Single-molecule and super-resolution microscopies in biology:
taking the best of fluorescent dyes, gold nanoparticles and carbon nanotubes

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The optical microscopy of single molecules has recently been beneficial for many applications, in particular in biology. It allows a sub-wavelength localization of isolated molecules and subtle probing of their spatio-temporal nano-environments on living cells. It also allows designing innovative strategies to obtain super-resolved optical images i.e. with resolution below the diffraction limit.

For many single-molecule microscopy applications, more photostable nanoprobes than fluorescent ones are desirable. For this aim, we developed several years ago far-field photothermal methods based on absorption instead of luminescence. Such approaches do not suffer from the inherent photophysical limitations of luminescent objects and allows the ultra-sensitive detection and spectroscopy of tiny absorbing individual nano-objects such as gold nanoparticles down to 5 nm in cells or carbon nanotubes. In order to access confined cellular environment (adhesion sites, synapses etc...), I will present our current efforts to reduce the functional nano-objects sizes as well as to use new near infrared nanoprobes.

The second part of my presentation will be dedicated to the presentation of super-resolution microscopy methods. It is indeed crucial to study a large ensemble of molecules on a single cell while keeping the sub-wavelength localization provided by single molecule microscopy. In order to study the dynamical properties of endogenous membrane proteins found at high densities on living cells we developed a new single molecule super-resolution technique, named uPAINT. Interestingly, uPAINT does not require the use of photo-activable dyes allowing easy multi-color super-resolution imaging and single molecule tracking. Different applications of uPAINT will be presented, in particularly the first demonstration of super-resolution imaging of functional receptors in interaction. This last result was obtained combining super-resolution microscopy and single molecule FRET.

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