: 'infinite sum' of the response == spherical convolution

Goal: solving the inverse problem == spherical deconvolution



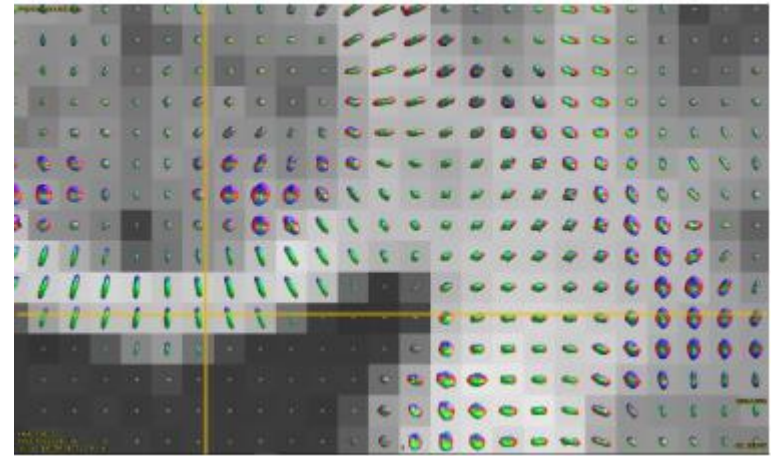
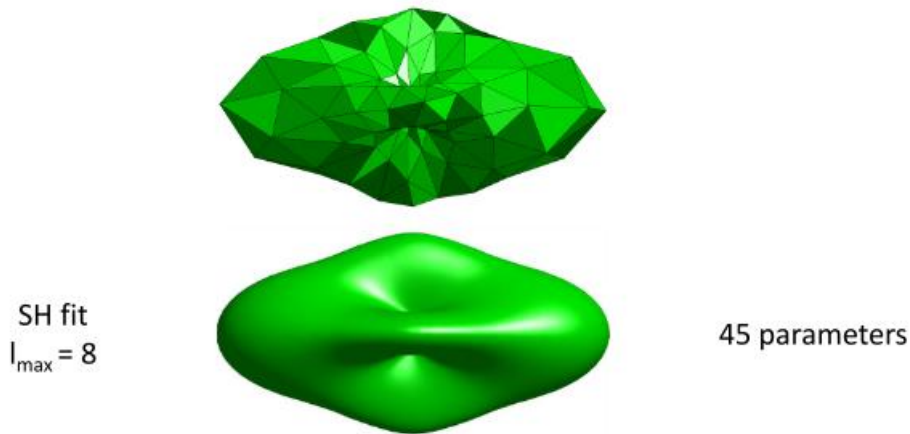
# Spherical harmonics

- Efficient representation for signals on the sphere (single-shell HARDI)
- Represent symmetric signal as linear combination of SH basis functions
- Efficient expression of spherical convolution as multiplication of corresponding SH coefficients !
- Symmetric functions on the sphere can be represented as a linear combination of symmetric spherical harmonics (SH) basis functions:



# Spherical harmonics

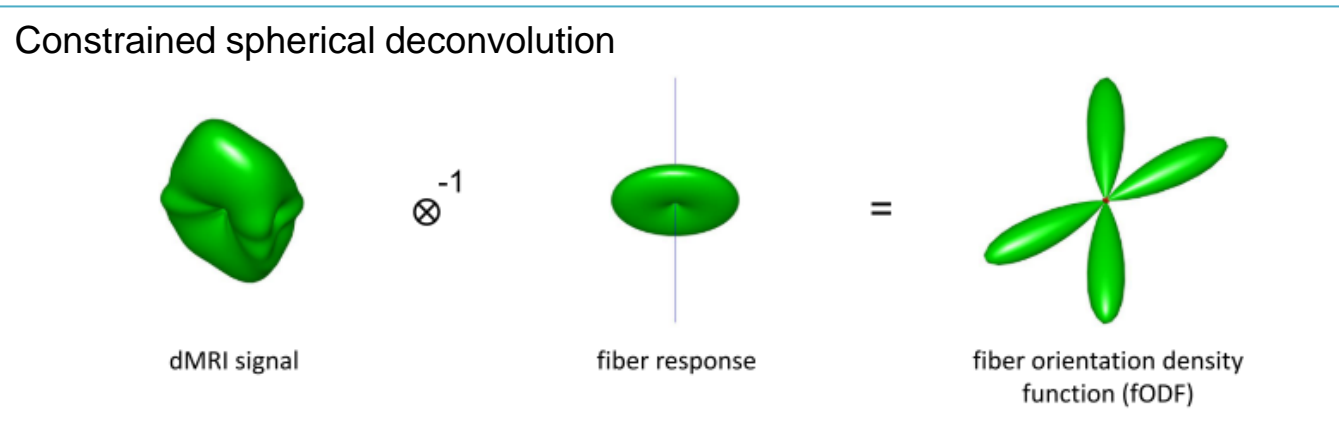
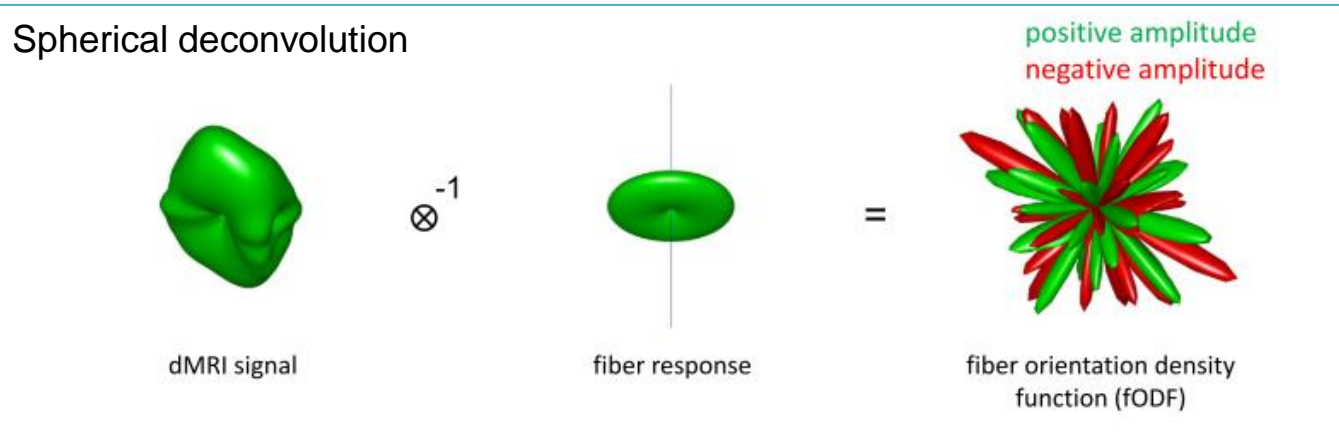
Single-shell dMRI signal represented by truncated series of SH basis functions:



```
$amp2sh dwi.mif sh.mif    (one b value)  
$amp2sh dwi.mif -shell 3000 sh_3000.mif  (multiple b values)
```

