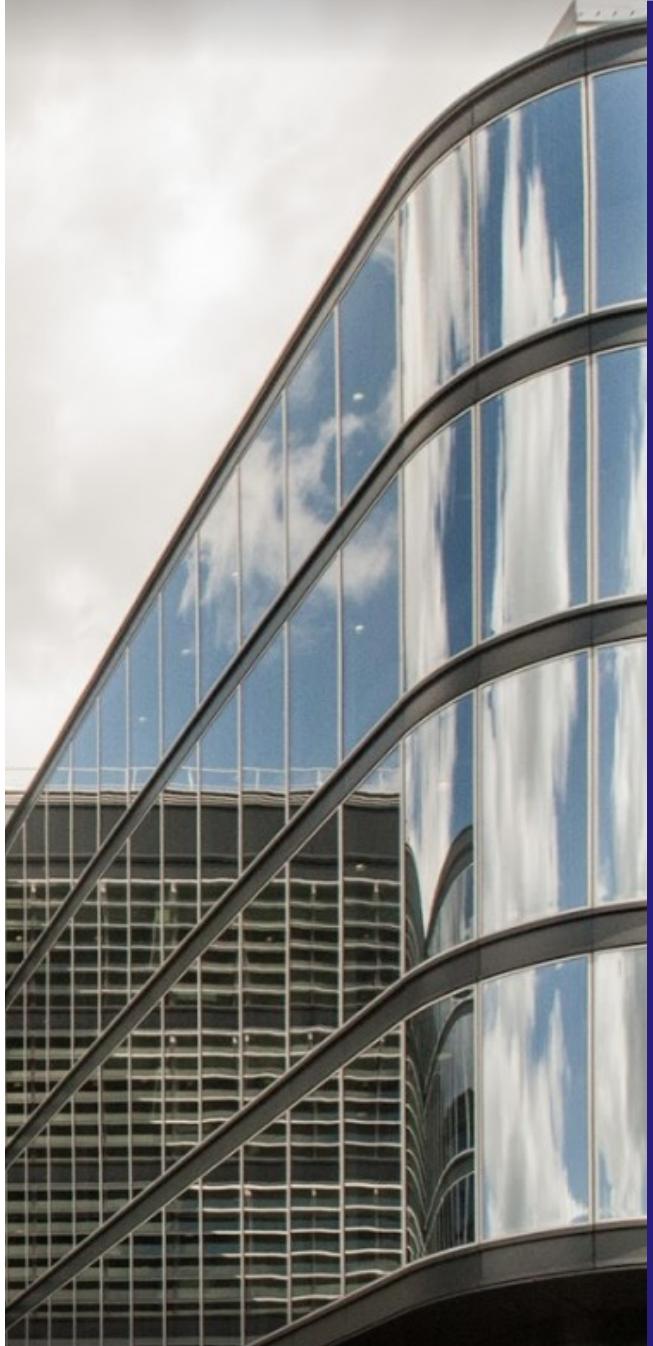

Spatially-resolved transcriptomics meets Deep Learning: denoising omics data matrix using Optimal Transport and Graph Attention Networks

Lucas RINCÓN DE LA ROSA

02/10/2024



01. Scientific background

RNA sequencing

Single cell vs Bulk.

- **Proportion of zeros** in bulk RNA-seq data is usually **10–40%** (*Jiang et al. Genome Biol 2022*).
- That proportion can be as high as **90%** in single cell RNA sequencing (**scRNA-seq**) data.
- The high data sparsity provoked the use of **zero-inflated** models **and** the development of **imputation methods** for reducing zeros.

