Performance of 3D Landmark Detection Methods for Point-based Warping in Autoradiographic Brain Imaging

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Abstract

Warping can be used to reduce interindividual structural variations of three-dimensional anatomical image datasets of brains. For this, a standard brain is generated and the individual datasets are matched to this reference system. Model-based warping uses structural information such as landmarks to construct the spatial correspondence between the datasets. In this paper we compare three different fully automatic landmark detection algorithms. The first two approaches use a threshold-based definition of landmarks. In the first case (Monte-Carlo based) searching points move in subvolumes simultaneously. In the second approach the searching points move along “rays”. The third method uses spatial derivations of voxels to determine the position of landmarks at prominent structural features. The subsequent warping is based on a distance-weighted method with an exponential weighting function. All methods tested are able to reduce structural variations. Best results are obtained by the derivation approach.

1. Introduction

Warping, as nonlinear geometric transformations [1,2] can be used to reduce geometric variations by transforming an individual dataset to a reference system, e.g. a “standard brain” [3]. Therefore, warping can be used for an accurate comparison of interindividual 3D datasets of brains.

Several steps are necessary to perform a warping process: First, a spatial correspondence between the datasets is determined. Second, the datasets are transformed using a specific warping function based on the established spatial correspondence. Third, the quality of the warping process applied has to be evaluated. In volume datasets obtained by functional imaging studies, frequently the spatial distribution of the gray-value information is of biological or medical interest. Therefore, this gray-value information cannot be used to construct the spatial correspondence (intensity based warping). Consequently, we investigated geometry based warping strategies, i.e., point-based warping for its application to reduce interindividual variations in brains of the naked mole rat (\textit{Nanospalax ehrenbergii}). The mole rats were acoustically stimulated with different tones and brain activity is visualized via incorporation of a radioactive marker [4].

For point-based warping corresponding points (landmarks) between the datasets have to be defined. Setting of many landmarks between large 3D datasets by a human expert is highly time-consuming and subjective. To overcome these problems, we developed fast automatic procedures for landmark definition.

2. Methods

2.1 Tissue preparation

The autoradiographs were obtained after injecting the radioactive 2-fluoro-2-deoxyglucose (2FDG) into the mole rats. The animals were acoustically stimulated and after a certain exposure time the animals were sacrificed. Then the brains were removed and sectioned. Next the slices were exposed on a X-ray film. After 2 weeks exposure, the films were developed
and digitized with a CCD camera (768 * 512 pixel, 201 slices, 8 bit/pixel). The last step is the image alignment by translating and rotating each slice in order to reconstruct the original 3D object. In this study, we use a computational method of principal axes alignment followed by a cross correlation method. This approach is fully automatic and a very fast technique to obtain the required transformations [5]. Moreover, all the obtained 3D volumes were registered using a 3D principal axes alignment approach.

2.2 Landmark detection

The first approach to define corresponding reference points uses a multiscale Monte-Carlo techniques to detect edges of biological structures simultaneously in a large number of individual datasets [6]. An edge is defined by the differences of gray values of adjacent voxels, which exceeds a constant predefined threshold value. This threshold value depends on the statistics and the quality of the dataset. At the beginning a regular coarse three-dimensional grid is placed on each dataset to define non-overlapping subvolumes (32x32x9 voxel). This grid, which was similar for all datasets, inherently defines the spatial relation between the individual dataset. Obviously as mentioned before, it is a prerequisite, that the individual datasets are prealigned within accuracy higher than the smallest grid size. Next, the Monte-Carlo-search is performed by random movements of a single point within each subvolume. The pseudo-random generator is taken from the tested standard libraries (MIPSpro C compiler 7.1) and was tested negatively for autocorrelation. It was initialized with a constant seed number. In order to minimize the influence of the seed number on the landmarks, the final positions of the landmarks are averaged over 10 generated landmark sets.

The searching point can reach all voxels of one subvolume within one iteration. The searching procedure stops within such a subvolume if an edge is found. Within all subvolumes containing no edges the searching point is eliminated after a maximum number of iterations. The high maximum number of iteration cycles depending on the subvolume size (250,000 for 9216 voxel) ensures that each edge is reliable detected.

Biological images may contain specific distortions which differ significantly in size. For our LM detection approach the detection of different distortion sizes is solved by a multiscaling procedure. Therefore, we introduced grids of different size, which are used successively. Empirically we came to the result, that two different sizes are optimally: First a coarse grid with 8,448 large first-order subvolumes to detect large distortions and then each first-order subvolume is divided into 4 smaller second-order subvolumes. If the Monte-Carlo-search within the 4 second-order subvolumes detects more than on edge in the corresponding first-order subvolume, the edge in the first-order subvolume is eliminated to prevent non-corresponding contours.

The second approach (ray-threshold) defines, as in the first method, a gray-value transition, which is greater than a given threshold, as an edge. However, here the searching points move along rays, which have their origins near the centers of substructures of the brain. For all datasets and each substructure a single position is selected for the origin. The origin is defined as the mean position of all centers of gravity of that particular substructure across the individual dataset (Fig. 1). Consequently, the origins have identical locations in all datasets and the angles between the rays are similar in all datasets to warrant their correspondence. The points move along the rays and stop if an edge is found. If on the corresponding rays of all datasets an edge is found, the position of that edge defines a landmark.

