Homology and Topology based Metrics for Evaluating Cortical Parcellations Generated using Diffusion MRI

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***Abstract*— When using diffusion MRI for segmenting the cerebral cortex, the modality of information used and workflow procedural factors can have significant effects on the resulting parcellation. There is as yet no consensus on best practice processing protocols, and no ground truth is available in vivo. Converging indirect evidence has been used to compare parcellation outcomes, including: (1) comparison of cortical parcellations based on different modalities; (2) reproducibility across independent acquisitions; (3) consistency across modality or subject; and (4) the extent to which the segmented regions are functionally distinct based on task or rsfMRI data. To these we add an additional strategy wherein parcellation results are assessed based on known organizational principles of the brain, specifically inter-hemispheric homology and topology, thereby permitting assessment of results per subject independently of another imaging modality or acquisition. We propose these measures to guide improvements in acquisition, reconstruction, and/or clustering approaches during the process of diffusion MRI parcellation.**

***Index Terms*— Earth Mover's Distance, diffusion MRI, tractography, parcellation, topology, homology**

I. Introduction

The cerebral cortex is comprised of a mosaic of cortical fields, each occupying a contiguous region of cortex [1]. A cortical field is posited to have a distinctive cytoarchitecture and anatomical connectivity fingerprint. These complementary and interrelated anatomical properties are thought to be important determinants of functionally independent cortical units, reflecting local processing capabilities and information input and output integration. The ability to accurately and reliably delineate cortical fields in vivo promises to be fundamentally useful for studying neuroanatomical variation and brain function in humans. Recent advances in imaging support the use of diffusion MRI (dMRI) to achieve this objective [2], and we focus on this approach here.

When using dMRI for segmenting the cortex into cortical fields, one makes procedural choices that can have a significant effect on the resulting segmentation, and there is no consensus on a "best practice" workflow, and no practically available "ground truth" for evaluating the resulting parcellations per subject, in vivo. Current evaluation approaches include: (1) comparison with cortical parcellations based on a different modality, (2) reproducibility of parcellations across independent acquisition sessions or diffusion sequences, (3) the extent to which the segmented regions are functionally different from each other, for example using task or rsfMRI data, and (4) consistency of the number and location of parcels across different subjects [2].

To these approaches, we propose adding a complementary method that exploits hemispheric homology, with metrics that assess the preservation of the topological arrangement of homologous brain areas and similarity of their connectivity profiles. The principle of homology assumes that at the physical scale of cytoarchitectonic fields, each region has a homologous counterpart in the contralateral hemisphere. Examples of parcellations in which homology has been observed include the Brodmann cytoarchitectonic parcellations [3], and the cytoarchitectonic and receptor-architectonic parcellations of the human inferior parietal cortex (IPL) [4], [5].

In the IPL parcellations [4], 10 postmortem human brains were bilaterally segmented into 7 cytoarchitectonic sub-regions, each with a contralateral homologous sub-region with which it shared similar cytoarchitecture. An analysis of probabilistic fiber tracts along these sub-regions superimposed onto the brains of 40 healthy humans revealed that the connectivity profiles/fingerprints of homologous regions were qualitatively more similar compared to non-homologous regions [6]. In addition, the topology of these regions across the two hemispheres was also similar (See Figure 1(a)). These observations suggest the macroscopic assessment of homology can be exploited to estimate the quality of individual cortical parcellation.

Our strategy is to assign homology based on the connectivity fingerprints of cortical parcels and then to evaluate the similarity of connectivity fingerprints within homologues and the resulting topological arrangements of the fields between hemispheres. We quantify the extent of homology using the Earth Mover's Distance (EMD) [7] and an accompanying topology based metric we call the topological distance (TpD).

In Section II, we describe our methodology for obtaining the EMD and TpD scores. Section III presents proof-of-concept results showing the validity of our approach to recover and assess the coarse-scale anatomic homology using whole brain cortical morphology-based parcellations. We also present and discuss application to finer scale parcellation of the human IPL. Finally, Section IV is our conclusion.

