Development of a micropore-based fluidic cell for rapid detection of nanoparticles in fluids

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Micropore-based technology emerges as a promising tool for rapid and cost-effective nanoparticle detection within fluidic environments. This innovative approach exploits the nanoparticle translocation dynamics into nano- or micrometer-sized apertures, marking a significant change in analytical methodologies[1,2]. From viral pathogen diagnosis to detecting nanoplastics in aqueous samples, resistive pulse sensing technique showcases unparalleled versatility and sensitivity [3,4].

Presently, silicon nitride-made nanopores are predominantly used as sensors for translocation dynamic studies[5]. However, their widespread use faces problems, primarily due to limited large-scale production capabilities and the prohibitively high cost of individual nanopore chips. In addition, the wetting of these pores often necessitates the use of hazardous chemicals, posing significant safety and environmental concerns.

In this study, we introduce a significant technological advancement: a cost-effective, mass-producible flow cell featuring a laser-drilled aperture of 1µm diameter within a 12.5 µm thick polyimide-made foil, suitable for the detection of particles measuring up to 100 nm in diameter.

Fundamental to our approach is the application of femtosecond laser technology, which offers notable advantages due to its ultrashort pulse duration (fs) and high instantaneous power (GW). These carachteristics enhance the precision of material processing, ensuring ultrafine results while minimizing any collateral damage to the surrounding material.

The system boasts compact dimensions, measuring 15 x 26 mm, and features a 12.5 µm thick layer of polyimide embedded within a PMMA/PET frame, housing two distinct compartments (Figure1A). The laser-drilled aperture in the polyimide sheet (Figure 1A) presents a truncated configuration, with the larger diameter (aprox 5 µm) facing the top compartment and the smaller diameter (1 µm) facing the bottom compartment. Access to both compartments is facilitated through apertures at the top, with a central larger one on the top side and two smaller ones on the bottom side (Figure 1A). The top compartment requires a maximum volume of 80 µL, while the bottom compartment, presenting a horseshoe-shaped configuration with open extremities, necessitates only 20 µL for filling. Two printed Ag/AgCl electrodes (Figure 1A) allowing the electrochemical measurments are designed to contact the electronics of a portable current-voltage amplifier, the Nanopore Reader 100 kHz (Elements srl).

To facilitate nanoparticle translocation through the aperture, a low pressure can be easiliy applied to the bottom compartment, if needed. A plastic tube is affixed to one of the access holes leading to the bottom compartment, while the second aperture remains sealed. By attaching a syringe to the tube, pressure can be applied on the solution, thereby enhancing the flow rate of nanoparticles passing through the aperture within a designated period.

Our results show that the fluidic cell can discriminate between particles of different diameters and can detect analytes up to 100 nm in size (Figure 1B,C). In addition, we show that applicatin of pressure significantly increases particle translocation (Figure 1D).

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This flowcell not only overcomes the limitations of passive systems relying on osmotic principles, but obviates the need for pre-wetting the nanopores with aggressive solutions such as piranha solution or the oxygen plasma treatment.

Beyond scalability and cost-effectiveness, this breakthrough empowers the deployment of nanopore-based detection methodologies in real-world field applications.

1 Luo L, German SR, Lan WJ, Holden DA, Mega TL, White HS. Resistive-pulse analysis of nanoparticles. Annu Rev Anal Chem (Palo Alto Calif). 2014;7:513-35. doi: 10.1146/annurev-anchem-071213-020107. Epub 2014 Jun 2. PMID: 24896310.

2 Pan R, Hu K, Jiang D, Samuni U, Mirkin MV. Electrochemical Resistive-Pulse Sensing. J Am Chem Soc. 2019 Dec 18;141(50):19555-19559. doi: 10.1021/jacs.9b10329. Epub 2019 Dec 5. PMID: 31771324.

3, Șoldănescu I, Lobiuc A, Covașă M, Dimian M. Detection of Biological Molecules Using Nanopore Sensing Techniques. Biomedicines. 2023 Jun 2;11(6):1625. doi: 10.3390/biomedicines11061625. PMID: 37371721; PMCID: PMC10295350.

4, Akhtarian S, Miri S, Doostmohammadi A, Brar SK, Rezai P. Nanopore sensors for viral particle quantification: current progress and future prospects. Bioengineered. 2021 Dec;12(2):9189-9215. doi: 10.1080/21655979.2021.1995991. PMID: 34709987; PMCID: PMC8810133.