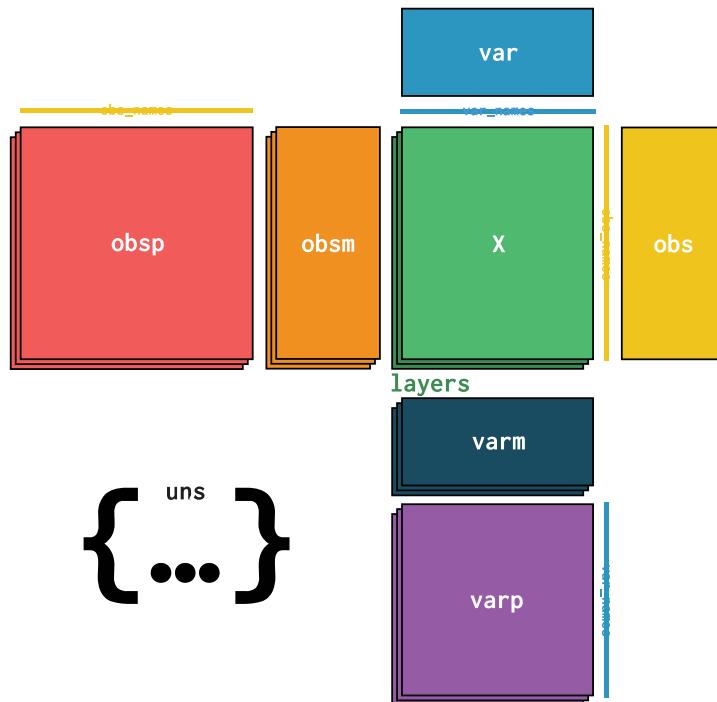


Figure 2: RNA-seq AnnData example. `.X`: containing the count matrix; `.obs`: containing annotations for the cells/spots and `.var`: contains annotations for the genes. (Virshup et al. 2021)