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II. METHODOLOGY

A. Data preprocessing

Our data were generated by high angular resolution DWI (64 unique directions, b=$1000mm/s^2$), 2 mm isotropic resolution in 19 healthy control subjects using a Siemens TIM Trio 3T scanner. DWI volumes were preprocessed to remove noise and eddy current distortions using FSL[1]. A 2 mm layer of voxels in the white matter subjacent to the gray matter of the T1-weighted images was extracted with FreeSurfer[2] and registered to the DWI images.

B. Parcellation of the IPL

To segment the IPL based on anatomical connectivity, we defined the seed voxels as all voxels of the angular gyrus, supramarginal gyrus, and Jensen sulcus of Freesurfer's Destrieux Atlas along the 2mm layer mentioned in Section II-A and the target voxels as all white matter voxels. Probabilistic tractography was performed with MRtrix[3] with default values for all free parameters. The product of this step was a 2D matrix, in which each row represented a map of the fraction of tracks that entered each target voxel from a given seed voxel (a.k.a. tractogram). We then reduced the tractogram dimensions nonlinearly such that the transformed space had only 3 dimensions [8]. We clustered the resulting 3D feature vectors using hierarchical clustering into 5 clusters. We used the well-known Davies-Bouldin (DB) index [9] to assess the quality of the resulting clustering. In general, parcellations that produce low DB scores are favorable over those that produce high DB scores. The former have clusters with high intra-cluster similarity and low inter-cluster similarity.

For each subject and each hemisphere we generated 100 random IPL parcellations using a randomly-seeded region growing approach [10]. This resulted in a total of 1900 pairs of random IPL parcellations. We also used the same procedure to generate a random whole brain parcellation for each subject such that each hemisphere only had 75 clusters.

C. Creation of connectivity fingerprints

In order to determine whether the resulting clusters in each IPL region contained distinct connectivity fingerprints, we performed another probabilistic fiber tracking operation from each cluster of each participant, with a reduced number of target regions namely the 75 cortical regions of Freesurfer's Destrieux atlas that are ipsilateral to the seed region. We rejected fiber tracks that started and ended in the same cluster. We randomly seeded 100,000 tracts from each cluster, keeping all other MRtrix parameters at their default values. We computed a probabilistic tractogram for each region by normalizing each region's tractogram by the total number of tracts that managed to reach any of the 75 target regions. The product was a 5x75 matrix for each IPL, in which each row represented the connectivity fingerprint of a given cluster. This procedure was also applied to each subject's Destrieux whole brain parcellation and the whole brain random parcellation described in Section II-B.

[1]http://fsl.fmrib.ox.ac.uk

[2]http://surfer.nmr.mgh.harvard.edu

[3]http://www.brain.org.au/software/mrtrix/

D. Quantifying homology and topological similarity

Our strategy was to assign homology of parcels between hemispheres using the EMD, and then use the TpD to measure the degree to which the EMD-driven solution also conserved the topological arrangement of IPL parcels.

1) Quantifying homology using the Earth Mover's Distance (EMD)

The EMD is a metric used to quantify the dissimilarity between two distributions [7]. In our application of this metric we seek to quantify the dissimilarity between the connectivity fingerprints of two contralateral brain regions that are posited to contain bilateral homologous sub-regions as represented in Figure 1(a). The EMD can be formalized as a linear programming problem described below.

Let $L = \{(l_1, w_{l_1}), \ldots, (l_m, w_{l_m})\}$ be a set of connectivity fingerprints from the left IPL of a given subject. For example, if working with the seven IPL sub-regions in Figure 1(a), $m = 7$, l_i is a connectivity fingerprint of the i'th sub-region, and $w_{l_i} = \frac{1}{7}$. We empirically decided to give all signatures equal weights (w_{l_i}). $R = \{(r_1, w_{r_1}), \ldots, (r_n, w_{r_n})\}$ is the set of fingerprints from the right IPL of the same subject with r_j being a connectivity fingerprint from one of its n sub-regions and $w_{r_j} = \frac{1}{7}$.

