

Cell Based Analysis for Mouse Brain Images^{*}

Kui Qian^{1[0000–1111–2222–3333]} and Yoav Freund^{2[1111–2222–3333–4444]}

¹ Department of Electrical and Computer Engineering, University of California San Diego, La Jolla CA 92093, USA

² Department of Computer Science and Engineering, University of California San Diego, La Jolla CA 92093, USA
`yfreund@eng.ucsd.edu`

Abstract. The abstract should briefly summarize the contents of the paper in 150–250 words.

Keywords: First keyword · Second keyword · Another keyword.

1 Introduction

2 Method

2.1 Extraction of Cell Shape Features

2.2 Mouse Brain Alignment Using Landmarks

2.3 Statistically Significant Regions

Landmarks are chosen by anatomists, which are typically biologically significant groups of neurons. Because cell shape feature extraction is under an unsupervised way, our method can suggest landmarks by detecting brain regions whose cytoarchitecture is significantly different from the average.

Statistical Significance of Patches We compare regions by using the Kolmogorov-Smirnov (KS) test to discriminate CDFs of cell shape features. Specifically, we define KS significance by sorting the features based on decreasing KS values. The score is then defined as the sum of the M most significant features,

$$score = \sum_{i=1}^M -\log KS(x_i, B_i) \quad (1)$$

where x_i and B_i are the CDFs of the i th feature of the patch and the contrast region respectively.

The image is divided into overlapping windows with a size of 100 microns and a stride of 50 microns. Images of 5 consecutive sections are included together to expand 2D patches to 3D cubes.

^{*} Supported by organization x.

Heuristics for Finding Significant Regions The following process is done sequentially, each iteration generating one significant region. The whole images are viewed as background while the significant regions are viewed as foreground. We repeat this process N times to generate N significant regions.

1. Find the cube (100 microns cubed) with the highest KS significance compared to the background.
2. Expand the cube to a region according the following rules:
 - Starting from the chosen cube, slide a window in all directions by a stride of half window size and then select the 8 closest cubes around to judge as background or foreground.
 - For the new foreground cubes, use the same way till no new ones appear.
 - A cube is recognized as foreground if $dist(x, S_B) > \alpha \cdot dist(x, S_F)$ where S_F represents the CDFs of cells in the most significant cube and S_B represents the CDFs of cells in the background. α is set to be 3.

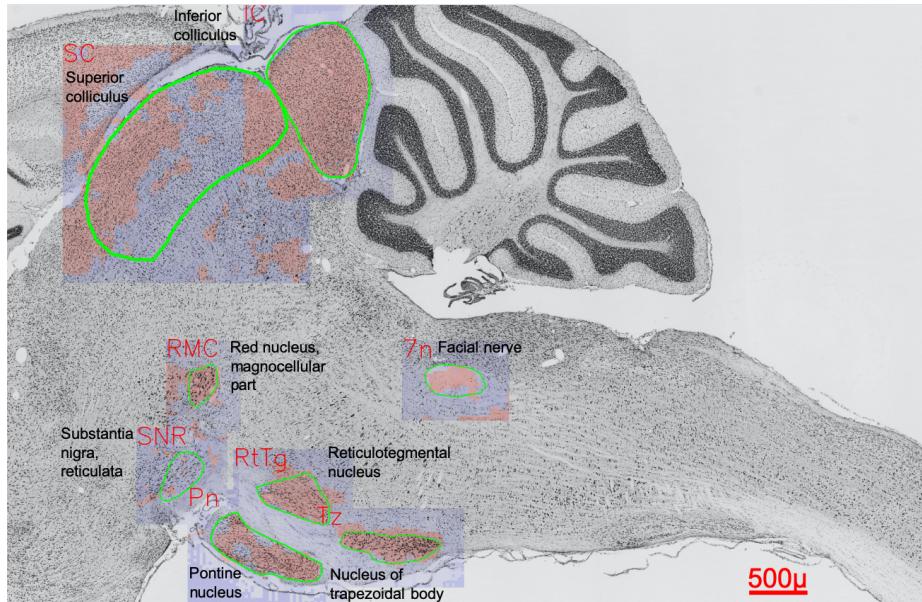


Fig. 1. One example detection score map of mouse brain sections. For one brain structure, patches in its local region are labeled as red when their detection scores are positive and blue otherwise. Green contours are annotations of structures by anatomists.

