A new Approach to define Landmarks for Point-based Warping in Brain Imaging

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Abstract. An accurate comparison of inter-individual 3D image datasets of brains requires warping techniques to reduce geometric variations. In this study we use a point-based method of warping with weighted sums of displacement vectors, which is extended by an optimization process. To improve the practicability of 3D warping, we investigate fast automatic procedures for determining landmarks. The combined approach was tested on 3D autoradiographs of brains of Mongolian gerbils. The landmark-generator is based on Monte-Carlo-techniques to detect corresponding reference points at edges of anatomical structures. The warping function is distance-weighted with landmark-specific weighting factors. These weighting factors are optimized by a computational evolution strategy. Within this optimization process the quality of warping is quantified by the sum of spatial differences of manually predefined registration points (registration error). The described approach combines a highly suitable procedure to detect landmarks in brain images and a point-based warping technique, which optimizes local weighting factors. The optimization of the weighting factors improves the similarity between the warped and the target image.

Keywords: Registration, Warping, Brain imaging, Landmark Detection

1 Introduction

As an approach for an accurate comparison of inter-individual 3D image datasets of brains we use geometric nonlinear transformation algorithms (warping) to reduce geometric variations within a group of individuals. Warping techniques are used for matching an individual dataset to a reference system, e.g. a standardized brain. Because the spatial distribution of grayvalue differences is an important result of our investigation density-based warping is not appropriate for this kind of analysis. Therefore point-based warping is investigated. For this class of warping corresponding points (landmarks) between the two datasets have to be defined in order to perform the transformation [1]. Setting of many landmarks between 3D image datasets by a human expert is highly impracticable and time-consuming. Furthermore, definition of landmarks depends on prior knowledge by the human expert, resulting in a subjective selection of corresponding points. As an approach to overcome these problems we investigate fast automatic procedures for determining landmarks to greatly improve the analysis in brain imaging.

Here, we apply point-based warping for reduction of interindividual variations in autoradiographic brain imaging of gerbil brains. The gerbils were acoustically stimulated and brain activity is visualized by the metabolic radioactive marker. The transformation function calculates the spatial correspondence between all voxels in the source and the target dataset using the information of the landmarks. This function can be based on e.g. second-degree polynomials [2, 3] or radial basis functions [4, 5]. In this study we used a distance-weighted method of warping with weighted sums of displacement vectors [6, 7], which is extended by an optimization process [8].

2 Material and Methods

The 8 datasets used in this study are image-stacks of 49 consecutive slices. After preprocessing, the landmark detection algorithm defines corresponding reference points in all datasets to generate a reference template. Then each source dataset is warped to this reference template. Finally, the quality of the warping is evaluated by comparison of the similarities between the original and the warped datasets.

2.1 Tissue-Preparation and Image Preprocessing

The autoradiographs were obtained after intraperitoneal injection of non-metabolizable radioactive 2-fluoro-2-deoxyglucose (2FDG) into gerbils, thereby visualizing brain activity. The animals were acoustically stimulated for 45 min. Afterwards the animals were sacrificed and the brains removed. Then the brains were sectioned with a cryostat and after drying at 60^{o}C the brains were autoradiographed. After 2 weeks exposure, the films were developed and digitized with a CCD camera (768 * 512 pixel, 8 bit/pixel). The image-stacks were reconstructed by translating and rotating each slice (image alignment) [9].

