Coat & Close technology for simultaneous coating and bonding of microfluidic devices

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Introduction

Microfluidic devices are used to process and manipulate small amounts of liquids. [1] These devices can be used in various applications, ranging from agrifood to forensics and medical diagnostics. For any of these applications, the amount of analyte is generally small, usually in the sub-milliliter range. For that reason, the channel dimensions (height and width) of a microfluidic device are usually tens to hundreds of micrometers. A microfluidic device generally consists of two halves: a substrate with channels, and a lid to close these channels. Thermoplastic polymers used in microfluidics, e.g., cyclic olefin copolymer (COC) or poly(methyl methacrylate) (PMMA), are hydrophobic, while applications using aqueous samples require channels with a hydrophilic surface for a better liquid flow and/or anti-biofouling properties to avoid unwanted adsorption of biomolecules to the channel walls.

A conventional route to fabricate a hydrophilic polymer microfluidic device involves hydrophilizing the channels, e.g. by plasma activation, SiO_2 deposition, or application of a nanocoating, and then applying a bonding technology, such as adhesive tape, thermal bonding, or laser welding, to close the channels (Figure 1a). [2] It is also possible to hydrophilize the channels after bonding, but this approach is not suitable for upscaling. In any case, the extra hydrophilization step adds complexity and costs to the manufacturing process, and the bonding technique must be compatible with the applied coating or hydrophilization technology. Moreover, the hydrophilicity may deteriorate over time, and/or the hydrophilized surface may be prone to unwanted adsorption of biomolecules (biofouling).

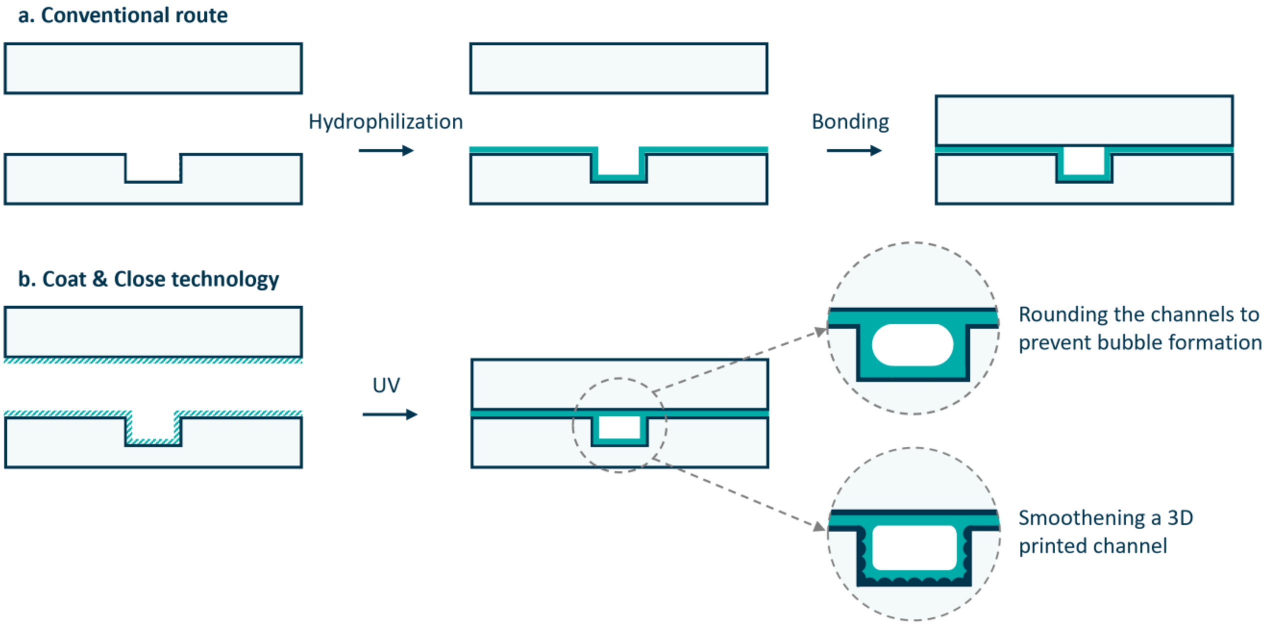

Figure 1. *A schematic representation of a) a conventional route of microfluidic device fabrication, where hydrophilization and bonding are performed in two consecutive steps, b) Surfix' Coat & Close technology, where coating and bonding are performed in one step, including the corresponding advantages shown in the cross sections of the channel.*

To overcome these challenges, Surfix Diagnostics has developed a proprietary technology called "Coat & Close" (C&C) [3], where coating and bonding are performed in one step (Figure 1b). C&C yields bonded microfluidic devices with stable hydrophilic, anti-biofouling channels. Besides being fast and cost-effective, the C&C technology is also advantageous because it prevents bubble formation and enhances flow by rounding the channels, and smoothens surface roughness. In the Horizon 2020 project PHOTO-SENS*, the C&C process is further developed into a scalable process for microfluidic device fabrication.

