# Absolute Beginner's Guide to Neuroimaging Methods - Diffusion Analysis

David Raffelt, PhD.
Florey Institute of Neuroscience and Mental Health
david.raffelt@florey.edu.au

## Highlights

- Tissue properties can be extracted from diffusion-weighted MRI by fitting a model to the measured data within each voxel
- Diffusion MRI models provide two types of tissue properties:
    1. Fibre orientations
    2. Quantitative properties (e.g. density, axon diameter, dispersion)
- The diffusion tensor model is only valid in voxels with a single population of fibres
- Higher-order models are required to derive biological meaningful information from voxels containing multiple fibre populations
- Fibre tractography is a technique to estimate the trajectory of white matter pathways
- Tractography streamlines can be used for identifying regions of interest, connectivity analysis and grey matter parcellation
- Analysis of quantitative measures can be performed at different scales: whole-brain, region of interest, voxel-level

## Target Audience

This talk is designed for clinicians, scientists, technologists and engineers who wish to gain a broad overview of diffusion MRI analysis methods.

## Outcomes

This talk will allow the attendee to identify different methods for analysing diffusion-weighted MRI, describe data and modelling requirements, as well as their advantages and disadvantages.

## Overview

Diffusion-weighted MRI (DWI) exploits the interaction of diffusing water molecules and tissue microstructure to obtain macroscopic information about tissue properties. The previous talk will describe how the MRI signal is sensitised to diffusion along a particular orientation by applying a magnetic field gradient. By acquiring images with a number of different gradient orientations, information about the extent and shape of diffusion within each voxel can be obtained.

### Models

To derive biologically meaningful information from DWI, a model is usually fit to the data acquired within each voxel. The previous presentation will introduce the most commonly used model: the diffusion tensor (i.e. diffusion tensor imaging, DTI). This talk will begin with a discussion on limitations of the diffusion tensor[1,2], focusing on issues with its interpretation in voxels that contain multiple-overlapping fibre bundles (also known as crossing fibres). It is important for diffusion MRI beginners to understand the limitations of DTI given the extensive DTI literature, prevalence of white mater voxels containing crossing fibres[3], and ready availability of vendor-supplied DTI processing software.

Given the limitations to the diffusion tensor, I will then discuss some higher-order models that more accurately model white matter in regions with crossing fibres[4–8]. Higher-order models can resolve multiple fibre orientations within a voxel, and can provide fibre-bundle-specific quantitative information[7,9].

**Tissue Properties**

The remainder of the talk will be split into two sections, with each covering analysis methods that utilise the two different types of information available from DWI (Fig. 1).

