Accepted Manuscript

Title: Long-lasting FR-4 surface hydrophilisation towards commercial PCB passive microfluidics

Author: Nikolaos Vasilakis Despina Moschou Daniela Carta Hywel Morgan Themistoklis Prodromakis

Please cite this article as: N. Vasilakis, D. Moschou, D. Carta, H. Morgan, T. Prodromakis, Long-lasting FR-4 surface hydrophilisation towards commercial PCB passive microfluidics, *Applied Surface Science* (2015), http://dx.doi.org/10.1016/j.apsusc.2015.12.123

Long-lasting FR-4 surface hydrophilisation towards commercial PCB passive microfluidics

Nikolaos Vasilakis, Despina Moschou, Daniela Carta, Hywel Morgan and Themistoklis Prodromakis

Nanoelectronics and Nanotechnology Research Group, Southampton Nanofabrication Centre, Department of Electronics and Computer Science, University of Southampton, SO17 1BJ, Southampton, UK

E-mail: N.Vasilakis@soton.ac.uk

Highlights

- oxygen plasma treatment on FR-4 laminates

- effect of power and exposure time studied to achieve long-lasting hydrophilic properties

- super-hydrophilic surface for 13 days demonstrated

- surface remains weakly hydrophilic between 13th and 26th day after the treatment

- hydrophilic behaviour is retained for 26 days in total

- oxygen plasma treatment was used on a commercially manufactured PCB microfluidic chip to enable passive filling of a microfluidic network

Abstract

Printed circuit boards (PCB) technologies are an attractive system for simple sensing and microfluidic systems. Controlling the surface properties of PCB material is an important part of this technology and to date there has been no study on long-term hydrophilisation stability of these materials. In this work, the effect of different oxygen plasma input power and treatment duration times on the wetting properties of FR-4 surfaces was investigated by sessile droplet contact angle measurements. Super and weakly hydrophilic behaviour was achieved and the retention time of these properties was studied, with the hydrophilic nature being retained for at least 26 days. To demonstrate the applicability of this treatment method, a commercially manufactured microfluidic structure made from a multilayer PCB (3-layer FR-4 stack) was exposed to oxygen plasma at the optimum conditions. The structures could be filled with deionised (DI) water under capillary flow unlike the virgin devices.

Keywords: PCB microfluidics; oxygen plasma; surface modification; hydrophilic; passive microfluidics; hydrophilicity retention

1. Introduction

Currently, the vast majority of microfluidic devices are based on polymers or paper substrates since these are the most affordable, easily disposable, and versatile materials for large-scale fabrication of inexpensive microfluidic devices [1-4]. Polymers such as polydimethylsiloxane (PDMS) [5, 6], polymethylmethacrylate (PMMA) [7, 8], polystyrene (PS) [9], polycarbonate (PC) [10, 11] and cyclin olefin copolymer (COC) [12] are fabricated using methods such as soft lithography, hot embossing, micromolding and laser micromachining techniques. Despite their widespread use, functional integration of components including electronics, heaters, electrodes, optoelectronics, and sensing elements remains a challenge [13]. Paper-based platforms have limited sample preparation capabilities but their use as diagnostic platforms is beginning to increase although there are issues with sensitivity and specificity [14].

An alternative approach to microfluidic diagnostics is based on the use of a mixed circuit board (MCB) demonstrated by Lammerink et al [15] and first developed by Merkel et al [16]. This uses printed circuit board (PCB) manufacturing technology for microfluidic systems, incorporating copper traces, electronic assemblies, functional microfluidic components and sensing electrodes in a fully integrated Lab-on-Chip (LoC), i.e. the Lab-on-PCB [17]. Such as simple substrate is ideal for commercial upscaling of LoC devices, since it benefits from the high degree of electronics integration, high precision, and the accumulated experience of several decades of industrial manufacturing [13, 18]. Examples of PCB-based devices include micromixers [17], nucleic acid amplification chips [19] and chemical sensors [20].

The core material of a PCB stack is E-glass reinforced epoxy laminate (FR4), an intrinsically hydrophobic material. Therefore, microfluidic devices fabricated exclusively by commercially available PCB techniques require pump for fluidic manipulation. Passive capillary fill systems require some form of stable surface modification process that produces a hydrophilic FR-4 core. Previous studies have shown how oxygen plasma treatment on FR-4 can improve the adhesion strength of underfills [21] or wire bonding [22].

Since oxygen plasma treatment is a widely used, well-known, and cost effective method to render polymer substrates hydrophilic [23, 24], in this work we explore its application in fabricating passive FR-4 based microfluidic channels. To our knowledge such microfluidic structures have not been demonstrated yet. We study the effect of oxygen plasma treatment on the properties of FR-4 surfaces for different input power and treatment times. In the quest of a long-lasting hydrophilic behaviour, the recovery behaviour of the surface was also studied. The optimal oxygen plasma parameters were used to treat a commercially manufactured PCB microfluidic network and successful hydrophilic modification of the microchannels was demonstrated.

