Spatially-resolved transcriptomics meets Deep Learning: denoising omics data matrix using Optimal Transport and Graph Attention Networks.

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INTRODUCTION

In this study we introduce a novel deep learning model for denoising spatial transcriptomics RNA sequencing data, leveraging the power of optimal transport and graph attention mechanisms. We called our model Graph Attention with Optimal Transport, Transformers and Time diffusion (1) (GO3T) which combines the mathematical accuracy of optimal transport to compute distance similarities with the dynamic learning capabilities of graph attention networks. This integration effectively mitigates noise and preserves spatial gene expression patterns. An overview of the architecture is represented in **Figure 1**.

To validate our model's performance, we conducted a comprehensive benchmark against state-of-the-art methods such as GraphST (2), SpaGCN (3), and STAGATE (4) as well as ScanPy (5). Our results demonstrate superior clustering metrics, highlighting the model's ability to maintain biological relevance.

METHODS

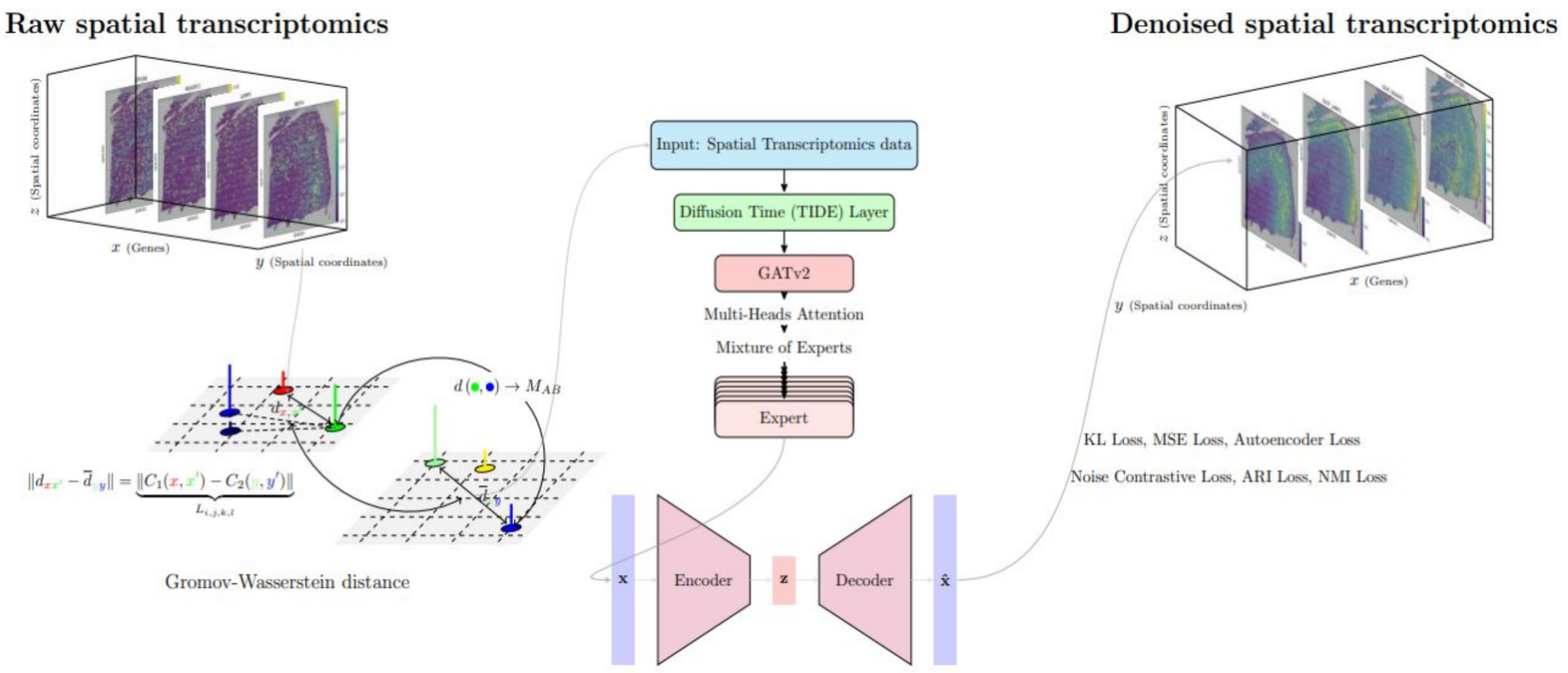

Figure 1: Overview of GO3T architecture.

