

Selective protein binding using a solid-state nanopore placed into a microfluidic device

Izadora Mayumi Fujinami Tanimoto^{1,2}, Benjamin Cressiot³, Nathalie Jarroux¹, Gilles Patriarche⁴, Bruno Le Pioufle², Juan Pelta^{1,3} and Laurent Bacri¹

¹ Université Paris-Saclay, Univ Evry, CNRS, LAMBE, 91025, Evry-Courcouronnes, France

² Université Paris-Saclay, ENS Paris-Saclay, CNRS, LuMIn, 91190, Gif-sur-Yvette, France

³ CY Cergy Paris Université, CNRS, LAMBE, 95000, Cergy, France

⁴ Université Paris-Saclay, CNRS, Centre de Nanosciences et de Nanotechnologies, 91120, Palaiseau, France.

*E-mail: izadora.fujinamitanimoto@univ-evry.fr,
izadora_mayumi.fujinami_tanimoto@ens-paris-saclay.fr

Abstract

Solid-state nanopores are a promising tool to detect and characterize biomolecular interactions in a controlled environment¹, amongst them DNA sequencing^{2,3}, detection of pathogens^{4,5} and mass spectrometry for polymers and oligonucleotides^{6,7}. Their nanometric diameter can be tunable to fit the analyte size and they present better chemical and mechanical stability than the biological ones^{8,9}. However the interactions between nanoparticles and the nanopore are not well established, and the membrane has a short experimental lifetime attributed to a high surface energy. To overcome these challenges, we propose a polymer functionalization to better control the pore size, to passivate the membrane, hence avoiding nonspecific interactions of nanoparticles, by manipulating the chemical and physical surface properties^{8,9}. Furthermore, to increase the specificity, a receptor can be immobilized on the nanopore surface to capture the target molecule^{1,5}, leading to an active sensor. The nanopore chip was inserted into a microfluidic device to facilitate its handling and protect it. The proof of concept was done using the streptavidin-biotin complex, where the streptavidin was captured by the grafted biotin¹⁰.

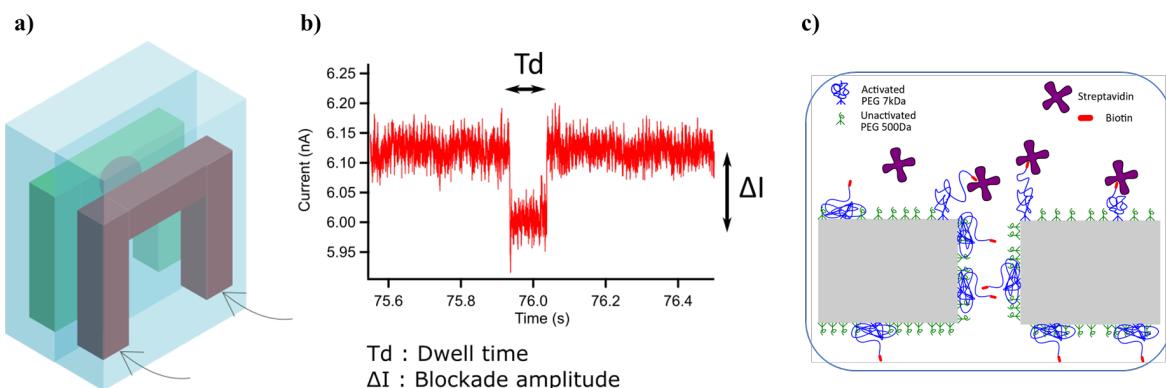


Fig. 1 a) Microfluidic device with a nanopore chip placed on it. b) Current blockade when a streptavidin molecule transiently resides inside a functionalized nanopore. c) Streptavidin interactions with a nanopore grafted with short and biotinylated long polymer (PEG) chains.

