
MRC Cognition and Brain Sciences Unit

UNIVERSITY OF CAMBRIDGE

# Introduction to Diffusion MRI – Part II

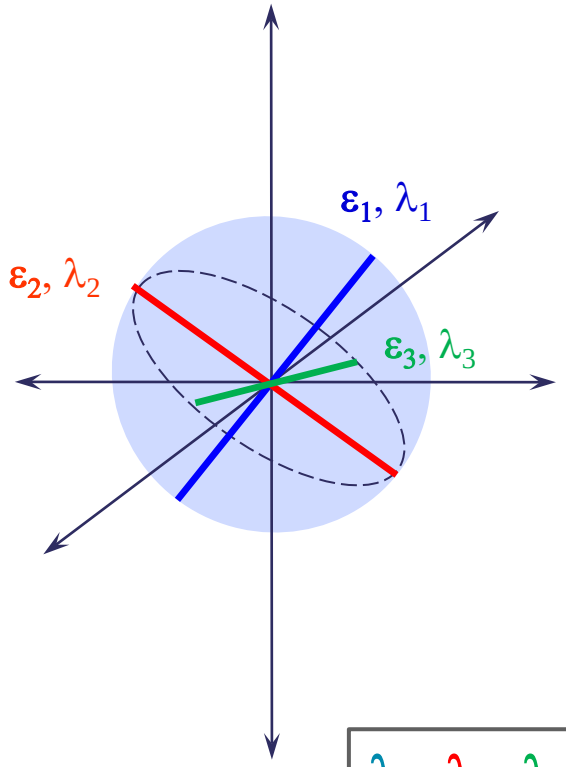
Marta M. Correia
MRC Cognition and Brain Sciences Unit

# Overview

- Introduction to Tractography
- Advanced Modelling:
  - Probabilistic Modelling
  - Multiple-fibre models
  - Diffusion MRI and microstructure

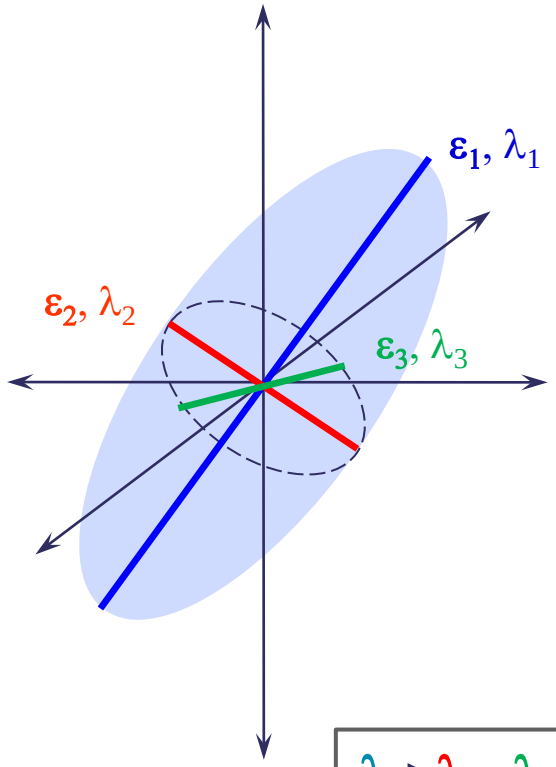
# Diffusion ellipsoid: Eigenvalues and eigenvectors

## Isotropic Diffusion




$\lambda_1=\lambda_2=\lambda_3$

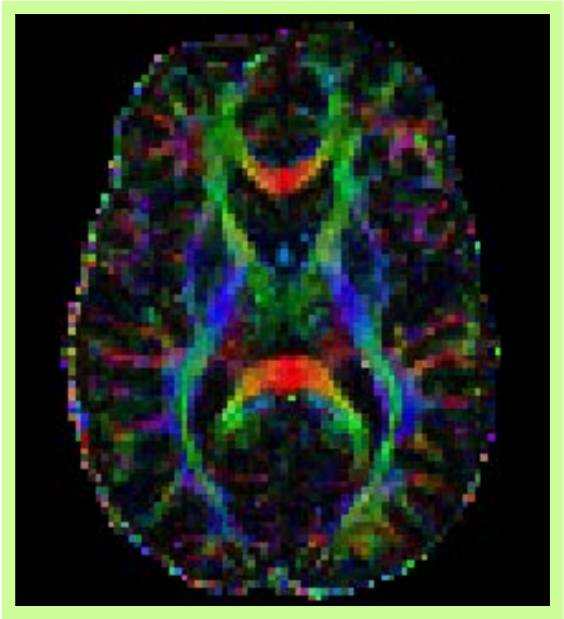
## Anisotropic Diffusion




$\lambda_1>\lambda_2\sim\lambda_3$

# Colour coded FA maps

- Let $\varepsilon_1$ designate the longest axis of the diffusion ellipsoid.
- $\varepsilon_1$ can be identified with the main direction of diffusion.
- This directional information can be added to the FA map using a colour code:



Red indicates directions in the *x* axis: right to left or left to right.

Green indicates directions in the *y* axis: front to back or back to front.

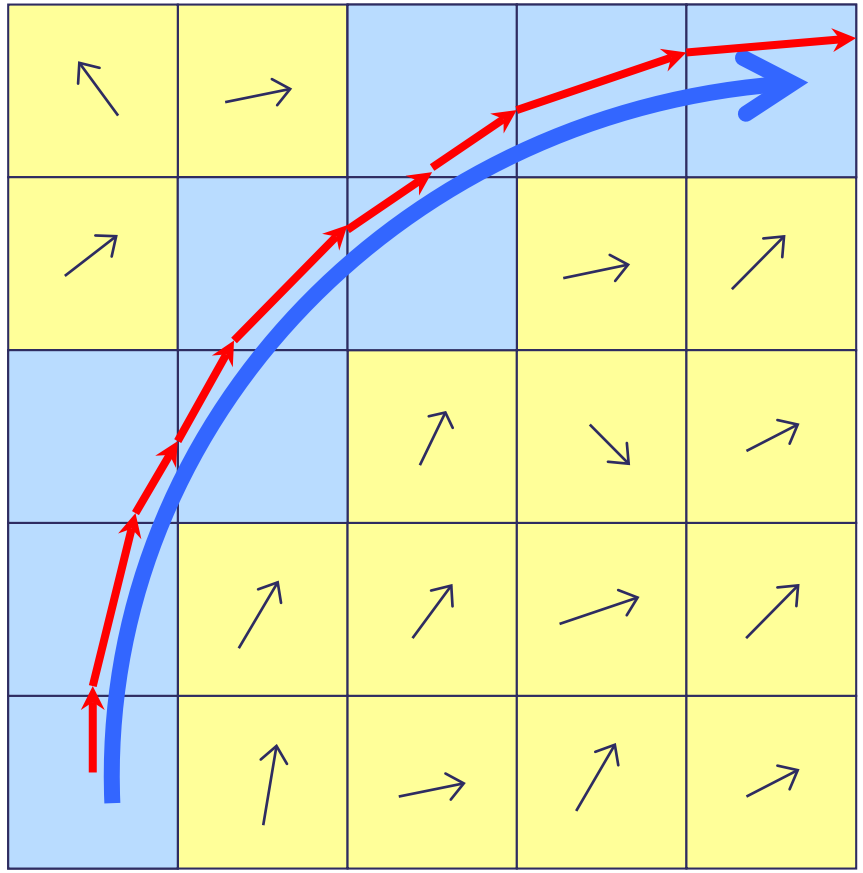
Blue indicates directions in the *z* axis: foot-to-head direction or vice versa.

