Estimation of anatomical connection strength in diffusion MRI tractography by a global message-passing algorithm

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Introduction Anatomical strength of diffusion MRI fiber tracts, defined as the amount of white matter oriented from one small region of the brain towards another, has wide range of potential applications, from study of normal brain function to various neurodegenerative diseases. However, currently available methods for estimation of fiber weight (strength) have serious drawbacks, see [1]. For example, the following issue has been recently raised: If probabilistic tracking is used, all white matter properties being the same, many more fibers are reconstructed between voxels that are close(r) and on the straight path without any branching, than between voxels that are further away, or on the same distance but on a curved path, or on branching paths, for details see [1]. Therefore, estimated strength of the connections will incorrectly favor the shortest, straightest and simplest path. In this work we develop a method that, among other desirable properties, does not suffer from this problem.

Our method estimates weights of fibers *globally,* considering *all the fibers and all the voxels that fibers are passing through simultaneously*. We achieve this by an iterative optimization procedure operating on bipartite graph that has nodes corresponding to fibers and white matter voxels. The method can be used to supplement and refine results from any tractography method, independently of the model of local fiber orientation (DTI, HARDI, Q-ball, CSD, DSI, etc.) and tracking algorithm (deterministic or probabilistic).

Methods *Method for fiber tract weight estimation:* The proposed method belongs to the class of message-passing algorithms operating on bipartite graphs. The algorithm starts with a set of fibers obtained by any reconstruction method. We construct the bipartite graph with classes of nodes corresponding to fibers and voxels. Node *s,* in the class of fibers, is connected to a node *v*, in the class of voxels, if fiber *s* passes through voxel *v*. In this work we further refined the first version of the method [4], by incorporating length of the fiber within a voxel $l_v(s)$, see step 1. below. The proposed algorithm consists of the following steps.

0. (Initialization) Each fiber node *s* sends $m^0(s \rightarrow v) = 1$ to all the voxels *v* it passes through.

1. Following calculations are performed at iteration *i* on voxel nodes

$$S^i(v) = \sum_{\{s \in v\}} m^{i-1}(s \rightarrow v) \cdot l_v(s); \quad SC^i(v) = \frac{C(v)}{S^i(v)};$$

$$m^i(v \rightarrow s) = SC^i(v) \cdot m^{i-1}(s \rightarrow v)$$

where *C(v)* is the amount of white matter in the voxel *v* and $l_v(s)$ is the length of *s* within *v*, see Figure 1.

2. Each fiber node *s* sends $m^i(s \rightarrow v)$ along each edge:

$$m^i(v \rightarrow s) = min_{v' \in s \setminus \{v\}} \left(m^i(v' \rightarrow s) \right)$$

and the weight of the fiber *s* is estimated as $w^i(s) = \min_{v \in s} (m^i(v \rightarrow s))$

Figure 1. 15 cingulum fibers passing through specific voxel *v* with different lengths $l_v(s_i), i = 1..15$

Figure 2 NCW matrix for probabilistic tractography with cut-off angle of 30°

Steps 1. and 2. are repeated until the amount of white matter assigned at iteration *i* defined as $\sum_{\forall v} S^i(v)$, does not change significantly over several iterations. *C(v)* can be obtained, for instance, from the T_1-weighted image by probabilistic segmenting and taking the probability of white matter in a voxel as a measure of the amount of white matter in that voxel. Estimates for *C(v)* coming from other sources, such as T_2-relaxometry, can be incorporated just as easily.

Weighted connections between gray matter areas: The definition of weight on individual fibers enables derivation of new measures for connection strength between larger gray matter areas. Here we present a measure appropriate for anatomic clustering of brain regions (for clustering see [3] and references therein). Let gray matter be divided into *N* areas V_k, *k=1..N*. Further, let each V_k be subdivided into the set boundary voxels V_k^b and interior voxels V_k^i so that boundary voxels of V_k are those having at least one neighbor that does not belong to V_k. Number of voxels on the boundary $|V_k^b|$ is used as an approximation of region area. Also, let a fiber between voxels v_i and v_j be denoted s_{ij}, *i<j*. We define *Normalized Connection Weight* (NCW), a measure of how oriented region V_k is toward V_l as $C_{NCW}(V_k, V_l) = \sum_{\{v_i \in V_k; v_j \in V_l\}} w(s_{ij})/|V_k^b|$. Note that this measure is not symmetric.