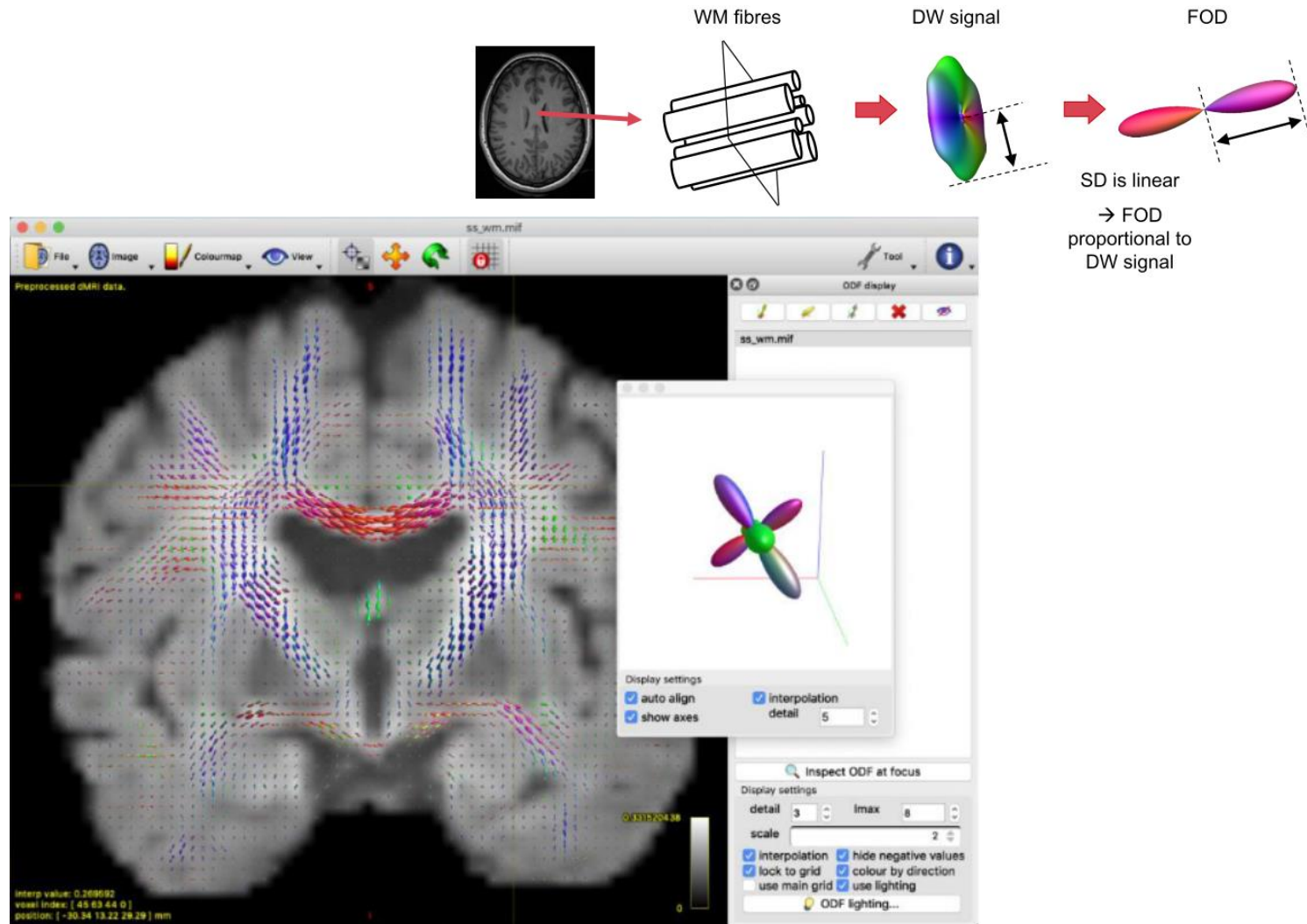
# Constrained Spherical Deconvolution

- When expressed in the SH basis, the math becomes very simple...
- but the optimization (solving the inverse problem) is not (regularization or constraint)





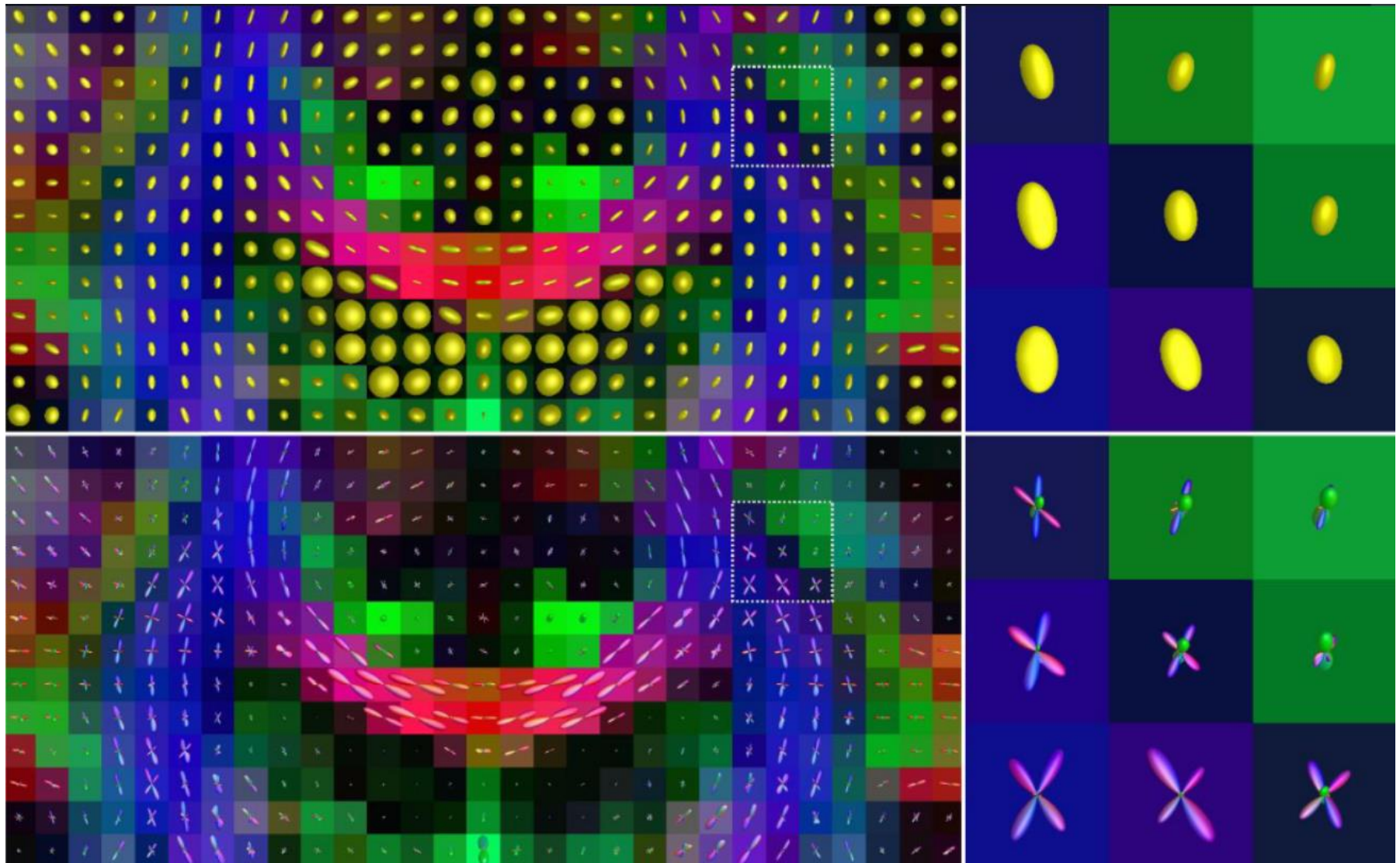
# Constrained Spherical Deconvolution



```
$dwi2fod csd -mask mask.mif dwi.mif wm.txt fod_wm.mif
```