**Colour coded FA map.**

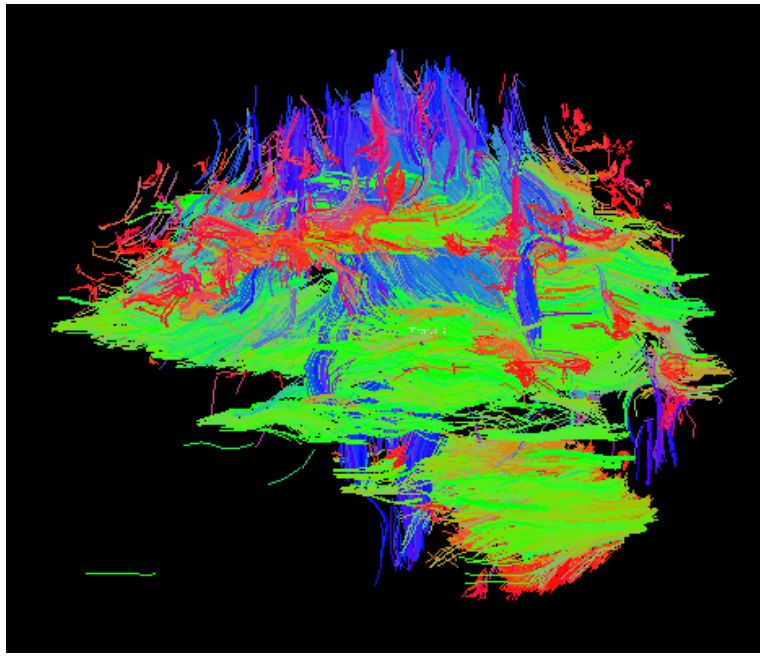
# Introduction to Tractography

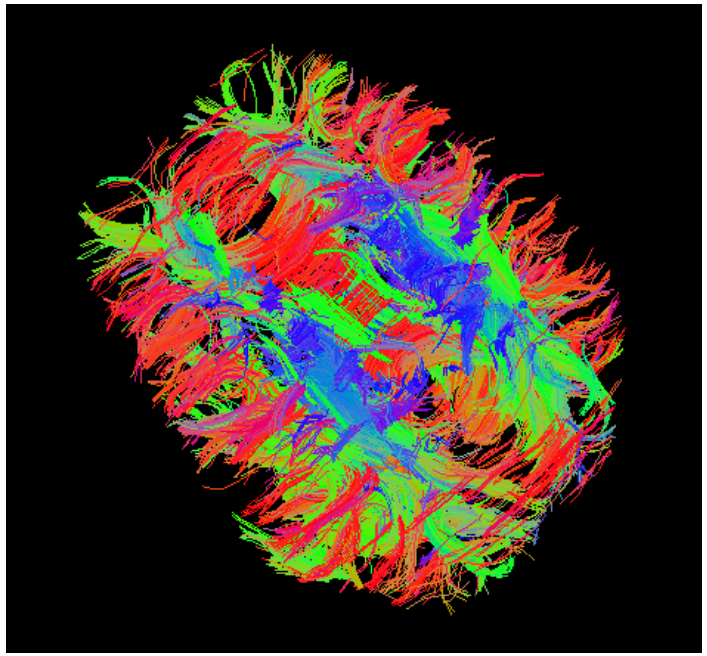
# Tractography: basic principles

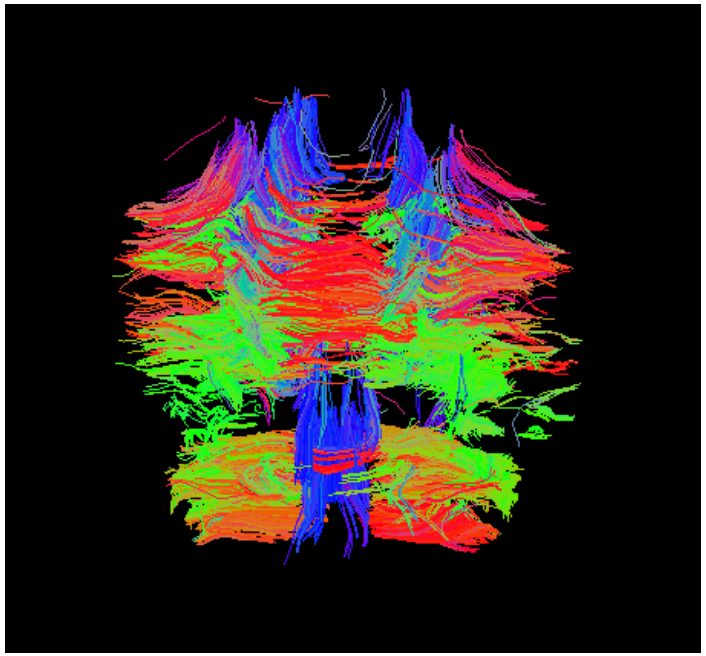
- After model fitting, the principal direction $\varepsilon_1$ can been calculated for all voxels.
- The trajectories of water molecules can be reconstructed using a method similar to the children's activity "connect the dots".
- We connect each voxel to the adjacent one toward which the fibre direction, $\varepsilon_1$, is pointing.



# Tractography in the Brain







**Fibre tracks obtained for a dataset of a healthy volunteer using simple streamlining (FACT).**

# Probabilistic Modeling of Diffusion MRI Signal

# Probabilistic Modelling

- The information provided by DTI can be very useful for the characterisation of brain white matter.
- However, the estimated tensor can be highly dependent on noise.
- Probabilistic modelling can be used to estimate a probability distribution function (PDF) for the DTI model parameters.
- The standard deviation (s.d.) of this PDF is a good marker for confidence in the results.

# MCMC Methods

- Markov Chain Monte Carlo (MCMC) methods are based on Baye's Theorem:

$$P(\omega \mid data) = \frac{P(data \mid \omega)P(\omega)}{P(data)}$$

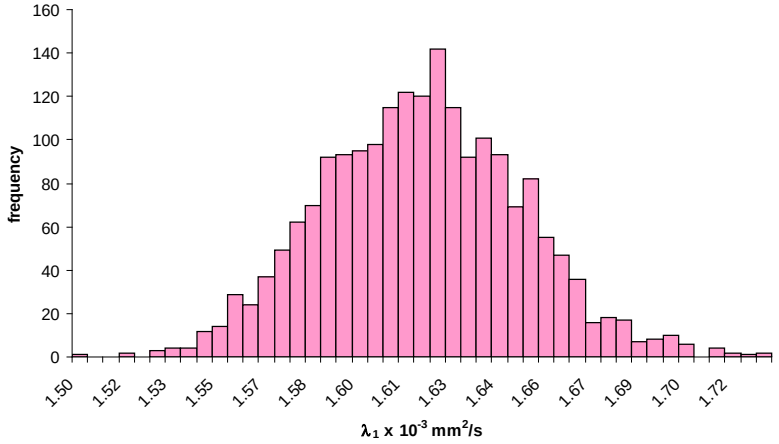
where $\omega$ represents the vector of model parameters.

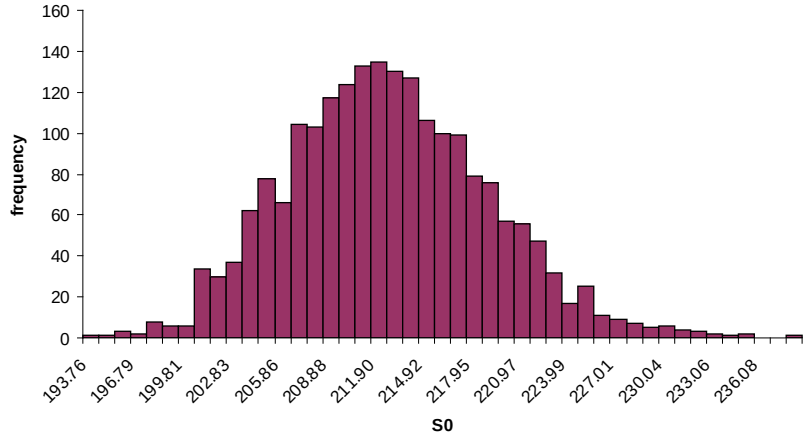
- The prior term *P(*$\omega$*)* offers an opportunity for scientists to include knowledge they have about the expected values of the parameters.

- The term *P( data |* $\omega$ *)* gives the probability of observing the data given a sampled set of parameters, and it is dependent on the model used.

# MCMC Methods

- Instead of producing a single set of parameters MCMC methods produce a PDF for each parameter.

