Fabrication of plastic high-aspect-ratio microfluidic devices for rare cell isolation using a PDMS stamp

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Single use disposable plastic devices implementing microfluidic technology has great potential applications in clinical diagnostics [1]. However, the challenges in commercializing plastic point-of care (POC) devices are the development of low cost, highly reliable and mass producible fabrication methods. In this work, we demonstrated a high fidelity micro-pattern fabrication method on plastic microfluidic devices using a next-generation biosensor material, a chemically inert cyclic olefin copolymer (COC). High resolution and high-aspect-ratio microstructure pattern transfer on COC substrate was achieved using a PDMS stamp. The whole device fabrication process includes a PDMS stamp double casting technique, a modified soft mold thermal imprint method, and a solvent assisted device sealing method. We also demonstrated the use of a plastic microfluidic device for the analysis of biochemical samples.

Cyclic olefin copolymer is chosen as the device material for its high optical transparency, high rigidity, and good biocompatibility. The master mold was fabricated by standard photolithography and a double casting of PDMS is required to fabricate high-aspect-ratio soft stamp. Pattern replication into TOPAS COC film (Topas Advanced Polymers) was achieved by thermal imprinting with a custom-built nanoimprint machine. Fluidic inlets were punched into a second blank COC film. Both the imprinted microstructure and the blank layer were treated with chemical vapor prior to thermal bonding. Figure 1 shows a SEM image of the imprinted microstructures on COC substrate.

As a demonstration, we fabricated a plastic microfluidic device made of COC film (Figure 2). The microfluidic device employing a deterministic lateral displacement structure is used to rapidly isolate circulating tumor cells (CTCs) from blood [2]. CTC is extremely rare in cancer patient blood samples (1 in 10^9 cells/ml), and its isolation is of great importance in early cancer detection and disease evaluation. The device has achieved around 90% CTC isolation efficiency, and clinical samples have been tested, with tumor cells identified from patient blood. The excellent performance of this size-based cell separation device is due to the high-aspect- ratio fluidic dynamic microstructures on the plastic substrate. Therefore, this fabrication technique of plastic microfluidic device has great potential in biochemical analysis and clinical diagnostics.

[1] S. Schumacher et al., "Highly-integrated lab-on-chip system for point-of-care multiparameter analysis", Lab on a Chip 12, 464-473, 2012
[2] Z. B. Liu et al., "Rapid isolation of cancer cells using microfluidic deterministic lateral displacement structure", Biomicrofluidics 7, 011801, 2013

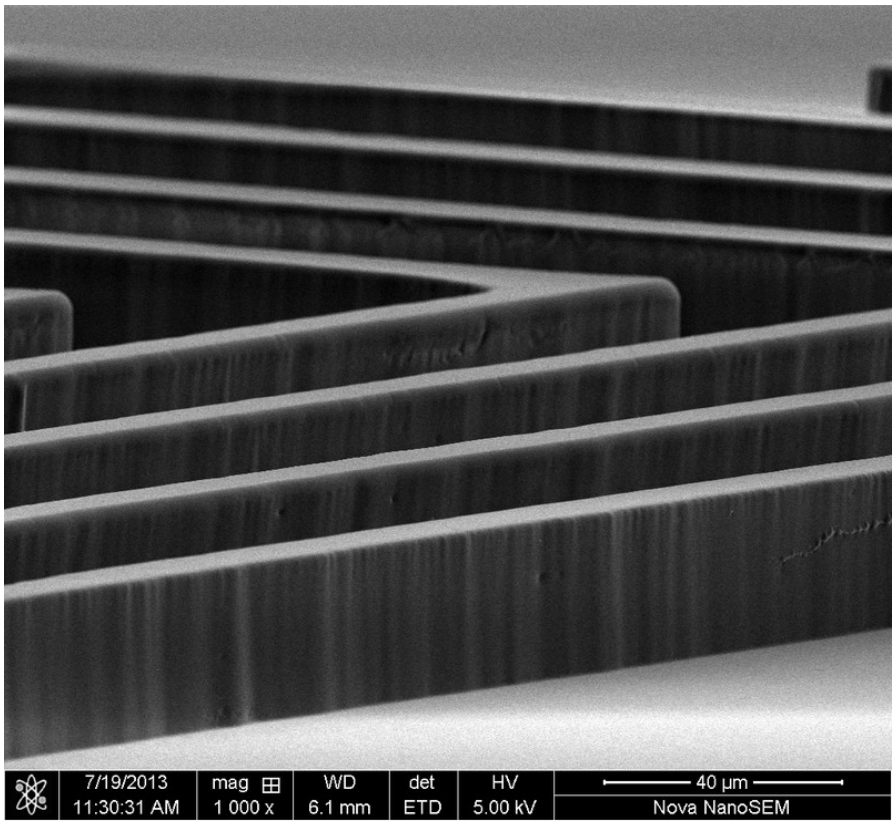

Figure 1: SEM image of the imprinted microstructures on COC substrate.

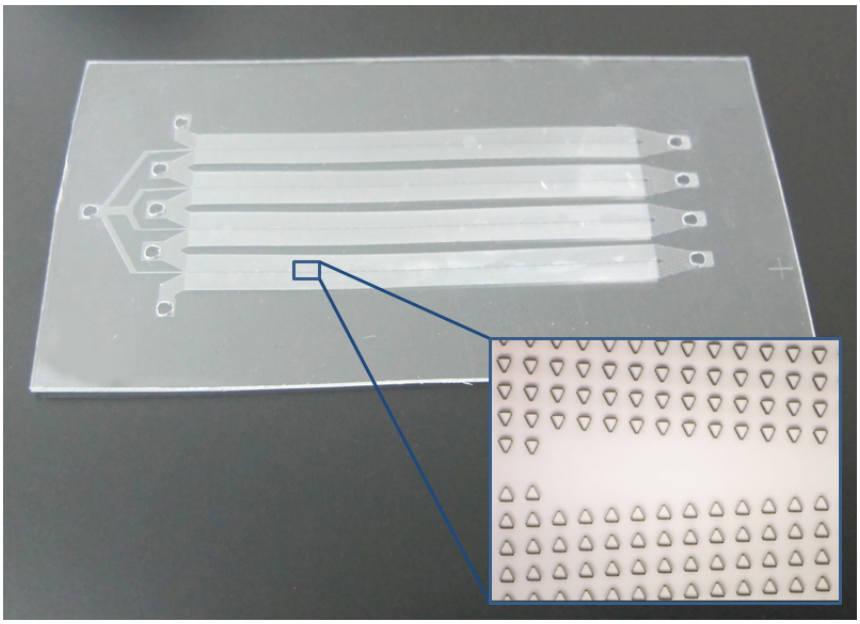

Figure 2: Plastic microfluidic device for circulating tumor cell isolation.