

Controlling DNA Translocation Velocities through Nanopores by *in-situ* Aperture Size Control

Justin N. Cronk¹, Alessio Angeli Bufalini¹, Morteza Aramesh¹

¹ Laboratory of Single-Molecule and Single-Cell Biophysics, ETH Zurich
maramesh@ethz.ch

Summary:

Dynamically selecting and modifying aperture size with high resolution allows for size-specific sensing and probing of biopolymers' conformational space. Indeed, in a solution containing single- and double-stranded DNA, we could reduce pore size such that only the single-stranded DNA could translocate, suggesting unparalleled specificity. Dynamic nanopores can also induce conformational changes in biopolymers: we show DNA translocations in its bulk random-walk state, folded states and linearised state through aperture size modification.

Keywords: Nanopore, DNA, Biopolymers, Conformation, Sequencing

Title

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Abstract

The interfacial nanopore is a nascent but proven technique ideally suited to localised detection and fingerprinting of secretions from cells; with dynamic pore sizing, clog-free stability, positionable with nanometre precision and functionalisable, interfacial nanopores provide *in-situ* aperture size control through the constriction of a solid-state micropore upon contact with and depression of an elastic surface. Nanopore AFMs have already been used to study fibronectin secretion [1], and later an AFM-based interfacial nanopore was used to conduct localised recordings next to single neurons [2].

Using a pipette-elastomer interfacial nanopore (PEIN), in which the aperture of a glass nanopipette is constricted *in situ* by depression into a soft elastomer, the conformational space of biopolymers can be probed. Indeed, dwell times of double stranded DNA in PEINs show significant increases with smaller apertures. Moreover, additional current levels corresponding to folds in the polymer are only seen at larger aperture sizes, implying greater structural information can

be derived and/or that conformational changes are induced in the DNA molecules. This is in accordance with DNA in its bulk random-walk state, folded states and linearised state. Aperture size can also be matched to analyte cross sections *in situ*, providing selectivity, increasing the range of possible analyte sizes measurable by one pore and allowing biopolymer dwell times to be increased by orders of magnitude over glass nanopipettes [3].

PEINs ultimately enable multidimensional analyte reads, aiding molecular fingerprinting, as well as furthering our understanding of strongly confined biopolymers. We hope to expand the library of biopolymers studied in PEINs and increase the complexity of protein mixtures, aiming to study real-time secretion patterns of live cells.

References

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