Finally, $D = [d_{ij}]$ is the ground distance matrix. d_{ij} is the Jeffrey-divergence distance between l_i and r_j and it is defined as: $d_J(l_i, r_j) = \sum_k (l_{i_k} * \log \frac{l_{i_k}}{a_k} + r_{j_k} * \log \frac{r_{j_k}}{a_k})$ where $a_k = \frac{l_{i_k} + r_{j_k}}{2}$. It measures how inefficient it is to code one histogram using the other histogram as a code-book [7]. Two identical distributions will have a d_J of 0. There is no upper bound for d_J. After computing the matrix D, we want to find the flow $F = [f_{ij}]$ with f_{ij} the flow between l_i and r_j, that minimizes the overall work:

$$WORK(L, R, F) = \sum_{i=1}^{m} \sum_{j=1}^{n} d_{ij} f_{ij}$$

subject to the following constraints:

$$f_{ij} \geq 0 \qquad 1 \leq i \leq m, 1 \leq j \leq n \tag{1}$$

$$\sum_{j=1}^{n} f_{ij} \leq w_{l_i} \qquad 1 \leq i \leq m \tag{2}$$

$$\sum_{i=1}^{m} f_{ij} \leq w_{r_j} \qquad 1 \leq j \leq n \tag{3}$$

$$\sum_{i=1}^{m} \sum_{j=1}^{n} f_{ij} = \min \left(\sum_{i=1}^{m} w_{l_i}, \sum_{j=1}^{n} w_{r_j} \right) \tag{4}$$

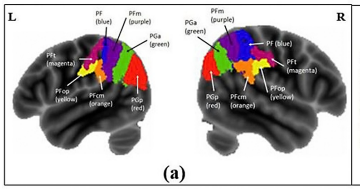
where constraint (1) ensures that supplies are moved from L to R and not vice versa, constraint (2) ensures that the total amount of supplies moved from L does not exceed the total weights of clusters in L, constraint (3) ensures that the total amount of supplies received by R does not exceed the total weights of its clusters, and constraint (4) ensures that the maximum amount of supplies have been moved [7]. Finally the EMD is the work normalized by the total flow:

$$EMD(L, R) = \frac{\sum_{i=1}^{m} \sum_{j=1}^{n} d_{ij} f_{ij}}{\sum_{i=1}^{m} \sum_{j=1}^{n} f_{ij}}$$

The closer to 0 the EMD score is between two IPL regions, the more similar the sets of connectivity fingerprints. The EMD score has no upper bound to indicate maximum dissimilarity. Since the IPL sub-regions have equal weights, this instance of the EMD reduces to the assignment problem, which allows us to retrieve the optimal pairing of the IPL sub-regions across the two hemispheres from the computed flow matrix F.

2) Quantifying topological similarity using the Topological Distance (TpD)

We projected the parcel labels from the seed voxel layer to the cortex using FreeSurfer. Then we computed the TpD, a measure of how similar the topological arrangement of clusters in IPL-L is to that of clusters in IPL-R, as follows: we re-labeled all clusters in IPL-L and IPL-R such that homologues (as assigned by the flow matrix F in Section II-D.1) have the same cluster label, we computed an NxN topology matrix for each IPL as depicted in Figure 1(b), where N is the total number of clusters in one IPL. The (i, j) entry of this matrix represents the number of voxels from cluster j in IPL-L that are spatially in contact (26-nearest neighbor) with voxels from cluster i in IPL-L. We then normalize each row of that matrix by the total number of neighborhood voxels for that row/cluster. After we obtained such a matrix for both IPL, we computed the TpD between IPL-L and IPL-R by calculating the cosine distance of the two matrices after vectorizing them. The TpD score ranges from 0 to 1. A score close to 0 suggests that the two IPL regions have similar topology (e.g. the parcellation of S1 in Figure 4(a)), while a score closer to 1 indicates the two IPL regions have dissimilarity topology (e.g. the parcellation of S17 in Figure 4(b) where the green cluster in the right hemisphere is divided into three spatially discontinuous regions, while its contralateral counterpart is a single spatially continuous region).



