TRACK-DENSITY IMAGING & NOISE: WHEN SUPER-RESOLUTION *QUALITY* DOES NOT YIELD *ACCURACY*

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Introduction: Track-density imaging (**TDI**) **[1][2]** was recently proposed as a means of obtaining super-resolution anatomical images from (lower resolution) diffusion weighted imaging (**DWI**) datasets. A typical TDI volume is basically a discretisation of a high number of tracks (resulting from fiber tracking), by counting the number of tracks in each voxel of a high resolution grid. Meaningful anatomical structures beyond the original voxel-scale might then be recovered. In this work, the effect of varying noise in the original data on the final TDI outcome is investigated *in vivo* and *in silico*, in terms of intensities as well as recovered or discovered structures.

Data: A single healthy subject was scanned using a Siemens 3T scanner. At a 2.5*mm* isotropic voxel size, 10 non-DWI volumes (averaged) were acquired, as well as DWI volumes for 75 uniformly distributed gradient directions (b = 2800 *s/mm²*). For the *in silico* data, the same dataset as specified in **[2]** was used: "Phantom A", available from the *Numerical Fibre Generator* website (http://www.brain.org.au/software/), sampled at 60 gradient directions (b = 3000 *s/mm²*). The voxel size was defined to be 2.5*mm*, in order to be consistent with the real data.

Noise realizations: 100 different noise realizations of both the real and phantom data were generated. For the real data, this was achieved using the residual bootstrap with correction for leverage, as detailed in **[5]**. For the phantom data, 100 realizations of random Rician noise at a signal-to-noise ratio of 17 were simply added.

TDI: TDI was applied to all 100 real and 100 phantom datasets as an automated pipeline. This pipeline starts by applying constrained spherical deconvolution (**CSD**), using a spherical harmonic order of 8. Next, 6 000 000 tracks are generated for each dataset by probabilistic full-brain/phantom tracking, using these parameters: step-size = 0.2*mm*, min. radius of curvature = 1*mm*, min. track length = 15*mm* (5*mm* for the phantom), max. track length = 300*mm*, min. FOD amplitude to initiate tracks = 0.2. Tracks are terminated if the FOD amplitude drops below 0.1 or when leaving a predefined brain mask (this mask was made in advance and is kept fixed for all runs of the pipeline). Finally, the number of tracks in each voxel of a new 0.5*mm* isotropic grid is calculated. This results in high resolution TDI volumes (2.5*mm* → 0.5*mm* isotropic). The *MRtrix* package (http://www.brain.org.au/software/) was used to perform the full pipeline on all datasets.

Results: In Fig.1, some maps are presented. The mean TDI (**μTDI**) is obtained by calculating the voxel-wise average across the 100 TDI's. The coefficient of variation (**CoV**) is defined as **σ/μ**, whereas the coefficient of dispersion (**CoD**) equals **σ²/μ**. The "reachability count" (**#R**) was defined in each voxel as the number of TDI volumes where the TDI intensity is greater than 0. Voxels reached by all (100) TDI's are colour-mapped to blue. The other maps (μTDI, CoV, CoD) are windowed for visual contrast. In Fig.2, the region of the thalamus is shown for 3 of the TDI's. For comparison of patterns, they are also overlaid by use of different colour channels. Possible structural ROI's are "extracted" by a simple threshold. Using the same colour channels, these ROI's are also overlaid on the μTDI. For the phantom data, we show directionally encoded colour (**DEC**) TDI maps **[1][2]** of 10 noise realizations in Fig.3. ROI's are also "extracted" at 2 threshold levels, and overlaid on the TDI's.

Conclusion: The CoV is the highest at the cortex and in structures like (amongst others) the caudate nucleus, the putamen and (parts of) the thalamus. This corresponds mostly to regions of lower μTDI and #R below the full 100. The CoD map shows quite a distinct pattern. The thalamus (amongst other regions) shows up very brightly. The CoD was larger than 1 everywhere, which indicates overdispersion. A large variation of patterns across different regions of all TDI's was observed; Fig.2 is only one of many examples. Playing a DEC TDI series such as the one in Fig.3 as a movie also showed striking differences. The potential pitfall, however, lies in the fact that *each single map looks perfectly plausible*. Even though many of the discovered patterns might (mostly) be caused by noise (rather than true anatomical structure), ***they do not give the traditional impression of noise!*** Noise in the original data has local, as well as "long distance" effects on some of the intensities and patterns that arise. TDI maps are not robust for quantification (as also stated in **[4]**). The findings of this work indicate however that great caution is also advised when using TDI's as super-resolution anatomical maps. New strategies (such as **[3]**) show promising results in being more robust (but also show less detailed contrast). The work in **[4]** effectively opens up the path to an endless family of new track-weighted maps, some of which *might* be more robust; but again this requires further investigation. One of the properties of such track-weighted maps in general (and TDI in particular) is that they easily "hide" the traditional pattern of noise from the user, giving them a potential impression of high *quality* images. *Accuracy*, however, does not come for free: some observed structures might in fact be caused more by this "hidden noise", rather than by true anatomy. Tools such as bootstrapping, combined with maps of CoV, CoD and #R can be of great value as indicators of regions where caution is due.

