Image Processing for Spatial Transcriptomics

Postdoctoral or Research Engineer Position

July 13, 2026

We announce the opening of a Postdoctoral or Research Engineer Position starting in October 2026. The position is funded for two years by the ANR Project MORPHO. This is a collaborative project between the IGFL (ENSL, Lyon) and CREATIS, INSA Lyon (Lyon, France).

Keywords Spatial Transcriptomics, Image Segmentation, Image Deconvolution, Deep Learning, 3D registration, Spot Detection.

Project overview The aim of Project MORPHO is to unravel the molecular and cellular mechanisms that control the morphological diversity of multifibre muscles in the Drosophila leg during development. Using a 3D spatial transcriptomics methodology, we aim to identify the intrinsic gene networks of each muscle lineage that regulate unique muscle morphologies. In this context, multiplexed error-robust fluorescence in situ hybridisation (MERFISH) has proven to be a highly effective technique [5].

Position overview The successful candidate will develop innovative image processing pipelines for analysing of MERFISH data. He/She will collaborate with a team of biologists at ENSL (see here) and a signal/image processing team at CREATIS (see here).

The candidate will develop new algorithms for each step of the pipeline and implement novel methods for visualising and analysing 3D maps of RNA molecules. They will also apply these methods to study the spatial organisation of RNA molecules in the Drosophila leg. Publications in high-impact journals are expected as a result of this work..

Workplan In the preliminary phase of the project, we set up an initial pipeline which was then evaluated using simulations. The next phase will see the candidate evaluate the pipeline using real datasets and improve its performance by developing new algorithms for each of the following components:

- **Registration:** The 3D volumes obtained for each hybridisation cycle originate from the same RNA molecules. However, they often vary in spatial position from cycle to cycle. We have explored rigid registration strategies in 2D, and these now need to be extended into 3D.
- **Deconvolution:** Under the microscope, each RNA molecule in the imaging plane appears as a blob, and signals from molecules outside the imaging plane can contaminate measurements. To address this issue, we will consider iterative algorithms, such as the Richardson-Lucy algorithm [6], as well as interpretable neural networks that can be trained using small datasets [2]. These approaches rely on a realistic, anisotropic and wavelength-dependent point spread function (PSF) of the microscope.
- **Decoding:** The objective of decoding is to assign an RNA type to each molecule within the 3D volume. This is achieved by searching the codebook for the corresponding code using a pixel-based approach [3]. Error correction is typically executed by assigning pixels with single-bit errors to the nearest valid code in the codebook.
- **Cell assignment:** Each molecule must be assigned to a specific cell. To do so, we will explore the watershed approach implemented in the MERlin pipeline [6]. However, considering the superior performance of deep learning methods in segmentation tasks—including cell segmentation from

DAPI-stained images [1]—we will also evaluate segmentation networks based on variants of the U-Net architecture [4]. Initially, this network will be trained on standard fluorescence microscopy image databases, and then fine-tuned using a manually annotated dataset specific to our MERFISH samples.

All methods will be implemented in Python and based on the PyTorch ecosystem. They will also be built to be compatible with the `napari` interactive viewer. We are also committed to making our algorithms publicly available via a dedicated Python package hosted on GitHub.

Requirements and skills The requirements for the position are as follows:

- Ph.D. or equivalent experience in Biology, Physics, Computer Science, or Applied Mathematics.
- Proficiency in programming languages, particularly Python, applied to image data analysis.
- Experience in confocal, spinning-disk, or super-resolution imaging is a plus.
- Excellent communication and collaboration skills. English is the working language.

The candidate will acquire advanced data science and machine learning expertise, gaining hands-on experience with self-supervised and unsupervised learning paradigms essential for training models when ground-truth data is scarce. The project will hone skills in sophisticated signal/image processing, cell segmentation, and deconvolution. The candidate will become highly proficient in scientific programming with Python, utilizing key libraries like NumPy, SciPy, and scikit-learn, and will master deep learning frameworks like PyTorch.

How to apply? Please send a curriculum vitae, a motivation letter, and your academic records (for Eng.) or Ph.D reports (for postdoc) to:
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References

[1] W. Han et al. "Cell segmentation for immunofluorescence multiplexed images using two-stage domain adaptation and weakly labeled data for pre-training". In: *Sci. Rep.* 12 (2022), p. 4399. DOI: 10.1038/s41598-022-08355-1.

[2] Y. Li et al. "Incorporating the image formation process into deep learning improves network performance". In: *Nat. Methods* 19 (2022), pp. 1427–1437. DOI: 10.1038/s41592-022-01652-7.

[3] J. R. Moffitt et al. "High-throughput single-cell gene-expression profiling with multiplexed error-robust fluorescence in situ hybridization". In: *Proc. Natl. Acad. Sci.* 113 (2016), pp. 11046–11051. DOI: 10.1073/pnas.1612826113.

[4] O. Ronneberger, P. Fischer, and T. Brox. "U-net: Convolutional networks for biomedical image segmentation". In: *International Conference on Medical image computing and computer-assisted intervention*. Springer, 2015, pp. 234–241. DOI: 10.1007/978-3-319-24574-4_28.

[5] Chenglong Xia et al. "Spatial transcriptome profiling by MERFISH reveals subcellular RNA compartmentalization and cell cycle-dependent gene expression". In: *Proceedings of the National Academy of Sciences* 116.39 (2019), pp. 19490–19499. DOI: 10.1073/pnas.1912459116.

[6] M. Zhang et al. "Spatially resolved cell atlas of the mouse primary motor cortex by MERFISH". In: *Nature* 598 (2021), pp. 137–143. DOI: 10.1038/s41586-021-03964-8.