A conformal nano-adhesive *via* initiated chemical vapor deposition for microfluidic devices

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A novel high-strength nano-adhesive is demonstrated for fabricating nano- and microfluidic devices. While the traditional plasma sealing methods are specific for sealing glass to poly(dimethylsiloxane) (PDMS), the new method is compatible with a wide variety of polymeric and inorganic materials, including flexible substrates. Additionally, the traditional method requires that sealing occur within minutes after the plasma treatment. In contrast, the individual parts treated with the nano-adhesive could be aged for at least three months prior to joining with no measurable deterioration of post-cure adhesive strength. The nano-adhesive is comprised of a complementary pair of polymeric nanolayers. An epoxy-containing polymer, poly(glycidyl methacrylate) (PGMA) was grown *via* initiated chemical vapor deposition (iCVD) on the substrate containing the channels. A plasma polymerized polyallylamine (PAAm) layer was grown on the opposing flat surface. Both CVD monomers are commercially available. The PGMA nano-adhesive layer displayed conformal coverage over the channels and was firmly tethered to the substrate. Contacting the complementary PGMA and PAAm surfaces, followed by curing at 70 °C, resulted in nano- and micro-channel structures. The formation of the covalent tethers between the complementary surfaces produces no gaseous by-products which would need to outgas. The nano-adhesive layers did not flow significantly as a result of curing, allowing the cross-sectional profile of the channel to be maintained. This enabled fabrication of channels with widths as small as 200 nm. Seals able to withstand > 50 psia were fabricated employing many types of substrates, including silicon wafer, glass, quartz, PDMS, polystyrene petri dishes, poly(ethylene terephthalate) (PET), polycarbonate (PC), and poly(tetrafluoro ethylene) (PTFE).

Introduction

Microfluidic devices have drawn extensive interest from researchers in the last decade due to their potential application in integrated analytical systems, biomedical devices, high throughput screening, and studies of chemical and biochemical reactions.[1–3] The advantages of miniaturized systems include the reduced consumption of reagents and analytes, low cost of manufacture, low consumption of power, high throughput, decreased production of by-product and increased portability.[1]

Microfluidic system fabrication incorporates many inorganic and polymeric materials. One of the most widely employed materials is poly(dimethylsiloxane) (PDMS).[1,4] Complex layouts of microfluidic channels are created by simply casting PDMS prepolymer onto a silicon master containing the negative image.[4] The elastomeric nature of PDMS can conformally seal minor perturbations in the substrates. However, PDMS also has some drawbacks, including undesirable swelling in many organic solvents, hydrophobicity, and insufficient modulus for fabrication of nanometer scale channels.[5,6]

Polystyrene (PS),[7] poly(ethylene glycol) (PEG),[8] cyclo-olefin copolymers (COC),[9] and poly(methyl methacrylate) (PMMA)[10] have been utilized in microfluidic devices to a lesser degree, because of fabrication difficulties associated with these polymers.[1,4] However, microfluidic devices fabricated with these materials potentially have many desirable attributes, including the reduction of undesirable swelling in organic solvents and decreased sagging when using higher modulus materials. Devices which can be mechanically flexed and which are comprised of smaller channels are also envisioned. Lower fabrication cost is another potential benefit.

One of the chief difficulties of employing alternate polymeric materials is that methods for sealing the microfluidic channels suffer from multiple limitations.[11] Strong seals can be achieved by fusion bonding[12,13] and anodic bonding,[14] but these require high temperatures and high electric fields, respectively, which have the potential to damage substrates with low thermal stability.[11] Surface modification with oxygen plasma[1,4,15,16] or strong acid treatment[15,17] allows formation of Si–O–Si covalent bonds at the interface with Si-containing substrates such as glass, quartz, or PDMS.[1] However, the sealing must be performed in a short period of time following the surface treatment as the modified surface is unstable and rapidly recovers hydrophobicity.[15] In addition, this method is not suitable for carbon-based polymeric substrates.[1] Prepolymer[5,11] or partially cured polymer materials[8] have also been utilized to seal chips, but the efficacy of these techniques is highly system-dependent. Adhesive bonding is one of the most common fabrication methods for