2.2 Landmark detection

The landmark detection algorithm is based on Monte-Carlo-techniques to find edges of biological structures. In this study, an edge is defined by a transition of grayvalues of voxels, which exceeds a certain threshold value. The threshold depends on the contrast of the image. Initially a three-dimensional grid is placed on each dataset to define 1920 non-overlapping subvolumes. Within each of these subvolumes the Monte-Carlo-search is performed by random movements of a single point. The searching procedure stops within a certain subvolume, if an edge is found. Subvolumes that contain no edge after a maximum number of iterations, do not contribute a reference point. Only if a given subvolume contains a reference point in all datasets, for this subvolume a reference point in the template is generated by averaging the positions of all corresponding reference points of the individual datasets. The spatial difference of an individual reference point and the corresponding one in the reference template defines a displacement vector. In order to detect different displacement sizes we use a multiscaling procedure. Two differently sized grids are used successively: First a coarse grid with larger first-order subvolumes (1920) is used to detect large distortions. Afterwards, each large subvolume is divided into four smaller second-order subvolumes (7680). If the search procedure within the second-order subvolumes detects more than one edge in the corresponding first-order subvolume, the displacement vector in the latter one is eliminated to avoid non-corresponding contours. Monte-Carlo-techniques are based on pseudo random number generators, which are initialized with a certain seed number. As an approach to minimize the influence of the seed number, the final positions of the landmarks are averaged over 10 generated landmark sets.

2.3 Warping

The subsequent warping is based on displacement vectors, which are defined by the spatial difference of corresponding reference points in the individual dataset and in the reference template. The transformation function determines the displacement of each voxel by the weighted sum of all displacement vectors. Each displacement depends on the spatial difference of a given voxel to each landmark and a landmark-specific weighting factor [8]. The weighting factor determines the influence of that specific landmark on the displacement. At the beginning all weighting factors have identical values, so that the displacement of a voxel is mainly influenced by the neighboring landmarks.

The following transformation function $T(x,y,z)$ describes the transformation of the voxel (x,y,z) based on the reference points $\{(x_i,y_i,z_i)|0 <= i <= M\text{-}1\}$ in the source 3D dataset and the corresponding points $\{(u_i,v_i,w_i)|0 <= i <= M\text{-}1\}$ in the reference template:

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

The weighting function $w_i(x,y,z)$ consists of the landmark-specific weighting factor β_i and the city-block distance of the point (x,y,z) to the reference point (x_i,y_i,z_i):

$$w_i(x,y,z) = e^{-\beta_i * [|(x-x_i)|+|(y-y_i)|+|(z-z_i)|]} \qquad (2)$$

Calculation of the Euclidean distance instead of the city-block distance does not improve the warping results but increases the computational effort (data not shown). It is essential to select the weighting factors optimally due to their strong influence on the warping result. To optimize the weighting factors, we used a computational evolutionary strategy, which consists of the following steps: At the beginning, a population of identical sets of weighting factors is generated. The fitness of the sets is determined by warping of each set and then by calculating a registration error to quantify the similarity. The registration error is the sum of the distance values between all registration points of the warped dataset and the corresponding ones of the reference template. Registration points are a small number (28) of manually defined points at characteristic positions in all datasets (one expert). In case of the reference template the registration points are generated by averaging the coordinates of the registration points of the individual datasets at a given position. This registration error has to be minimized by the optimization procedure. Therefore after each generation, the set with the lowest registration error is duplicated and replaces the worst set. Then the weighting factors are mutated randomly with normal distributed step sizes. These steps are iterated for a constant number of generations, which was selected to obtain a stable fitness.

3 Results

Fig. 1a shows as an example a surface view of a brain image dataset with the defined landmarks (M=626). For the sake of a better illustration, different regions and the outer contour of the brain were segmented manually and then surface rendered. Most of the landmarks are located on the edges of the structures. Fig. 1b depicts another dataset with the defined registration points (28).

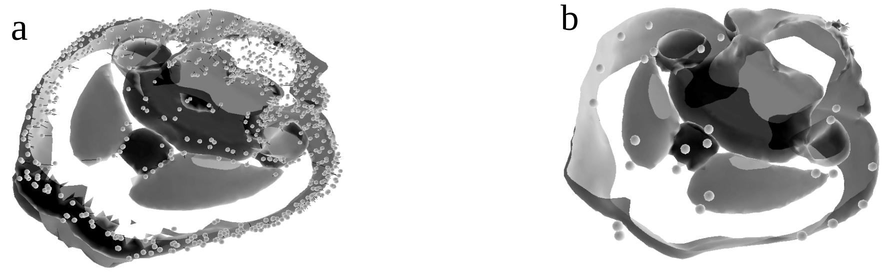

Fig.1 a) Brain image dataset with 626 landmarks. b) Another dataset showing the 28 manually defined registration points. Rendering software: AMIRA (TGS Europe)