2. Materials and methods

2.1 Contact angle measurement

The static contact angle (CA) was measured on sessile deionized (DI) water 3 μL droplets, engaged gradually on level FR-4 (Flame Retardant 4) surfaces. A Drop Shape Analysis System (DSA 30 Kruss Co., Germany) was employed for CA calculation from captured images. A polynomial function was fitted to the two 3-phase sections of the profile in the region of the baseline. The slope of the polynomial function at the 3-phase contact points determines the contact angle and two contact angles on the left (θ_L) and right (θ_R) side of the droplet were evaluated. Every measurement was repeated three times and the average value was calculated.

All measurements were taken at the centre of the FR-4 substrates under constant and controlled laboratory conditions. The wettability of each sample was evaluated at the same position before treatment, immediately after treatment and systematically once every day to further investigate surface characteristics as a function of time. Results were classified on the basis of contact angle, taking into account recent published recommendations summarised in Table 1 [25].

Table 1: Hydrophilicity and hydrophobicity classification of solid surfaces according to the contact angle

Type of surface	contact angle CA (deg)
Superhydrophilic (rough surface $r^* > 1$), Hydrophilic	$\approx 0°, < 5°$
Weakly hydrophilic	$0° \sim 5° < \theta < (56 \sim 65°)$
Weakly hydrophobic	$(56 \sim 65°) < \theta < 90°$
Hydrophobic	$90° < \theta < 120°$

Superhydrophobic
(rough surface $r^* > 1$) $\theta > 150°$

---

* r : ratio of the true solid surface area to the apparent area

2.2 Atomic force microscopy (AFM) measurement

Atomic Force Microscopy (AFM) maps were acquired by a MultiMode Nanoscope V AFM (Veeco Metrology Group) in tapping mode using commercial Al coated Si tips (Budget sensors, Tap300Al-G) with 125 μm long cantilevers, resonant frequency of 300 kHz and force constant of 40 N/m.

2.3 Oxygen plasma treatment

Oxygen plasma treatment was performed with a Diener Femto (Diener Electronic, Germany) capacitively coupled plasma reactor. The radio-frequency (RF) power supply was operated at 13.56 MHz and the oxygen gas flow rate was 81 standard cubic centimetre per minute (sccm) under 100 kPa pressure. The maximum achievable input power in this particular plasma reactor was 100 W. All samples were treated with varying input power (P) and treatment time (t_t). Before every treatment the matching network was tuned manually to maintain the reflected power below 2% and to maximize the forward power (98% in case of input power 100 W).

2.4 Samples studied

Oxygen plasma assisted surface modifications were performed on commercially available FR-4 substrates, supplied by Newbury Electronics Ltd. FR-4 is a composite material, consisting of woven fiberglass with an epoxy resin binder, primarily and routinely used in PCB manufacturing. No mechanical post-treatment was employed to reduce intrinsic surface roughness.

The PCB microfluidic structures studied consist of a 3 layer FR-4 stack, illustrated in Fig. 1a to c. It comprises two 500 μm thick FR-4 core layers (Layer 2 and 3) and a thinner 200 μm thick FR-4 core (Layer 1), allowing optical inspection of the microfluidic channels. The two top layers (Layer 2 and 3) are formed following standard electronic PCB fabrication (mechanical drilling of vias, copper pattern definition and via electroless copper plating).

The fluidic delivery network layer on the bottom is formed on the thin FR-4 core (Layer 1) by laminating a 51 μm photo-patternable negative dry photoresist (DuPont, PC1020), routinely utilized as a standard copper etch mask by PCB manufacturers. The

microfluidic channels were patterned utilizing a laser direct imaging (Limata, UV-P300 LDI) system.

The microfluidic chip features several variations of the design (minimum feature size = 150 μm). The basic design consists of a 3.1 mm long microchannel (Layer 1) connected in series with three pairs of concentric vias (Layer 2 and 3), stacked one on top of the other. The Layer 3 vias serve as channel inlets and outlets.

Each layer was patterned according to the respective CAD design and the patterned layers were bonded together to form the final stack via a pressure/temperature bonding press. Subsequently, individual chips were separated from large panels.
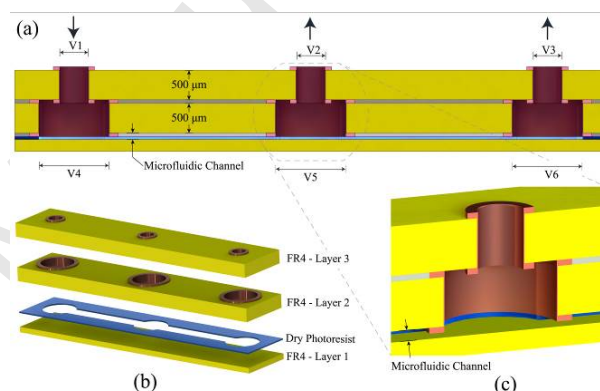

Fig. 1: Commercially manufactured microfluidic PCB design. (a) Cross-sectional view. V1 (Ø 500 μm) is the inlet of the device and V2, V3 (Ø 500 μm) are the outlets. V4, V5 and V6 (Ø 1200 μm) (b) 3D exploded view diagram of the structure (c) 3D cross-sectional detail view of the middle via V2 and V5

3. Results and discussion

It is evident throughout the literature that oxygen plasma treatment acts chemically by oxidising the polymer surface. X-ray Photoelectron Spectroscopy (XPS) measurements reveal that oxygen content on the surface is increased, carbon content is depleted while oxygen functional groups are formed such as carbonyl (-C=O), carboxyl (-COOH) and carbonate (CO_3)[21, 26-28]. The appearance of functional groups increases the surface free energy of the material.

