

A Semantic Contour Tree Approach for Visual Comparison of Brain White Matter Connectivities in Cohorts

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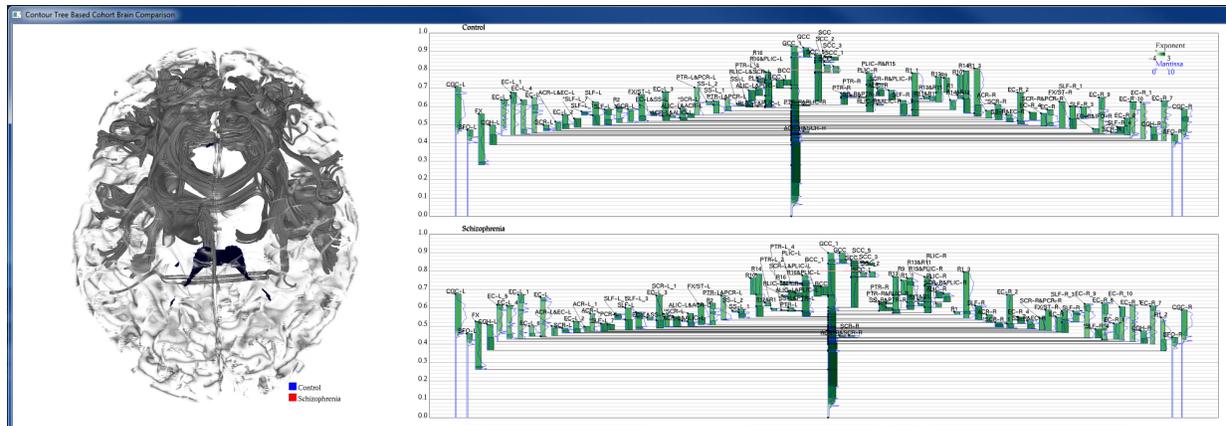


Fig. 1: Semantic contour tree visualization for brain cohort comparison. At left is an isosurface rendering of the selected contour class (indicated by a pink tick on the arcs in the contour trees) overlaid with brain fiber tract network. At right, the two contour trees are generated from two cohorts with 128 control (top) and 123 schizophrenia (bottom) cases.

Abstract— We present a semantics-driven contour tree visualization approach to support exploring and comparing cohort-level brain white matter connectivities. A contour tree is a topological method that stores the nesting relationships of the contours in a scalar field, here a brain water molecule movement measure of fractional anisotropy (FA) values. Previous contour tree visualizations have lacked the capability to effectively relate two-dimensional (2D) tree structures to the three-dimensional (3D) counterparts reflecting the semantic structures. Our approach is semantics-driven in that contour trees are labeled with brain anatomical regions, thus are stable in their structures for comparative studies. We further explore the contour tree approach as a tool for interactive exploration and for comparative studies of patient and normal cohorts. Our approach is novel not only in summarizing the 3D topological structures but also in showing spatial attributes associated with brain connectivity represented in fiber tracts, thus allowing brain scientists to examine and compare critical differences between cohorts.

Index Terms—Brain connection, diffusion MRI, brain white matter, contour tree, graph layout.

1 INTRODUCTION

Recent advances in brain imaging capturing capability permit brain scientists to study multi-modality cohorts [10] to address critical comparative tasks in clinical use and research settings. One of these tasks is to compare brain white-matter integrity; this can provide substantial insights into brain functions to observe and locate deficits in brain networks [17]. Such comparisons can be conducted at numerous levels such as patient and normal cohorts, individual and normal cohorts, individual and patient cohorts, and so on.

White matter integrity is often studied using diffusion tensor magnetic resonance imaging (DTI), an in-vivo non-invasive method to

measure the water molecule movement in brain tissues. Since water does not pass through membranes, interpreting water motion represented as a tensor field informs anatomical connectivity, often computed through tractography analysis at each image voxel location. The tractography process generates several tens of thousands of lines in the head volume, making it impractical as a visual representation due to occlusions in the three-dimensional (3D) space. In the meanwhile, the water movement pattern can be represented using a scalar value, fractional anisotropy (FA) at each voxel location.