Coat & Close process

The C&C formulation contains a mixture of polymerizable compounds with anti-biofouling moieties. If needed, the substrates are activated, e.g., by oxygen plasma treatment, to enhance wetting and adhesion. The formulation is applied to one or both substrates using spray coating, which leads to a conformal layer on the 3D structured channel substrates. This is an advantage compared to other coating techniques such as spin coating or roller coating, which are only suitable for planar substrates. Spray coating is also a suitable technique for upscaling. After spray coating, the two halves of the microfluidic device are brought in contact, and the reactants are cured under UV light. This yields a microfluidic device where the channel walls are coated with a hydrophilic anti-biofouling coating, and the adhesive properties of the coating are used to bond the two halves of the device. No further washing or drying steps are needed after curing. The UV wavelength (365 nm) is compatible with the presence of biomolecules in the microfluidic device.

Results

Coating and bonding

To demonstrate the formation of the hydrophilic C&C coating on the channel walls, the wettability of coated and (commercially available) uncoated channels was compared. The coated COC channels (Figure 2b) can be filled by capillary force without applying any external pressure, thus demonstrating the presence of the hydrophilic coating on the channel walls. This holds for both injection molded and 3D printed channels, as shown in Figure 2b and Figure 2c, respectively. Uncoated channels (Figure 2a), on the other hand, remain hydrophobic and cannot be filled by capillary force. The channels closed by C&C are leak-tight for regular microfluidic applications, also if active pumping is used.

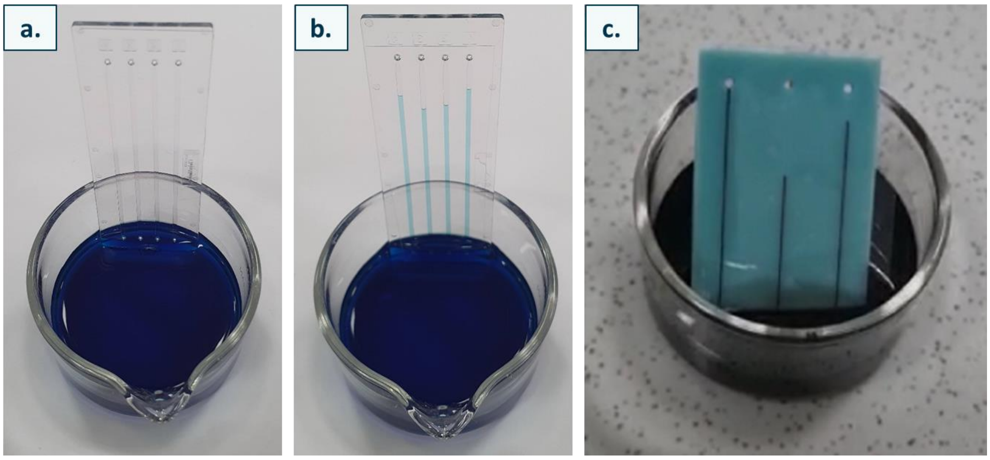

Figure 2. *a) Hydrophobic, uncoated COC channels (closed with a conventional technique, commercially available) immersed in an aqueous dye solution, b) hydrophilic COC channels, coated and bonded with C&C, immersed in an aqueous dye solution, c) a 3D printed substrate, coated and bonded with C&C, immersed in an aqueous dye solution.*

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Tuning layer thickness

Since the reactant formulation is applied by spray coating, the layer thickness of the reactant can be tuned to match the channel dimensions and roughness. In general, the coating should be thin enough to avoid channel clogging, and thick enough to compensate for the surface roughness. This is especially relevant for devices prepared by 3D printing. This manufacturing technology is ideal for rapid prototyping, but 3D printed devices generally have a high surface roughness, which may hamper their performance. By varying spray coating parameters, i.e., the speed of the spray coater nozzle, and the flow speed of the liquid input for the nozzle, the layer thickness can be tuned from <1 µm to 50 µm (Figure 3a). Independent of the thickness, the coatings are equally hydrophilic, as proven by water contact angle measurements (50-55° static contact angle). The thicker the coating, the lower the surface roughness (Figure 3b).

