Comparison of Deep-learning based cytoarchitectonic mapping of cortex in the big brain against gold standard cytoarchitectonic map (D2.1.1 –SGA2)

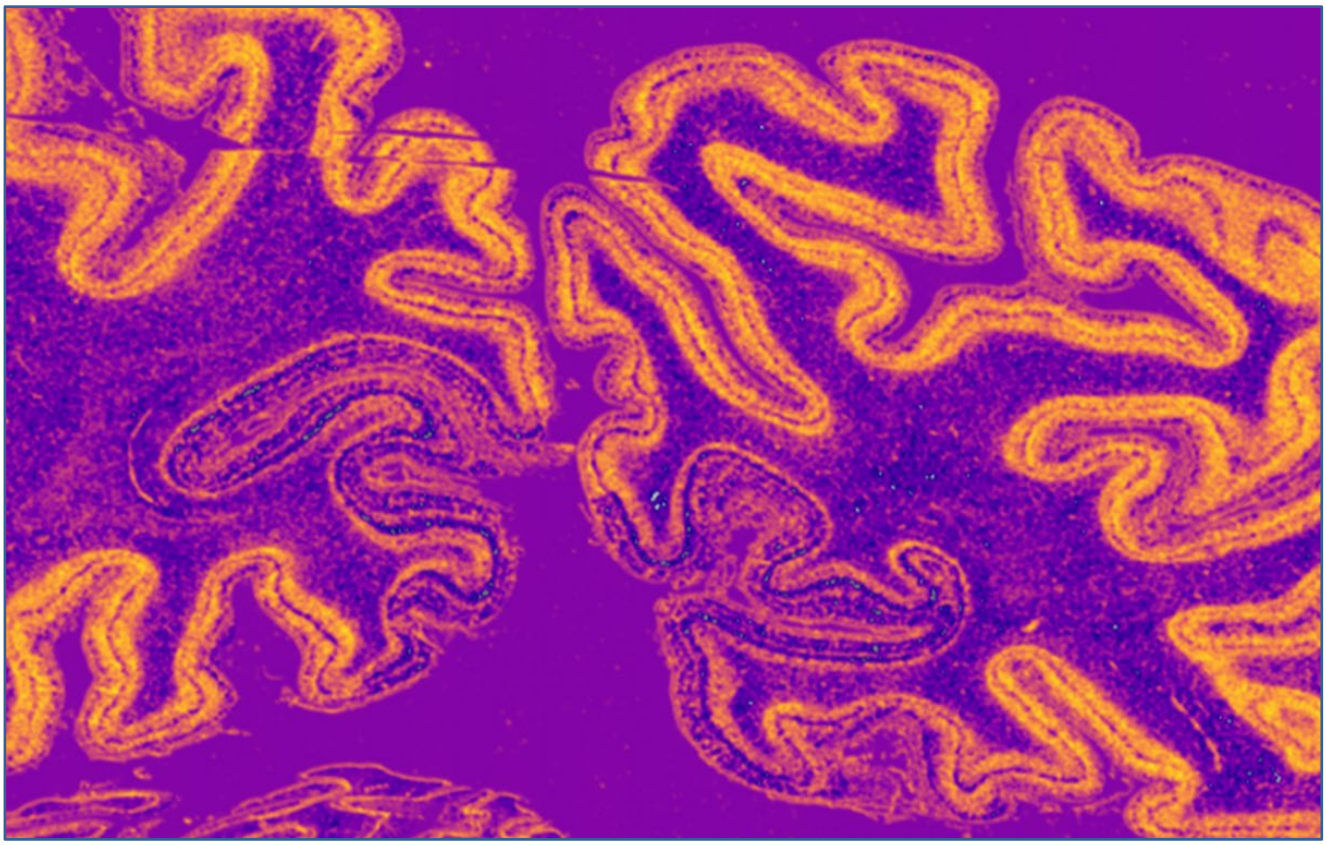

Figure 1: Deep-Learning Based Brain Mapping Tool's Filter Response Uncovering Cortical Layers

The image shows a filter response from a convolutional neural network trained to segment the secondary visual cortex in the BigBrain dataset. The filter has developed a bias for non-granular cortical layers aiding high-throughput delineations of cortical areas based on cytoarchitectonic features, which is further covered in section 3.

