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Low cost integration of multilevel lab-on-a-chip using a new generation of dry film photoresists

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Abstract

We present the use of a novel dry film photoresist DF-1050 (EMS) for the integration of multilevel microfluidic systems. We showed that high resolution and high aspect ratio (7:1) can be achieved for free standing structures. We proved also that the dry film autofluorescence level is compatible with most of lab-on-a-chip applications and established the biocompatibility of this dry film. Ultimately, we demonstrated that this low-cost material combined with multilevel lamination technology would allow introducing massively 3D microfluidic in lab-on-a-chip devices.

1 Introduction

The fabrication of multilevel microfluidics devices is quite challenging in a fast and cheaply way. In the past few years dry film photoresists have been studied as good candidates to achieve three dimensional architectures. Abgrall et al. [1] was the first to fabricate 3D microfluidics devices with SU-8 films. More recently, Wangler et al. [2] have presented the interest of using a commercially dry film TMMF to make microchannels. However both of these ways suffer from the high cost of the photoresists. Here, we present the study of a novel negative epoxy based dry film DF-1050 (Engineered Materials Systems, Inc) whose low price presents a major advantage (Table 1): it's minimum ten times cheaper than SU-8 and TMMF. Besides, the process time for a double layer with dry film photoresist is faster due to the absence of soft-bake step. Indeed, the fabrication of SU-8 dry film needs a cure after spin coated the liquid photoresist onto a PET/adhesive/PET substrate in order to evaporate the solvents and harden the layer prior to lamination [1, 3].

<i>Comparison of photoresists</i>	SU-8 (3050) (50 μm)	TMMF (45 μm)	DF-1050 (50 μm)
<i>Prices (for a 4'' wafer)</i>	16 €	12 €	1.2 €
<i>Process duration for a double layer</i>	6h30	2h30	2h10

Table 1: Comparison of three photoresists

2 Manufacturing of 3D microfluidic devices

The process fabrication can be summarized as illustrated in Fig. 1: lamination and photolithography technologies are combined to realize 3D devices. First, a layer is laminated (100°C for the rolls temperature and 2 bars pressure were applied) onto the substrate, photopolymerized and finally developed in cyclohexanone. Then, a second layer is laminated onto the first structured layer, photopolymerized and developed. To avoid a collapse of the upper layer in the opening structure of the first one we have tested different temperatures and pressures of the rollers: 65°C and 2 bars pressure for rolls are suitable in a width range of microchannels of 10 μm to 300μm.

