

Automated cell type calling for high-resolution spatial omics

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Spatial omics techniques¹ allow spatially resolved quantification of protein or RNA species abundance in tissue. Spatial omics techniques can roughly be divided into two categories:

- Low-resolution, high-coverage techniques (LR-SO) allow measuring the entire transcriptome at super-cellular resolution (several cells per spot):
- High-resolution, low-coverage techniques (HR-SO) such as MIBI², MERFISH³, or MELC⁴ allow targeted measurement of fewer proteins or RNA species at single-cell resolution.

This project focuses on a specific pre-processing task for HR-SO data, the automated assignment of cell type labels (e.g., T cells, B cells, melanocytes, etc.) to individual cells. This is a challenging problem, because in HR-SO data, conventionally used cell type markers may not have been measured, complicating straightforward application of automated cell type assignment algorithms designed for whole transcriptome single-cell RNA-sequencing data. Specifically, the project will proceed in the following steps:

1. Individuate state-of-the-art methods that allow automated cell type assignment for HR-SO data.
2. Individuate HR-SO datasets with high-confidence expert-provided cell type annotations.
3. Based on these datasets, design and implement a validation pipeline to benchmark the methods individuated in step 1.
4. Include a prototype method (<https://github.com/bionetslab/THEORETIC>) for cell type assignment in HR-SO data developed at the BIONETS lab into the validation pipeline and compare its performance against the state of the art.

Requirements

- Python programming.
- Highly independent and rigorous workstyle.
- Willingness to independently dive into cellular biology (reading textbooks, etc).

Depending on the results, continuation of the project in the context of a MSc thesis is possible.

References

1. Bressan, D., Battistoni, G., and Hannon, G.J. (2023). The dawn of spatial omics. *Science* 381, eabq4964. <https://doi.org/10.1126/science.abq4964>.
2. Ptacek, J., Locke, D., Finck, R., Cvijic, M.-E., Li, Z., Tarolli, J.G., Aksoy, M., Sigal, Y., Zhang, Y., Newgren, M., et al. (2020). Multiplexed ion beam imaging (MIBI) for characterization of the tumor microenvironment across tumor types. *Lab. Invest.* 100, 1111–1123. <https://doi.org/10.1038/s41374-020-0417-4>.
3. Chen, K.H., Boettiger, A.N., Moffitt, J.R., Wang, S., and Zhuang, X. (2015). RNA imaging. Spatially resolved, highly multiplexed RNA profiling in single cells. *Science* 348, aaa6090. <https://doi.org/10.1126/science.aaa6090>.
4. Schubert, W., Bonnekoh, B., Pommer, A.J., Philipsen, L., Böckelmann, R., Malykh, Y., Gollnick, H., Friedenberger, M., Bode, M., and Dress, A.W.M. (2006). Analyzing proteome topology and function by automated multidimensional fluorescence microscopy. *Nat. Biotechnol.* 24, 1270–1278. <https://doi.org/10.1038/nbt1250>.