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microfluidic devices.[18] In spite of its ease of use and the resulting high bonding strength, the adhesive bonding process has some critical drawbacks. In this liquid-based process, the adhesive deforms at the curing temperature, often causes clogging of the channel and/or deviation of the shape of channel from its initial design.[19] Additionally, delamination of adhesive layer from the substrates often causes the device failure.[19] To avoid these problems, several requirements on the adhesive layers can be suggested. First, the adhesive should be robustly anchored to the substrate before the sealing process. Second, the flow or deformation of the adhesive should be minimal during the sealing step. Next, the adhesive should conformally cover the substrates. Finally, the adhesive should be sufficiently thin to avoid blockage of the channel. For these reasons, it is essential to obtain conformally coated adhesive layer with nanometer scale thickness, which is firmly tethered on a substrate. However, these goals are extremely challenging to achieve with liquid-phase process, which often results in highly non-isotropic coverage of adhesive films on complex geometries.[20,21]

Conformal coverage of many varieties of organic films at nanometer scale thicknesses has been achieved by initiated chemical vapor deposition (iCVD).[20,22,23] onto geometrically complex substrates including carbon nanotubes,[24] microparticles,[22] electrospun nanofibers,[23] and trenches with high aspect ratio.[20] The iCVD process is performed using room temperature substrates with commercially available cheap monomers.[20,25] Thus, the iCVD surface modification layer can be applied to almost any type of substrate (metals, plastics, ceramics, etc.). Gas phase temperatures are generally less than 300 °C, which is sufficient for activating the initiator but still mild enough to limit thermal decomposition of the monomer.[22,26] Consequently, reactive functional groups present in the monomer are retained to a high degree in the iCVD polymer film.[25] The retention of functional group is critical as these represent the potential adhesive sites.

Herein, we report a novel nano-adhesive layer deposited by the iCVD process. An epoxy-containing polymer, poly(glycidyl methacrylate) (PGMA) was used as a nano-adhesive layer. The PGMA coated substrate was brought into contact with the substrates covered with plasma polymerized poly(allylamine) (PAAm),[27,28] and the ring-opening curing reaction of PGMA layer with conjugate PAAm layer was performed at the temperature of 70 °C to form a strong covalent bond between the two substrates. Both PGMA and PAAm layer could be easily obtained from commercially available cheap monomers. No leakage was observed up to the test pressure of 50 psia from the resulting microfluidic devices.[15]

Results and discussion

Adhesive bonding

Fig. 1 demonstrates schematically the procedure for bonding two different substrates. Channels were pre-patterned on one substrate, and the other substrate was kept flat. In general, the carbon-based polymeric substrates do not require the pretreament. However, in the case of polymeric substrates with low surface energy such as PTFE require the oxygen plasma treatment to activate the polymeric surface for better adhesion.[29] PGMA and PAAm films were deposited on this substrate *via* iCVD and plasma polymerization from commercially available monomers, respectively (Fig. 1a and b). No noticeable delamination was observed in PGMA and PAAm films even after 30 minutes of ultrasonication in water. Strong bonding of adhesive layer on the substrate is essential for this nano-adhesive layer to form well sealed microfluidic devices, since the flaws in the interface between adhesives and substrates has been observed to be one of the major causes of leakage in microfluidic devices.[19]

Finally, the PGMA-grafted substrate was placed on the other PAAm-covered flat substrate. The stacked substrates are lightly pressed ($\sim$ 0.1 bar) and put into an oven at 70 °C for 12 hrs to induce a curing reaction between the epoxy and amine groups in the nano-additive film to complete the bonding of two substrates (Fig. 1c).[30] The ring-opening curing reaction is advantageous for this bonding process because of its relatively fast reaction rate at low temperature (25 $\sim$ 100 °C). In addition, since curing occurs by an addition reaction, no gaseous reaction by-products evolve which might lead to leakage in the bonded substrates.[29,30] Recently, H. Chen *et al.* had also demonstrated a solventless adhesive bonding process using CVD polymer coatings to induce a strong covalent bonding between two substrates.[31] However, their process is a condensation reaction with gaseous water by-product which can induce defects at the bonded interface, or bonding failure. In addition, the curing temperature of 140 °C is higher than the glass-transition temperature (T_g) for many of the broadly used polymeric substrates including PS, PMMA, PET, polyvinylalcohol (PVA), polyacrylonitrile.[32] Using curing temperatures higher than T_g can deform the polymeric substrates and the initial design of channel cannot be retained. In addition, the CVD reactants require special synthesis, which is a barrier to further commercialization.

