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Chemical-Assisted Bonding of Thermoplastics/Elastomer for Fabricating Microfluidic Valves

Pan Gu¹, Ke Liu¹, Hong Chen¹, Toshikazu Nishida^{2,*}, and Z. Hugh Fan^{1,3,*}

¹ Interdisciplinary Microsystems Group, Department of Mechanical and Aerospace Engineering, University of Florida, Gainesville, Florida 32611-6250, USA

² Interdisciplinary Microsystems Group, Department of Electrical and Computer Engineering, University of Florida, Gainesville, Florida 32611-6130, USA

³ Department of Biomedical Engineering, University of Florida, Gainesville, Florida 32611-6131, USA

Abstract

Thermoplastics such as cyclic olefin copolymer (COC) and polymethylmethacrylate (PMMA) have been increasingly used in fabricating microfluidic devices. However, the state-of-the-art microvalve technology is a polydimethylsiloxane (PDMS)-based three-layer structure. In order to integrate such a valve with a thermoplastics-based microfluidic device, a bonding method for thermoplastics/PDMS must be developed. We report here a method to bond COC with PDMS through surface activation by corona discharge, surface modification using 3-(trimethoxysilyl)propyl methacrylate (TMSPMA), and thermal annealing. The method is also applicable to PMMA. The bonding strength between thermoplastics and PDMS was represented by the peeling force, which was measured using a method established by the International Organization for Standardization (ISO). The bonding strength measurement offered an objective and quantitative indicator for protocol optimization, as well as comparison with other PDMS-associated bonding methods. Using optimized bonding conditions, two valve arrays were fabricated in a COC/PDMS/COC device and cyclic operations of valve closing/opening were successfully demonstrated. The valve-containing devices withstood 100 psi (~689 KPa) without delamination. Further, we integrated such valve arrays in a device for protein separation and demonstrated isoelectric focusing in the presence of valves.

Thermoplastics have been increasingly employed for microfluidics applications.¹ Compared with glass and silicon, thermoplastics offer several advantages including manufacturability, low cost, and biocompatibility.^{1–4} Among several thermoplastics, cyclic olefin copolymers (COC) and polymethylmethacrylate (PMMA) are frequently exploited for making microfluidic devices. These devices were often fabricated by bonding a cover sheet with a substrate containing microchannels and other microfeatures using various bonding methods including thermal fusion,^{3–7} solvent bonding,^{8–14} surface treatment,^{15–20} and adhesives.^{21, 22} Each of these methods has advantages and disadvantages as reviewed in the literature.^{1, 2}

A microfluidic system consists of a number of necessary building blocks. One of them is microvalves that may regulate flows, contain fluids, and isolate one region from the other.^{23, 24} Microvalves can be actuated using a variety of mechanisms, including electric, pneumatic, and thermal methods.²³ The state-of-the-art microvalve technique for lab-on-a-chip systems is elastic membrane-based polydimethylsiloxane (PDMS) valves. Quake's

* To whom correspondence should be addressed. hfan@ufl.edu; Fax: 352-392-7303. .

research group reported the concept in 2000,²⁵ followed by several studies using thousands of integrated microvalves for high-throughput applications.²⁶⁻²⁹ The elastomer valves consists of three layers of PDMS. Control channels in the top layer are used to regulate the fluid channels in the bottom layer through the elastic property of the middle PDMS layer. The elastomer valve has been adopted by a number of researchers³⁰⁻³⁸ while modifications have also been reported, including the efforts by Mathies' group who integrated the valve with a glass device to form glass/PDMS/glass structures for DNA analysis and other applications.³⁶⁻³⁸

In this paper, we report our effort in integrating the elastomer valve with COC devices with a particular focus on the optimization of the PDMS/COC bonding. The valves were designed for developing protein separation devices, which we have reported using two-layer COC devices with gel-based pseudo-valves.³⁹ To realize the goal of integrating elastomer-based true valves in the device, the key challenge is to achieve strong bonding between COC and PDMS so that the device will not delaminate when a pressure is built up after valves are closed.^{5, 39} The recent efforts on bonding PDMS to thermoplastics have targeted bonding PMMA/PDMS.¹⁷⁻²⁰ To our knowledge, there is no report on bonding COC/PDMS to fabricate multilayer hybrid devices.

