A Deep-learning Based Computer Framework for Automatic Anatomical Segmentation of Mouse Brain

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Abstract. In the research of neuroscience, it is significant for quantitative analysis based on accurate brain regions segmentation. A deep-learning enabled computer framework have been developed that can automatically segment fluorescence microscopy image data of mouse brain into several anatomical brain regions. Our approach includes an optimized registration algorithm for readily providing training datasets and a semantic segmentation neural network to infer brain regions efficiently. Using our deep-learning model, we can directly obtain the segmentation results of 18 brain regions in real time, and at high accuracy with averaged mean Dice value over 0.85.

Keywords: Deep learning; Fluorescence microscopy, Brain segmentation; Image registration.

1. Introduction
Currently, the understanding of pathological brain process is a major challenge in neuroscience research and which fundamentally based on accurate anatomical segmentation of brain images[1,2]. Mouse as the model animal in most frontier research, there have many large projects achieved significant results in mouse brain analysis. As more and more laboratories make obviously progress in high-throughput microscopy imaging, the mouse brain fluorescence microscopy images with higher resolution, larger data volume and data diversity make brain regions segmentation manually a time-consuming and hopeless process. The basis of brain anatomical segmentation requires an objective and reliable segmentation protocols to depict different regions of the brain and enables the fair comparison across different experimental individuals. Currently, registration is a widely-used method for brain anatomical segmentation, but complicated feature engineering and alignment calculation make this method time-consuming and computationally intensive. With the advancement of deep learning technology, automatic feature extraction at different levels of network and outputting in real time encourage active deep learning research in the field. The rapid development of deep neural networks has frequently applied to the analysis of brain images, such as image super-resolution, anatomical segmentation of human brain[3,4], etc. However, it remains difficult to segment the complex mouse brain by semantic segmentation, mainly for two reasons. Firstly, brain region inference based on semantic segmentation requires region labeling with pixel-level accuracy for training sets. In addition, sufficient training sets are needed to capture the variability of various brain structures and the versatility between different datasets[5]. Here we propose a complete and automatic framework, including the registration of acquisition image to the standard template from Allen CCFv3[6], training network based on precise label datasets, and anatomical segmentation output of network. The optimized registration algorithm generated the training library of the net-
work, which solves the problem of obtaining label data with pixel-level accuracy. The framework automates the whole process without additional manual labeling of data and achieves the real-time anatomical segmentation of mouse brain.

2. Method
To obtain the accurate anatomical segmentation of mouse brain datasets for conducting the neural network training in our deep-learning model, it is necessary to map the dataset to a standard space under a common coordinate frame. The process was conducted through a dual-channel image registration[7], in which average template provided by Allen CCFv3 was precisely registered to experimental dataset and the generated atlas gave fully anatomical structural information. Then the registered-and-segmented whole-brain datasets were input into the neural network for initiating the network training. Here we trained a classic encoder-decoder model based on the DeepLabv3+ structure, as shown in following Figure 1. As a semantic segmentation network, the network based on a simple structure and introduces shallow semantic information on the encoding branch to improve the segmentation accuracy.

Figure 1. Architecture of the DeepLabv3+. The input is sagittal plane image from mouse brain, and the features are extracted by Xception on the left branch. The ASPP (atrous spatial pyramid pooling) module captures multi-scale information of images.

3. Result
We first imaged the coronal sections of a whole mouse brain using serial two-photo (STP) microscopy, and obtained the 3D image of the whole brain. Through the prior image registration, the anatomical segmentations of several brain regions were obtained for network training (Figure 2). Here 18 primary brain regions were chosen as segmentation objects.
A complete brain provides about 500 sagittal plane images, and we collected 9 mouse brain samples for training network. The learning rate was set to 0.001 with learning momentum ~ 0.9. After ~40 hours and ~30000 iterations, the model to reach its convergence. Then, a new mouse brain dataset was used to test the performance of the trained network. The segmentation results by our network inference were finally compared to the registered ground truths, as shown in Figure 3.

Figure 3. Comparisons between anatomical segmentation results by deep learning inference and conventional image registration. (a) Three sagittal planes of the validation dataset. Scale bar, 1 mm. (b) Annotation segmentation from optimized dual-channel registration. (c) Performance of DeepLabv3+ model.
We then calculated the Dice values of network-based segmentations with ground truths from registration. Dice score is a similarity measure of image segmentation. The averaged median value of Dice scores for 18 brain regions are above 0.85, and especially high at Isocortex (~0.965), HPF (~0.938), STR (~0.913) regions. Meanwhile, the performance at PAL (~0.777), MBsta (~0.774), and P-sen (~0.780) regions are relatively low, possibly owing to the relatively large variation of morphology in these regions. Due to the large differences in one brain area on the different sagittal plane, there are some outliers in the box plot.

![Figure 4. Dice scores of 18 anatomical segmentation regions based on DeepLabv3+](image)

4. Conclusion
A deep-learning based segmentation framework for the anatomical segmentation of mouse brain were provided. Unlike the conventional iterative image registration-based segmentation/mapping, our approach uses a reliable semantic segmentation network DeepLabv3+ to directly infer anatomical regions of mouse brain at high accuracy. We expect this computational framework could provide neuroscience researchers a promising tool for enabling advanced brain investigation.

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