Master 2 internship subject

Development of a biochip compatible with surface enhanced Raman spectroscopy and surface plasmon resonance for extracellular vesicles characterization

Start/duration: internship lasting 6 months, starting in January or February 2024

Location: FEMTO-ST institute, 15B avenue des Montboucons, 25000 Besançon

Keywords: Plasmonics, nanofabrication, biochip, PVD, SERS

Context:

Extracellular vesicles (EVs) are nanovesicles emitted by cells. EVs are of interest both in therapeutics, as a vector for active substances, and in diagnostics [1]. These last years, the Nano2BIO team of FEMTO-ST Institute (Besançon) had developed a multiplex biochip to characterize EVs with complementary methods (atomic force microscopy – AFM, surface plasmon resonance imaging- SPRi) [2], [3]. This internship is part of a starting ANR project to add Raman spectroscopy to the characterization methods. This technique would give molecular information on the composition of the membrane of EVs and its content [4]. As Raman intensity is weak, our goal is to develop a biochip that would enhance the Raman signal (surface enhanced Raman spectroscopy – SERS), while being compatible with AFM and SPRi [5].

Objectives of the internship:

The first step will be to refabricate SERS substrates produced in previous work of the team [6]. It was a glass slide on which gold nanoparticles had been deposited by thermal evaporation with annealing. This resulted in crystalline gold nanoparticles with a radius of 12 ± 7 nm separated from one another by 1 to 3 nm (figure 1). The Raman signal enhancement will be tested using methylene blue.

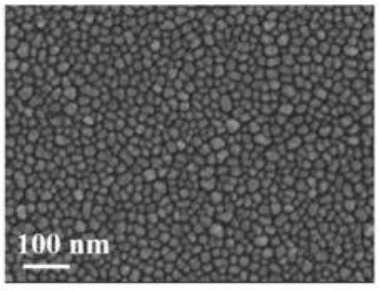

Figure 1 : SEM image of the SERS substrate manufactured by the team.

Then, the deposition parameters will be modified to change the gold nanoparticles and increase the Raman enhancement. AFM will be used to characterize the chips surface. Finally, the biochips will be tested with Cytochrome-c (strong Raman scatterer that can be present in EVs) and then on EVs adsorbed or immunocaptured. Further development of the Raman

optical system will also be envisaged. The manufacturing and characterization of chips will benefit from the equipment available at the ARCEN and MIMENTO platforms.

Required profile:

Applications are welcome from students in their 2nd year of a research master's program or 3rd year of an engineering school. Candidates should have a sound background in physics, experience in optics or plasmonics would be a plus. As the project is oriented towards an application in biology, candidates interested in this field are welcome. Candidates should consider pursuing a thesis, as funding will be offered depending on the progress of the internship.

To apply, send your CV and covering letter to benjamin.brunel@univ-fcomte.fr before **25/10/2023**.

References:

[1] E. R. Abels et X. O. Breakefield, « Introduction to Extracellular Vesicles: Biogenesis, RNA Cargo Selection, Content, Release, and Uptake », *Cell. Mol. Neurobiol.*, vol. 36, n° 3, p. 301-312, avr. 2016, doi: 10.1007/s10571-016-0366-z.

[2] S. Obeid *et al.*, « NanoBioAnalytical characterization of extracellular vesicles in 75-nm nanofiltered human plasma for transfusion: A tool to improve transfusion safety », *Nanomedicine Nanotechnol. Biol. Med.*, vol. 20, p. 101977, août 2019, doi: 10.1016/j.nano.2019.02.026.

[3] G. Raizada *et al.*, « Multimodal Analytical Platform on a Multiplexed Surface Plasmon Resonance Imaging Chip for the Analysis of Extracellular Vesicle Subsets », *JoVE J. Vis. Exp.*, n° 193, p. e64210, mars 2023, doi: 10.3791/64210.

[4] M. J. Baker *et al.*, « Developing and understanding biofluid vibrational spectroscopy: a critical review », *Chem. Soc. Rev.*, vol. 45, n° 7, p. 1803-1818, mars 2016, doi: 10.1039/C5CS00585J.

[5] K.-L. Lee, C.-Y. Hung, M.-Y. Pan, T.-Y. Wu, S.-Y. Yang, et P.-K. Wei, « Dual Sensing Arrays for Surface Plasmon Resonance (SPR) and Surface-Enhanced Raman Scattering (SERS) Based on Nanowire/Nanorod Hybrid Nanostructures », *Adv. Mater. Interfaces*, vol. 5, n° 21, p. 1801064, 2018, doi: 10.1002/admi.201801064.

[6] E. N. Aybeke, Y. Lacroute, C. Elie-Caille, A. Bouhelier, E. Bourillot, et E. Lesniewska, « Homogeneous large-scale crystalline nanoparticle-covered substrate with high SERS performance », *Nanotechnology*, vol. 26, n° 24, p. 245302, mai 2015, doi: 10.1088/0957-4484/26/24/245302.