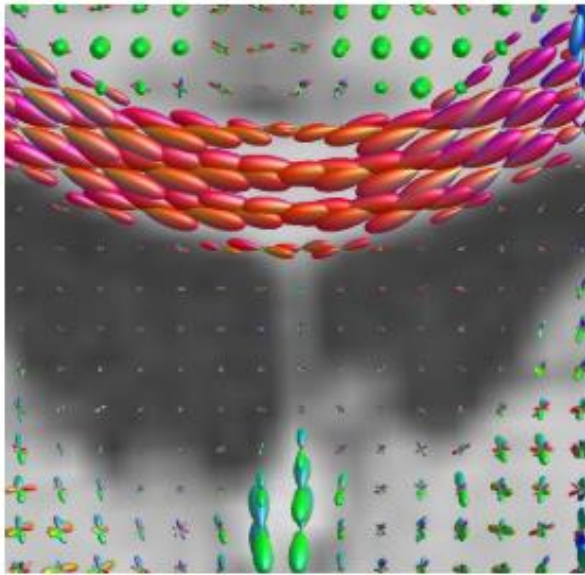


# DTI vs CSD

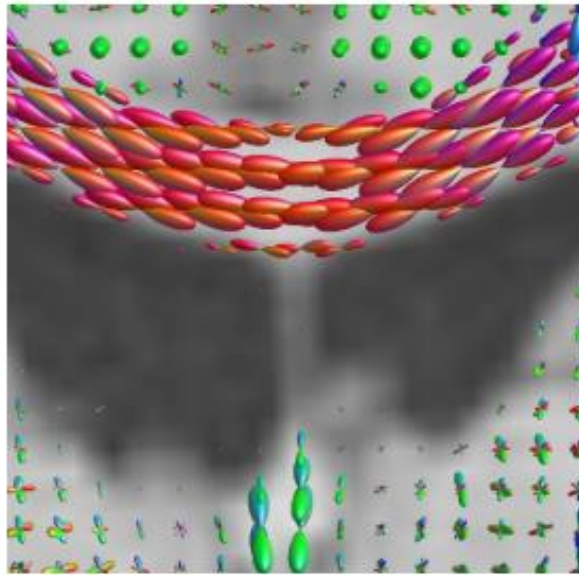


# Multi-tissue CSD: 1-tissue vs 2-tissue vs 3-tissue CSD

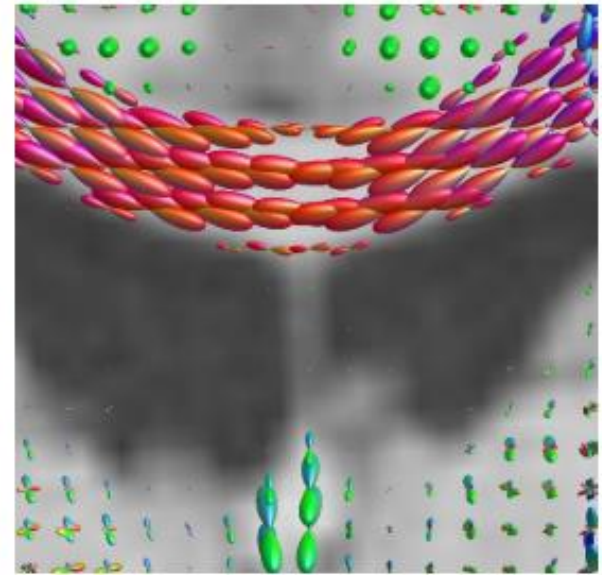
Jeurissen et al. NeuroImage, 103:411-426, 2014



1 shell  
1 tissue



2 shells  
2 tissues

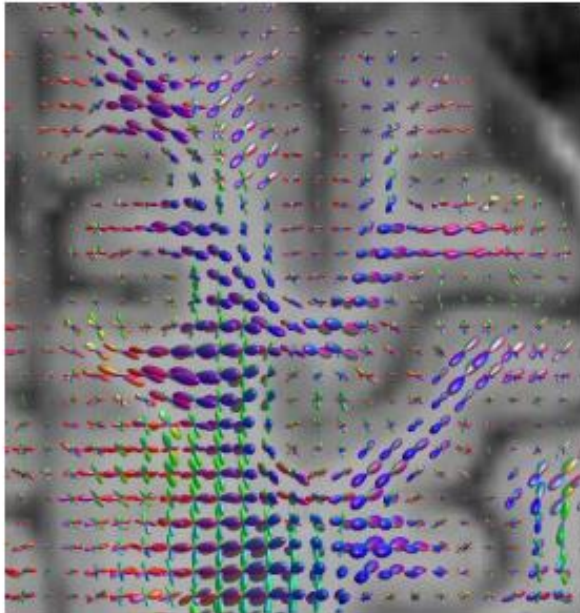


4 shells  
3 tissues

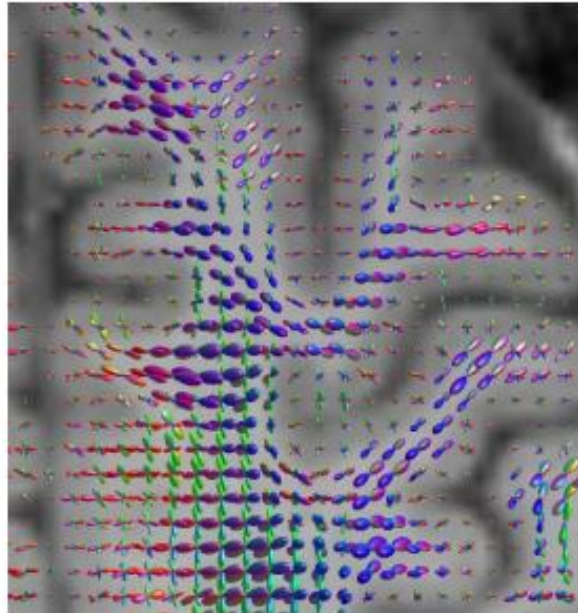


# Multi-tissue CSD: 1-tissue vs 2-tissue vs 3-tissue CSD

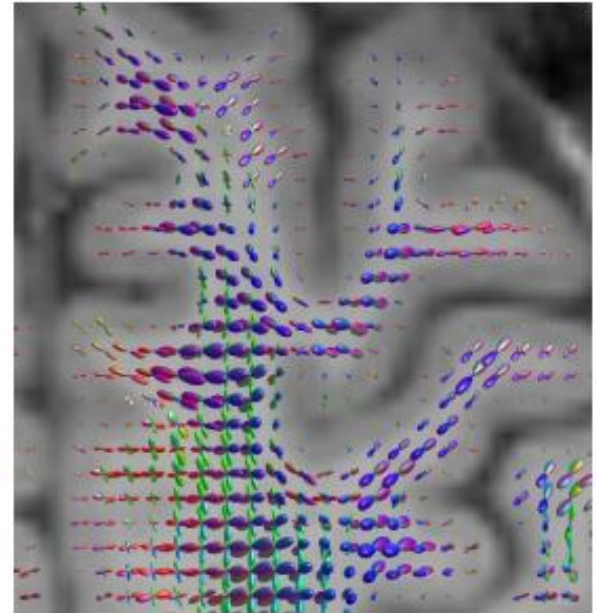
Jeurissen et al. NeuroImage, 103:411-426, 2014