(a)

	Red	Green	Purple	Blue	Magenta	Yellow	Orange
Red	0	1	0	0	0	0	0
Green	0.5	0	0.5	0	0	0	0
Purple	0	0.5	0	0.3	0	0	0.2
Blue	0	0	0.5	0	0.3	0	0.2
Magenta	0	0	0	0.4	0	0	0.6
Yellow	0	0	0	0	0.6	0	0.4
Orange	0	0	0.5	0.2	0	0.3	0

(b)

Fig. 1. (a) Sagittal slice (X=141 for L, Left hemisphere and X=37 for R, Right hemisphere in MNI space) of the IPL cytoarchitectonic parcellation [4]. Sub-regions homologous across the two hemispheres have the same color. (b) The topology matrix for L.

III. RESULTS AND DISCUSSION

Absent a feasible "ground truth" for evaluating subject-specific dMRI-based parcellation in vivo, we adopted an alternative strategy whereby results are assessed through joint consideration of measures leveraging known organizational principles of the brain, specifically inter-hemispheric homology and topology. In the present work, we propose and evaluate a new measure, EMD and TpD, that quantify the preservation of homology and topology, respectively, across hemispheres, and demonstrate their utility in assessing IPL parcellation results.

Using these measures we found that one can use tractogram-based connectivity fingerprints extracted from Freesurfer's Destrieux parcellations (a whole brain cortical morphology-based parcellations) to identify and quantify inter-hemispheric homologous brain regions. In Figure 2 all the 19 subjects had much lower EMD and TpD scores when using the connectivity fingerprints of their Destrieux parcellations compared to the random parcellations. This suggests that the notion of parcel homology can be generalized across the entire brain at this course-scale anatomic level.

The IPL parcellation results are depicted in Figure 3 (metric space) and Figure 4 (anatomical space). The Principal Component Analysis (PCA) biplot in Figure 3 is a graphical representation of our samples (the EMD, TpD, and DB scores of the random and tractogram-based parcellations after a PCA analysis) and variables (the EMD, TpD, and DB) on the same plot. It showed that the parcellations based on the tractograms were mostly concentrated in the encircled area, while the random parcellations were scattered across that Figure. This suggested that there was better correspondence of connectivity profiles along the tractogram-based parcellations than the random parcellations. Besides, the matching of homologues for the 7 subjects that were not in the encircled area was not successful. In Figure 4(b) each of the 7 subjects had either an incorrectly matched IPL subregion (e.g. S5, S15, and S18) or a cluster that was spatially discontinuous (S9, S11, S17, and S19).

The variable plots in Figure 3 showed that the EMD and TpD variables have a high correlation with each other, while the DB variable is mostly uncorrelated to either the EMD or the TpD variable. Both observations were expected. The TpD metric was designed to measure the degree to which the EMD driven solution also conserved the topological arrangement of IPL parcels, while the DB measure is independent of the TpD or the EMD measure.

We see several benefits for using these metrics to evaluate cortical parcellations: (1) they tend to reveal sub-optimal parcellations such as those in Figure 4(b) and, over groups of subjects, can guide improvements in parcellation workflow, (2) they can be used to evaluate parcellations results from other data modalities such as rsfMRI data, and (3) they can be used to describe hemispheric and/or inter-subject differences because they stem from anatomically meaningful information.

We also see some limitations to the proposed metrics: (1) optimization of metric values is only approximate with respect to accurate identification of cortical fields. A perfect parcellation would not have perfect EMD and TpD scores because anatomic connectivity and function has, inherently, some degree of hemispheric asymmetry and (2) the metrics will not detect systematic bias that preserves and/or promotes consistency across hemispheres. This might result in parcellations that do not reflect cortical fields, while exhibiting strong correspondences across the two hemispheres. Both limitations can be overcome through the concurrent use of

other evaluation criteria.

