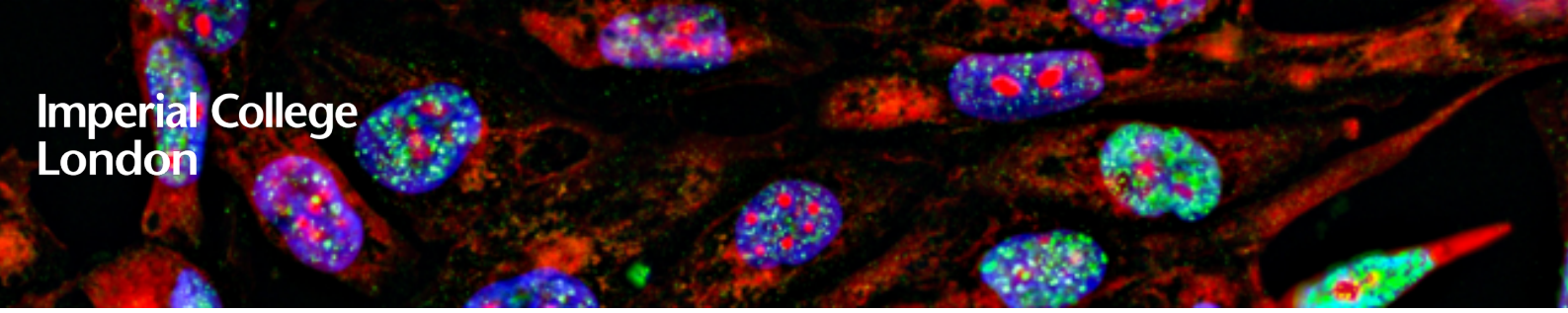

Imperial College London

Hybrid Nanopore Opto-Electronic Platform for Single Molecule Biological Screening

A molecular beacon-modified DNA carrier to specifically identify short nucleic acids and small proteins using a synchronised opto-electronic platform with nanopipette.

Proposed use

Potential applications include the detection of mismatched duplexes, point mutations in DNA/RNA oligonucleotides and nucleic acid-protein complexes. Due to the increasing availability of aptamer sequences, a greater range of targets can be addressed by integrating relevant specific aptamers into the carriers. This combined detection strategy can be further extended in a multiplexed sensing platform by introducing different binding probes at specific sites of the carrier. This, in turn, allows for a multiplexed capability to screen an array of molecules in complex samples with higher sensitivity and selectivity.

Problem addressed

The identification of short nucleic acids and proteins at the single molecule level is a major driving force for the development of novel detection strategies. Nanopore sensing has been gaining in prominence due to its label-free operation and single molecule sensitivity. However, it remains challenging to detect small molecules selectively. Our invention combines the electrical sensing modality of a nanopore with fluorescence-based detection. Selectivity is achieved by grafting either molecular beacons, complementary DNA, or proteins to a DNA molecular carrier.

Technology overview

The invention comprises a molecular beacon (MB) incorporated into a DNA carrier for rapid detection of protein and short nucleic acids. The MB is incorporated into specific sequences of ssDNA that can identify and bind to the target of interests (small molecules / proteins) along the DNA carrier selectively. The invention enables detection of specific small molecules and proteins in a label-free and high throughput manner with both electrical and optical measurements.

Benefits

- Using the custom MB carrier, the detection of target molecules does not require the need of labelling, thereby reducing preparation time and labelling error.
- The incorporation of aptamer into the custom MB allows a variety of targets to be detected, offering multiplexing approach.
- The incorporation of electrical and optical detection offers higher spatial resolution in identifying the binding of small biomolecules.
- The identification of targets through reading coincident electrical and optical signals is rapid, straightforward and unambiguous.
- The coincident electrical and optical detection eliminates false-positive events.

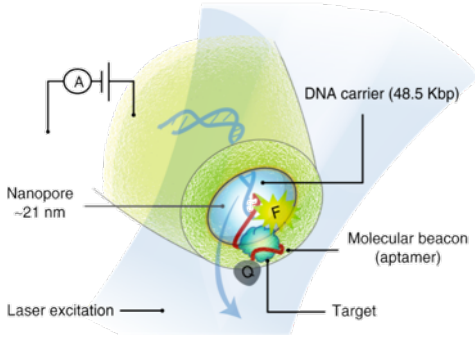

Figure 1 | Schematic of the electro-optical configuration where a nanopore is integrated with a single-molecule fluorescence confocal microscope.

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Intellectual property information

Patent : PCT/GB2020/050479 (pending)

Links to published papers

Cai, S., Sze, J. Y., Ivanov, A. P., & Edel, J. B. (2019). Small molecule electro-optical binding assay using nanopores. Nature communications, 10(1), 1-9.

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