Reproducibility of an Automated Regional Analysis of White Matter with Diffusion Imaging

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Introduction:

In this work, we test the reproducibility of an automated approach for regional mapping of white matter in diffusion imaging studies. These typically aim to understand local changes in microstructure with health and disease. While many approaches exist for localizing measurements across a population [5], one popular approach is to co-register, or spatially normalize [1], images and make voxel-wise comparisons. While this approach has high spatial specificity, two issues are misalignment and a large number of statistical hypotheses. Region-of-interest studies alternatively provide better alignment of structures and fewer comparisons; however, they typically focus on particular anatomy and require either manual selection [7] or complex tractography models [4]. In this work, we examine a region-based approach that parcellates the whole white matter using a novel clustering algorithm that groups voxels based on both their spatial and directional structure. We report experimental results showing that the proposed regional approach has high reproducibility and performs as well or better than the voxel-based approach.

Methods:

Under an IRB-approved protocol, Diffusion MRIs were acquired from eight healthy volunteers with three repetitions (24 sessions in total). Imaging was conducted on a GE 1.5T scanner with 2x2x2mm voxels, 64-directions, b=1000s/mm2, and resolution 128x128x72. Volumes were preprocessed (correction for motion and eddy current artifacts and skull stripping) with FSL [9]. Tensors and fractional anisotropy (FA) were computed and deformed to a population template using DTI-TK [10]. Regions were automatically extracted from the template using a novel clustering algorithm. This represents each region by a prototypical position and direction and finds regions by minimizing the sum of squared distances between each voxel's position/direction and the nearest prototype. An iterative algorithm was used to compute the optimal regions, as described in [3]. Next, an FA threshold of 0.15 was applied to include only white matter, and the mean FA was computed in each region. We assessed reproducibility with two statistics [2]: mean coefficient-of-variation (MCV) within each subject, which is considered acceptable below 10%, and intra-class correlation (ICC), which is considered acceptable above 0.7 [6]. MCV and ICC were first computed for the regional analysis and then for the traditional voxel-wise approach, and then repeated with spatial smoothing (Gaussians with std. of 1mm and 2mm).

Results:

Figures 1 and 2 show regions extracted from the template and an example of those transferred to a single subject. 112 regions were extracted with a mean volume of 3807 mm3 with standard deviation 1250 mm3. Reproducibility results are presented in Table 1, and the spatial distributions of ICC and MCV for FA are visualized in Figure 3. We found the smoothed voxel-based and unsmoothed region-based approaches to have comparable ICC (0.76). The region-based approach had lower MCV (1.3% unsmoothed) than the voxel-based approach in all cases (3.6% with smoothing).

Conclusions:

Our results suggest that the proposed approach has equal or better reliability, compared to the voxelwise approach and previous studies [8]. The lower MCV suggests that the regional statistics are more robust, while the high ICC suggests that the regional measures retain discriminative power. One explanation is that the averaging for each region tends to be restricted within major structures, unlike the smoothing in voxel analyses. This is likely because fiber orientations provide a rich feature for defining boundaries that would

otherwise be continuous with scalar measures like FA. In fact, we found the regions to coincide with interfaces between bundles, as shown in Figure 2. While these results suggest this approach is reproducibly and reliable, it remains an open question whether it is more sensitive to clinically interesting changes in microstructure than existing techniques.

Modeling and Analysis Methods:

Diffusion MRI Modeling and Analysis

Table 1: Results from the experiments measuring mean coefficient-of-variation (MCV) and intra-class correlation (ICC) for the regional and voxel-wise analyses

Method	MCV	ICC
Regional, no smoothing	1.3% +- 0.0	0.76 +- 0.001
Regional, 1mm smoothing	1.2% +- 0.0	0.78 +- 0.001
Regional, 2mm smoothing	1.1% +- 0.0	0.80 +- 0.001
Voxel-wise, no smoothing	9.0% +- 0.1%	0.60 +- 0.008
Voxel-wise, 1mm smoothing	4.9% +- 0.1%	0.72 +- 0.006
Voxel-wise, 2mm smoothing	3.6% +- 0.1%	0.76 +- 0.005