RESULTS

Experiments were tested using 12 samples from a Dorsolateral Prefrontal Cortex (DLPFC) dataset. **Figure 2** compares different metrics for each of the samples used whereas **Figure 3** represents the performance, using the same metrics, over all the datasets. Results show that our method is significantly more performant than other state-of-the-art methods. Our model achieves the highest Normalized (NMI) and Adjusted (AMI) Mutual Information, and that only for samples 151508 and 151509 the Adjusted Rand Index (ARI) is lower than others.

$$ARI = \frac{\text{RI - Expected RI}}{\text{Max(RI) - Expected RI}} \quad NMI(Y, C) = \frac{2 \times I(Y;C)}{[H(Y) + H(C)]}$$

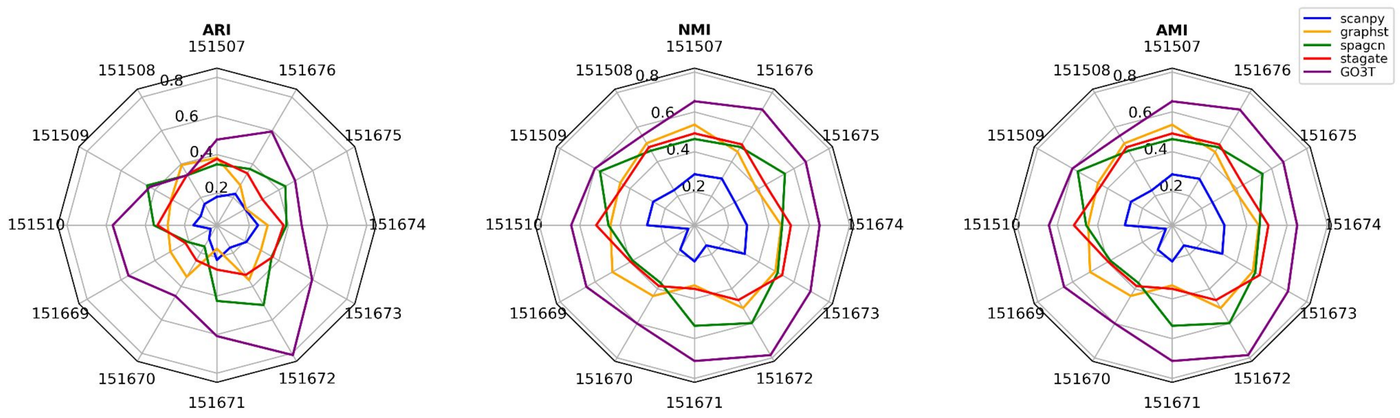

Figure 2: radarplots grouped by the three metrics used (ARI, NMI and AMI) for the 12 DLPFC samples using four common methods and ours (GO3T).

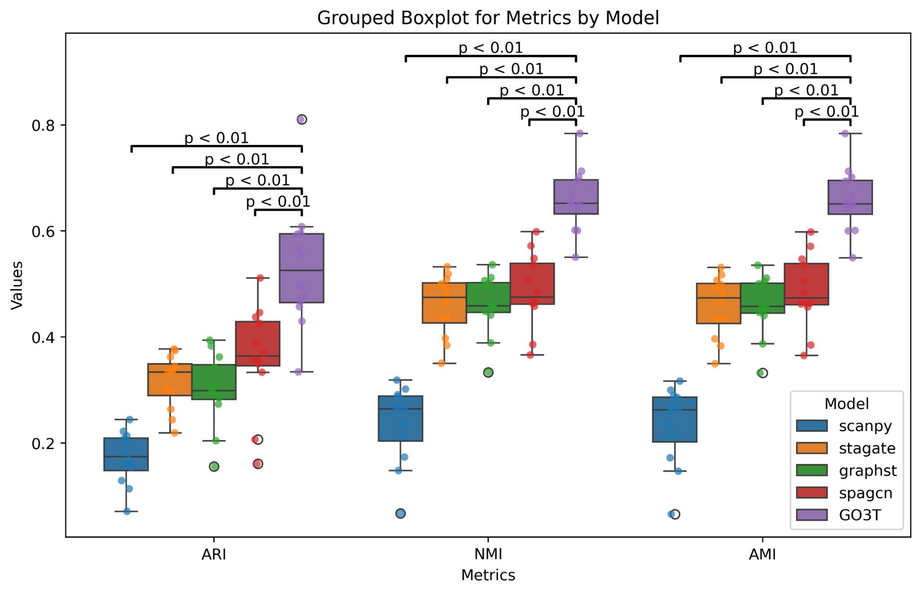

Figure 3: boxplots grouped by the three metrics used (ARI, NMI and AMI) for the 12 DLPFC samples along with the two-sided p-value obtained with t-test comparison between four common methods and ours (GO3T).

Figure 4 represents the ground truth along the raw and imputed matrices using different models and GO3T. We can visually verify that our model has a smoother imputation preserving the different cortex layers except for the outer one. **Figure 5** shows the expression of different genes for the same dataset comparing the raw matrix with the one imputed by our method, visually proving that it accomplishes to denoise the data.