Our method to bond COC with PDMS is based on surface modification using 3-(trimethoxysilyl)propyl methacrylate (TMSPMA). TMSPMA has been used as a coating on glass slides⁴⁰ and for grafting on fiber/polypropylene composites,⁴¹ but never be exploited for facilitating thermoplastic bonding. Prior to the chemical treatment, surfaces to be bonded were activated using corona discharge. Thermal annealing was then performed to facilitate the formation of chemical bonds between functional groups on the surfaces and enhance the bonding strength. We found that the method is also applicable to PMMA. The bonding strength between COC and PDMS was represented by the peeling force, which could be quantitatively measured. Using optimized bonding conditions, two valve arrays were fabricated in a COC/PDMS/COC device and their operations were demonstrated.

Further, the utility of the valve arrays were demonstrated in a protein separation device. Conventional two-dimensional protein separation consists of isoelectric focusing (IEF) as the first dimension and polyacrylamide gel electrophoresis (PAGE) as the second dimension. As they are implemented in a device, an array of microvalves is required for introducing two types of separation media, without cross-contamination, into orthogonal channels in order to achieve two-dimensional separation based on different mechanisms.^{39, 42} The elastomer valve arrays in this work meet this need.

Experimental

Reagents and Materials

Cyclic olefin copolymer (COC) films (Zeonor 1420R, 188 μm thick) and COC resins (Zeonor 1020R) were purchased from Zeon Chemicals (Louisville, KY) while a 100- μm thick COC (Topas 8007) was from PLITEK (Des Plaines, IL). Poly(methyl methacrylate) (PMMA) films (250 and 100 μm thick) were obtained from Evonik Industries (Essen, German). Polydimethylsiloxane (PDMS, Sylgard 184) was bought from Dow Corning (Midland, MI). A solution of 98% 3-(trimethoxysilyl)propyl methacrylate (TMSPMA) was purchased from Acros organics (Fair Lawn, NJ) while solvents and common chemicals were from Fisher Scientific (Atlanta, GA). Green fluorescent protein (GFP, 1 mg/mL stock) and R-phycoerythrin (RPE, 4 mg/mL stock) were acquired from Clontech (Mountain View, CA) and Invitrogen (Carlsbad, CA), respectively. A solution of 6% (volume ratio) TMSPMA was obtained by diluting it in ethanol whereas other solutions were prepared using water purified from Barnstead Nanopure Water System (Model: D11911, Dubuque, Iowa). A corona

discharge generator (BD-10A) was purchased from Electro-Technic Products Inc. (Chicago, IL) and it was operated by following the instructions of the manufacturer.

Bonding of Thermoplastics and PDMS

The process flow of bonding a thermoplastic substrate with a PDMS layer is shown in Figure 1. A mixture of PDMS pre-polymer was prepared according to the instructions of the manufacturer. After eliminating air bubbles via vacuum, the mixture was spin-coated onto a clean 100- μm -thick Topas film (or 188- μm -thick Zeonor 1420R when high annealing temperature was used) using a spinner (Laurell Technologies) at a speed of 4000 RPM for 30 seconds (Figure 1a). The Topas thin film served as a sacrificial layer (discarded later), facilitating the formation of a thin layer of PDMS via spin-coating. PDMS on the sacrificial layer was cured in an oven at 60 °C for 4 hours. The resulting PDMS thickness was 15 μm , measured by a profilometer (Dektak IIa, Veeco Instruments).

A plastic sheet (188- μm -thick Zeonor 1420R) containing microchannels was first activated by corona discharge treatment, followed by immersing it in a solution of 6% TMSPMA for 20 minutes (Figure 1b). The corona discharge treatment was carried out by pointing the corona discharge generator towards the sheet surface and evenly scanning the probe across the substrate. It took about 1 minute to scan the whole surface area of a 1" $\times$ 3" sheet. After the sheet was taken out from the TMSPMA solution, it was blow-dried using nitrogen. The sheet was then placed in contact with the PDMS/sacrificial layer (prepared as in Figure 1a) after both surfaces were activated by corona discharge (Figure 1c). The assembly was placed in an oven at 90 °C overnight for annealing, which facilitated the formation of chemical bonds between activated functional groups on the surfaces and promoted bonding. At the end of annealing, the sacrificial layer was removed and irreversible bonding of thermoplastics/PDMS was achieved (Figure 1d).