References

- (1) Malekian, B.; Schoch, R. L.; Robson, T.; Ferrand -Drake del Castillo, G.; Xiong, K.; Emilsson, G.; Kapinos, L. E.; Lim, R. Y. H.; Dahlin, A. Detecting Selective Protein Binding Inside Plasmonic Nanopores: Toward a Mimic of the Nuclear Pore Complex. *Front. Chem.* **2018**, *6*, 637. <https://doi.org/10.3389/fchem.2018.00637>.
- (2) Kasianowicz, J. J.; Brandin, E.; Branton, D.; Deamer, D. W. Characterization of Individual Polynucleotide Molecules Using a Membrane Channel. *PNAS* **1996**, *93* (24), 13770–13773. <https://doi.org/10.1073/pnas.93.24.13770>.
- (3) Jain, M.; Koren, S.; Miga, K. H.; Quick, J.; Rand, A. C.; Sasani, T. A.; Tyson, J. R.; Beggs, A. D.; Dilthey, A. T.; Fiddes, I. T.; Malla, S.; Marriott, H.; Nieto, T.; O’Grady, J.; Olsen, H. E.; Pedersen, B. S.; Rhie, A.; Richardson, H.; Quinlan, A. R.; Snutch, T. P.; Tee, L.; Paten, B.; Phillippy, A. M.; Simpson, J. T.; Loman, N. J.; Loose, M. Nanopore Sequencing and Assembly of a Human Genome with Ultra-Long Reads. *Nature Biotechnology* **2018**, *36* (4), 338–345. <https://doi.org/10.1038/nbt.4060>.
- (4) Arima, A.; Harlisa, I. H.; Yoshida, T.; Tsutsui, M.; Tanaka, M.; Yokota, K.; Tonomura, W.; Yasuda, J.; Taniguchi, M.; Washio, T.; Okochi, M.; Kawai, T. Identifying Single Viruses Using Biorecognition Solid-State Nanopores. *J. Am. Chem. Soc.* **2018**, *140* (48), 16834–16841. <https://doi.org/10.1021/jacs.8b10854>.
- (5) Arima, A.; Tsutsui, M.; Harlisa, I. H.; Yoshida, T.; Tanaka, M.; Yokota, K.; Tonomura, W.; Taniguchi, M.; Okochi, M.; Washio, T.; Kawai, T. Selective Detections of Single-Viruses Using Solid-State Nanopores. *Sci Rep* **2018**, *8* (1), 16305. <https://doi.org/10.1038/s41598-018-34665-4>.
- (6) Firnkes, M.; Pedone, D.; Knezevic, J.; Döblinger, M.; Rant, U. Electrically Facilitated Translocations of Proteins through Silicon Nitride Nanopores: Conjoint and Competitive Action of Diffusion, Electrophoresis, and Electroosmosis. *Nano Lett.* **2010**, *10* (6), 2162–2167. <https://doi.org/10.1021/nl100861c>.
- (7) Cressiot, B.; Ouldali, H.; Pastoriza-Gallego, M.; Bacri, L.; Van der Goot, F. G.; Pelta, J. Aerolysin, a Powerful Protein Sensor for Fundamental Studies and Development of Upcoming Applications. *ACS Sens.* **2019**, *4* (3), 530–548. <https://doi.org/10.1021/acssensors.8b01636>.
- (8) Roman, J.; Jarroux, N.; Patriarche, G.; Français, O.; Pelta, J.; Le Pioufle, B.; Bacri, L. Functionalized Solid-State Nanopore Integrated in a Reusable Microfluidic Device for a Better Stability and Nanoparticle Detection. *ACS Appl. Mater. Interfaces* **2017**, *9* (48), 41634–41640. <https://doi.org/10.1021/acsami.7b14717>.
- (9) Roman, J.; Français, O.; Jarroux, N.; Patriarche, G.; Pelta, J.; Bacri, L.; Le Pioufle, B. Solid-State Nanopore Easy Chip Integration in a Cheap and Reusable Microfluidic Device for Ion Transport and Polymer Conformation Sensing. *ACS Sens.* **2018**, *3* (10), 2129–2137. <https://doi.org/10.1021/acssensors.8b00700>.
- (10) Fujinami Tanimoto, I. M.; Cressiot, B.; Jarroux, N.; Roman, J.; Patriarche, G.; Le Pioufle, B.; Pelta, J.; Bacri, L. Selective Target Protein Detection Using a Decorated Nanopore into a Microfluidic Device. *Biosensors and Bioelectronics* **2021**, *183*, 113195. <https://doi.org/10.1016/j.bios.2021.113195>.