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Description in GA	Deep-learning based cytoarchitectonic mapping of cortex in the big brain and comparison against gold standard cytoarchitectonic map (Task T2.1.4); map made available in the HBP human brain atlas
Abstract:	This Deliverable reports on the validity of a prototype deep-learning based brain mapping tool that is in development for automatic cortex delineations in the BigBrain dataset. The prototype was able to reliably and reproducibly predict the primary and secondary visual cortex on 2401 histological sections. Predictions were compared to gold standard cytoarchitectonic maps created with the help of an observer-independent multivariate statistical image analysis tool developed in our lab 20 years ago. The comparisons showed great overlaps of area delineations with only minor incongruities. Analysis of the operational mode of the network revealed feature representations corresponding to well-known cytoarchitectonic features in the cortex. These observations indicate that the Deep Learning workflow will aid neuroscientists in big data brain mapping approaches by increasing mapping throughput with a minimal amount of input data needed. This way it will enable the generation of dense 3D maps at microscopic resolution. Our positive observations contribute to the ongoing development of the Deep Learning method. The resulting high-resolution maps of these first visual areas in the BigBrain are now under data curation. Their release in the HBP atlas is scheduled for May 1st, 2019. They will be accessible through Knowledge Graph search[1] as well as through visual exploration of the Big Brain in the HBP atlas viewer[2]

[1] https://www.humanbrainproject.eu/en/explore-the-brain/search/
[2] https://bigbrain.humanbrainproject.eu

Keywords:	Deep learning, brain mapping, brain mapping tool, neuroscience, BigBrain, visual system, atlas, automatic mapping, machine vision
Target Users/Readers:	Neuroscientists, anatomists, neurologists, computer scientists, Machine-Learning researchers

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1. Component Reference

This Deliverable is part of component SGA2 T2.1.4 Cytoarchitectonic mappings in BigBrain visual areas (component id: C2272) that provides delineations of the visual cortex in the BigBrain dataset as a gold standard to verify automatic delineations based on a new Deep Learning method which is currently under development in Task SGA2 T2.6.4 (component id: C2376). We created human expert delineations of human visual areas V1 and V2 in some of the coronal sections of the Big Brain reference template. These expert annotations are provided for download with this deliverable at https://fz-juelich.sciebo.de/s/3QWZ0wrAb4l23tb. Based on the complete set of delineations of these first visual areas for all coronal sections obtained from the Deep Learning method, we have generated 3D maps for the BigBrain at unprecedented detail, which are now under data curation. Their release in the HBP atlas is scheduled for May 1st, 2019. They will be accessible through Knowledge Graph search[3] as well as through visual exploration of the Big Brain in the HBP atlas viewer[4]

2. Background

In the last twenty years, cytoarchitectonic brain mapping has relied on a well-accepted observer-independent multivariate statistical image analysis tool (Schleicher *et al.*, 1999; Schleicher *et al.*, 2005), which is considered a gold standard for cytoarchitectonic mapping. Mapping of one brain area in one histological cell-stained section of the human brain based on this method can easily take up to 4 hours of work for one human expert. This renders the method practically infeasible to label full stacks for histological sections, and to keep up with high throughput microscopy setups. Large brain areas can easily extend across more than 1000 histological sections, which would lead to an effort in the range of a year for one expert using the established method. To this end, researchers are currently developing a more automatic procedure based on Deep Learning (SGA2 Task T2.6.4, component id: C2376), which learns from existing expert annotations and will aid neuroscientists in such “big data” settings. The motivation in this document is to compare results observed during the ongoing development of this Deep Learning method to the concrete knowledge of an expert, to discover indications about the potential of these neural networks.

3. Results

We successfully mapped four areas of the human visual system using gold standard cytoarchitectonic mapping techniques and compared the mappings to predictions of a recent prototype of the Deep Learning workflow, which is a modification of the Deep Learning model first described by Spitzer *et al.* (2018). Mappings were created on every 60th section of the BigBrain dataset and included the primary (hOc1) and secondary (hOc2) visual cortex, as well as the first adjacent cortical area in the ventral visual stream (hOc3v) and the cytoarchitectonic correlate of the motion sensitive area V5/MT+ (hOc5).

The prototype Deep Learning method has produced valid and reproducible mappings of hOc1 and hOc2 on previously unseen sections resulting in complete, dense maps of hOc1 and hOc2 on 2401 sections of the BigBrain dataset with a resolution of 1 x 1 x 20 µm. Validations of the tool’s results have been conducted by comparing the results to reference delineations acquired using the gold standard approach (Schleicher *et al.*, 1999; Schleicher *et al.*, 2005). We observed high overlaps of area delineations (see Figure 2), with only minor incongruities (e.g. bottom right image pair in Figure 2). Here, it should be noted that the Deep Learning method performs a pure pixel segmentation, while the gold standard explicitly identifies a straight border orthogonal to the

[3] https://www.humanbrainproject.eu/en/explore-the-brain/search/
[4] https://bigbrain.humanbrainproject.eu

surface. Therefore, a visual assessment is more appropriate than assessing a pixelwise error at the current state of development.