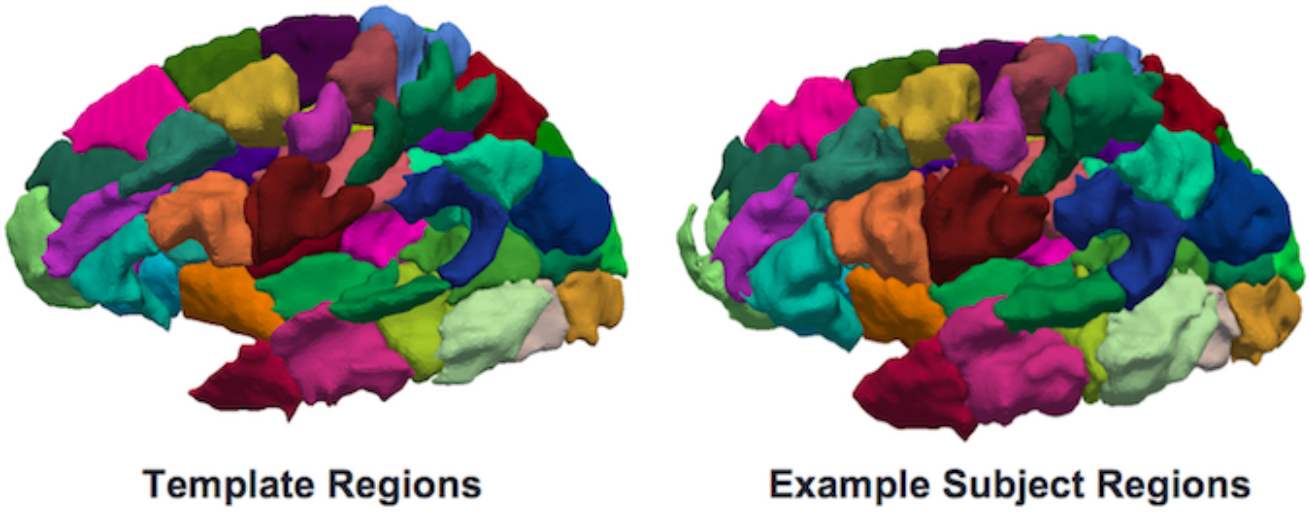

Figure 1: A surface rendering of the regions in the template (left) and mapped to an example single subject (right)

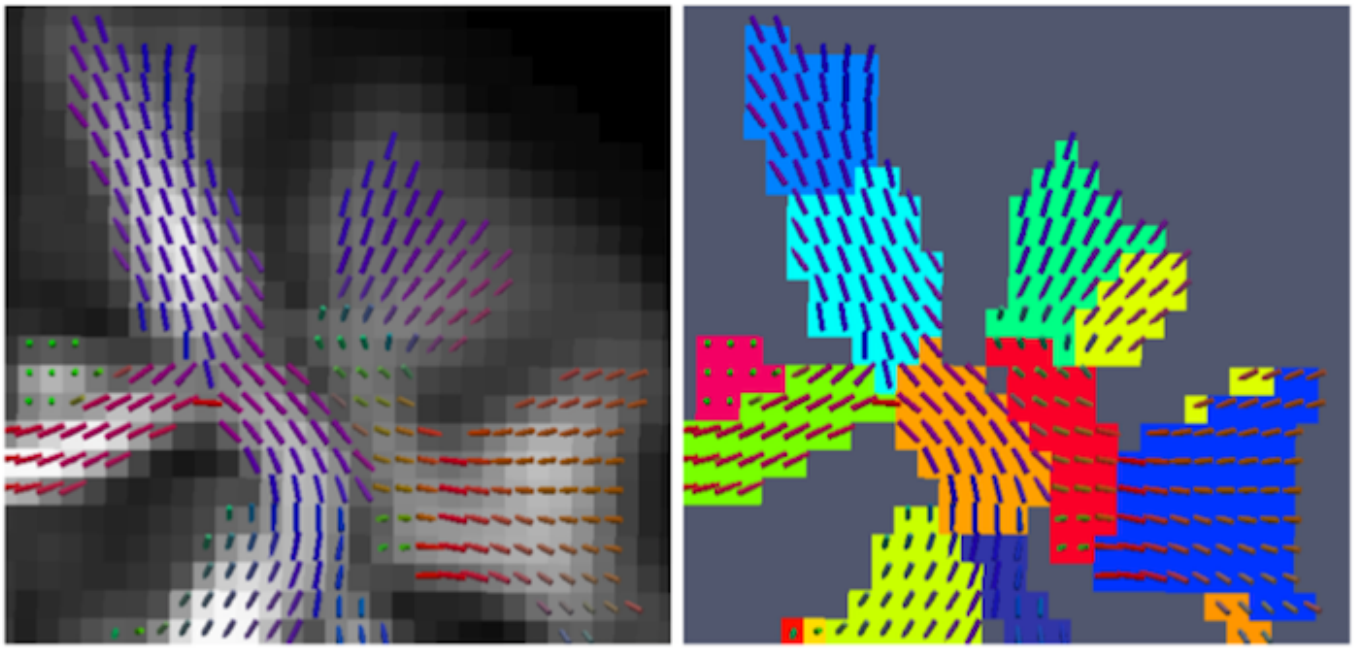

Figure 2: A slice rendering of the template showing fiber orientations (left) and extracted regions (right). We found the regions to rarely cross anatomical interfaces, such as the shown corona radiata/superior longitudinal fasciculus and the corpus callosum/cingulum bundle. Note, however, that major bundles may include several regions, so not all anatomical interfaces coincide with region boundaries.

