LOW TEMPERATURE "CLICK" WAFER BONDING OF OFF-STOICHIOMETRY THIOL-ENE (OSTE) POLYMERS TO SILICON

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ABSTRACT
We present a low temperature (< 37°C) wafer-scale microfluidic batch packaging process using covalent, dry bonding of off-stoichiometry thiol-ene polymers (OSTE), enabling rapid, bio-compatible integration of fluidics on wafer-scale in combination with excellent polymer properties.

KEYWORDS: wafer-scale bonding, off-stoichiometry thiol-ene (OSTE), packaging, biocompatible

INTRODUCTION
Common bonding techniques for lab-on-chip (LOC) microfluidic devices require surface bio-functionalization to be performed in-situ after the chip has been packaged due to the bio-incompatible features of the bonding technique, including high temperature requirements (e.g. thermal bonding of thermoplastics), use of organic solvents (e.g. PMMA bonding) or plasma activation (e.g. PDMS bonding). This severely limits widespread use of LOC's since functionalization after packaging is a slow and expensive chip-level processes compared to standard batch surface functionalization such as array spotting [1].

One suggested method that enables surface modification before bonding is the use of patternable liquid UV-curable glue as an intermediate layer [2]. While being a biocompatible and low-temperature process, a liquid glue layer risks blocking the channels upon solidification. Another proposed method involves a thiol-ene polymer formulation (NOA 81) in which one substrate contains a thin layer of uncured polymer material that is subsequently UV-polymerized [3]. These surfaces however, have a short shelf life and the bond to silicon substrates is based on adhesive forces, not covalent bonds, which make them vulnerable to solvents.

We recently introduced a family of OSTE (Off-Stoichiometry Thiol-Ene) polymers, compatible with the soft-lithography process and developed specifically for lab-on-chip applications to replace PDMS [4,5]. In contrast to PDMS, these novel OSTE-polymers feature tunable mechanical properties, excellent chemical barrier properties and a large number of chemically reactive anchors (thiol or allyl) at the surface after polymerization.

Moreover, the OSTE-polymer has excellent chemical barrier properties, low shrinkage (< 2%), is surface patternable using UV-light, and is designed to soften when heated to its glass transition temperature (Tg) of 37 °C to conform with micro-irregularities in the surface. This allows them to form a perfect seal with the substrate and improve the covalent bond yield (Fig 1).

We here present and demonstrate biocompatible, wafer-level microfluidic packaging of pre-functionalized bio-surfaces using an OSTE-polymer that features a very high density of thiol surface groups. On wafer-level, we achieve a void-free, dry, covalent bond between the OSTE polymer substrate and a substrate containing a standard biological linker surface, using only a low temperature (37 °C) bonding step.

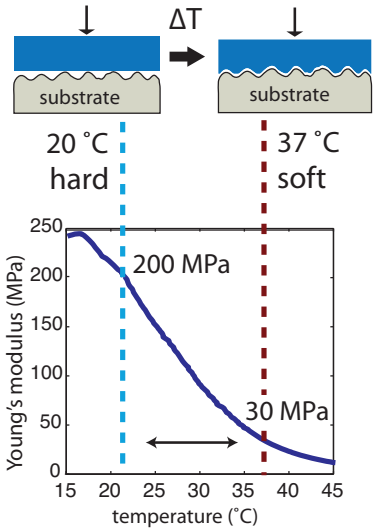

Figure 1: Mechanical properties of the 70% excess OSTE polymer at usage temperature (20 °C) and bonding temperature (37 °C).

"CLICK" CHEMISTRY USING OFF-STOICHIOMETRY THIOL-ENES
The free thiol groups available on the OSTE polymer surface are capable of participating in so-called "click" reactions with many reactive molecules. The term "click chemistry", first used by Sharpless [6], is a class of efficient and selective chemical reactions that are used to join molecules together in a rapid manner with high yield, high purity and little or no byproduct, which is ideal for forming permanent bonds. In this work we use a OSTE material with excess of thiols to covalently "Click" bond sheets of micropatterned polymers to silicon wafer coated with a bio-reactive monolayer of 3-isocyanatopropyl triethoxysilane (ITPES), which is a commonly used linker for attaching proteins.

