

Optical single molecule characterization of natural and synthetic polymers through nanopores

Supervisors :

Fabien Montel (fabien.montel@ens-lyon.fr). Ecole Normale Supérieure de Lyon. Laboratoire de Physique

Arnaud Favier (arnaud.favier@univ-lyon1.fr). Université Lyon 1. Ingénierie des Matériaux Polymères

Synthesis and characterization of natural polymers at the monomer level is routinely performed in living cells by a broad range of biological enzyme like DNA and RNA polymerases, ribosomes and glycosyltransferases. The same characterization remains a challenge for synthetic polymers even if several promising approaches based on single molecule manipulation and characterization techniques has been used in the past years. Biological and artificial nanopore [1] are now widely used to sequence at the base pair level DNA, RNA and even oligopeptides molecules. Despite some recent results and their high sensitivity existing nanopore methods based on electrical detection are limited by their adaptability to the studied polymer and their rate of measurements.

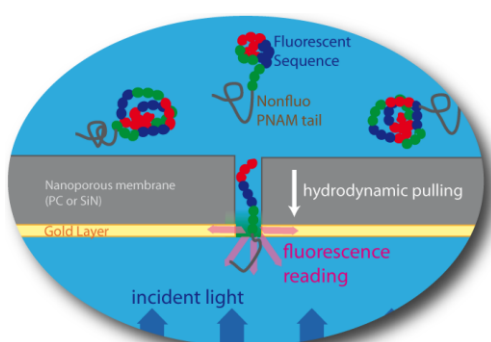


Figure 1 : Optical setup for the characterization of the polymer chains. Polymer chains are pulled through the nanopores by a hydrodynamic injection. When one polymer block reaches the end of the pore (reaching the level of the gold layer) it is illuminated and read by our Zero Mode Wave guide setup.

In a collaboration started between Fabien Montel (LPENSL UMR 5672, Lyon) and Arnaud Favier (IMP UMR 5223, Villeurbanne) we have proposed a method based on the optical detection of single polymer molecules during their translocation through nanopores. Our goal is to build a versatile and high throughput tool that can be used on various type of natural and synthetic polymers.

Following a proof of principle established with a funding from Labex iMust we propose in this Internship/PhD project to extend the Zero Mode waveguide for nanopores previously developed by the LPENSL group [1-5]. We will achieve high frequency detection and characterization of natural and synthetic polymer by improving the same device. This will benefit from the precision polymer synthesis tools developed in the IMP group (collaboration with a PhD student in polymer chemistry). The nanopore measurements will be compared to a, unique in France, high throughput optical tweezers + confocal system that will enable to build a single molecule ground truth measurement.

References

- 1] Molcrette B, Chazot-Franguiadakis L, Auger T and Montel F. Quelques éléments de physique autour des nanopores biologiques. **Reflets de la Physique** 2023, Vol. 75, p18
- 2] Auger T, Mathé J, Viasnoff V, Charron G, Di Meglio JM, Auvray L, Montel F. Zero-mode waveguide detection of flow-driven DNA translocation through nanopores. **Physical Review Letters**. 2014 Jul 11;113(2):028302.
- 3] Molcrette B, Chazot-Franguiadakis L, Liénard F, Balassy Z, Fretton C, Grangeasse C, and Montel F. Experimental study of a nanoscale translocation ratchet. **Proceedings of the National Academy of Sciences** 2022, 119 (30) e2202527119.
- 4] Chazot-Franguiadakis L, Eid J, Socol M, Molcrette B, Guégan P, Mougél M, Salvetti A, and Montel F Optical Quantification by Nanopores of Viruses, Extracellular Vesicles and Nanoparticles. **NanoLetters** 2022, 22, 9, 3651–3658
- 5] Kolbeck PJ, Benaoudia D, Chazot-Franguiadakis L, Delecourt G, Mathé J, Li S, Bonnet R, Martin P, Lipfert J, Salvetti A, Boukhet M, Bennevault V, Lacroix JC, Guégan P and Montel F. Thermally switchable nanogate based on polymer phase transition. **NanoLetters** 2023, 23, 11, 4862–4869