Atlas-guided Histology Reconstruction of Mouse Brain

Xi Qiu[1, 2]
nqiu@rotman-baycrest.on.ca

Tony Pridmore[2]

Alain Pitiot[2]

[1] Rotman Research Institute,
University of Toronto, Canada

[2] University of Nottingham, UK

Abstract

Histology acquisition often introduces tissue distortions that prevent a smooth 3D reconstruction from being built. In this paper, we propose a method of atlas-guided optimization to the piecewise registration scheme we developed previously. It takes the information of several consecutive slices in a neighbourhood into account. In order to achieve an accurate anatomic presentation, we run the method iteratively with the assistance from a pre-segmented brain atlas. The registration parameters are optimized to accommodate different brain sub-regions, e.g. cerebellum, hippocampus, etc. The results are evaluated by both visual and quantitative approaches. The proposed method has been proved to be robust enough for reconstructing an accurate and smooth mouse brain volume.

1 Introduction

Building and studying 3D representations of anatomical organs, such as the brain, plays an important role in modern biology and medical science. While 3D imaging methods such as MRI and CT provide accurate 3D structural information, 2D imaging methods such as histology and optical microscopy typically generate images with much higher resolution and better specific contrast. When studying the mouse brain, it is ideal to combine the advantages of both 3D and 2D imaging technologies. The classical approach is to reconstruct a 3D mouse brain volume from a series of histology slice images which provide more tissue details than MR images [1], [2], [3]. However, histology acquisition generally induces a lot of artifacts (holes, folding, tearing, sketching, etc.). Detecting and correcting the artifacts becomes a central issue when reconstructing a 3D volume from a series of histology slices. Indeed, they can make the distorted regions significantly different from the corresponding regions in adjacent slices. In a typical pairwise registration approach, registration errors tend to propagate to adjacent slices and prevent a smooth 3D brain volume from being reconstructed. Therefore, post-acquisition distortion correction is necessary [1], [2].

Researchers have proposed approaches to detect distorted slices by evaluating the quality of image registration between slices [4]. Other methods [5], [6] are based on the idea of eliminating the distorted slices rather than correcting them where possible. Quite often, most of serial histology slices have different types of distortions in different regions. If they are all removed, there may be not sufficient information left to reconstruct a 3D volume. In [7], Qiu et al. have proposed a framework to detect the distorted slices and predict the possible distorted structures. Along the similarity-measure-based techniques,

we developed a registration scheme that takes more local information into account in a piecewise fashion [8] and an extended method that borrows the information from a 3D atlas to improve the accuracy and robustness of distortion correction. In this paper, we present the atlas-based optimization method.

2 Methodology

A mouse brain has been reconstructed using the method described in [8]. Nevertheless, the fact of lack of support and proof from a 3D ground truth still prevents the reconstructed volume from becoming a solid foundation for future studies. Therefore, a 3D reference is still necessary here for correcting the shape of reconstruction and, much expectantly, improving local smoothness as well. Consequently, we introduce a structural-improving technique of reconstructed volume guided by a pre-segmented 3D atlas of mouse brain. The already reconstructed volume is fused with the atlas. In each brain sub-region, we further refine the parameters of our piecewise distortion correction method to achieve accurate brain structure and better volume smoothness.

Method Framework

1. Register the 3D brain atlas of the same mouse strain to our reconstruction by the 3D fusion technique [2].
2. Warp the atlas labels to the space of our reconstruction by the transformation of step 1.
3. Label the brain regions in the reconstruction according to the warped atlas segmentation.
4. Refine the parameters for distortion correction [8] to adapt the different brain regions.
5. Reconstruct a new volume using the refined parameters.

The method is operated in a coarse-to-fine fashion. The above steps are looped until a stopping criterion has been met. In the first iteration, a set of initial parameters is assigned for step 3. Those parameters are recommended as a prior knowledge by our neurologists based on the atlas. Thereafter, all the following iterations halve the parameters from the last iteration. We implement the method in this way to ensure the parameters can be optimized rapidly. The stopping criterion is defined as an evaluation of mean smoothness [3] of the reconstructed volume, i.e. when mean smoothness measure $S_k \leq 1$, we stop the loop and output the reconstruction as the final result.