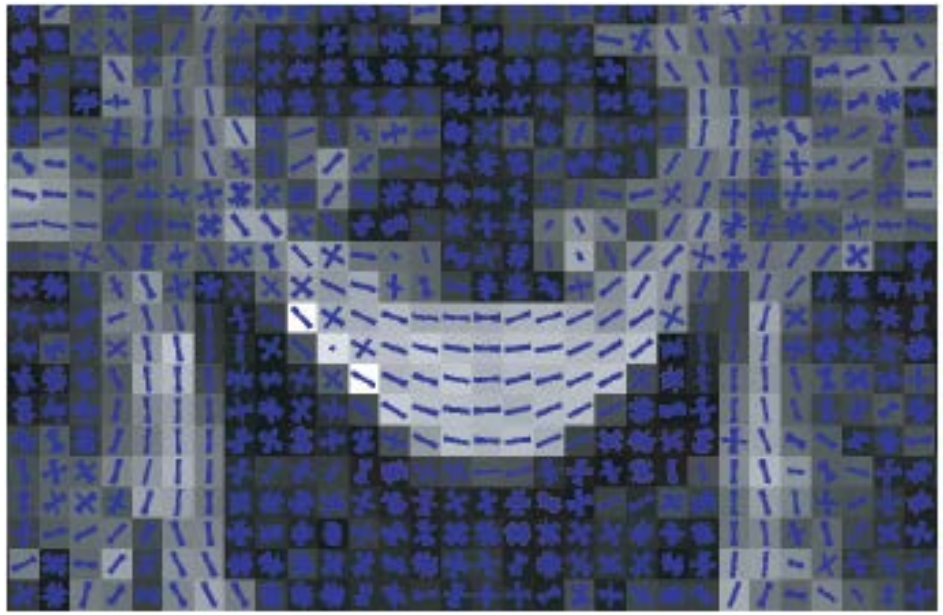



- The standard deviation of these PDFs is a good marker for confidence in the results.
- **FA maps, MD maps**, etc., can be obtained by taking the average of each PDF as the most likely value of the model parameters.

# PDF for fibre orientation

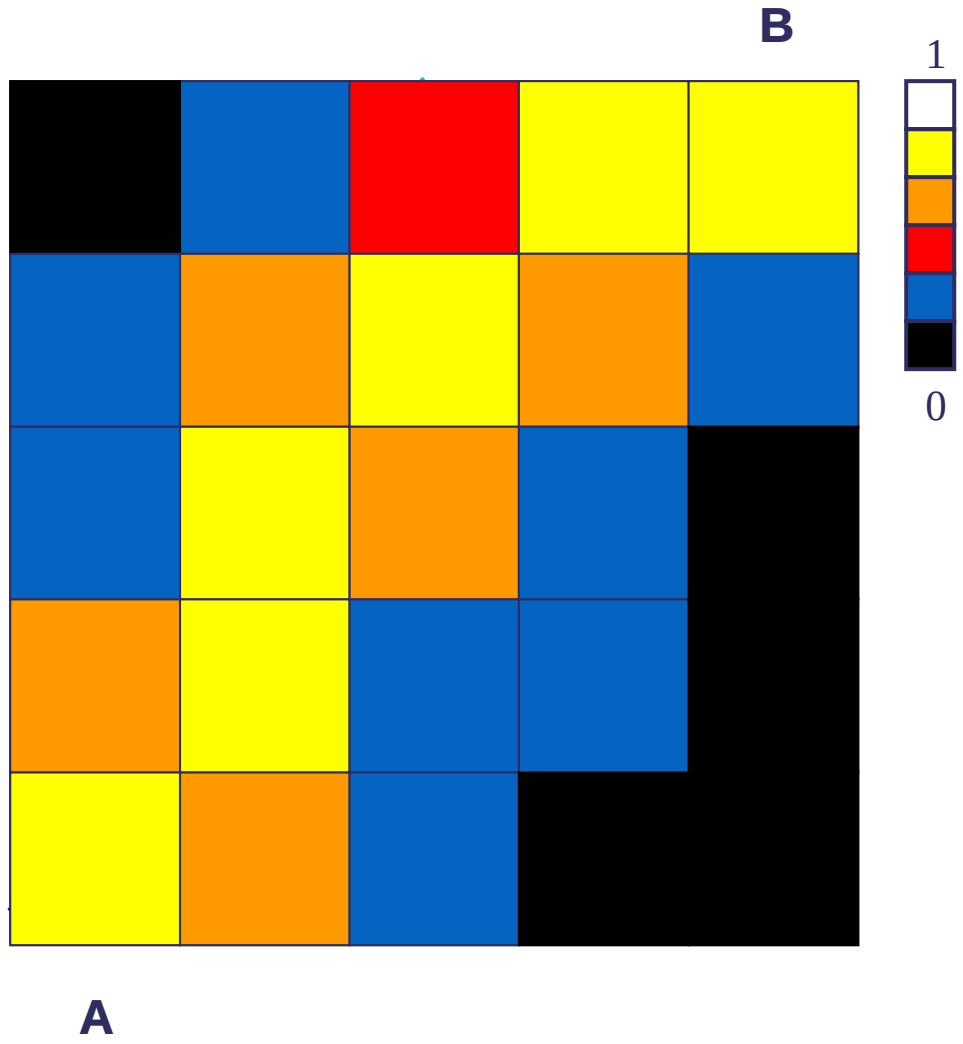
- For each voxel, we can obtain a PDF for the fibre orientation, by combining samples from the PDFs for $\theta$ and $\phi$:



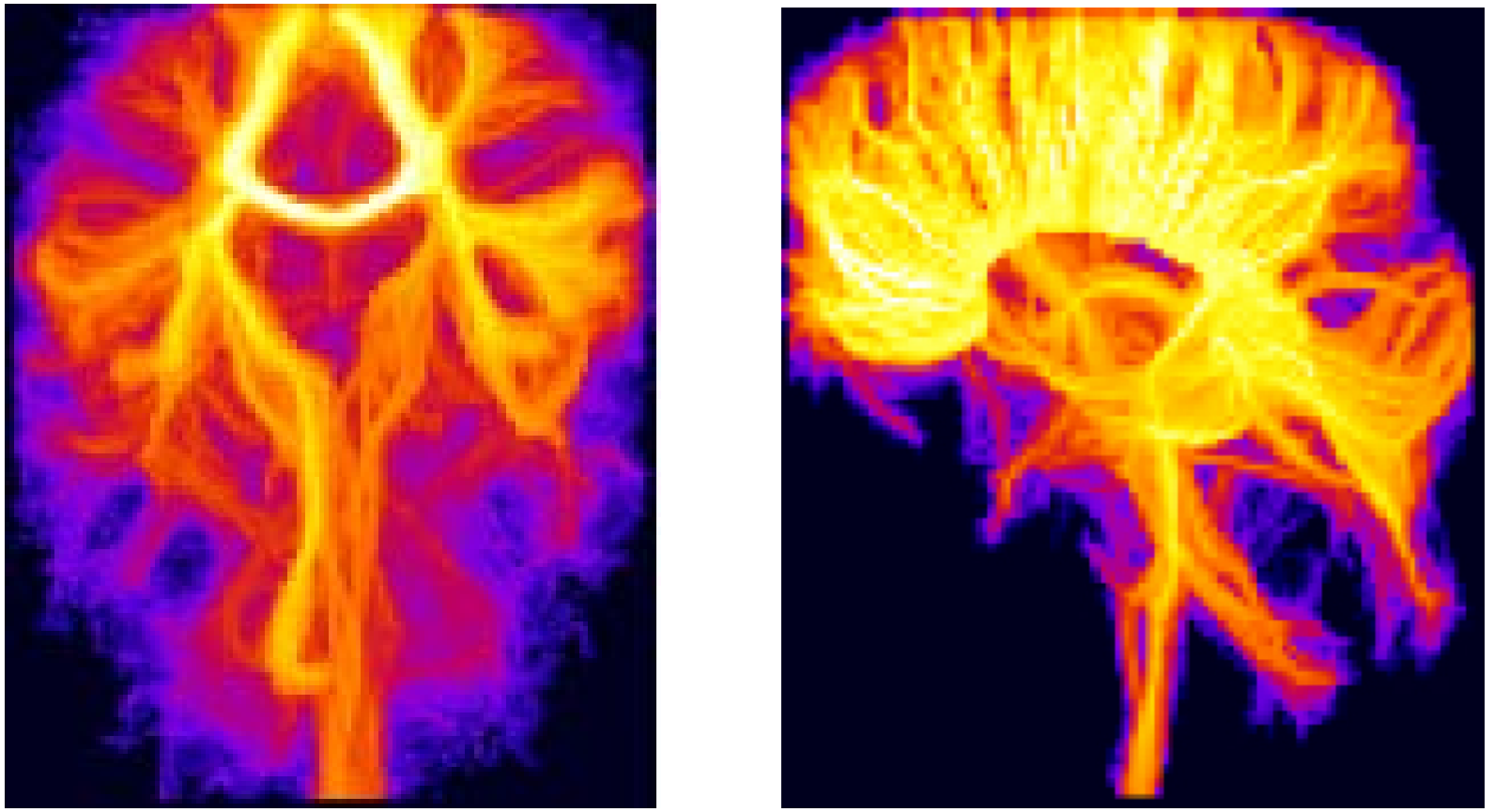
- Regions of one-fibre populations have very narrow distributions, while regions of crossing fibres show greater variability.

