Processing and Comparison of Hierarchical Trees for Whole-Brain Connectivity-Based Cortex Parcellation

David Moreno-Dominguez, Alfred Anwander & Thomas R. Knösche

Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany
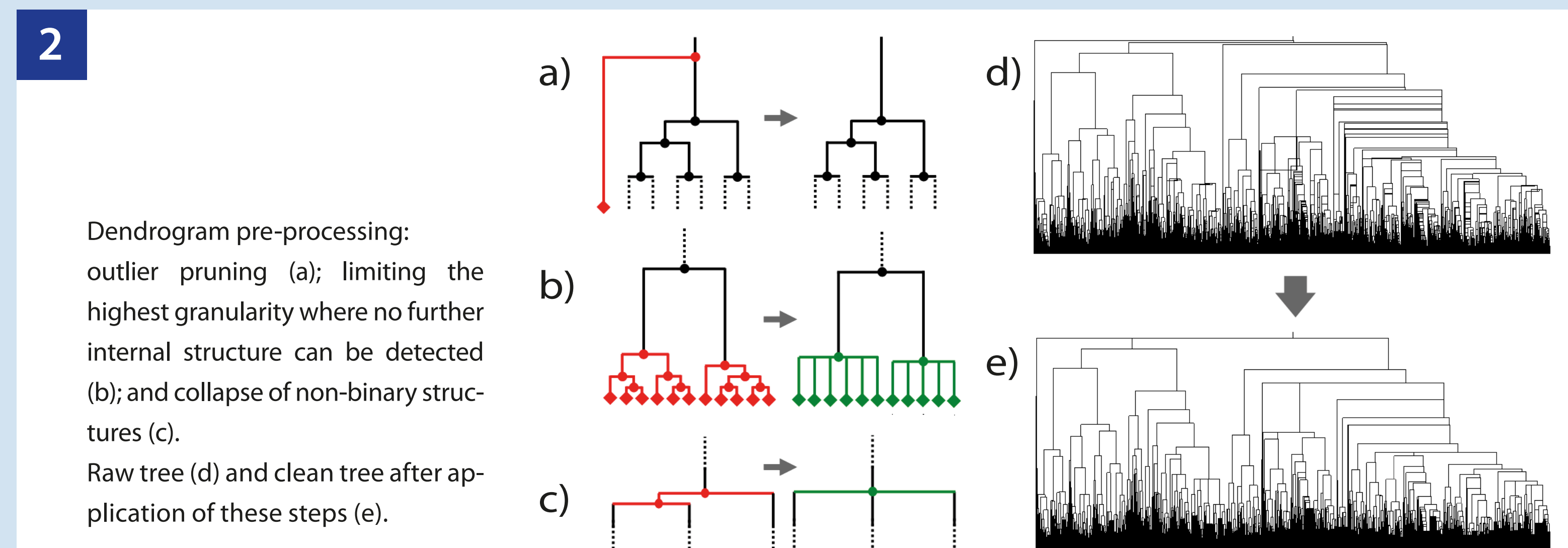moreno@cbs.mpg.de

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]. Existing methods, however, are typically restricted to finding a predefined number of clusters and/or limited to smaller regions of grey matter [3]. 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 dealing not only with 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