Valve Fabrication

To fabricate a microvalve, a control layer (a 188- μm -thick COC sheet with microchannels) and PDMS were bonded as discussed above. Channels in the control layer were fabricated by laser-ablation (JPSA IX-260 ArF excimer laser). The width of the channels was either 90 μm or 150 μm . Alternatively, channels in the control layer were fabricated by a computer numerically controlled (CNC) milling machine (LPKE ProtoMat S100) and the designed channel width was 250 μm or 300 μm .

The fluid layer in the microvalve was fabricated using compression molding as reported previously.⁵ Briefly, a pattern of microchannels was created in a glass plate via photolithography. Electroplating on the glass plate generated a nickel mold, which was employed to produce plastic parts from COC resins (Zeonor® 1020) using a hydraulic press (Carver, Wabash, IN). The surface of the fluid layer was activated by corona discharge, followed by TMSPMA treatment as discussed above (Figure 1e).

The fluid layer was then placed in contact with the PDMS/control layer assembly after both surfaces were treated with corona discharge (Figure 1f). The channels in the control layer were aligned to the desired valve locations in the fluid layer. Afterwards, the 3-layer assembly was annealed in an oven as described above. When a pressure was supplied in the control layer, PDMS deflected and blocked the channel in the fluid layer (Figure 1g).

Bonding Strength Measurement

The bonding strength between thermoplastics/PDMS was measured in order to study the effects of different materials and bonding conditions. The standard peel test established by the International Organization for Standardization (ISO) was employed to determine the

bonding strength.⁴³ Samples were prepared by following the ISO 180° peel test protocol and illustrated in Figure 2a. The size of the COC film is 250 mm × 25.4 mm and the bonding area of PDMS is 25.4 mm × 25.4 mm. The COC film was bonded with PDMS using the procedure described above. The COC/PDMS assembly was then bonded to a plastic plate that was fixed to the bottom grip of a two-column, floor-standing tensile machine made by MTS Systems Corp. (Eden Prairie, MN). The COC film was bent to 180° and the other end of it was attached to the top grip, which was programmed to be pulled up at a crosshead speed of 5 mm/minute (Figure 2b). The pulling force was measured by a load cell that was mounted at the top grip. The load cell had a maximum force of 100 N with a detection sensitivity of 0.02 N. Figure 2c shows an example of a plot that recorded the force as a function of the moving distance of the load cell. Large fluctuations near the edges of the device (the initial and ending points) were not used for calculation per the recommendation by ISO.⁴³ The stable peeling forces in the middle were employed to calculate the average peeling force as indicated in Figure 2c. Each bonding condition was studied three times to enhance the precision.

Valve Operation

As illustrated in Figure 1g, a microvalve was actuated by a pressure supplied in a channel in the control layer. A pressure supply system was connected to the inlet of the control channel via an Upchurch Nanoport (Oak Harbour, WA). The pressure system was built in-house, similar to what was reported previously.⁴⁴ It consisted of a pressure controller (Cole-Parmer 68502-10), a nitrogen cylinder, and a Dynamco dash valve (Model D1B1202, Commerce, GA) that was controlled by a DC power supply (Model E3630A, Agilent Technologies, San Jose, CA). The pressure at the nitrogen cylinder was set at 100 psi, and the actual pressure to the device was fine-tuned by the dash valve for values ranging from 0 to 100 psi. The DC power supply for each dash valve was controlled by a computer.

To show the operation of a microvalve in the device, a solution of a food dye was introduced into channels in the fluid layer. Operation of the valve was indicated by the disappearance of the dye in the channel when the valve was closing. An inverted microscope (IX51, Olympus) equipped with a Hamamatsu CCD camera (model C4742-80-12AG) was used for recording the dye signals.

Protein Separation

We fabricated a microfluidic device to demonstrate protein separation in the presence of valve arrays. The fluid layer consists of one IEF channel and 29 PAGE channels as reported previously.³⁹ PDMS-based elastomer valves were fabricated using the bonding procedure described above. The control layer was made in PDMS since it contained two control channels that must be aligned with the IEF channel in the fluid layer.