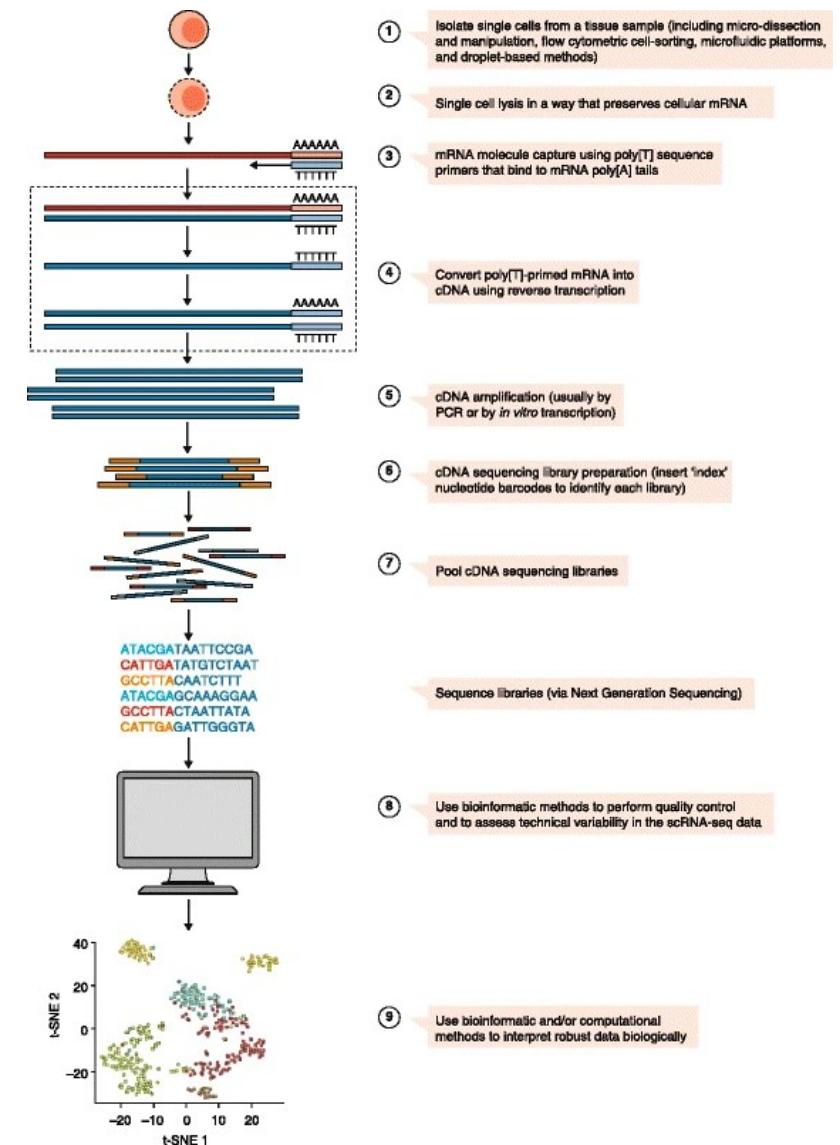


Figure 1: General workflow of single-cell RNA-sequencing (scRNA-seq) experiments (Haque et al. Genome Med 2017)

02. Data availability

DLPFC data by 10x Visium

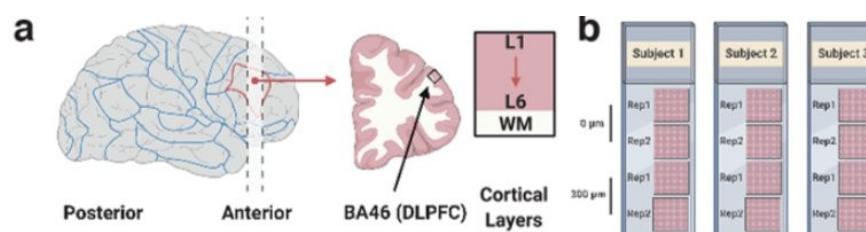


Figure 3: (a) Tissue blocks for experiments. (b) Schematic representation of experiments. (Maynard et al. Nat Neurosci 2021)

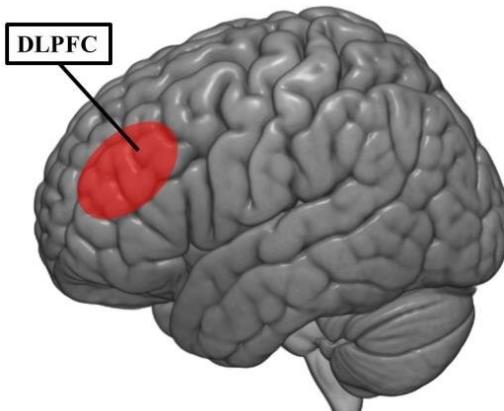


Figure 4: Location of the Dorsolateral Prefrontal Cortex (Duprat 2017)