Changes in the surface free energy (SFE) of a solid affects its wetting behaviour. In essence, high SFE

solids are hydrophilic and tend to promote wetting, while low SFE solids have a hydrophobic behaviour. The contact angle method is widely used to characterize the wettability of a solid surface. Previous studies reported that oxygen plasma treatment of the FR-4 surface improves the C–O and carbonyl (C=O) ratios and decreases the root mean square (RMS) roughness. Consequently, the measured contact angles were decreased by the increased total surface energy as well as the creation of new binding states by the plasma treatment. [21]

However, the rendered hydrophilicity by the oxygen plasma treatment is subject to aging effects causing hydrophobic recovery of the treated surface. Ageing effects can be attributed to a thermodynamically driven reorientation of the oxygen functional groups away from the surface into the sub-surface and the decay of these hydrophilic groups by atmospheric contaminants [28-30].

Plasma treated PDMS is the most popular substrate utilized for microfluidic device development. However, the retention of the oxygen plasma rendered hydrophilicity cannot exceed a 7-day period if stored in air [31, 32]. Therefore, in this work a hydrophilicity retention period of several weeks is considered as long-lasting surface modification, regarding applications in microfluidic channels.

The contact angle of DI water on plain FR-4 surfaces was first measured prior to any treatment, and found to be $118.3 \pm 3.4°$ (Fig. 2(a)). An initial oxygen plasma treatment was performed on these untreated surfaces (P=100 W, t_t=2 and 20 min) in order to investigate the possibility of making them more hydrophilic. The contact angle was measured immediately after plasma treatment. Fig. 2(b) and (c) depict a representative DI water droplet spreading on the FR-4 surface after 2 sec and 10 sec respectively (plasma treatment P=100 W, t_t=2 min). As shown, the contact angle is almost 0°, hence it can be deduced that O_2 plasma treatment changes the hydrophobic FR-4 surface to super-hydrophilic.
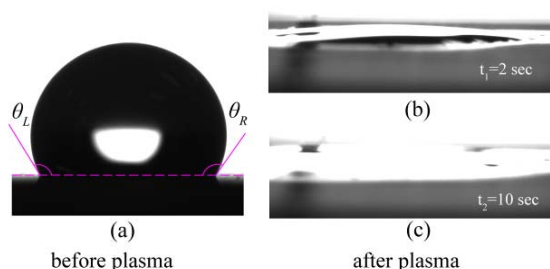

Fig. 2: 3μL DI water droplets on FR-4 surfaces (a) untreated, θ_L and θ_R are the contact angles on the left and right droplet side respectively (b) oxygen plasma (P=100 W, t_t=2 min) treated (t_1=2 sec after droplet attachment), and (c) oxygen plasma (P=100 W, t_t=2 min) treated (t_2=10 sec after droplet attachment).

It is well known that roughness has a strong influence on wettability of surfaces [33]. AFM was used in this work to characterize the surface morphology and the roughness of the FR-4 surface before and after oxygen plasma treatment. The root mean square (RMS) roughness calculated on 1×1 μm^2 areas of untreated and treated surfaces was found to be 9.70 nm and 5.30 nm respectively (Fig. 3). Although it has been reported that oxygen plasma on other polymeric surfaces can increase the RMS roughness [34], our findings are in agreement with the results of previous studies demonstrating a decrease as an effect of O_2 plasma treatment on the FR-4 surface [21].
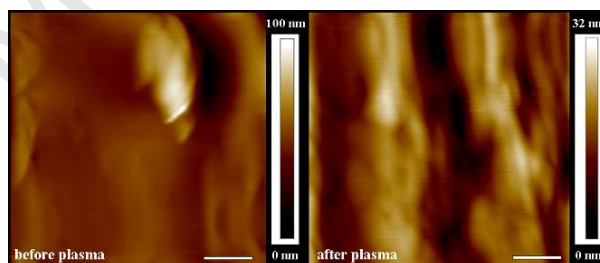

Fig. 3: AFM images of the FR-4 surface before and after O_2 plasma treatment. Scale bar = 200 nm

The aim is to produce passive hydrophilic devices. Therefore the time course of the recovery of the original surface properties is important. Hence, contact angle measurements were made on the treated samples for a period of 28 days. The sample exposed for 2 min became weakly hydrophilic after 5 days, with a CA greater than 5° (Fig. 4)