3 Experiments and Results

3.1 Detection Score Map

3.2 Detection Score Accuracy Based on Landmark Shifts

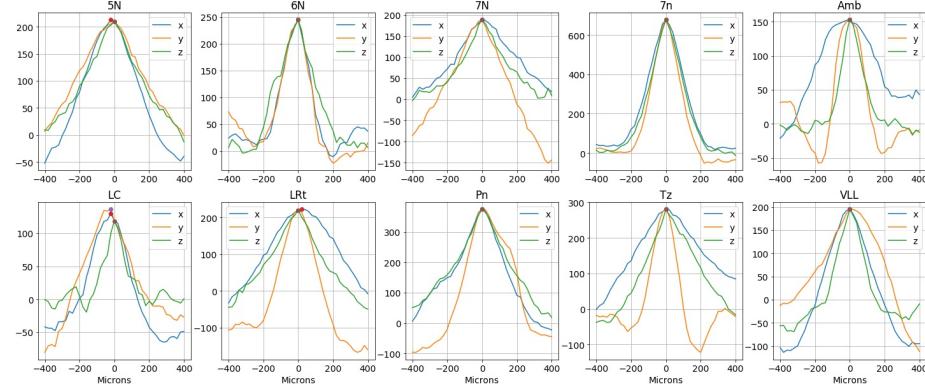


Fig. 2. Detection scores as function of translation in one direction among X, Y and Z. 10 mouse brain structures are included.

3.3 Visual Feedback of Detection

Usually the detected region for a structure is larger or smaller than the contour marked by anatomists. To help anatomists determine whose results are better between the detector and themselves, we give them feedback showing how the detector works. Because cells are anatomical units and elements of feature vectors as input of the detector are CDFs of cell shape features, the feature importance values returned by the XgBoost Classifier directly show which shape features the detector cares. Fig. ?? provides an example of visual feedback of detection. The most important feature for the structure in this image according to the detector is rotation. It is obvious that most cells in the red regions have different orientations compared with those in the blue regions. This explains why some patches inside the contour are detected as outside and suggests a new substructure in this structure. Anatomists can refine or add contours given the feedback, leading to better annotations.

3.4 Statistically Significant Regions

Statistical Significance Map As described above, KS significance could tell the dissimilarity between cytoarchitectural features in two regions. Thus we proceed to achieve a statistical significance map based on KS significance scores

