A Novel Dimer System for Single Small Molecule Detection

A new method for the efficient and accurate detection of proteins with nanopores by utilising aptamer-modified gold nanoparticle (AuNP) dimer carriers.

Proposed use

The ability to measure specific, selective biomarker molecules at single molecule level in physicians' surgeries and clinics has the potential to revolutionise the disease diagnosis, monitoring, and therapy. Our invention can identify a range of molecules, from large proteins (> 35 kDa) down to small antigen molecules (< 15 kDa) with high sensitivity and selectivity. Furthermore, by quantifying the signature proportion, the concentration of the target biomarkers at trace levels can be calculated.

Problem addressed

Nanopores provide a label-free platform for sensing single biomolecules. However, it remains challenging to detect small molecules selectively. Our invention comprises two flexible, efficient and low-cost strategies to sense biomolecules with different size using a high resolution nanopore system. One strategy is to use an aptamer-modified AuNP dimer molecular carrier to detect relatively bigger proteins: the protein-bounded complexes generate specific ionic current signal which facilitates accurate target recognition. The other strategy is to use a pair of AuNP monomer probes to sense small antigen molecules.

Technology overview

Our invention provides an efficient and accurate detection of proteins with nanopores by utilising aptamer-modified gold nanoparticle (AuNP) dimer carriers. The target protein will bind to these dumbbell-shaped dimer carriers with the corresponding aptamer located in the middle part and then will it be transported through the fine-tuning nanopipette. Recorded by a high-bandwidth instrument, the high-res signal of AuNP monomers, AuNP dimers and AuNPs with target protein can be differentiated by analysing the translocation events.

Benefits

- Using the traditional nanopipette-based normal electrical detection, it is hard to resolve the single molecule events of proteins and other small molecules. In this invention, the small molecule signal can be amplified by the AuNPs dimer carriers directly or by the AuNP monomer probes indirectly.
- Compared with other carriers, the AuNPs dimer carrier is easy to fabricate and more importantly, its translocation signal wouldn't interfere by itself (such as lambda-DNA).
- The AuNPs dimer carriers can detect a wide range of proteins by hybridising different kinds of aptamer. The modification process of AuNPs dimer is easy and fast.
- The AuNP monomer probes can detect a wide range of small antigens by modifying the AuNPs with different pairs of antibodies.
- The signals can be distinguished easily, which provides straightforward and unambiguous results of the detection.

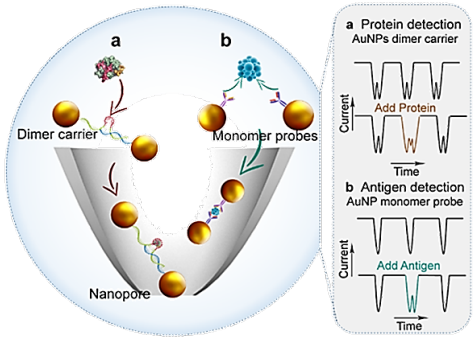

Figure 1 | Schematic of AuNPs dimer protein carrier and AuNP antigen probes. Driven by the electrical field, the AuNPs dimer carriers with target protein (a) or the dimers with the antibody-antigen-antibody sandwich bridge (b) translocate from inside nanopipette to outside.

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Links to published papers

Pending publication

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