A Framework for Mapping Scalable Human Brain Anatomical Networks via Diffusion MRI*

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***Abstract*— Anatomical network analysis is considered as a significant way to study brains. The attributes of anatomical networks vary across network nodal scales and therefore a scalable network mapping method is needed. Here, a new framework for mapping scalable brain anatomical networks via d-MRI is presented. The modelling of nodes is based on the structural basis of brain connections (white matter) and the scale of network nodes is determined by the clustering number of white matter fibers' endpoints. d-MRI datasets from glioma patients and healthy people were tested in this framework. All mapped networks have small-world characteristics, and demonstrate the effects of glioma on brain network connectivity.**

I. INTRODUCTION

The whole human brain is one of the most complex natural systems, usually modelled as a network [1]. The characterization of the global architecture of the connectivity patterns has gained significant interests in recent years. The study of brain connectivity could provide an insight of how human brain specifies different regions and integrates them to emerge functional brain states [2]. From a clinical aspect, the brain network properties can also be used as diagnostic markers, and the investigation can help us understand the pathogenesis and treatment of brain disorders [3].

Based on different magnetic resonance imaging (MRI) modalities, two different types of human brain networks can be mapped: functional networks and anatomical networks. Typically, a functional brain network is constructed from correlated activity between functional grey-matter regions over time, through resting-state-functional-MRI (rs-fMRI), electroencephalography (EEG) or magnetoencephalography (MEG). An anatomical network is based on white-matter fiber bundles that connect spatially isolated grey-matter regions, using diffusion-MRI (d-MRI). Previous works have mainly investigated the mapping and characteristics of functional human brain networks [4]–[7]. The derivation and analysis of anatomical brain networks, however, have been poorly studied, because of the challenges in mapping the elements of anatomical brain networks with respect to nodes and connections [2], [8].

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Some studies have revealed an intimate relationship between a human brain's functional network and anatomical network, which share common topological features [3], since an individual neural node's pattern of connections with other nodes partly determines its functionality in the network and the entire anatomical connectivity places constraints on each node's interactions with others [9]. Functional networks and anatomical networks profile one person's brain from two perspectives. On the other hand, anatomical connectivity is the structural basis of functional connectivity. For a complete understanding of human brain, a comprehensive map of structural connectivity is required [2].

Diffusion MRI is capable of illustrating brain white-matter pathways in-vivo and non-invasively by exploiting the anisotropic properties of white-matter fiber bundles [10]. The motion of water molecules inside fiber bundles can be labeled during diffusion image acquisition. On the basis of the measurements, the microstructure at every imaged brain location can be captured and fiber bundle trajectories can be inferred (a so-called tractography technique) [11]. White matter is the structural basis of connections in brain networks and anatomical brain networks can be mapped through the reconstruction of white matter structures. The challenges are how to define the nodes (functional regions in grey matter) in the networks and the connections (white-matter pathways) between the nodes [8].

Currently, no single parcellation scheme for human brain regions is universally accepted. It is not clear what the optimal scale (neuronal, micro-column or regional scale) is for brain connectivity characterization. Previous works have investigated the connectivity patterns in the cerebral cortex of human beings [12], and studied the whole human brain anatomical networks [13] via d-MRI. For these, the cerebral cortex or grey matter tissues were segmented into tens of different regions by registering the subjects with atlases, like automated anatomic labeling (AAL) atlas [14]. Some researchers have attempted to map a high-resolution structural brain network by simply segmenting the cortex into $1.5cm^2$-size homogenous patches according to their gyral coordinates [15], which only relied on the their positions on the cortical surface.

In the present paper, our interest lies on the modelling of scalable human brain anatomical networks. First, we propose a new scalable network nodal definition method, capable of mapping high-resolution brain networks, according to the anatomy of white matter. Tractography provides the entire white-matter structure of any person, in terms of fiber tracts. Scalable nodes of brain networks are defined by clustering

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each tract's end points. Then, we validate our methods by modelling the brain networks of glioma patients and normal people. Not only previous small-world analysis is employed, other three important graph properties will also be investigated.

