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Weighted Functional Brain Network Modeling *via* Network Filtration

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Abstract

In traditional brain network modeling, an weighted brain network is often thresholded at a prespecified level to produce a binary graph for visualization and quantification. However, if we threshold the brain network and obtain only the strongly connected edges, we may lose additional information. Motivated by the persistent homology and Rips filtration, we propose a new multiscale brain network modeling framework called the *network filtration*, which represents the weighted network into the finite number of nested binary networks over every possible threshold. In the network filtration framework, we look at the changes of topological invariants over different thresholds. Particularly, we are interested in the changes of connected structures in the brain network, which can be represented in four different but equivalent ways: barcode, single linkage dendrogram (SLD), single linkage matrix (SLM) and minimum spanning tree (MST). Numerical experiments show that the proposed method can discriminate the local and global differences of the brain networks of 24 attention deficit hyperactivity disorder (ADHD), 26 autism spectrum disorder (ASD) and 11 pediatric control (PedCon) children obtained through the FDG-PET data.

1 Introduction

In traditional brain network modeling, nodes are anatomically or functionally predefined regions of interest (ROIs) and the edges are determined by various techniques such as correlation methods, structural equation modeling or dynamic causal modeling [1, 2, 3, 4]. Correlation-based methods are probably the most widely used approaches in the field. However, the problem of the correlation-based approach is the arbitrariness of where to threshold correlations. For thresholding correlations, few proposed methods such as the multiple comparisons correction and the sparsity control are available [5]. These thresholding methods assume that the strongly connected edges are only important; however, it is recently suggested that the weakly connected edges may also have discriminative information between networks [6]. Moreover, graph theoretical measures such as small-worldness and degree distribution drastically change depending on where correlations are thresholded [3].

Motivated by these results [6, 3], we propose a novel scalable weighted network modeling technique that does not threshold correlations at any fixed level. The proposed approach represents the weighted network into the finite number of binary networks at every possible threshold *via* the filtration on networks. Then we quantify the topological invariants like Betti numbers on the network filtration. In this study, we particularly look at the changes of the connected components in the brain network, which is related to single linkage dendrogram (SLD), single linkage matrix (SLM)

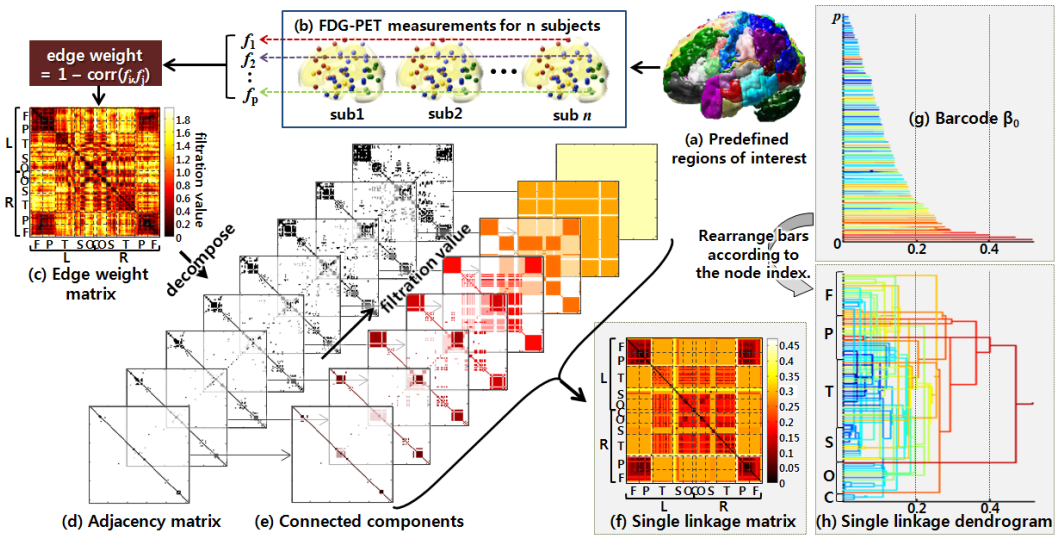

Figure 1: Schematic diagram of proposed functional brain network filtration framework using PET. (a) Using the predefined anatomical atlas, the brain is parcellated into ROIs. (b) Each center of ROI serves as a node and (c) its FDG-PET measurement is used in assigning the edge weight. (d) The edge weight matrix is decomposed into the finite number of binary matrices at every possible filtration value. (e) Subsequently, we can find the connected networks (CNs) at each filtration value as a topological invariant. If we put all connected network matrices together, (f) SLM is obtained. The other representations of SLM are (g) barcode and (h) SLD. If we rearrange bars in the barcode according to the node index, SLD is obtained.

