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-structuring 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: ATTCATACGCAAGAAGGCGCTCGTCTTTGGTATGTAG
  - Probe: GATTTAGGGGCTGGCCCTTTGGTG
- 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

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.

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.