# Probabilistic Tractography

- For each sample of the directional PDF we can produce a track (or streamline).
- Repeat this for a large number of samples.
- The probability of voxels A and B being connected can be calculated by dividing the number of streamlines that reach B, by the total number of streamlines generated from A.

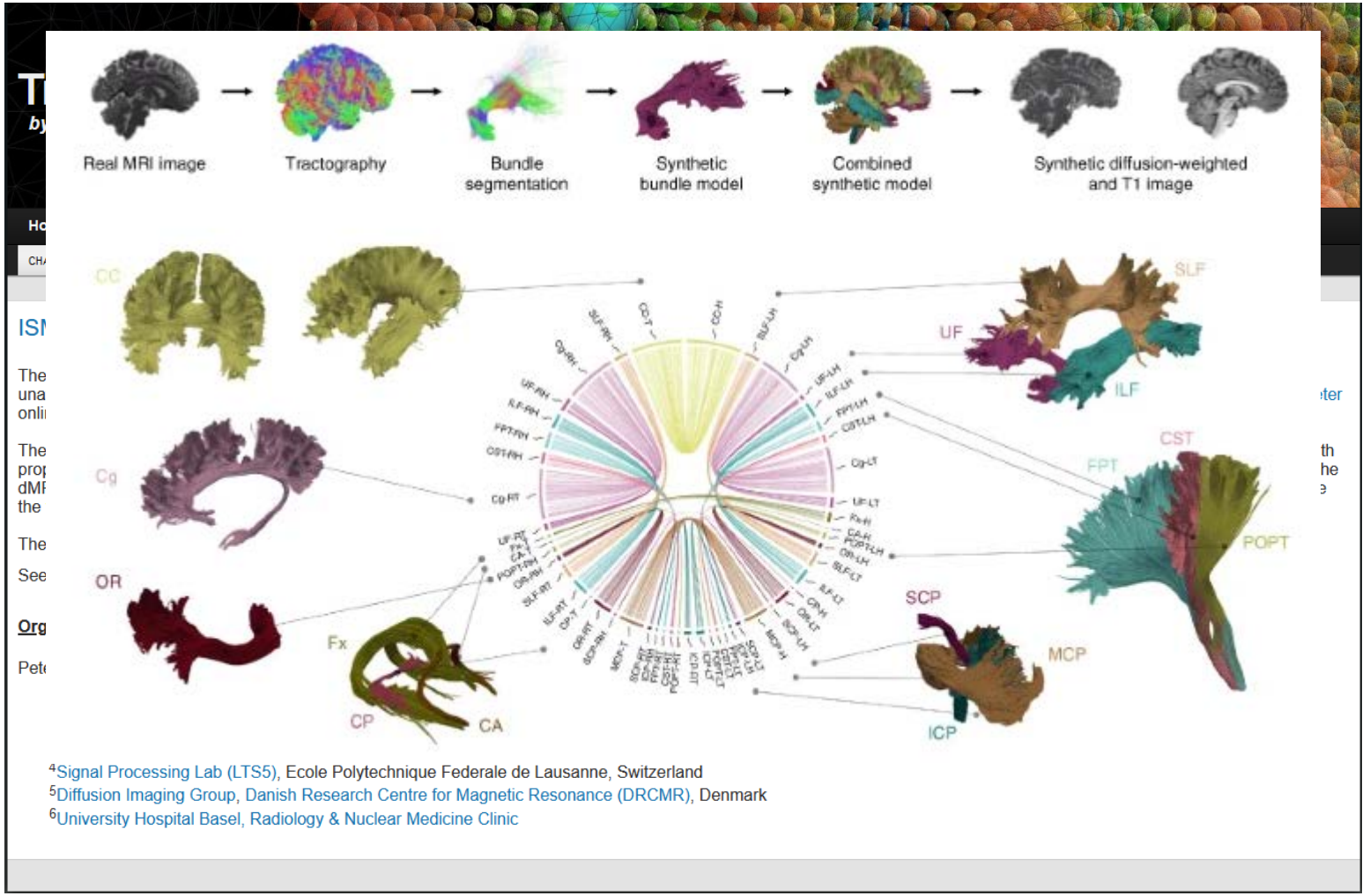


# Probabilistic Tractography in the Brain



**Probabilistic tractography dataset obtained for a healthy volunteer.**

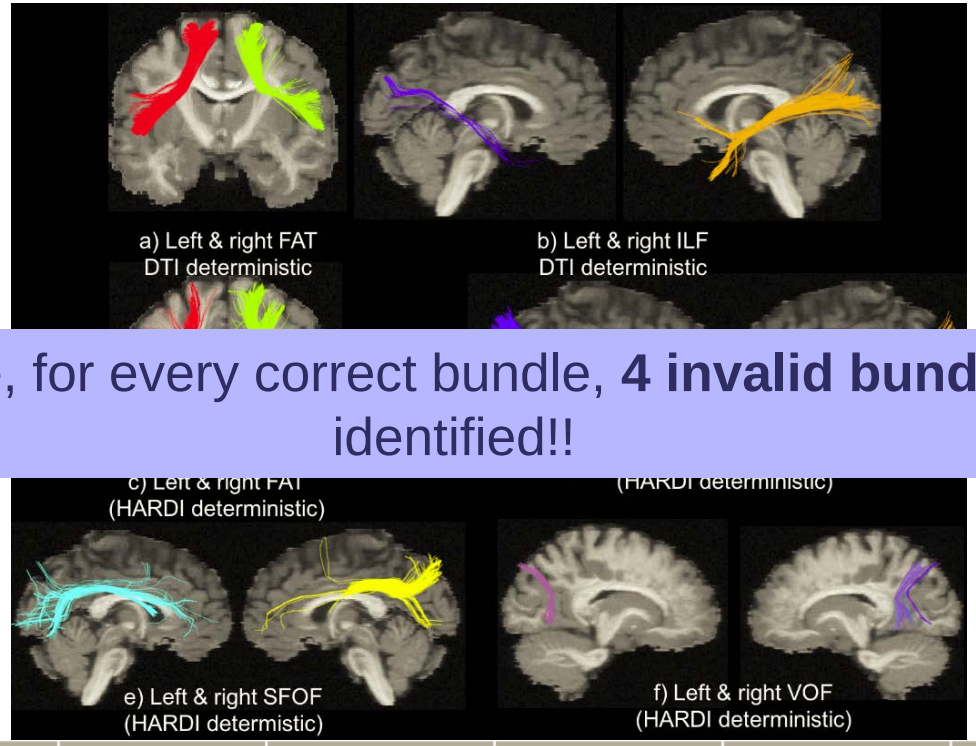
# Tractography: A cautionary tale




[4]Signal Processing Lab (LTS5), Ecole Polytechnique Federale de Lausanne, Switzerland
[5]Diffusion Imaging Group, Danish Research Centre for Magnetic Resonance (DRCMR), Denmark
[6]University Hospital Basel, Radiology & Nuclear Medicine Clinic