FABRICATION
As a demonstrator, we fabricated a 350 µm thick layer of OSTE-polymer (tetrathiol:triallyl 1.7:1; 50% stoichiometric thiol excess), containing 60 microfluidic chips of 10x4 mm2 footprint each, by UV-casting on a standard 4" wafer sized SU8-master (Fig 2A). The entire polymer layer was released on a PC release film carrier from the master at 45 °C (T_g) and transferred to the substrate. As a pre-functionalized substrate, we used a 4" silicon wafer that contained DRIE etched fluidic ports and coated with a bioreactive layer of IPTES [1]. (Fig 2B). After aligning, and bringing the OSTE polymer and the IPTES

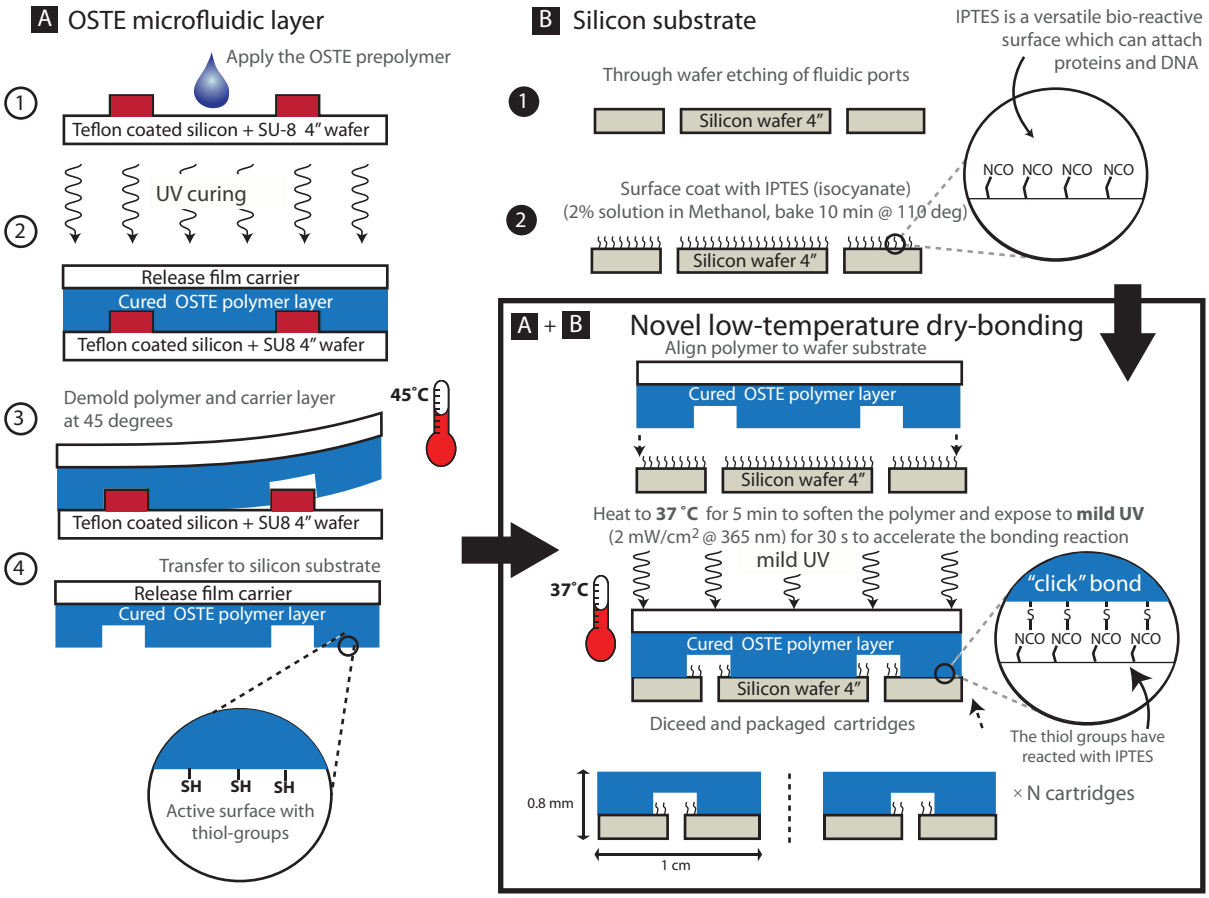

Figure 2: (A) The microfluidic layer is UV-casted in an OSTE-polymer. (B) The Si substrate is etched and coated with isocyanate. (A+B) The OSTE polymer is transferred, aligned and bonded to the Si substrate prior to the dicing.

coated silicon substrate in contact, the stack was heated on a hotplate for 5 minutes at 37 °C, allowing the softened OSTE substrate surface to conform to the micro-irregularities on the silicon substrate surface and initiating the "click" reaction between the IPTES isocyanate and the thiols (Fig 2A+B). After subsequent cooling to room temperature, the OSTE polymer regains its rigidity. The release film carrier was released and the bonded stack was diced into chips using a standard wafer dicing tool.