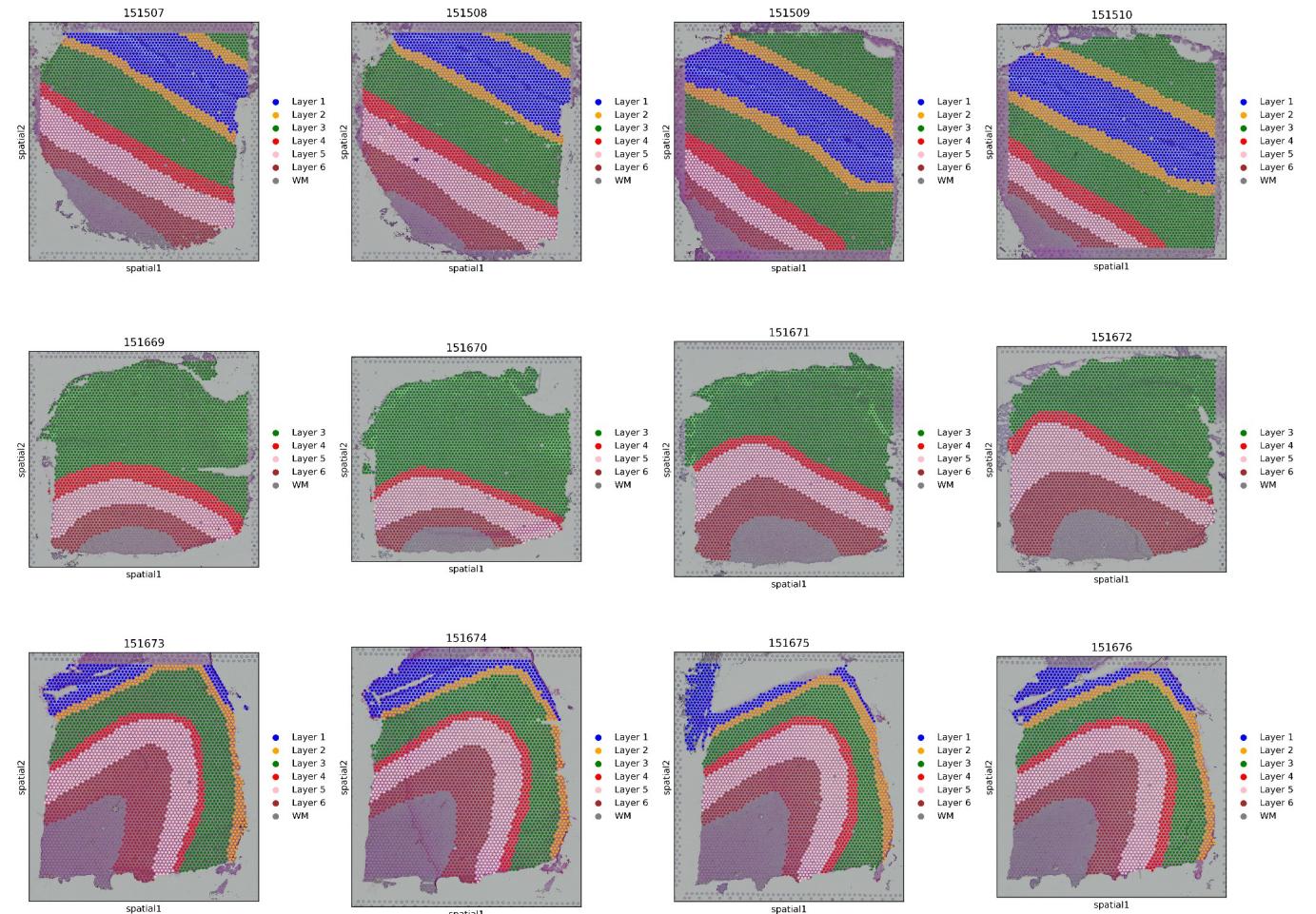


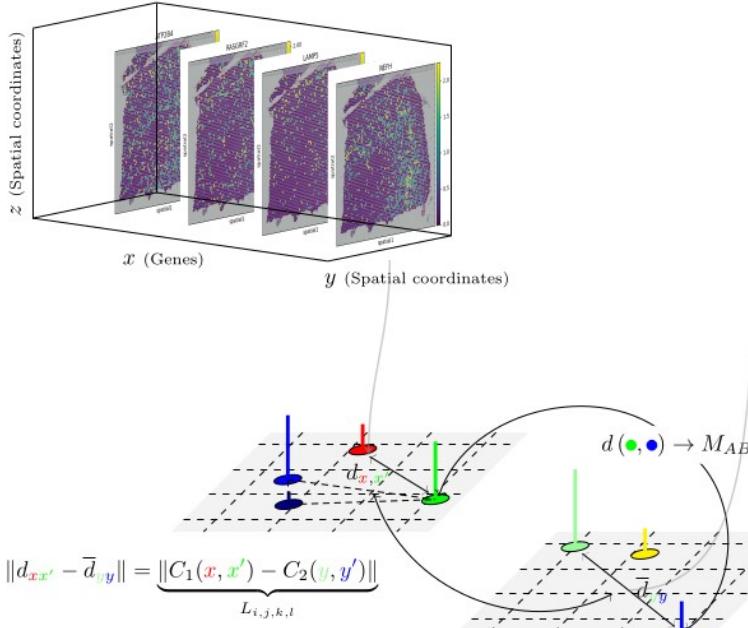
Figure 5: 12 samples from the DLPFC dataset by (Maynard et al. Nat Neurosci 2021) showing the 6 regions plus white matter.