and minimum spanning tree (MST) [7, 8, 9]. The proposed method is applied in discriminating three different functional brain networks of attention-deficit hyperactivity disorder (ADHD), autism spectrum disorder (ASD) and pediatric control (PedCon) subjects obtained through FDG-PET.

2 Methods

Brain network construction: The brain is parcellated into p ROIs by using the predefined anatomical atlas (Fig. 1 (a)) [10, 8]. Each center of ROI serves as a node of the brain network in (b). At node i, we have vector $\boldsymbol{f}_i \in \mathbb{R}^n$ corresponding to FDG-PET measurements of multiple subjects. The weight matrix is denoted as $\boldsymbol{W} = [w_{ij}]_{i,j=1,\dots,p}$, where

$$w_{ij} = 1 - \boldsymbol{f}_i^\top \boldsymbol{f}_j$$

is the edge weight between nodes in (c). When $\boldsymbol{f}_i$ is normally distributed with mean 0 and the variance $1/n$, w_{ij} is one minus Pearson correlation. We can always translate and normalize $\boldsymbol{f}_i$ to satisfy these conditions. Then the weighted functional brain network forms a metric space $X = (V, \boldsymbol{W})$, where V is the node set [8].

Network filtration: The concept of network filtration is motivated by the Rips filtration in persistent homology [8]. Given the weighted network $X = (V, \boldsymbol{W})$, we perform the filtration on the edge weights to obtain a sequence of binary networks. At the filtration value ϵ, the obtained binary network is denoted as $\mathcal{B}(X, \epsilon)$. Then, the binary network $\mathcal{B}(X, \epsilon)$ is a subset of the Rips complex $\mathcal{R}(X, \epsilon)$ defined by a simplicial complex whose $(p-1)$-simplices correspond to unordered p-tuples of nodes that satisfy $w \leq \epsilon$ in a pairwise fashion [11, 9]. If we choose the filtration values from the ordered set of edge weights, $\{w_{\min} = w_1 < \cdots < w_q = w_{\max}\}$, we have the nested sequence of networks (Fig. 1 (d) and Fig. 2 (a)):

$$\mathcal{B}(X, w_1) \subseteq \mathcal{B}(X, w_2) \subseteq \cdots \subseteq \mathcal{B}(X, w_q).$$

The sequence of such nested network will be called as the *network filtration*. The weighted graph $X = (V, \boldsymbol{W})$ can be uniquely decomposed.

