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Spatial Transcriptomics-Informed Inference of Cell Types and States from Nuclear-Stained Whole Slide Images

Identifying cell types and their spatial organization in tissues is fundamental to understanding biological function, particularly in tissues where structure and function are tightly related, such as brain tissue. Furthermore, investigating changes in cell type composition or spatial organization in pathological settings can reveal underlying pathological mechanisms. Cell phenotyping in brain tissue usually relies on of cell-specific markers, such as antibodies. Alternatively, technologies such as Spatial Transcriptomics (ST) can map spatial gene expression across different cells in a tissue, which can then be used to annotate cell types. However, both approaches are costly and therefore not always accessible.

We aim at developing a Deep Learning (DL) model to predict cell types and healthy/pathological states from DAPI Whole Slide Images (WSIs), leveraging information from ST data. Such a model would assist to wet-lab scientists, providing fast and reliable cell type and state annotation without expensive markers or technologies. Moreover, it could provide insights into the role of different cell types in pathological mechanisms in brain tissue.

DAPI is a nuclear stain routinely used in laboratories to localize cell nuclei. While it only captures the cell nucleus, trained neuropathologists can still use it to identify cell types. Previous attempts have been made to predict cell cycle stage or phenotype from single cells on DAPI stain, or in flow cytometry experiments (Narotamo, 2020; Narotamo, 2021; Li, 2024; Eulenberg, 2017). However, both approaches only rely on single cell information and do not consider higher spatial and structural context. Moreover, models have been developed to classify cell types/states in Hematoxylin-Eosin (H&E) stained WSIs. A recent study successfully inferred cancer cell type and state from H&E WSIs leveraging information from ST data (Zhang, 2025). Other studies have attempted to predict spatial gene expression from H&E WSIs, but their accuracy is limited due to the complexity of spatial gene expression patterns (Zeng, 2022; Tan, 2023; Xie, 2023; Jiang, 2023; Chung, 2024).

At first, we plan to use a pre-trained ResNet50 architecture with a trainable classification head to predict cell types from DAPI WSIs, using ST-derived cell type annotations. We will first assess the feasibility of the prediction on an in-house dataset of paired wild-type mouse brain DAPI WSIs and MERFISH data. Afterwards, we will evaluate if the model can also capture pathological cell states, using similar data derived from an Alzheimer's Disease (AD) mouse model.

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