1. Fibre orientations
2. Quantitative measures (e.g. density, axon diameter, dispersion)

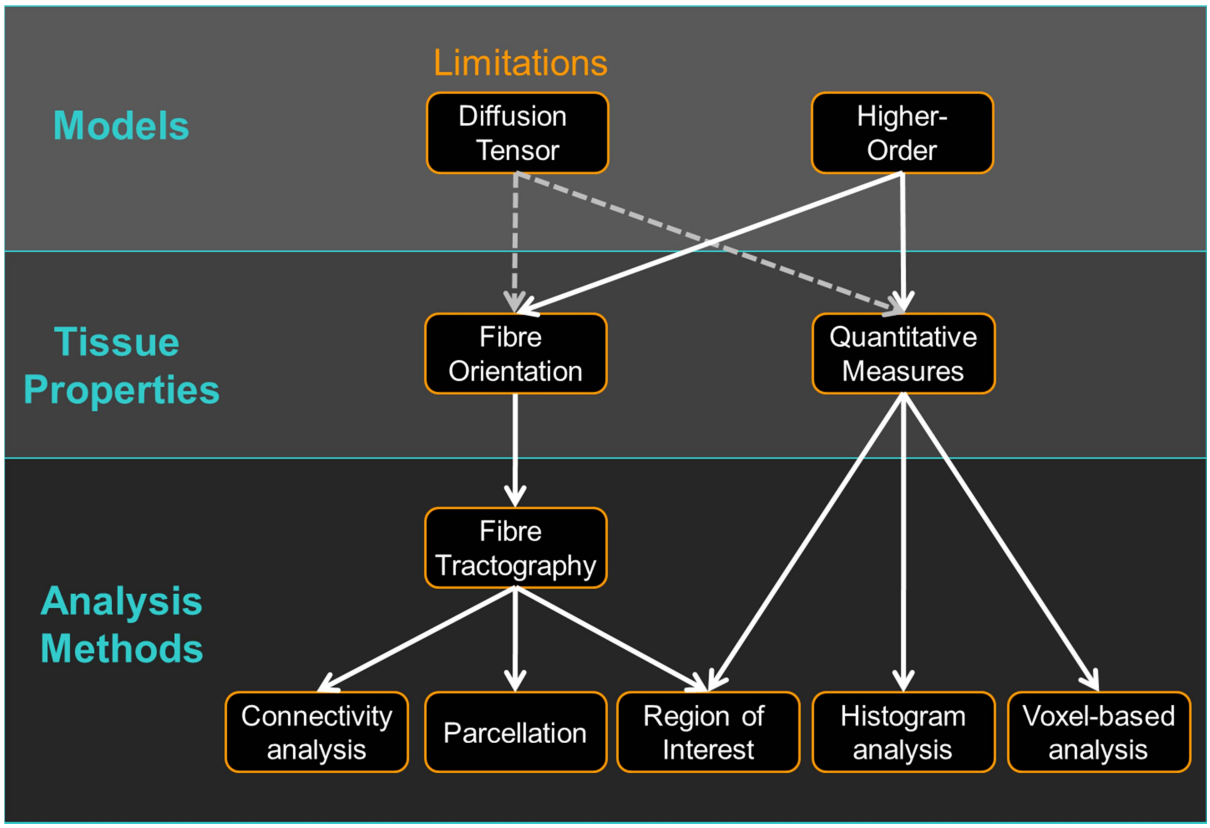


Figure 1.Talk overview

**Tractography-based Analysis Methods**

The first section will introduce how fibre orientation information within each voxel can be used to estimate the trajectory of fibre pathways (a method known as ***fibre tractography***)[6]. Fibre tractography can be accomplished using two different approaches:

1. Targeted tractography (involving a seed, include and exclude regions)
2. Whole-brain tractography

A brief overview of typical fibre tractography applications will be given. The simplest application of tractography is to use tractography-derived streamlines to define a bundle or ***region of interest***. Regions can be identified using targeted tractography or by automatic clustering of whole-brain tractography streamlines. The location of specific regions/bundles can be beneficial in applications such as neurosurgery, and to enable region of interested based group comparisons of quantitative tissue properties.

The second tractography application discussed, called ***connectivity analysis***, is an area that has gained momentum in recent years. This talk will cover the basics principles of whole-brain structural connectivity analysis via generation of a fibre tractography-based connectivity matrix[10]. Potential limitations and pitfalls will also be covered[11,12].

Tractography-derived connectivity information can be used for ***parcellation*** of cortical and sub-cortical grey matter. An example of thalamic parcellation will be given based on voxel-level connectivity to different cortical regions[13].

**Analysis of Quantitative Measures**

The second section of this talk will give an overview of different approaches used to analyse quantitative measures. Region of interest based comparisons of quantitative measures will be covered in the previous section. I will give a brief overview of ***histogram analysis***[14], an approach that is sensitive to subtle diffuse changes at the cost of spatial specificity. Finally, I will outline the basic steps required to perform whole-brain ***voxel-based analysis***[15], including image registration, smoothing, and the need to correct for multiple comparisons.

## References and Further Reading:


1. Assaf Y, Pasternak O. Diffusion tensor imaging (DTI)-based white matter mapping in brain research: a review. J Mol Neurosci. 2008;34(1):51–61.

2. Tournier J-D, Mori S, Leemans A. Diffusion tensor imaging and beyond. Magn Reson Med. 2011 Jun;65(6):1532–1556.

3. Jeurissen B, Leemans A, Tournier J-D, Jones DK, Sijbers J. Investigating the prevalence of complex fiber configurations in white matter tissue with diffusion magnetic resonance imaging. Hum Brain Mapp. 2013 Nov;34(11):2747–2766.

4. Wedeen VJ, Hagmann P, Tseng W-YI, Reese TG, Weisskoff RM. Mapping complex tissue architecture with diffusion spectrum magnetic resonance imaging. Magn Reson Med. 2005;54(6):1377–1386.

5. Tuch DS. Q-ball imaging. Magn Reson Med. 2004;52(6):1358–1372.

6. Behrens TEJ, Berg HJ, Jbabdi S, Rushworth MFS, Woolrich MW. Probabilistic diffusion tractography with multiple fibre orientations: What can we gain? NeuroImage. 2007 Jan 1;34(1):144–155.

7. Assaf Y, Basser PJ. Composite hindered and restricted model of diffusion (CHARMED) MR imaging of the human brain. NeuroImage. 2005 Aug 1;27(1):48–58.

8. Tournier JD, Calamante F, Connelly A. Robust determination of the fibre orientation distribution in diffusion MRI: Non-negativity constrained super-resolved spherical deconvolution. NeuroImage. 2007 May 1;35(4):1459–1472.

9. Raffelt D, Tournier J-D, Rose S, et al. Apparent Fibre Density: a novel measure for the analysis of diffusion-weighted magnetic resonance images. NeuroImage. 2012 Feb 15;59(4):3976–3994.

10. Hagmann P, Cammoun L, Gigandet X, et al. Mapping the structural core of human cerebral cortex. PLoS Biol. 2008 Jul 1;6(7):e159.

11. Jones DK, Knösche TR, Turner R. White matter integrity, fiber count, and other fallacies: the do's and don'ts of diffusion MRI. NeuroImage. 2013 Jun;73:239–254.

12. Smith RE, Tournier J-D, Calamante F, Connelly A. SIFT: Spherical-deconvolution informed filtering of tractograms. NeuroImage. 2013 Feb 15;67:298–312.

13. Jbabdi S, Woolrich MW, Behrens TEJ. Multiple-subjects connectivity-based parcellation using hierarchical Dirichlet process mixture models. NeuroImage. 2009 Jan 15;44(2):373–384.

14. Zhou Y, Lin F, Zhu J, et al. Whole brain diffusion tensor imaging histogram analysis in vascular cognitive impairment. J Neurol Sci. 2008 May 15;268(1-2):60–64.

15. Cercignani M. Strategies for Patient-Control Comparison of Diffusion MRI Data. In: Jones DK, editor. Diffus MRI Theory Methods Appl. USA: Oxford University Press; 2010. p. 465–482.