High-Density Optical Nanopore Translocation Biosensor for Ultra-high Sensitivity miRNA Quantification

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Nanopore sensors are an emerging class of single-molecule biosensors. These devices consist of a nanoscale sized hole in an impermeable membrane that separates two chambers of electrolyte solution.[1] Voltage is applied across the membrane, and single molecule sensing is typically achieved by detecting changes in the ionic current as analytes translocate through the pore and block the passage of ions.[1, 2] Nanopore sensors have thus become a promising class of single molecule biosensors for the quantitative analysis of clinically relevant biomarkers. Despite the significant interest in these sensors, most studies have used optics to detect translocation events through a single nanopore. The implication of this is that molecules must diffuse to within a few microns of the nanopore for it to be drawn into and through the pore by the applied electric field.[3, 4] As such, for analytes present at sub-picomolar concentrations, one must wait for a significant period to observe a translocation event.[5]

In this work, we demonstrate the ability to optically monitor the translocation of two-colour fluorescent nanoparticles in a high-density array containing 1235 nanopores. We also discuss characteristics of the device design, nanopore/nanoparticle surface chemistry, and bio-recognition concept that enabled us to detect and automatically extract nanoparticle translocation events at femtomolar concentration levels. We successfully deployed our system to detect miRNA-21, achieving a detection limit of 100 fM within 10 minutes of experimental runtime. This work demonstrates the potential for application in clinical diagnosis and therapy monitoring using very low abundance nucleic acid biomarkers.

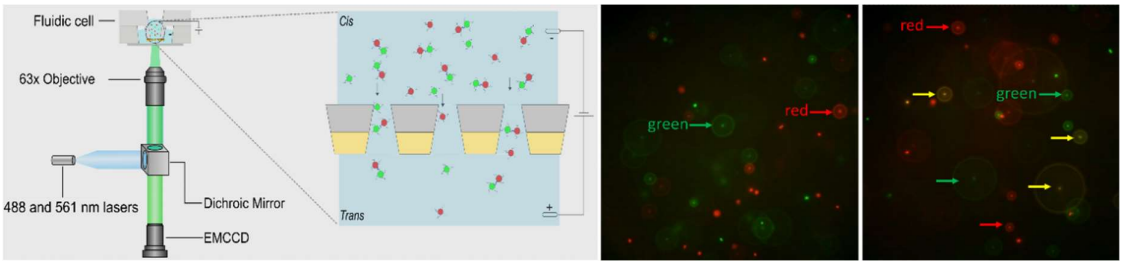

Figure 1: Schematic of the experimental setup and fluorescence microscopy images used in this work.

References:

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