Many types of polymer substrates can be bonded with the procedure outlined above. For example, a pre-patterned polyurethane (PU) substrate was bonded with a thin PC film (Fig. 2a). A test microfluidic device was fabricated by sealing pre-patterned PDMS substrate with PET film *via* nano-adhesive bonding (Fig. 2b and c). This microfluidic device did not fail even after the repeated flexing and the bondage was stable for a long storage (longer than 100 days). Even when mechanical stress was applied to the point where the polymer substrate failed, the seal remained intact, evidence of excellent bond strength. In addition to the examples shown in Fig. 2, many other substrate pairs were successfully bonded including tissue-culture grade PS (TCPS)–PDMS, PTFE–PDMS, and PC–PET film.

Nano-adhesive films could also be grafted onto inorganic substrates including Si wafer, glass and quartz substrates through a pre-treatment with a vinyl containing silane coupling agent, trichlorovinyl silane (TCVS).[20] The covalently tethered surface vinyl groups of TCVS react with the vinyl monomers used to form grafted PGMA and PAAm layers. Then, as shown in Fig. 1, the nano-adhesive layer was cured to complete the bonding of two inorganic substrates. With this procedure, strong bonding of many organic and inorganic materials pairs was achieved including Si wafer–Si wafer, Si wafer–glass, and Si wafer–PDMS. The observations shown above clearly demonstrate that the nano-adhesive pair of iCVD PGMA and PAAm layers can be applicable to a broad range of organic and inorganic substrate materials, which enables the broad application of many kinds of flexible pre-patterned substrates to microfluidics.

