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Optimized fabrication protocols of microfluidic devices for X-ray analysis

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ABSTRACT

Microfluidics combined with X-ray scattering techniques allows probing conformational changes or assembly processes of biological materials. Our aim was to develop a highly X-ray transparent microfluidic cell for detecting small variations of X-ray scattering involved in such processes. We describe the fabrication of a polyimide microfluidic device based on a simple, reliable and inexpensive lamination process. The implemented microstructured features result in windows with optimized X-ray transmission. The microfluidic device was characterized by X-ray microbeam scattering at the ID13 beamline of the European Synchrotron Radiation Facility.

1. Introduction

Microfluidics is nowadays a well-established tool for studying chemical reactions and performing biological analysis [1,2]. The use of small-scale devices allows significantly reducing the costs of materials and the amount of sample required for analysis [3]. Other advantages regard portability, ease to handling and speed of analysis [4–6].

Various techniques or the analysis of biological samples in microchannels have been reported [7–10]. Microfluidics combined with in situ X-ray scattering techniques is a highly promising tool for studying biological assembly processes and protein solution structures. Indeed, X-ray scattering provides information on molecular conformation, structure, chemical composition and physical properties of biological matter in solution and solid state [11]. Materials used for cell-windows, such as polydimethylsiloxane (PDMS) introduce, however, a strong scattering background and are easily degraded due to the high flux-density of X-ray microbeams at a 3rd generation synchrotron radiation source such as the European Synchrotron Radiation Facility (ESRF) [12]. General proposed guideline for optimizing X-ray scattering measurements from a microfluidic chip are: (i) use of low absorption materials, (ii) thin chip thicknesses, (iii) short wavelength to reduce scattering angles [13]. Indeed, Pollack et al. described a device with ultrathin silicon nitride windows for minimizing background scattering from the chip [14]. Barrett et al. fabricated chips from polyimide (PI) using laser ablation to reduce X-ray absorption [12]. Toft et al. developed microfluidic devices made of thin polystyrene substrates for high-throughput small angle X-ray scattering (SAXS) analysis [15].

The device presented in this paper was fabricated from PI by using an inexpensive and reliable lamination process allowing an easy modification of the cell layout. Moreover, microstructured features were integrated in the device allowing further reducing X-ray scattering and absorption. These features result in transmission windows with reduced thickness in comparison with other devices used for X-ray scattering experiments. The device was characterized by X-ray scattering measurements performed at the ESRF with a microfocused X-ray beam.

2. Materials and methods

The chip design and materials used were chosen to be compatible with X-ray scattering techniques as well as to ensure proper microfluidic handling of liquid samples.

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2.1. Microfluidic device fabrication

The microfluidic chips were fabricated from 25 mm wide, 75 mm long and 13 μm thick PI-films (Kapton NT, Dupont) using optical lithography, plasma etching and lamination. The fabrication process can be divided into two main parts: (i) implementation of transmission windows by microstructuring PI layers which are used as substrate and cover of the microfluidic channels (Fig. 1, steps 1–5) and (ii) fabrication and assembly of the microfluidic device (Fig. 1, steps 6–8).

2.1.1. Transmission window fabrication

The transmission windows are 3 mm long and 1 mm wide layers into which the PI was etched selectively to obtain very small thicknesses, in the order of 5 μm, of the same PI.

A PI-substrate (13 μm thick, 75 mm long and 25 mm wide) was punched to fabricate the inlets and outlets of the microfluidic network. Successively, a negative dry photoresist (PR) Ordyl SY500, 50 μm thick was laminated at a temperature of 120 °C. The laminated PR was aligned by photolithography under a glass mask, exposed under UV light (130 mJ/cm^2) for 30 s. The sample was then baked on a hot plate at 85 °C for 2 min to eliminate the traces of solvent inside the resist and to promote the crosslink. Finally, it was developed for 4 min in Ordyl Developer and rinsed for 30 s in Ordyl Rinse. This process allowed reproducing on the PR the positive replica of the transmission windows.

After the photolithography, a gold layer of about 400 nm was sputtered on top of the PI film and the remaining PR. The following lift-off process allowed removing the PR and reproducing the negative replica of the transmission window on the gold deposited on the PI. The gold was used as mask for the subsequent etching process.

The etching process was performed by an ICP-RIE (inductive coupled plasma-reactive ion etching) in an O_2 (90 sccm) and SF_6 (26 sccm) environment, at a pressure of 7 mTorr and a power of 300 W for 20 min.

