

The effect of tractography algorithm on human cortical connectome reconstruction by diffusion weighted MRI

Matteo Bastiani^{1,2}, Rainer Goebel¹, and Alard Roebroeck¹

¹Department of Cognitive Neuroscience, Faculty of Psychology and Neuroscience, Maastricht University, Maastricht, Netherlands, ²Forschungszentrum Jülich, Jülich, Northrhine-Westfalen, Germany

INTRODUCTION

Reconstructing the macroscopic human cortical connectome [1] by Diffusion Weighted Imaging (DWI) is a challenging research topic that has gained a lot of attention recently. The connectome is often abstracted into a graph where cortical patches are nodes and white-matter connections are edges [2]. We center this investigation on three semi-independent distinctions within the large set of available diffusion models and tractography methods (see Table 1): i) single fiber direction versus multiple directions in the intra-voxel diffusion model, ii) deterministic versus probabilistic tractography and iii) local versus global measure-of-fit of the reconstructed fiber trajectories. We evaluate the effects on the obtained cortical connectivity matrix in terms of connection density, small-worldness and cortical connection hubs.

METHODS

MR Data Acquisition and preprocessing

A Siemens 3T MAGNETOM Allegra MR scanner (40 mT/m, 400T/m/s head gradient, 8Ch RF-coil) was used to acquire whole brain diffusion-weighted scans (doubly-refocused bipolar PGSE EPI sequence, 120 diffusion directions; b-value = 3000 s/mm², 11 b = 0 volumes, 52 axial slices, 2.5mm cubic voxels) and a 3D MPRAGE scan for white/grey matter (WM/GM) boundary surface reconstruction (1mm cubic voxels) in two volunteers. FSL ecc was applied. All directional modeling and tractography was performed in 'native' diffusion data space. Using the WM/GM boundary ~30k unique diffusion data voxels were identified that were then mapped to 4k random equi-surface WM/GM patches.

Diffusion models and Tractography algorithms

Two models of intra-voxel diffusion were fitted: diffusion tensors (DTs) and constrained spherical deconvolution (CSD) fiber orientation distributions (FODs [3]) with up to three main fiber directions fitted [4]. All algorithms use the same white matter masks (FA 0.2 and 0.1), step size (1 mm for all the local methods, 5x5x5 neighbor size for SDG and MDG) and angular thresholds (30 and 90 degrees). SDD and MDD streamlines connecting any voxel mapped to one parcel to any voxel mapped to another, connects the two parcels in the final adjacency matrix. SDP, MDP, SDG and MDG two parcels were connected if any non-zero visitation count or percentile graph weight connecting any voxel in one parcel to any voxel in another was present.

RESULTS

Figure 1 shows the small-worldness index of the final 4k-node adjacency matrices for all methods. It can be seen that small-worldness (a coefficient larger than 1) is a very robust phenomenon over all methods. Small-worldness is increased, sometimes dramatically, by: i) increasing probabilistic threshold, ii) going from probabilistic to deterministic tractography iii) increasing FA and decreasing angle thresholds iii) moving from global to local tractography, and iv) moving from multi direction to single direction models. A 'deterministic limit of probabilistic results' effect can be observed for the local methods: the small-worldness for SDD and MDD can be considered to form a 100% limit value for the entire probabilistic threshold curves. Figure 2 shows deterministic streamlines (A) and global paths (B) connecting lateral frontal cortical surface. MDD is more successful in identifying trans-callosal inter-hemispheric projections but shows a sensitivity/specificity trade-off with angle-threshold. SDG and MDG show good sensitivity and specificity at the same liberal thresholds for the same data. The effect of increasing probabilistic threshold is seen to prune paths and decrease connection density (Figure 2B). Figure 2C shows the degree per cortical patch (i.e. the number of other-patch connections) which illustrates how increasing probabilistic thresholds and single direction models intensify connection hubs (i.e. high-degree patches).

Diffusion model	Single-direction		Multi-direction	
	Deterministic	Probabilistic	Deterministic	Probabilistic
Tractography				
Local	SDD: DTI Streamline	SDP: PICo [5]	MDD: CSD Streamline [7]	MDP: iFOD [8]
Global	SDG: DTI Graph [6]		MDG: CSD Multigraph [9]	

Table 1

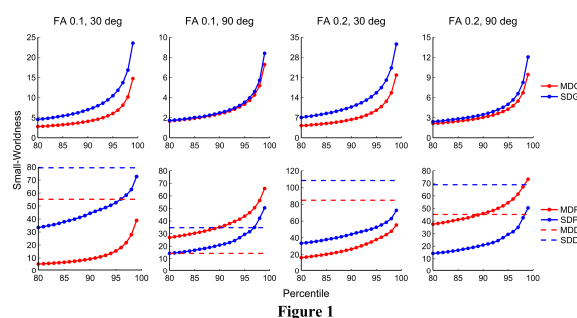


Figure 1

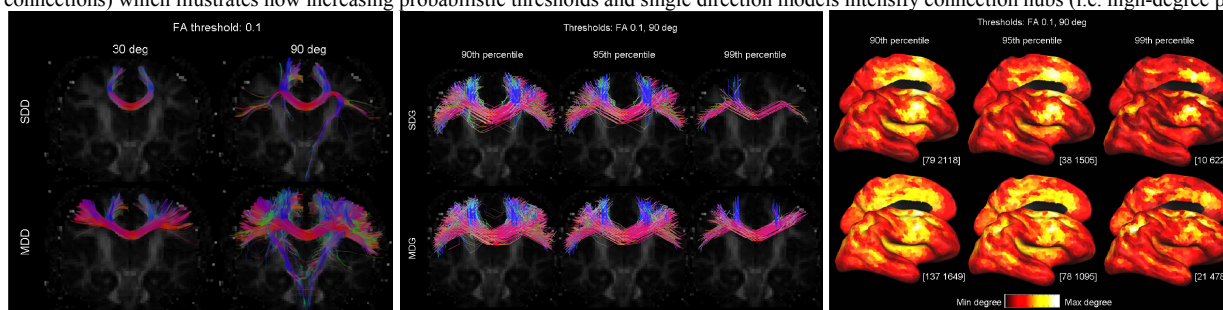


Figure 2

A

B

C

DISCUSSION

There is increasing interest in using graph-based measures such as small-worldness and connection hub indices to diagnose and characterize disease, aging and learning [2]. We show here that the choice of tractography algorithm class along three general dimensions is an important consideration in this endeavor. The choices in Table 1 and in thresholds (FA, angle, probabilistic) can affect the results dramatically, which is crucial for the sensitivity of any studies using these measures as dependent variables and for the validity of study comparisons. Much of the variation is explained by the effect on resulting overall connection density and choices could be lead by sensitivity and specificity in identifying true connections (Figure 2A&B), which is inherently difficult with a lack of a gold standard for the entire human brain.

REFERENCES: [1] Sporns et al., PLoS Comput Biol 1:e42 (2005). [2] Sporns & Bullmore, Nat. Rev. Neuroscience 10(3):186-198 (2009). [3] Tourmier et al., Neuroimage 35:1459-1472 (2007). [4] Schultz et al., IEEE Trans Vis Comput Graph 14:1635-1642 (2008). [5] Parker et al., JMRI 18:242-254 (2003). [6] Iturria-Medina et al., Neuroimage 36:645-660 (2007). [7] Hagmann et al., PLoS One 2:e597 (2008). [8] <http://www.brain.org.au/software/> [9] Sotiropoulos et al., Neuroimage 49:2444-2456 (2010).