Identifying Structure in Short DNA Scaffolds using Solid-State Nanopores

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The detection of molecular features in DNA origami complexes has many potential applications in nanobiotechnology, disease biomarker detection and DNA sequencing. The inherent sensitivity of solid-state nanopore sensors enables the identification of substructure in such complexes, thus providing an avenue for proposing novel molecular sensing assays. We present an approach of molecular assembly in which solid-state nanopores are capable of differentiating DNA scaffolds containing zero, one and two dsDNA protrusions in origami complexes which are over an order of magnitude smaller than those used in typical nanopore experiments. This highly scalable technique requires minimal sample preparation and is customizable for a wide range of targets and applications. As a proof-of-concept, an aptamer-based DNA displacement reaction is performed in which a dsDNA protrusion is formed along a DNA scaffold in the presence of ATP. While ATP is too small to be directly sensed using conventional nanopore methods, our approach allows us to detect ATP by identifying molecular substructure along the DNA scaffold.

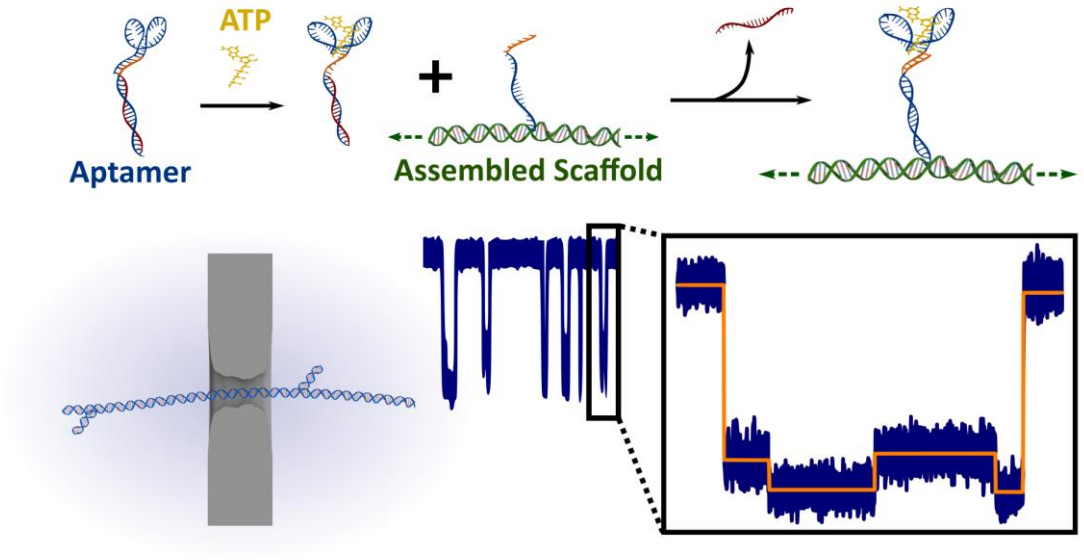

Figure: Scaffolds assembled using the principles of DNA origami contain customisable functional regions for the addition of molecular tags. In this case, a ssDNA overhang hybridises to an aptamer sequence in the presence of a small target molecule (ATP) via a DNA displacement reaction. The resulting biomolecular structures are resolved in ionic current measurements using solid-state nanopores.