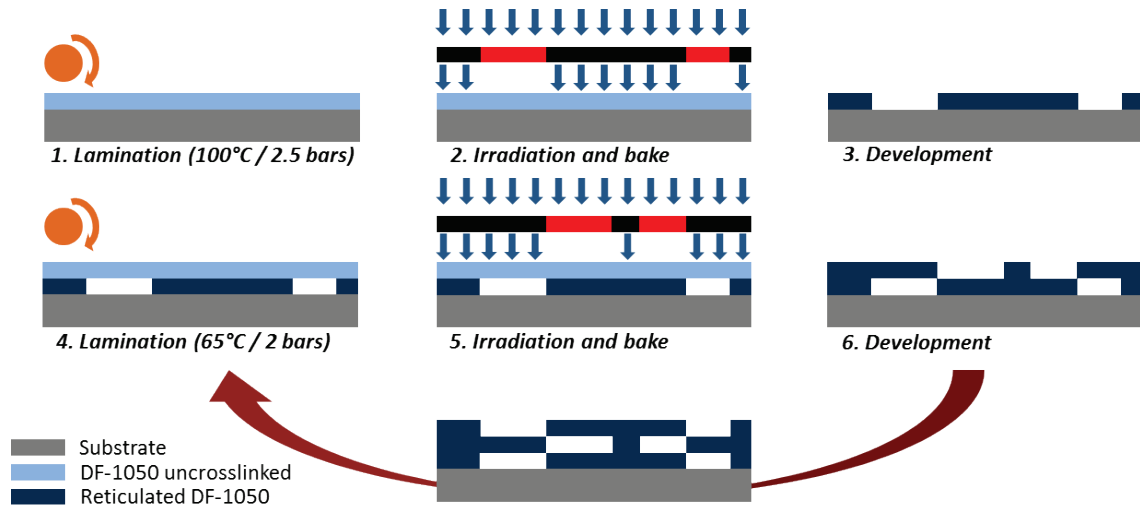


Fig. 1: Example of 3D process fabrication

By repeating steps 4 to 6, it is possible to make complex 3D microfluidics chips by stacking several dry film photoresist.

3 Experimentation and results

3.1 Absorption wavelength and resolution of the dry film photoresist

The absorption of the photoresist was investigated by using a Hewlett Packard HP8452A diode array spectrophotometer. Fig. 2 shows that the film is sensitive to i-line irradiation (365 nm) before irradiation. However, unlike SU-8 the film is slightly yellow colored after irradiation and bake.

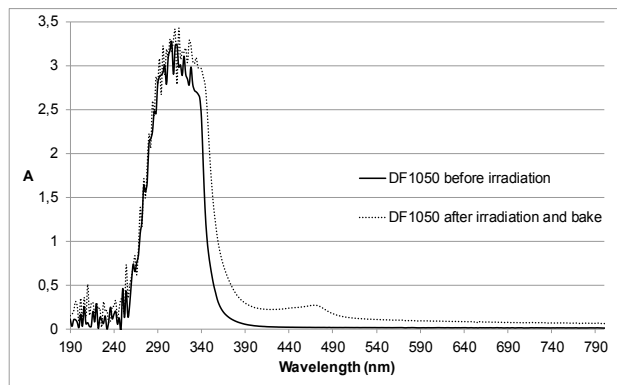


Fig. 2: Absorption spectrum of the dry film photoresist before and after irradiation.

We tested the resolution of this dry film photoresist by using a Karl Süss MA-6 mask aligner and the datasheet of the material provided by the manufacturer. Two parameters influencing the resolution were investigated: exposure energy and time of post exposure bake. We have determined that 250 mJ/cm² and 7 min at 100°C have given the best results. As illustrated in Fig. 3, DF-1050 dry film enables an aspect ratio of 7:1 for free standing structures and 5:1 for channel structures. The sidewalls profile is slightly negative but according to the SEM images the angle is estimated to 92°.

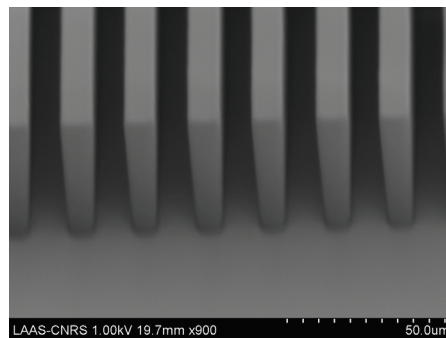


Fig. 3: SEM image of DF-1050 test structures

Another advantage of this DF-1050 dry film photoresist is that the total thickness variation across a 100 mm wafer is less than $\pm 1.2\mu\text{m}$ which is well below what can be obtained with liquid photoresists.

3.2 Microchannels fabrication with DF-1050

To study the compatibility of DF-1050 with microfluidic application we manufactured various microchannels by following the protocol described in Fig. 1. The Fig. 4 shows an example of 200 μm width microchannel with two layers of 50 μm thickness of DF-1050. High quality results were obtained down to 10 μm width channels.

