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Brain morphometry by distance measurement in a non-Euclidean, curvilinear space

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Abstract. Inspired by the discussion in neurological research about the callosal fiber connections with respect to brain asymmetry we developed a technique that measures distances between brain hemispheres in a non-Euclidean, curvilinear space. The technique is a generic morphometric tool for measuring minimal distances within and across 3-D structures. We applied the technique for distances from the cortical gray/white matter boundary to the cross-section of the corpus callosum. The method uses a 3-D extension of the F*-algorithm. The algorithm uses a cost matrix determined by the image data. The resulting distances are mapped to the cortical surface and differences on the two hemispheres can be visually compared. Distances were also projected back to the corpus callosum to represent asymmetry by comparing left and right measurements. We can present results obtained by processing 11 3-D magnetic resonance data sets representing a normal control group.

1 Introduction

Image analysis has become a common component to study diseases of the human body by obtaining anatomical and functional information. Since the advent of non-invasive magnetic resonance imaging, morphometry has become increasingly important. The new analysis methods described here are fully 3-D processing techniques and overcome limitations of conventional slice-by-slice analysis.

This project is driven by studying schizophrenia. In schizophrenia, changes in the morphology of various brain structures are thought to provide important clues to the disease related brain abnormalities, but the changes are subtle and can barely be detectable with current interactive segmentation techniques [1, 2]. Quantitative measurements on postmortem brains and on anatomical structures segmented from magnetic resonance image data corroborate the hypothesis that the asymmetry between the brain hemispheres is reduced at first episodes of schizophrenia [4, 8]. To date, the errors in measurements are often larger than the effect to be studied, and interesting findings often could not be confirmed by other research groups. Therefore, it becomes necessary to provide more accurate measurements of brain asymmetry. Bullmore et al. [3] proposed a measurement called *radius of gyration* to assess cerebral asymmetry. This measurement has been only applied to 2-D coronal slices of 3-D brain images. Prima et al. [12] applied non-linear elastic registration to find corresponding regions in the two hemisphere. Differential operators applied to the 3-D deformation field results in measures of lateral asymmetry.

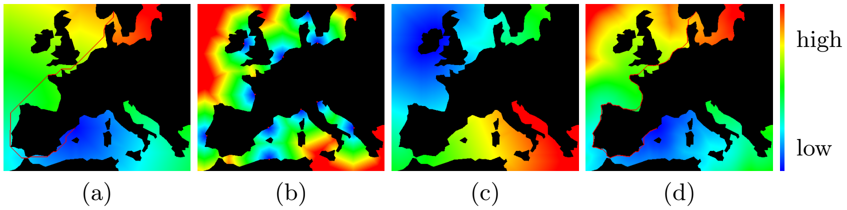
Symmetry of structures under a class of spatial transformations is a well-defined mathematical property. However, dealing with biological structures and the inherent variability, the mathematical approach to exact symmetry is too strict and has to be modified. Guillemaud et al. [8] segmented the manifold of the interhemispheric fissure and determined length between the cortical surface and the fissure along perpendicular lines emanating from the midplane. Measures from the left and right cortical surface result in estimates of local asymmetries and in a quantitative 2-D asymmetry map. This paper also suggested the use of a curvilinear coordinate system of the brain directly related to brain morphology. The encouraging results inspired the research work presented in this paper. A more realistic simulation of white matter fiber connections, however, would have to include information about local fiber directions, as nicely presented in [10] and [11], for example. The search for minimum cost paths is an 3-D extension of the F* algorithm [5] and has similarities to the interactive live-wire segmentation in [9]. In the context of analyzing the white matter structure of the brain we also would like to refer to Mangin et al. [7] who proposed a discrete implementation of conservative flow systems to analyze the white matter, in particular to detect the corpus callosum. Due to lack of space, details of implementations are generally omitted here, but are described in[13] (full color version).

2 Optimal path algorithm and asymmetry measurement

In our proposed approach, callosal fibers are simulated by curvilinear paths of minimal distance running inside the white matter from the white matter boundary to the interhemispheric cut through the corpus callosum. We use distance measurements propagated along trajectories determined by the graph search algorithm F*, extended to fit our specific needs. The distances at the white matter boundary are projected back onto the corpus callosum for a comparison of asymmetry between the two hemispheres.