Visualization of the Maynard 2021 dataset in SODB: <https://gene.ai.tencent.com/SpatialOmics/dataset?datasetID=6>

04. Proposed method

Graph with Optimal Transport, Transformers and Time diffusion (GO3T)

Raw spatial transcriptomics



Denoised spatial transcriptomics

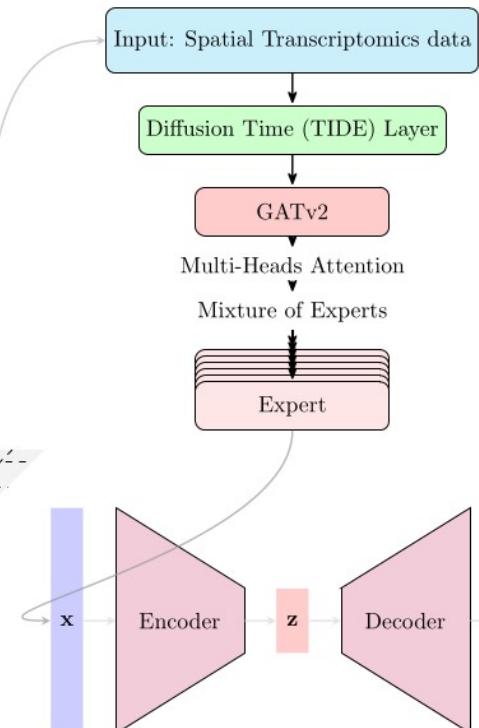
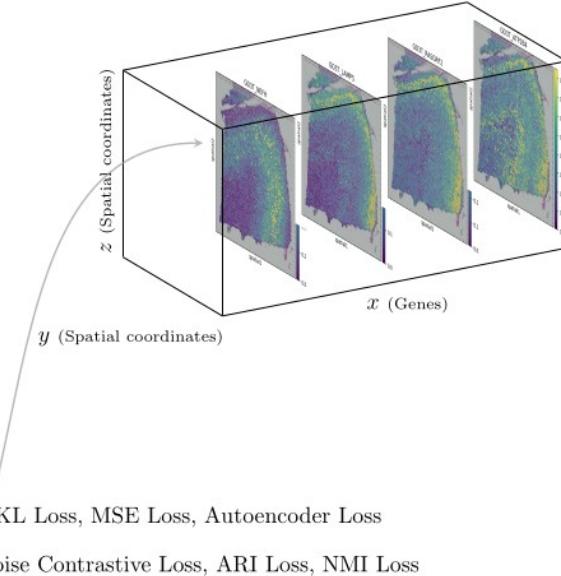


Figure 6: overview of GO3T architecture.