3 Experimental Results

1.1. Experiment Setup and Parameters

In our experiment, a set of 350 Nissl-stained coronal images acquired by cyro-sectioning a single frozen C57BL/6J [9] adult mouse brain from LONI Research Lab at the UCLA was used. Each image was sized to 900 x 900 pixels in a resolution of 10 μm per pixel during acquisition. The distance between the consecutive sections is $25\mu m$. In order to reduce registration error, we ran a prior step of applying a Gaussian filter (σ = 3) to the images to downsize them and reduce noise.

The computation of 87 iterations consumed a total ~40 hours, averaging ~15 minutes for the local correction of each slice. Block size [10],[11] of 11x11, lattice site of every 10 pixels and exploration neighbourhood size of 71x71 were chosen, which was sufficient to

cover misaligning range for different slices in the dataset. Geometrical rigid regularization [10] was applied on a circular range with a radius of 50 pixels and followed by an averaging filter with a radius of 20 pixels to optimize the raw displacement fields derived by the block-matching registration.

Based on the synthesized consideration of all the atlas' features [2], the MR C57BL/6J Mouse Brain Atlas built by Brookhaven National Laboratory (BNL) was chosen as the 3D reference in our study.

1.2. 3D Reconstruction Results

The chosen BNL atlas volume was registered to our reconstruction result from the method described in [8]. The derived transformation was then applied to warp the atlas labels to the reconstruction, results shown in Fig. 1.
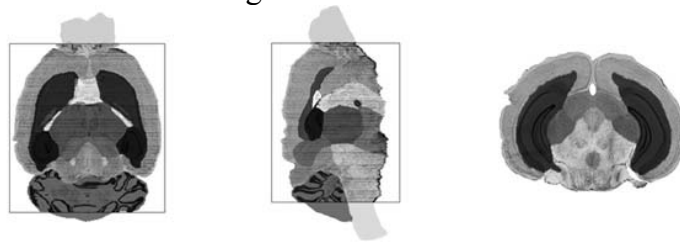

Fig. 1. Warped atlas labels superimposed on top of the reconstructed volume

In our experiment, parameters were halved every iteration to quickly regress to the optimized combination. Table 1 shows the final set of the optimized parameters.

	b_{size}	N_R	R_{Reg}	R_{Ave}	d_{Maj}
Cerebral Cortex	15x15	40x40	50	30	3
Cerebellum	7x7	40x40	30	20	3
Midbrain	25x25	50x50	80	50	3
Thalamus	25x25	55x55	80	50	3
Corpus Callosum	7x7	35x35	20	20	3
Hippocampus	5x5	25x25	15	15	3

Table 1. The optimized parameters

where b_{size}: Block Size, N_R: Exploration Neighborhood Size, R_{Reg}: Regularization Radius, R_{Ave}: Average Filter Radius, d_{Maj}: Majority Filter Window.

Visual Validation

It is not always easy to assess the quality improvement of all the sub-regions visually. For better demonstration, we focus on the comparison of the reconstructed Hippocampus because Hippocampus has clear texture to observe and also it is a relatively small structure and one of the hardest to reconstruct.
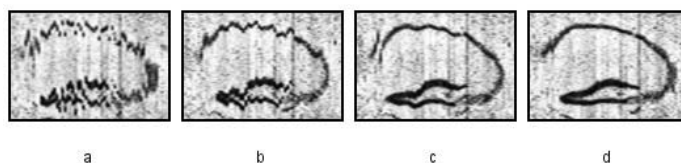

Fig. 2. Hippocampus reconstructions in Sagittal view: (a). rigid-body alignment; (b). piecewise distortion correction only; (c). atlas-guided correction based on the initial parameters; (d) atlas-guided correction based on the optimized parameters

In Fig. 2, the hippocampus reconstructed by the optimized parameters in Table 1 shows the accurate anatomic structure and the smoothest texture among the four.

A further noise-removing tool – majority filter [12] can be employed to ensure a smoother appearance of the reconstructed volume in the applications where intensity inhomogeneity is zero-tolerant, e.g. high-resolution visualization and atlas building.

