Proposition de sujet de thèse – 2019

Titre : MF-SFM-MED : multifrequency spectroscopy platform for structural analysis of biosystem

Responsable : E. Lesniewska
Axe(s) scientifique(s) : 1
Equipe(s) de recherche : OSNC
Co-responsable(s): O. Pietrement, E. Bourillot

Context, positioning and objectives:

This project is founded by ANR-15-IDEX-03 PIA2/iSite-BFC (Coordinator: E. Lesniewska) and **ANR-18-CE02-0014-03/Mobi (Partner: E. Lesniewska)** national projects. The project has been positioned in Research Project of Excellence **AAP Region 2019 Nano-Neuro-Med** and **AAPG ANR-19 /DH-Cell**.
The **MF-SFM-MED** project aims to develop the combination of recent developments on thermal poration for delivering nanoparticles into cells, and a multi-frequency platform (frequencies ranging from acoustic waves, microwaves to infrared). The electromagnetic waves in each of these bands have different characteristics, such as how they are produced, how they interact with matter, and their practical applications. We propose to develop this platform in relationship with the world leader *(Bruker GmbH)*. High-speed atomic force microscopy (**HS-AFM**) will provide the supramolecular organization by direct imaging of the structure dynamics and dynamic processes. Microwave AFM will provide the electrical properties of biological membranes, while ultrasonic AFM will provide 3D tomographic information of local density variations. The project also proposes the innovative approach to employ spatially modulated Joule-heating of substrate-solution-cell surface system for inducing cell membrane poration controlled in time and space. We will determine the performance on different human *cells (coll. C. Garrido, Inserm U1231).*

Summary

The **MF-SFM-MED** project aims at developing a novel approach for delivering molecules to living cells or tissues with high efficiency, viability and throughput, in a controlled, affordable and accessible way, without irreversible damage to the cell. Localized transient membrane poration will be achieved by using well confined and controlled Joule heating of micro- and nano-fabricated substrates in contact with cells, respecting the cell life temperature threshold, and will enable intracellular delivery of molecules. The proof-of-concepts will concern gene therapy trials for rare diseases We expect to answer relevant medical questions. We have defined specific aims: (i) **Development of ohmic current-excited substrates**, (ii) **numerical analysis of heat propagation and temperature dynamics,** (iii) **application on model membranes and thermoreflectance imaging** *(coll. Institut Langevin, ESPCI Paris)*, (iv) **application on cells. The proof-of-concepts will concern gene therapy trials for rare diseases**.

Overall strategy:

The objective of this project is the implementation of scanning probe microscopy techniques and to promote local heat-mediated intracellular delivery technology by the production medically important results worldwide. We expect to be able, using the thermal poration and multi-frequency platform, to contribute novel knowledge about structure-function relationships of individual molecules and cells. In this context, one clearly sees the growing expectation of:

(i) Development of a novel technology;
(ii) Applications for gene therapy.

The PhD student will be assisted throughout the course of his PhD on nano-micro-fabrication, numerical simulations, imaging and local spectroscopy, biological and medical approaches.

Knowledges required: Motivations, open for multidisciplinary collaboration, numerical simulation

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