05. Results

Boxplots for metrics comparison

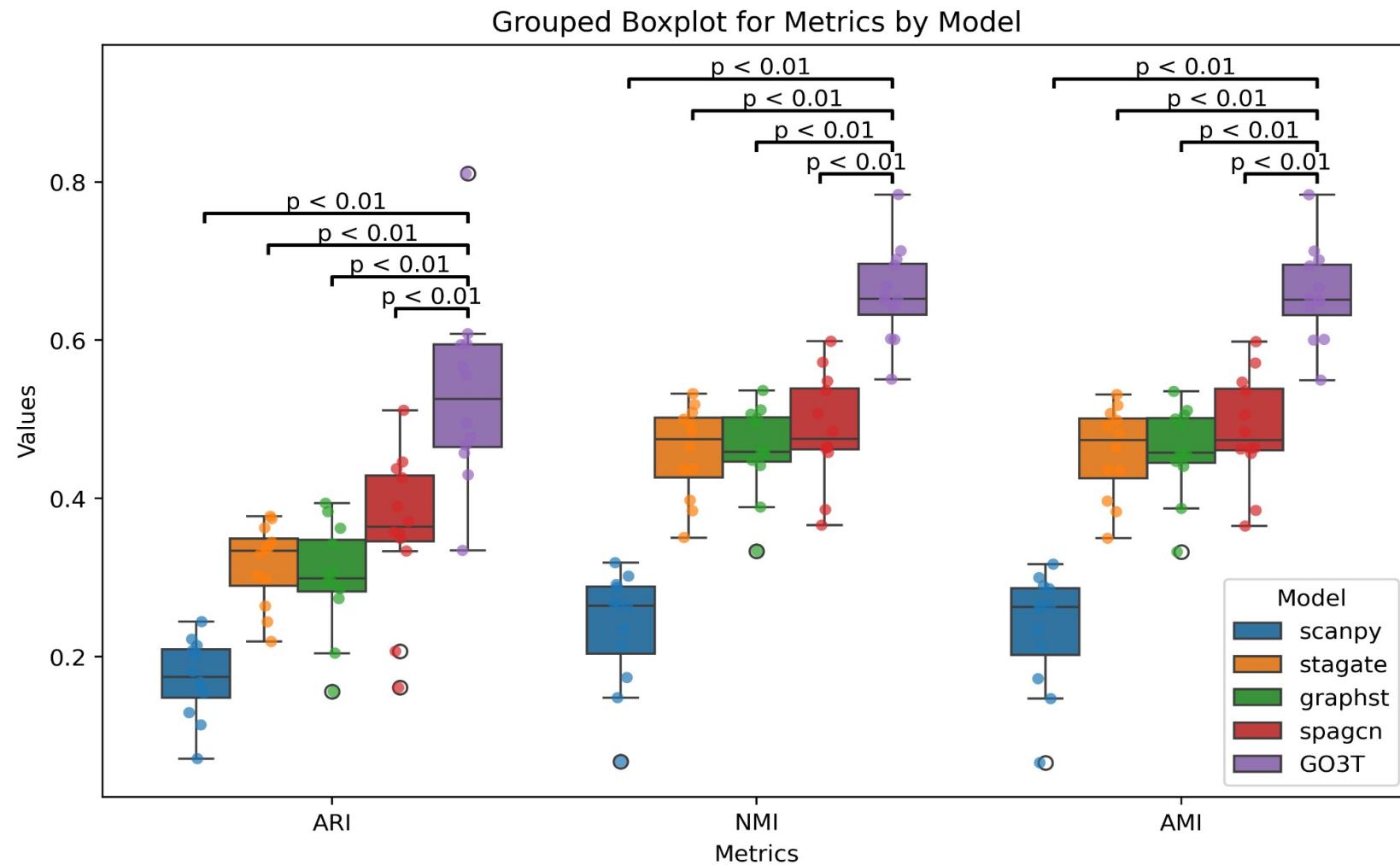


Figure 7: boxplots grouped by the three metrics used (ARI, NMI and AMI) for the 12 DLPFC datasets along with the t-test value comparison between four common methods and ours (GO3T).