Brain scientists' comparative data analysis sometimes begins with examining the entire brain volume and then uses fiber tract structures and FA values to locate region-of-interest (ROI), ultimately focusing on several found or pre-defined structures. For tasks requiring locating ROIs, searching and finding the abnormalities in dense field requires interpreting average FA values aggregated in small regions as well as interactivity to remove uninteresting regions, both processes leading to great visual uncertainty in 3D [5].

Current approaches to displaying large-dense datasets of brain imaging focus on three solutions. The first is to focus on the display hardware, e.g., by increasing the size and using immersion and stereo to augment human perceptual capabilities [5]. However, this approach is not always available in brain scientists' offices, where desktops are the usual environments. The second approach is to simplify the visualization to extract meaningful features such as topological structures [18]. This simplification approach is powerful, but has the draw-

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back that topology might not reflect critical brain structures since it is derived using generic mathematical concepts. The third approach focuses on low-dimensional reduction and interactivity, i.e., using an embedding or projection approach to yield 2D displays that can also show fiber clusters [6]. None of these approaches, however, support a simultaneous display of brain integrity information (measured in FA) and reduces occlusion as well as facilitating interactivity.

Our current design combines the second and the third approaches to provide an interactive 2D clutter-free solution to assist analysis that supports integration of FA values. Since FAs form a scalar field, we use a contour-tree approach in our occlusion-free 2D construction. Although this contour-tree approach has shown great promise in summarizing the 3D scalar field into an uncluttered 2D tree structure [19], it has the drawbacks of being unstable and sensitive to noise. Unstable 3D structural changes would prevent users from forming a mental map of the underlying data. Our solution instead creates stable trees to relate the 2D tree structure to the 3D anatomical structures. A second issue is that the contour tree approach can generate overly complex structures and thus requires meaningful simplification [4, 14]. Our approach to these challenges is to add semantic labeling to the contour tree, and we call our approach semantic contour trees, useful for brain scientists to compare and search for ROIs from the visualized brain maps.

A major contribution of this research is addressing new comparison tasks through the design of a 2D semantics-enabled contour tree such that parameter values (here FA) can be clearly perceived and queried in different parts of the brain. Specifically, this article contributes the following: (1) a clutter-free 2D contour-tree visual representation for interactive comparison of patient and control cohorts, (2) a semantic-labeling to build the visual correspondence to produce stable contour trees, and (3) interactive visualization of parameters of interest to support visual comparison.

2 BACKGROUND AND RELATED WORK

2.1 DTI and Comparative Studies

Brain connectivity is necessarily a large graph [2]. Brain scientists on our team are interested in understanding brain structural integrity in schizophrenia patients. An approach the team has been taking is to capture and compare patient cohorts with normal cohorts to understand FA value changes in human brains. Interestingly, the brain science literature shows mixed results: some researchers found that FA values increase in certain regions while others report FA decreases, perhaps due to differences in population sampling and data processing mechanisms. It is thus crucial to learn exactly where and how FA varies.

For ROI-based analyses, segmenting the regions requires manual labor and expertise. Being able to automatically summarize the ROI statistics and allow comparison of multiple instances of the data can be very helpful. In this work, we provide labeling methods such that different anatomical regions can be compared.

2.2 Clutter-free 2D Representation

Due to challenges in exploring and interacting with 3D structures, 2D representations have been used to produce clutter-free solutions to either facilitate spatial clustering or improve interaction. Jianu et al. embed the 3D fiber tracts into 2D representation to allow easier selection and interaction [11], as the 2D plane allows precise location comprehension and interaction with visual markers [7]. This approach is powerful in providing anatomical references. However, users must synthesize 3D information in their brain to reconstruct meaning. Chen et al. used multidimensional scaling techniques to show groupings in which spatially closer points are also closer on the 2D plane [6]. This dimension reduction approach provides flexible interaction between 2D and 3D representation fiber tracts to allow quicker and easier fiber selection. One issue, however, is that a line in 3D space becomes a point in 2D and integrating any other parameters (e.g., FA values) is challenging.

