Mapping Brain Connectivity with Statistical Fibre Tracking and Virtual Dissection

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Abstract:
Most fibre tracking techniques were developed in a deterministic framework reducing the diffusion information to one single main direction, thus not taking into account the fibre directional uncertainty related to the diffusion tensor. We implemented a different approach that was statistical in nature and that took in account the whole diffusion information. This algorithm was then used to model globally the brain connectivity. The mass of connections thus generated was then virtually dissected to uncover different tracts. The connectivity pattern and the individual fibre tracts were then compared to known anatomical data; a good matching was found.

Introduction:
Fibre tracking algorithms have all the same aim: inferring from a Diffusion Tensor (DT) field fibre tract trajectories. Most of the algorithms used to infer bundles of fibres from DT images are based on a discrete resolution of the integral curves of the vector field corresponding to the reduction of the DT to its largest eigenvector e.g. [1,2,3]. As opposed to those deterministic integral path approaches, this work investigates brain circuitry with a random-walk-based algorithm. As long as in a voxel all the axons travel in a unique direction the measured DT exhibits strong anisotropy and the first eigenvector is aligned with the axonal trajectory. But when considering a voxel that contains several populations of axons with different directions the shape of the tensor will change according to the proportion of each population, moving toward a donut-like or spherical shape [4]. In this situation the principal eigenvector looses its signification and tracking, unless leaving the DT model for higher angular resolution imaging, becomes more hazardous. The principal eigenvector is also very sensitive to noise. The aim is to take into account the statistical nature of the data.

Material and Methods:
Brain imaging was performed on a 1.5 T clinical MRI scanner (Magnetom Symphony; Siemens). The DT data were produced with a diffusion-weighted single-shot EPI sequence. We acquired 44 axial slices in a 128 by 128 matrix size covering the whole brain (voxel size: 1.64 x 1.64 x 3.00 mm). Acquisition specification: TR of 1000 s, TE of 89 s, b-value of 1000 s/mm^2 at a maximum gradient field of 30 mT/m and 4 time averaging. An anatomical T1 MPRAGE was also performed.
The random-walk algorithm was based on two hypotheses:

- considering a voxel, the probability of a fibre to propagate in a given direction is proportional to the corresponding diffusion coefficient,
- axonal trajectories or more cautiously trajectories of axonal bundles follow regular curves.

Based on these two ideas we constructed a random walk model of a particle diffusing in a non homogeneous medium, here a DT field, $\mathbf{D}^{\alpha}$, with a curve regularizing constraint emphasizing co-linearity (1). The continuous trajectory of a particle in the 3D space is given by its time varying position vector $\mathbf{q}_i$, where i is the discrete time step (0<i<m). The curve that the particle propagation generates grows along a unit vector Ω_i that is a random direction vector modelling the statistical nature of the diffusion process and the curve regularizing constraint (2). Ω_i is a weighted sum of the random vector $\mathbf{d}_i$, defined on the unit sphere and distributed according to the local diffusive properties (3). $\Omega_{i-1} \cdot \Omega_i > 0$ is just an additional constraint to avoid backward jumps. μ is the step size (here 0.75) whereas α is an anisotropy enhancing exponent. In order to tighten the distribution α was put to 2. λ is a constant tuning the relative importance of the random diffusion component versus the curve regularizing term (here is 1). In order to map the connectivity of the entire brain such random curves were initiated in 40% of the white matter voxels. The result was a statistical estimate of the entire brain connectivity, modelled by a ``huge spaghetti plate" of about 100'000 curves.
In order to visualize anatomical connections in the form of separate identifiable tracts or bundles, a virtual dissection in this modelled brain had to be performed. This was done in two main steps: first a selection by knowledge-based Region Of Interest (ROI) placement and secondly selection by fibre validity classification. Axonal trajectories result from a stochastic process and therefore some of the curves accurately match reality whereas others are aberrant. To select a posteriori the ``good" trajectories, we assigned to each curve a ``Validity Index" (VI) (4). We expect that trajectories that follow directions of high diffusion to be more likely than those which do not. Therefore we integrated the diffusion coefficient along the trajectory and normalized it to the length (4). For tracts that were selected by one or several ROI, the histogram of the fibre population VI could be plotted. Fibres below a certain quantile (here 20%) were then discarded so that only the most credible fibres with a high VI were retained.

(1) $\mathbf{q}_{i+1} = \mathbf{q}_i + \mu\Omega_i$,

(2) $\Omega_i = \begin{cases} \dfrac{\lambda\mathbf{d}_i + \Omega_{i-1}}{\left\|\lambda\mathbf{d}_i + \Omega_{i-1}\right\|}, \\ \Omega_{i-1} \cdot \Omega_i > 0 \end{cases}$

(3) $\mathbf{d}_i = \mathbf{D}_i^{\alpha}\mathbf{r}_i$, where $\mathbf{r}_i$ is uniformly distributed over the surface of a unit sphere.

(4) $VI = \dfrac{1}{m}\sum_{i=1}^{m} \Omega_i^T \mathbf{D}_i \Omega_i$

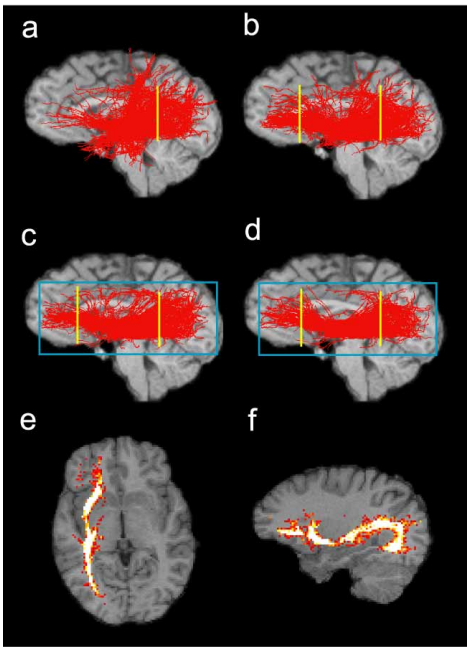

Figure: Virtual dissection of the occipito-frontal fascicle and various connectivity maps as an example of the methodology. a) fibres passing a posteriorly placed yellow ROI. b) fibres selected in a) and also passing in the second anterior yellow ROI. c) fibres selected in b) and that do not pass outside the blue frame. d) fibres selected in c) that have a VI above the 20th quantile. e) and f) statistical density maps of the fibres selected in d).

Results:
In the Figure we took the example of the occipito-frontal fascicle, an important association bundle for illustrating the technique. The different steps are explained. A first yellow ROI was placed in the caudal part of the brain a). A large population of fibres was selected among which the occipito-frontal projections as well as fibres of the superior and inferior longitudinal fascicles and fibres belonging to the corona radiata and posterior cortico-thalamic projections (not visible here in those sagittal figures). Willing to visualize only the occipito-frontal connections, a second yellow ROI was then placed in the frontal brain b). In some situation, instead of choosing a second ROI it was more appropriate to cut out fibres that pass out of a region, we illustrated it here in c) with a blue box. The final step of our virtual dissection was to eliminate unlikely fibres that are defined as having a VI inferior to the 20th quantile d).

Conclusion:
We used a tracking approach that is statistical in nature in order to map globally brain connections. As a second step tracts of interest are virtually dissected from the modelled brain. The connectivity pattern and the individual fibre tracts were then compared to known anatomical data; a good matching was found.

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