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# Effects of tractography filtering on the topology and interpretability of connectomes

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## Introduction

The analysis of connectomes and their associated network metrics forms an important part of clinical studies [1,8]. These connectomes are based on tractography algorithms to estimate the structural connectivity between brain regions [7]. However, tractography algorithms, are prone to false positive connections [7] and this affects the quality of the connectomes.

Several tractography filtering techniques (TFTs) [6,2,10] have been proposed to alleviate this issue in studies [5,3,9], but their effect on connectomic analyses of pathology has not been investigated. The aim of our work is to investigate how TFTs affect network metrics and their interpretation in the context of clinical studies.

## Methods

Our dataset consisted of 18 patients with Traumatic Brain Injury (TBI) and 18 demographically matched healthy controls. For each subject, the connectomes were created using probabilistic anatomically constrained tractography to obtain a tractogram of 2 million streamlines, parcellating the brain into 86 regions based on the Desikan atlas [4], and using the streamline count to represent the connectivity between regions. We refer to this 86 x 86 matrix as the “unfiltered connectome”. TFTs filter a tractogram by assigning weights to streamlines based on how well they explain the underlying data. Streamlines associated with a coefficient of zero value are marked as a false positive, and are hence excluded from the tractogram. The TFTs we compare are SIFT2 [10], COMMIT [2] and the Group-Sparsity (GS) formulation of COMMIT [6]. SIFT2 filters the tractogram based on the fiber density information without incorporating microstructure. On the other hand, COMMIT models the underlying microstructure and excludes false positives based on how well the streamlines explain the acquired dMRI fitted with this multi-compartment model. Finally GS builds on this microstructure model of COMMIT and incorporates the brain's bundle structure to eliminate false positives. Starting from unfiltered connectomes, new “kept” connectomes were recreated after filtering each tractogram using these 3 TFTs. We also computed the connectomes using the streamlines that have been excluded by the process of filtering by COMMIT and GS, called “excluded” connectomes. The topology of connectomes was quantified using the integration measure of global efficiency and the segregation measure of Louvain modularity, computed on healthy controls. The interpretability of the connectomes

was evaluated by comparing the connectomes of the patients and controls at the level of each edge, using the Mann-Whitney U test with false discovery rate based multiple comparisons correction.

## Results

Fig. 1 illustrates that all TFTs increase the segregation and decrease the integration of the connectomes, which translates into a significant change on the network topology. Fig. 2 shows the comparison of patients and controls for each of the connectome sets. We observe that SIFT2 and COMMIT increase discriminability between patients and healthy controls, as compared to the unfiltered connectomes, while GS removes all differences. Notably, although SIFT2 and NNLS both capture group differences, different sets of edges show significant differences and could potentially involve different subnetworks. In addition, although there are no significant group differences in the excluded connectomes of COMMIT, all group differences in GS are transferred to the excluded connectome.

## Conclusions

Our results demonstrate that tractography filtering techniques change the topology of brain networks, and thus alter network metrics. The uniform removal of false positives that COMMIT undertakes, has a different effect than the structured removal of GS. This clearly affects the interpretability of results, as we demonstrated in the TBI dataset. As such, more research and extra caution are needed prior to incorporating tractography filtering into connectomic analysis pipeline in clinical studies.

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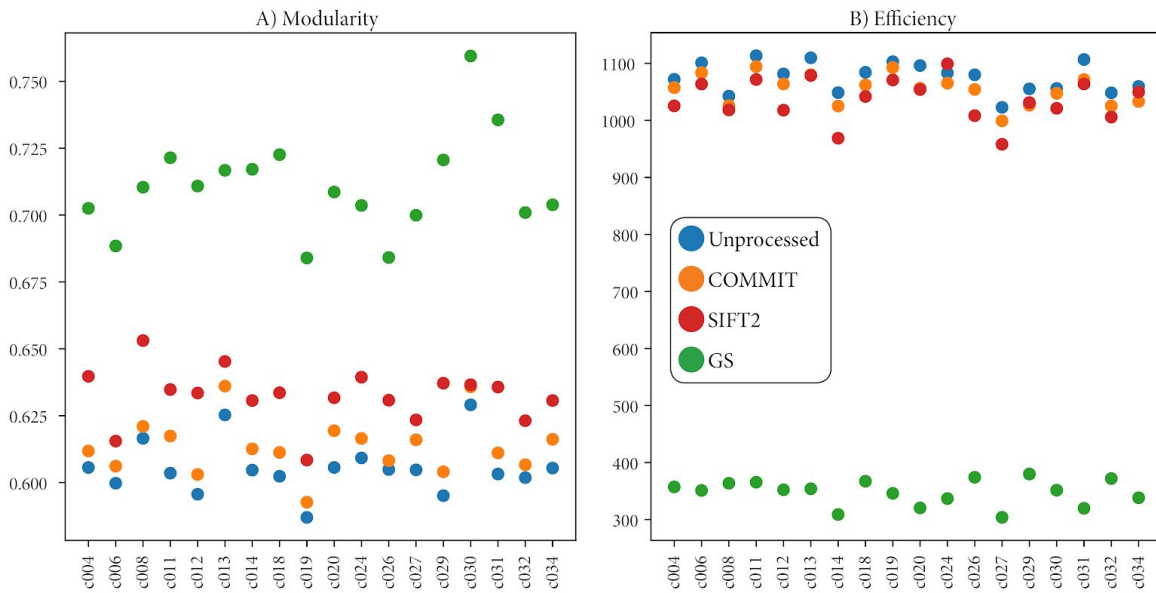
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### Figure 1