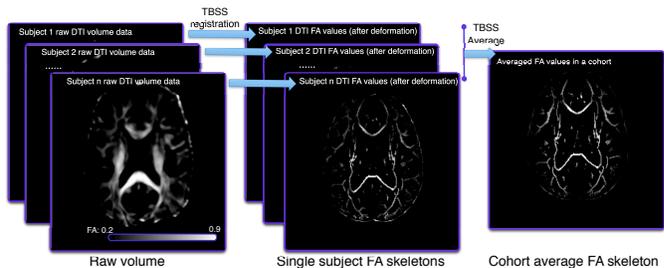


Fig. 2: FA volumes: from raw data to average cohort FAs. Background regions are indexed as zero FA value.

2.3 Contour Tree Visualization

The contour tree is a topological abstraction of a scalar field that represents the nesting relationships of connected components of isosurfaces or level sets of equal scalar value. The contour tree tracks the evolution of contours and represents the relationships between the connected components of the level sets in a scalar field. Each leaf node is a minimum or maximum, each interior node is a saddle, and each edge represents a set of adjacent contours with isovalues between the values of its two ends on each arc. Two connected components that merge as one contour are represented as two arcs that join at a tree node. Therefore, display of a contour tree can give the user direct insight into the topology of the field and reduces the interaction time necessary to understand the structure of the data [4]. For example, in medical CT scans, an isosurface can show and reconstruct the separation between bones and soft tissues.

Many contour-tree algorithms exist to serve different purposes. Carr et al. introduced the concept of using contour trees for exploration purposes, and then proposed several geometrical measurements to simplify contour tree [4]. These methods demonstrated a powerful paradigm of using simplification for contour selection. Pascucci et al. provide level-of-detail algorithm based on a novel branching algorithm and a 3D Orrery layout for hierarchical exploration of field data [14]. Heine et al. compared several planar contour tree layouts and identified an orthogonal layout as most effective in representing branch hierarchy, minimizing self-intersections, and associating ancillary information such as geometric properties of contours [9].

Here we adopt Carrs approaches for contour tree generation [3, 4] and take the results from Heine et al. [9] on the use of orthogonal layout in order to produce effective visual query of different anatomical brain structures.

3 ORTHOGONAL SEMANTIC CONTOUR TREE VISUALIZATION

We introduce our approach to visualizing cohort-level brain white matter structures. Compared to previous contour tree methods, we have made the following technical advances:

- Stable tree structure generation by using a skeleton template to generate semantically meaningful branches;
- Arc level histogram to provide detailed FA value distributions for comparative studies;
- A layout and labeling method to better convey the tree structure for further analysis.

We discuss the cohort FA value computing in Section 3.1. Though this method is also new, we only give a broad-brush description of it since it is not the focus of the paper. We focus instead on the contour tree construction and visualization.

3.1 Data Preprocessing: FAs in Brain Cohorts

The goal in this preprocessing is to automatically compute the average FA values in a brain cohort using ROI-based approach. These

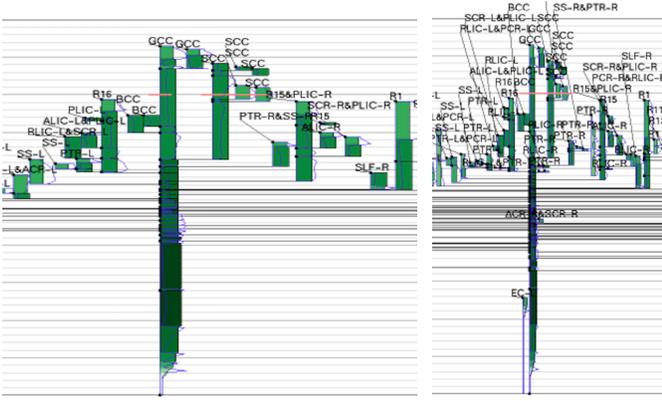


Fig. 3: Simplification results with pruning threshold of 5 voxels (left) and 20 voxels (right) in selected contour tree regions.

ROIs will later be used to label and construct anatomically meaningful contour trees. We use an automatic approach because extracting ROIs requires substantial anatomical knowledge and is very time-consuming [16]. Our purpose here is to design a visualization tool in which any imaging cohorts can be loaded and compared effectively.