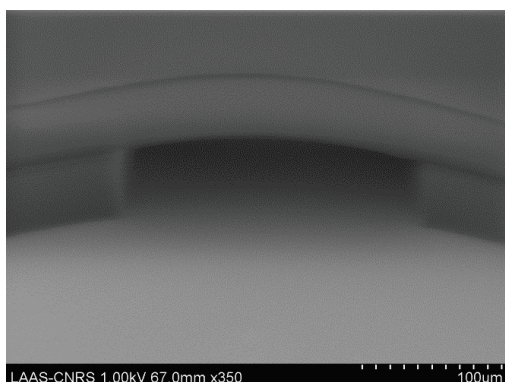


Fig. 4: SEM image of a microchannel inlet

After photolithography step, the photoresist has to be baked to catalyze the polymerization reaction. However, when we laminate a layer onto another air was trapped in open microstructures. This could be an issue at the post exposure bake step. Indeed, the air pressure in microchannels increases faster than the cationic polymerization of the materials. This phenomenon can cause a deformation of the layer as illustrated in Fig. 5 (left picture). To minimize this swelling a hot plate with a thermal ramp bake can be used. The start temperature was 65°C up to 100°C (10°C/min) and down to 25°C (5°C/min). Fig. 5 (right picture) shows the benefit of this bake method: the deformation is very small.

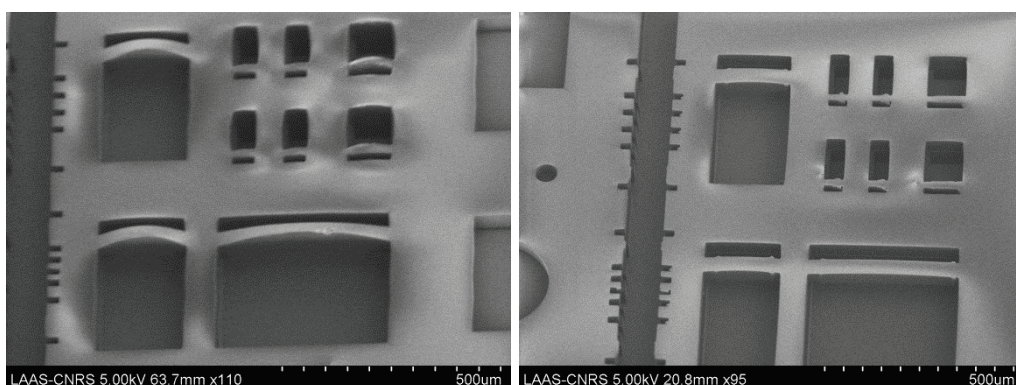


Fig. 5: Deformation of the top layer with a classic hot plate (left) and with using a thermal ramp bakes (right)

Different organics liquids are used in microfluidic devices. So, we tested the resistance of 2D microchannels to different solvents at various pressures with a MFCS™ 7 bars from Fluigent.

The photopolymerized dry film is alcohol (ethanol and isopropanol) acetone and dimethylsulfoxyde resistant and no delamination of the two layers occurred until 3.5 bars fluid pressure. We have not been able to go further because of fluid connectors used (Homemade molded PDMS pads, bonded with photosensitive glue with Teflon tubing of 1/16" external diameter).

3.3 Autofluorescence of the DF-1050

The film remains colored (illustrated in Fig. 1) after complete processing. As it could be an issue for fluorescence based experiments, we characterized the autofluorescence of DF-1050 with a PTI (Photon Technology International) Quantamaster 1 at 470 and 545 nm excitations wavelengths. We also characterized SU-8 and PDMS (layers of 50 μ m thickness) in the same way in order to compare the three materials. Results are regrouping in Fig. 6 and show that the fluorescence intensity of SU-8 and DF-1050 were quite similar and low (detection limit of the apparatus). S. Cargou et al. have used a 3D microfluidic devices made in SU-8 to characterize the behavior of at least three different fluids [3]. The autofluorescence of the SU-8 did not interfere in the fluorescence detection. It is also the case with the DF-1050, confirmed experimentally by the observation of diluted solution of fluorescein without any interference (Fig. 6).

