Enabling Cost-effective Glass Microfluidics for Life Sciences: The Example of a Complete Sequencing Device Fabricated at Wafer Scale

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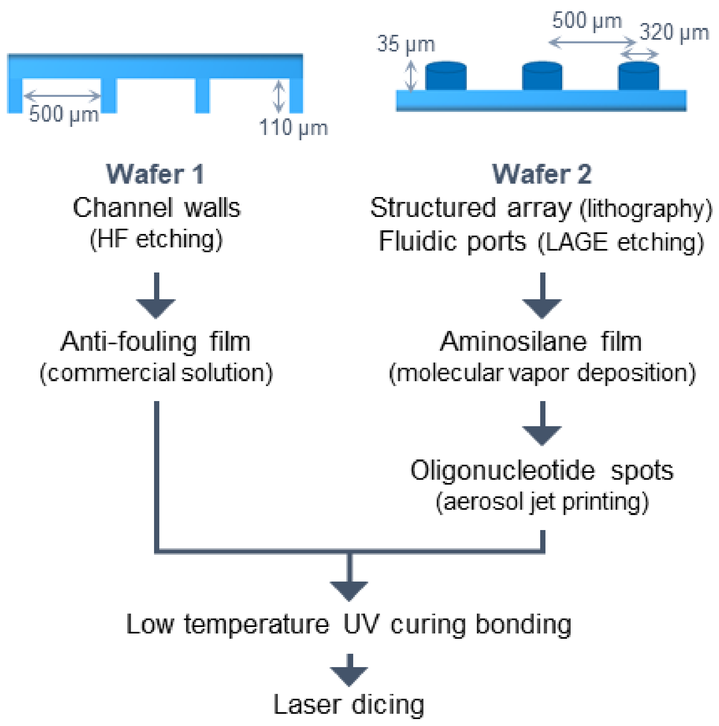
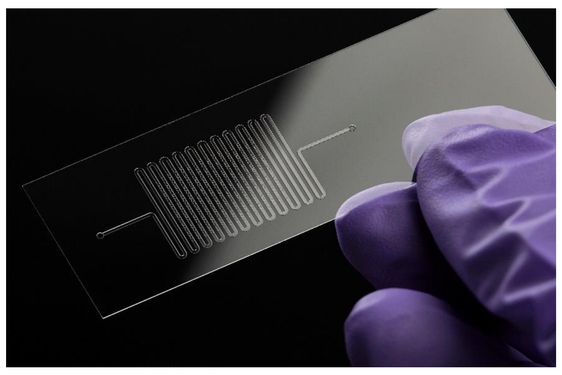
Glass advantages over plastics are acknowledged in the microfluidics community. However, the costs associated with device manufacturing often limit its use in bio-applications. The bottleneck remains channel sealing, especially when it is required after bio-functionalization. Here we demonstrate for the first time wafer-level integration of structured bio-functionalization by UV-bonding for sequencing applications. We present a new cost-effective manufacturing process that maintains biomolecule integrity during the fabrication of the glass microfluidic device. It was developed to produce a flow-through microarray chip. This process combines surface micro-structuration and functionalization with the immobilization of oligonucleotides and low-temperature bonding.

Wafer-scale fabrication of the microarray chip



- 13 chips (25x75 mm) per 8-inch wafers
- 384-microarray channel (IncaSlide, patented design)
- Bio-functionalization followed by channel sealing at wafer scale



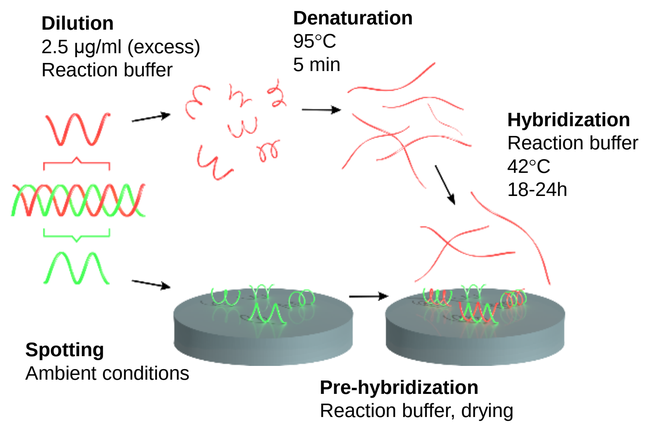
Characterization of the microarray

- Fluorescently labelled oligonucleotides

Sequence part of core protein J, Bacteriophage PhiX 174

Target	5'-TTTTAAGCGTAAAGGCGCTCGTCTTTGGTATGTAG-3'	5' Modification: amine
		3' Modification: ATTO532
Probe	5'-CTACATACCAAAGACGAGCGCCTTTACGCTT-3'	5' Modification: ATTO647N
		3' Modification: none

- Hybridization assays run in the sealed chips (stopped flow)

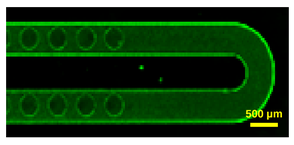


Results

Efficient channel sealing

- Reproducible application of the adhesive
- No adhesive leaking in the channel
- Stable channel sealing over at least 4 months without leakage

Example of fluorescence images obtained 4 months after sealing: absence of adhesive in the channel (left) and no leakage upon injection of a solution of fluorescently labelled target oligonucleotide in the channel (right)



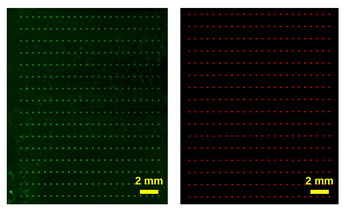
Preserved microarray performances

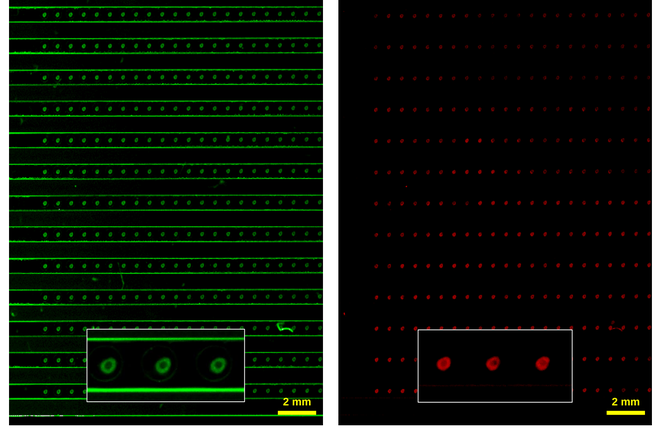
The spotted target oligonucleotides are reactive and specific after chip bonding with our process:

- Preserved target spots (green spots)
- Efficient pairing of the probe during hybridization (red spots)
- No non-specific binding (tested with 5 nucleotide pairs mismatch)

Example of fluorescence images obtained after spotting, sealing and hybridization of the spotted target oligonucleotide.

Example of similar results obtained on a Nexterion Slide A+ (Schott) coverslip used as assay reference.





Conclusion

The specialized bonding method enables sealing of microfluidic channels in the presence of pre-immobilized oligonucleotides, thus offering other perspectives than plastics. 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.