The algorithm pipeline contains two steps, TBSS registration and TBSS average, as illustrated in Fig. 2. The first step performs deformation analysis using FSL to generate the skeleton for each single subject with a template brain white-matter volume [12]. The second step averages the skeleton volume data for all subjects in the same cohort. We use averaged tract-based spatial statistics (TBSS) [15], which maps the white-matter structure to a common “skeletonized” template and conducts ROI-based statistics using aggregated measurements mapped to the skeleton [10].

Our preprocessing process has three benefits: 1) It is more resilient to the noise in data, thus increasing the chances of creating anatomical meaningful branches in the contour tree; 2) TBSS provides a common template to register all voxels of interest thus facilitating the generation of similar topologies among datasets for comparison purposes in tree visualizations; and (3) TBSS reduces the spatial variability of individuals brain structures by using nonlinear registration.

3.2 Contour Tree Construction, Simplification, Labeling, and Layout

Construction and Simplification. We use the contour tree construction algorithm to automatically generate a summary graph of the underlying scalar field [3, 4]. The algorithm has four stages: (1) sorting vertices in the scalar field, (2) computing the join tree and split tree, (3) merging the join and split trees to build the contour tree, and (4) pruning less significant arcs in the contour tree. The resulting visualization extracts the major structures of the scalar field. See [3, 4] for a formal algorithmic description.

The first three stages are exactly the same as in Carr [3]. In the last pruning stage, we also follow the arc reduction methods using the leaf-pruning method [4], and apply that to the overlapping between the regions one arc represents and an ROI label template defined in the same coordinate system as the TBSS skeleton [10]. For each arc in the tree, we calculate the overlapping between voxels on the arc and any labeled regions in the labeling volume. If the number of overlapping voxels is below a user-defined threshold, we prune the arc. We continue this process until no more pruning is possible. Then we collapse all regular vertices, which have only one upper arc and one lower arc, by combining the two arcs into one.

For example, the user can prune the tree using a threshold of 20 voxels, i.e. any leaf branches that have less than 20 voxels overlapping with the labeled regions are removed from the tree. The resulting visualization is shown in Fig. 3. The selected region is pruned using a threshold of 5 and 20 voxel sizes.

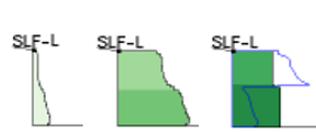


Fig. 4: Linear scale histogram, logarithm scale histogram, and OOMM style histogram of the same arc (superior longitudinal fasciculus left) voxel value distribution as part of the contour tree.

Labeling. We label each arc once the simplification is complete. Since brain regions of interest usually have higher FA values than their surroundings, they are usually local maximum and thus represented by upwards arcs. We therefore label only arcs that connect to a leaf node. To calculate the name for a given arc, we traverse all the voxels represented by that arc. For each voxel, we obtain the label from the labeling volume by counting the occurrence for all labels in that arc and considering the two labels with the most count as candidates for an arc label. We compare the counts of the labels against the total number of voxels of that branch: if the maximum count of the label is less than 20% of the total voxels, we leave that arcs name blank. Otherwise, if the second highest counted label has voxel number no less than 20% of that in the highest counted label, the arc is named by combining both labels. Otherwise the arc is named after the highest counted label.

Layout. Our orthogonal layout algorithm expands upon Wu and Zhang [19] and Heine et al. [9] with several modifications to better present the brain data. First, we make sure branches with labels of left brain regions are placed on the left side of the contour tree and right region branches are on the right side; second, each branch size is calculated with the actual histogram size (see Section 3.3) needed instead of a fixed width, for better screen-space utilization; third, each arc in the contour tree is replaced by a histogram showing the distribution of FA values of the white-matter structure represented by that arc.

3.3 Contour Tree Based FA Comparison

To compute the FA distribution on each arc, we compute the 1D convolution using a Gaussian kernel with $\sigma = 0.01$. The bin size is 0.005. For a voxel, where $FA = f_0$ value and $f_0 \in [0, 1]$, we first calculate the range of bins that cross the FA range $[f_0 - 3 \times \sigma, f_0 + 3 \times \sigma]$. For each bin i crossed, we calculate the weight of this point on it. Say that the bin’s middle FA value is f_i ; then the weight $w_i = \exp(-\text{pow}((f_0 - f_i) \div \sigma, 2))$. Next, we normalize all weights so that w_i for that point on these bins sum to 1. Finally, we assign the normalized w_i to each bin. We do this for all points associated with that arc to obtain the FA distribution on that arc.