In contrast, treating the surface for 20 min led to the superhydrophilic regime that remained even after 12 days (apparent CA <5°) (Fig. 4). Since retention of hydrophilicity seems to depend on plasma treatment conditions, the next step was to define the optimum O_2 plasma treatment conditions that result in the lowest possible change in contact angle over time.
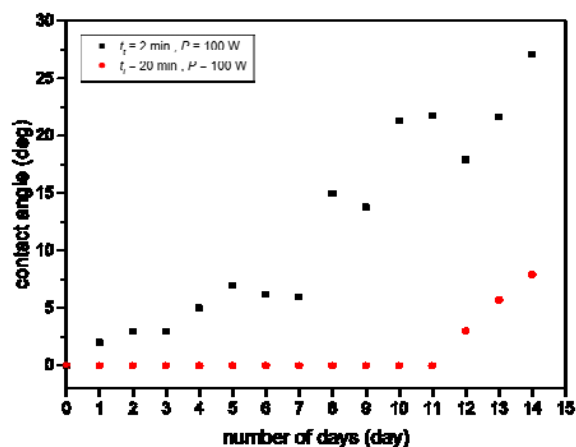
Fig. 4: Contact angle measurements for 14 days after oxygen plasma treatment as a function of ageing time. Plasma input power P=100 W and duration: • (red) t_t=2 min, ■ (black) t_t=20 min

3.1 Oxygen plasma input power

First the effect of oxygen plasma power density on the surface wettability was studied. Three different input power values (P=50 W, 75 W, 100 W) were investigated, for treatment times (t_t) of 2 min and 20 min. The average measured contact angle on the 6 untreated FR-4 surfaces was 118.3±2.7° (the error in this case, and subsequently is the 95% confidence interval). Immediately after plasma treatment all the samples became superhydrophilic (apparent CA≈0°). The samples were subsequently measured daily for a 14-day period.

As expected, the highest plasma input power (P=100 W) results in a hydrophilic surface that retains its characteristics longest (CA=7.9±2,2° for t_t=20 min and CA=27.1±0.8° for t_t=2 min), (Fig. 5(a)). Moreover, the CA appears to decreases linearly with input power P for the shorter treatment times (t_t=2 min). Fig. 5:

(b),(d),(f) illustrate the sessile droplets on the treated FR-4 surfaces on the 14th day at P=50 W, 75 W and 100 W respectively, for t_t=2 min, while Fig. 5:

(c),(e),(g) for t_t=20 min.

Treatment time seems to be as important as input power for the 100 W case. For the lower input power used the hydrophilic properties are almost the same 14 days after treatment. The highest plasma input power (P=100 W) combined with the extended treatment duration time (t_t=20 min) leads to the most

pronounced retained hydrophilic behaviour on the 14th day (CA=7.9±2.2°).
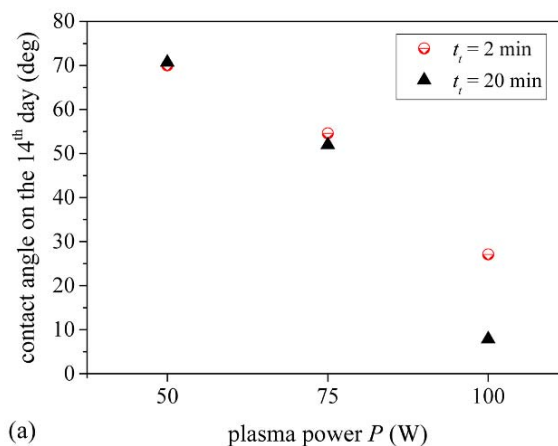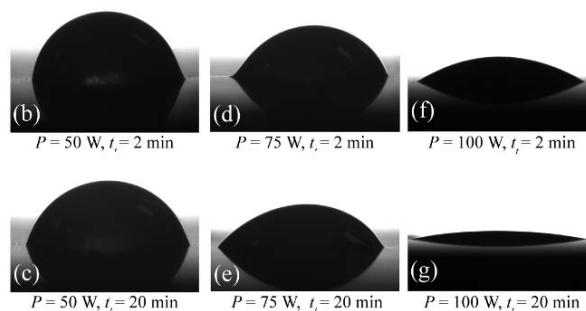

Fig. 5: Contact angle measurements on the 14th day after oxygen-plasma treatment. (a) Measured contact angles vs. different oxygen plasma input power (P) for durations (t_t) of 2 and 20 minutes;

(b) P=50 W, t_t=2 min; (c) P=50 W, t_t=20 min;

(d) P=75 W, t_t=2 min; (e) P=75 W, t_t=20 min;
(f) P=100 W, t_t=2 min; (g) P=100 W, t_t=20 min

3.2 Oxygen plasma duration effect

The effect of oxygen plasma treatment time on the hydrophilicity retention time of FR-4 was examined in more detail. A batch of four samples was modified by oxygen plasma at the previously determined optimum input power (P=100 W). Before surface modification the average contact angle of the four samples was 119.5±5.2°. Immediately after the plasma treatment all samples exhibited extreme hydrophilicity (CA≈0°), as observed previously.