Further analysis of the filter responses inside the trained prototype convolutional neural network revealed a gradient in complexity of feature representations from superficial to deep layers of the networks. These feature representations correspond well to known cytoarchitectonic features in the cortex and stress potential shared feature detection methods in human and deep-learning based brain mapping (see Figure 1).

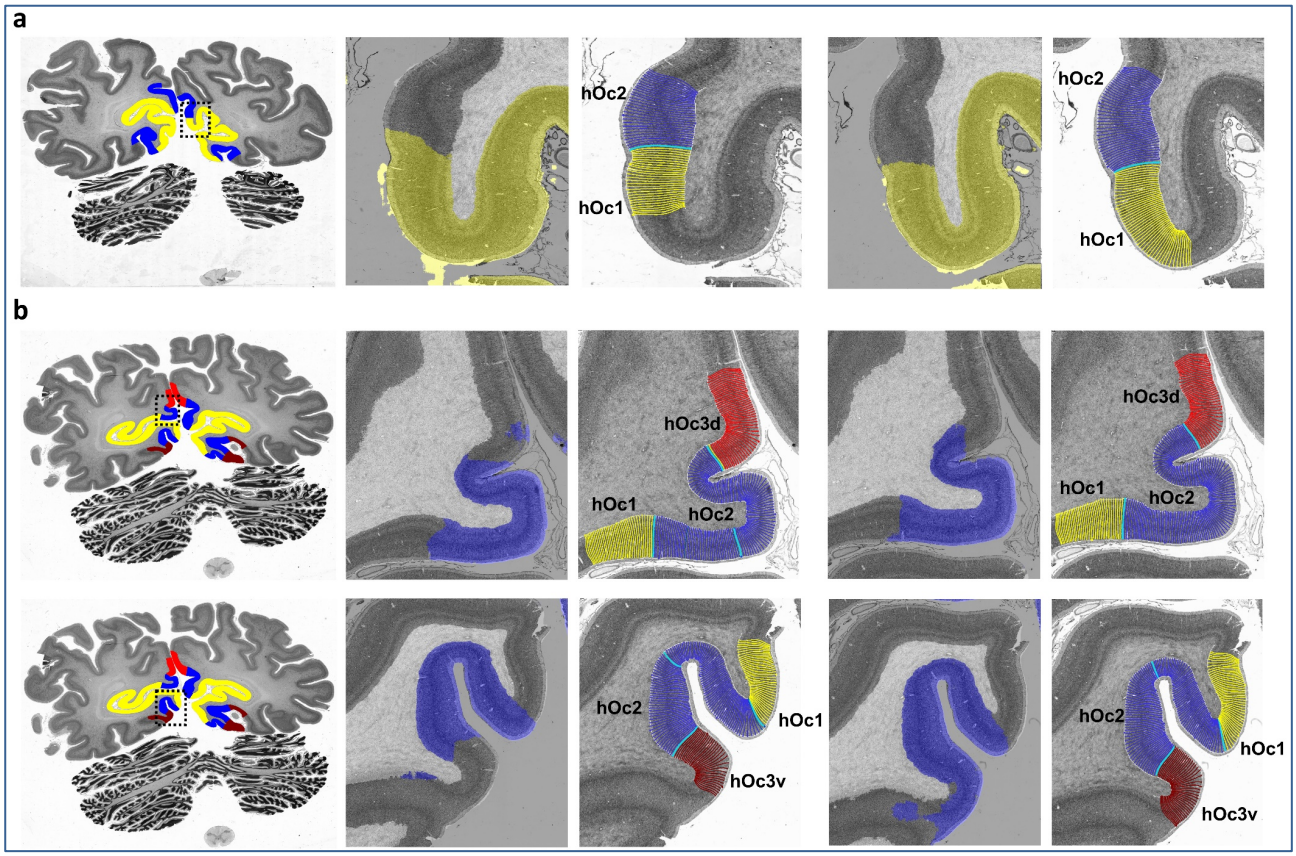

Figure 2: Comparison of Mappings generated using the Deep Convolutional Neural Network approach, and the Gold Standard Method

Visual comparison of classifications for cytoarchitectonic areas in the human visual system obtained by the Deep Learning method being developed by SGA2 Task T2.6.4 (columns 2 and 4) with areal borders provided by a human expert and confirmed using the established observer independent method by Schleicher *et al.* (columns 3 and 5). (a) Prediction of area hOc1 around the border to hOc2, (b) prediction of area hOc2 near the borders to hOc1 and hOc3d in the dorsal part, and near the borders to hOc1 and hOc3v in the ventral part.

