Nanopore tweezers: voltage controlled trapping of analytes for nanopore sensing

Mauro Chinappi[a], Alina Asandei[b], Tudor Luchian[c], Fabio Cecconi[d]

[a] Center for Life Nano Science@Sapienza, Istituto Italiano di Tecnologia, Via Regina Elena 291, 00161, Roma, Italia
[b] Department of Interdisciplinary Research, Alexandru I. Cuza University, Iasi, Romania
[c] Department of Physics, Alexandru I. Cuza University, Iasi 700506, Romania
[d] ICNR-Istituto dei Sistemi Complessi UoS "Sapienza", Via dei Taurini 19, 00185 Roma (Italy)

e-mail: mauro.chinappi@iit.it

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In recent years, a wide number of single-molecule protocols and devices based on nanopore technology have been proposed in literature [1-3]. The working principle of nanopore sensing (also referred as resistive pulse) is actually very simple. A nanopore connects two chambers containing an electrolyte solution. When a voltage is applied between the chambers a ionic current sets in. If a macromolecule translocates through the pore or it is blocked at the pore mouth, the ionic current is altered. From the current signal variation, information about the molecule (e.g. base sequence in the case of nucleic acids or folding state for protein and peptides) can be inferred. For sequencing puposes (e.g., DNA bases, aminoacids, various monomers), the single-nanopore recording should discriminate between the pulses of electric current and the noise, and should assign distinct current pulses to particular monomers or segments of them which cross the nanopore at a given time. Two limitations are common to both biological and solid-state nanopore sensors: (i) the spatial resolution, related to their ability to resolve individual monomers within the pore, entailing a current sensitive to a single monomer at a time (ii) the temporal resolution of the current recordings. Indeed, the detection of single monomers is usually prevented by the high translocation speed generated in common electrophysiology techniques. Consequently, the control of polymer translocation speed is of critical importance for nanopore sequencing, as free electrophoretic threading is still too rapid for single-monomer detection.

In this study, we rationalize and extend an approach, dubbed nanopore tweezer, originally proposed in [4], to control the residence time of a particle inside a nanopore. The method can be applied to both biomolecules and nanoparticles. The only requirement is the strong polarity of the passing species, a property that can be obtained, for instance by adding a positive and negative tails at opposite ends of it.

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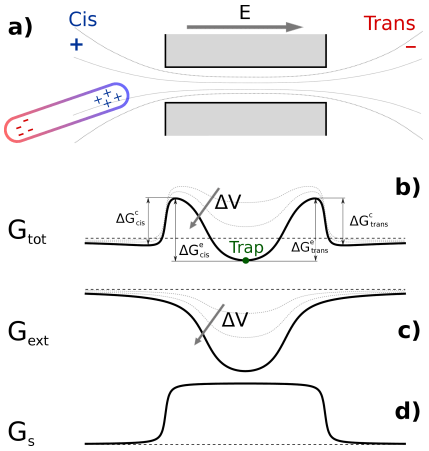

Figure 1. General scheme of the nanopore tweezer. A voltage ΔV is applied between cis and trans compartments. An inhomogeneous electric field E sets in (dashed lines in panel a). The electrical field is more intense inside the pore and goes to zero far from the pore. A polar particle in the cis compartment is attracted towards the pore entrance (a). The electric contribution to the free-energy due to ΔV and the entropic one, are qualitatively sketched in panels c and d. The combination of the twos results in the free-energy profile G_{tot} (panel b). The capture and escape barriers are functions of ΔV. The profiles refer to a symmetric case where barrier at cis and trans sides are identical, however asymmetries in the system result in unbalance between cis and trans behaviors.

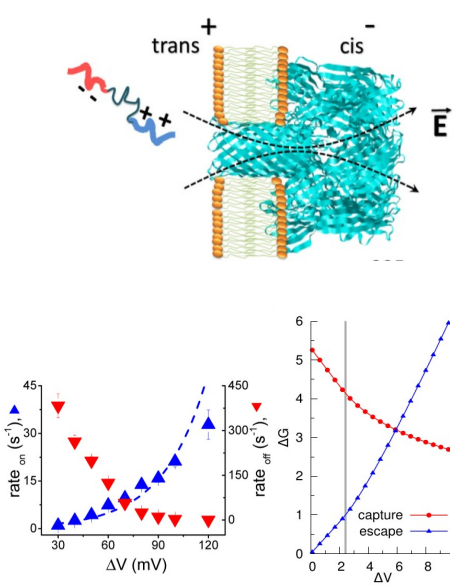

Figure 2. Example of a nanopore tweezer. The pore is an α-hemolysin and the molecule is a 36 amino acid peptide (12E-12N-12R) [4]. As ΔV increases the capture rate increases while the escape rate increases. Hence, at larger ΔV, long residence time in the sensing region can be achieved. Lower panels report capture and escape free-energy barriers from the experiments [4] and the theoretical model.