



Solid-state nanopore sequencing

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Abstract

We aim to develop a solid-state nanopore system capable of high-precision DNA sequencing without relying on biological components. By leveraging voltage-induced metal phosphate precipitation, we realized nanopore gating functions such as fluidic diodes and memristors, with dynamic pore size control. Additionally, integrating a nanoscale heater enabled localized thermal denaturation of long DNA molecules, achieving enzyme-free unzipping with minimal power. These advancements pave the way for robust, scalable, and low-power sequencing devices suitable for portable diagnostics and personalized medicine.

Background & Results

Nanopore sequencing is an advanced technique that reads DNA base sequences by monitoring ionic current changes as single-stranded DNA (ssDNA) translocates through a nanometer-scale pore. Conventional devices, such as those from Oxford Nanopore Technologies, use protein-based nanopores with motor enzymes to unzip double-stranded DNA (dsDNA). However, these biological systems are limited in durability, scalability, and long-term stability, prompting a need for solid-state alternatives.

Significance of the research and Future perspective

To address this, Associate Professor Makusu Tsutsui and his team at Osaka University developed a solid-state nanopore device using semiconductor fabrication. By applying voltage, they controlled metal ion flow to induce reversible precipitation and

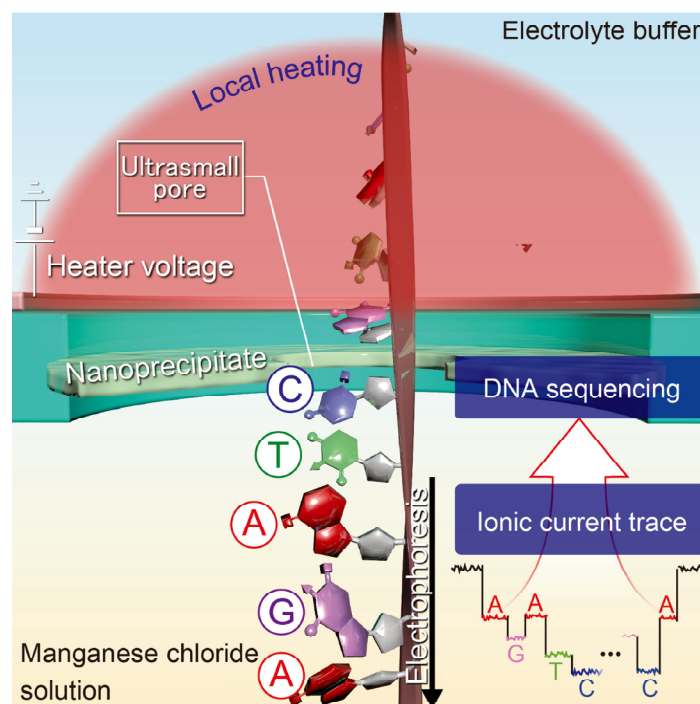
dissolution of metal phosphates inside the pore. This "nanogating" enables the pore to act as a fluidic diode or memristor, with functionalities such as high rectification and memory effects. The pore size can also be dynamically tuned using electric pulses, allowing real-time optimization for different target molecules.

The team further advanced the system by embedding a platinum nanoheater around the nanopore, enabling localized Joule heating for in situ thermal denaturation of DNA. This method successfully unzipped long DNA molecules—including over 50,000-base viral genomes and plasmids—in a 0.82 M NaCl solution using only a few milliwatts of power. Unlike conventional methods requiring motor proteins or bulk heating, this technique minimizes DNA damage and supports high-throughput, single-molecule analysis.

Together, these innovations significantly expand the capabilities of solid-state nanopores. The ability to control pore gating and DNA unzipping with electric and thermal stimuli offers a robust and scalable platform for next-generation sequencing. Electrophoretic and viscosity-based control of DNA migration also enables fine-tuning of capture and translocation rates, potentially improving accuracy.

Thanks to their low power requirements and miniaturization potential, these systems are well-suited for portable sequencers and on-site diagnostic tools. These findings demonstrate that even long DNA strands can be denatured reliably without enzymes, paving the way for real-world applications in early cancer detection and personalized medicine.

These results are detailed in *Nature Communications* (2025) and *ACS Nano* (2025), and related patents are under consideration. Development is ongoing toward scalable nanopore chip production and integration into compact, high-reliability sequencing devices.

**Patent** PCT/JP2025/039039

Treatise Tsutsui, Makusu; Hsu, Wei-Lun; Hsu, Chien et al. Transmembrane voltage-gated nanopores controlled by electrically tunable in-pore chemistry. *Nat. Commun.* 2025, 16, 1089. doi: 10.1038/s41467-025-56052-0
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