

Diffusion Analysis Using *MRtrix*

Analyze This! Practicalities of fMRI & Diffusion Data Analysis

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Highlights

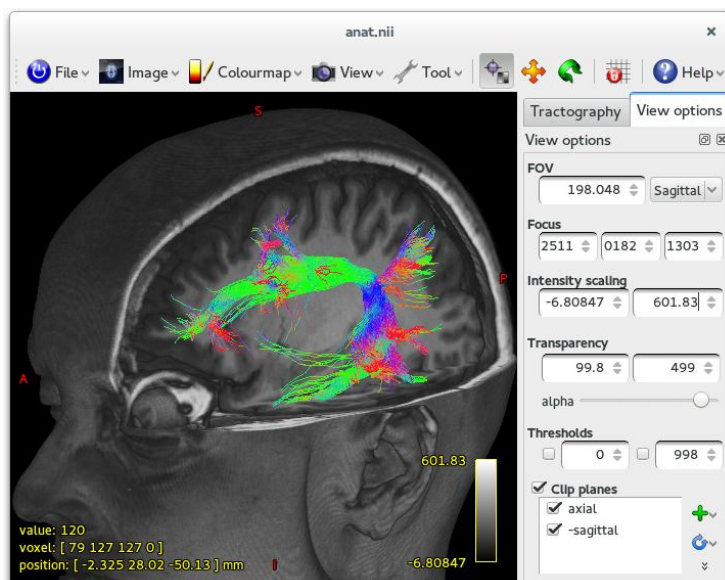
- High-quality software to perform many types of diffusion analysis
- Based primarily on spherical deconvolution
- Designed with a particular focus on performance and usability
- Can be installed on all major operating systems

Target audience: Scientists and clinicians interested in using the MRtrix software package to perform state-of-the-art tractography and other advanced diffusion MRI analyses.

Purpose: To provide an overview of the types of analyses that can be performed within *MRtrix* (more specifically, *MRtrix3* (1)), how these analyses can be performed, and outline the design principles behind the software.

Introduction

The field of diffusion MRI has expanded massively since its early days, with the introduction of the diffusion tensor (2,3) over 2 decades ago, to the more advanced higher-order models in use today (reviewed in 4). A number of software packages are now available, each implementing a subset of the vast number of techniques proposed to date. *MRtrix* (5,6), along with its more recent version *MRtrix3* (1), is a collection of tools to perform analysis of diffusion MRI using or building on spherical deconvolution (7), particularly the non-negativity constrained version of the algorithm (8). Here, we focus on the newer *MRtrix3* (1) release, since this version includes the most recent developments.



MRView, the viewer included with MRtrix3, showing a volume render of an anatomical scan with two clip planes, to reveal a directionally-encoded colour rendering of a delineation of the arcuate fasciculus, produced using constrained spherical deconvolution and the iFOD2 probabilistic streamlines fibre-tracking algorithm.

Features

MRtrix3 is written almost entirely in C++, using multi-threading throughout for maximum performance. It is primarily command-line driven, allowing for easy scripting and chaining of commands via Unix pipes. It provides native support throughout for DICOM, NIfTI, and variety of other formats (including some native

to *MRtrix*). It can be installed on MicroSoft Windows, Mac OS X, and most recent GNU/Linux distributions, and is available free of charge under an open-source license (the GNU General Public License, version 3).

MRtrix3 also includes a modern viewer for image, FOD, and tractogram display. It is based on OpenGL 3.3 and Qt, and includes tools to edit ROIs, overlay images, and to display FODs, streamlines, and vector fields. It also includes a full-featured ray-tracing volume renderer, as shown in Figure 1.

Technologies included in MRtrix

The concept of spherical convolution (7) is core to MRtrix. In this framework, the DW signal measured as a function of orientation is modelled as the convolution of a canonical single-fibre response function (i.e. the diffusion profile for a typical straight population of fibres), with the fibre orientation distribution (FOD; alternatively, the fibre orientation distribution function, fODF). The FOD can be used for a number of applications, including first and foremost the estimation of fibre orientations using spherical deconvolution (7,8), providing the information required for tractography (5,9) and related technologies (10,11), but also to refine the tractography results and imbue them with more quantitative properties (12), to drive non-linear image registration algorithms (13), to perform direction-specific voxel-based analyses (14), and to estimate microstructural features such as the fibre (or more generally *neurite*) density (14). These types of analysis are all implemented within the *MRtrix3* (1) software package; the original *MRtrix* (6) package provides only a core subset of these functionalities.

Constrained spherical deconvolution (CSD): spherical deconvolution is an ill-posed problem, prone to noise amplification (7). Non-negativity constrained spherical deconvolution (8) was proposed to address this issue, and has proved very successful even with relatively modest data (15,16). *MRtrix3* provides a fast and robust implementation of CSD.

Probabilistic and deterministic tractography: both *MRtrix* and *MRtrix3* include algorithms for probabilistic tractography based on the FOD, which have been shown to perform well (9,17). In MRtrix3, the default algorithm is the 2^{nd} -order integration over fibre orientation distributions (iFOD2) approach (18), designed to minimise biases inherent in first-order methods in curved regions. Tractography can be performed using regions of interest (e.g. for neurosurgery planning (9)), or over the whole brain, which opens up promising applications (see below).

Anatomically-constrained tractography (ACT): it is well known that tractography is prone to false positives, particularly probabilistic approaches. The anatomically constrained tractography framework (11) is designed to identify biologically implausible streamlines and discard them from the output, and hence maximise the biological accuracy of the resulting streamlines.

Spherical deconvolution informed filtering of tractograms (SIFT): it is now clear that streamlines-based tractography algorithms do not produce quantitative results directly: streamline counts are not representative of the actual white matter fibre count (19). SIFT addresses this by modifying an input whole-brain tractogram such that the final streamline counts are in proportion to the FOD data, removing many of these biases and ensuring that the number of streamlines connecting different regions is proportional to the amount of white matter they represent. The streamline counts obtained after SIFT are therefore ideally suited to connectivity analyses, and the emerging field of connectomics.

Track density imaging (TDI) / Track-weighted imaging (TWI): whole-brain tractograms can be used to produce striking high-resolution images of the brain (10), which can be used to observe anatomical details not visible using other techniques (20). This approach can also be used in combination with other types of

data to produce high-resolution images weighted by a combination of the streamlines and their properties as measured along their lengths (21), using a very general framework with interesting potential applications (22).

Apparent fibre density (AFD): it can be shown that the FOD amplitude is directly related to the amount of white matter it corresponds to. In other words, the FOD provides a direct (albeit relative) measure of apparent fibre density (a.k.a. *neurite* density). This forms the basis of a *fixel*-based analysis framework¹, allowing the detection of group-wise differences or correlations in both space *and* orientation: differences can be ascribed to a specific fibre population within the regions identified as significant. A full-blown AFD analysis requires a number of non-trivial steps, including: non-linear registration of the FOD images to a group template, preferably using the FODs themselves to drive the registration (13), with the appropriate reorientation (23) and modulation (14) of the FODs; computation of fixel-wise statistics using connectivity-based fixel enhancement (24) to boost statistical power; and permutation testing to assign significance (14). This approach has been applied in a number of populations with promising results (25–28).

Conclusion

MRtrix provides tools to allow many types of advanced diffusion MRI analysis, including robust tractography suitable for many types of connectivity analyses, and *fixel*-based group analyses. It is designed with a particular focus on performance and usability, and is being used successfully by researchers in both scientific and clinical settings.

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¹ fixel: a fibre population within a voxel

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