4. Conclusion

The amount of data faced in high throughput microscopy and existing microscopic 3D models of the human brain like the BigBrain model (Amunts *et al.*, 2013) renders the current gold standard method for cytoarchitectonic brain mapping practically infeasible. A Deep Learning-based workflow that is currently in development (SGA2 Task T2.6.4, component id C2376) increases the mapping throughput with a minimal amount of required input data for training purposes. The tool's validity in mapping the primary and secondary visual cortex in the BigBrain suggests the generation of a high-resolution reference atlas of many more brain areas, and further development of the tool will enable us to perform a complete 3D cytoarchitectonic mapping of the BigBrain in SGA3, providing an important and missing link between the probabilistic maps at the neuroimaging scale and the microscopic level.

With this deliverable, we created high resolution delineations of the primary and secondary visual cortex in every coronal section of the BigBrain, which allows us to release the first high-resolution 3D maps as part of the HBP atlas in May 2019. This sets the foundation for a detailed observation framework for further investigations in the visual system. For the remaining SGA2 period, we plan to produce and validate several additional cytoarchitectonic areas, including some outside the visual system.

5. Publications / posters

Schiffer, C., Spitzer, H., Kiwitz, K, & Dickscheidm, T. (2019). ***Deep Learning speeds up gapless cytoarchitectonic mapping in serial histological sections***. 25th Annual Meeting of the Organization for Human Brain Mapping (OHBM), Rome.

Kiwitz, K., Spitzer, H., Schiffer, C., Amunts, K., & Dickscheid, T. (2018, September). *Advances in Cytoarchitectonic Mapping Using Deep Convolutional Neural Networks*. Human Brain Project Education Programme. poster session, Düsseldorf.

Schiffer, C., Spitzer, H., Kiwitz, K., Amunts, K., & Dickscheid, T. (2018, February). *Supporting Cytoarchitectonic Mapping on Histological Brain Sections using Transfer-Learning with Convolutional Neural Networks*. NIC-Symposium. poster session, Forschungzentrum Jülich.

Schleicher, A., Amunts, K., Geyer, S., Morosan, P., & Zilles, K. (1999). Observer-Independent Method for Microstructural Parcellation of Cerebral Cortex: A Quantitative Approach to Cytoarchitectonics. *NeuroImage*, *9*(1), 165–177. https://doi.org/10.1006/nimg.1998.0385

Schleicher, A., Palomero-Gallagher, N., Morosan, P., Eickhoff, S. B., Kowalski, T., Vos, K. de, Amunts, K., Zilles, K. (2005). Quantitative architectural analysis: A new approach to cortical mapping. *Anatomy and Embryology*, *210*(5-6), 373–386. https://doi.org/10.1007/s00429-005-0028-2

Spitzer, Hannah, Amunts, Katrin, Harmeling, S., & Dickscheid, Timo (2017). Parcellation of visual cortex on high-resolution histological brain sections using convolutional neural networks. In *2017 IEEE 14th International Symposium on Biomedical Imaging (ISBI 2017): From Nano to Macro : Tuesday, 18 April-Friday, 21 April 2017, Melbourne Convention and Exhibition Centre, Melbourne, Australia* (pp. 920–923). Piscataway, NJ: IEEE. https://doi.org/10.1109/ISBI.2017.7950666, preprint available at https://arxiv.org/abs/1705.10545

Spitzer, Hannah, Kiwitz, Kai, Amunts, Katrin, Harmeling, S., & Dickscheid, Timo. (2018). Improving Cytoarchitectonic Segmentation of Human Brain Areas with Self-supervised Siamese Networks. In A. F. Frangi, J. A. Schnabel, C. Davatzikos, C. Alberola-López, & G. Fichtinger (Eds.), *Lecture Notes in Computer Science: Vol. 11073. Medical image computing and computer assisted intervention – MICCAI 2018* (Vol. 11072, pp. 663–671). Cham: Springer. https://doi.org/10.1007/978-3-030-00931-1_76, preprint available at https://arxiv.org/abs/1806.05104