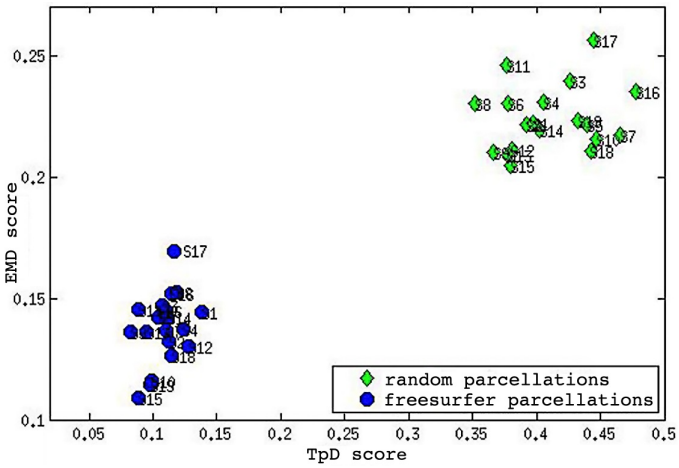


Fig. 2. The EMD and TpD scores for all 19 subjects (blue circles: Destrieux parcellation, green diamond: random parcellation [10]). Both types of parcellations had a total of 75 parcels in each hemisphere.

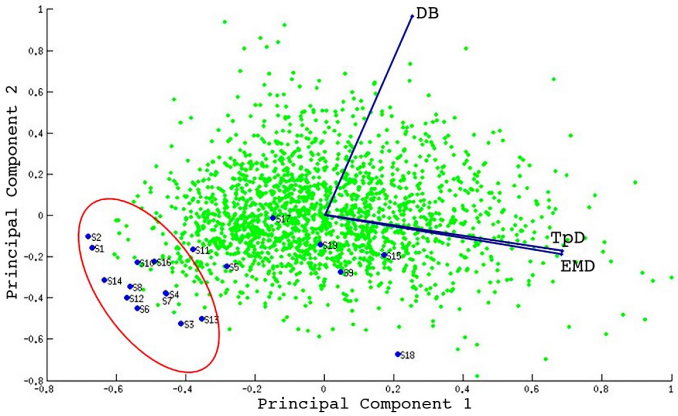


Fig. 3. The PCA Biplot of the TpD, EMD, and DB scores of all 19 subjects given both the 19 tractogram-based (blue circles) and the 1900 random (green diamonds) parcellations.

IV. CONCLUSION

We describe and demonstrate complementary metrics (EMD for homology and TpD for topology) for assessing the quality of subject-specific cortical parcellation. These metrics are useful in guiding improvements in acquisition, reconstruction, and/or clustering approaches. Future work will be geared towards using these metrics to (1) systematically study the effects of choices made during the creation of workflows for dMRI based parcellations, and (2) investigate the metrics sensitivity to cross-subject homology.

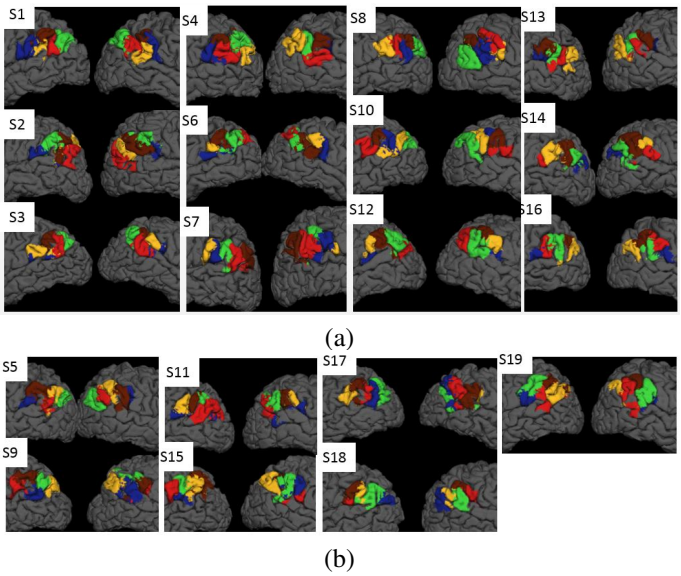


Fig. 4. Homologous IPL sub-regions as computed using the EMD for all the 19 subjects: (a) The 12 subjects encircled in Figure 3 and (b) the remaining 7 subjects. Note that within a subject homologous regions are assigned the same color, but this is not true for clusters across different subjects.

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