

# Next-generation Structured Illumination Microscopy for biological imaging

## Mots clés :

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- **Co-encadrant(s)** :
- **Unité de recherche** : Unité d'Analyse d'Images Quantitative
- **Ecole doctorale** : École Doctorale Informatique, Télécommunications, Électronique de Paris
- **Domaine scientifique principal**: Sciences et technologies de l'information et de la communication

## Résumé du projet de recherche (Langue 1)

Fluorescence microscopy is one of the most used tools in modern experimental biology. During the last few decades, several super-resolution techniques have been proposed to overcome the theoretical limit related to diffraction. The goal of this project is to take advantage of several mathematical tools and frameworks developed at the BioImage Analysis Unit (BIA) to improve one of these optical super-resolution techniques, namely Structured Illumination Microscopy (SIM)[1]. SIM is a wide field technique that increases the lateral spatial resolution up to a factor 2. Although the resolution enhancement obtained with SIM cannot rival that of pointillistic approaches one of its main advantages is the ability to provide enhanced resolution from a modest number of images and low illuminance. It is thus the technique of choice for imaging dynamic processes in live samples. Super resolution is achieved by projecting periodic illumination patterns onto the sample. This structured illumination is generated by the interference of two or more coherent light beams. The acquisition of a sequence of images captured with different pattern orientations and phases allows computing the final super resolved image through a dedicated algorithm.

Over the last few years in collaboration with teams at ESPCI-Paristech and Centrale-Supélec/Université Paris-Saclay, Olivo-Marin's team has developed an alternative approach for image reconstruction in SIM [2] that requires a reduced number of raw images to build a super resolved optically sectioned image. The method is based on an inverse problem approach [3] where the solution is inferred via a joint myopic criterion for image and modulation (or acquisition) parameters. The estimate is chosen as the minimizer of a nonlinear criterion, numerically calculated by means of a block coordinate optimization algorithm. The efficiency of this approach has been demonstrated on fixed cells samples as well as on living cells: with only 4 acquired images it has been possible to obtain a final image similar to the one obtained with 9 raw images. This novel, fast and unique SIM microscope therefore allowed dynamic super-resolution imaging [4].

Notwithstanding these advances, the reconstruction algorithm is not fully robust and the resulting super-resolution image is strongly dependent on the signal-to-noise ratio of each sample. Moreover, this technique has to be scaled to several excitation wavelengths at the same time with a fast acquisition rate, demanding the processing of an increased amount of data. We propose to address these technical challenges through the introduction of new algorithms as well as their applications to different optical setups (3D SIM, blindSIM, ...).

The project will consider the design and implementation of dedicated dynamic acquisition algorithms for SIM as well as the application to relevant biological questions, like the orchestration of the molecular mechanisms of pathogen entry in cells. One challenging part of this project will be to develop new algorithms to improve image quality and acquisition time, and further improve the capability of the structured illumination microscope and in particular to design and validate fast Compressive Sensing-based dynamic protocols in SIM microscopy via specific acquisition devices.

The resulting advances in SIM should lead to massively increased image acquisition rates with guaranteed resolution and quality for a given acquisition rate and should enable the design of optimized dynamic imaging protocols, dedicated to specific biological paradigms and experimental conditions.

## Informations complémentaires (Langue 1)

This PhD will be co-supervised by Dr. Jost Eninga (Institut Pasteur), and co-advised by Drs. Alexandra Fragola (ESPCI) and François Orieux (CentraleSupélec).