Fig. 6 shows the surface wettability of the samples on the day 14. A clear trend is observed where the contact angle decreases with increasing treatment time. The sample treated for t_t=20 min at P=100 W maintains a strong affinity to water even 14 days after plasma exposure, with a contact angle of 7.9±2.2°. On the contrary samples treated for 2 min, 5 min and 10

min had a surface wettability within the weakly hydrophilic regime i.e. CA=27.1±0.8°, 16.9±1.7° and 14.6±1.6° respectively.
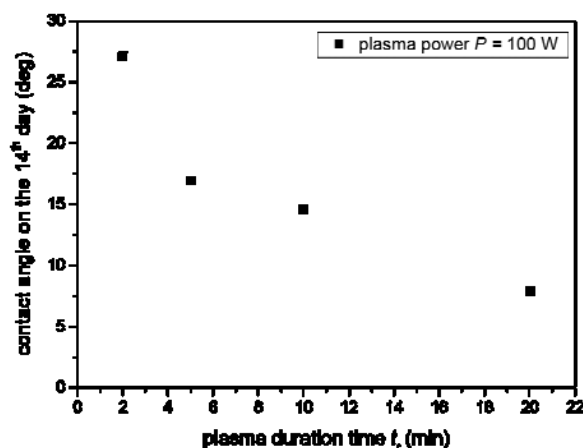

Fig. 6: Contact angle measurements on the 14th day after oxygen-plasma treatment as a function of plasma treatment time (t_t).

Having defined the optimum oxygen plasma treatment conditions, a longer term ageing study was performed to investigate the retention period of hydrophilicity induced by oxygen plasma on FR-4 surfaces. Samples were oxygen plasma treated for 20 min at an input power 100 W. Subsequently contact angle measurements were performed daily for 26 days. The results are plotted in Fig. 7.

Following the classification of surface wettability (Table 1), three retention periods can be identified, namely super-hydrophilic, weakly hydrophilic and weakly hydrophobic. The surface is super-hydrophilic for the first 13 days where the apparent contact angle is below 5° (CA≈0°).

Afterwards the wettability enters the weakly hydrophilic regime. The duration of this period is again 13 days where the 26th day the measured sessile droplet contact angle is 64.0±2.37°. Hence the hydrophilic retention period of the treated surface for 20 min under 100 W input power can be considered as 26 days. However, shorter plasma treatment duration time (t_t=2 min) with the same plasma intensity (P=100 W) results in long-lasting (17 days) weakly hydrophilic behaviour, as illustrated in Fig. 7 (•, red).

According to the observations above, FR-4 laminates treated by oxygen plasma (P=100 W, t_t=20 min) exhibit long-lasting (26 days) weakly hydrophilic properties and for the first 13 days can be classified as super-hydrophilic. Consequently, this

material could be used as substrate for passive microfluidic components. The post-treated microfluidic structures would be expected to remain hydrophilic for a sufficient period of time, owing to the FR-4 hydrophilicity retention presented.
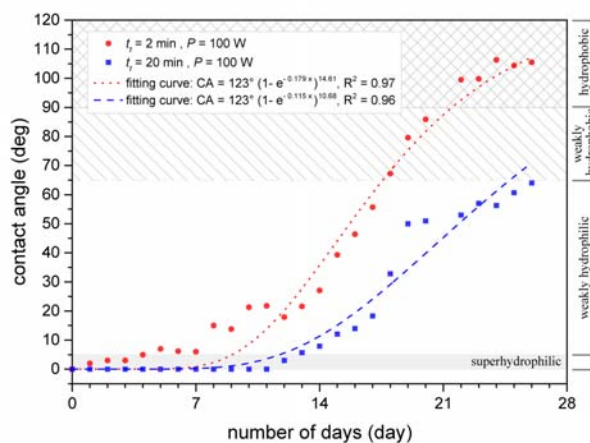

Fig. 7: Contact angle measurements for 26 days after oxygen plasma treatment as a function of ageing time. Plasma input power P =100 W and duration: • (red) t_t = 2 min, ■ (blue) t_t = 20 min

3.3 Hydrophilisation of PCB microchannels

In order to explore whether the specified oxygen plasma post-treatment could be used to produce passive PCB microfluidic structures, a basic microfluidic network was designed and manufactured in collaboration with Newbury Electronics Ltd, a UK based PCB industrial manufacturer. Fig. 8(a) illustrates a cross-sectional schematic of the structures. The PCB microfluidics were delivered from the manufacturer and examined by attempting to fill them with DI water under capillary action.