# Tractography: A cautionary tale

- Examples of **invalid bundles**

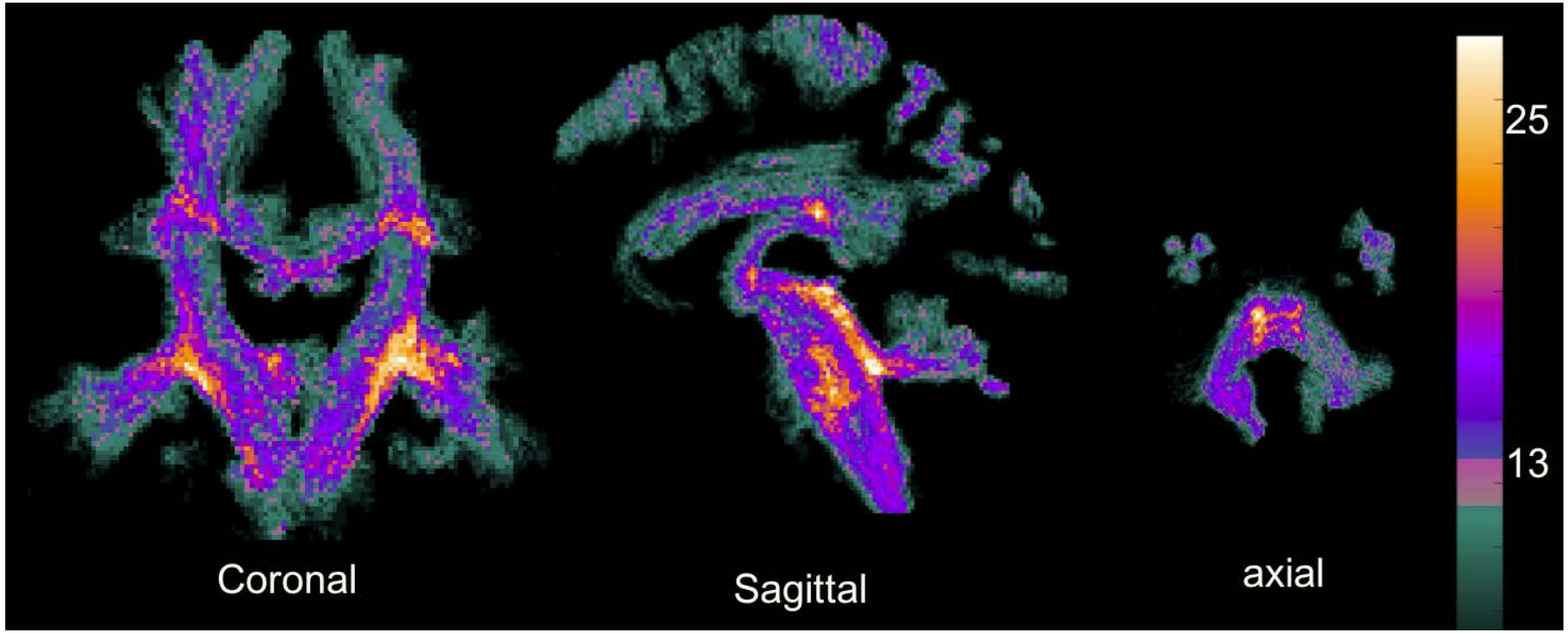



On average, for every correct bundle, **4 invalid bundles** were identified!!

| Bundles | FAT | ILF | MLF | SFOF | VOF |
|---|---|---|---|---|---|
| Occurrence (%) | 88% | 85% | 95% | 81% | 81% |

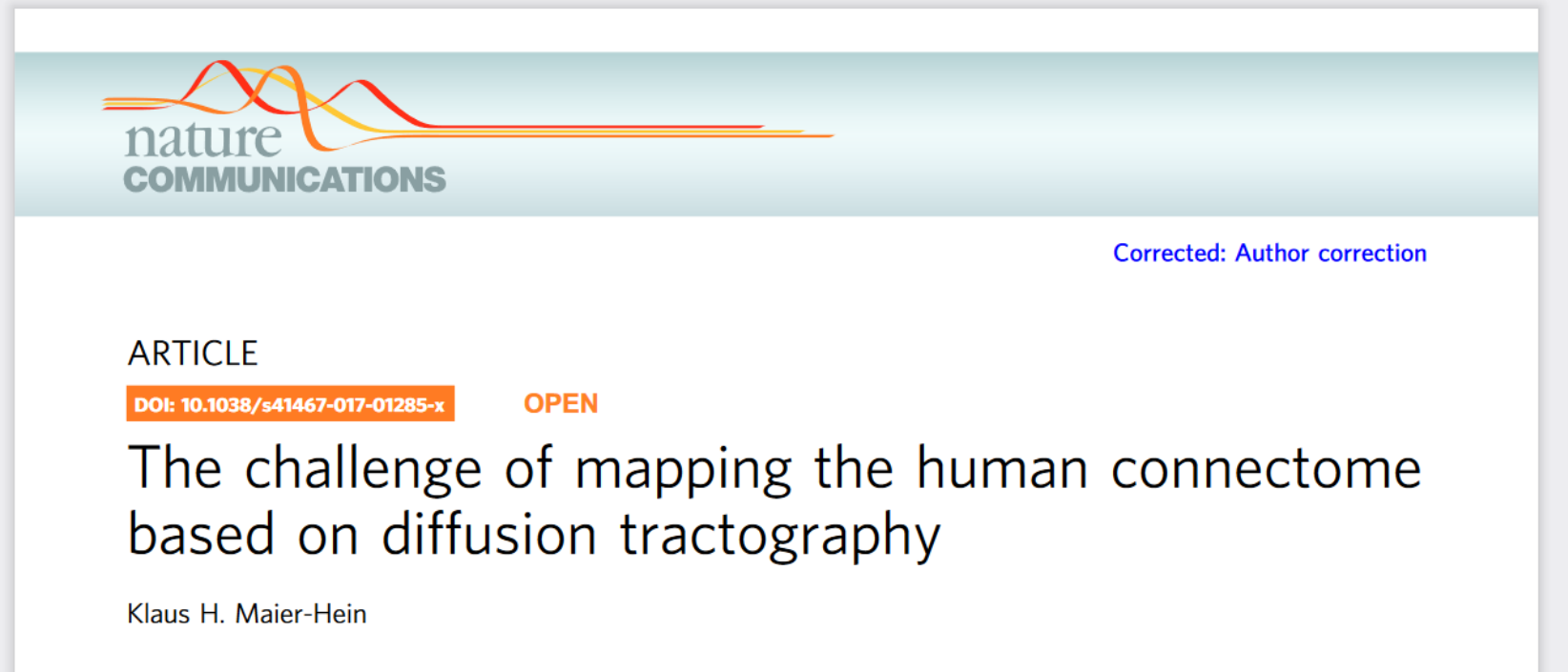
# Tractography: A cautionary tale

- Most common occurring locations of intersecting **invalid bundles**



# Tractography: A cautionary tale

**http://tractometer.org/ismrm_2015_challenge/**



nature COMMUNICATIONS

Corrected: Author correction

ARTICLE

DOI: 10.1038/s41467-017-01285-x OPEN

The challenge of mapping the human connectome based on diffusion tractography

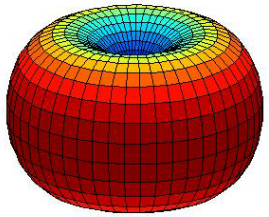
Klaus H. Maier-Hein

# Multiple fibres

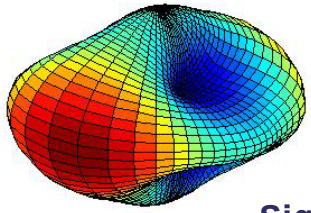
## Beyond the Diffusion Tensor

# Why the diffusion tensor is not the end of the story

- DTI has a key limitation: it assumes a single fibre per voxel, and it cannot be used to explain the signal profile obtained from multiple crossing fibres.