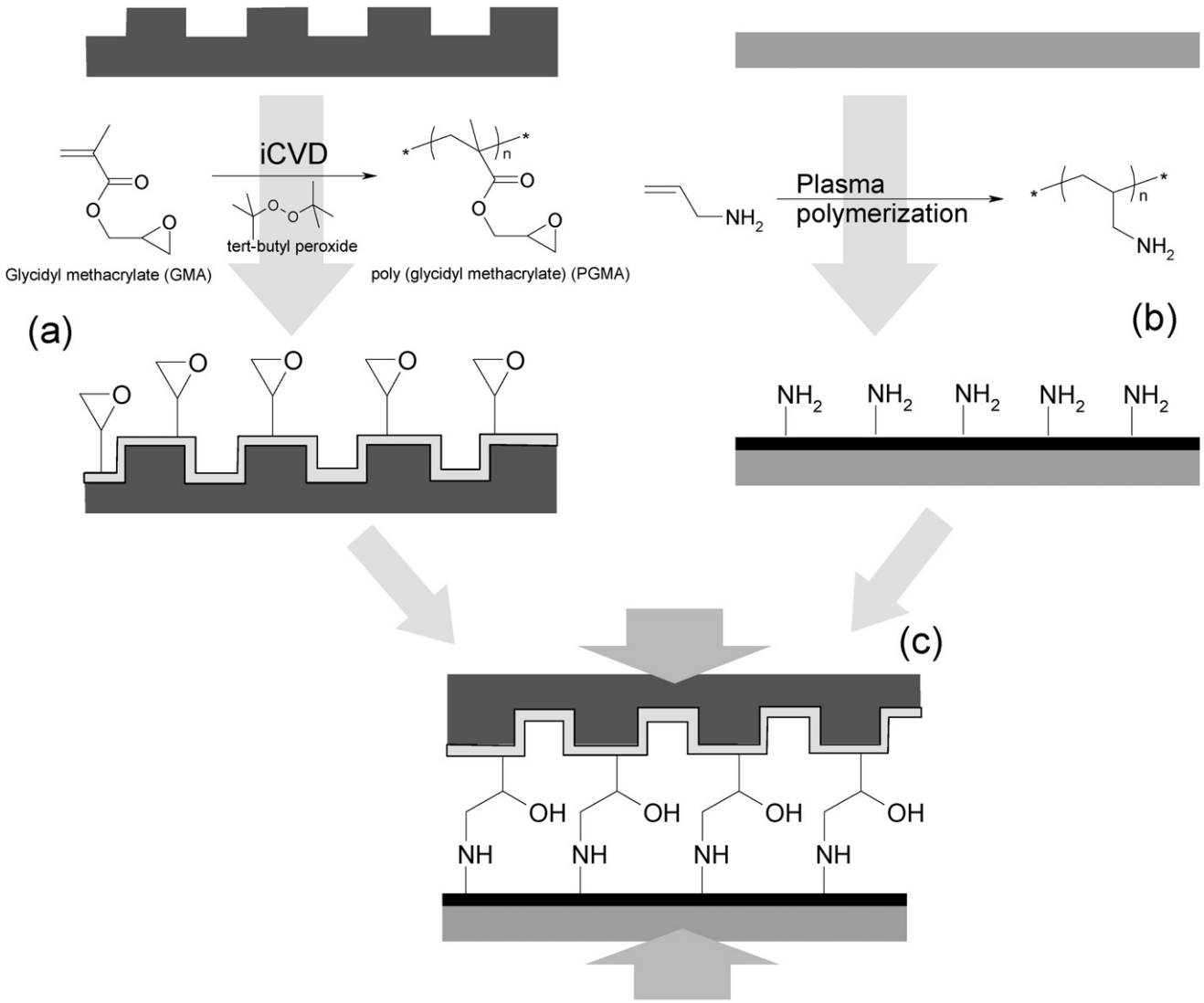

Fig. 1 Schematic of process for nano-adhesive bonding. Deposition of the (a) iCVD of PGMA onto a pre-patterned substrate and of the (b) plasma polymerized PAAm onto flat substrate, followed by curing at 70 °C to complete the bonding of two substrates (c). Note that the final adhesive bonding step produces no gaseous by-products and so avoids any potential issues arising due to outgassing.

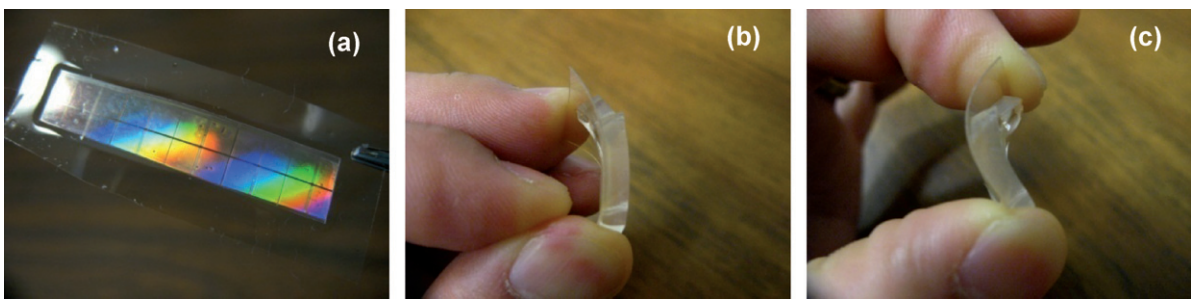

Fig. 2 Pre-patterned PU substrate bonded with PC film (a) and compressive (b) and tensile (c) stresses were applied to a test microfluidic device composed of pre-patterned PDMS substrate bonded with PET film.