1 shell  
1 tissue

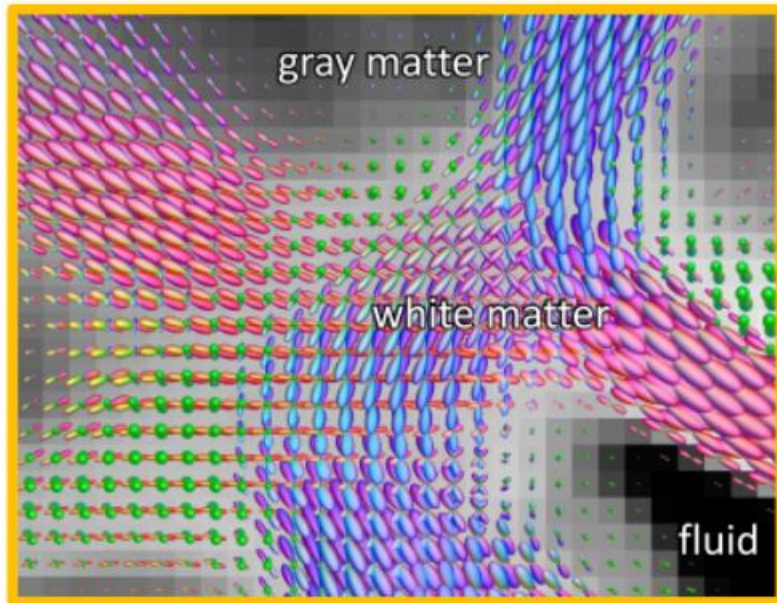


2 shells  
2 tissues

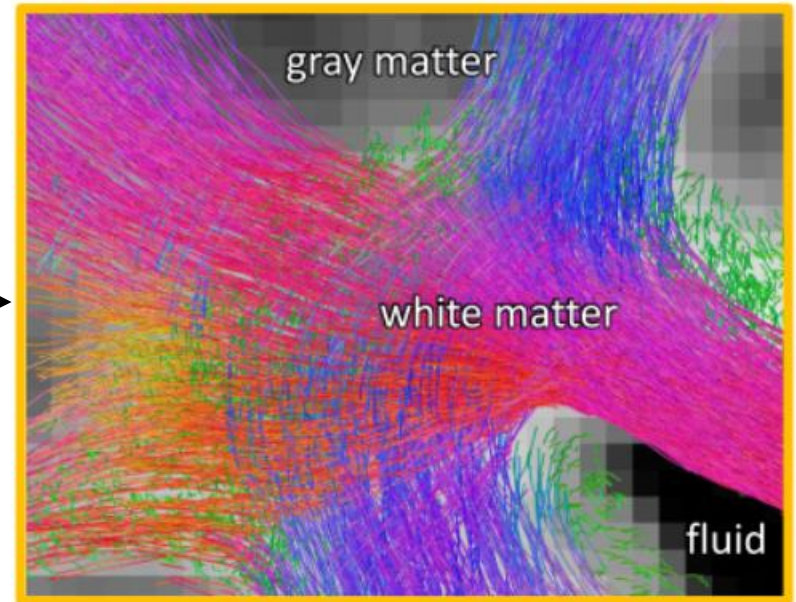


4 shells  
3 tissues

# Tractography



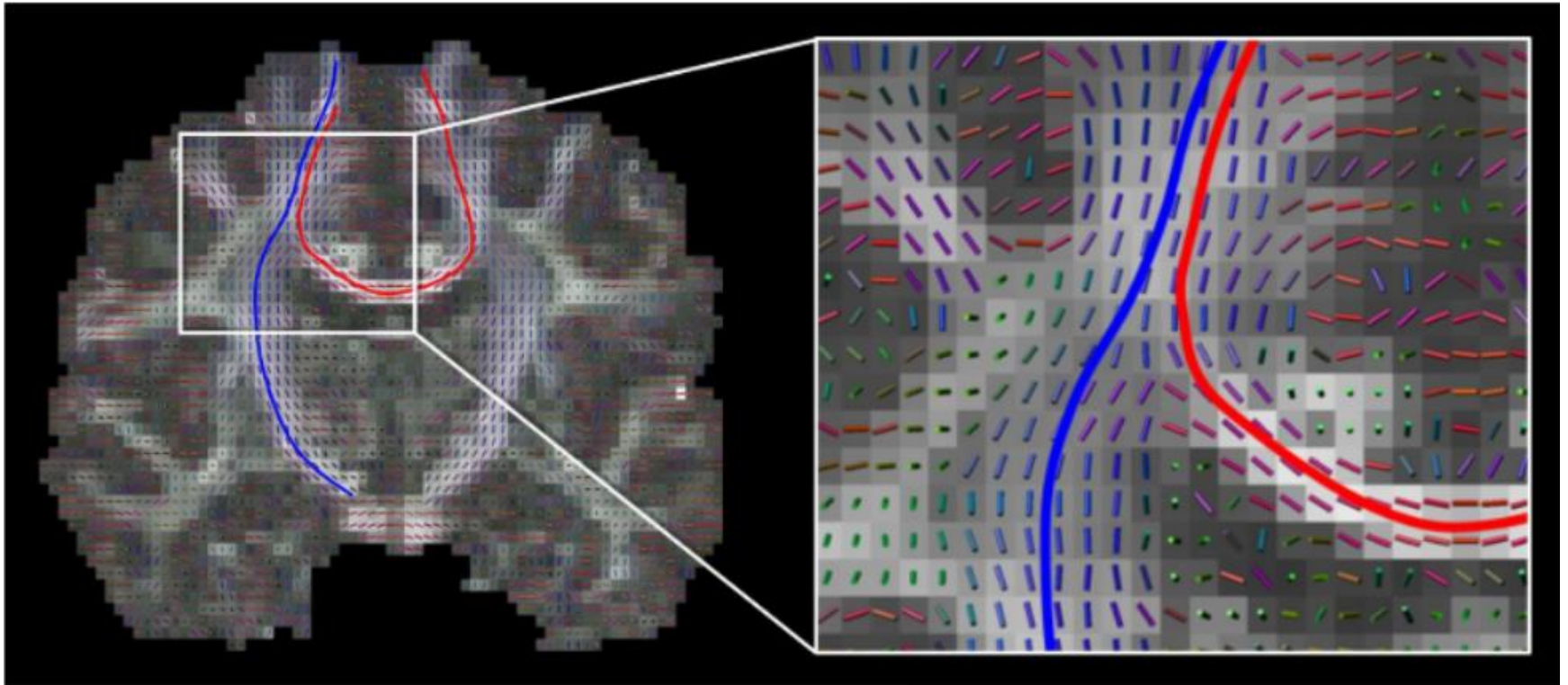
amount of white matter fibers  
as a function of orientation



white matter fiber  
connections



# Streamline tractography



local fiber orientations = vector field  $\rightarrow$  fiber tracks = streamlines

# Tractography

diffusion tensor

1. LOCAL MODELLING

fODFs

Euler

2. INTEGRATION METHODS

Runge-Kutta

nearest

3. INTERPOLATION METHODS

linear/cubic

ROI-based

4. SEED POINT SELECTION

whole-brain

fiber probability  
< threshold

5. TRACK TERMINATION  
CRITERIA

local curvature  
> threshold

inclusive ROIs

6. TRACK EDITING

exclusive ROIs

deterministic :  
same trajectory

7. DETERMINISTIC AND  
PROBABILISTIC

probabilistic :  
distribution

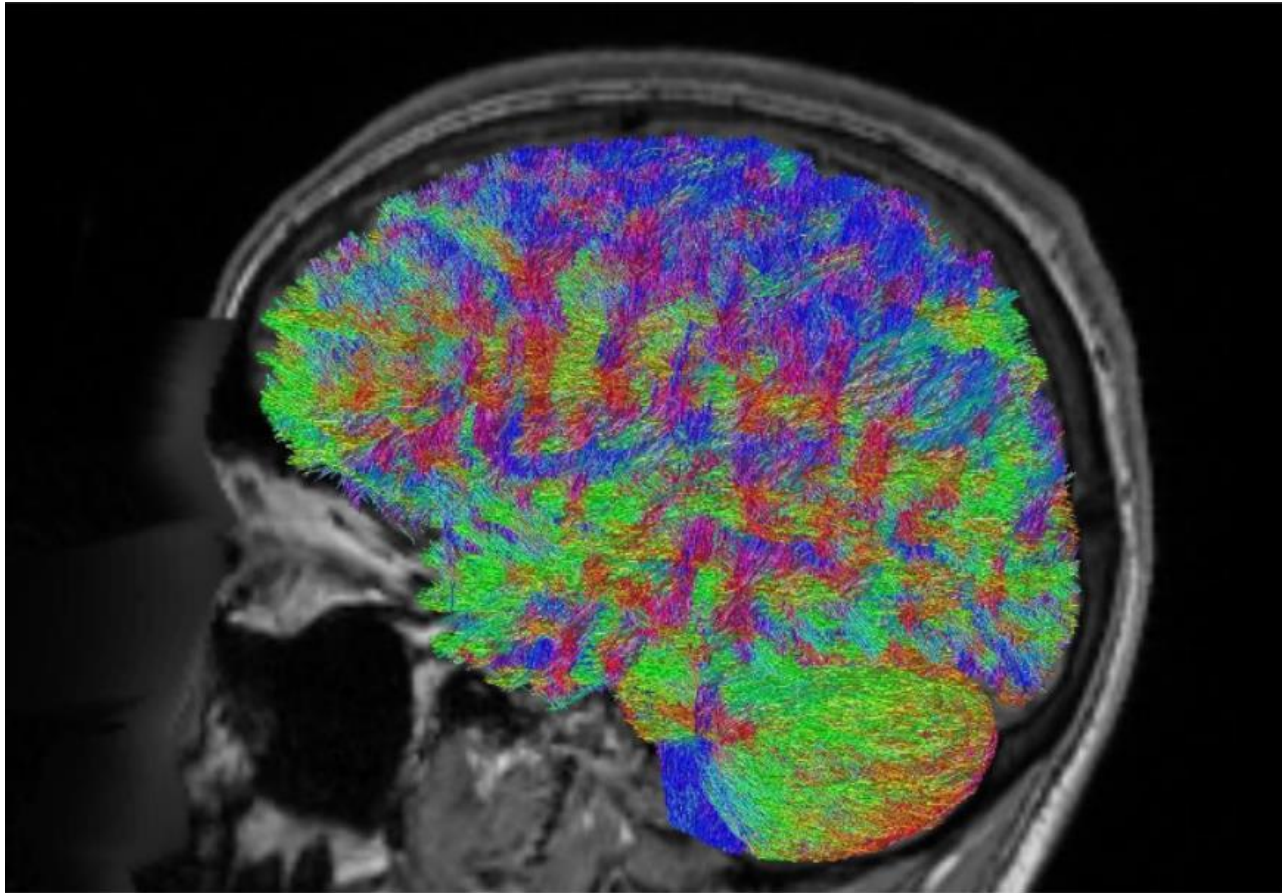
# Tractography

Purpose	Command
Generate a tractogram	tckgen
Print out information about a tractogram	tckinfo
Edit a tractogram	tckedit

```
$ tckgen -algorithm iFOD2 fod_wm.mif -seed_image mask.mif -  
select 100K ifod2.tck
```