II. MATERIALS AND METHODS

A. Datasets

The present study included 20 d-MRI data sets. Ten of them were from patients diagnosed with brain glioma, provided by Beijing Tiantan Hospital. The scans were performed on a Siemens 3.0T MRI scanner. d-MRI were acquired by using an Echo-Planar Imaging (EPI) -based sequence: coverage of the whole brain, 5.20-mm slice thickness with no interslice gap, 25 axial slices, time repetition (TR) = 3600 ms, echo time (TE) = 95 ms, 64 diffusion directions with b = 1000 s/mm^2, in-plane acquisition matrix = 128 $\times$ 128. The other ten of the datasets were from the open datasets of normal people in the community National Alliance for Medical Image Computing (http://hdl.handle.net/1926/1687). The scans were acquired on a 3 Tesla General Electric system using an EPI-based diffusion imaging sequence: coverage of the whole brain, 1.70-mm slice thickness with no interslice gap, 85 axial slices, TR = 17000 ms, TE = 78 ms, 51 diffusion directions with b = 900 s/mm^2, in-plane acquisition matrix = 144 $\times$ 144.

B. Preprocessing

DTIPrep (http://www.nitrc.org/projects/dtiprep) is used to perform preprocessing of Diffusion Weighted MRI (DWI) datasets [16], which includes image and diffusion information checking, eddy-current artifacts correction and head motion artifacts correction.

C. Reconstruction of Anatomical Connections by Tractography

Our framework of mapping brain anatomical networks from d-MRI is based on the structural connectivity (white matter) in human brains. Tractogarphy is a computational method of tracing fiber tracts by following probable tract orientations, on the basis of d-MRI, which actually reconstructs the white matter. Since white matter provides connectivity information in the brain networks modeling, it is significant to choose a tractography method which can infer a more complete structure of white matter.

Unscented Kalman filtering (UKF) tractography [17] is employed here to map a white matter structure from one's diffusion weighted MRI data. Specifically, part of our datasets are from brain glioma patients. Gliomas usually deform other brain tissues and appear together with edema. The fluid in edema changes the anisotropic properties of its nearby region and d-MRI captures the white matter fibers' microstructure at each location by the measurements of the anisotropic properties. Tracing the fiber tracts inside of edema becomes a challenge and some studies have reported that UKF tractography addresses the challenge better than other tractography methods do [18].

D. Network Node Definition

Our brain network node modelling is based on white matter fiber clustering. Tractography provides fiber trajectories in terms of the course of anatomical fiber tracts (mm diameter) and the scale is fine enough to map a high-resolution (around 10000-node) brain network. Ideally, the two endpoints of each fiber tract reach grey matter and can be regarded as abstraction of adequately segmented functional regions. For mapping scalable networks, these points need to be clustered into coarse-scale nodes and the scale depends on the number of clusters we set. Modelling network nodes from fiber tracts, we adopt a five-step process: (1) extracting all the endpoints of fibers (to be clustered), (2) assigning each endpoint with affinities with other points and calculating the entire pairwise endpoint affinity matrix, (3) creating a spectral embedding of all endpoints, (4) using the k-means algorithm in the embedding space to find k clusters, (5) computing the center of mass of each cluster's points as our network nodes.

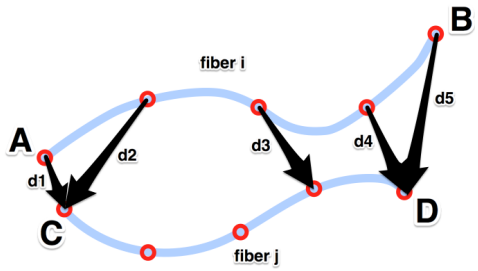


Fig. 1. Illustration of computation of the MCP distance from fiber i to fiber j. In this figure, 5 equidistant points are used to represent each fiber and the distance from each point in fiber i to its closest point in fiber j is computed.