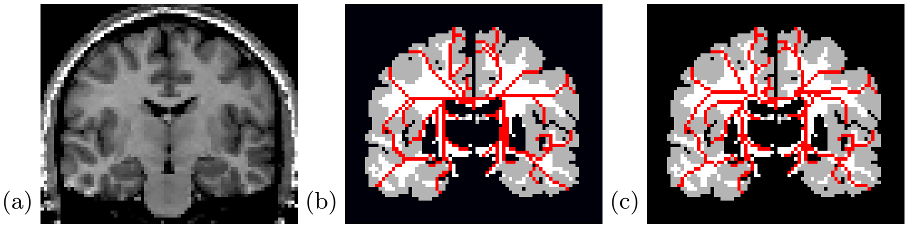
The F*-algorithm used in our implementation is based on the approach of Tenenbaum [5], where pixels or voxels of a dataset are represented by nodes of a graph. The edges of the graphs are defined as the 8-neighborhood in 2-D space and as the 26-neighborhood in 3-D space. The F*-algorithm enables the calculation of a distance map from a certain point of reference ('seed') to any other point in the graph. This distance map assigns a distance-value to each node in the graph which is based on a cost function that determines the point-related cost of a path.

To fit our needs we have implemented several extension of the original F* algorithm: 1.) Extension to 3-D space. 2.) Use of a seed region instead of a single seed point to allow multiple seed regions (see Fig. 1). 3.) Calculation of accurate costs for paths running along diagonals, but each dimension needs additional



(a) (b) (c) (d)

Fig. 1. 2-D F* distance maps representing the distance of the sea route to the closest seed point: (a) single seed point (at Barcelona) with highlighted optimal path running to Stockholm, (b) multiple seed points, (c) seed region (border of Ireland), (d) single seed, costmatrix penalizing optimal paths running far off the coast.



(a) (b) (c)

Fig. 2. Visualization of arbitrary optimal paths based on a constant cost matrix (b) and based on an a-posteriori probability cost matrix (c) on an 2D MRI image (a)

correction if voxel dimensions are non uniform. 4.) Propagation of additional information and measurements from the seed region to all points.

The F* algorithm needs the cost function to be stored as a matrix which represents the point-related costs for each point. The cost matrix was modeled to force optimal paths to run less likely through certain regions using two terms a constant distance term and a penalty-term. The penalty term assigns high costs to points were paths should be less likely to run through (see Fig. 1). The resulting path lengths are not measured in unit size, requiring a modification of the F* algorithm to additionally calculate the unit size distances.

The optimal path is not an explicit result of the F* algorithm, but they are extracted from the distance map using a steepest descent approach to trace trajectories back to the seed points (see Fig.2 and 3).

So far, we have calculated distances at the white matter boundary. However such a visualization is rather unusual and requires training. More common is a projection of attributes to the cortical surface, which also allows a comparison between multiple brain surfaces. We have developed a method to project the calculated distances from the gray/white matter boundary outwards to the cortex through gray matter using the F* algorithm. The projection runs along the optimal path from the white matter boundary to the cortex (see Fig. 3).

The main problem in defining asymmetry measurements is to determine correspondence. Establishing correspondence between brain hemispheres is not well defined since the brain is not strictly symmetric and depicts structures which appear only in one hemisphere. The approach chosen in our application is to compare the distances projected back to the corpus callosum along optimal paths.

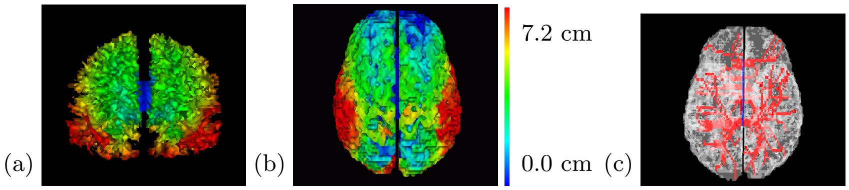


Fig. 3. Application on a 3-D brain atlas. Visualization of calculated distances on the white matter boundary (a) and as projection to the cortex (b). Visualization (c) of arbitrary paths and corpus callosum.

Measurements projected from both sides to one point of the corpus callosum can therefore be compared directly for asymmetry.

We define our asymmetry measurement as the difference of the mean of the distances after averaging the distance values separately for each side. These differences can be visualized as a 2-D difference graph or can be projected back to the cortex for visualization.

3 Results

The proposed algorithm has been applied on 2-D datasets without symmetry axis like maps (see Fig. 1) and mazes to test and extend the functionality of the F* algorithm. Further 2-D tests involved datasets with symmetry axis at the seed region, like artificial images, images of butterflies, bats, plants and 2-D-slices of a brain atlas. The mean distance asymmetry measure showed to be superior to extrema or median measures. Corresponding catchment areas of a point on the symmetry axis showed high variability in cases when areas were hidden behind obstacles. In such cases the correspondence and thus the asymmetry measurement turned out to be poor.