The device was rinsed with 1% KOH and DI water, followed by coating the channel surfaces using 2.3% hydroxypropyl cellulous solution. After closing the valve arrays, IEF separation medium was then introduced into the IEF channel. The separation medium was comprised of 2% carrier ampholytes, 8% glycerol, 2.3% hydroxypropyl cellulous (MW 80,000), and two proteins, GFP (60 ng/μL) and RPE (40 ng/μL).³⁹ 10 mM acetic acid and 10 mM ethanolamine served as anolytes and catholytes, respectively. An electric field of 150 V/cm was applied across the IEF channel for 1 minute. Detection was carried out by an inverted epifluorescence microscope (Olympus IX51) equipped with a charge-coupled-device (CCD) camera (Hamamatsu C4742-80-12AG) using a 10× objective, similar to what we reported previously.⁴⁵

Results and Discussion

Bonding Condition Optimization

The bonding strength, represented by the peeling force, is an objective and quantitative indicator. Thus it can be used to determine the necessity of each step in a bonding protocol as well as the optimum condition of each step required. The bonding protocol described in the Experimental Section for COC/PDMS was obtained after a large number of experiments. An example of the bonding condition optimization is the study of the annealing temperature. After corona discharge activation and TMSPMA treatment, COC was placed in contact with PDMS, followed by annealing at a certain temperature. During annealing, chemical bonds (Si-O-Si) could be formed between the activated functional groups on the surfaces of the thermoplastic and PDMS layers. Our preliminary studies using attenuated total reflection Fourier transform infrared spectroscopy and X-ray photoelectron spectroscopy suggested there were grafting of TMSPMA on the plastic surface and dehydration reactions between TMSPMA and silanol groups on the activated PDMS surface; the results will be published elsewhere when the studies are completed. Annealing also promoted bonding as suggested by our experimental results.

Figure 3 shows the effects of the annealing temperature on the bonding strength. The results indicate that the peeling force required to delaminate COC/PDMS linearly increased with the annealing temperature from 50 °C to 90°C. The bonding strength was negligible when annealing took place at a lower temperature.

We also found that the corona discharge exposure is necessary before TMSPMA treatment. Our results indicated that the corona discharge exposure increased the bonding strength by about 20% compared to those without corona discharge treatment (data not shown).

To put the peeling forces in the users' perspective, we also carried out the blister test.⁴⁶ This test was carried out by observing dye spreading when delamination took place and the two layers formed bulges at the edges of a dye-filled channel. We did not observe any blistering in valve-containing channels up to 100 psi (~689 KPa) when the optimized bonding protocol was used. The device might sustain an even higher pressure but our setup was designed to have a maximum pressure of 100 psi as discussed in the Experimental Section. Considering the fact that most microfluidic devices are operated under 50 psi,⁴⁷ we conclude that the chemical-assisted COC/PDMS bonding is well suited for microfluidic applications.

PMMA versus COC

We also determined if TMSPMA-assisted bonding is applicable to another thermoplastic material, PMMA, which is used extensively in microfluidics. The bonding strength measurement suggested that (1) TMSPMA-assisted bonding is applicable to PMMA and (2) there are some differences in the required steps and the optimum operation parameters between COC and PMMA.

One difference is shown in Figure 3, in which the peeling forces are plotted as a function of the annealing temperature. Although PMMA/PDMS showed a similar trend that the peeling force linearly increased with the annealing temperature, the temperature required was much lower than COC/PDMS. Significant bonding between PMMA/PDMS was obtained even after overnight annealing at room temperature (25 °C) whereas COC/PDMS gained the similar degree of bonding when annealing took place at 55 °C. The PMMA/PDMS bonding strength reached a plateau when the temperature was higher than 70°C. The difference in the required annealing temperature is likely related to their plasticity, since PMMA has a lower glass transition temperature than COC. It may also be related to the difference in their chemical structures and surface property.

The second difference is that PMMA did not require corona discharge before chemical treatment. We did not observe any significant improvement in bonding strength if it was performed for PMMA/PDMS bonding. As mentioned above, it was required for COC when it was bonded with PDMS. This difference likely resulted from the existence of acrylate functional groups in PMMA. However, corona discharge treatment was required for both COC and PMMA after chemical treatment since it enhanced the bonding strength. Note that these are experimental observations, and further theoretical reasoning will be explored in the future.