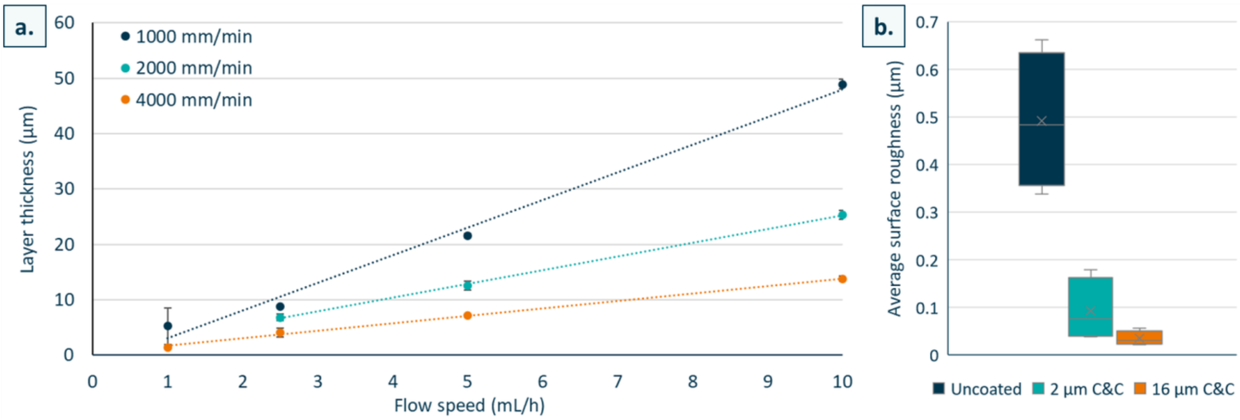

Figure 3. *a) C&C film thickness on a planar COC microscope slide as a result of varying nozzle speed and flow speed, b) surface roughness, as measured by laser scanning microscopy, on unclosed 3D printed microfluidic substrates for 0, 2, and 16 µm C&C film thicknesses. Each bar represents the average of four different substrates.*

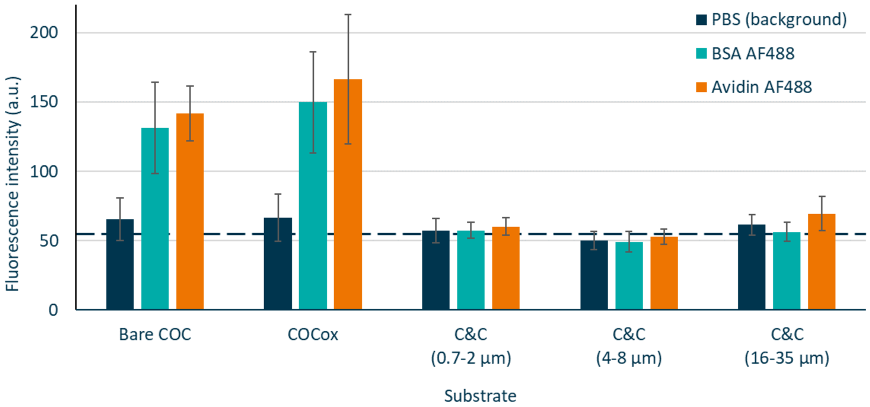

Figure 4. *Anti-biofouling properties of C&C coatings with several thicknesses, compared to bare COC and a plasma oxidized COC slide (COCox). Each bar represents the average fluorescence intensity for two substrates with three spots each ± SD.*

Anti-biofouling

The anti-biofouling (i.e. protein-repellent) properties were tested on COC microscope slides with several thicknesses of C&C coating, and compared to a bare COC slide and a COC slide which was hydrophilized by treatment with oxygen plasma (Figure 4). All substrates were exposed to solutions of proteins (BSA and avidin) labelled with a fluorescent dye (AF488), followed by washing. The amount of adsorbed protein was quantified by measuring the fluorescence intensities using a fluorescence microscope. A buffer solution (PBS) without proteins was used to determine the background signal. The high fluorescence intensity of the blank substrates indicates strong protein adsorption (biofouling) on those substrates, whereas the fluorescence intensity on all C&C coatings equals that of the background (dotted line and PBS bar). So, the C&C coating has good anti-biofouling properties for all layer thicknesses tested.