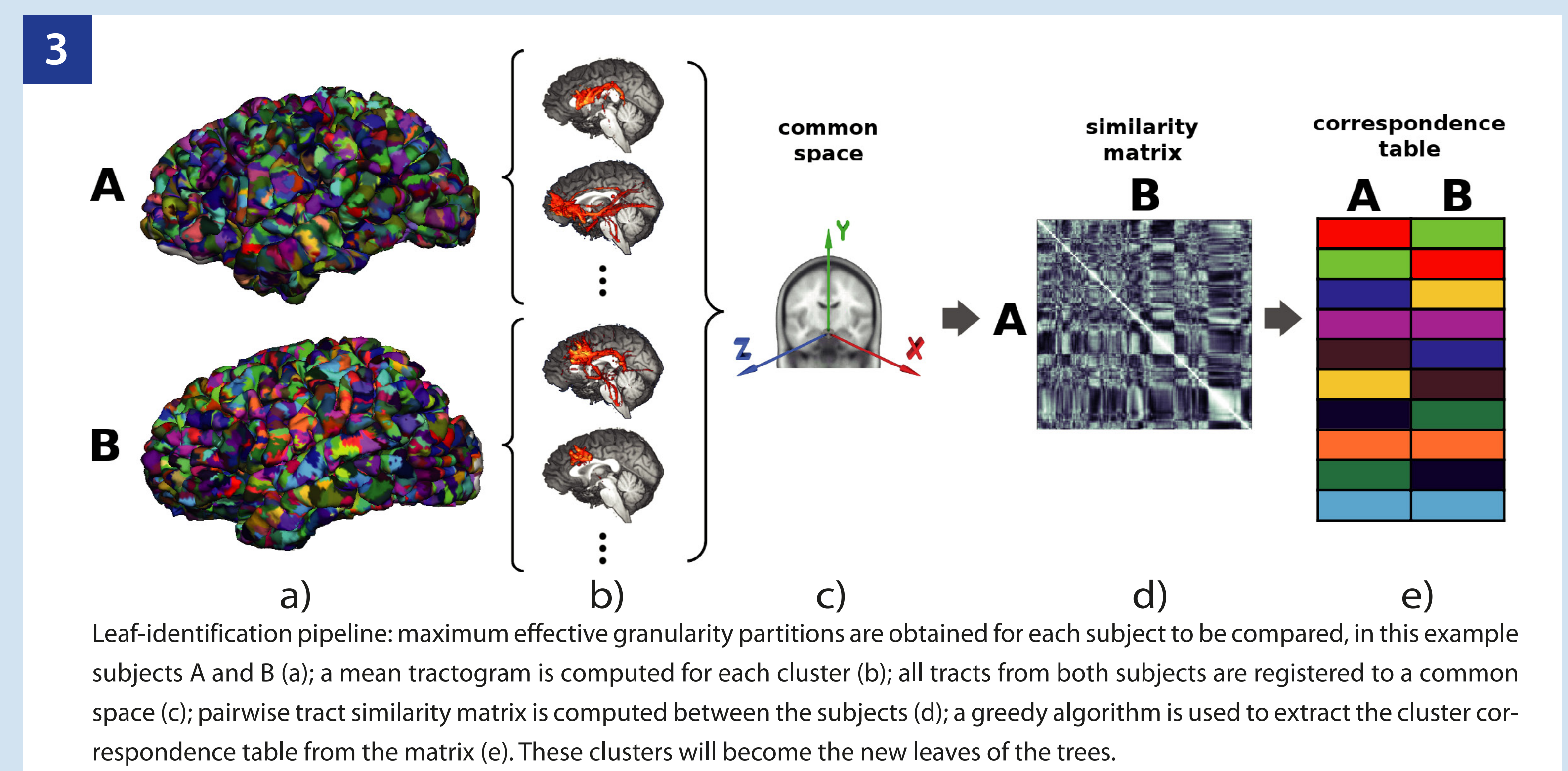Schematic of the hierarchical clustering process.
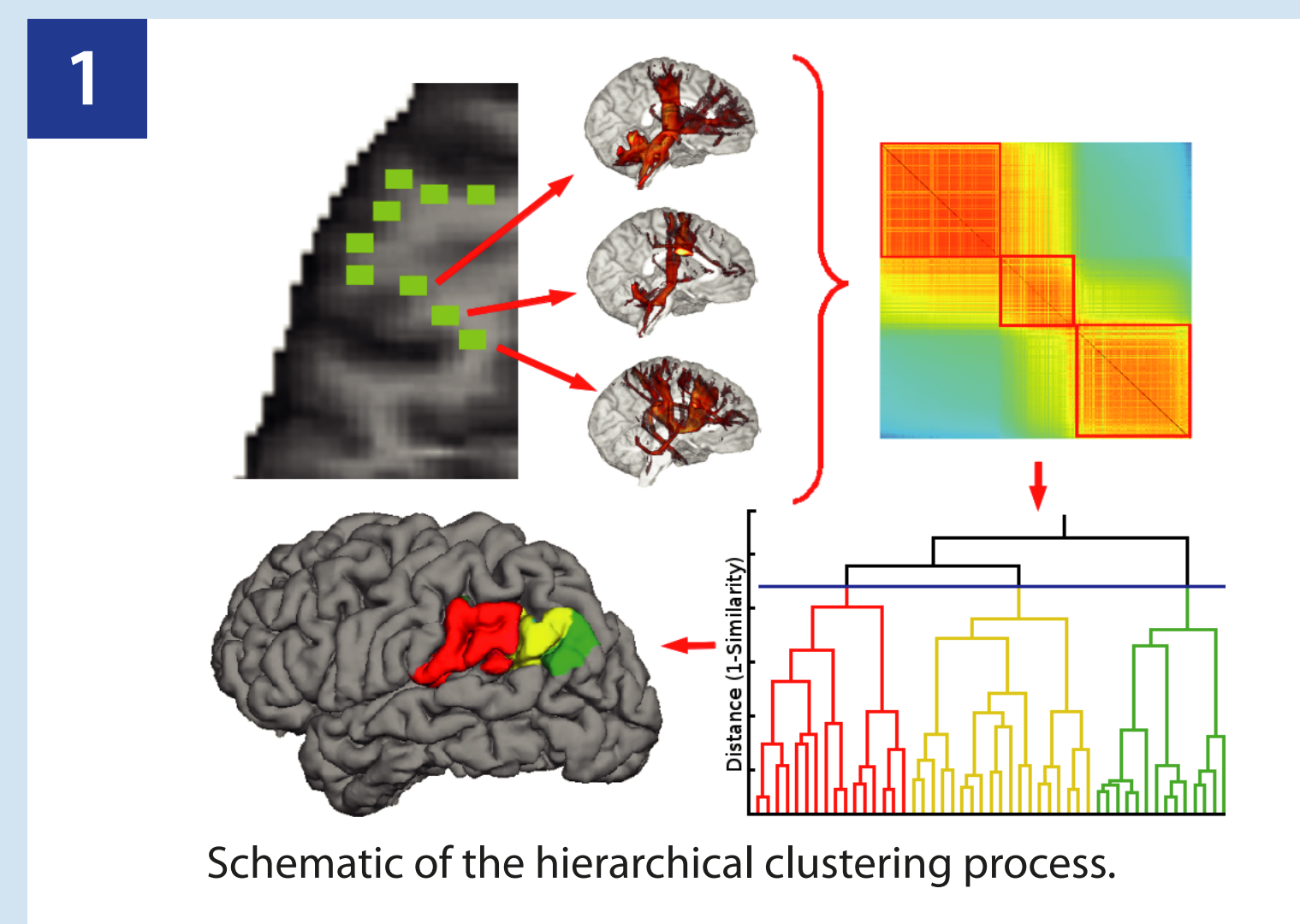
levels is encoded in a hierarchical tree or dendrogram. Tree-cleaning processing steps are applied and different partition selection algorithms are implemented. Also, the possibility for assessment of whole-brain connectivity-structure similarity across subjects or measurements is introduced through dendrogram comparison.

