Event-based single-molecule localization microscopy for biological applications

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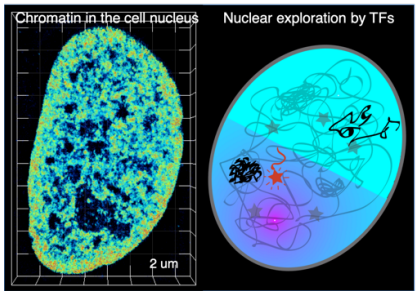
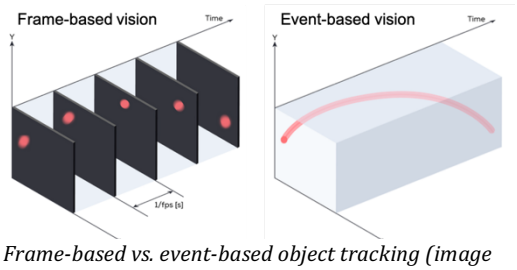
At the Institut Langevin, ESPCI Paris, we have recently shown that event-based sensors, an emerging new vision technology, have the potential to bring a new palette of applications to the field of single-molecule fluorescence microscopy (Cabriel et al, 2022). We are now looking for motivated students to help us develop novel approaches in the arising field of event-based single-molecule localization microscopy.

The advent of super-resolution imaging has revolutionized the field of optical microscopy, as recognized with the Nobel Prize in Chemistry 2014. Notably among them, single-molecule localization microscopy (SMLM) makes use of photo-switchable fluorophores so that only a fraction of them fluoresce at a time. These molecules are localized at high precision (~10 nm), and a super-resolved image can be reconstructed with a spatial resolution that beats classical Abbe's diffraction limit by one order of magnitude. One related and powerful technique to study the molecular diffusion and dynamics in biological matter is single-particle tracking (SPT), consisting in retrieving the changes in position of individual molecules within the sample of interest and reconstruct their trajectories to study their motility in the cell.



Probing cell organization and dynamics with single-molecule microscopy

Thanks to SMLM and SPT, the field of cell biology has now access to previously hidden details and other physical variables at the macromolecular level inside the cell. The analysis of a set of single molecule data contains structural information of the sample but also reveals hidden phenomena about molecular dynamics and stoichiometry of biochemical processes. However, the amount of information that one can retrieve from a single-molecule microscopy experiment is limited in part by the current acquisition technology of standard scientific CMOS or EMCCD cameras. In conventional cameras, the use of a fixed acquisition framerate determines the characteristic time scale at which the (bio)physical phenomenon is observed, which is a major limitation for processes that are typically multi-scale in time and space.



Frame-based vs. event-based object tracking (image adapted from https://www.prophesee.ai)

Event-driven or neuromorphic vision cameras are based on an asynchronous digitization of pixels, triggered by a change in intensity. Thus, contrary to conventional cameras, all pixels are independent, which makes this technology inherently faster than classical cameras. Instead of an image, event-based sensors return a list of events corresponding to the position of the pixel and the time at which its value changed. Thus, the way of acquiring and interpreting data is very different from a classical camera and requires an important experimental and algorithmic work.

After demonstrating the feasibility of event-based SMLM for super-resolution imaging, we now want to exploit the novel applications of event-based SMLM for both super-resolution imaging and molecular dynamics studies. We are looking for motivated students with an interest in microscopy, instrumentation, and data treatment and analysis, but also with a keen curiosity for the field of molecular biology and the physico-chemical processes giving rise to the functional cell.