ODF-BASED MORPHOMETRY AND APPLICATION TO BRAIN ASYMMETRY

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Introduction:

The Orientation Distribution Function (ODF), the angular profile of the diffusion probability density function of water molecules, can be estimated from High Angular Resolution Diffusion Imaging (HARDI) data [2]. We present an extension of voxel-based morphometry to ODFs and apply it to brain asymmetry. While little is known about white matter connectivity asymmetry, several recent studies have examined left-right differences from DTI-derived measures in large human populations (N = 374; [1]). ODF-based morphometry allows us to extend the study of hemispheric asymmetry by examining differences in fiber characteristics across hemispheres rather than just differences in shapes and volumes. We estimate voxel-wise maps of asymmetries between the ODFs in the left and right hemispheres, using a generalized Hotelling's T-squared test for ODFs.

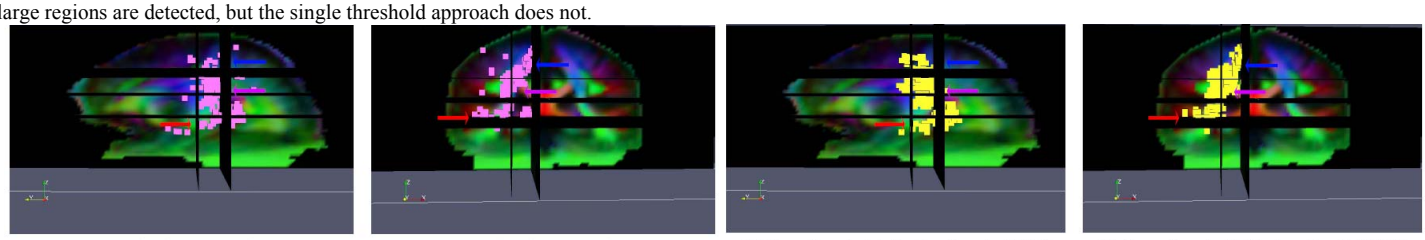
Voxel Based Morphometry (VBM) is a neuroimaging analysis technique to investigate regional differences in brain anatomy. VBM-type methods have made a significant contribution to the understanding of brain changes in several disorders and their relation to clinical measures. For example, VBM has been used to study a number of different disorders, including neurodegenerative diseases, multiple sclerosis, schizophrenia, movement disorders and epilepsy. Let $\mathbf{x}_1, \ldots, \mathbf{x}_{n_x}$ and $\mathbf{y}_1, \ldots, \mathbf{y}_{n_y}$ be the (Euclidean) feature vectors drawn from two populations, $\overline{\mathbf{x}} = \frac{1}{n_x}\sum_{i=1}^{n_x} \mathbf{x}_i$ the sample mean of the first population, and $\overline{\mathbf{y}} = \frac{1}{n_y}\sum_{i=1}^{n_y} \mathbf{y}_i$ the sample mean of the second population. In VBM, one wants to test the hypothesis that $\overline{\mathbf{x}} = \overline{\mathbf{y}}$, a commonly used statistic is the Hotelling's T-squared statistic, a generalization of the Student's *t*-statistic commonly used in multivariate hypothesis testing. The ODF is a probability density function and it is well known that it does not lie in Euclidean space. We have generalized the Hotelling's T-squared statistic to ODFs by exploiting the specific geometry of the statistical manifold of ODFs.

Methods:

To generalize the Hotelling's T-squared test to ODFs, we first assume that the ODF volumes of different subjects are already registered to a common template. Having registered the ODF volumes, we next compute the mean and covariance matrices of the ODF-valued data, as described in [2]. Let $\boldsymbol{\psi}_1, \ldots, \boldsymbol{\psi}_{n_\psi}$ and $\boldsymbol{\phi}_1, \ldots, \boldsymbol{\phi}_{n_\phi}$ be the ODFs drawn from two populations and let $\overline{\psi}$ and $\overline{\phi}$ be the sample means of the two populations. We generalize the Hotelling's T-squared statistic and VBM to ODFs in a similar fashion to what was developed for DTI in [3]. By generalizing the equations to calculate the Hotelling T-squared statistic to ODFs, we get the following equation, $T^2 = \frac{n_\psi n_\phi}{n_\psi + n_\phi}\overrightarrow{\overline{\psi}\,\overline{\phi}}^{\top}\mathbf{W}^{-1}\overrightarrow{\overline{\psi}\,\overline{\phi}} = \frac{n_\psi n_\phi}{n_\psi + n_\phi}\log_{\overline{\psi}}\overline{\phi}^{\top}\mathbf{W}^{-1}\log_{\overline{\psi}}\overline{\phi}$, where $\mathbf{W} = \frac{\sum_{i=1}^{n_\psi}\overrightarrow{\overline{\psi}\,\boldsymbol{\psi}_i}\overrightarrow{\overline{\psi}\,\boldsymbol{\psi}_i}^{\top} + \sum_{i=1}^{n_\phi}\overrightarrow{\overline{\phi}\,\boldsymbol{\phi}_i}\overrightarrow{\overline{\phi}\,\boldsymbol{\phi}_i}^{\top}}{n_\psi + n_\phi - 2}$. Having formulated the equivalent of the Hotelling's T-squared test for ODFs, we can perform a statistical group comparison of ODFs using multivariate hypothesis testing via permutation tests. The statistics image can be thresholded using a single threshold test or a suprathreshold cluster test.

Results and Discussion:

Statistically significant asymmetries in ODFs ($p < 0.05$) are shown in Fig. 1. ODF based morphometry reveals a number of white matter microstructural differences. First of all, the *planum temporale*, a highly lateralized brain structure involved with language processing, is clearly detected. This localization is consistent with the literature, as the language comprehension areas are among the most highly functionally lateralized areas of the brain. Secondly, the posterior limb of the internal capsule and the corticospinal or pyramidal tract are also detected. These areas are major components of the primary sensory-motor pathways. This result agrees well with previous studies reporting the asymmetry of these fiber tracts [4], further validating this approach. The main regions of the brain that are deemed asymmetric by the two tests are generally in agreement with each other. The suprathreshold cluster test generally gives contiguous regions, at the cost of reduced localizing power since only large regions are detected, but the single threshold approach does not.



(a) Single Threshold (b) Single Threshold (c) Suprathreshold Cluster, threshold 250 (d) Suprathreshold Cluster, threshold 250

Fig. 1: Results of performing the ODF statistical test for brain asymmetry. Figs. 1(a) and 1(c) show a sagittal view and Figs. 1(b) and 1(d) a coronal view. The pink voxels in Figs. 1(a) and 1(b) are deemed significant by the single threshold test and the yellow voxels in Figs. 1(c) and 1(d) are deemed significant by the suprathreshold cluster test. The red arrow shows the planum temporale, the purple arrow the internal capsule, and the blue arrow the corticospinal tract.

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