Dendrogram pre-processing: outlier pruning (a); limiting the highest granularity where no further internal structure can be detected (b); and collapse of non-binary structures (c).
Raw tree (d) and clean tree after application of these steps (e).

Methods

High resolution dMRIs were acquired on a Siemens TimTrio scanner (1.5 mm iso, 60 dir, b=1000 s/mm^2, GRAPPA/3, AV =3) in three healthy participants. All voxels at the cortex/white matter boundary (FA ≥ 0.15) were selected as individual seed points for probabilistic tractography [3]. Tractogram similarity was computed as the normalized inner product between each pair of tracts. A bottom-up agglomerative hierarchical tree of clusters was generated by using neighborhood restrictions on the centroid method applied in tractogram space [4]. An outline of the clustering process is shown on Figure 1.

The resulting dendrograms were processed in order to remove confounds and improve further analysis (Figure 2), effectively reducing tree complexity by 97% with only a 0.1% information loss. Before dendrogram comparison is applied, leaf identification of trees from different subjects is obtained as shown on Figure 3. Two different methods are used to assess dendrogram similarity: cophenetic similarity [5], which compares the tractogram similarity of every pair of leaves as encoded by each tree (emphasis on numerical values, Fig. 5a) and triples similarity [6], which compares the joining order in the tree of every possible triple of leaves (emphasis on topology, Fig. 5b).