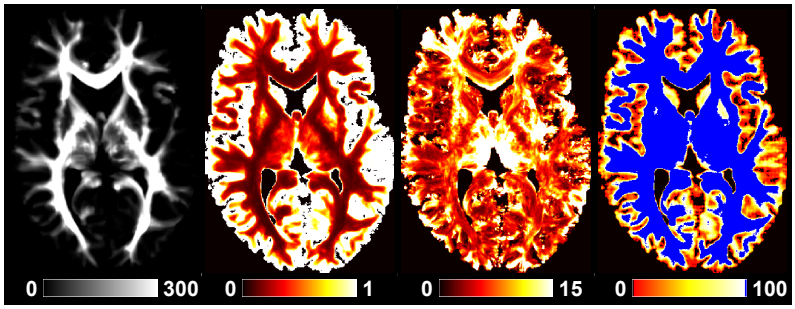

Fig.1: Maps of **μTDI**, **CoV**, **CoD** and **#R** (across TDI's of 100 noise realizations).

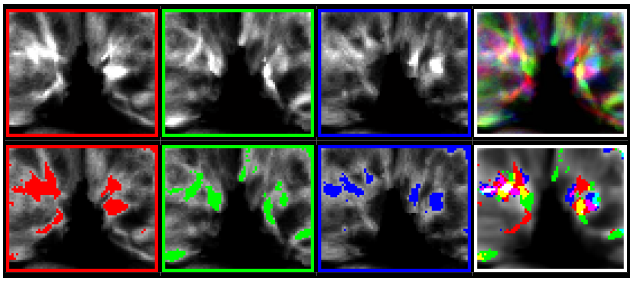

Fig.2: ***First row***: thalamus region in 3 noise realized TDI's + combined. ***Second row***: ROI's from thresholding *first row* + combined (on μTDI).

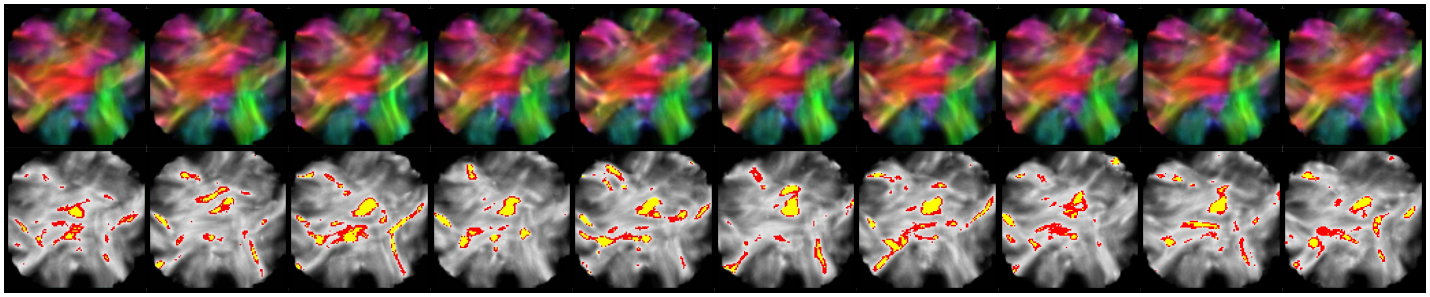

Fig.3: ***First row***: DEC TDI's of 10 noise realizations of the phantom. ***Second row***: ROI's at 2 threshold levels (*red* and *yellow*) overlaid on the corresponding TDI's.

References: **[1]** Calamante F et al: Track-density imaging (TDI): Super-resolution white matter imaging using whole-brain track-density mapping. NeuroImage 53(4), 1233-1243 (2010). **[2]** Calamante F et al: Track density imaging (TDI): Validation of super resolution property. NeuroImage 56(3), 1259-1266 (2011). **[3]** Pannek K et al: The average pathlength map: A diffusion MRI tractography-derived index for studying brain pathology. NeuroImage 55(1), 133-141 (2011). **[4]** Calamante F et al: A generalised framework for super-resolution track-weighted imaging. NeuroImage (in press) (2011). **[5]** Jeurissen B et al: Probabilistic Fiber Tracking Using the Residual Bootstrap with Constrained Spherical Deconvolution. Human Brain Mapping 32(3), 461-479 (2011).