# Diffusion model for super-resolution fluorescent microscopy inverse problem

#### PhD proposal for 2025 (Duration: 3 years)

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# **Context and PhD objectives**

Conventional optical microscopy techniques, as confocal microscopes, are widely used in biology for cellular and sub-cellular structures investigation. However, their spatial resolution is limited by the light diffraction phenomena and it is typically around 200nm in the transverse plane and 400nm in the optical axis. Over the recent years, several super-resolution techniques have been developed to overcome this drawback. Among them we focus on fluctuation of fluorescent molecules methods as they don't need any specific materiel or fluorophore. The super-resolved image reconstruction is formalized in mathematical terms as an inverse problem with regularization. In the morpheme group we have proposed model-driven approach (e.g., COLORME [1]) as well as model-based data-driven approaches (e.g., GANs [2] or Plug& Play [3]).

A different and increasingly popular class of methods producing outstanding results in many applied fields is based on the use of modern generative learning approaches. Among them, diffusion models [4] have attracted the attention of several researchers working in the field of inverse problems due to their ability of combining variational inference approaches with the ability of neural networks to learn unknown posterior distributions distributions. Their use in the field of image microscopy, however, remains limited.

The purpose of this PhD thesis is to develop an inverse super-resolution method based on the use of diffusion model, inspired, e.g., from recent works in inverse problems as [5]. This approach will be developed with different regularization terms according to the biological structures of interest. The advantage will be the automatic estimation of model parameters and the possibility of associating uncertainties with the results. Acquisitions with specific microscope views will also be developed in collaboration with the Laboratoire de biologie du développement de Villefranche sur mer, enabling super-resolved 3D reconstruction.

### Candidate profile

Master/engineer degree in computer science, applied mathematics, data science with background in image processing, imaging inverse problems, deep learning and optimisation. Good coding skills for numerical simulation (Pytorch, Python, MATLAB, ...). A general interest in health and biology is welcome.

#### **Practical information**

MORPHEME research team is a joint research group between INRIA Sophia Antipolis Méditerranée., I3S Lab (Université Côte d'Azur and CNRS).

Remuneration:

#### **Application procedure**

Please send your CV, motivation letter, marks of the last two years of study and the name and e-mail address of a contact for recommendation to Laure Blanc-Féraud (blancf@i3s.unice.fr), Luca Calatroni (calatroni@i3s.unice.fr), Xavier Descombes (xavier.descombes@inria.fr).

# References

- [1] V. Stergiopoulou, L. Calatroni, H. de Morais Goulart, S. Schaub, and L. Blanc-Féraud, "Col0rme: Super-resolution microscopy based on sparse blinking/fluctuating fluorophore localization and intensity estimation," *Biomedical Imaging*, vol. 2, 2022.
- [2] M. Cachia, V. Stergiopoulou, L. Calatroni, S. Schaub, and L. Blanc-Féraud, "Fluorescence image deconvolution microscopy via generative adversarial learning (FluoGAN)," *Inverse Problems*, vol. 39, no. 5, 2023.
- [3] V. Stergiopoulou, S. Mukherjee, L. Calatroni, and L. Blanc-Féraud, "Fluctuation-based deconvolution in fluorescence microscopy using plug-and-play denoisers," in *Scale Space and Variational Methods in Computer Vision*, 2023.
- [4] S. Y, J. Sohl-Dickstein, D. Kingma, A. Kumar, S. Ermon, and B. Poole, "Score-based generative modeling through stochastic differential equations," 2021.
- [5] H. Chung, J. Kim, M. McCann, M. Klasky, and J. C. Ye, "Diffusion posterior sampling for general noisy inverse problems," 2023.