Leaf-identification pipeline: maximum effective granularity partitions are obtained for each subject to be compared, in this example subjects A and B (a); a mean tractogram is computed for each cluster (b); all tracts from both subjects are registered to a common space (c); pairwise tract similarity matrix is computed between the subjects (d); a greedy algorithm is used to extract the cluster correspondence table from the matrix (e). These clusters will become the new leaves of the trees.
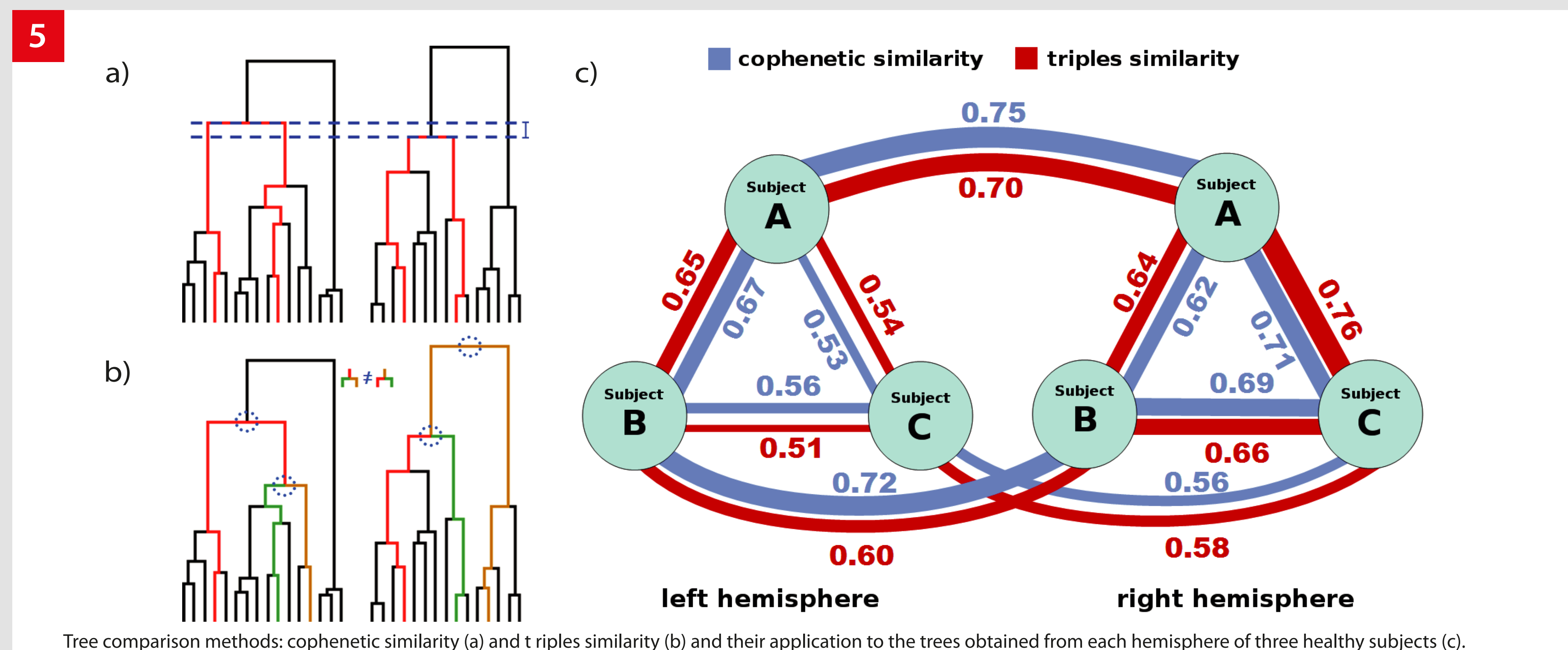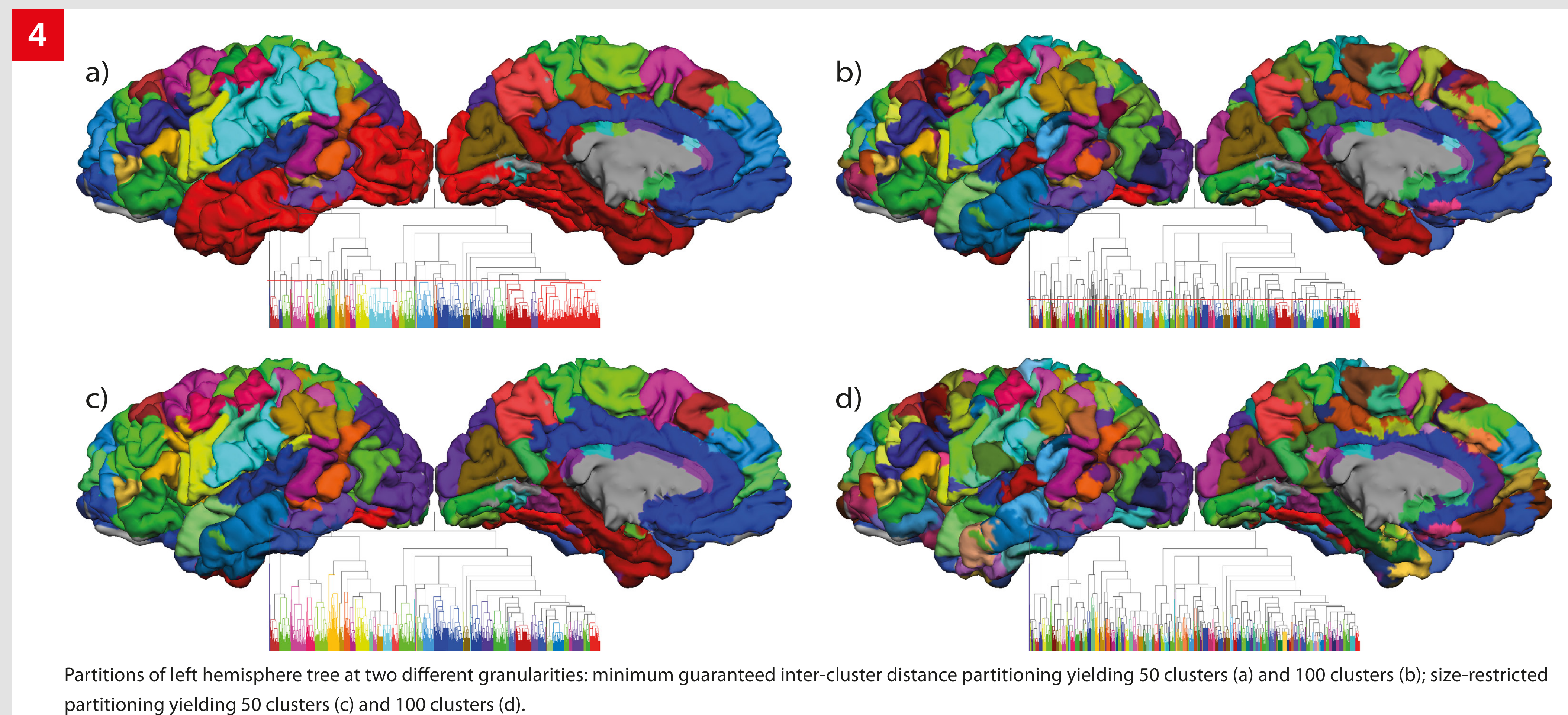
Results