algorithm	local model	type	integration	interpolation
FACT	none	deterministic	1 <sup>st</sup> -order*	nearest
Tensor_Det	tensor	deterministic	1 <sup>st</sup> -order*	tri-linear
Tensor_Prob	tensor	probabilistic ('uncertainty')	1 <sup>st</sup> -order*	tri-linear
SD_STREAM	fODF	deterministic	1 <sup>st</sup> -order*	tri-linear
iFOD1	fODF	probabilistic ('anatomy')	1 <sup>st</sup> -order	tri-linear
iFOD2	fODF	probabilistic ('anatomy')	2 <sup>nd</sup> -order	tri-linear

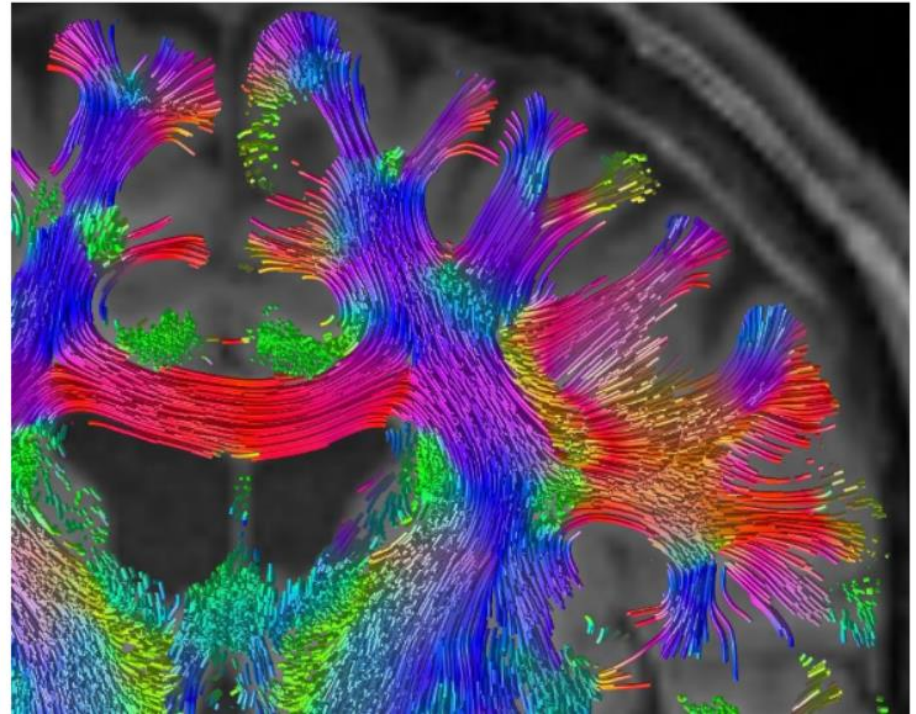
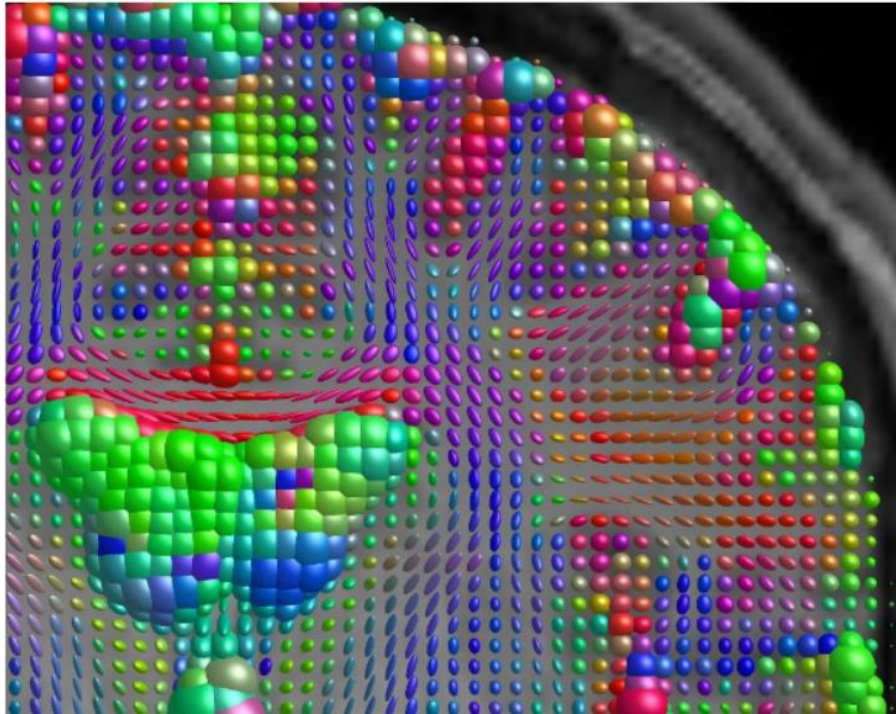
# Whole-brain tractography



```
$ tckgen -algorithm iFOD2 fod_wm.mif -seed_image mask.mif -  
select 100K ifod2.tck
```

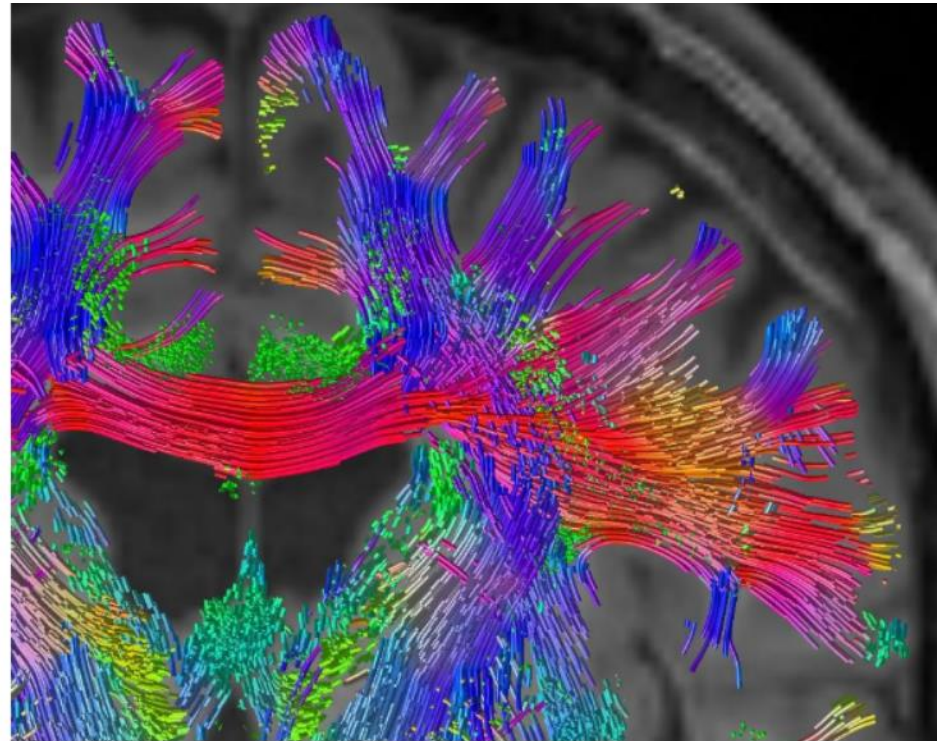
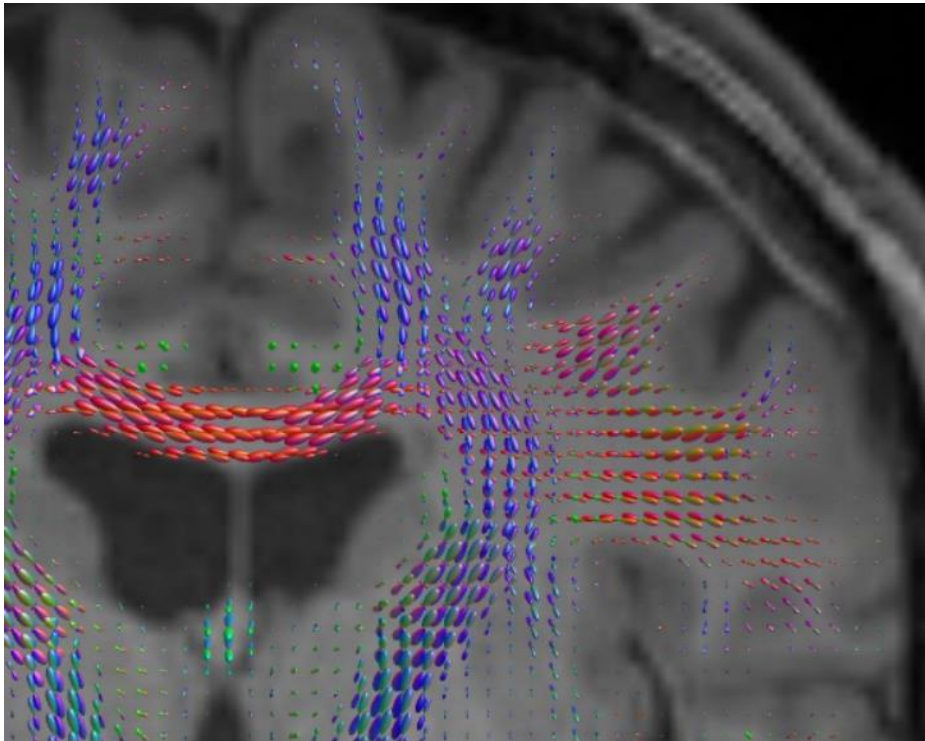