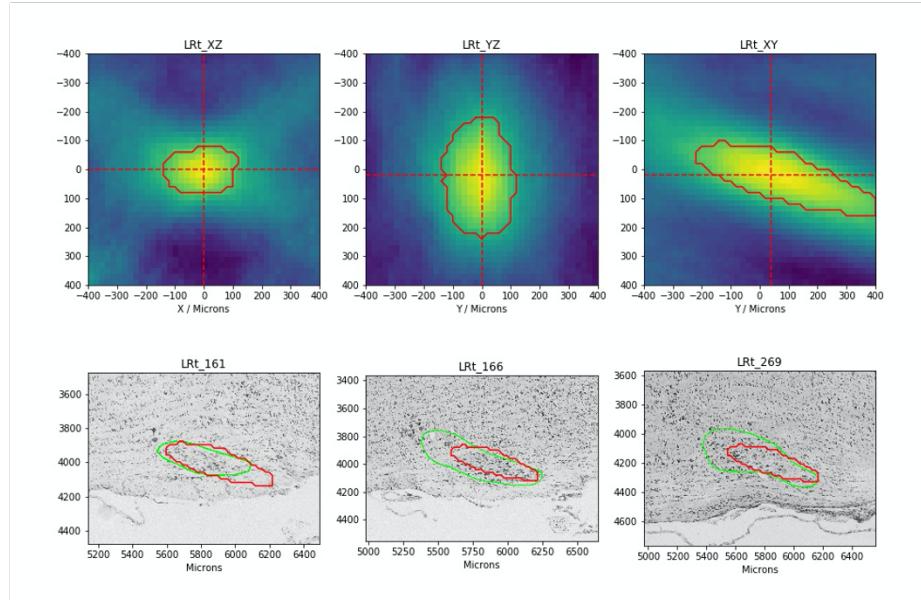


Fig. 3. Detection scores as function of translation in three planes for one structure, Lateral reticular nucleus (LRt). Intersection points of two red dashed lines are the locations of maximum and red contours mark half the maximum. The three images at the bottom are local regions of LRt taken from three mouse brain sections. Green contours are annotations by anatomists.

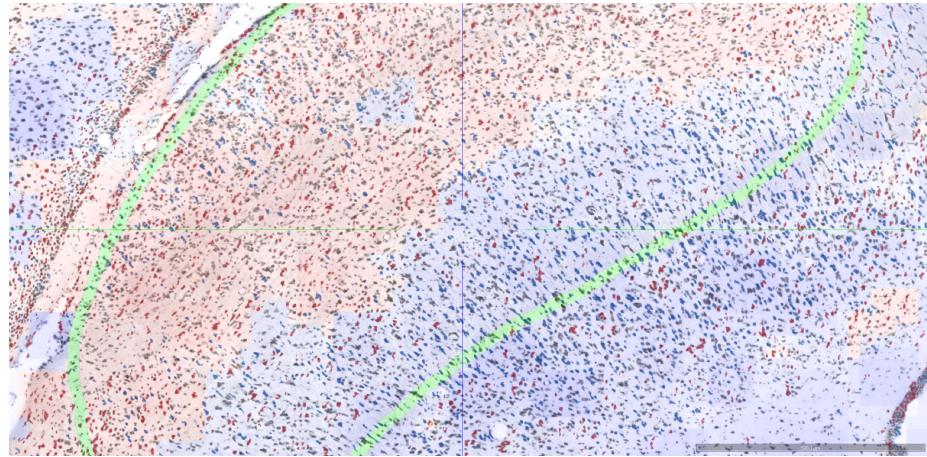


Fig. 4. One example of visualizing features' function in detection. The image shows a region of a mouse brain structure, superior colliculus (SC). Patches are labeled as red when their detection scores are positive and blue otherwise. Red cells are those with rotation values ranging from 20 to 60 while blue ones are those with rotation values ranging from -50 to 10. Green contours are annotations by anatomists. The visualization software is WebKnossos.

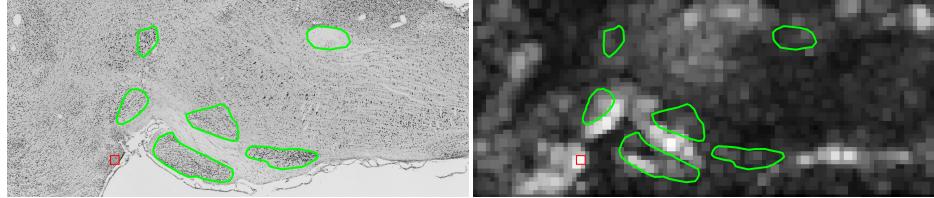


Fig. 5. One example of segmented mouse brain images (left) and its corresponding statistical significance map (right). Green contours are annotations of structures by anatomists and red rectangles (100×100 microns squared) mark the patches with the highest statistical significance.

against the whole brain sections to show distinct patches. Fig. ?? provides an example of such a process. To avoid the influence of meaningless stem parts, images are segmented to exclude these parts as shown. Patches with high gray values are those with high KS significance scores. We see that locations of distinct patches do not match the annotations of structures. For those patches inside a certain structure, they may appear different from local regions around the structure, but when compared to the whole brain section, they do not have to show dissimilarity. The detector is sensitive to textures different from the average. For those unmarked regions with many distinct patches, they may suggest new structures or other biological regions.