Different levels of granularity for the left hemisphere of a single subject were explored using the *OpenWalnut* software [7]. A first horizontal cut scheme guarantees clusters with a minimum given similarity between their mean tractograms, but tends to bigger clusters in regions sharing large bundles and small clusters on regions with local connections (Figure 4a); a second method relieves this bias obtaining partitions where all the clusters are smaller than a defined size (Figure 4c).

Example results for the full connectivity structure comparison between each hemisphere of three healthy subjects are shown in Figure 5c. Both comparison methods yield similar values and well above the chance level of 0.25 (obtained from comparison of randomly matched trees). Several conclusions might already be drawn from the graph: such as subject C having a notably higher variability of connectivity structure across hemispheres, and that while the right hemispheres for all three subjects show relatively high similarity, the left hemisphere of subject C deviates in structure from the other two.

Partitions of left hemisphere tree at two different granularities: minimum guaranteed inter-cluster distance partitioning yielding 50 clusters (a) and 100 clusters (b); size-restricted partitioning yielding 50 clusters (c) and 100 clusters (d).

Tree comparison methods: cophenetic similarity (a) and triples similarity (b) and their application to the trees obtained from each hemisphere of three healthy subjects (c).

Discussion

Hierarchical clustering is an elegant way to account for the numerous levels of functio-anatomical organization present in the brain structure. We have introduced an agglomerative hierarchical method suitable for whole-brain connectivity analysis and developed cleaning and complexity-reduction processing steps that facilitate dendrogram interpretation. We have also shown how this method brings the possibility to assess full-brain connectivity similarity across subjects or measurements. The most important challenges for the future include developing more refined algorithms to automatically find relevant partitions within a single subject and validating our results (e.g. through the study of data from repeated measurements).

References

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