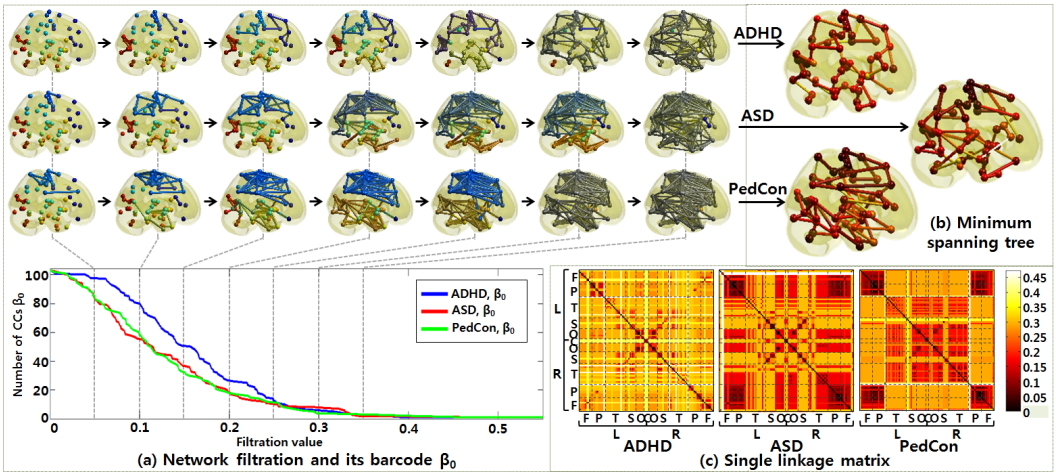

Figure 2: Network discrimination using the network filtration on ADHD, ASD and PedCon datasets. If we count the number of connected networks (CNs) during the filtration, the barcode β_0 is obtained (a). The barcode shows the difference of global connection between ADHD and other networks. The local difference between networks can be compared using (b) MSTs and (c) SLMs. Although MSTs have the identical number of edges, PedCon seems to have more edges due to the long-range connections. From SLMs, we observe that ASD has looser connections in the left (L) frontal (F) region and ADHD has looser connections in the fronto-parietal regions (F-P) compared to PedCon.

Representation of β_0: We consider the network consisting of $0-$ and $1-$complexes (nodes and edges). Our main concern is the changes of the zeroth Betti number β_0, which measures the number of connected networks (CNs). The changes of β_0 are visualized using the barcode in Fig. 1 (g). The vertical and horizontal axes in the barcode represent the indices of CN and filtration values respectively. The barcode of β_0 is basically a decreasing function showing when CNs are merging to form a bigger network component.

The number of CNs at the certain filtration value is same to the number of bars. If we rearrange the bars according to the node index instead of CN index in the vertical axis, we obtain SLD as shown in Fig. 1 (g,h). While the barcode of β_0 shows the global changes of the connected structure of network when the bars are ended, the SLD shows the local changes when the bars are merged. SLD can be also represented in the algebraic form $\boldsymbol{D}$ called SLM (Fig. 1 (f)):

$$\boldsymbol{D} = [d_{ij}] = [\min_{P_{ij}} \max_{l} w_{p_l, p_{l+1}}],$$

where $P_{ij} = \{i = p_0, \cdots, p_k = j\}$ is a path between two nodes i and j. The minimum is taken over every possible path between i and j. d_{ij} is the single linkage distance between v_i and v_j. If we collect the edges which make a change in β_0 during the network filtration, the obtained edge set generates MST in Fig. 2 (a,b). MST is a network with the minimum number of edges among all possible networks which have the same SLD.

3 Results

Our FDG-PET data consists of 3 groups: 24 ADHD, 26 ASD and 11 PedCon subjects. PET images were spatially normalized to the standard template space after converting to Analyze format and smoothed with a Gaussian filter of 16 mm FWHM using Statistical Parametric Mapping (SPM 2,UK) package [10]. The mean FDG uptake within 103 ROIs were extracted.

After filtration on the weighted network, its SLM, MST, SLD and barcodes β_0 are obtained (Fig. 2). We calculated the difference between two connected structures of networks using the Gromov-Hausdorff distance, which is defined as the maximum distance between two different SLMs [7, 8]. Using the permutation test, we found that the overall connected structures between ADHD and PedCon and between ASD and PedCon are statistically different at the significance level .05. We also found the local differences between groups at the level .05 as follows:

- ASD showed looser connections between left inferior prefrontal regions in BA44 and BA45 and other brain regions. It might reflect the behavioral symptom in ASD [12].
- ADHD showed looser connections between sensorimotor region and various frontoparietal regions including anterior cingulate compared to PedCon. It might reflect the deficits of cognitive attentional control and sensori-motor integration [13].
- ASD and ADHD have commonly abnormal connected structure in cerebellum. Cerebellum is one of the pathophysiological regions in ADHD and ASD.

4 Conclusions

In this paper, we proposed a new brain network modeling framework by introducing the concept of network filtration, which is motivated by the Rips filtration in the persistent homology. From the network filtration, we extracted the persistent topological features that tabulates the changes in the number of CNs over the filtration. The topological features are related to MST. Hence, we were able to combine two distinct concepts (Rips filtration and MST) into our network filtration framework [7, 8]. As an application, we showed that SLD-based features can discriminate the network differences and can be used as an topological biomaker for characterizing abnormal brain networks.

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