The affinity of two endpoints is determined by the similarity of their corresponding tracts, which is reasonable since a bundle (cluster) of tracts usually connects one functional region with another region. We quantify the pairwise tract similarity by computing the mean closest point (MCP) distance d_{mcp} of the two tracts, which is a commonly used measure in white matter tracts segmentation [19]. The computation of this distance is illustrated in Fig. 1. It is calculated by:

$$d_{mcp_{ij}} = \frac{1}{n}\sum_{k=1}^{n} d_k \tag{1}$$

where n is the number of the equidistant points used to represent each fiber (n equals to 15 in our methods, but for simplification, each fiber is represented by 5 points in Fig. 1.) and d_k is the distance from point K in fiber i to its closest point in fiber j. The MCP distance is a directional distance. We symmetrize it by taking the minimum value of the two distances $d_{mcp_{ij}}$ and $d_{mcp_{ji}}$:

$$d_{i,j} = min(d_{mcp_{ij}}, d_{mcp_{ji}}) \tag{2}$$

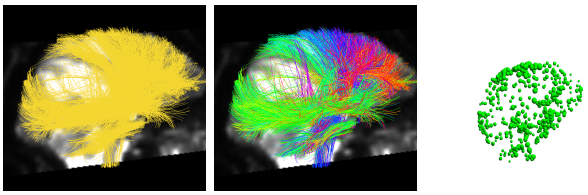
The similarity $S_{i,j}$ of fiber i and fiber j is converted from $d_{i,j}$ by a Gaussian Kernel:

$$S_{i,j} = e^{-{d_{i,j}}^2/\sigma^2} \tag{3}$$

Fig. 2 illustrates the whole brain tractography results of one glioma patient and their internal similarity assignment.

For the affinity W of the endpoints in fibers, if two endpoints are in the same side of the fibers, then the affinity equals the similarity of their corresponding fibers; otherwise, the affinity is set to be 0 (The range of S is $(0, 1]$.). For the example in Fig.1, point A with C are in the same side, and point A with B or D are in opposite sides. A and B are the two endpoints of the same fiber so they are judged in opposite sides; The Euclidean distance between A and D is larger than that between A and C so A and D are also judged in opposite sides. Therefore, $W_{A,B/D} = 0$ and $W_{A,C} = S_{i,j}$.

By computing the leading eigenvectors of the entire pairwise endpoint affinity matrix $\mathbf{W}$, the spectral embedding of all endpoints can be created. We employ the embedding method described in [20]. In the embedding space, the k-means algorithm is employed to find k groups of points. The center of mass for each cluster of points, which represents this region (cluster), is a node in our network. An example of so-generated 400 network nodes is illustrated in Fig.2.



(a) (b) (c)

Fig. 2. Illustration of white matter fiber tracts from one glioma patient, the fibers' internal similarity assignment and an example of 400 network nodes from this patient. For the sub-figure (b), more similar the colors of two tracts are, higher their similarity value W is.

E. Node-node Connectivity

The connection between two nodes is characterised by the number of fiber tracts which connect the two nodes (the two cluster of points that the two nodes represent) and their neighbor nodes. For example, there are only three nodes in a network and the number of fiber tracts which connect node a with b is $N_{a,b}$ and node b is close to node c. If the Euclidean distance between node b and c is less than a threshold α, then the fiber tracts connecting a and c will contribute to the connection of node a and b. The arc weight between node a and b is $m_{a,b} = N_{a,b} + \beta N_{a,c}$. Here (for the 400-node network), we set α to be $5mm$ and β to be 0.1. A so-mapped undirected weighted network is illustrated in Fig. 3.

III. RESULTS

Using the human brain anatomical network mapping framework described above, 400-node anatomical networks were estimated for the 10 healthy people and 10 glioma patients. Graph theory is commonly used for the analysis or feature extraction of complex networks. Some methods in graph analysis have been widely used in the analysis of brain networks. Here, we employ the property of small-worldness to validate our results and other three aspects to characterize our mapped networks.

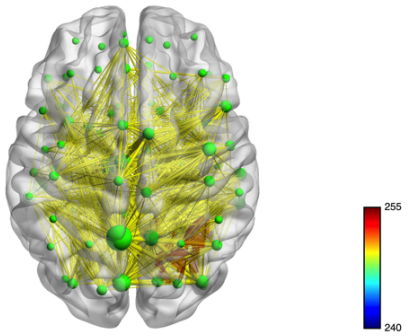


Fig. 3. Illustration of a glioma patient's 400-node brain anatomical network. The widthes of the lines are proportional to their arc weights and the sizes of the points are proportional to the degrees of these points. The red chunk represents the glioma. Only large-degree nodes are illustrated in this figure.