5 Rahman M, Sampad MJN, Hawkins A, Schmidt H. Recent advances in integrated solid-state nanopore sensors. Lab Chip. 2021 Aug 21;21(16):3030-3052. doi: 10.1039/d1lc00294e. Epub 2021 Jun 17. PMID: 34137407; PMCID: PMC8372664.

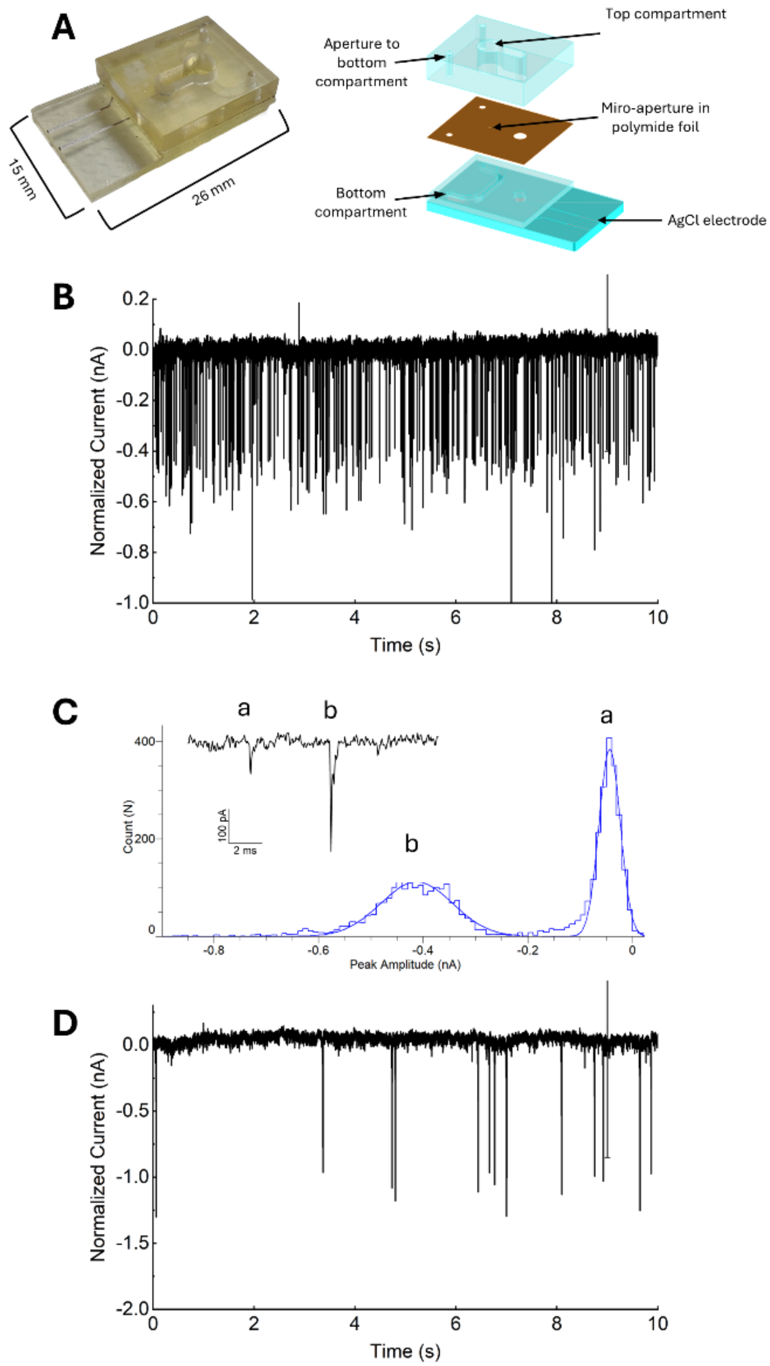

Figure 1

A. *Left*, picture of the assembled micropore flow cell. *Right*, stack view of the flow cell. Arrows indicate the top and bottom compartments , the Ag/AgCl electrodes and the micro-sized aperture laser-drilled in a 12.5 μm tick polymide foil.

B. Representative 10-second recording of resistive pulses measured in the micropore flow cell after the addition of polystyrene nanoparticles, 100 and 350 nm in size, in a 1:1 mixture (concentration: E12 particles/mL in 1X PBS). The two apertures providing access to the bottom compartment (see panel A) were clogged after the addition of the sample in order to apply a pressure.

C. Histogram analysis of the peak amplitude shows two clear distinct populations, namely the 100 and the 300 nm particles. Inset shows a blow-up of two representative events.

D. Representative 10-second recording of resistive pulses measured in the same condition as Panel A, but removing the pressure applied to the bottom compartment. Note the marked decrease in event frequency compared to panel A.