Disposable Glass Microfluidics for Nucleic Acids Bioassays

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Despite plastic's favored use in microfluidic consumables, the superior optical and chemical properties of glass mean it should be the material of choice. Undesirable damage to pre-immobilized biomolecules caused by some bonding methods have so far limited the use of glass. In collaboration with IMT AG, CSEM is developing new cost-effective glass solutions to maintain biomolecule integrity.

Glass advantages over plastics are acknowledged in the microfluidics community. However, the costs associated with device manufacturing often limit its use in bio-applications. Although micro-structuration and surface functionalization (typically by dip-coating or vapor deposition) are both available at the wafer scale, glass channel sealing remains costly. Existing industrial-scale solutions are not suitable for the life sciences as the processing conditions are not compatible with pre-immobilized biomolecules (*e.g.*, high temperature for fusion or anodic bonding, O2/CF4 plasma for direct bonding). Methods using an adhesive inter-layer seem promising but typically lack standardization in the application of the adhesive [1] and remain limited to the laboratory scale.

A glass microfluidic device was fabricated based on the patented design of the IncaSlide [2]. It consists of a meandering channel including an array of 384 cylindrical positive microstructures (bumps). The chip fabrication process is shown in Figure 1. A total of 13 chips (25x75 mm) per 8-inch wafers are produced (Figure 2). After spotting the oligonucleotides on the bump array of wafer 2, a homogeneous layer of adhesive is transferred onto Wafer 1 without wetting the channel walls. Wafers 1 & 2 are then aligned and brought into contact. The adhesive is cured by exposure to UV light.

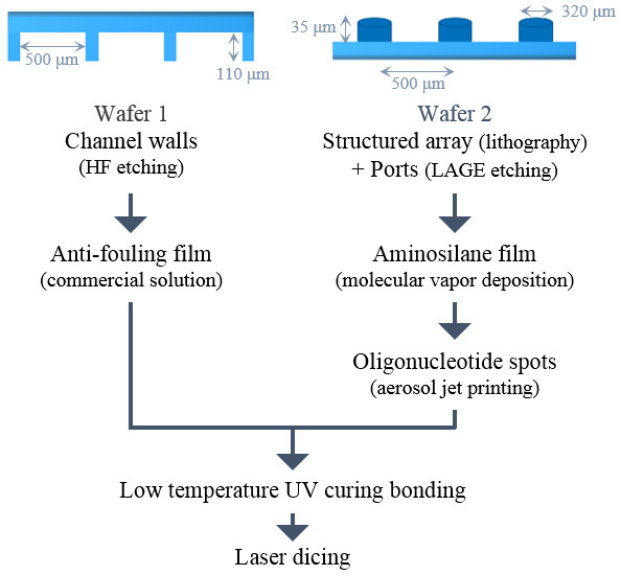

Figure 1: Fabrication process of the microfluidic microarray device.

Injection of a fluorescent solution in the channel enables to assess the sealing efficiency (Figure 3A). We demonstrate that the sealing is stable for at least 4 months without any leakage. Our method allows a reproducible application of the adhesive without spreading in the channels after curing. Besides, the integrity and functionality of the spotted biomolecules are verified at the end of the fabrication process (Figure 3B). The pre-immobilized target oligonucleotide is still visible (green spots) and pairs properly with the probe (red spots) after bonding and hybridization. We also demonstrate that there is no non-specific binding of other probes on the spots and at the glass/adhesive interface (data not shown). The immobilized biomolecules maintain their reactivity and specificity after the whole fabrication process.

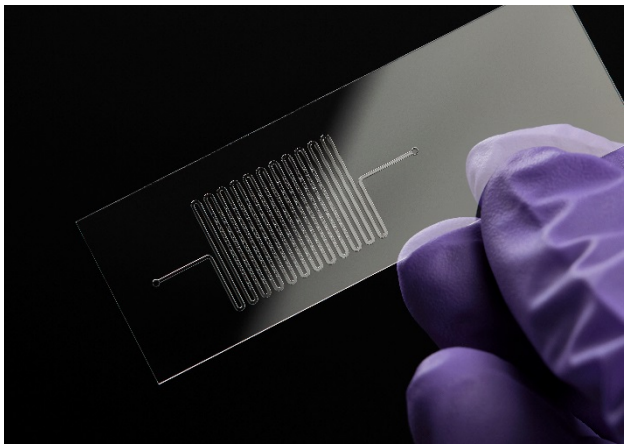

Figure 2: Picture of the sealed glass microfluidic microarray device.

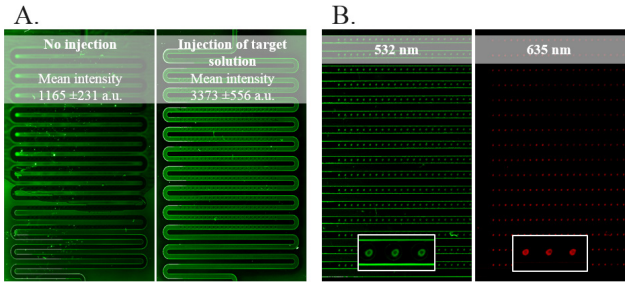

Figure 3: Example of fluorescence images obtained before and after injection of a fluorescent solution in the channel, 4 months after sealing (A) and results obtained after bonding and hybridization of the pre-immobilized target (B).

In this study, we demonstrate for the first time wafer-level integration of structured bio-functionalization by UV-bonding for sequencing applications. This work pushes further wafer-scale glass bonding and opens the way to cost-effective precision glass consumables for life science applications, such as high throughput sequencing, but also in vitro diagnostics and cell handling.

• IMT Masken und Teilung AG

[1] Y. Temiz, R.D. Lovchik, G.V. Kaigala, E. Delamarche, "Lab-on-a-Chip Devices: How to Close and Plug the Lab?", Microelectronic Engineering, 132, 156-175, 2015.

[2] F. Crevoisier, F. Heitger, H. Siegrist, H. Chai-Gao, "Apparatus and Platform for Multiplex Analysis", EP2397224A1, 2011.