Results *Data acquisition:* We tested the method on High Angular Resolution Diffusion Imaging (HARDI) data using 55 isotropically distributed diffusion-encoding directions at b=1000s/mm² collected on healthy adults with a 3T GE Signa EXCITE scanner. Further technical details on diffusion MRI and T_1 image used for *C(v)* can be found in [3]. We used 116 cortical structures as areas V_k, *k=1..116*, parcellated by using SPM5[5] software and the brain atlas created in standardized Montreal Neurological Institute (MNI) space [6] provided in the Automatic Anatomical Labeling software package [7].

Fiber tracking: We tested the proposed algorithm on initial sets of fibers coming from (deterministic) DTI/FACT algorithm [8] implemented in software package [9] and probabilistic tractography algorithm with HARDI ODFs from [2]. Various cut-off angles were used (15°, 20°, 30°, 40°, etc.). In all the cases, the message-passing algorithm converged, up to the 4th decimal point of $\sum_{\forall v} S^i(v)$, in less than 200 iterations.

Initial connectivity results, prior to the message-passing, vary greatly, depending on tracking algorithm and cut-off angle. We compared Frobenius norm of 116x116 binary matrices, where matrix entries at locations *(i j)* and *(j,i)* are "1" if there is at least one reconstructed fiber between brain regions *i* and *j*. During message-passing iterations weight of some of the fibers converges to zero, and Frobenius norm of binary matrices difference diminishes. On Figure 2. we present NCW matrix for probabilistic tractography with cut-off angle of 30°. For the list of 116 regions see [7] or [3]. Further numerical results, as well as analysis of eliminated fibers, shall be presented at the conference and a subsequent journal publication.

Discussion The developed method is global, non-stochastic and offers possibility to incorporate a physical attribute (fiber thickness) into tractography. As a consequence, the weights estimated by this method do not exhibit incorrect behavior briefly described in the introduction and discussed in detail in [1]. Numerical experiments suggest that the algorithm eliminates some dubious fibers and diminishes variability coming from *ad-hoc* parameters and randomness in tracking algorithms. Note that the message-passing algorithm has no free parameters. If all the available white matter is distributed among the streamlines, the iterative algorithm is not going to alter the weights in anyway.

Further, the weight assignment method enabled us to offer alternative average connectivity measures. These measures will be tested as tools in study of traumatic brain injuries and diagnostics of multiple sclerosis where advanced MRI metrics are needed.

References [1]D.K. Jones, *Imaging in Medicine;*2:341-355(2010). [2]Y. Iturria-Medina *et al. NeuroImage*; 36:645-660(2007). [3]M. Ivkovic *et al. PLoS ONE,* in press, 2010. [4] M. Ivkovic, A. Raj, submitted to *2011 ISBI.* [5]K. J. Friston, C. Buchel, *Acad. Press* 2003.[6] D. L. Collins, *Trans. on Medical Imaging*; 17: 463-468 (1998). [7] N. Tzourio-Mazoyer *et al. NeuroImage;* 15:273-289(2002). [8] S. Mori *et al Ann. of neurology*; 45:265-269(1999).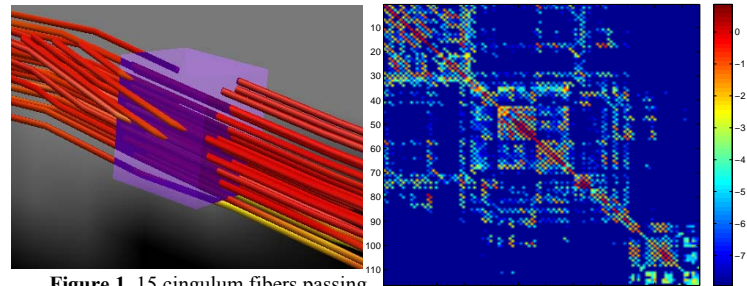[9] R. Wang *et al, ISMRM* 15:3720 (2007).