Nanopore-based Single-Molecule Size-Discrimination (Np-SMSD) of short homopeptides under different experimental conditions.

Fabien Piguet^{a*}, Hadjer Ouldali^a, Juan Pelta^b and Abdelghani Oukhaled^{a*}

- a. LAMBE UMR 8587, University of Cergy-Pontoise, 95300 Pontoise, FRANCE
- b. LAMBE UMR 8587, University of Evry-Val-d'Essonne, 91000 Evry, FRANCE
- * fabien.piguet@u-cergy.fr, abdelghani.oukhaled@u-cergy.fr

Nanopores have been recently used to perform the single-monomer-resolution size-discrimination of synthetic polymers [1,2,3], of short oligonucleotides [4] and of short homopeptides [5]. The high resolution and high sensitivity of this technology have major applications, as demonstrated by already commercialized nanopore-based DNA sequencing devices. It also opens new perspectives towards early *in vitro* diagnostics and protein sequencing. Experimental conditions have been shown to have a crucial impact on Np-SMSD. For example, we demonstrated that high temperature enables the single-monomer-resolution size-discrimination of synthetic polymers of high molar mass, not possible at room temperature [3]. In this talk, following our recent results [5], I shall present the effect of voltage, temperature and electrolyte concentration on the single-amino-acid-resolution size-discrimination of short homopeptides using a biological nanopore.

- [1] Robertson, J. W. F. *et al.* Single-molecule mass spectrometry in solution using a solitary nanopore. *Proc. Natl. Acad. Sci. USA* **104**, 8207-8211 (2007)
- [2] Baaken, G. *et al.* High-resolution size-discrimination of single nonionic synthetic polymers with a highly charged biological nanopore. *ACS Nano* **9**, 6443-6449 (2015)
- [3] Piguet, F *et al.* High temperature extends the range of size discrimination of nonionic polymers by a biological nanopore. *Sci. Rep.* **6**, 38675 (2016)
- [4] Cao, C. *et al.* Discrimination of oligonucleotides of different lengths with a wild-type aerolysin nanopore. *Nat. Nanotechnol.* **11**, 713-718 (2016)
- [5] Piguet, F. *et al.* Identification of single amino acid differences in uniformly charged homopolymeric peptides with aerolysin nanopore. *Nat. Commun.* **9**, 966 (2018)