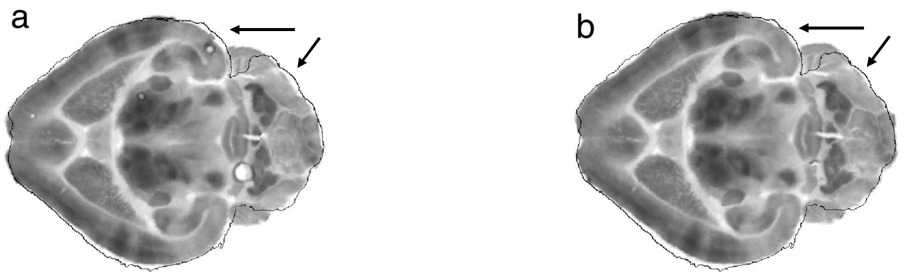

Fig. 2 a) Slice of the warped dataset before optimization of the local weighting factors. b) Slice of the warped dataset after 1000 iterations. Black contour: Outline of the corresponding slice of another warped brain.

The optimized warping was realized with a population of 500 sets of weighting factors, which started with the identical value of 0.04. Fig. 2 shows as an example a slice of the warped dataset before optimization (all weighting factors = 0.04) (fig. 2a) and on the right after optimization (fig. 2b). The contour of the corresponding slice of another warped dataset is shown to illustrate the increase in overlap after application of the optimization. It can be seen, that the overlap increases after the application of the optimization procedure (see arrows). The overall quality of optimized warping is quantified by applying 3 similarity functions before and after warping (mean values across all datasets): 1) registration error: decrease of 19.46 %; 2) linear cross-correlation coefficient: increase of 3.24 %; 3) overlap index: increase 0,65 %.

4 Discussion

The described approach combines a fast fully automatic procedure to detect landmarks and a point-based warping technique, which optimizes the influence of displacement vectors. The presented landmark generator is a highly suitable tool for calculating landmarks simultaneously in a large number of brain datasets without any prior knowledge. The optimization of the weighting factors improves the similarity of the warped datasets and hence decreases the inter-individual differences in all cases tested. The method results in an accurate warping with very good local adjustments, which justifies the relatively high computational effort of the optimization procedure. It may prove to be a useful tool to make complex biological structures comparable and accessible to an efficient automatic quantitative evaluation.

5 References

1. Toga, A.W., Brain Warping. 1999, San Diego London: Academic Press.
2. Wolberg, G., Digital Image Warping. 1990, IEEE Computer Society Press.
3. Lohmann, K., et al. Spatial based polynomial 2D-warping: a possibility to reduce interindividual variations in functional neuroimaging? In: IEEE Int. Conf. Image Processing. 1996.
4. Hardy, R.L., Multiquadric equations of topography and other irregular surfaces. J. Geophys. Res., 1971, 76: p. 1905-1915.
5. Bookstein, F.L., Principal warps: thin-plate splines and the decomposition of deformations. IEEE Transactions on pattern analysis and machine intelligence. 1989, 11(5): p. 567-585.
6. Shepard, D. A two-dimensional interpolation function for irregularly-spaced data. In: 1968 ACM National Conference. 1968
7. Franke, R. and G. Nielson, Smooth interpolation of large sets of scattered data. Int. J. for Numerical Methods in Engineering, 1980, 15: p. 1691-1704.
8. Pielot, R., et al. Optimiertes Warping durch gewichtete Summen von Verschiebungsvektoren - eine neue Methode zur Reduktion von interindividuellen Variabilitäten von Hirndaten. In: Bildverarbeitung für die Medizin 1999, 1999, Heidelberg: Springer-Verlag.
9. Hess, A., et al., A new method for reliable and efficient reconstruction of 3-dimensional images from autoradiographies of brains sections. Journal of Neuroscience Methods. 1998, 84: p. 77-86.