Unsupervised motion estimation for the exploration of molecular processes in 3D light-sheet microscopy

Duration
Internship: Flexible between January to August 2022. PhD: Starting Fall 2022.

Short description of the host team
The bioimage mining group led by P. Roudot (Institute for Mathematics of Marseille/CENTURI) at Aix-Marseille University (Marseille, France) develops new computational methods for the automated discovery of molecular processes in terascale movies of complex living systems. Embedded in the interdisciplinary network of the Turing Center for Living System (CENTURI), we design robust and scalable algorithm to measure the heterogeneity of cellular processes captured by experiments that are optically, biochemically and computationally integrated.

The team led by J. Salamero at Institut Curie (Paris, France) focuses on the spatiotemporal imaging of organelles and endomembrane dynamics. The group combines conventional and super-resolved microscopy to reveal the mechanisms orchestrating the endosome recycling pathway, a key yet poorly understood process.

Project description
Within the last decade, major breakthroughs in 3D live microscopy have enabled the imaging of highly dynamic cells embedded in environments mimicking human tissues. Compared to standard imaging on glass coverslip, pathological cells display vastly different behaviors. However, the resulting 3D scenes are now too complex to be understood by visual inspection due to the large number of structures overlapping visually and moving with high degrees of freedom. Hence, while algorithms for 2D motion estimation have proven powerful in recognizing dynamic processes observed in the image data, new approaches must be designed to mine for invisible patterns in those biomolecular clouds. This internship focuses on unsupervised stochastic filtering approaches for the detection of heterogeneous motions in 3D movies where the repartition of motion types is unknown a priori. We will first study those challenges in static cells layered on a glass coverslip then in the context of a soft environment.

The problem will be approached through the study of contact sites between late endosomes and mitochondria (see Figure), a key process in cellular energy production. Despite high resolution 3D imaging, the heterogeneity and clutter have challenged the understanding of this process. Anecdotal evidence shows a stop-and-go behavior combining arrival, stable docking and rapid departures that are challenging to measure but could not be studied quantitatively. The first task of this internship will be the automated tracking of endosomes based on our previous work on piecewise-stationary motion tracking. To that end, the trainee will learn both the theory and practice of stochastic smoothing in the context of multiple target tracking. This first phase will be followed by a diagnosis of motion model weaknesses and explore how the approximation made by the linear motion models affects local errors as well as overall statistics. Based on his training, the student will study new strategies to increase robustness toward false positives using stochastic modeling of endosome distribution or non-linear motion model using deep network infrastructure.

Following up, a fully funded PhD position is available to tackle the challenges linked to dynamic estimation in tissue-like environments as opposed to glass coverslip. As such the PhD project will focus on the development of multiscale motions model for the shared dynamic footprint of molecules. In addition to enable the quantification of dynamics that are not currently within reach, we aim at providing a generic framework for the fully automated exploration of molecular processes in physiological bioimaging.

Application
Send a cover letter and a CV addressed to Philippe Roudot (I2M/CENTURI): philippe.roudot@univ-amu.fr.
Training during the internship

- Understanding the image formation process in fluorescence microscopy.
- Modeling biodynamics under constraints of computational scalability.
- Bayesian filtering for biodynamics.
- Interdisciplinary communication.
- Formulating biological hypothesis and quantitatively interrogate them.

References


