3iA Côte d'Azur
Interdisciplinary Institute for Artificial Intelligence

Ph.D. research topic

- Title of the proposed topic: **Reconstruction of filaments in fluorescence microscopy by off-the-grid methods**
- Research axis of the 3IA: : axis 3 AI for Computational Biology and Bio-inspired AI
- **Supervisor (name, affiliation, email):** Laure Blanc-Féraud, DR CNRS, blancf@i3s.unice.fr
- Potential co-supervisor (name, affiliation): Gilles Aubert, Pr. emeritus UCA, Gilles.Aubert@unice.fr, Sébastien Schaub, IR CNRS, sebastien.schaub@imev-mer.fr
- The laboratory and/or research group: Morpheme team (I3S, INRIA SAM, iBV)

Apply by sending an email directly to the supervisor.
The application will include:

- Curriculum vitæ.
- Motivation Letter.
- Academic transcripts of a master's degree(s) or equivalent.
- At least, one letter of recommendation.
- Internship report, if possible.
- Marks of the Master 1 and 2.

- **Description of the topic:**

Conventional optical microscopy techniques, as confocal microscopes, are widely used in biology for cellular and sub-cellular structures investigation in live cells. However, their spatial resolution is limited by the light diffraction phenomena, 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 bypass this limit and the Morpheme team has acquired a great expertise in this domain (see e.g. [1,2,3,4]). Among them, super-resolution by fluctuation of molecules is a powerful strategy that allows to reconstruct super-resolved image without specific material, illumination, or fluorophores, just acquiring a sequence of images of the fluctuating sample.

The super-resolved image reconstruction problem is formalized in mathematical terms as an ill-posed inverse problem which is regularized by introducing a sparsity-promoting penalization. In the off-the-grid approach, we have recently defined a norm in the vector measure space which promotes curve reconstruction: the solutions of this regularized problem are a finite sum of curves [5]. This allows to reconstruct filaments in an image one by one, following a greedy strategy defined by the Sliding Franck-Wolfe minimization algorithm [6].

- **Objective of the PhD thesis**

Work in this area is still in its infancy. The objective of this PhD thesis is to develop theoretical and numerical new results to reconstruct filaments of biological samples in the super-resolved approach by fluctuation of molecules and off-the-grid reconstruction method. Defining the data term is a question as it relates the reconstructed curves, modeled by a *vector* measure, to the observed data which are *scalar*. Moreover, from the sequence of images we can exploit the covariance as the data term [2], but also use the full information of distribution given by the observed images through a Generative Adversarial Network (GAN) [3]. How optimizing a measure through a GAN is a new and open problem. To develop an autonomous tool useful for biologists, some numerical difficulties must be overcome among them complicated geometries (for example crossing curves).

Finally, we will integrate the temporal dynamics in the model to consider the possible movement of the sample during the acquisition time. Methods and algorithms will be validated on data acquired on a calibrated fluorescent slide. The final goal of this work is to offer a software for curve reconstruction in super-resolution from microcopy fluctuating images. A special case study is to visualize the microtubules and their tips of *Ostreopsis fibronectin*, a key element in the reproduction process of this toxic algae in view to explain their proliferation.

[1] S. Gazagnes, E. Soubies, and L. Blanc-Féraud, "High density molecule localization for super-resolution microscopy using CEL0 based sparse approximation," in 2017 IEEE 14th International Symposium on Biomedical Imaging (ISBI 2017), pp. 28–31, 2017.

[2] 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," Biological Imaging, vol. 2, 2022.

[3] M. Cachia, V. Stergiopoulou, L. Calatroni, S. Schaub, and L. Blanc-Féraud, "Fluorescence image deconvolution microscopy via generative adversarial learning (FluoGAN)," 2022. HAL preprint: https://hal.archives-ouvertes.fr/hal-03790156

*[4] V. Stergiopoulou, L. Calatroni, S. Schaub, and L. Blanc-Féraud, "3*D Image Super-Resolution by fluorophore fluctuations and MA-TIRF Microscopy reconstruction (3D-COL0RME)", *2022 IEEE 19th International Symposium on Biomedical Imaging (ISBI), 2022.*

[5] Bastien Laville, Laure Blanc-Féraud and Gilles Aubert, "Off-the-grid curve reconstruction through divergence regularisation: an extreme point result", SIIMS (SIAM), March 2023.

[6] Bastien Laville, Laure Blanc-Féraud and Gilles Aubert, "Off-the-grid charge algorithm for curve reconstruction in inverse problems". SSVM 2023, 9th International Conference on Scale Space and Variational Methods in Computer Vision. May 2023.

- **Candidate profile:** Master student (M2 level) in signal/image processing, applied mathematics, data science and artificial intelligence with a strong background in mathematical image processing, inverse problems, optimization, learning, digital manipulation of images (in MATLAB, Python. . .) and use of libraries for deep learning (PyTorch), with a general interest in biology.