To visualize the FA values on each arc, we begun with the linear and logarithm scale histogram but later adopted the more effective order of magnitude marker (OOMM) [1] due to the large range of the FA distribution (Fig. 4). The OOMM algorithm represents a numerical value in scientific notation (e.g., $100 = 1 \times 10^2$) and plots both the mantissa (here 2) and the exponent (here 1). The probability density distributions of FA values are converted to scientific notation, where the blue-colored line shows the mantissa and the 8-step color bar encodes the exponent. We double-encode the exponent so that the two parts of the scientific notation are easier to differentiate. The 8-step color scale is adopted from Colorbrewer [8].

3.4 Interactions

A brain scientist can interact with the contour tree to select different anatomical regions, similarly to [4]. Users can drag in one arc to see its 3D level-sets in the 3D view, where a transparent brain cortex mesh is also rendered to provide spatial context. User can also change the threshold for the pruning process to adjust the number of arcs shown.

4 RESULT AND DISCUSSION

4.1 Case Study: Comparison of A Schizophrenia and A Normal Control Cohorts

We describe a case study in which our visualization is used to compare a schizophrenia cohort of 123 samples against a normal control cohort of 128 samples.

We have several observations. First, we can see that overall, the two tree representations are similar in the structures represented and the layout of those arcs representing the structures. Both trees have GCC (genu of corpus callosum) as the main branch, as this region has the highest FA values, followed by the branches representing SCC (splenium of corpus callosum). The regions corresponding to these two major regions are also drawn as contours with the same isovalue (indicated by pink ticks on the contour tree). The two further branches that are isolated from the other branches and connect to them only through the global minimal point are CGC-L and CGC-R (cingulum or cingulate gyrus left and right). We observe that the CGC structure is indeed spatially disconnected from the rest of the brain white matter.

Next, the distribution histograms show that most white-matter voxels reside in the center branch, as indicated by its dark green color and wider histograms: those arcs represent the regions where white matter heavily crosses into the cortex and connects the gray matter, where the FA values drop to their lower ranges.

Last but not least, we see by detailed visual inspection that the height, thus the FA values of the tree in the schizophrenia cohort are generally lower than those in the controlled group. The difference is more obvious in the GCC and SCC branches. This is consistent with previous discoveries that schizophrenia patients have reduced white-matter FA values, especially in the corpus callosum region [13].

4.2 Discussion

This semantic-driven contour construction approach has allowed us to construct an occlusion-free representation, interactively examine the ROIs, and visualize fiber integrity through FA values. Our method is not limited to showing only FA values but can handle any information captured, for example, through the design of encoding on those arcs.

There are several future directions to improve the usefulness of our approach. The first is related to interactivity: to allow multiple regions of selection. Since the contour trees are dense, it will be useful to design approaches to allow comparison of the numerical values of the same regions clearly between cohorts. Second, we also plan to construct the contour tree of specific ROIs to reduce the visual complexity. The third is related to fiber tracts based graph connectivities. Currently we can overlay fiber tracts on top of the volume rendering (Fig. 1). One interaction design would be to display the fiber tracts to show all regions connected to the ROI selected in the contour tree and subsequently mark those connected regions in the tree as well to provide informative contextual queries related to ROI. We also need to empirically validate our visual design approach using case studies or lab-based experiments.

5 CONCLUSION

We have designed a semantic-driven contour-tree visualization for brain white matter cohort comparison. Our approach improves the previous contour-tree simplification and layout methods by taking into account anatomical ROI information. The layout and labeling are automatic making it easier for brain scientists to understand the meaning of each arc and the correspondences between arcs in different contour trees. The occlusion-free 2D representation makes it easy to compare FA values in brain regions.