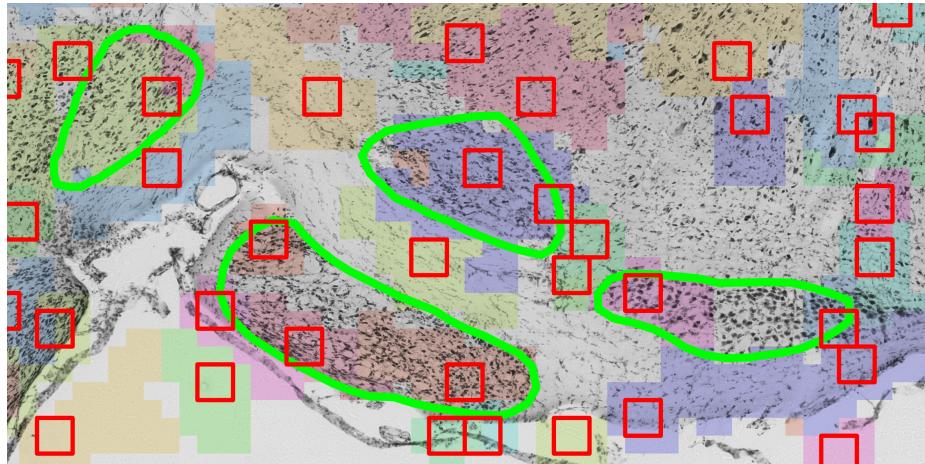


Fig. 6. One example image labeled based on statistical significance. Significant regions are marked with various colors and red rectangles (100×100 microns squared) mark the significant patches which are origins of these regions. Green contours are annotations of structures by anatomists.

Significant Regions According to the heuristics for finding significant regions, distinct patches in the map are extended to significant regions. In Fig. ??, significant regions are colored by various colors. The areas of significant regions depend on similarity of distinct patches to their surrounding regions. In other words, significant regions collect areas with similar cytoarchitecture, which can provide guidance for recognizing structures. In addition, we see that many structures or textures are divided into several significant regions and large regions usually achieve relatively low KS significance scores. This shows that our method using statistical significance is sensitive to the change of cytoarchitectural features, especially the direction of cells. Thus, these regions are helpful to assist anatomists to better understand the structures in the mouse brain.

4 Conclusion

Sample Heading (Third Level) Only two levels of headings should be numbered. Lower level headings remain unnumbered; they are formatted as run-in headings.

Sample Heading (Fourth Level) The contribution should contain no more than four levels of headings. Table ?? gives a summary of all heading levels.

Displayed equations are centered and set on a separate line.

$$x + y = z \tag{2}$$

Please try to avoid rasterized images for line-art diagrams and schemas. Whenever possible, use vector graphics instead (see Fig. ??).

Theorem 1. *This is a sample theorem. The run-in heading is set in bold, while the following text appears in italics. Definitions, lemmas, propositions, and corollaries are styled the same way.*

Proof. Proofs, examples, and remarks have the initial word in italics, while the following text appears in normal font.

For citations of references, we prefer the use of square brackets and consecutive numbers. Citations using labels or the author/year convention are also acceptable. The following bibliography provides a sample reference list with entries for journal articles [?], an LNCS chapter [?], a book [?], proceedings without editors [?], and a homepage [?]. Multiple citations are grouped [?, ?, ?], [?, ?, ?, ?].

References

1. Author, F.: Article title. Journal **2**(5), 99–110 (2016)
2. Author, F., Author, S.: Title of a proceedings paper. In: Editor, F., Editor, S. (eds.) CONFERENCE 2016, LNCS, vol. 9999, pp. 1–13. Springer, Heidelberg (2016). https://doi.org/10.1007/978-3-319-45678-9_1
3. Author, F., Author, S., Author, T.: Book title. 2nd edn. Publisher, Location (1999)
4. Author, A.-B.: Contribution title. In: 9th International Proceedings on Proceedings, pp. 1–2. Publisher, Location (2010)
5. LNCS Homepage, <http://www.springer.com/lncs>. Last accessed 4 Oct 2017