To clearly show the advantages and the possible drawbacks of our atlas-guided scheme, we compared our results in Fig. 3 (c) with Guest's (a), Ju's (b) corresponding views of results and also Paxino's histology atlas [13] as a reference.
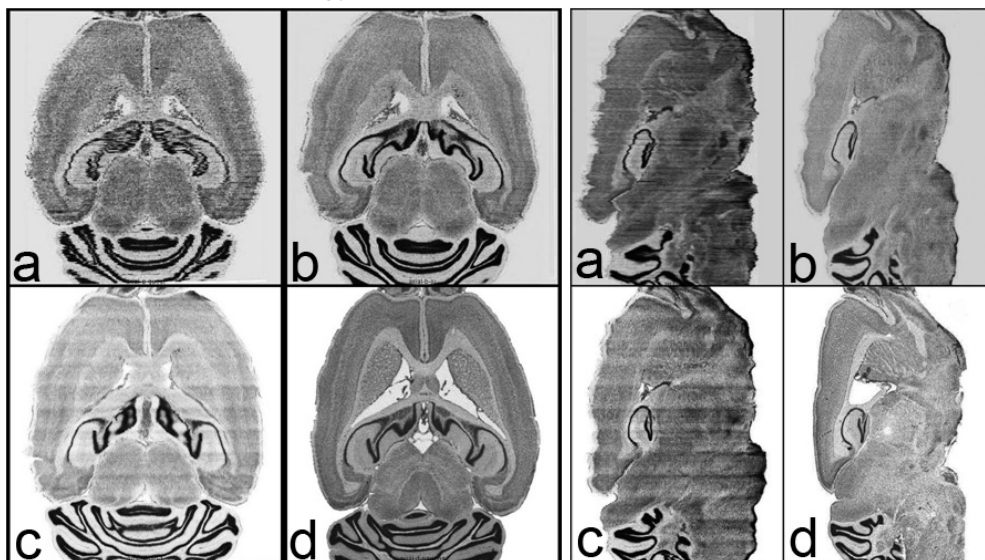

Fig. 3. Result comparison: (a) reconstructed volume by [14]; (b) by [3]; (c) our result; (d) No. 157 axial and No. 110 sagittal section of Paxino's atlas [13].

Among the three sets of results, our reconstructed volume was noted that the inside anatomical features became a lot more coherent. Moreover, the result showed that the shapes of many key structures had been recovered thanks to the scheme of labelling out the brain regions and dealing with them in a respective manner. Our result was found to have more matches of anatomical regions with Paxino's atlas compared to either Guest's or Ju's results, in particular, Hippocampus, Corpus Callosum and Cerebellum.

Quantitative Validation

To ensure our reconstructed volume has achieved the satisfaction quantitatively, we computed a smoothness evaluation S_k that was also used as the stopping criterion in our iterative program. With the optimized parameters and majority filtering of three sections on each side, we achieved a reconstruction with a mean smoothness evaluation $S_k = 0.92$, i.e. in the reconstructed volume, on average, each point deviates from the middle of its two corresponding pixels on the neighbouring sections by only about 0.46 pixel (9.8% closer than Ju's result: 0.51 pixel [3]).

4 Discussion and Conclusion

In this paper, we proposed an atlas-guided anatomy recovery method for mouse brain reconstruction. Pre-segmented atlas labels were firstly warped to the space of our reconstructed volume after the piecewise registration. Labelled anatomical regions in our reconstruction were then assigned an initial set of parameters of the piecewise registration by neurologists based on the anatomical features of the individual brain regions. Our

automated framework was then operated to optimize the parameters iteratively by correcting local distortion piecewisely and re-warping the corrected sections pairwisely.

For result inspection, both visual and quantitative evaluations had been performed in comparison with other competitive approaches. Despite lacking global alignment in some regions compared to other methods due to the local nature of the atlas labels we referenced to, our results still showed clear advantages of local smoothness and better matching with the real histology sections than the other methods in the comparison. Moreover, our method requires the least manual manipulation among the compared methods.

In summary, the proposed method has been proved as a reliable and robust way to reconstruct a smooth and accurate volume of mouse brain from a series of consecutive histology sections.

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