Prevention of air bubbles

The formation of air bubbles is a frequent problem in microfluidics. For example, they may hamper the flow, or disturb the read-out of optical or electrochemical sensors. Especially when working at elevated temperatures, the formation of air bubbles is hard to avoid. Here, the rounded edges induced by the C&C technology (Figure 5a) are advantageous, since they prevent the formation of air bubbles when heating an aqueous solution to 60 °C (Figure 5c). In contrast, many air bubbles are created in channels that are coated and closed via a conventional route with double-sided tape (Figure 5b).

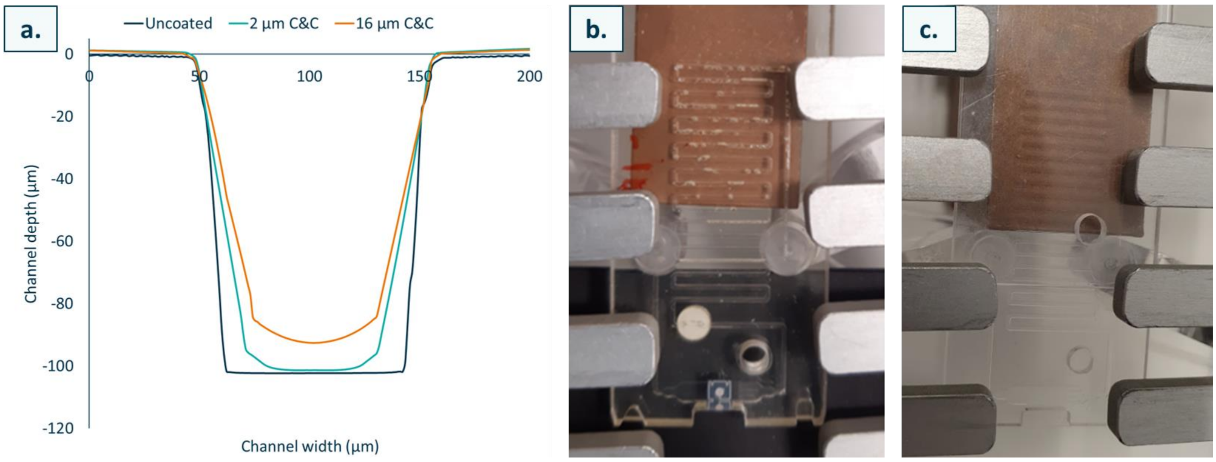

Figure 5. *a) Channel cross-section, as measured by laser scanning microscopy, for unclosed COC channels with 0, 2, and 16 µm C&C film thicknesses, b) COC channels coated with a conventional hydrophilic nanocoating and bonded with double-sided adhesive, heated to 60 °C, c) COC channels, where C&C is applied to bond a COC foil onto the milled channels, heated to 60 °C.*

Conclusion

Surfix' Coat & Close technology is a scalable one-step coating and bonding process for polymer microfluidic devices, yielding hydrophilic and anti-biofouling channels. The thickness of the coating can be adjusted to smoothen the surface roughness of (3D printed) devices. The resulting channel geometry is rounded to prevent bubble formation. These features also make Coat & Close a particularly attractive technology for making microfluidic devices based on capillary (passive) flow. The next step is to implement the Coat & Close technology in microfluidic device fabrication, and to further automate the process for upscaling.

References

[1] A.-G. Niculescu, C. Chircov, A. C. Bîrca and A. M. Grumezescu, "Fabrication and Applications of Microfluidic Devices: A Review," *Int. J. Mol. Sci.,* vol. 22, p. 2011, 2021.

[2] Y. Temiz, R. D. Lovchik, G. V. Kaigala and E. Delamarche, "Lab-on-a-chip devices: How to close and plug the lab?," *Microelectronic Engineering,* vol. 132, pp. 156-175, 2015.

[3] L. Scheres, R. P. Rijo Da Costa Carvalho, W. Knoben and J. T. Zuilhof, "Process for manufacturing a microfluidic device". Patent WO2023118292, 2023.

Abbreviations

AF488	Alexa Fluor 488 (i.e., a fluorescent dye)
BSA	Bovine Serum Albumin
C&C	Coat & Close
COC	Cyclic Olefin Copolymer
PBS	Phosphate Buffered Saline
PMMA	Poly(methyl methacrylate)
SD	Standard Deviation
UV	Ultraviolet