Master 2 thesis/PFE
(5 to 6 months)

Measuring protein adsorption on surfaces with integrated optical sensors

The adsorption of proteins on surfaces plays an important role in the biomedical field [1]. For diagnostics, the control of the adsorption of immobilized capture antibodies is crucial for accurate immuno-assays. Because of their tendency to adsorb onto surfaces, therapeutic proteins can be inactivated and lost during their manufacturing, storage and administration to the patient. Moreover, understanding the adsorption process of matrix and bioactive proteins is essential to control the adhesion and the growth of cells for tissue engineering.
To investigate the interactions of proteins with surfaces, several label-free methods like surface plasmon resonance, quartz crystal microbalance with dissipation can be used [1]. An alternative approach has been studied in the past by CROMA and LMGP. The CROMA laboratory has a long experience in integrated photonics and in particular in integrated photonic sensors. Complete fabrication and characterization tools for optical integrated circuits on glass substrates are available, including clean room facilities [2]. In this context, we proposed a device based on an asymmetric Mach-Zehnder interferometer structure. Our first results show that the device is sensitive enough to detect the binding of the bovine serum albumin protein on the glass surface [3]. We aim at assessing the sensitivity of the interferometer by testing other proteins of different sizes and several protein assemblies. In addition, even if this approach seems to be very promising, the performances of the device should be improved. Among the several possibilities that can be explored in the proposed internship, there is the precise delimitation of the interaction area between the proteins and one arm of the interferometer. Alternative approaches can also be studied, for instance by fabricating a Bragg grating interacting with an integrated waveguide, to be perturbed by the protein binding (Bragg gratings on glass have long been exploited by CROMA for integrated DFB lasers). There is furthermore the need of improving the data treatment so to quantify more precisely the acquisition noise or perform time-resolved acquisitions. Finally, it would be interesting to study packaging and microfluidics solutions to allow to conduct measurements without requiring a fully equipped optical bench.

To fulfill the objective of the internship, the student will have to:

- Become acquainted with the subject through detailed bibliographic research on the working principle of the sensor and the modeling of bio-layers.
- Fabricate devices with clean room micro-fabrication processes and with the ion-exchange facilities available at CROMA (both Mach-Zehnder and Bragg grating approaches).
- At the LMGP, prepare and deposit several proteins. The functionalization of the fabricated sensor to obtain hydrophilic or hydrophobic surfaces can be performed as well.
- Characterize the optical response of the sensor and correlate it with the theoretical models.
- Develop a robust data treatment strategy allowing to observe the evolution of protein binding with respect to time.

Advisors:
Charlotte VENDRELY charlotte.vendrely@grenoble-inp.fr +33 (0) 56 52 93 58
Davide BUCCI davide.bucci@phelma.grenoble-inp.fr +33 (0)4 56 52 95 39

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[2] Allenet, T., Geoffray, F., Bucci, D., Canto, F., Moisy, P., & Broquin, J. E. (2019). Microsensing of plutonium with a glass optofluidic device. Optical Engineering, 58(6), 060502.
[3] Hoang, T.G. Study of protein adsorption on glass surface via an integrated photonic sensor. Grenoble Alpes University. Master Thesis. 2024