Conformal coverage and fabrication of the nano-channel

Trenches (8 μm deep × 2 μm wide) in silicon were used to examine the conformal coverage of iCVD PGMA. Fig. 3a and b demonstrate the cross-sectional SEM images of standard trench covered conformally with PGMA film (a) and the thickness variation of PGMA film (b) on these standard trenches with respect to the position in the trench. The lowest thickness of

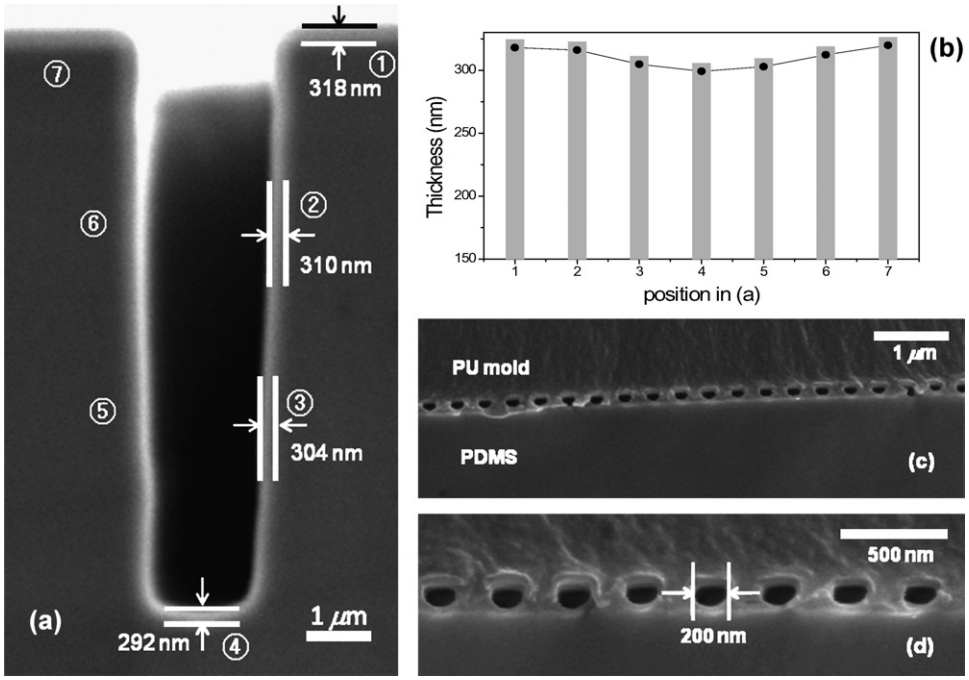

Fig. 3 Cross sectional SEM images of (a) a 318 nm thick PGMA film deposited conformally on a standard trench (2 μm × 8 μm) and (b) the thickness variation of PGMA film with respect to the trench position in (a). Each number in the x-axis corresponds to the numbers in (a). (c, d) a cured iCVD PGMA film on pre-patterned PDMS with a flat PET film coated with PAAm with different magnification. The cross sectional SEM image of (c) and (d) clearly shows that 200 nm-channels at the interface between PDMS and PU film are retained.

PGMA at the bottom of trench was 91% of the thickness at the trench mouth, which clearly demonstrates that PGMA film can conformally cover the trench structure. This conformal coverage is one of the unique properties of the CVD process, which is very difficult to achieve in other liquid phase based methods.[21]

Fig. 3c and d show the cross sectional SEM images of sealed substrates with 200 nm nano-channels. The thickness of PGMA and PAAm layers were 50 nm and 20 nm respectively, and the shape of the resulting nanochannel is essentially unchanged by the curing processes, suggesting that the viscous flow of both PGMA and PAAm is negligible as the movement of the grafted nanolayers is highly restricted.

