Dendrogram processing for whole-brain connectivity-based hierarchical parcellation

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INTRODUCTION

The arrival of diffusion MRI and particularly probabilistic tractography [1] has enabled researchers to perform in-vivo cortical parcellation based on the brain connectivity structure, which is believed to be strongly correlated with function [2]. An in-vivo, brain-wide atlas based on connectivity would surely be a great step forward into revealing new functional regions, understanding the interplay between functional areas, and providing a more suitable foundation onto which to build the human connectome. Existing methods, however, are typically restricted to finding a predefined number of clusters and/or limited to smaller regions of grey matter [3,4]. Furthermore, all the available methods rely on finding the optimal number of regions, but when faced with a whole-brain approach, the challenge arises of not only having a high and unknown expected number of regions, but of that number being subjective to the desired granularity of the partitioning.

In this work, a hierarchical clustering approach is suggested in order to overcome these difficulties, where the information of the connectivity structure at all granularity levels is encoded in a hierarchical tree or dendrogram. A fast algorithm is introduced, along with processing schemes to extract information form the resulting dendrogram. These dendrograms could enable an intelligent comparison of connectivity structure between subjects.
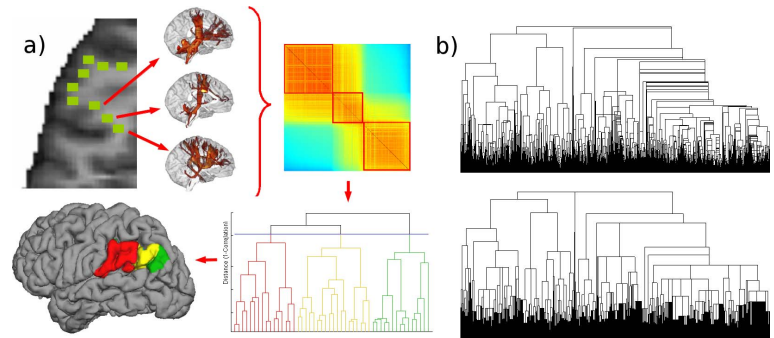

Figure 1: a) Schematic of the connectivity based hierarchical clustering process. b) Raw dendrogram as a result of the algorithm (upper) and cleaned dendrogram after applying the processing steps (lower).

METHODS

High resolution dMRIs were acquired on a Siemens TimTrio scanner (1.5mm iso, 60 dir, b=1000s/mm^2, GRAPPA/3, AV =3) in one healthy participant. All voxels at the cortex/white matter boundary (FA >= 0.15) were selected as individual seed points for probabilistic tractography. The similarity among the tractograms was computed as the normalized inner product between each pair of tractograms. A bottom-up agglomerative hierarchical tree of clusters was generated by using neighborhood restrictions on the centroid method applied in tractogram space [5]. An outline of the clustering process is shown on Figure 1a.

The interpretation of the resulting dendrogram is not simple, since it contains outliers resulting from isolated voxels and tracking artifacts, non-monotonic steps due to the nature of the centroid method [6], information from a very high number of granularity levels, and a forced binary division of each cluster. In order to ease the information extraction several processing steps were developed and applied: outlier pruning, monotonicity correction, detection and flattening of non-binary structures, and smoothing of the levels of highest granularity (close to the single voxel level), effectively reducing the number of branching while keeping the maximum usable information (Figure 1b).

RESULTS

Effects of the cleaning process on the tree structure are exemplified in Figure 1 and enabled better performance of partitioning algorithms. Figure 2 a,b shows the full partitioning of the cleaned dendrogram corresponding to the left hemisphere using different methods (yielding 50 clusters each): maximizing inter-cluster distance or minimizing cluster size difference. The resulting partitions were mapped back onto the brain surface. Clusters with especially sharp boundaries are shown in Figure 2c. All the results were interactively explored using the OpenWalnut software.
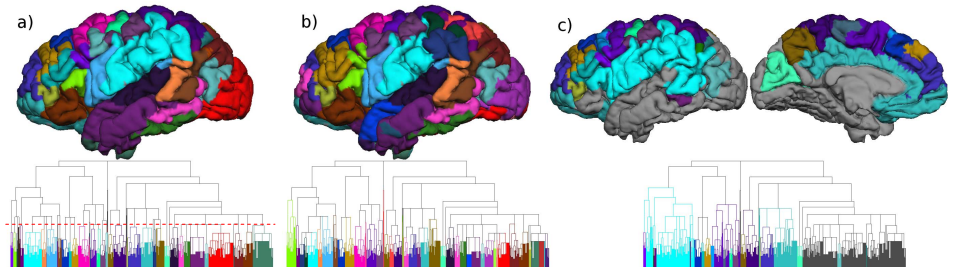

Figure 2: Results of different clustering extraction methods on the left hemisphere dendrogram: Maximum inter-cluster distance partitioning: 50 clusters (a), Minimum size difference partitioning: 50 clusters (b), sharp-boundary clusters (c).

CONCLUSIONS

Hierarchical clustering is an elegant way to account for the numerous levels of functio-anatomical organization present in the brain structure. However, intelligent processing of the obtained dendrograms must be performed in order to efficiently extract useful information. Horizontal partitioning is probably not the optimal way to find a best cut of the tree, as different clusters might have different cohesion and relevant granularity levels (Figure 3), and a better solution might be achieved by combining several methods. A current challenge that is being faced in this project is also the comparison between trees from different subjects, in order to quantify inter subject connectivity variability.
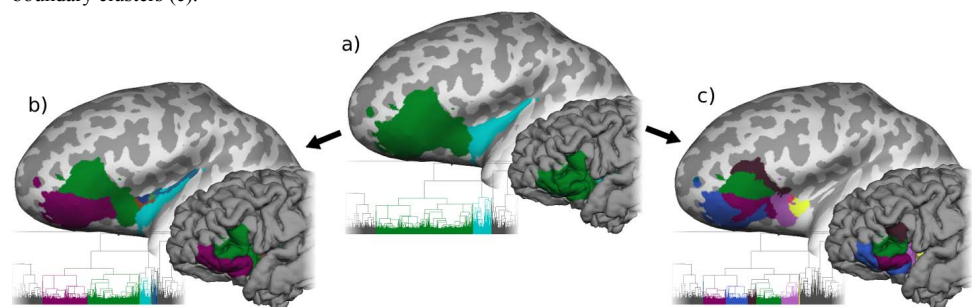

Figure 3: Exploration of two clusters on the inferior-frontal gyrus (IFG) and the insula (a). While inter cluster distance partitioning of the whole region is dominated by the lower cohesion of the insula cluster, showing no further inner structure (b), isolating the IFG cluster shows plausible further partitioning (c).

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