Other comparisons for metrics and gene regions

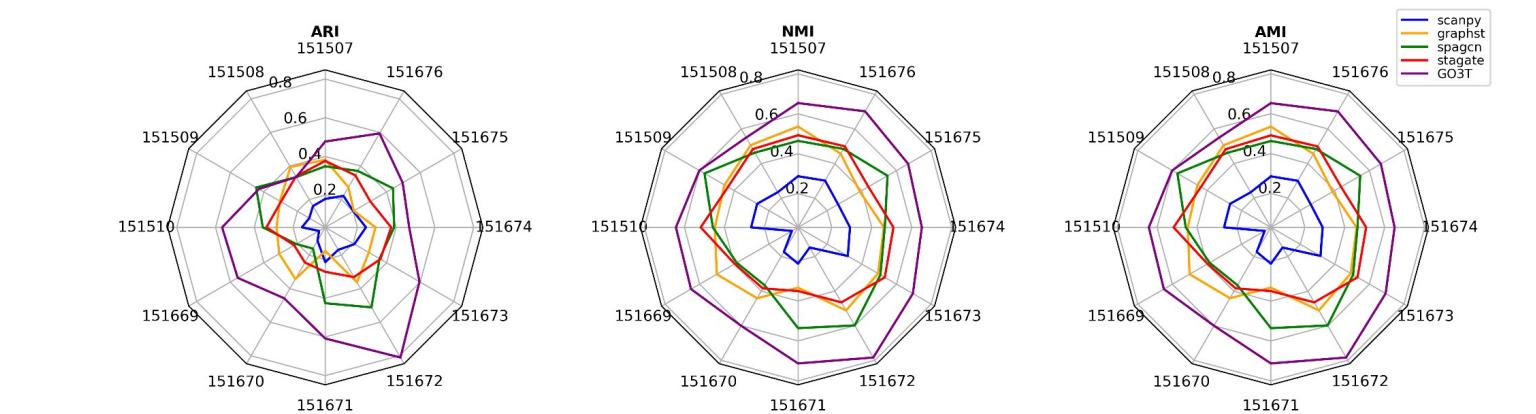


Figure 8: radarplots grouped by the three metrics used (ARI, NMI and AMI) for the 12 DLPFC datasets using four common methods and ours (GO3T).

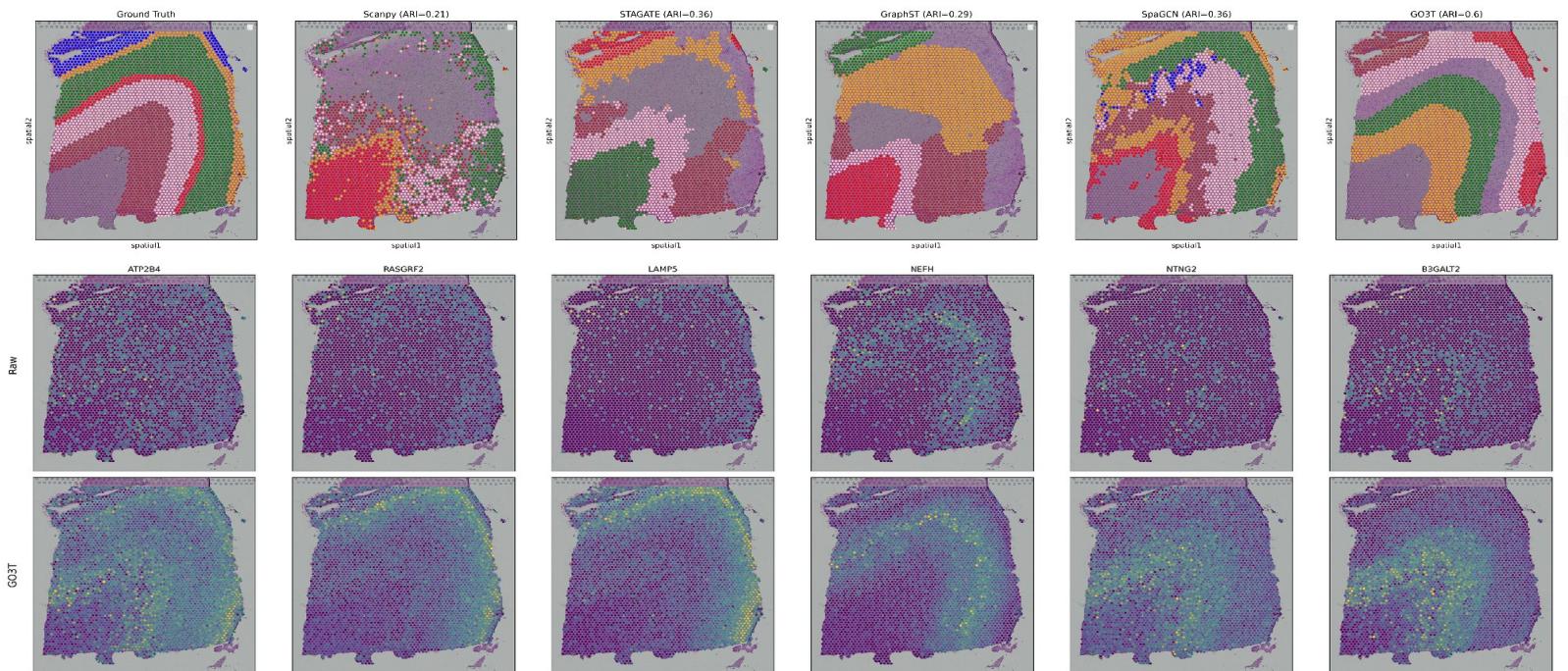


Figure 9: spatial plots for the 151673 dataset showing the ground truth regions along with the predicted ones for 4 common methods and ours (GO3T).



