
Compact feature representations for human brain cytoarchitecture using self-supervised learning

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Abstract

The high number of neurons and the complex segregation of the human brain based on cytoarchitecture require an automated analytics approach. Therefore, we are analyzing images of 1 μm resolution histological sections stained for cell bodies using deep learning. The severely limited training data for supervised brain region segmentation represents a challenge for such analysis. We solve it by learning a feature embedding from patches of cortex using a self-supervised Siamese network. The distance between two features corresponds to the distance of the respective image patch locations in the 3D anatomical space. In this contribution, we show that the learned features encode distinctive cytoarchitectonic attributes of the input patches, and form anatomically relevant clusters across the brain.

1 Introduction

Analysis of histological human brain sections at a cellular level serves as a basis for identifying the cytoarchitectonic segregation of the cerebral cortex [2]. Cytoarchitectonic areas are distinguished by their characteristic arrangement of neurons in a laminar pattern, the presence or absence of cell clusters, and the visibility of columns. Identifying areal borders requires visual inspection of the region of interest under a light microscope combined with image analysis and an observer-independent method for reproducible border detection [3]. To support and automate the mapping process we successfully trained a Convolutional Network on the area segmentation task [4], combining patches of cortex from 2 μm resolution histological cell-body stained sections with prior topological knowledge.

Despite the encouraging results reported in [4], the naturally limited amount of labeled training data remains a challenge. Using unsupervised learning we can circumvent this issue and answer questions like: What patterns does a deep model discover in histological brain data? Do these patterns correspond in any way to brain regions as identified by a neuroscientist? Following this motivation, we make use of the 3D relationship between histological sections of the *BigBrain* dataset [1] given by a 3D reconstruction and train a Siamese network on the following self-supervised task (see Figure 1): Given two input patches sampled from any location of the cortex in one brain, we learn to predict the geodesic distance of the two inputs along the brain surface.

In a recent contribution [5], we argued that pre-training on this self-supervised distance learning task boosts performance for supervised area segmentation, and reported that the features learned in a self-supervised manner can already distinguish primary visual cortex from other cortex. While that contribution focused on transfer learning for brain mapping in the areas of the visual system, the aim of this study is to investigate how well the purely self-supervised approach produces neuroscientifically meaningful results across the whole human brain. We show in the following that the learned feature representation of high resolution patches of cortex efficiently summarizes information about the cytoarchitecture of the patch.

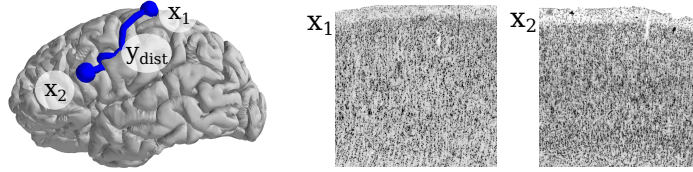


Figure 1: Two example patches from different histological sections and brain regions (right), their locations on the 3D reconstructed mesh and their geodesic distance over the cortical surface (left).

2 Methods

To calculate the feature embedding, we use the self-supervised distance learning task described in [5]: Given two $2\ \mu\text{m}$ resolution histological patches sampled from the cortex of a human brain, a Siamese network is trained to predict the geodesic distance of the locations of the patches over the cortical surface of the brain (see Figure 1). To succeed with this training objective, the model needs to learn the characteristics of cytoarchitecture in the different regions of the brain. Figure 1 shows an example of how the distribution of neurons in the cortical laminae varies at different locations on the cortex.

Siamese Network Training We use the Siamese network architecture described in [5] with two input branches that share weights. The branches contain six blocks comprising two convolutional layers (each followed by a BatchNorm layer and ReLU activation function) and a max pooling layer. After the convolutional blocks follows a dense layer that outputs a 32-value feature vector $f(x)$ for each input x . The predicted distance between the two inputs is the squared Euclidean distance of the feature vectors.

For training, we use $2\ \mu\text{m}$ resolution cell-body stained histological scans from the *BigBrain* dataset [1] which consists of a human brain that has been 3D reconstructed at $20\ \mu\text{m}$ resolution. This dataset allows us to sample pairs of patches from arbitrary 2D sections and recover their geodesic distance over the cortical surface (see Figure 1). We train our model for 70 epochs on a dataset of 100000 pairs of $1019 \times 1019\ \text{px}$ patches ($2\ \text{mm}^2$, covers entire depth of cortex) sampled from 3400 sections.

Hierarchical Clustering We calculate the feature representation $f(x)$ of 5000 patches sampled randomly from 300 held-out test sections. To verify that these features retain anatomically relevant information from the input patches, we calculate a hierarchical clustering using Ward’s algorithm, minimizing within-cluster variance using the squared Euclidean distance function as metric.