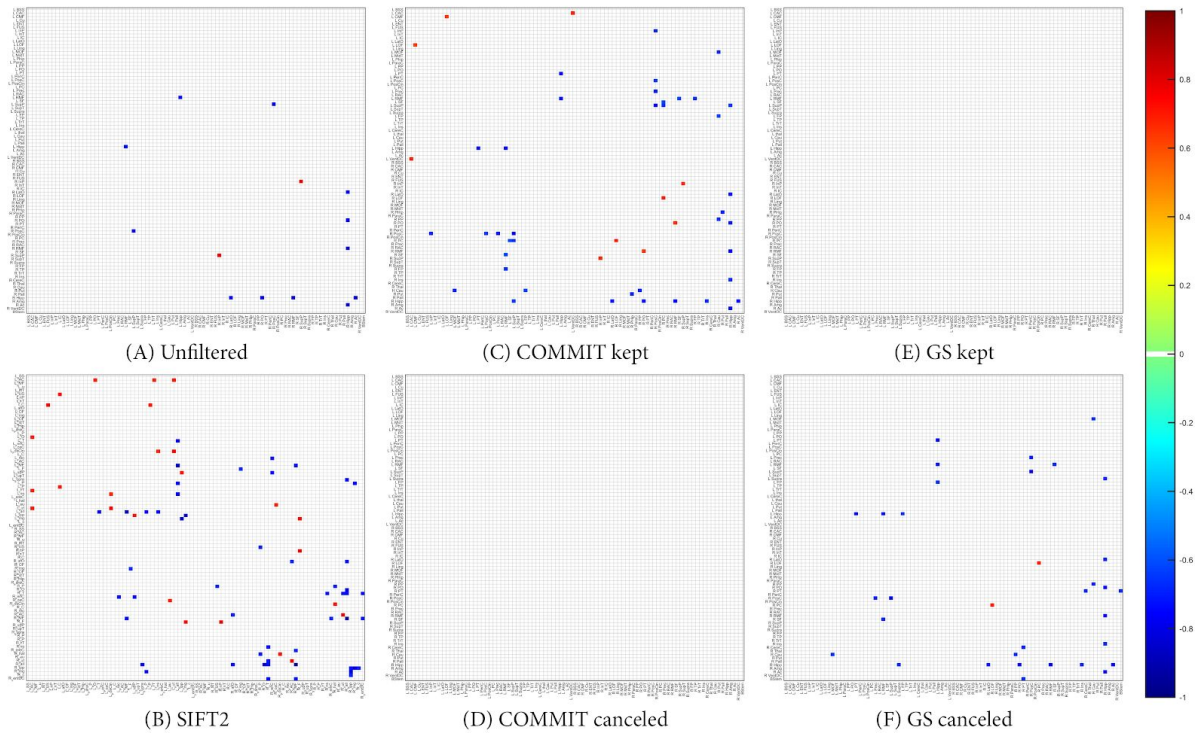
Effect of tract filtering on the topology of connectomes of the healthy controls. Figure A shows the intra-subject variability of the modularity across different Tractography Filtering Techniques. The displayed values are the average of 100 runs of the Louvain modularity method. Figure B shows the intra-subject across-TFT variability of efficiency. Both integration and segregation of the network topology is affected by tract filtering.



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## Figure 2

Effect of tract filtering on the interpretability of connectomic analysis of a clinical dataset. These figures show the results of the edge-wise statistical comparison of connectomes of patients with brain injury using the Mann–Whitney U test with FDR multiple comparisons correction on A) unfiltered connectomes; B) SIFT2 connectomes; C) and D) connectomes based on streamlines kept and removed after COMMIT, respectively; E) and F) Connectomes created using streamlines kept and removed by GS, respectively.



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