Sensing DNA Molecules using Plasmonic Nanowell-Nanopore Biosensors

***Tal Gilboa*, Ossama N. Assad, Joshua Spitzberg, and Amit Meller**

Department of Biomedical Engineering,

The Technion – Israel Institute of Technology, Haifa, 32000, Israel

E-mail: tal.hitron@gmail.com

Optical sensing in solid state nanopores, which can provide complementary information on the analyte translocation through the pore, has gained growing momentum toward applications such as rapid DNA sequencing, DNA barcoding, and epigenetic modification sensing. However the detection of individual fluorophores has proven to be challenging due to background noise resulting from photoluminescense of the solid dielectric membranes, and labeled molecules residing in the detection volume.

Here, we combine the molecular-focusing feature of a solid-state nanopore with a plasmonic nanowell structure to achieve localized fluorescence enhancement of labeled DNA molecules as they translocate through a sub-5 nm pore. The stacked plasmonic nanowell-nanopore biosensor suppresses almost entirely the background fluorescence from bulk and yield net >10 fold enhancement of the fluorescence intensity, offering extremely high S/B ratio for single-molecule detection at extremely low excitation laser intensities while maintaining sub ms resolution[1]. We further explore the two conformations of the plasmonic nanowell structure using Finite-difference time-domain (FDTD) simulations, and their ability to suppress background noise using bulk measurements. Those two conformations could be used to sense either directly labeled DNA molecules in which the optical detection is performed in the trans chamber, or DNA molecules hybridized to labeled beacons in which the optical detection occurs at the cis chamber where the beacons are unzipped.

References:

(1) Assad, O. N.; Gilboa, T.; Spitzberg, J.; Juhasz, M.; Weinhold, E.; Meller, A. Light-Enhancing Plasmonic-Nanopore Biosensor for Superior Single-Molecule Detection. *Adv. Mater.* **2016**, 1605442–1605449.