# Whole-brain tractography - DTI



```
$ tckgen dwi.mif dti.tck -select 100K -algo tensor_det -  
seed_image mask.mif -mask mask.mif -angle 60
```

# Whole-brain tractography - CSD

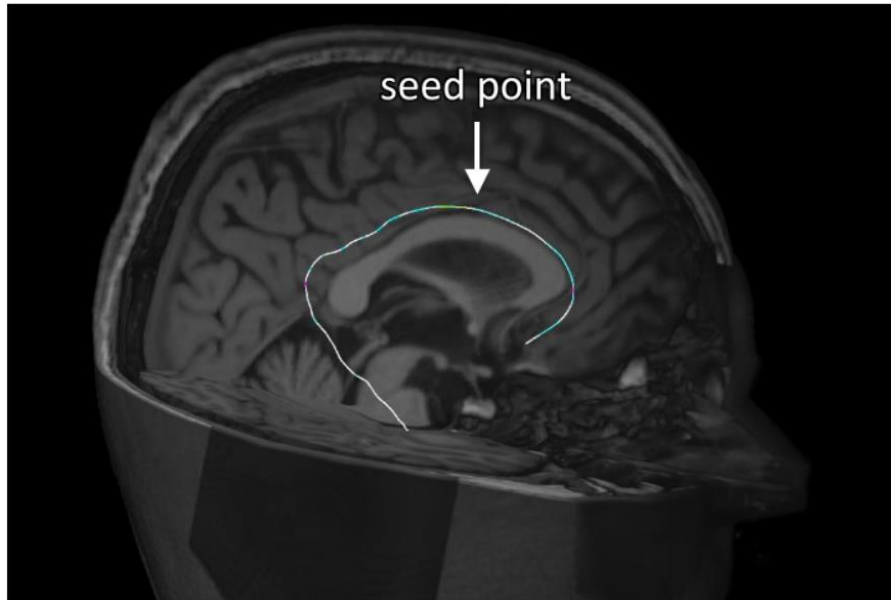


```
$ tckgen fod_wm.mif csd.tck -select 100K -algo sd_stream -  
seed_image mask.mif -mask mask.mif -angle 60
```



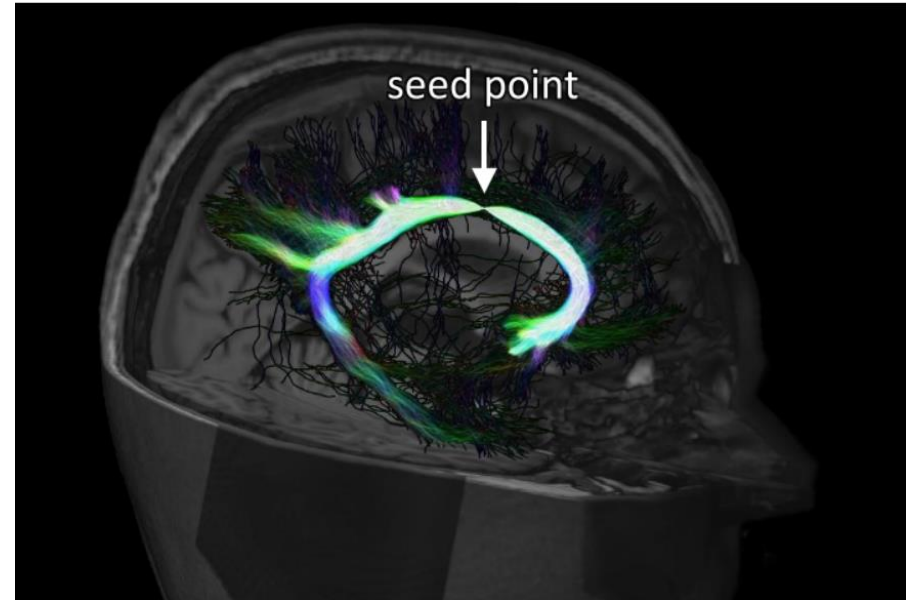
# Deterministic vs Probabilistic

deterministic



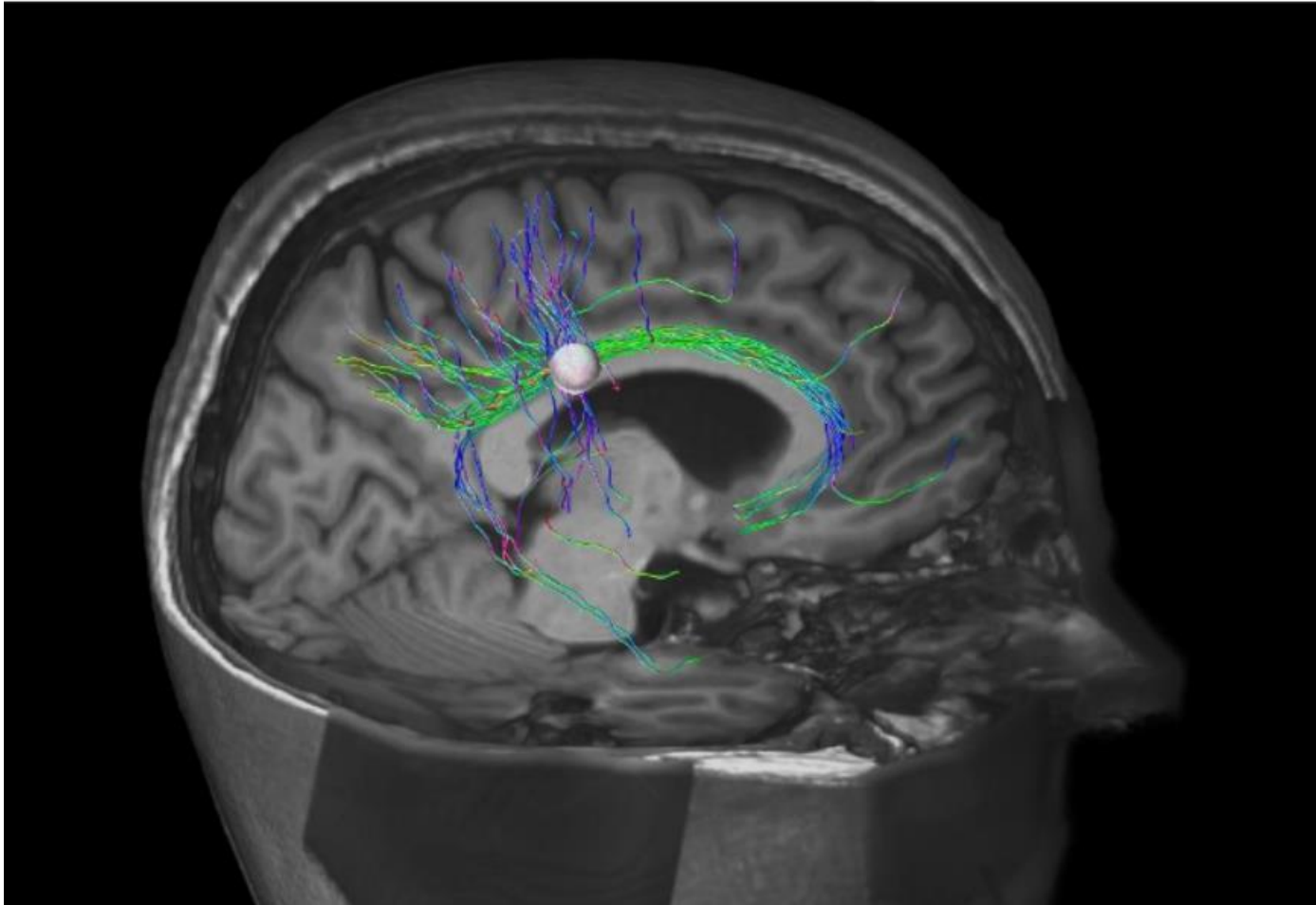
```
$ tckgen fod_wm.mif csd.tck -select  
100K -algo FACT -seed_image  
mask.mif -mask mask.mif -angle 60
```

