

# TORTOISE: an integrated software package for processing of diffusion MRI data

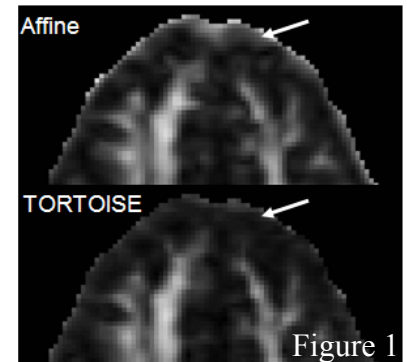
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**Introduction:** Diffusion MRI modalities, including diffusion tensor imaging (DTI), are commonly used for both research and diagnostic purposes. Diffusion MRI data suffer from a number of artifacts, such as bulk subject motion, eddy current distortion, and susceptibility induced EPI distortion [1-2]. Appropriate pre-processing of diffusion weighted images and robust processing of diffusion tensor data is vital for accurate quantitative analysis. Thus, there is a need for reliable and flexible software packages to accomplish these goals. Here we present a comprehensive tool for diffusion MRI data correction, as well as for tensor calculation. The package is called TORTOISE (Tolerably Obsessive Registration and Tensor Optimization Indolent Software Ensemble); it is non-commercial, and is freely available for download at [www.tortoisedi.org](http://www.tortoisedi.org).

**About TORTOISE:** TORTOISE can be run on both Linux and Mac platforms. It is composed of two modules named DIFF PREP and DIFF CALC. DIFF PREP aims at having a robust and reliable image registration-based correction for motion, eddy current distortion and EPI distortion. DIFF CALC offers tools for estimation of the tensor, as well as many tensor derived metrics, and ROI utilities. The software is highly customizable to the user's individual needs, and also provides the ability to export both diffusion weighted images (DWIs) and the tensor quantities to several other commonly used software packages. Below we highlight some of the features offered by TORTOISE that are not generally available with other packages.

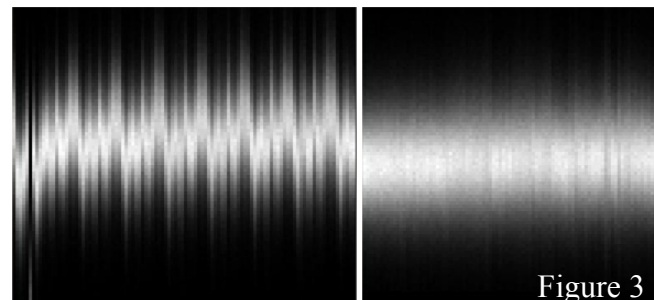
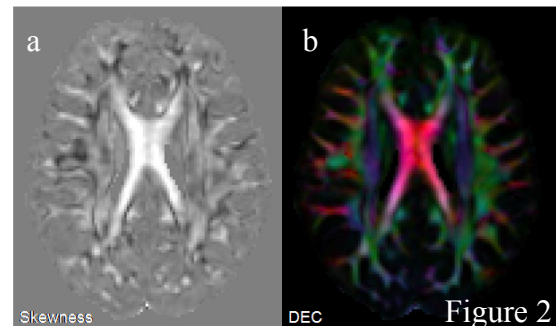
## DIFF PREP

- Single pipeline for correction of all DWI artifacts including motion, eddy distortion and EPI  $B_0$ , and concomitant field distortions. All deformations are calculated and combined to enable the image correction to be applied with a single interpolation step. This minimizes interpolation errors in the corrected data.
- Inclusion of a quadratic term for eddy current distortion correction. Eddy current correction is usually performed using an affine deformation model; however, it is known that for complete correction higher order terms need to be included [1]. An example of the improved results achieved by TORTOISE vs. software that uses a simple affine model is shown in Figure 1. The affine corrected image contains a rim of artifactually high anisotropy (arrow) that is not present in data corrected using TORTOISE.
- EPI distortion correction performed using registration to a structural MRI target [2], without the need of  $B_0$  field mapping. The best structural target for this correction is a T2-weighted scan with fat suppression that can typically be acquired in about 2 minutes.
- Reorientation of the corrected DWIs into any desired standard space.
- Appropriate reorientation of the b-matrix after motion correction and reorientation to standard space [1,3].



## DIFF CALC

- Properly weighted linear and non-linear least squares methods of tensor estimation.
- All standard tensor derived metrics, plus other useful metrics including e.g., 1) a measure of the degree of oblateness or prolateness of the diffusion ellipsoid in each voxel based on the skewness of the eigenvalues ((Mean-Median)/Mean) (Fig 2a). In the skewness map, bright voxels correspond to regions of prolate ellipsoids (cigars); dark voxels correspond to regions of oblate ellipsoids (pancakes). These show interesting architectural features of white matter that are not apparent in standard anisotropy maps, 2) the lattice anisotropy index which is less biased by noise than the commonly used FA [4], 3) Several directionally encoded color (DEC) maps proposed in [5] in addition to the traditional absolute value DEC map (Fig 2b).
- Graphical representation of goodness of fit measures for detecting potential problems in data quality or experimental design. Figure 3 shows one of these tools; each column represents the aggregate histogram of the residuals of the tensor fit for all voxels for each b-matrix. The midline of the vertical axis thus represents a perfect fit and the intensity is proportional to the frequency of the histogram. With simple thermal noise a Gaussian distribution of the residuals is expected and any shift away from the midline will indicate a systematic problem with the fitting. This is demonstrated in Figure 3 where the histogram on the left indicated a systematic problem with the first set of volumes. Upon removal of these volumes, the histogram becomes uniform, and results in an accurate tensor fitting.



**Summary:** TORTOISE is an integrated and flexible software package for processing of DTI data, and in general for the correction of diffusion weighted images to be used for DTI and potentially for high angular resolution diffusion imaging (HARDI) analysis.

**References:** [1] Rohde, GK, et al, MRM 2004. 51(1), p 103-14 [2] Wu, M, et al, MICCAI 2008 11(Pt 2): p321-9 [3] Leemans, A, et al, MRM 2009 61(6): p1336-49 [4] Pierpaoli, C, et al, MRM 1996, 36(6): p893-906 [5] Pajevic, S, et al, 1999, MRM. 42 p526-540