Fig. 1 Single slice together with the rays. The three groups of rays on the left have their origins at the left and right striatum and at the septum. The right group of rays pass the whole brain. For this last group of rays the dataset is binarized, so that only the outer contour of the brain can be detected.
The third approach is based on 3D differential operators for the detection of point landmarks in MR images [7,8]. The operators are based on first partial derivatives of the voxels. According to this approach the differential operator exploits the matrix N, which is computed in an observation window around the voxel \( x=(x,y,z) \):

\[
N = \begin{pmatrix}
\sum g_{xi}^2 & \sum g_{xi}g_{yi} & \sum g_{xi}g_{zi} \\
\sum g_{xi}g_{yi} & \sum g_{yi}^2 & \sum g_{yi}g_{zi} \\
\sum g_{xi}g_{zi} & \sum g_{yi}g_{zi} & \sum g_{zi}^2
\end{pmatrix}
\]

The sum index \( i \) denotes the spatial location of a voxel in the observation window (5*5*3 voxel). The partial derivatives \( g_x, g_y, g_z \) determine the derivative of a certain point in the respective spatial direction. The operator \( F(x) \)

\[
F(x) = \frac{\text{det}(N)}{\text{tr}(N)}
\]

determines the operator output of the point \( x \) in the center of the observation window, where \( \text{det}(N) \) is the determinant and \( \text{tr}(N) \) the trace of the matrix.

The reference points are determined by searching for local maxima of operator values, which are greater than a preset threshold value. To ensure a correct correspondence of the reference points across the different datasets a 3D grid approach is used again, like in the case of the Monte-Carlo method. Only if a sub-volume contains a reference point in all datasets, these reference points are defined as landmarks [9].

The standard brain, i.e. the reference template for warping, is generated by averaging the positions of corresponding individual landmarks. The spatial difference of each individual landmark and its corresponding one in the reference template defines the displacement vector and these vectors serve as the information for the following warping.

2.2 Warping

The warping method is based on a distance-weighted method [10,11,12]. The displacement of each voxel is determined by the weighted sum of all displacement vectors. The transformation function \( T(x,y,z) \) determines the displacement of each voxel \((x,y,z)\) by the weighted sum of all displacement vectors:

\[
T(x,y,z) = \frac{\sum_{i=0}^{M-1} w_i(x,y,z)[(u_i,v_i,w_i)-(x_i,y_i,z_i)]}{\sum_{i=0}^{M-1} w_i(x,y,z)}
\]

The displacement vectors are the spatial difference between the reference points \{\((x_i,y_i,z_i)\)\} in the source 3D dataset and the corresponding points \{\((u_i,v_i,w_i)\)\} in the reference template. Each displacement depends on the spatial difference of a given voxel to each landmark and a constant weighting factor, which is initially set to 0.04. The weighting function \( w_i(x,y,z) \) consists of the weighting factor \( \beta \) and the city-block distance of the point \((x,y,z)\) to the reference point \((x_i,y_i,z_i)\):

\[
w_i(x,y,z) = e^{-\beta \sqrt{[(x-x_i)^2+(y-y_i)^2+(z-z_i)^2]}}
\]

The whole warping procedure of a group of objects consists of three steps: first the definition of the spatial relation between the datasets and generating a reference template as a standard system, next the transformation of the individual datasets to this reference template and at last the evaluation of the obtained results (Fig. 2).

Fig. 1 Scheme for reducing inter-individual variations. The landmark detecting algorithm defines landmarks in a group of individual brain image datasets \((B_1, B_2, \ldots, B_n)\) and generates a reference template by averaging the positions of these landmarks. Afterwards, each individual dataset is warped with this reference template. In summary, the similarity between the datasets increases due to reduction of interindividual variations.
3. Results

We applied the procedures to 4 individual mole rat brain datasets. The Monte-Carlo method found 1,845 landmarks in approx. 68,000 s/dataset (SGI Origin 200, CPU: R10k/195). The ray-threshold method found 1,074 landmarks in approx. 5 s/dataset and the 3D Operator approach found 347 landmarks in approx. 8,000 s/dataset. To give a better illustration a single slice is shown in Fig. 3. The dots depict the locations of landmarks, which z-coordinates correspond roughly to this slice. Inset a shows the landmarks, which are determined by the Monte-Carlo method (10 out of 1,845 landmarks), the inset b the landmarks after application of the ray-threshold method (20 out of 1,074) and inset c the landmarks obtained by the 3D Operator approach (20 out of 347).

The quality of warping is quantified by applying 2 similarity functions: linear cross-correlation coefficient and volume overlap index. The table shows the increase of similarity after warping:

<table>
<thead>
<tr>
<th>Method</th>
<th>Linear cross correlation [%]</th>
<th>Volume overlap index [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monte-Carlo method</td>
<td>1.25</td>
<td>1.66</td>
</tr>
<tr>
<td>Ray-threshold method</td>
<td>1.64</td>
<td>3.21</td>
</tr>
<tr>
<td>3D Operator</td>
<td>1.73</td>
<td>3.37</td>
</tr>
</tbody>
</table>

Table 1: Results of the similarity measures between the datasets after warping (increase of similarity, averaged values)

4. Discussion

In this study, we investigated 3 different, fully automatic procedures to detect landmarks for point based distance-weighted warping. The landmarks are successfully used for generating a reference template and the similarity of the individual datasets increases after warping in all cases tested. The quality of warping, as indicated by the employed similarity functions, varies between the different landmark generators. The best cross-correlation coefficient and the best volume overlap index is achieved by the 3D operator approach. The ray-threshold method produces good result in this study as well, but in much less computation time. After application of this approach most landmarks are located at the outer edge of the brain, which results in a relatively good volume overlap index. The ray-threshold method can be used, when computation time...
(or computation power) for obtaining a good set of landmarks is limited. The most accurate warps are obtained with landmarks after application of the 3D Operator approach, which proved to be a suitable tool in this study to make complex biological structures inter-individually comparable and facilitate a group comparison in functional autoradiographic brain imaging studies.

5. References


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