29a-G16-10

Nanopore Thermophoresis for DNA Sequencing

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The National Institutes of Health (NIH) has launched the $1000 genome sequencing project towards practical realization of an ultrafast, label-free, and low-cost DNA sequencer for personalized medicine. The targeted device structure configures a pair of nanoelectrodes embedded in a nanopore. It has been proposed that reading the transverse tunneling current across a single DNA molecule when it passes through a nanopore enables direct sequence read-out as seen in Fig1. This new detection paradigm will revolutionize the DNA sequencing capability; full human genome sequencing, formidable task to achieve by conventional PCR-based techniques, is estimated to be completed within a few hours.

Despite the huge potential, it still faces several great challenges. The commonly used electrical approaches have encountered some intrinsic difficulties, for examples, how to prepare single-stranded DNA without self-hybridization, and how to control DNA translocation through nanopore with very low speed. Hereby we propose to thermophoretically drive DNA molecules through nanopores to address these challenges [1]. As shown in Fig3, the end of *cis* chamber is kept around the melting point of double-stranded DNA by a micro-heater, while that of *trans* chamber is maintained at the room temperature by a micro-cooler. Besides, a layer of thermo-insulating material is utilized as the separating membrane and nanopores are fabricated through it. The novelty and advantages of our proposed design are as follows. First, the hotter environment in cis chamber would cause untwisting of dsDNA, resulting in single strands for the single-nucleotide-by-single-nucleotide identification within the pore. Then, the attained ssDNA are prevented from self-hybridization under that elevated temperature. Thereby, problems due to entangled molecule conformation, which would devastate the ensuing sequencing effort within the pore, are successfully circumvented. Finally, our calculation indicates that most of the temperature difference drops within the pore due to the presence of heat insulating membrane. This significant temperature drop in the pore region yields a thermophoretic driving force trapping polymers into and then pulling them through the pore. That is, three requirements for nanopore sequencing have been fulfilled in one design.

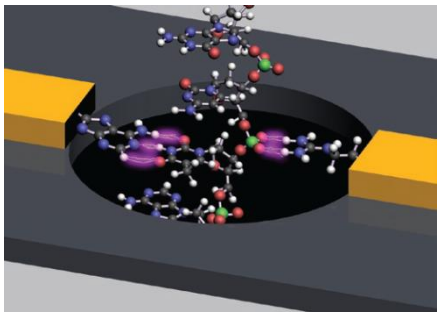

Fig1: Schematic of nanopore-based DNA sequencing

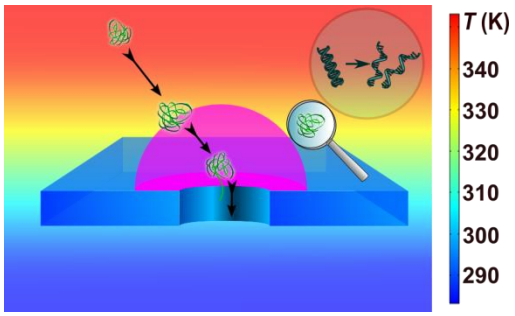

Fig2: Our proposal of thermophoretic manipulating DNA.

[1] “Thermophoretic Manipulation of DNA Translocation through Nanopore”, Yuhui He *et al*, **ACS Nano.**