

# A method to study alterations in networks of structural connectivity

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## Introduction

The global structural connectivity of the brain can be explored *in vivo* with a connectivity matrix derived from diffusion MRI tractography [1]. In such a matrix, M, every index i or j represents a small region of interest (ROI) at the white-gray matter (WGM) interface and every entry  $M(i,j)$  provides a measure of connectivity derived from tractography. Once the matrix computed, it is easy to obtain connectional information between any two ROIs. It is also possible to extract properties about larger group of ROIs or even about the entire network. The challenging question is to define a methodology to construct normalized connectional matrices that allow inter-subject comparisons. Indeed, every brain has a slightly different shape such that finding a point to point gray matter correspondence between subjects is a non trivial problem. We propose to use a template based approach to find this correspondence and accordingly to construct a network for every subject with equal number of nodes that are in equivalent location. This methodology allows us to study the network alteration in a patient with a glioma.

## Material and Methods

In this study, a group of 10 healthy subjects and one patient with a left fronto-temporal glioblastoma have been scanned. We performed for every subject a whole brain study on an Achieva 3T Philips scanner. We used a diffusion weighted single shot EPI sequence to perform multi-shell q-ball imaging, sampling 1 b0 image, 6 diffusion encoding directions at  $b\text{-value} = 1000 \text{ mm}^2/\text{s}$  and 66 directions at  $7000 \text{ mm}^2/\text{s}$ . In every voxel an orientation distribution function (ODF) is reconstructed with a modified QBI algorithm [2]. The acquisition block was made of 32 slices of a  $128 \times 128$  matrix with a spatial resolution of  $2 \times 2 \times 3 \text{ mm}^3$ . The timing parameters were TR/TE = 3000/100 ms and the acquisition time was 10 minutes.

An atlas based segmentation on a high resolution T1w acquisition is used to define a mask of white matter and the WGM interface. Whole brain tractography [3] is performed in the white matter of every subject.

We want to cover the WGM interface of every subject with  $N=1500$  small ROIs of about  $1\text{cm}^2$ , which should be placed in equivalent positions in each subject. We start by extracting the WGM interface of a template brain atlas (MNI-305 Atlas). This interface is partitioned with an iterative algorithm into N ROIs of equal size. Each ROI gets a unique number and Brodmann area identifier.

The affine transformation between every brain and the template is computed and used in order to map the N standard ROIs into the subject space. As there is not yet a perfect match between the mapped ROIs and the subject WGM interface, the center of gravity of each ROI is projected onto the nearest point of the subject's WGM interface. From these centers of gravity the iterative ROI generation algorithm is repeated to get this time a set of N ROIs on each subject with equivalent position. These N matched and labeled ROIs are the N entries of the subject normalized connectivity matrix.

For each subject, the simulated fibers passing through each pair of ROIs are selected. The connectivity matrix represents the network of structural connectivity where every node represents a ROI and every edge the connection between two ROIs. The edge weights can represent different type of measures such as Connection Density (CD) (1), mean or maximal Mean Diffusion (MD) along the tract, mean or minimal Fractional Anisotropy (FA), etc. At the end of the process we have as many matrices as subjects.

$$(1) CD(i, j) = \sum_{f \in F(i, j)} 1/l(f)$$

with  $F$  fibers are connecting ROI( $i$ ) to ROI( $j$ ), each fiber  $f$  of this set  $F(i, j)$  has a specified length  $l(f)$ . This normalization with the fiber length is necessary in order to account for the linear bias towards longer fibers introduced by the tractography algorithm.

Grouping all matrices belonging to the controls, we have for every matrix entry  $M(i, j)$  N sample that represent the distribution of normal values. This allows to study quickly a specific tract across different populations or as in our example to compare an altered network with a reference group. Instead of studying a specific tract it is also possible to extract global network properties as we will see below.

## Results

Fig 1 shows an example of a WGM interface being partitioned into N normalized ROIs. Every ROI( $i$ ) has equal surface and its position is equivalent to the same ROI( $i$ ) in the other subjects. Fig 2 shows the resulting connectivity matrix where  $M(i, j) = CD(i, j)$ . We now consider some node characteristics in the controls and the tumor patient (Fig 3). Fig 4 is a plot of the node degree distribution. For example if we take node degree=2, we see a box plot that represents the distribution of the number of nodes that have a degree=2 across the control population. The red circle corresponds to the number of nodes in the tumor patient having degree=2. Considering the entire plot we notice that in the tumor patient there are less nodes with a high degree while there are more nodes of small degree. This phenomenon is due to a connection loss in the tumor patient. The correlate of this observation is that the total number of edges as well as the total CD is significantly smaller in the tumor patient versus the control group (Fig 5).

## Conclusion

We have shown a new methodology to construct a "distribution of normalized connectivity matrix" for a population where the matrix entries represent the statistical distribution of a fiber tract characteristic in a population. This makes possible not only to study global connectivity but also specific tract characteristics across population. In particular we have been able to analyze the network alteration of a tumor patient.

## References

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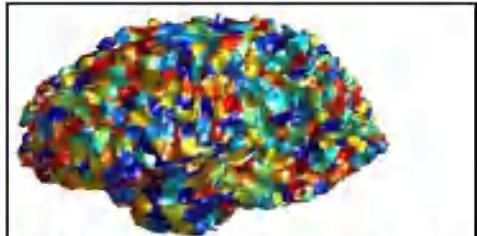


Fig 1: Partition of WGM interface into normalized ROIs

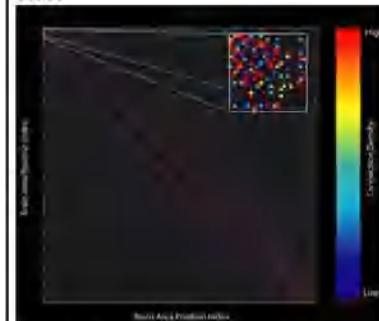


Fig 2: Normalized connectivity matrix



Fig 3: Tumor patient

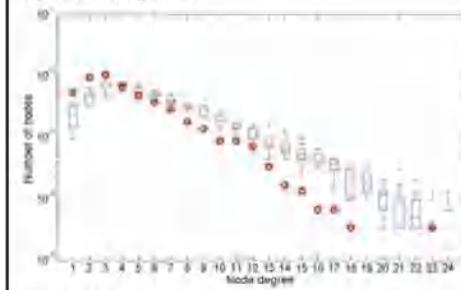


Fig 4: Node degree distribution

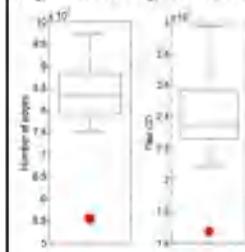


Fig 5: Number of edges and total CD