A 500μm thick blunt needle, maintained at a fixed distance (~400μm) from the channel inlet (to avoid any external pressure), supplied DI water droplets to the inlet. At the beginning a droplet starts to form in the centre of the inlet via 1 (Fig. 8(b)) and by gradual expansion attaches to the internal wall (Fig. 8(c) and (d)). As the size of the droplet increases and by the time its volume becomes larger than Via 1, the droplet enters the underlying Via 4 (Fig. 8(e)). On the bottom of Via 4 the hydrophobic FR-4 surface (which also serves as the microchannel bottom), meets a capillary barrier. The barrier is created by the hydrophobic surfaces of the microchannel walls and cannot be overcome by the low hydrostatic pressure of the expanding droplet itself (no external pressure applied). Fig. 8(f) illustrates the droplet at the time

(104 sec after start) when the two vias (Via 1 and Via 4) are fully filled. Afterwards water cannot flow through the microchannel and consequently, the droplet starts expanding out of Via 1 as shown in Fig. 8(g). Therefore, commercially manufactured microfluidic structures on FR-4 cannot be considered intrinsically passive, as expected, due to the inherent hydrophobic nature of FR-4.
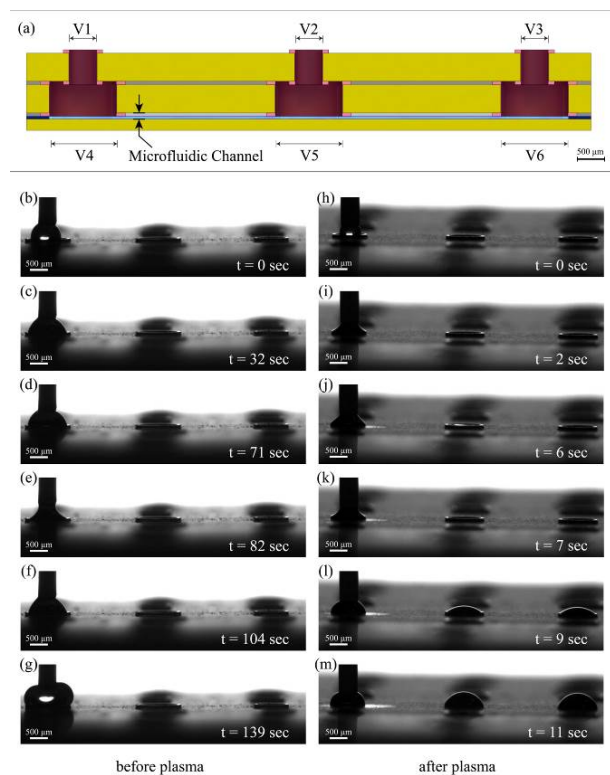

Fig. 8: Still images from the DI water-filling experiment on the manufactured PCB microfluidic (a) cross-sectional view of the PCB microfluidic structure device. (b) to (g) filling before plasma treatment, (h) to (m) after plasma treatment.

The same, sealed PCB microfluidic structures were treated with the oxygen plasma (P=100 W, t_t=20 min). After treatment the same sample was examined for passive filling, by repeating the previous experiment. The flowrate through the blunt needle was set to 20 μL/min. Fig. 8(h) and (i) illustrate the inlet filling procedure (Via 1 and 4). By comparing Fig. 8(i) and (j) in the area of Via 2 it can be observed that Via 2 in Fig. 8(j) was filled. The surface of the water reflects light and is visible in the middle of Via 2. This demonstrates that the DI water has moved through the microchannel connecting Via 4 and 5. One second later (t=7 sec, Fig. 8(k)), this water

surface disappeared, although the flowrate through the needle had not changed. Actually, the water level in Via 2 dropped due to further water flow through the microchannel connecting Via 5 and 6. As a consequence, after 2 seconds (t=9 sec, Fig. 8(l)) water level in both outlet vias (Via 2 and 3) rose concurrently forming a meniscus. Fig. 8(m) illustrates the formed meniscus in its greatest extend.

The experiment was performed daily on structures of different size (via diameters and microchannel width) and the same behaviour was repeatedly observed. It is worth noting that even 26 days after plasma treatment, wide microchannel (500μm) structures could be successfully filled, and the water menisci appearing through the outlet vias were formed concurrently. Therefore, plasma treatment delivers PCB passive microfluidic channels, maintaining their hydrophilicity over 26 days.

4. Conclusions

We have demonstrated that oxygen plasma treatment of sealed, commercially manufactured PCB microfluidic structures can render them hydrophilic and suitable for passive microfluidics systems. Different plasma input power settings and treatment times were investigated to determine long-lasting hydrophilic FR-4 surfaces using commercially manufactured microfluidic PCBs. Both plasma input power and treatment time affected the surface hydrophilicity, with increased input power and longer treatment times showing better long term retention. The optimal oxygen plasma treatment conditions were P=100 W and t_t=20 minutes. FR-4 substrates treated under these conditions were found to remain superhydrophilic for 13 days and weakly hydrophilic for a further 13 days. Hence, the hydrophilic behaviour was retained for 26 days. The oxygen plasma treatment was used on a commercially manufactured (Newbury Electronics Ltd) PCB microfluidic test chip, formed from FR-4. Treated structures could be passively filled with DI water. Further experiments indicate that the long-lasting weakly-hydrophilic behaviour of the treated FR-4 surface, can deliver a simple passive microfluidic platform. The inherent characteristics of a PCB based microfluidic device (electronics and sensing electrode integration, upscaling, low cost) are further enhanced by the prominent capabilities of passive microfluidics (no external power source for liquid flow), result to the ideal candidate for a disposable diagnostic Lab-on-PCB platform.