**Signal profile from a single fibre**



**Signal profile from two crossing fibres**

- This limitation results in artificially low FA values in regions of crossing fibres, and in greater variability of FA and MD estimates.
- It is also a major obstacle for tractography and connectivity mapping, since the model fails at fibre crossings.
- A variety of alternative models and algorithms aim to resolve the orientations of crossing fibres.

# Multiple fibre approaches

## Model-Based Approaches

- The multi-tensor model

## Non-Parametric Approaches

- Diffusion Spectrum Imaging (DSI)
- Q-ball Imaging
- Constrained Spherical Deconvolution (CSD)
- Persistent Angular Structure (PAS)

# Multiple fibre approaches

## Model-Based Approaches

- The multi-tensor model

## Non-Parametric Approaches

- Diffusion Spectrum Imaging (DSI)
- Q-ball Imaging
- Constrained Spherical Deconvolution (CSD)
- Persistent Angular Structure (PAS)

# The Multi-tensor Model

- The multi-tensor model is a simple generalisation of DTI.
- The signal in each voxel is modelled by a mixture of *n* Gaussian densities:

$$S(b,\vec{r}) = S_0 \sum_{i=1}^{n} f_i \, e^{-b\,\vec{r}^{\,T}\,\underline{D}_i\,\vec{r}}$$

where $f_i$ represents the volume fraction of compartment *i.*

- This model assumes the number of distinct fibre populations, *n*, is known.
- The parameters $\underline{D}_1$, …, $\underline{D}_n$ cannot be expressed as a linear function of the signal, so non-linear optimisation is required.
- The principal eigenvector of each $\underline{D}_i$ provides a separate fibre orientation estimate.

# The Multi-tensor Model

- Practical considerations, such as the number of measurements and the noise level, limit the number of orientations the method can resolve reliably, and most studies use $n$=2.

## Acquisition requirements

- A minimum of $n \times 7$ unique gradient directions are required to estimate the model parameters.
- In 2005 Alexander and Barker recommended using $b$ in the range 2200-2800 s/mm$^2$.

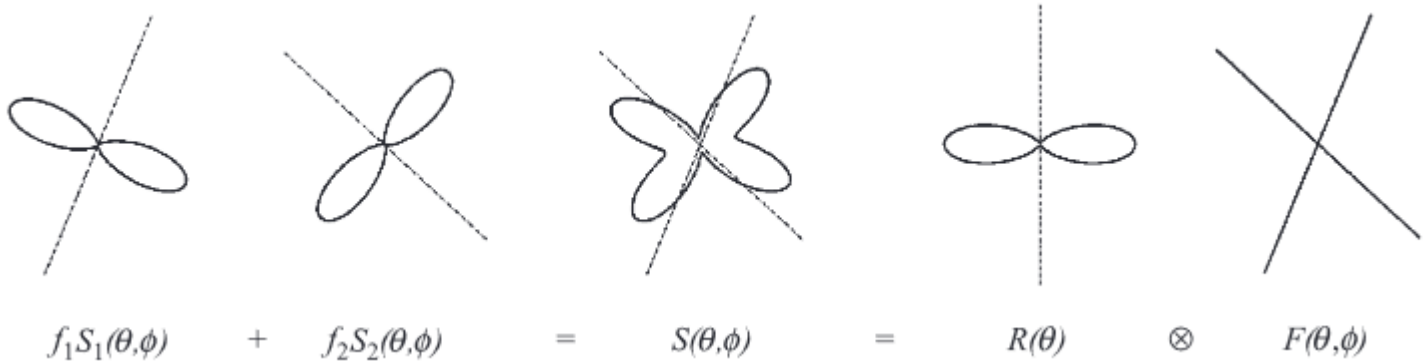
## Limitations

- Increased acquisition time and lower SNR.
- Using 64 directions the 2-tensor model can resolve 60 degree crossings, but does not consistently resolve 30 degree crossings.

# Constrained Spherical Deconvolution (CSD)

- CSD is able to estimate the distribution of fibre orientations within a voxel without making assumptions about the number of fibres present.
- The original method (Tournier et al. 2007) requires a single-shell high angular resolution diffusion data (>60 directions).
- Ideally, the *b*-value used should be in the region of 2,500 – 3,000 s/mm² (for *in vivo* human brains).
- Multi-shell multi-tissue CSD (MSMT-CSD) was introduced by Jeurissen et al. in 2014.
- MSMT-CSD requires multi-shell high angular resolution diffusion data, containing multiple *b*-values.
- To resolve WM, GM & CSF the acquisition should contain at least 2 shells plus the *b*=0 volumes (i.e. 3 unique *b*-values).

# Constrained Spherical Deconvolution (CSD)



$f_1S_1(\theta,\phi) + f_2S_2(\theta,\phi) = S(\theta,\phi) = R(\theta) \otimes F(\theta,\phi)$

Tournier et al. 2007

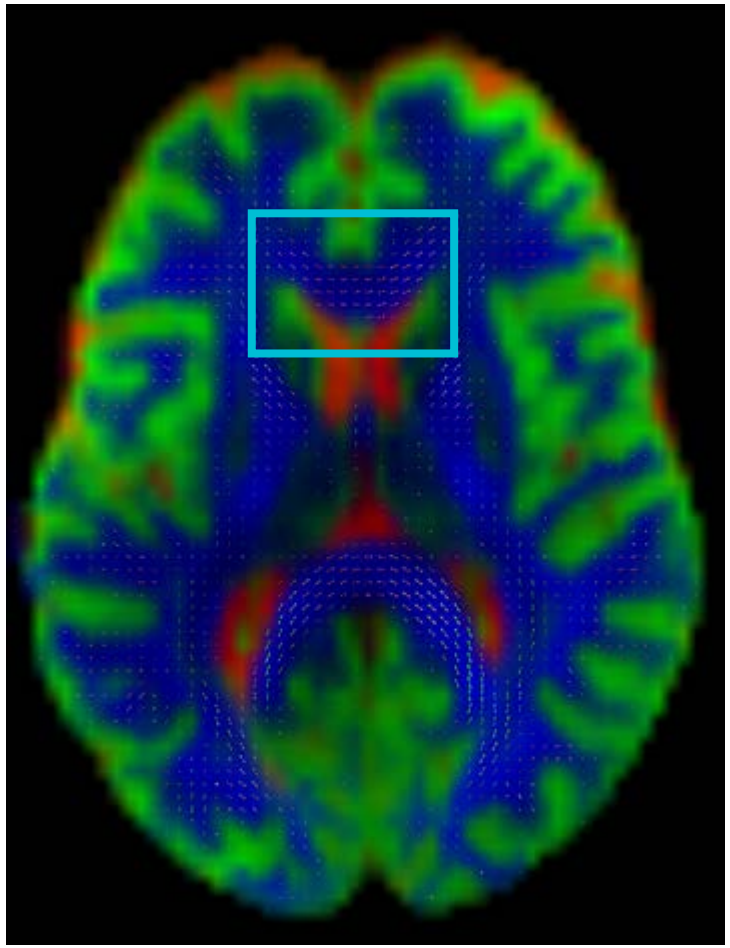
- Two distinct fibre orientations
- $S_1(\theta,\phi)$, $S_2(\theta,\phi)$ – diffusion weighted signal attenuation
- $f_1$,$f_2$ – volume fractions