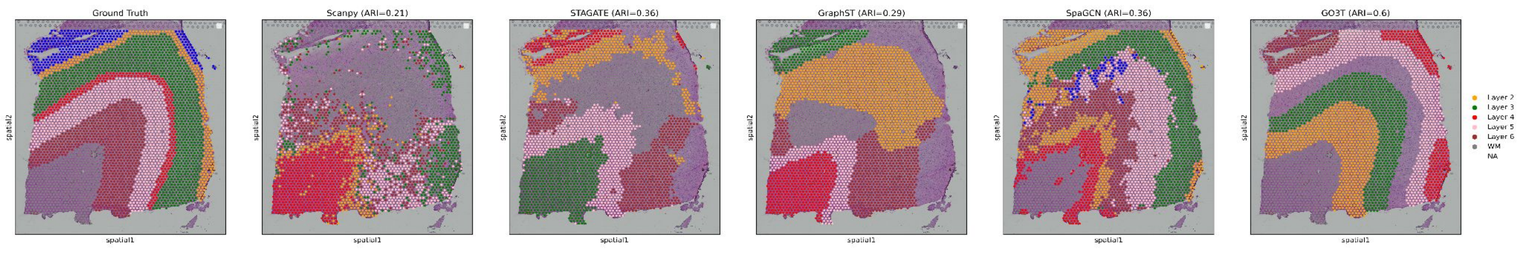

Figure 4: spatial plots for the sample 151673 showing the ground truth regions along with the predicted ones for 4 common methods and ours (GO3T).

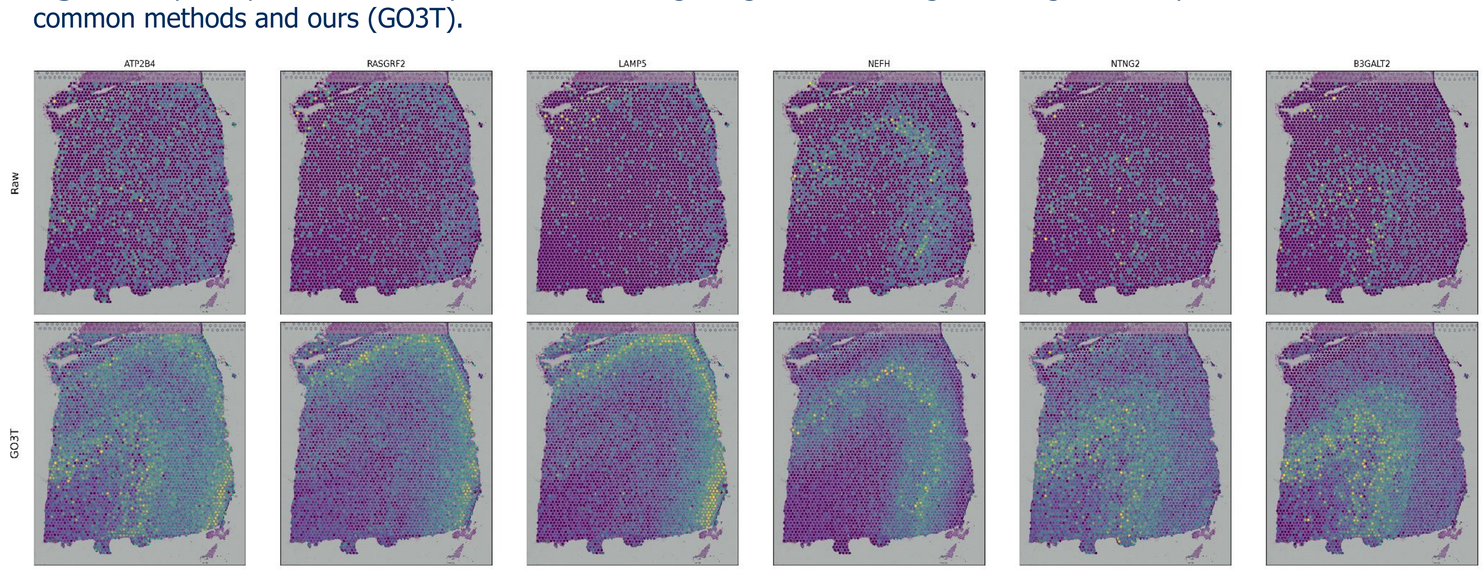

Figure 5: spatial plots comparing 6 gene expression using scanpy (above) and our method GO3T (below) for denoising in the 151673 sample showing a better spatial organization of the different selected genes.

CONCLUSIONS

Our model GO3T is significantly more performant that current state-of-the-art models for denoising sp-RNA seq matrices. The current barrier can be set around ARI=0.6, which is still lower than what we would like but it already proves good performance for keeping layers or recover genes expressions.

FUTURE WORK

- Scalability of the model.
- Ablation study: to determine which layers of GO3T intervene the most for denoising the matrix.
- Cell deconvolution: to recover the type cells in the tissue.
- Analysis of a broad range of additional spatially resolved approaches (i.e. MERFISH, StereoSeq, etc) and further comparisons with additional methods.
- Analysis of various cancer datasets.

REFERENCES

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