Aptamer-Based Multiplex Screening Platform

A fully flexible, scalable and low-cost detection platform to sense multiple protein targets simultaneously by grafting specific sequences along the backbone of a double-stranded DNA carrier.

Proposed use

The method is able to detect a large range of biomarkers, with the potential to diagnose and monitor disease states at a very early stage of disease development. The invention has already been demonstrated to detect human α-thrombin, high concentrations of which have been linked to thrombotic disease. The invention can be utilised to detect any protein biomarkers across a range of conditions, such as cancer, infection or neurodegenerative diseases.

Problem addressed

While nanopore sensing is well developed for detection of nucleic acids, its use in screening proteins is complicated by heterogenous charge, fast translocation time and non-specific adsorption of the analyte to the pore, all contributing to a lack of specificity, particularly when applied to complex biological matrices such as serum or cerebrospinal fluid (CSF). Methods to compensate for these issues entail extensive molecular engineering or complex immobilisation. Moreover, they also often necessitate high analyte concentrations and unusually high ionic strength, differing from physiological salt concentrations and potentially altering protein conformation. To address these limitations we have developed a flexible and selective approach to nanopore protein screening for accurate detection of multiple analytes.

Technology overview

In the invention, aptamer sequences are extended to hybridise to a complementary DNA carrier, together forming a specific detection probe. Advantageously, the carrier is generic and can be used in all situations, while the aptamer is specific to the target protein. In use, the aptamer-carrier signature is identifiable as highly negative, and its profile is disturbed by the presence of bound proteins. Location and magnitude of the peak generated allows the protein to be identified.

Benefits

- Detects proteins at very low concentrations (down to pM range).
- Applicable to any protein regardless of size or charge.
- Potential for detection of 40+ proteins at one time.
- No need for sample purification or altering of salt concentrations.
- Very low false positive rate (<1%).

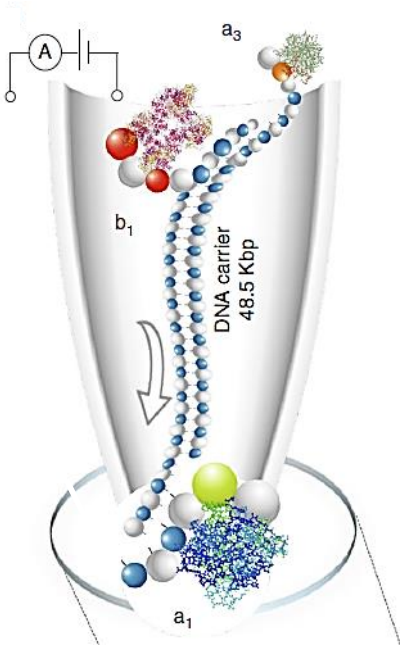

Figure 1 | Schematic representation of a DNA carrier (engineered to contain aptamer sequences (a1, b1, a3) that bind to three proteins translocating through a nanopore driven by the electric field.

Contact:
Imperial College London
Dr Stuart Sims
Industry Partnerships and Commercialisation Executive
Enterprise
e: s.sims@imperial.ac.uk
t: +44 (0)207 594 3461
m: + 44 (0)7872 850067
Technology reference: **8194**

Imperial College London

Intellectual property information

Patent : EP3610257A1, US20200041497A1

Links to published papers

Sze, J. Y., Ivanov, A. P., Cass, A. E., & Edel, J. B. (2017). Single molecule multiplexed nanopore protein screening in human serum using aptamer modified DNA carriers. Nature communications, 8(1), 1-10.

Inventor information

Professor Joshua Edel, Professor Tony Cass, Dr Jasmine Sze