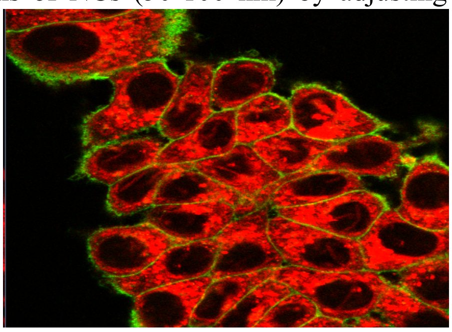
NÉEL INSTITUTE Grenoble

Topic for Master 2 internship – Academic year 2019-2020

Confined nucleation and growth of molecular nanocrystals for biophotonics: fluorescence imaging and photodynamic therapy

General Scope: We have developed an original process of sonocrystallization in solution (nucleation favored by the application of ultrasound to the crystallization solution) to confine the nucleation and growth of organic nanocrystals (NCs) in droplets. This results in highly fluorescent tracers for biological imaging based on two-photon fluorescence scanning microscopy. These tracers (40-100 nm) are based on molecular NCs, which combine the good photostability of crystals with a high number of molecules (10^5-10^6) constituting each NC, thus enhancing strongly the cross sections of absorption and fluorescence emission. This leads to bright tracers that greatly increase fluorescence contrasts for deep 3D imaging in biological tissues (see image below). On the other hand, we have started, in collaboration with biologists, to test the possibility of preparing molecular NCs for photodynamic therapy (PDT). Finally, some specific molecular NCs (non-centrosymmetric structure or highly conjugated molecules) will be involved in the characterization of optical nonlinear (ONL) properties of nanocrystals (two-photon absorption, second harmonic generation, exaltation of excitonic properties, etc.) in collaboration with physicists.

Research topic and facilities available:
The main objective will be to control the confined crystallization of molecular NCs in droplets of organic solvents. For that, organic compounds will be dissolved in organic solvents miscible with water (alcohols, THF, dioxane…). The resulting solutions will be suddenly sprayed and dispersed in water through ultrasounds. As water is generally a non-solvent for molecular phases, the corresponding NCs will nucleate and grow when the solvent droplets will be gradually mixed in water. We recently made a step-forward in the control of this process by producing nanometer-sized crystals (50 nm in diameter). Based now on a fully developed reactor, the goal is now to produce monodisperse initial droplets to obtain narrow size distributions of NCs (50-100 nm) by adjusting accurately the confined nanocrystallization conditions. The resulting NCs will be characterized by X-ray diffraction, electron microscopies (SEM and TEM), dynamic light scattering, Raman and fluorescence spectroscopies. Finally, we will plan to couple this confined nanocrystallization method in solutions to sol-gel chemistry to cover in a second step the NCs with a thin amorphous shell to produce biocompatible NCs and allow then their bio-functionalization for *in vitro* or *in vivo* studies (fluorescence imaging, see image beside, and PDT experiments).



Possible collaboration and networking:
Lab. Chimie ENS Lyon, INSERM Lyon, IBMM Montpellier

Possible extension as a PhD: Possible, depending on funding

Required skills: Chemistry, material science. The candidate should demonstrate a strong interest in the development and characterizations of nanomaterials with spectroscopic (fluorescence) properties for biological or nanomedicine applications.

Starting date: 2019-20

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