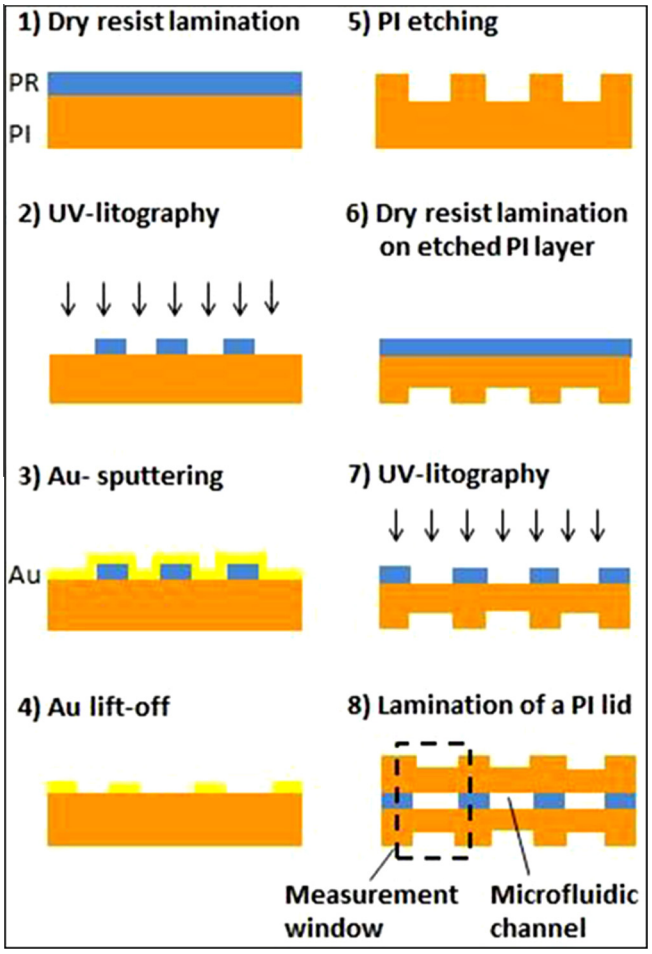

Fig. 1. Schematic representation of the microfluidic device fabrication.

2.1.2. Microfluidic device assembly

The etched films were cleaned in the Au etcher and then in acetone. A PR layer was laminated on the top of the PI film integrating the transmission windows and then exposed under UV light, using a mask, that reproduced the negative replica of the channels. The time of exposition and develop is the same of the photolithography process mentioned previously. So, the laminated PR was aligned under UV source for 30 s; it was baked at 85 °C for 2 min; it was developed for 4 min and was rinsed for 30 s. Finally, a second PI film integrating the transmission windows was laminated on top of the other layers as a lid, to seal the microchannels. Finally, the system was cured in an oven at 120 °C for 2 h.

The developed device had 500 μm wide, 100 μm deep, and 25 cm long channels.

2.2. Frame design

For handling liquid samples, the microfluidic device was assembled in a rigid frame which allowed to interconnect the microchannels with external tubes [16,17]. The frame shape was designed to fit on the X-ray beam end station and at the same time to ensure mechanical rigidity to the device. The frame was fabricated in PMMA (polymethylmethacrylate) by milling [18]. It was integrated with gaskets which allowed sealing the interface between microchannels and external tubes. The gasket was pressed between the microfluidic device and the frame by screws. The assembled device is shown in Fig. 2a.

2.3. Microfluidic device characterization

The rate and direction of the flow in the channel were controlled by a syringe pumps connected the device through external tubes [19]. The pump was computer controlled and managed with a Labview interface.

The chip performance was characterized in transmission geometry using a monochromatic X-ray beam of $\lambda = 0.984086$ wavelength and an about 1 μm focal spot [20]. X-ray scattering experiments were performed by rastering the microfluidic chip through the X-ray beam using a motorized x/y/z stage [20]. Alignment of the chip in the focal spot and selection of a ROI for raster-scanning was done by an off-axis microscope, calibrated to the focal spot [20]. For data collection a fast-framing CCD with X-ray converter screen was used. Typical exposure times per raster-step were about 1 s [20].

3. Results and discussion

3.1. Device assembly

The choice of PI as a substrate was dictated by the need to have a material with high X-ray transmission properties and compatible with the lamination process. Lamination is one of the most commonly used techniques for the fabrication of microfluidic devices in polymers, because it is simple and inexpensive. [21].

The photolithography on the PI layer was possible thank to the use of a dry resist which could be laminated on it. Alternatively, a