LARGE-SCALE FABRICATION OF NANOSTRUCTURES USING PDMS-BASED PHASE SHIFT LITHOGRAPHY, AND APPLICATION TO NANOFLUIDICS

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ABSTRACT

The advantages derived from utilizing nanoscale phenomena to manipulate fluid samples at the molecular level or mediate drug delivery with exquisite precision have fuelled developments in nanofabrication that were mostly accomplished using electron lithography. The cost of this equipment has constituted a bottleneck for the expansion of nanofluidics in the scientific community. Here we describe a simple, low-cost and high-throughput technology to fabricate nanostructures over large areas that requires standard photolithography equipments, and we demonstrate its suitability for nanofluidic applications.

KEYWORDS: Nanofabrication, Nanofluidics, Single-biomolecule manipulation, DNA-obstacle interaction.

INTRODUCTION

Over the past ten years nanotechnologies have been applied to fabricate nanofluidic systems that enable to control molecules conformation and environment at the nanoscale. Nanofluidic systems unique potentialities were proposed to pave a new way to design optimal biochemical assays for µTAS. One major problem in nanofluidics stems from the difficulty of fabricating nanostructures, which require costly equipments that remain poorly distributed in the µTAS community. For example, electron beam lithography (EBL) is the most commonly used nanofabrication technology, as it achieves exquisite spatial resolutions, but it is a slow process because nanopatterns are imprinted by point-by-point serial exposures. NanoImprint Lithography (NIL), which has been developed in the middle of the 90’s and has been shown to be adapted to fabricate 25 nm features [1], is one popular alternative to EBL. NIL consists in molding a polymer with a mold generally obtained by EBL. This step-and-repeat process allows relatively cheap nanodevice fabrication. Despite the reduced price and time to fabricate nanodevices, NIL requires an expensive mold, and specific equipments for im-

Figure 1: (A) Principles of PDMS-based Phase Shift Lithography. The PDMS mask is deposited on the photoresist and exposed to produce tranches or reliefs depending on the polarity of the photoresist, and the patterns are transferred into the silicon by reactive ion etching. (B) Low magnification optical micrograph of 500 µm long nano-trenches. Scale bar = 100 µm. (C) SEM images of integrated nanofluidic 200 nm square nanochannels etched in silicon. (B) SEM of the replication mold with 180 nm square nanochannels and their connections to microchannels. Scale bars in C-D = 5 µm.
printing nanopatterns that are not yet widely distributed. Here we use PDMS-based Phase Shift Lithography (PPSL) [2], a technology that solely relies on standard photolithography devices, to generate linear and punctual nanopatterns. Moreover, we propose the first, to the best of our knowledge, application of PPSL to nanofluidics.

**FABRICATION PROCESS**

PPSL consists in fabricating an elastomeric template in poly-dimethylsiloxane (PDMS), which is composed of parallel ~4 µm in width and ~500 nm in height channels (Fig. 1A). This template is deposited on a photoresist, and serves as a mask for a subsequent exposition to parallel UV light (Fig. 1A). The optical path differs in air and in PDMS, leading to interference at the air-PDMS interface, which can be destructive for an adjusted channel height. This technology was established with positive and negative photoresists, AZ1505 and SU8, respectively, enabling us to fabricate linear nano-patterns as small as 50 nm and 200 nm, respectively, with lengths up to 3 mm (Fig. 1B).

The photoresist patterns were subsequently transferred in silicon or glass by reactive ionic etching, and arrays of nano-trenches or nano-reliefs were obtained using negative or positive photoresists, respectively (Fig. 1C-D). In order to fabricate functional fluidic systems, access holes were drilled through the wafers, and nanochannels were sealed by anodic bonding. On the other hand, nano-reliefs arrays were used as molds that have been replicated by soft lithography to form PDMS nanochannels, which were enclosed to glass slides using oxygen plasma activation.

Notably, 2D nano-post arrays were also devised by performing PPSL two times consecutively in two different directions. The resulting patterns corresponded to the intersect between both successive exposures, and their geometries could be finely tuned (Fig. 2). In addition to being low-cost and high-throughput, this technology was highly reproducible because the quantitative analysis of individual post structure showed standard deviations in size lower than 4% and 10% for cylinders and ovals, respectively.

**NANOFLUIDIC EXPERIMENTS**

Single molecule manipulation experiments in nanochannels were first conducted using purified genomic DNA fluorescently labeled with YOYO-1. The confinement induced by the walls of the nanochannels was expectedly associated to an entropic spreading of the molecules ([3,4], Fig. 3A), and we confirmed that smaller nanochannels of 120 nm induced a larger degree of stretching (not shown).

We then explored the dynamics of DNA-post interaction at the nanoscale using ~50 kbp λ-DNA. Although the physics of DNA-post interaction driven by electric fields has been extensively studied with micron-scale obstacles [5,6], for this constitutes a model system for gel electrophoresis, the subject remains poorly characterized with asymmetric posts,
and even more so for sizes comparable to DNA bending persistence length. Notably recent simulations by Dorfman’s group [7] showing that the strain experienced by a DNA molecule depends on the geometry of the obstacles still need experimental validations that our technology is particularly well-suited to provide. Our first results were obtained with 200 nm cylindrical posts (Fig. 2A), and consisted in tracking ~600 DNA-post interaction events with 20 ms inter-frame time intervals (Fig. 3B). We obtained a statistical distribution for the hooking time of these molecules (Fig. 3C), which exhibits a long-tail associated to long lived interactions, as described in [7]. We now wish to investigate this process for smaller and asymmetric obstacles in order to improve DNA separations in future generations of µ-TAS.

CONCLUSION
Taken together our results demonstrate that PPSL is a cost effective, versatile and easy-to-access technology for the fabrication of nanofluidic devices. In addition, we apply our nanofluidic systems to two different applications, namely single molecule nanomanipulation by entropic spreading in nanochannels, and single molecule nano-obstacle interactions.

REFERENCES

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