Bonding Strength Survey

Since the peeling force measured here is an excellent indicator of the bonding strength between two layers in a microfluidic device, we measured and compared a number of bonding methods that are related to PDMS and often used in the microfluidics community. Table 1 lists the bonding materials and methods we evaluated and the corresponding peeling forces. All samples tested had a 1" × 1" bonding area. Soft bonding between PDMS/glass refers to the situations where plasma treatment was not used so that PDMS can be peeled away from a glass substrate for reuse. In hard bonding between PDMS/glass, plasma treatment was carried out on the surface of PDMS and permanent bonding between the two were generally realized.⁴⁷ We used the corona discharge to treat PDMS surface as previously reported.^{48, 49} Our results suggested that long-term annealing resulted in stronger bonding between PDMS/glass. Annealing for 3 days at room temperature produced bonding strength almost twice higher than that after overnight annealing. Using PDMS prepolymer as glue, PDMS/PDMS generated strong bonding as expected. For comparison, we also included in the table the bonding strength between PMMA/PDMS and COC/PDMS at the optimum bonding conditions as discussed above.

Valve Array

As mentioned above, COC/PDMS bonding was developed for fabricating a reliable valve array for protein separation. Figure 4a shows a picture of a COC substrate with the layout we used for two-dimensional protein separation.³⁹ The device consists of one AB channel for the first dimension (IEF) and a number of CD channels for the second dimension (PAGE). Since different separation media are employed to achieve different separation mechanisms in each dimension, a valve array is required at the intersections to prevent two separation media from contaminating each other. The valve array is represented by the dashed lines on each side of the IEF channel in Figure 4a.

To demonstrate the operation of two valve arrays, we created two 300- μ m-wide channels in the control layer. These two channels were pneumatically controlled using the pressure supply setup described in the Experimental Section. These control channels were not aligned with the IEF channel in this experiment for simplicity. All channels in the fluid layer were filled with a food dye solution. Figure 4b shows an exploded-view picture of five channels when valves were open (no pressure in control channels). Rough surface in the control channels was due to the fabrication method used in this work; they would disappear if we fabricated them using the same method for fabricating the fluid channels. We then supplied a pressure of 30 psi into the control channel on the right side; the valves on the right side were closed as indicated in Figure 4c. When the pressure was also applied to the control channel on the left, both valve arrays were then closed (Figure 4d). When the pressure in the control channels was relieved, valve arrays were opened again and dye flowed back into the channels (Figure 4e). Cyclic operations of valve closing-opening were demonstrated. Furthermore, we found that the same device properly closed and opened more than 10 times 6 months later, without any indication that the bonding failed.

The depth of microchannels in our device is 45 μm , and the width is 110 μm . As a result, the aspect ratio (depth/width) is 0.41. This number is much higher than what is typically used in elastomer-based valves. For instance, valves in the Quake's report had an aspect ratio of 0.1.²⁵ Deeper channels with higher aspect ratios are harder to close than those with smaller aspect ratios, thus requiring a higher pneumatic pressure. In addition, the pressure required to close valves in a fluid channel is also related to the width of the control channels.²⁵ A wider control channel possesses more actuation area, thus it requires a lower pressure to close the valves. We studied four different control channels widths and determined the minimum pressure required to block the same fluid channel. The result in Figure 5 shows a relationship between the control channel width and the pressure required to close the valves. This result offers another guideline in the design of microvalves.

Protein Separation

After two valve arrays were placed on both sides of the IEF channel as indicated in Figure 4a, we demonstrated separation of two model proteins, R-phycoerythrin (RPE) and green fluorescence protein (GFP), both of which are naturally fluorescent. The pH gradient was established using carrier ampholytes with a pH gradient of 3–10. The separated proteins were detected using a CCD camera installed on a microscope. The separation pattern obtained is the same with what we observed when identical proteins were separated in a single channel⁵⁰ or when a pseudo-valve array was used.⁵¹ RPE and GFP were focused at their expected positions in the channel according to their isoelectric points. This result suggests that elastomer-based valves can be exploited for two-dimensional protein separation.