- Overall diffusion weighted signal attenuation

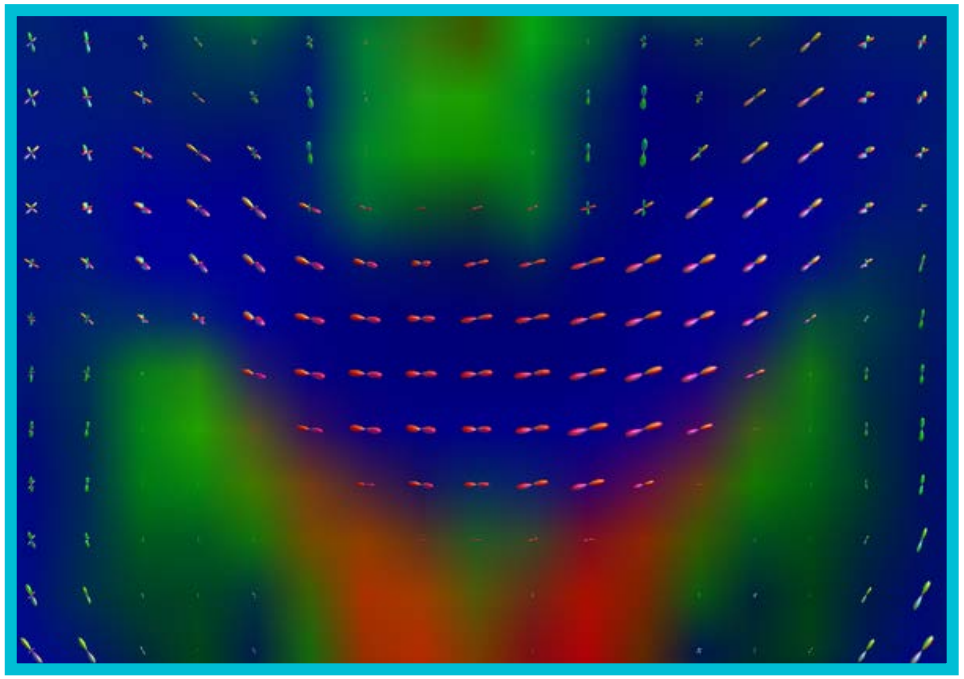
- Axially symmetric response function describing the signal attenuation measured for a single fibre population.

- Fibre orientation density function describing the fibre orientations present in the voxel

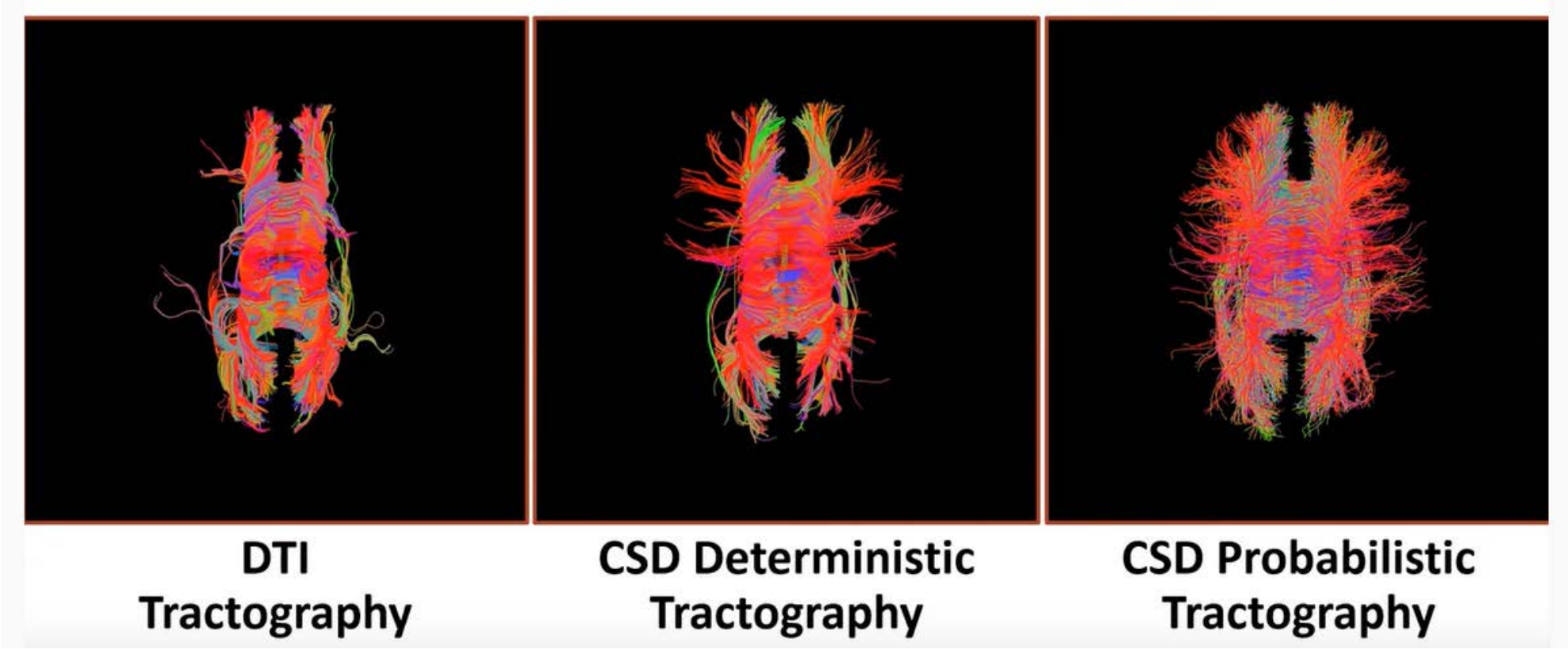
# Constrained Spherical Deconvolution (CSD)



White matter
Grey matter
CSF



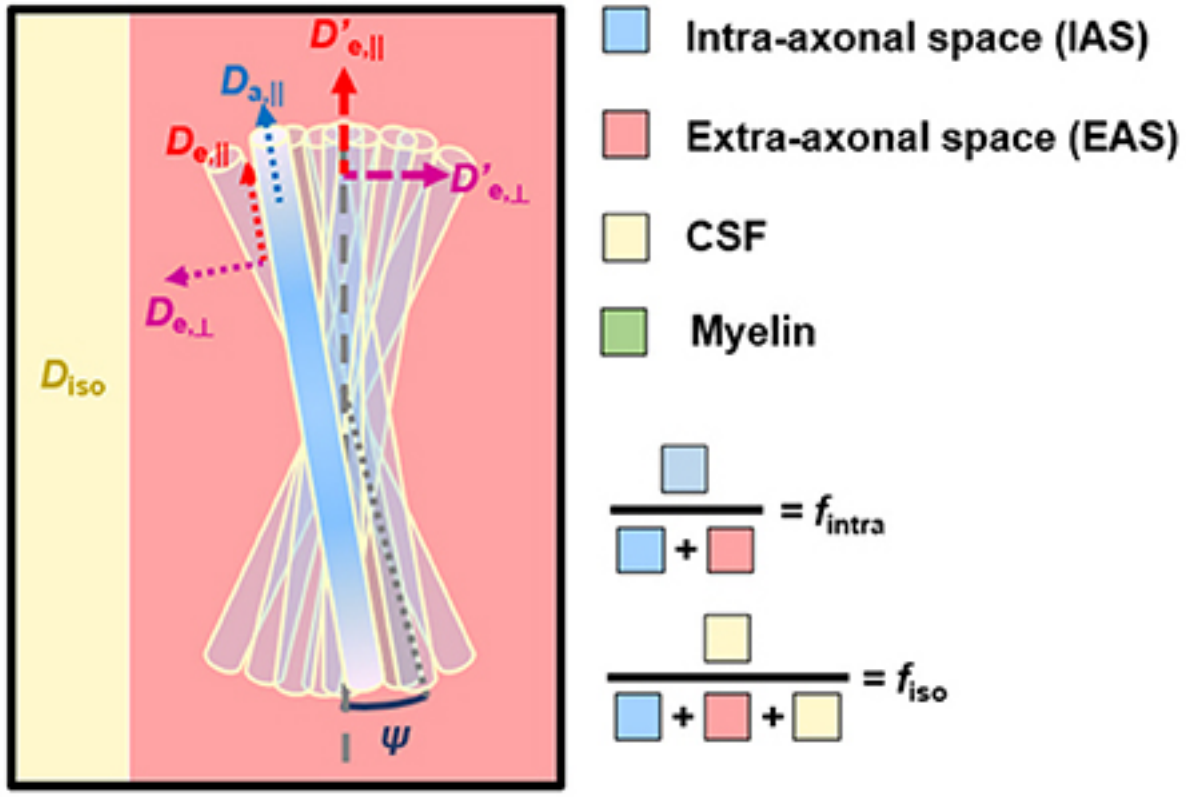
# Constrained Spherical Deconvolution (CSD)