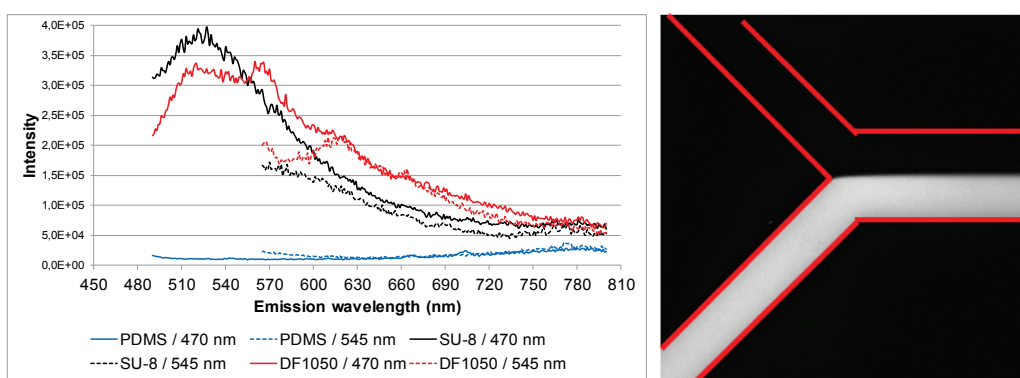


Fig. 6: DF-1050, SU-8 and PDMS fluorescence spectrums at 470 and 545 nm excitation wavelengths and fluorescence microscopy image of two fluids in DF-1050 microchannels for a 470 nm excitation wavelength (the two fluids are water and fluorescein in water)

3.4 Biocompatibility of the photoresist

Because microfluidic device is used in a lot of biological applications we also tested the cytotoxicity of the DF-1050 according to the protocol of ISO 10993-5. L-929 mouse fibroblast cells were used. Polyurethane film containing 0.1% zinc diethyldithiocarbamate and high density polyethylene sheet were used as positive and negative control respectively.

MTS cytotoxicity test was performed to quantify the viability cells rate after exposition to the three materials. The statistical results have shown a viability rate of 3.9% for the positive control articles whereas for the negative control and the DF-1050 the viability rate was 97.1% and 93 % respectively.

This study proved that DF-1050 is suitable for biological applications.

3.5 3D micromixer fabrication with DF-1050

Three-dimensional structures can be useful for a tremendous amount of applications in microfluidics. A well-known and specific field where we can see the relevancy of this technique is micromixing. Many different methods and designs have been reviewed when it comes to micromixers [4], among them the Baker's transformation has been thoroughly described. In a 2007 theoretical paper, P. Carriere [5] suggested a very innovative 3D design to implement this transformation in a microfluidic device. Given the lack of enabling fabrication technologies, a similar design was first realized in 2012 by Liao et al. [6], using femtosecond laser writing, a non-conventional microfabrication technique.

We decided to apply our dry film lamination protocol to build such a device, and we showed this micromixer is functional using a simple example.

In order to fabricate the device, 4 masks and 5 levels of films were needed: a first plain level to avoid the fluid being in contact with different materials (the glass substrate and the dry film), then 3 levels (that are represented on the 3D drawing on Fig. 7) for the 3D network of microchannels, and a "roof" level with openings for inlets and outlets. The shown pattern comprises 3 loops, and this pattern repeats 10 times in the same device. Channels are $45\ \mu\text{m}$ wide and $50\ \mu\text{m}$ high (thickness of the dry films).

