Biological nanopores for single-molecule sensing

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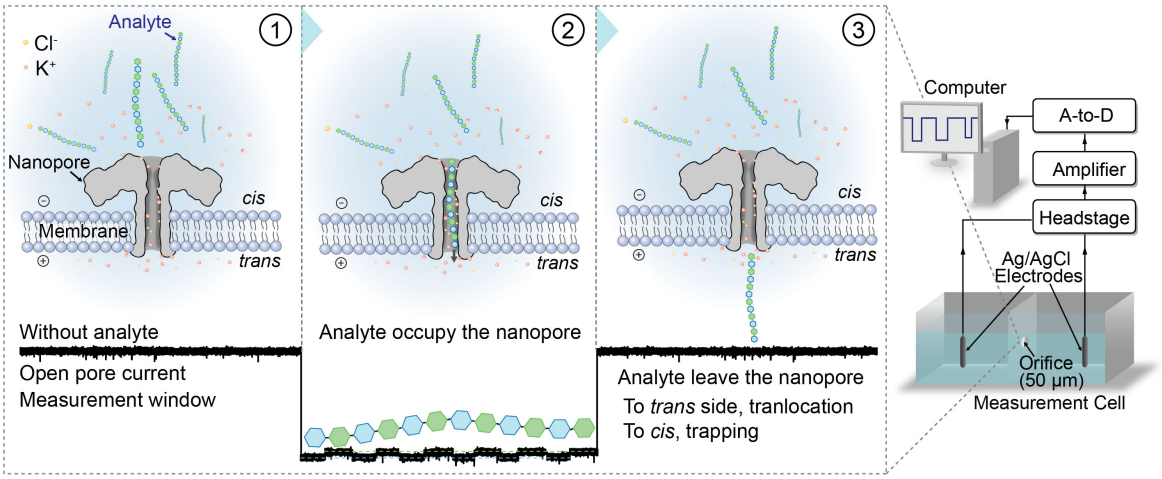
Single molecule nanopore technique has revolutionized DNA sequencing which advanced the development of precision medicine, and recently is making significant impacts on proteomics research [1]. By measuring the ionic current induced as a single molecule passes through a nanopore detector, the chemical and physical properties of the detected molecule can be obtained, including the size, mass, composition, structure, sequence and conformation. As an analytical tool, the nanopore technique highlights several unique advantages: (i) no requirement of additional labelling and amplification; (ii) the cheap electric readout, which can be easily miniaturized and massively parallelized for a high-throughput analysis; (iii) measuring a fundamentally different property of the analyte compared to other techniques, the ionic current difference induced by the target molecule; (iv) direct detection of mixture samples without the need for additional separation steps.

Here, we rationally designed a set of mutated pores and evaluated them *in silico* by molecular simulations and *in vitro* by single-channel recording and molecular translocation experiments to study the pore structural variation, ion selectivity, ionic conductance and capabilities for sensing several biomolecules, including DNA and peptides [2]. Our results show that the ion selectivity and sensing ability of aerolysin are mostly controlled by electrostatics and the narrow diameter of the double β-barrel cap. By engineering single-site mutants, a more accurate molecular detection of nucleic acids and peptides has been achieved. These findings open avenues for developing aerolysin nanopores into powerful sensing devices.



[1] S.F. Mayer, C. Cao, M. Dal Peraro, Biological nanopores for single-molecule sensing *Iscience*, **2022**, *25*, 104145.
[2] C. Cao, N. Cirauqui, M.J. Marcaida, et al. Single-molecule sensing of peptides and nucleic acids by engineered aerolysin nanopores. *Nat Commun.,* **2019**, *10*, 4918.