A. Small-worldness

Previous works have reported that functional and anatomical human brain networks both exhibit "small-world" attributes [7], [13]. Small-worldness is related to two concepts: average shortest path length ($ASPL$) and clustering coefficient (CC). λ represents the ratio of $ASPL$ of a graph to its random graph which contain the same number of nodes ($\lambda \equiv ASPL_{real}/ASPL_{random}$). γ represents the ratio of CC of a graph to its random graph ($\gamma \equiv CC_{real}/CC_{random}$). The "small-world" condition lies in satisfying $\sigma \equiv \frac{\gamma}{\lambda} > 1$.

The results from the 20 data sets (Table I) confirm the expected small-world property of the 20 mapped human brain anatomical networks and the mean parameters of interest are $\gamma_{mean} = 1.18$, $\lambda_{mean} = 0.94$ and $\sigma_{mean} = 1.29$.

B. Characterizing Brain Anatomical Networks

Three graph attributes are employed to characterize the 10 healthy people's and 10 glioma patients' brain networks: average betweenness centrality, average degree and global efficiency. The results of the characterizations are illustrated in Fig. 4. Glioma in the brain can infiltrate or displace white matter fibers. The mapped brain networks demonstrate the effects of glioma.

IV. CONCLUSION

We propose a framework for mapping scalable human brain anatomical networks via d-MRI and "small-world" attribute is used to validate our results. The scales of the networks are based on the clustering of white matter fibers' endpoints. Three graph attributes are employed to characterize the glioma's effects on brain connectivity.

For future work, more categories of datasets and more scales of networks will be examined and tested, to somewhat find optimal nodal scales for different problems.

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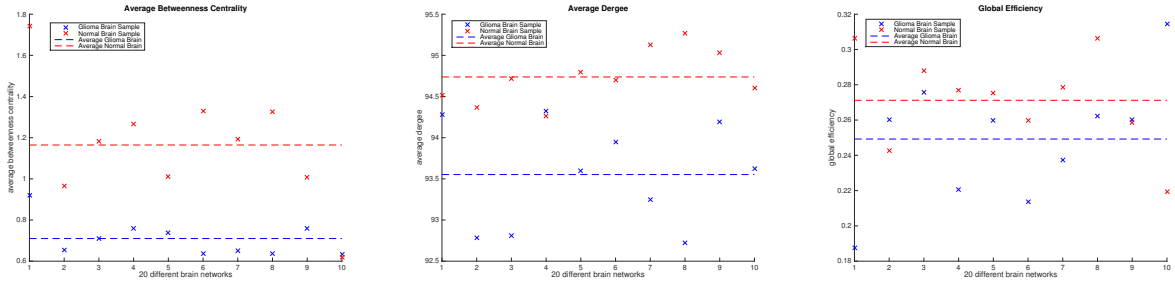
TABLE I

OBTAINED HUMAN BRAIN ANATOMICAL NETWORKS PROPERTIES

Subjects	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
γ	0.96	0.94	0.93	0.99	0.98	0.95	0.93	0.94	0.96	0.97	1.99	1.03	1.46	1.68	1.06	1.71	1.54	1.54	1.23	0.82
λ	0.92	0.65	0.71	0.76	0.74	0.64	0.65	0.64	0.76	0.63	1.74	0.96	1.18	1.27	1.01	1.33	1.19	1.33	1.01	0.62
σ	1.04	1.44	1.31	1.31	1.33	1.48	1.43	1.48	1.26	1.53	1.14	1.07	1.24	1.32	1.05	1.29	1.29	1.16	1.23	1.32



(a) (b) (c)

Fig. 4. Illustration of three brain network characteristic attributes between healthy people and glioma patients. (a) is for average betweenness centrality. (b) is for average degree. (c) is for global efficiency.

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