

ADDRESSING THE PROBLEM OF PATH-LENGTH DEPENDENCY IN PROBABILISTIC TRACTOGRAPHY – THE ICE-T FRAMEWORK

M. G. Liptrot¹, K. Sidaros¹, and T. B. Dyrby¹

¹DRCMR, MR dept. 340, Copenhagen University Hospital Hvidovre, Hvidovre, Denmark

Introduction

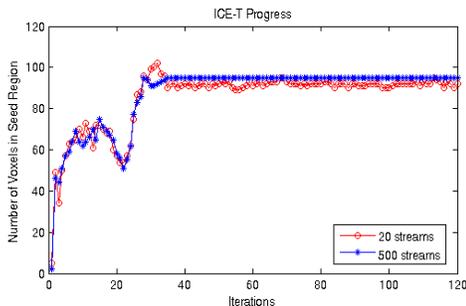
Probabilistic tractography [1] affords a potentially quantitative method for non-invasively generating a “connection probability map”, a frequency measure of successful vs. attempted fibre-tracking trials to remote brain areas from a given seed region. However, one of the limitations with the approach is that of path-length dependency, where the values thus produced are modulated by a gradual decline in the likelihood of successful propagation as the distance from the seed region increases [2]. This bias is unfortunately inherent to the method, as it is derived from a propagation, along a potential fibre, of the very uncertainty per voxel which is required in order to generate the probability maps. Hence, in so favouring short-range connections over longer-range ones, the method’s ability to perform fibre-tracking to distal regions is compromised. Surprisingly, little focus has been directed towards the path-length dependency problem (e.g. [2]). Here, we address the issue with a novel tractography framework, *Iterative Confidence Enhancement for Tractography* (ICE-T). This retains the stages of conventional probabilistic streamlining tractography, but then attempts to overcome the path-length dependency via the introduction of an extra stage, and a subsequent feedback loop to allow iteration of the fibre tracking stage. In this way, the ICE-T framework can be used with any conventional streamlining tractography method. The present study was based on the same DWI dataset acquired on perfusion-fixed mini pig brains recently used to validate conventional probabilistic tractography using in-vivo tracers [4].

Method

Consider the probabilistic tractography analysis framework as a modular processing pipeline with the following stages: (1) acquisition of diffusion-weighted (DW) images; (2) fibre reconstruction; (3) generation of fibre-orientation probability density functions (FO-pdf); (4) fibre tracking: repeated streamlining from a given seed region, via voxelwise sampling of the FO-pdfs; (5) generation of connection probability maps. The non-deterministic nature of probabilistic tractography, and hence also the cause of the path-length dependency, is introduced in stages (3) & (4). Traditionally, to segment a tract emanating from the seed region, the results of (5) are (arbitrarily) thresholded at some appropriate level. Our approach takes its inspiration from the region-growing algorithms commonly used in image processing to obtain segmentation [5]. The principle is simple - the neighbourhood of a given seed region is considered and those voxels which match a user-defined predicate are aggregated within it. Once merged, a feedback loop is followed, and the neighbours of the newly-updated seed region are considered. Hence the region iteratively grows whilst the predicate rule is fulfilled. The ICE-T framework employs a user-specified threshold (here defined as the *ICE-T threshold*) of the connection probability map as a predicate, and supra-threshold voxels are then aggregated into the existing seed region. The loop then iterates, using the new region as a seed, and this process is continued until no more candidate voxels are generated. Hence the ICE-T framework can be seen as an extra stage after (5), with a feedback loop to (4).

Data

Diffusion weighted images were obtained from the perfusion fixed brains on an experimental 4.7T Varian Inova scanner. Postmortem DWI data excludes the well known in-vivo related physiological noise sources whilst retaining the anatomical structures as if in vivo. A b-value of 4009 s/mm² was selected according to [6], with a voxel size of 0.51x0.51x0.50 mm³ (for details [1]). The DWI dataset included 61 dw-directions and 3 non-dw image volumes. Multi-fibre reconstruction, based upon a mixture tensor model of up to two fibre populations [7], was performed. An ROI was hand-drawn in the somatosensory area (in green, Fig 2), and tractography seeded from it using the traditional and proposed methods. The ICE-T method was implemented using both 20 and 500 streamlines per voxel per iteration, with an ICE-T threshold of 0.2. This was then compared against conventional probabilistic tractography, with free-tracking from the same region using 60,000 streamlines. In both cases, the tractography routines utilised the Camino Toolbox [3], whilst the ICE-T framework was implemented in Matlab.



Results

Figure 1 (left) shows the number of voxels segmented out by the ICE-T algorithm using either 20 or 500 streamlines per voxel per iteration. Note the close agreement between the two, and how stability is reached after only 35 iterations. Their spatial agreement is 0.92. Similar results are achieved for different ICE-T thresholds. Figure 2 shows the comparison between ICE-T (20 streams, iteration 35, in blue) and the free-tracking using conventional tractography with 60,000 streamlines (in red, over the blue), with a viewing threshold of 0.1. Note the clear influence of the path-length dependency in the contra-lateral hemisphere compared to the ICE-T result. Previous work [4] has confirmed the existence of such contra-lateral cortico-cortical connections, and also demonstrated the path-length dependency issues incurred by conventional methods when attempting to extract them. The number of streamlines calculated by each method are approximately (60,000 streams x 61 seed voxels) = 3,660,000 for free-streaming, vs (35 iterations x 100 seed voxels, max. x 20 streams) = 70,000 for ICE-T.

Conclusion

The ICE-T algorithm’s use of region-growing encourages homogeneity of the seed region, and we purport that it is this feature which helps to subdue the path-length dependency as observed in conventional probabilistic tractography. As the entire, growing seed region is streamlined at each step, supra-threshold values represent voxels with a higher probability of connection *throughout* the region. Hence the resulting voxels can be interpreted as the group intersection of those with both short-range (i.e. with their neighbours) and long-range (with remote voxels) connection probability. We therefore surmise that the ICE-T framework is a worthwhile alternative to traditional high-number streamlining and indeed can address the problems of path-length dependency, with the additional benefit of requiring fewer calculations. In future, we hope to be able to use the method to enable comparison of connectivity probabilities across subjects.

References

- [1] G. Parker, et al, A framework for a streamline-based probabilistic index of connectivity (PICo) using a structural interpretation of MRI diffusion measurements, *J Magn Reson Imaging*, 18(2), 2003, pp242-54
- [2] D. Morris, et al, Probabilistic fibre tracking: Differentiation of connections from chance events, *Neuroimage* 42, 2008, pp1329-1339
- [3] P. Cook, et al, Camino: Open-Source Diffusion-MRI Reconstruction and Processing, 14th Scientific Meeting of the International Society for Magnetic Resonance in Medicine, Seattle, WA, USA, p. 2759, May 2006
- [4] T. Dyrby et al, Validation of in vitro probabilistic tractography, *Neuroimage*, 37(4), 2007, pp1267-77
- [5] R. Gonzalez & R. Woods, Ch. 7.4, *Digital Image Processing*, 1992, Addison-Wesley
- [6] T. Dyrby et al, Acquiring optimal DWI data for tractography on post mortem brain tissue, *ISMRM 2008*
- [7] G. Parker, D. Alexander, Probabilistic Monte Carlo based mapping of cerebral connections utilising whole-brain crossing fibre information, *Inf Process Med Imaging*, 2003, 18, pp684-95

