Predicting Cell Type from Spatial Transcriptomic Data

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Motivation

Spatial transcriptomics is a cellular profiling method that scientists utilize to not only measure the amounts of gene activity in a cell but also localize the activity to subcellular components [1]. Our project explores a variety of methods to predict cell type from spatial transcriptomic data, including cell morphology and where RNA localizes in a cell.

Data

The MERFISH dataset has ~17,000 cells annotated with cell type. Each cell has between 3 to 10 z-slice images of the cell and its RNA localization spots labelled by gene.

We extracted multimodal data, including a cell-by-gene expression matrix, images with compiled cell boundaries and RNA spots across z-slices, and periphery scores. For each gene in each cell, the periphery score is a value between -1 and 1 measuring how peripheral or central a gene is within a cell relative to all the other genes that are expressed in that cell. These were provided by our external mentors.

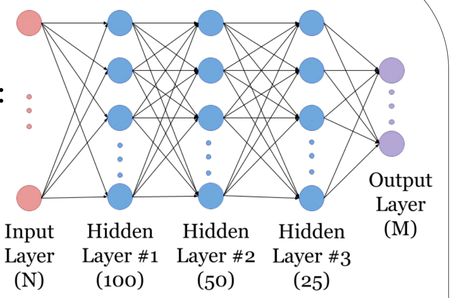
Evaluation Metrics

We used sklearn's accuracy and balanced accuracy metrics to evaluate our models. The metrics assess the model's overall accuracy, the adjusted accuracy with all classes weighted equally to address any data imbalances.

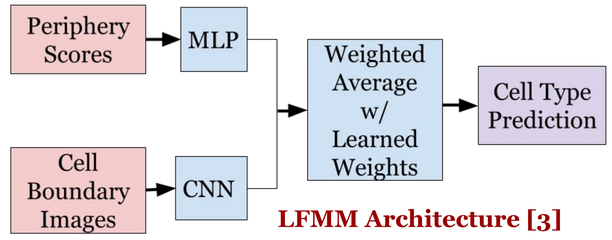
Models

A number of deep learning models were used to explore the best predictors for cell type:

1. Gene Expression MLP (Baseline): 3-layer Multi-Layer Perceptron that predicts cell type from cell-by-gene expression matrix
2. Periphery Score MLP: 3-layer Multi-Layer Perceptron that predicts cell type from periphery scores
3. Cell Boundary CNN: 1-layer Convolutional Neural Network that predicts cell type from cell boundary image data
4. Late-Fusion Multimodal Model (LFMM): concatenates periphery score MLP and cell boundary CNN outputs using learned weights
5. Early-Fusion Transformer (EFT): Self-attention model that differentially weights the (x, y) coordinates and gene type of each RNA localization spot.



MLP Architecture [2]



LFMM Architecture [3]

Results

Model	Accuracy	Balanced Accuracy
Baseline	83.67%	47.8%
Periphery Score MLP	54.6%	18.5%
Cell Boundary CNN	11.3%	1.28%
LFMM	53.3%	22.4%
EFT	83.4%	53.2%

Discussion/Future Work

While our periphery score and transformer models show some good results, they weren't significantly better than the baseline gene expression model. However, the high accuracy in spite of the relative increase in complexity shows that spatial transcriptomics data has potential to reveal more information about cell type.

Our next steps are to continue to tune the multimodal models to try to achieve better results, and to further analyze results to determine how much information spatial data encodes when compared to expression data.

References

[1] Method of the year: Spatially resolved transcriptomics / Marx, Vivien (2021)
[2] ACTINN: automated identification of cell types in single cell RNA sequencing / Ma, Feiyang and Pellegrini, Matteo (2019)
[3] Text Classification with Transformer / Nandan, Apoorv (2020)