References

[1] Whitesides, G.M., 'The Origins and the Future of Microfluidics', *Nature*, 2006, 442, (7101), pp. 368-373.

[2] Neils, C.M., Tourovskaia, A., Weigl, B., and Folch, A., 'Combinatorial Microfluidic Devices for Cell Biology', *2nd Annual International Ieee-Embs Special Topic Conference on Microtechnologies in Medicine & Biology, Proceedings*, 2002, pp. 148-151.

[3] Gervais, L., de Rooij, N., and Delamarche, E., 'Microfluidic Chips for Point-of-Care Immunodiagnostics', *Advanced Materials*, 2011, 23, (24), pp. H151-H176.

[4] Yetisen, A.K., Akram, M.S., and Lowe, C.R., 'Paper-Based Microfluidic Point-of-Care Diagnostic Devices', *Lab Chip*, 2013, 13, (12), pp. 2210-2251.

[5] Duffy, D.C., McDonald, J.C., Schueller, O.J.A., and Whitesides, G.M., 'Rapid Prototyping of Microfluidic Systems in Poly(Dimethylsiloxane)', *Anal Chem*, 1998, 70, (23), pp. 4974-4984.

[6] Rushworth, C.M., Jones, G., Fischlechner, M., Walton, E., and Morgan, H., 'On-Chip Cavity-Enhanced Absorption Spectroscopy Using a White Light-Emitting Diode and Polymer Mirrors', *Lab Chip*, 2015, 15, (3), pp. 711-717.

[7] Zagnoni, M., Sandison, M.E., Marius, P., Lee, A.G., and Morgan, H., 'Controlled Delivery of Proteins into Bilayer Lipid Membranes on Chip', *Lab Chip*, 2007, 7, (9), pp. 1176-1183.

[8] Beaton, A.D., Cardwell, C.L., Thomas, R.S., Sieben, V.J., Legiret, F.E., Waugh, E.M., Statham, P.J., Mowlem, M.C., and Morgan, H., 'Lab-on-Chip Measurement of Nitrate and Nitrite for in Situ Analysis of Natural Waters', *Environmental Science & Technology*, 2012, 46, (17), pp. 9548-9556.

[9] Young, E.W.K., Berthier, E., Guckenberger, D.J., Sackmann, E., Lamers, C., Meyvantsson, I., Huttenocher, A., and Beebe, D.J., 'Rapid Prototyping of Arrayed Microfluidic Systems in Polystyrene for Cell-Based Assays', *Anal Chem*, 2011, 83, (4), pp. 1408-1417.

[10] Kim, N., Murphy, M.C., Soper, S.A., and Nikitopoulos, D.E., 'Liquid-Liquid Segmented Flows in Polycarbonate Microchannels with Cross-Sectional Expansions', *International Journal of Multiphase Flow*, 2014, 58, pp. 83-96.

[11] Ansari, K., Ying, J.Y.S., Hauser, P.C., de Rooij, N.F., and Rodriguez, I., 'A Portable Lab-on-a-Chip Instrument Based on Mce with Dual Topbottom Capacitive Coupled Contactless Conductivity Detector in Replaceable Cell Cartridge', *Electrophoresis*, 2013, 34, (9-10), pp. 1390-1399.

[12] Jeon, J.S., Chung, S., Kamm, R.D., and Charest, J.L., 'Hot Embossing for Fabrication of a Microfluidic 3d Cell Culture Platform', *Biomedical Microdevices*, 2011, 13, (2), pp. 325-333.

[13] Wu, L.L., Babikian, S., Li, G.P., and Bachman, M., 'Microfluidic Printed Circuit Boards', *2011 Ieee 61st Electronic Components and Technology Conference (Ectc)*, 2011, pp. 1576-1581.

[14] Hu, J., Wang, S.Q., Wang, L., Li, F., Pingguan-Murphy, B., Lu, T.J., and Xu, F., 'Advances in Paper-Based Point-of-Care Diagnostics', *Biosens Bioelectron*, 2014, 54, pp. 585-597.

[15] Lammerink, T.S.J., Spiering, V.L., Elwenspoek, M., Fluitman, J.H.J., and vandenBerg, A., 'Modular Concept for Fluid Handling Systems - a Demonstrator Micro Analysis System', *Ninth Annual International Workshop on Micro Electro Mechanical Systems, Ieee Proceedings*, 1996, pp. 389-394.

[16] Merkel, T., Graeber, M., and Pagel, L., 'A New Technology for Fluidic Microsystems Based on Pcb Technology', *Sensors and Actuators a-Physical*, 1999, 77, (2), pp. 98-105.

