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ONDES ET IMAGES

Single-Molecule Fluorescence Lifetime Imaging Nanoscopy

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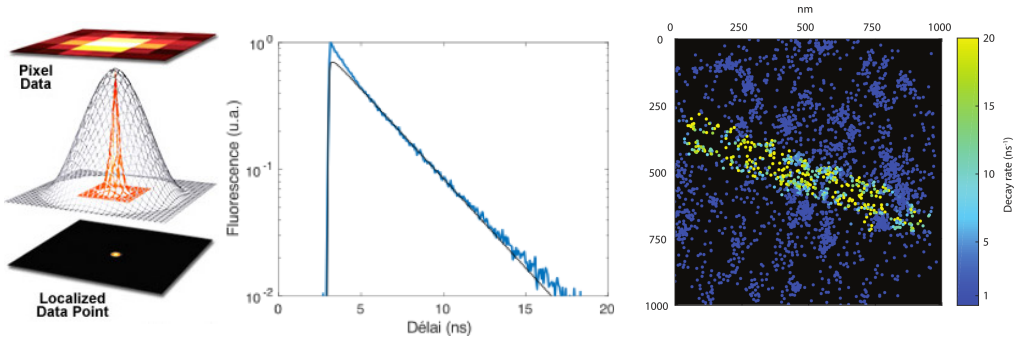
At the Institut Langevin, ESPCI Paris, we have conceived a novel microscopy system capable of simultaneously detecting single fluorescent molecules as well as their fluorescence lifetime, and thus obtaining super-resolved fluorescence lifetime images.

The field of optical fluorescence microscopy has been revolutionized with the emergence of different **super-resolution** approaches, recognized with the Nobel Prize in chemistry 2014. This set of techniques allows us to image objects with a resolution at the nanometer length scale (~10 nm), well below the classical limit imposed by the diffraction of light (typically ~200 nm). Among these, **single-molecule localization microscopy (SMLM)**[1] approaches (such as PALM[2], STORM[3], etc.) are based on the capacity of detecting single-molecules and the ability of *switching on* and *off* fluorescent emitters.

The above-mentioned techniques rely mainly on fluorescence intensity measurements. In **fluorescence lifetime imaging microscopy or FLIM**[4], the fluorescence lifetime rather than the intensity is used to create an image. Fluorescence lifetime is characteristic of the emitter environment and FLIM is used in a growing number of fields around the disciplines of biology, medicine and materials science.



Left: single-molecule localization. Middle: fluorescence lifetime (linked to LDOS). Right: LDOS nano-cartography of a silver nanowire

So far, we have applied our system to study plasmonic structures and obtained a super-resolved cartography of the local density of electromagnetic states (LDOS) of silver nanowires. However, this new approach opens up new and exciting applications not only in the fields of materials science and nanophotonics, but also for biological imaging and biophysics applications.

We are now looking for motivated students, PhD candidates and postdocs to work with us in the development of a new prototype of the system. **We aim to fully explore and exploit the capabilities of this original imaging method.** A non-exhaustive list of examples includes intracellular protein-protein interactions at the molecular level, plasmonic-induced three-dimensional super-resolution imaging, long-range plasmon-assisted energy transfer phenomena, etc.

The range of applications is broad and our device, for which we have filed a patent application, has a strong industrialization potential. That is why we are accepting applications from students with different background and motivation, ranging from biophysics to nanophotonics, and from fundamental to applied science interests. For more information, contact Ignacio Izeddin at ignacio.izeddin@espci.fr or Valentina Krachmalnicoff at valentina.krachmalnicoff@espci.fr

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2. Betzig, E. *et al.* Imaging Intracellular Fluorescent Proteins at Nanometer Resolution. *Science* **313,** 1642–1645 (2006).
3. Rust, M. J., Bates, M. & Zhuang, X. Sub-diffraction-limit imaging by stochastic optical reconstruction microscopy (STORM). *Nat. Methods* **3,** 793–796 (2006).
4. Dong, C. Y. *et al.* Fluorescence-Lifetime Imaging Techniques for Microscopy. in *Methods in Cell Biology* (eds. Wilson, L. & Matsudaira, P.) **72,** 431–464 (Academic Press, 2003).