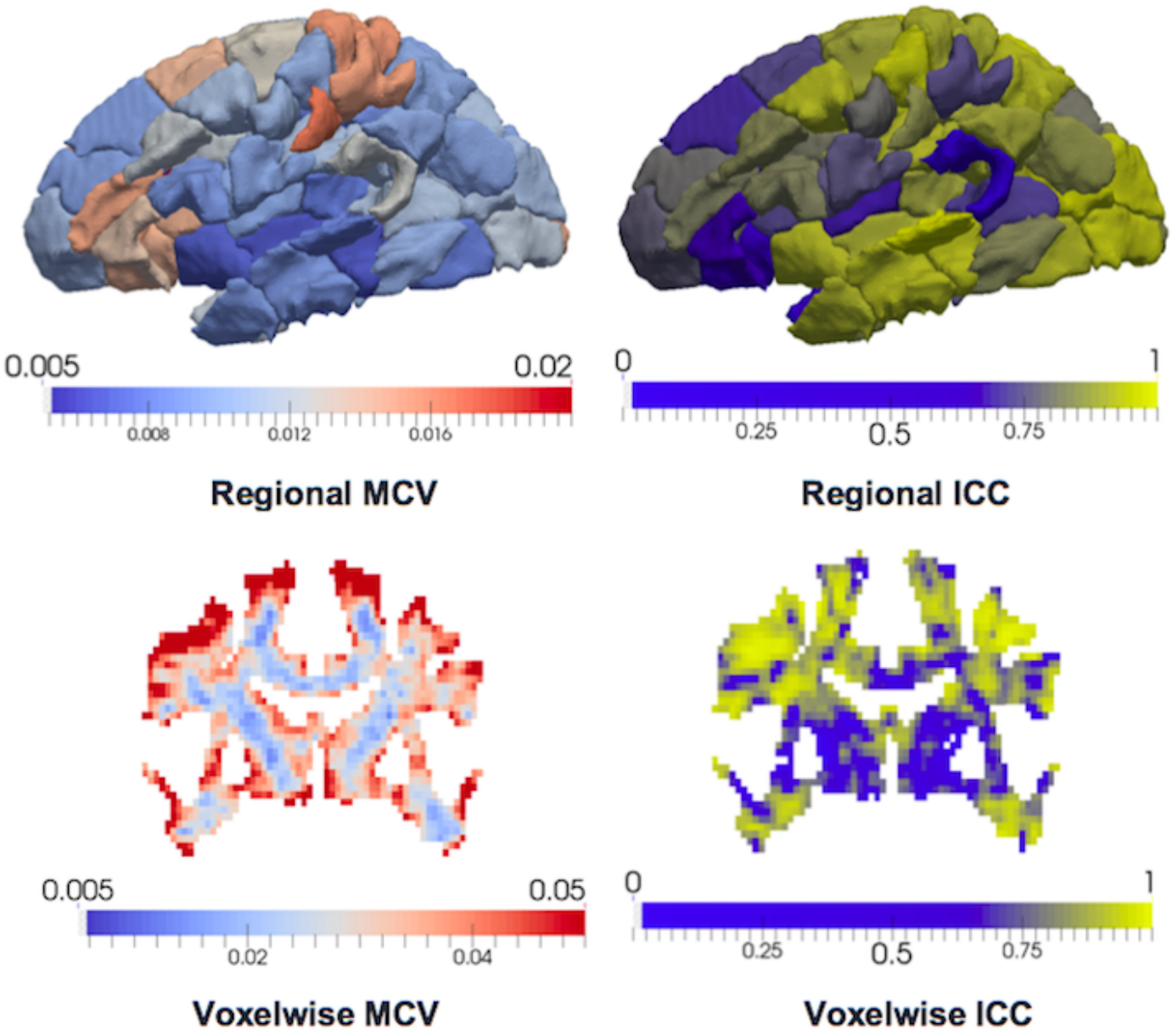

Figure 3: The spatial distribution of mean coefficient of variation (MCV) and intra-class correlation (ICC) from the regional and voxel-wise analyses. In the MCV plots, blue indicates lower error, and in the ICC plots, yellow indicates higher reliability. Note that the MCV plots do not share the same color map.

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