probabilistic



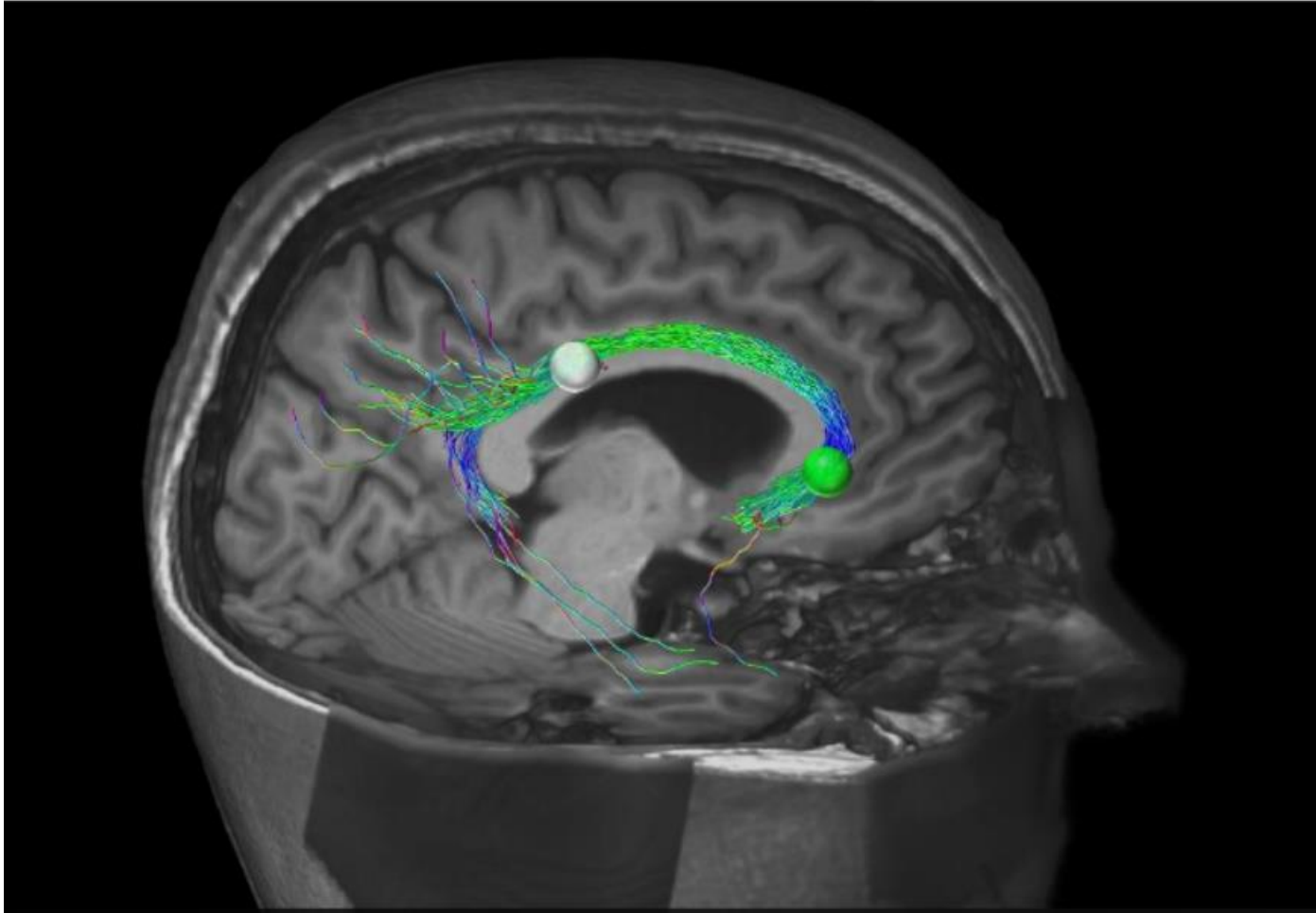
```
$ tckgen fod_wm.mif csd.tck -select  
100K -algo iFOD2 -seed_image  
mask.mif -mask mask.mif -angle 60
```

# ROI-based tracking: spheres



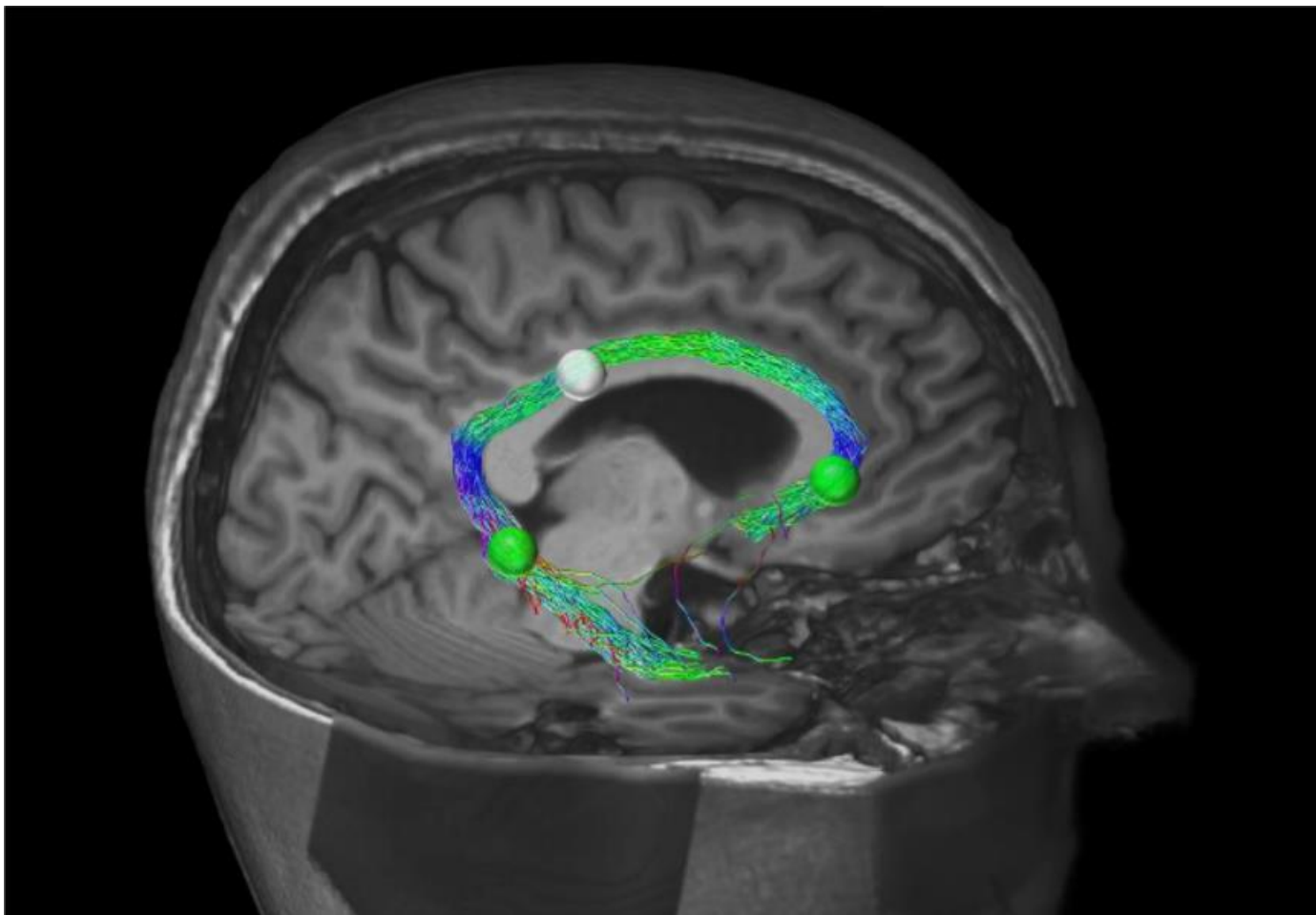
```
$ tckgen -algorithm iFOD2 fod_wm.mif -seed_sphere 4,5,24,5  
-select 100K cing.tck
```

