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Layer-specific cortical cell distributions of cytoarchitectonic areas anchored in BigBrain

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Introduction
The BigBrain model offers a framework to extract quantitative measures of brain architecture at 20µm isotropic resolution. While the BigBrain model itself already enables the extraction of 3D histological features, higher resolution is necessary to map individual cells. In this project, we aimed to use 2D 1µm sections to characterize cellular distributions within selected areas in the human brain, and furthermore enrich the BigBrain model with approximations of layer wise cell densities across the entire cortex.
Methods
Within 12 cortical areas of the Julich brain atlas, patches in the region of the corresponding probability map with the highest probability of being the specific area were sampled and transferred to BigBrain space. Cortical image patches ranging from the surface of the brain to slightly below the lamina VI-white matter boundary were extracted. Cortical layers within these patches were labeled by trained experts and validated in a four-eye procedure. Automatic cell body detection was applied to all extracted patches so that laminar cell numbers and cell sizes could be generated for all investigated areas. The extracted laminar cell packing densities of the 1um histological sections were used to calibrate the available gray levels of the corresponding 20um sections of the BigBrain. This allows to extract layer-wise cell densities within all areas included in the Julich-Brain atlas.
Results
We produced a dataset containing 120 cortical patches that were selected in well-defined cytoarchitectonic areas of the Julich-Brain Atlas. For each patch, the dataset includes the 1µm image together with manual annotations of isocortical layers and cell segmentations obtained from a state of the art deep learning approach. Thus, the resolution in the analyzed patches was increased from the native 20µm BigBrain resolution to 1µm in x and y direction. The transfer of the data to a whole brain parcellation shows that there are significant differences in the cell packing density of the different laminae of the brain. A trend of decreasing cell densities from posterior to anteriorly located areas can be observed in all lamina of human cortex. However, this trend is more pronounced in granular layers II and IV than in pyramidal layers III, V and VI. Additionally, there are quite large regional variabilities. For example, the insular cortex, shows differences of up to 15% between the number of detected cells within different laminae in the parcellation of the Julich-Brain atlas.
Conclusions
The regional increase in resolution to 1um has enabled analyses at the cellular level. The high-resolution area-specific cell numbers as well as the brain-wide interpolated cell numbers showed established cell architectural characteristics but also significant regional and lamina-specific peculiarities. The produced dataset includes high-resolution histological images, manually verified lamina annotations and precise cell numbers. All patches and the resulting analyzed datasets are located in the BigBrain reference space, so that beyond a semantic anchoring a transferable spatial localization is possible. Finally, the dataset was integrated into the multilevel atlas framework of the EBRAINS infrastructure, allowing programmatic access with the siibra-python library and thus enrichment with data from other available modalities.

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