Conclusion

We have developed a reliable method to bond thermoplastics with PDMS. The optimized protocol resulted in a strong bond; the bonding strength is higher than those using several bonding methods associated with PDMS. With microfluidic valves in place, we found that the COC/PDMS bond sustained at least a pressure of 100 psi. Two valve arrays integrated in a device enabled protein separation in one dimension without the possibility to interfere with the other dimension.

A large number of reports exist on a variety of bonding methods and materials. However, it is difficult to compare them and tell which one would produce the strongest bond. The bonding strength measurement using a method established by ISO offered an objective and quantitative indicator for comparing different methods as we demonstrated in this work. More concerted efforts are needed in this front to generate a consensus and guidelines. Universally accepted bonding methods are extremely important for commercialization of microfluidic devices since the fabrication reliability is essential.

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Figure 1.

The process flow of bonding a thermoplastic substrate with a PDMS layer (a-d), followed by additional steps for valve fabrication (e-g). (a) PDMS prepolymer was spin-coated on a sacrificial plastic layer, followed by curing. (b) The surfaces of a plastic sheet were activated, followed by treatment with TMSPMA. The plastic sheet was represented by a control layer containing a microchannel in the direction into the paper. (c) After activation, PDMS and the plastic sheet were in contact, followed by annealing. (d) Irreversible bonding of thermoplastics/PDMS was formed and the sacrificial layer was removed. (e) The surface of a fluid layer containing microchannels was activated and treated with TMSPMA. (f) The fluid layer was bonded with PDMS/control layer as in (c). (g) The valve was closed when a pressure was supplied to the channel in the control layer and PDMS deflected to block the channel in the fluid layer. The drawing is not to scale.

Figure 2.

(a) Three-dimensional view of a sample prepared for bonding strength measurement. A 15- μm -thick PDMS was bonded with a 188- μm -thick COC film using the procedure described in Figure 1. The assembly was then bonded to a 4 mm-thick plastic plate, which was then fixed to a peel test machine. (b) Schematic showing the plastic plate was fixed on the bottom grip of the peel test machine and kept stationary. The COC film was attached to the top grip that was programmed to move up at a speed of 5 mm/minute. The force was measured by a load cell attached to the top grip. (c) A representative plot showing the force as a function of the traveling distance of the load cell. The range of the data used for calculating the peeling force is indicated.

Figure 3.

The effects of the annealing temperature on the bonding strength. The bonding strength is indicated by the peeling force required to delaminate thermoplastics/PDMS. Thermoplastics include COC (closed circles) and PMMA (open circles). Each line is the linear regression of the data points within the line. Each value is the average of three repeat experiments. Error bars indicate one standard deviation.

Figure 4.

(a) Picture of a COC substrate that functioned as a fluid layer. The device was designed for protein separation. Channel AB is for the first dimensional (IEF) while channels CD are for the second dimension (PAGE). Valve arrays are indicated by the dashed lines on the both sides of the IEF channel. The size of the device is 1" × 3". (b) Picture of two control channels in the atmosphere pressure and five fluid channels filled with a dye solution. (c) Valves on the right side were closed when a pressure was supplied through the right control channel. (d) Both valve arrays were closed when a pressure was applied to both control channels. (e) Both valve arrays were opened again and dye flowed back to channels when the pressure in control channels was relieved.

Figure 5.

The pressure required to close valves as a function of the width of control channels. The fluid channel dimension was the same in all experiments. The line is the best-fit power relationship among experimental data.

Figure 6. IEF separation of two proteins, R-phycoerythrin (RPE) and green fluorescent protein (GFP) in the presence of PDMS-based valve arrays. The anode was on the left and the cathode was on the right. The scaling bar is 360 μm.

Table 1

The bonding strength in devices fabricated by different methods

Bonding Materials and Methods	Peeling Forces
Soft bonding between PDMS and glass	<0.02 N
Hard bonding between PDMS and glass, overnight annealing	(1.9 ± 0.3) N
Hard bonding between PDMS and glass, 3-day annealing	(5.7 ± 0.5) N
Hard bonding between PDMS and PDMS	(10.3 ± 0.6) N
Chemical-assisted bonding between PMMA/PDMS	(24 ± 2) N
Chemical-assisted bonding between COC/PDMS	(29 ± 3) N