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CytoNet: A Foundation Model for Microscopic Analysis of Cytoarchitecture in the Human Brain

Studying the structure of biological networks in the human brain is key to decoding the mechanisms underlying brain function, dysfunction, and behavior. Imaging and mapping distributions of cells and nerve fibers at the micrometer scale across entire human brains can bridge the gap between nanoscale imaging of small fields of view (e.g., by EM) and in vivo imaging of the whole brain (e.g., MRI, fMRI, DWI), the latter capturing structure and function at the millimeter scale across large numbers of subjects. A fundamental organizational principle in the cerebral cortex is cytoarchitecture; defined by the columnar and laminar arrangement of cells as well as their shape, density, size, and type. High-throughput microscopic imaging of whole human brain sections allows to map cytoarchitecture at whole-brain level, but implies to process petabyte-scale image datasets to capture inter-individual microstructures variability of different brains. To leverage the rich information of such large datasets for brain research, we propose CytoNet, a foundation model for cytoarchitecture in the human cerebral cortex. CytoNet is trained with a specifically designed self-supervised learning task that exploits the relationship between spatial proximity and architectural similarity in the brain to promote the extraction of cytoarchitectonic features from microscopic image patches extracted along the cortical ribbon. The model learns to extract anatomically plausible latent features in a fully data-driven fashion, capturing fundamental properties of cytoarchitecture with their regional variance and inter-subject variability. The features are comparable across brain regions and subjects, can be computed at arbitrarily dense sampling locations in the cerebral cortex of different brains, and facilitate a broad range of neuroscientific analysis tasks. In particular, we demonstrate state-of-the-art performance on brain area classification, cortical layer segmentation, estimation of morphological parameters, and unsupervised parcellation. As a foundation model, CytoNet offers new perspectives for characterizing microscopic architecture across subjects, establishing the foundation for holistic analyses of cytoarchitecture and its relationship to other organizational and functional principles at the whole-brain level.

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