[17] Aracil, C., Perdigones, F., Moreno, J.M., Luque, A., and Quero, J.M., 'Portable Lab-on-Pcb Platform for Autonomous Micromixing', *Microelectronic Engineering*, 2015, 131, pp. 13-18.

[18] Bachman, M. and Li, G.P., 'Integrated Mems in Package', *Circuit World*, 2012, 38, (4), pp. 184-192.

[19] Moschou, D., Vourdas, N., Kokkoris, G., Papadakis, G., Parthenios, J., Chatzandroulis, S., and Tserepi, A., 'All-Plastic, Low-Power, Disposable, Continuous-Flow Pcr Chip with Integrated Microheaters for Rapid DNA Amplification', *Sensors and Actuators B-Chemical*, 2014, 199, pp. 470-478.

[20] Prodromakis, T., Liu, Y., Yang, J., Hollinghurst, D., and Toumazou, C., 'A Novel Design Approach for Developing Chemical Sensing Platforms Using Inexpensive Technologies', in, *Biomedical Circuits and Systems Conference (BioCAS), 2011 IEEE*, (IEEE, 2011)

[21] Noh, B.I. and Jung, S.B., 'Characterisation of Fr-4 Substrate with Various Plasma Treatment Conditions', *Materials Science and Technology*, 2007, 23, (7), pp. 792-798.

[22] Nowful, J.M., Lok, S.C., and Lee, S.W.R., 'Effects of Plasma Cleaning on the Reliability of Wire Bonding', *Advances in Electronic Materials and Packaging 2001*, 2001, pp. 39-43.

[23] Trantidou, T., Prodromakis, T., and Toumazou, C., 'Oxygen Plasma Induced Hydrophilicity of Parylene-C Thin Films', *Applied Surface Science*, 2012, 261, pp. 43-51.

[24] Jokinen, V., Suvanto, P., and Franssila, S., 'Oxygen and Nitrogen Plasma Hydrophilization and Hydrophobic Recovery of Polymers', *Biomicrofluidics*, 2012, 6, (1).

[25] Drelich, J., Chibowski, E., Meng, D.D., and Terpilowski, K., 'Hydrophilic and Superhydrophilic Surfaces and Materials', *Soft Matter*, 2011, 7, (21), pp. 9804-9828.

[26] Kontziampasis, D., Trantidou, T., Regoutz, A., Humphrey, E.J., Carta, D., Terracciano, C.M., and Prodromakis, T., 'Effects of Ar and O2 Plasma Etching on Parylene C: Topography Versus Surface Chemistry and the Impact on Cell Viability', *Plasma Processes and Polymers*, 2015.

[27] Baytekin, H.T., Wirth, T., Gross, T., Treu, D., Sahre, M., Theisen, J., Schmidt, M., and Unger, W.E.S., 'Determination of Wettability of Surface-Modified Hot-Embossed Polycarbonate Wafers Used in Microfluidic Device Fabrication Via Xps and Tof-Sims', *Surface and Interface Analysis*, 2008, 40, (3-4), pp. 358-363.

[28] Tserepi, A., Gogolides, E., Bourkoula, A., Kanioura, A., Kokkoris, G., Petrou, P., and Kakabakos, S., 'Plasma Nanotextured Polymeric Surfaces for Controlling Cell Attachment and Proliferation: A Short Review', *Plasma Chemistry and Plasma Processing*, 2015, pp. 1-14.

[29] Arefi-Khonsari, F., Kurdi, J., Tatoulian, M., and Amouroux, J., 'On Plasma Processing of Polymers and the Stability of the Surface Properties for Enhanced Adhesion to Metals', *Surface & Coatings Technology*, 2001, 142, pp. 437-448.

[30] Kim, B., Kim, K., Park, C., and Ryu, C., 'Improvement of Wettability and Reduction of Aging Effect by Plasma Treatment of Low-Density Polyethylene with Argon and Oxygen Mixtures', *Journal of adhesion science and technology*, 2002, 16, (5), pp. 509-521.

[31] Zhou, J.W., Ellis, A.V., and Voelcker, N.H., 'Recent Developments in Pdms Surface Modification for Microfluidic Devices', *Electrophoresis*, 2010, 31, (1), pp. 2-16.

[32] Tsougeni, K., Tserepi, A., Boulousis, G., Constantoudis, V., and Gogolides, E., 'Tunable Poly(Dimethylsiloxane) Topography in O-2 or Ar Plasmas for Controlling Surface Wetting Properties and Their Ageing', *Japanese Journal of Applied Physics Part 1-Regular Papers Brief Communications & Review Papers*, 2007, 46, (2), pp. 744-750.

[33] Kubiak, K.J., Wilson, M.C.T., Mathia, T.G., and Carval, P., 'Wettability Versus Roughness of Engineering Surfaces', *Wear*, 2011, 271, (3-4), pp. 523-528.

[34] Bi, X.P., Crum, B.P., and Li, W., 'Super Hydrophobic Parylene-C Produced by Consecutive O-2 and Sf6 Plasma Treatment', *Journal of Microelectromechanical Systems*, 2014, 23, (3), pp. 628-635.