Acknowledgments

Thank you for your time

- Any questions ? Join me at Poster #18
- Find poster and slides at lucas-rdlr.github.io

Agustí ALENTORN - PhD supervisor

References

- Haque, A., Engel, J., Teichmann, S.A. et al. A practical guide to single-cell RNA-sequencing for biomedical research and clinical applications. *Genome Med* 9, 75 (2017). <https://doi.org/10.1186/s13073-017-0467-4>
- Jiang, R., Sun, T., Song, D. et al. Statistics or biology: the zero-inflation controversy about scRNA-seq data. *Genome Biol* 23, 31 (2022). <https://doi.org/10.1186/s13059-022-02601-5>
- Li, X., Wang, CY. From bulk, single-cell to spatial RNA sequencing. *Int J Oral Sci* 13, 36 (2021). <https://doi.org/10.1038/s41368-021-00146-0>
- Virshup, I., Rybakov, S., Theis, F.J., Angerer, F. and Wolf, F.A. bioRxiv 2021 Dec 19. doi: 10.1101/2021.12.16.473007.
- Maynard, K.R., Collado-Torres, L., Weber, L.M. et al. Transcriptome-scale spatial gene expression in the human dorsolateral prefrontal cortex. *Nat Neurosci* 24, 425–436 (2021). <https://doi.org/10.1038/s41593-020-00787-0>
- Duprat, Romain. (2017). Accelerated intermittent theta-burst stimulation in major depressive disorder. Focus on the reward system.
- Dong, K., & Zhang, S. (2022). Deciphering spatial domains from spatially resolved transcriptomics with an adaptive graph attention auto-encoder. *Nature communications*, 13(1), 1739. <https://doi.org/10.1038/s41467-022-29439-6>
- Long, Y., Ang, K.S., Li, M. et al. Spatially informed clustering, integration, and deconvolution of spatial transcriptomics with GraphST. *Nat Commun* 14, 1155 (2023). <https://doi.org/10.1038/s41467-023-36796-3>
- Hu, J., Li, X., Coleman, K. et al. SpaGCN: Integrating gene expression, spatial location and histology to identify spatial domains and spatially variable genes by graph convolutional network. *Nat Methods* 18, 1342–1351 (2021). <https://doi.org/10.1038/s41592-021-01255-8>
- Haviv, D., Kunes, R. Z., Dougherty, T., Burdziak, C., Navy, T., Gilbert, A., & Pe'er, D. (2024). Wasserstein Wormhole: Scalable Optimal Transport Distance with Transformers. ArXiv, arXiv:2404.09411v4.
- Krahn, Maximilian & Behmanesh, Maysam & Ovsjanikov, Maks. (2022). TIDE: Time Derivative Diffusion for Deep Learning on Graphs. 10.48550/arXiv.2212.02483.
- Wu, X., Huang, S., Wang, W., and Wei, F. Multi-Head Mixture-of-Experts (2024). <https://doi.org/10.48550/arXiv.2404.15045>
- Veličković, P., Cucurull, G., Casanova, A., Romero, A., Liò, P. and Bengio, Y. Graph Attention Networks (2018). <https://doi.org/10.48550/arXiv.1710.10903>
- Shi, Y., Huang, Z., Feng, S., Zhong, H., Wang, W. and Sun, Y. Masked Label Prediction: Unified Message Passing Model for Semi-Supervised Classification (2021). <https://doi.org/10.48550/arXiv.2009.03509>