The effect of the nanopore shape on resistive pulse sensing of mononucleotides in plastic dual in-plane nanopore sensors

Hooman Abdolvand, Junseo Choi and Sunggook Park
Mechanical and Industrial Engineering Department and Center for BioModular Multi-Scale Systems for Precision Medicine (CBM²), Louisiana State University, Baton Rouge, LA 70803
sunggook@lsu.edu

Nanopores offer a groundbreaking framework employing resistive pulse sensing (RPS) to identify and detect single molecules. In RPS, as a charged molecule traverses a nanopore containing an ion solution, there is a brief interruption in ion flow, leading to a change in the electrical signal that imparts the distinctive signatures of the molecule. Capitalizing on their ability to achieve mononucleotide resolution, a sequencing platform utilizing biological nanopores has been developed and is currently available in the commercial market. Both biological and solid-state nanopores have been developed, each with its unique advantages and drawbacks. Solid-state nanopore sensors exhibit superior stability against mechanical, chemical, and thermal factors. Additionally, the ability to control pore size and shape during fabrication renders them a distinctive alternative to biological nanopores. We recently demonstrated dual in-plane nanopore sensors on various plastic substrates, fabricated by nanoimprint lithography (NIL). These sensors consist of two in-plane nanopores connected by a nanochannel. Using these sequential RPS sensors, we have successfully identified and differentiated various mononucleotides based on their flight time through the nanochannel, all without the need for labeling. While the configurations and sizes of nanopores play a significant role in influencing the electrical signals in RPS, there is limited understanding of how these factors specifically impact RPS signals in in-plane nanopore platforms formed within plastic substrates.

Our present study focuses on investigating the effect of nanopore geometric shapes in our plastic dual-nanopore sensors on the RPS signals and the identification of single molecules. We will present how the pore shape affects the peak amplitude, dwell time, electrical noises of the RPS signals from individual in-plane nanopores as well as the time-of-flight of the molecules through the nanochannels and resulting discrimination accuracy. The Si master molds for the dual in-plane nanopore thermoplastic devices with different cross-sectional geometries, U-shaped and V-shaped, were fabricated via a combination of photolithography and focused ion beam milling (FIB). The conventional FIB milling process with the bitmap mode resulted in shallow U-shaped nanopores while FIB with an Al sacrificial layer led to V-shaped nanopores. The master mold structures were first replicated into a UV resin mold. Then, the UV resin mold was used to produce the nano sensor structures into final polymer substrates. Cyclic copolymer (COP) substrate was used. The enclosed nanofluidic devices were formed via cover plate bonding. The conductance measurements showed that the sizes of both types of the nanopores were sub-10 nm in an effective diameter. Both devices were able to detect and discriminate four 2-deoxyribonucleoside 5'-monophosphates, dNMPs, molecules. Our results will provide a guideline for the design and fabrication of in-plane nanopores for improved RPS signals and molecular discrimination via their flight time in our nano sensors.