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A novel approach in analyzing histological images using neural networks and deep learning

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The complexity of the cerebral cortex underlies its function and distinguishes us as humans. Here, we present a principled veridical data science methodology for quantitative histology that shifts focus from image-level investigations towards neuron-level representations of cortical regions, with the neurons in the image as a subject of study, rather than pixel-wise image content. Our methodology relies on the automatic segmentation of neurons across whole histological sections. We discuss methodologies to achieve that end, from ad-hoc heuristics and traditional image processing techniques to deep-learning segmentation methods. After neuronal body segmentation, an extensive set of features were engineered, which reflect the neuronal phenotype of individual neurons and the properties of neurons'neighbourhoods. This is especially important, as we have shown since similar individual properties are expressed in different cortical layers, but the neurons can nevertheless be distinguished by the characterization of their neighbourhood. These neuron-level representations are used in an interpretable machine learning pipeline that can distinguish all cortical layers and produce accurate segmentations of the layers. To validate our approach, we created a unique dataset of cortical layers manually annotated by three experts in neuroanatomy and histology. The presented methodology offers high interpretability of the results, and we discuss properties that are changing across the layers and bring them in relation to known cytoarchitectural elements. Such insights provide a deeper understanding of human cortex organisation, which may help formulate new scientific hypotheses and cope with systematic uncertainty in data and model predictions. We also aim to develop an automatized pipeline that eliminates the need for manual
intervention between the steps, thus removing human-in-the-loop biases.

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