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REFERENCES

- [1] R. Borgo, J. Dearden, and M. W. Jones. Order of magnitude markers: an empirical study on large magnitude number detection. *IEEE Transactions on Visualization and Computer Graphics*, 20(12):2261–2270, 2014.
- [2] P. Burkhardt. Big graphs. *The next wave*, 20(4), 2014.
- [3] H. Carr, J. Snoeyink, and U. Axen. Computing contour trees in all dimensions. *Computational Geometry*, 24(2):75–94, 2003.
- [4] H. Carr, J. Snoeyink, and M. van de Panne. Simplifying flexible isosurfaces using local geometric measures. In *Proceedings of the conference on Visualization*, pages 497–504, 2004.
- [5] J. Chen, H. Cai, A. P. Auchus, and D. H. Laidlaw. Effects of stereo and screen size on the legibility of three-dimensional streamtube visualization. *IEEE Transactions on Visualization and Computer Graphics*, 18(12):2130–2139, 2012.
- [6] W. Chen, Z. A. Ding, S. Zhang, A. MacKay-Brandt, S. Correia, H. Qu, J. A. Crow, D. F. Tate, Z. Yan, and Q. Peng. A novel interface for interactive exploration of DTI fibers. *IEEE Transactions on Visualization and Computer Graphics*, 15(6):1433–1440, 2009.
- [7] N. Gehlenborg and B. Wong. Points of view: Power of the plane. *Nature methods*, 9(10):935–935, 2012.
- [8] M. Harrower and C. A. Brewer. Colorbrewer.org: an online tool for selecting colour schemes for maps. *The Cartographic Journal*, 40(1):27–37, 2003.
- [9] C. Heine, D. Schneider, H. Carr, and G. Scheuermann. Drawing contour trees in the plane. *IEEE Transactions on Visualization and Computer Graphics*, 17(11):1599–1611, 2011.
- [10] N. Jahanshad, P. V. Kochunov, E. Sprooten, R. C. Mandl, T. E. Nichols, L. Almasy, J. Blangero, R. M. Brouwer, J. E. Curran, G. I. de Zubicaray, et al. Multi-site genetic analysis of diffusion images and voxelwise heritability analysis: A pilot project of the ENIGMA-DTI working group. *Neuroimage*, 81:455–469, 2013.
- [11] R. Jianu, Ç. Demiralp, and D. H. Laidlaw. Exploring 3D DTI fiber tracts with linked 2d representations. *IEEE Transactions on Visualization and Computer Graphics*, 15(6):1449–1456, 2009.
- [12] P. Kochunov, J. L. Lancaster, P. Thompson, R. Woods, J. Mazziotta, J. Hardies, and P. Fox. Regional spatial normalization: toward an optimal target. *Journal of computer assisted tomography*, 25(5):805–816, 2001.
- [13] K. Nakamura, Y. Kawasaki, T. Takahashi, A. Furuichi, K. Noguchi, H. Seto, and M. Suzuki. Reduced white matter fractional anisotropy and clinical symptoms in schizophrenia: a voxel-based diffusion tensor imaging study. *Psychiatry Research: Neuroimaging*, 202(3):233–238, 2012.
- [14] V. Pascucci, K. Cole-McLaughlin, and G. Scorzelli. Multi-resolution computation and presentation of contour trees. In *Proc. IASTED Conference on Visualization, Imaging, and Image Processing*, pages 452–290, 2004.
- [15] S. M. Smith, M. Jenkinson, H. Johansen-Berg, D. Rueckert, T. E. Nichols, C. E. Mackay, K. E. Watkins, O. Ciccarelli, M. Z. Cader, P. M. Matthews, et al. Tract-based spatial statistics: voxelwise analysis of multi-subject diffusion data. *Neuroimage*, 31(4):1487–1505, 2006.
- [16] J. M. Soares, P. Marques, V. Alves, and N. Sousa. A hitchhiker’s guide to diffusion tensor imaging. *Frontiers in neuroscience*, 7, 2013.
- [17] O. Sporns, G. Tononi, and G. M. Edelman. Theoretical neuroanatomy: relating anatomical and functional connectivity in graphs and cortical connection matrices. *Cerebral Cortex*, 10(2):127–141, 2000.
- [18] X. Tricoche, G. Kindlmann, and C.-F. Westin. Invariant crease lines for topological and structural analysis of tensor fields. *IEEE Transactions on Visualization and Computer Graphics*, 14(6):1627–1634, 2008.
- [19] K. Wu and S. Zhang. A contour tree based visualization for exploring data with uncertainty. *International Journal for Uncertainty Quantification*, 3(3):203–223, 2013.