# ROI-based tracking: spheres



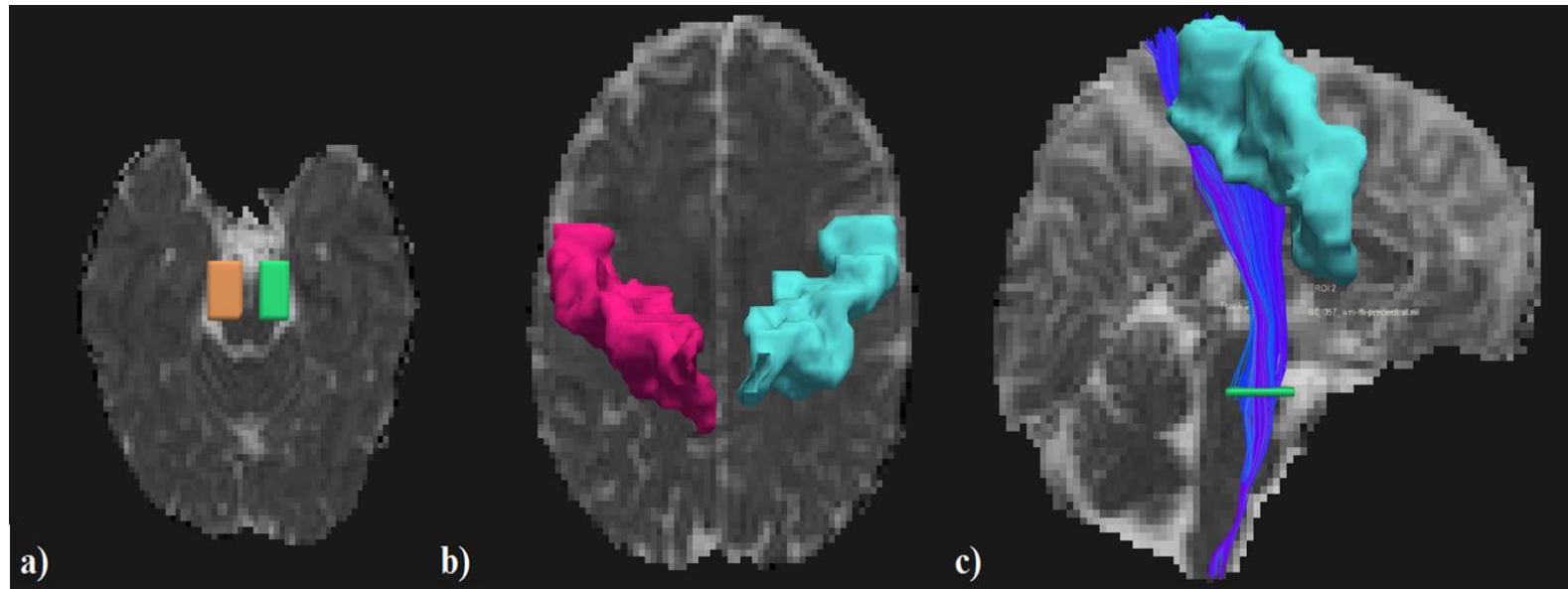
```
$ tckgen -algorithm iFOD2 fod_wm.mif -seed_sphere 4,5,24,5 -  
include 4,44,-6,5 -select 100K cing.tck
```

# ROI-based tracking: spheres



```
$ tckgen -algorithm iFOD2 fod_wm.mif -seed_sphere 4,5,24,5 -  
include 4,44,-6,5 -include 14,-4,-16,5 -select 100K cing.tck
```

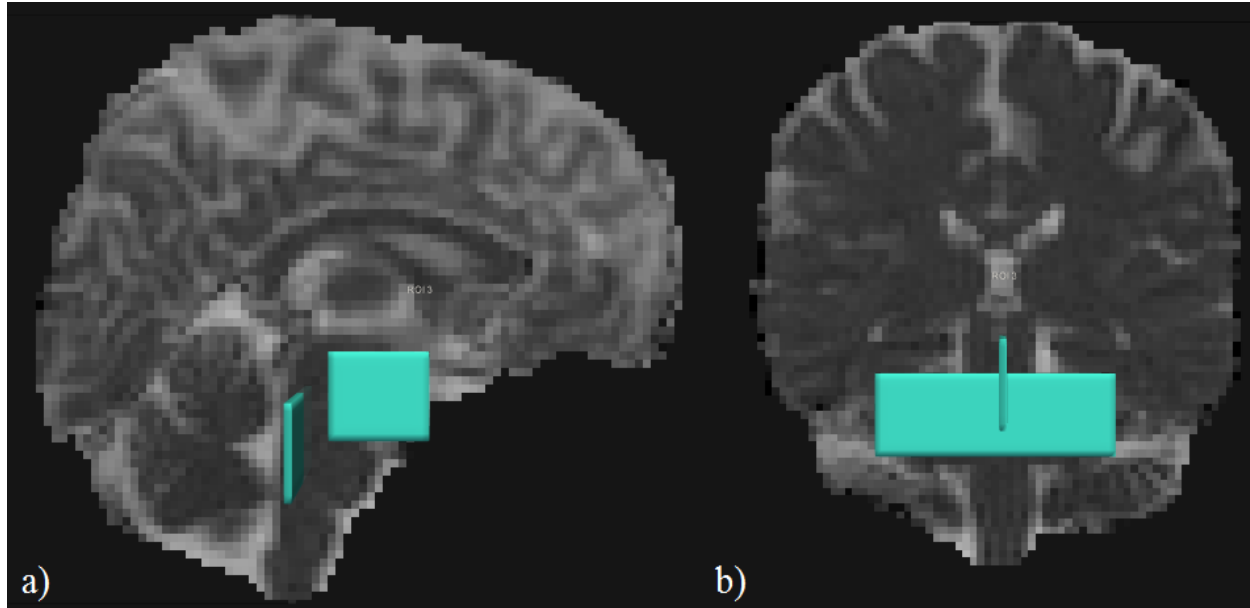
# Virtual dissection: mask ROIs



- a) Cerebral peduncle in the midbrain area, axial slice; b) Precentral gyrus/primary motor cortex, axial slice; c) Reconstructed CST tract, sagittal view.

```
$ tckedit tract.tck -include ROI01.mif -include ROI02.mif CST.tck
```

# Virtual dissection: mask ROIs



- Exclusion ROIs for the CST tracts: a) ROI selection blocking any fiber to cross the hemispheres, in the middle sagittal slice; b) ROI selection of fibers near the cerebral peduncle that are not part of the CST tract, in the coronal slice. Using the operator NOT for ROI filter for all the drawn ROIs.

```
$ tckedit CST.tck -exclude NOT01.mif -exclude NOT02.mif  
CST_new.tck
```



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**OBRIGADA/THANK YOU!!**