From Gabriel Girard, DIPY tutorial 2021

# Diffusion MRI and Microstructure

# Modelling multiple diffusion compartments




Intra-axonal space (IAS)

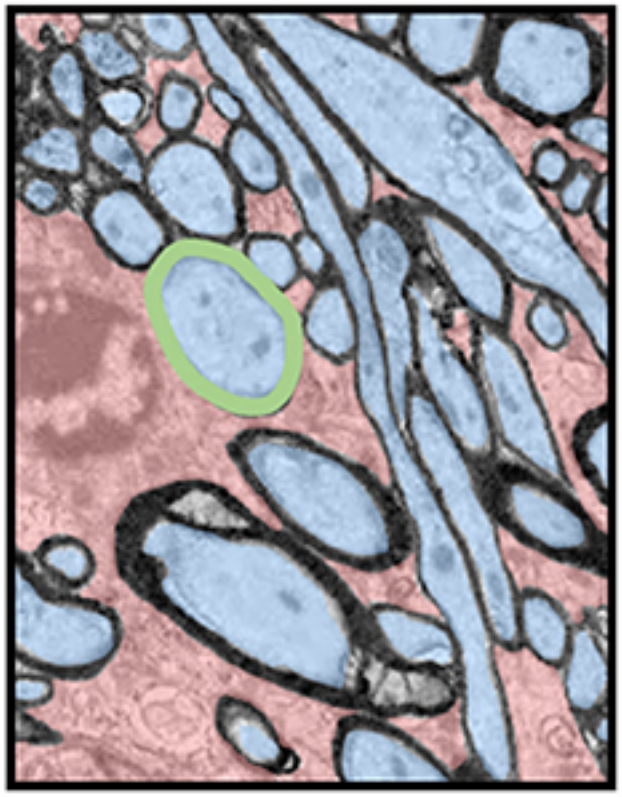
Extra-axonal space (EAS)

CSF

Myelin

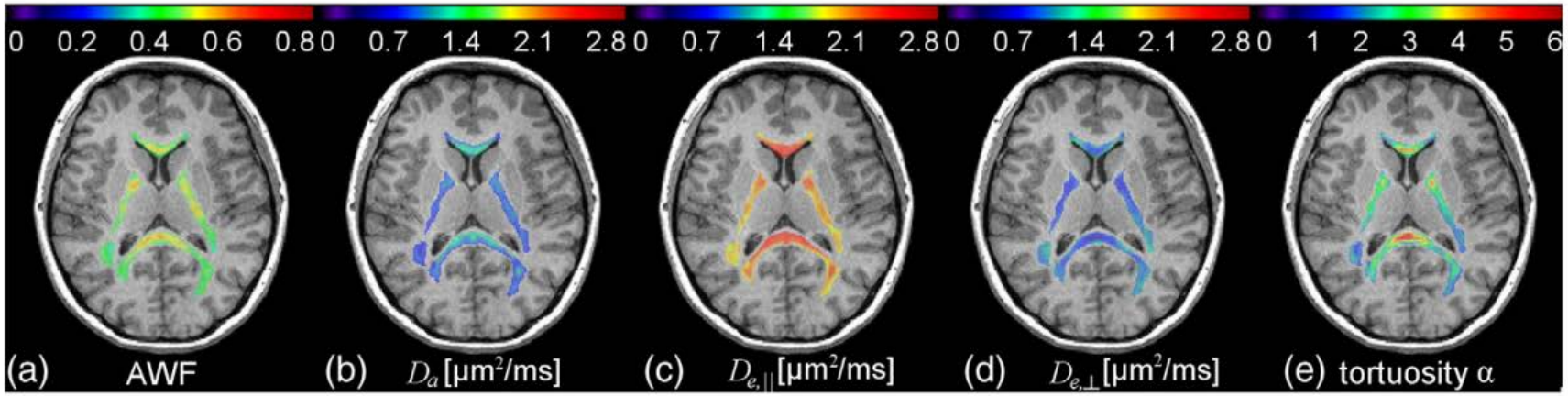
$= f_{intra}$

$= f_{iso}$



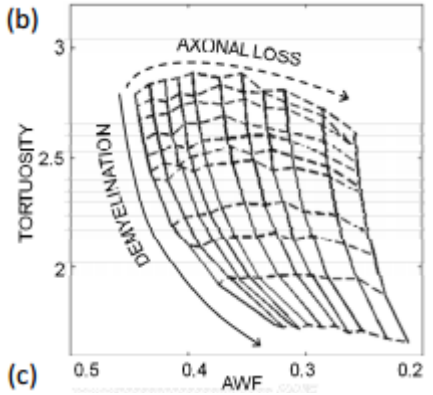
# White Matter Tract Integrity (WMTI)

- Introduced by Fieremans et al. (2011).



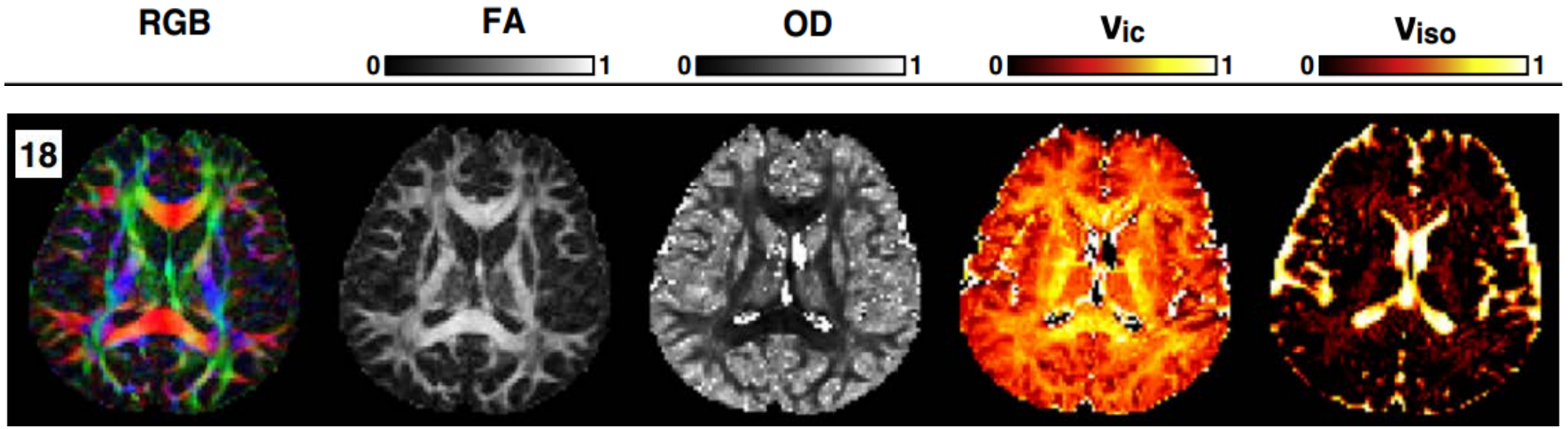

- AWF and tortuosity differentiate between axonal loss and demylination (Fieremans et al. 2012).

- Typical acquisition time: 10-15minutes (usually two b-values in the range 1000-2500 s/mm$^2$ x 30-60 directions).



# Neurite Orientation Dispersion and Density Imaging (NODDI)

- Introduced by Zhang et al. (2012).




- Typical acquisition time: **30 minutes** (b=711s/mm$^2$ x 30 dir, b= 1000 s/mm$^2$ x 30 dir, b=2000s/mm$^2$ x 60 dir, and b=2855 s/mm$^2$ x 60 dir).

# Summary

- Tractography is a popular method used to reconstruct white matter fibre pathways.
- Easy to run, with multiple methods and software packages to choose from.
- HOWEVER, this technique is severely affected by false positives and spurious findings, and results should be interpreted with scepticism.
- Advanced diffusion MRI acquisitions and modelling beyond DTI allows us to model multiple fibre orientations and multiple tissues types.

MRC Cognition and Brain Sciences Unit

UNIVERSITY OF CAMBRIDGE

# Thank you

Advanced Diffusion MRI (Marta Correia) - Feedback
https://www.surveymonkey.com/r/JG8VYS7