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NANOPARTICLE DETECTION BY SOLID-STATE NANOPORE INTEGRATED INTO A REUSABLE MICROFLUIDIC DEVICE

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ABSTRACT

Solid-state nanopores can be used as electrical biosensors at the single molecule resolution. Such high resolution sensors provide a promising approach to address societal challenges in health and biotechnology. Nevertheless, the analytes detection is still limited by non-specific interactions between these molecules and the membrane supporting the nanopore. Therefore, we performed a polymer functionalization of the nanopore surface that allows to passivate the membrane and to control the pore size. Moreover, we integrated the solid-state nanopore in a reusable microfluidic device, thereby reducing the sample volume needed to perform the detection. The combination of these two approaches is applied to the sensing of single thyroglobulin protein.

KEYWORDS: Solid-state nanopore, microfluidics, protein detection, polymer functionalization

INTRODUCTION

Solid-state nanopores have been used to characterize the biomolecular interactions in a controlled environment.¹ One can tune their diameter to better fit the analyte size and they present better stability than the biological ones.^{2,3} Nanopore sensing is performed from an electric detection. Whenever the analyte transiently resides inside the nanopore there is an ionic current drop. However, the interactions between nanoparticles and the nanopore are not well established. A high surface energy of the membrane,² missing events due to high translocation speed and the pore-to-pore variability limit the experiments reproducibility. Another challenge is that in classical microfluidic devices the nanopore chip needs to be irreversibly sealed into it, whereas the analytes chamber are not hermetically sealed leading to potential cross contamination during the solution exchange process. Hence, this work will focus on improving the membrane chemical and physical surface properties, by functionalizing its surface to avoid non-specific interactions and to control the nanopore size, and on the integration of solid-state nanopores into a microfluidic device (Fig. 1a-b). The efficiency of such set-up was confirmed by the detection of single thyroglobulin transport.

EXPERIMENTAL

Si₃N₄ membranes are pierced with a TEM. Polyethylene glycol (PEG) 7 kDa chains are grafted over the nanopore surface.³ This nanopore is inserted in between two identical subunits that formed the microfluidic device.³ Part of the surfaces of those subunits are not covalently bonded, in order to achieve the reversible packaging (Fig. 1a).³ The polydimethylsiloxane (PDMS) microfluidic circuit device is casted on a 3D-printed polyethylene terephthalate (PET) mold on a silicon wafer. The ionic current is measured using Ag/AgCl electrodes.

RESULTS AND DISCUSSION

The fabrication of PDMS based devices needs a master mold, usually obtained by photolithography techniques, which are time consuming and require a clean room. Here, we show that a 3D-printer can make molds in laboratory and usable for fast conception of microfluidic devices (Fig. 1a). This approach allows us to work with a hermetic system, avoiding possible contamination and fluid evaporation (Fig. 1b) and to reduce the analyte volume to 100 μ L, which is important for biologic fluids. Besides, this device facilitates the changes in fluids. The final set-up confirms the capacity to detect protein at single molecule level, from variation of ionic current trace after addition of thyroglobulin ($\varnothing = 18$ nm) (Fig. 1c). The current blockades show the presence of thyroglobulin. The high signal to noise ratio - 98% - shows a high confinement controlled by the PEG chain grafting .

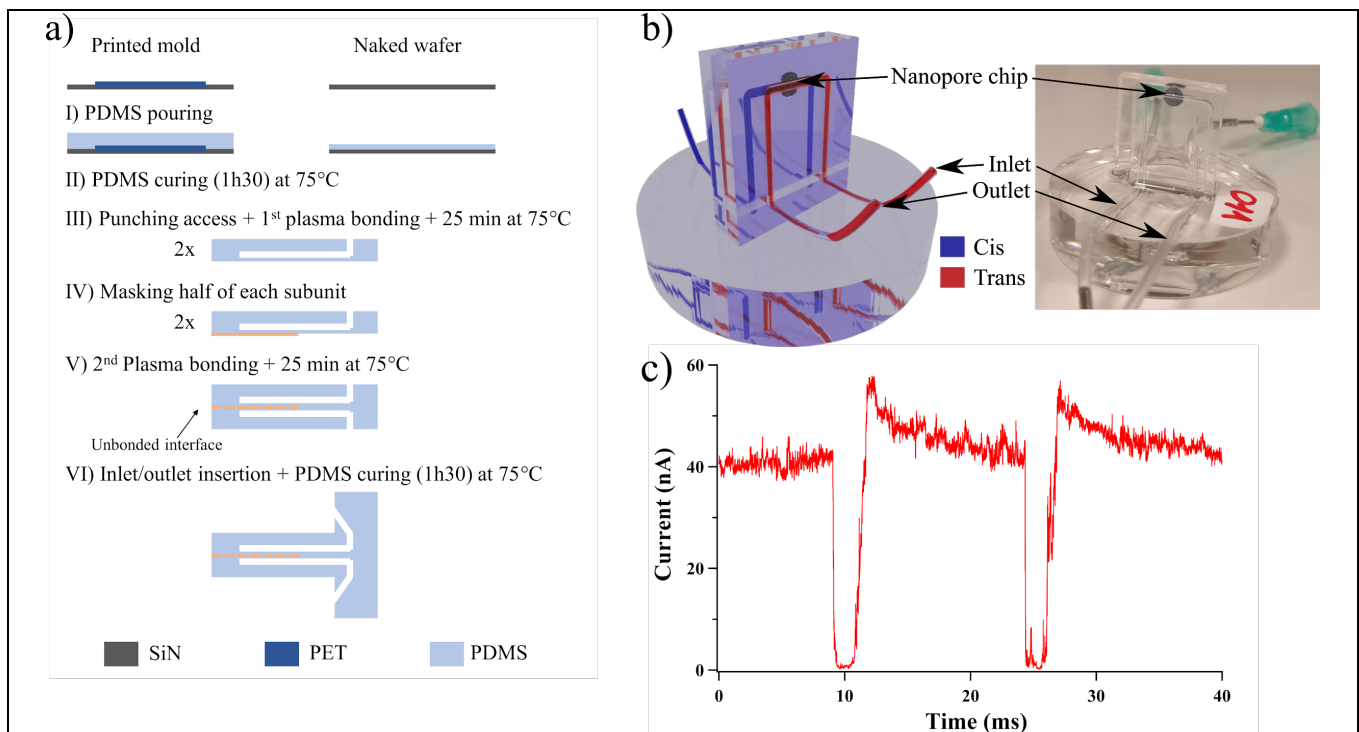


Figure 1: a) Microfluidic device protocol. b) 3D sketch of microfluidic device with the nanopore inserted on it (left) and a picture of the device with the nanopore chip (right). c) Current trace measured after the addition of thyroglobulin by one nanopore ($\text{\O} = 28 \text{ nm}$, length 20 nm) grafted by PEG 7 kDa chain. $\Delta V = 1 \text{ V}$, 50 mM LiCl, 0.1 M Tris, pH 7.4.

CONCLUSION

Here, we stated the feasibility of the nanopore integration in reusable microfluidic device without permanent sealing between the nanopore and the device, which makes possible changes of small amount of electrolyte solutions and on nanopore manipulation. We demonstrate the control on PEG chain conformation along the nanopore surface. The system allows the detection of thyroglobulin transport through the nanopores with a high signal-to-noise ratio.

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