RESULTS

The process had a 100% yield of void-free sealed microfluidic chips (Fig. 3b) after dicing and the very sharp interface between the channel on the OSTE polymer with the Si substrate layer indicates good channel sealing (Fig. 3c). A pressure test experiment was carried out to evaluate the strength of the bonded chips with pressures up to 4 bars, which is above what is normally required in LOCs. The samples showed no significant change during the pressure test.

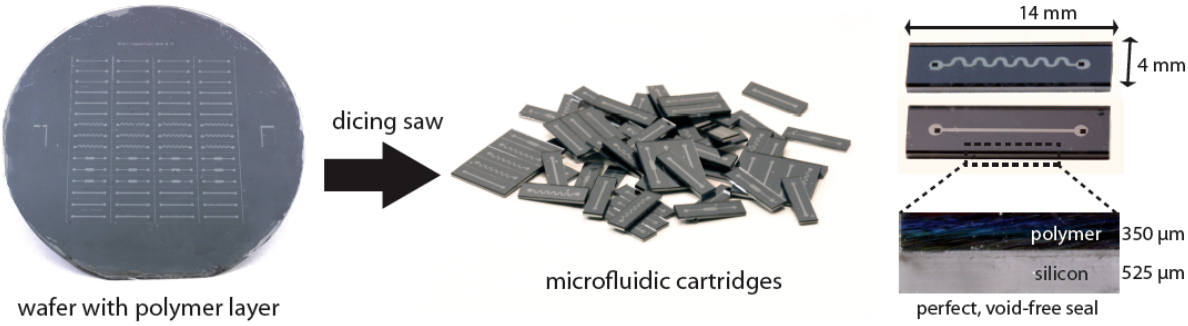

Figure 3: Wafer containing 60 cartridges: before dicing and after dicing.

Fluidic tests were performed to check the barrier properties of the OSTE-polymer after bonding, and the results were compared to PDMS. An aqueous solution of Rhodamine B (50 µM aqueous) was introduced by capillary action into the microchannel and sealed for 24 hours. Figure 4 illustrates the result of the diffusion tests after the channels were emptied and analyzed using confocal fluorescence microscopy. In Figure 4A, no diffusion of Rhodamine B was detected in the OSTE-channel walls after 24 hours, unlike in PDMS where the Rhodamine diffused more than 40 µm into the channel wall as illustrated in Fig. 4B.

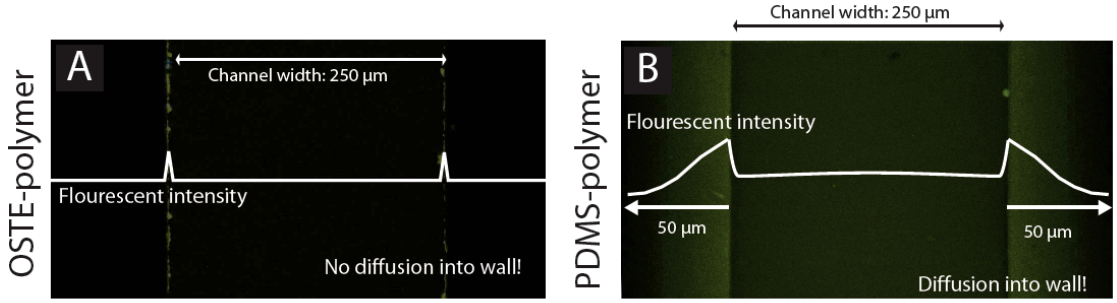

Figure 4: (A) No diffusion of Rhodamine B was detected in the OSTE-polymer, (B) whereas diffusion was clearly observed in PDMS.

Leakage tests were conducted by introducing solvent in the microchannel. Rhodamine B was mixed with ethanol, sealed in the OSTE channel and left for 24 hours. Similar test were performed using PDMS bonded to Si substrate for comparison. After 24 hours, the ethanol with Rhodamine B still resided in the channel (Fig. 5) whereas the ethanol in the PDMS channel had completely evaporated.

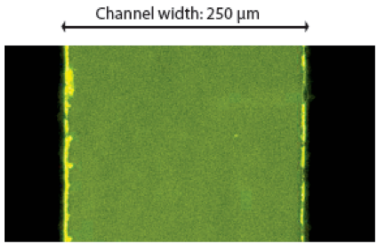

Figure 5: Ethanol with Rhodamine B sealed in the OSTE-channels for 24 hours without evaporation

CONCLUSION

We demonstrate for the first time a one-step, biocompatible covalent wafer-scale packaging process of microfluidic labs-on-chip using a novel OSTE-polymer. By not exceeding 37 °C and avoiding potentially harmful UV-light the process allows for batch surface bio-functionalization of the substrate before packaging, thus circumventing complex chip-level handling and reducing production costs for large scale production of labs-on-chip.

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