3 Results

Figure 2a shows the result of the hierarchical clustering thresholded at seven clusters on the left hemisphere. For comparison, probabilistic maps of selected brain regions from the JuBrain atlas [2] are shown in Figure 2b-d. Although the coordinates on the cortical surface were not used to compute them, the clusters form smooth regions on the brain surface. Most notably, clusters 2 and 6 separate the motor cortex (Figure 2c) from the somatosensory cortex (Figure 2b) accurately along the central sulcus. These two brain regions have very different cytoarchitecture: The motor cortex belongs to the agranular cortex and contains giant pyramidal cells, while the somatosensory cortex is a granular cortex with smaller cells and a more distinct laminar pattern. The more anteriorly located frontal lobe is formed by cluster 1. Other clusters roughly represent the lobes of the brain and functionally meaningful regions; e.g., cluster 3 covers the occipital lobe containing the visual system (Figure 2d).

4 Conclusion

As in [5], we trained a Siamese network on a self-supervised distance learning task, and applied it to the analysis of the cortical segregation in human brain histological sections. The Siamese network generates a feature embedding of the input patches, where the squared Euclidean distance between features corresponds to the geodesic distance of the corresponding patches. Using hierarchical clustering, we have shown that these features form clusters that roughly represent different anatomical

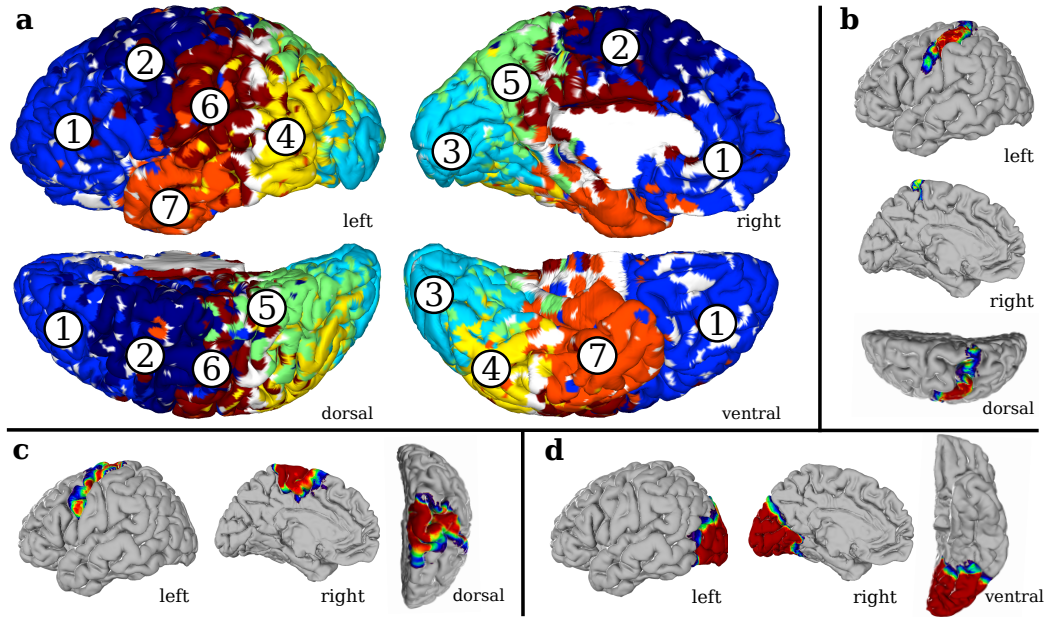


Figure 2: A: Hierarchical clustering of the features learned by the self-supervised Siamese network. For each patch, its position on the cortical surface is colored according to its cluster. Clusters roughly correspond to different cortical regions of the brain. B-D: Probabilistic maps of selected brain areas from the JuBrain atlas (images from <http://jubrain.fz-juelich.de>). B: Anterior parietal cortex (somatosensory areas 1, 3a, 3b), corresponding to cluster 6. C: Precentral region (premotor and motor cortex, areas 6, 4p, 4a), corresponding to cluster 2. D: Occipital lobe (striate and extrastriate visual areas including fusiform areas FG1, FG2), corresponding to cluster 3.

and functionally relevant regions in the brain, such as the motor, somatosensory and visual regions. This is remarkable since the feature embedding does not take into account the real locations, and has not been trained to be anatomically relevant. Therefore, the feature vectors trained on the self-supervised distance task seem to efficiently and robustly encode relevant characteristics of the cytoarchitecture in the cortical image patches.

We presented results for the *BigBrain* dataset [1], where we have access to a precise high resolution 3D reconstruction of the histological brain volume for calculating the geodesic distance. Future work will investigate the impact of reduced spatial resolution of the 3D information (e.g., larger distances between histological sections) on the results.

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