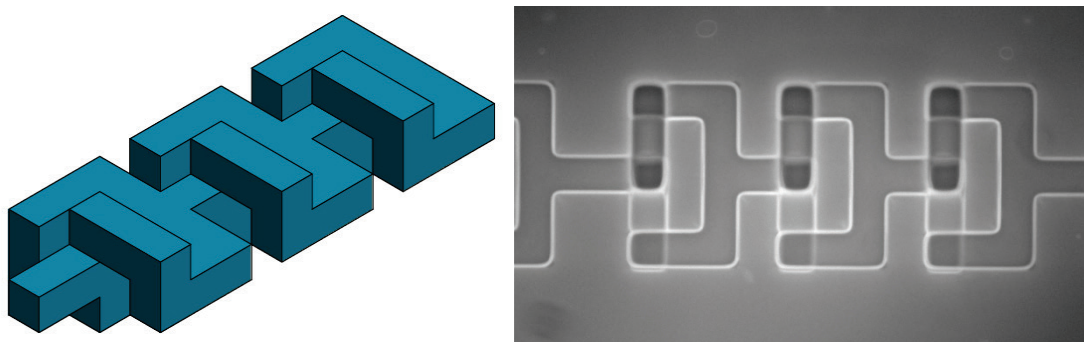


Fig. 7: Design of the 3D microfluidic mixer [5] and optical micrograph of the device at the end of the fabrication process

The chip was designed to fit in a homemade Teflon and aluminum chip holder; UpChurch 10-32 coned nuts and ferrules, as well as Teflon tubing ($1/16''$ O.D. $0.3\ \text{mm}$ I.D.) were used to flow the solutions in the two inlets and out of the outlet.

A solution of D.I. water, and a solution of fluorescein in water at a concentration of $0.6\ \text{mmol/L}$ were injected with $1\ \text{mL}$ SGE glass syringes and a Cetoni Nemesys syringe pump. All the solutions have been filtered ($0.22\ \mu\text{m}$ filters) previous to their use.

Various flow rates have been applied, and efficient mixing is observed even at very low Reynolds numbers. The same flow rate is applied for water and fluorescein solution. In Fig. 8, we show the first pattern (3 loops) of the device: we can observe as expected that the fluorescein concentration field is divided in 2, 4, and 8 values of concentration before the inlet of the 1st, 2nd and 3rd loops. At the exit of the 3rd

loop, diffusion is such as we cannot distinguish all of the 16 different levels of concentration we would have with a non-diffusive baker's transformation. For a total applied flow rate of 40 $\mu\text{L}/\text{min}$ ($\text{Re} \approx 15$, $\text{Pe} \approx 3.104$), we obtain a homogeneous solution after the fifth pattern (15 loops), so we achieved mixing in a laminar flow, even with very poor contribution from diffusion.

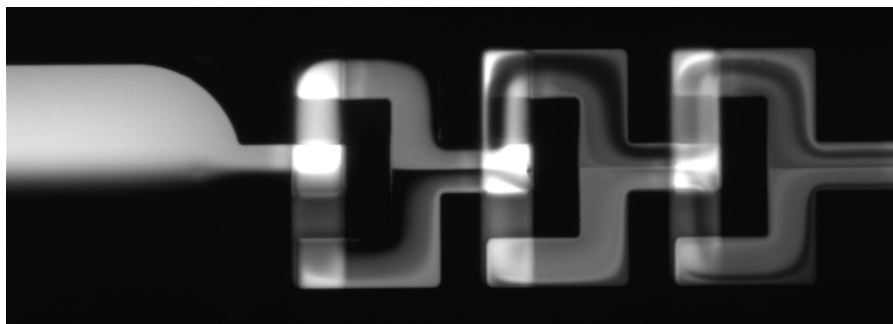


Fig. 8: Fluorescence microscopy image of a DF-1050 3D micromixer for a 470 nm excitation wavelength (the two fluids are water and fluorescein in water). The flow rate is 40 $\mu\text{L}/\text{min}$.

We therefore realized a complex structure of a 3D micromixer and demonstrated our dry film lamination technology is tailored to implement innovative microfluidic functions involving 3D flows management.

4 Conclusion

The fabrication of 3D microfluidic chips using commercially dry film photoresist DF-1050 was demonstrated and investigated in several ways essential in microfluidic field. We have proved that this material is capable of high aspect ratio: 7:1 for free standing structures and 5:1 for channel structures. It's also resistant to the common organics solvents and although it remains colored after processing we have shown that it is not an issue for fluorescence based experiments. Last but not least, we proved that this dry film photoresist is biocompatible. Finally we realized a complex structure of a 3D micromixer and demonstrated the capability of this powerful technology to implement innovative microfluidic functions involving 3D flows management.

Acknowledgments

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