The first 3-D test has been performed on an isotropic brain atlas. Distances and paths were calculated and visualized (Figures 2(a-c), 3). There were significant visual differences observed between the two hemispheres. The difference graph of the mean was determined as asymmetry measurement and visualized (Fig. 4). Both the asymmetry graph and the distance visualization on the cortex demonstrate that the left hemispheric paths are longer for most parts of the brain. Compared to the 2-D case, we observed a lower variance of the size of catchment areas, but nevertheless the correspondence was not solved to our full satisfaction. One reason is that the corpus callosum is a small structure compared to the the white matter, so rather large areas are projected onto a single point on the corpus callosum.

Further 3-D tests are in progress. Datasets of 10 control patients of an Organic Amnesia study, varying in age and sex, have been processed. Both the corpus callosum and the brain hemispheres were segmented manually. The segmentation of the brain tissues has been performed using statistical classification with the Bayes-classifier. The a-posteriori probabilities were used to calculate the cost matrix. Distances have been visualized (see Fig. 5) and there were again significant visual differences between the two hemispheres in all processed

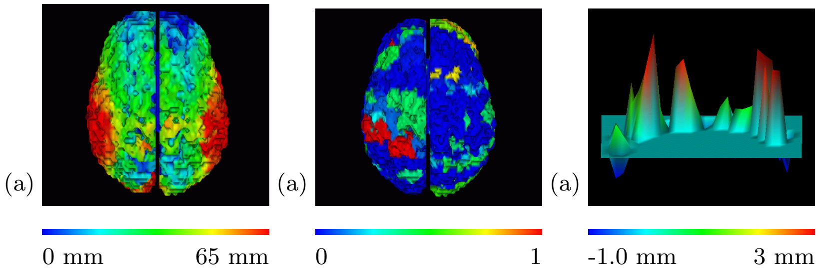


Fig. 4. Application on a 3-D brain atlas. Visualization of distances (a) and of normalized asymmetry measurement (b) as a projection on the cortex. Areas of smaller distance are displayed in blue. (c) Visualization of the difference graph (left minus right) projected on the corpus callosum.

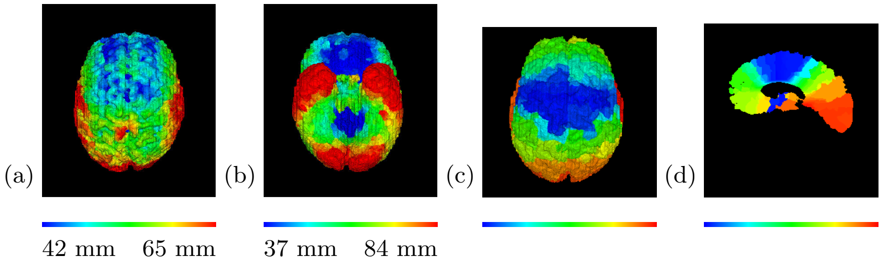


Fig. 5. Application on real 3-D datasets: Visualization of distances projected on the cortex from superior (a) and inferior (b) viewpoints. Visualization of the correspondence as projection on the cortex (c) and of the color-coded labels on a slice (d).

datasets. The asymmetry measurements have not yet been calculated. We observed that the manual segmentation of the corpus callosum is not placed exactly at the location of the interhemispheric fissure for several datasets, resulting in displacements as large as a few millimeters. These displacements are of equal size as the range of the mean differences of the distances for the atlas. As for the test with the atlas we observed again that the correspondence should be improved.

4 Conclusions and Discussion

In this paper, we have presented a new approach to measure minimum cost paths in a non-Euclidean curvilinear space. We use such paths as a simulation of callosal white matter fiber tracts which are of interest in current neurological research. We also proposed a technique to calculate a rough correspondence and an associated asymmetry measurement. Results are promising, but especially the correspondence needs improvement. The method has been applied to 11 3-D dataset so far, and the implementation runs stable and reliable.

The distances determined with our method are based on the city-block metric with the inherent disadvantages of showing large deviations from Euclidean distance measurements and of non-isotropic propagation of distances in space. Kiryati et al. [6] have adressed this issue and have proposed a correction of the calculated distances. We plan to incorporate this correction into a future method. Future directions of our research include the generation of a more robust measurement of asymmetry, combining curvilinear distances with explicitly established lateral correspondence between brain hemispheres.

Acknowledgments

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