Bond strength of sealed microfluidic devices

The adhesion strength of nano-adhesive must be sufficient for microfluidic device application.[5,11,15,17,19] Thus, microfluidic devices were fabricated *via* the nano-adhesives bonding procedure (Fig. 1) and tested for leakage with flowing water as the pressure in the microchannel was increased.[15] The PDMS pre-patterned replica was paired with a variety of organic and inorganic flat substrates (Table 1) and in all cases no leakage was observed at the maximum channel pressure achievable by the infusion syringe pump set-up, 50 psia. This value is sufficient for many microfluidic applications[3,6] and compares to the top end of the 30 ~ 50 psia range generally obtainable from PDMS bonding with gaseous plasma treatment.[1,4,15] The film thickness of PGMA was varied from 50 nm to 300 nm maintaining the thickness of PAAm to 50 nm, and the adhesion strength was practically identical. To test stability of the adhesive functional groups (Fig. 1a and 1b) grafted to surfaces of a PDMS replicate and PET flat substrates were stored for three months before performing the curing step. The resulting channel was leak-free at a pressure of 50 psia. Thus, the nanoadhesive bonding method renders the immediate sealing unnecessary, which is in sharp contrast to the requirements for the well-established gaseous plasma method.[15] The stability of the sealed device itself was also monitored. The bond strength of the test device exceeded 50 psia after three months of storage.

Table 1 Summary of leakage test of microfluidic devices with PDMS and various kinds of substrate materials at the channel pressure of 50 psia

PDMS bonded with…	At 50 psia of channel pressure
Si wafer	No leakage
PTFE	No leakage
PS Petri dish	No leakage
PC film	No leakage
PET film	No leakage

Experimental

Plasma polymerization of PAAm[33]

Plasma polymerized PAAm film was obtained in a parallel plate chamber with 150 mm diameter electrodes. Allylamine (Aldrich, 99%) was purchased and used without further purification. First, if required, the substrates were 100 W of oxygen plasma treated for 60 s at 50 mTorr of oxygen. Immediately after the oxygen plasma treatment, the plasma polymerization was initiated by applying 5 W of 13.56 MHz power source with continuous RF discharge. The process pressure was 100 mTorr, and allylamine

was introduced at a flow rate of 20 sccm. After 10 minutes, plasma polymerized PAAm film was obtained with a thickness of 100 nm.

iCVD of PGMA

The procedure of the iCVD process was described in detail elsewhere.[26] Before the iCVD process, if required, the substrates were oxygen plasma treated, as in plasma polymerization. The plasma treated substrates were immediately transferred to the iCVD vacuum chamber. GMA (Aldrich, 98%) and tert-butyl peroxide (Aldrich, 98%) were purchased and used without further purification. GMA and initiator were vaporized at room temperature and introduced into the iCVD chamber at a flow rate of approximately 2.95 sccm and 1.75 sccm, respectively. The flow rates were controlled with MKS 1490A mass flow controllers. The polymerization reaction was initiated with the resistively heated tungsten (W) filament at 220 °C. The process pressure of 200 mTorr was maintained by a butterfly valve with PID control (MKS 248 flow control valve). Film thicknesses were monitored *in situ* by interferometry; approximately 200 nm of the PGMA film was deposited in 5 min.

Silane treatment for surface grafting of inorganic substrates

0.5 ml of TCVS (from Aldrich, 97%) was placed in the dessicator. Oxygen plasma treated substrate—Si wafer, glass, quartz, and PDMS—was exposed to TCVS vapor at 25 °C for less than 5 minutes. The process pressure in the dessicator was 100 mTorr. Exactly the same iCVD and plasma polymerization conditions were applied to the silane treated substrates for grafted PGMA on the substrates.

Curing nano-adhesive layers

PGMA-coated substrates were bound to PAAm-coated substrates to seal the substrates. A PGMA grafted substrate was gently placed on the PAAm grafted substrate and lightly pressed (~0.1 bar) to ensure the contact of the two substrates. The bonding was completed by placing the coupled substrate into an oven at 70 °C for 12 hrs for curing the nano-adhesive layer.

Fabrication of test microfluidic devices and leakage test

Linear microfluidic channels were prepared in PDMS by standard soft lithographic techniques. Sylgard 184 (Dow Chemical) was cast over a silicon wafer mold prepared by standard lithographic methods, degassed under vacuum and cured overnight at 70 °C. The cured PDMS was peeled off the master, individual devices separated and fluidic connections were punched. Channels were straight and rectangular: 200 μm wide, 75 μm high. A nano-adhesive PGMA layer was applied onto this PDMS microfluidic channel, as described above. Separately, PAAm deposited Si wafer, PTFE, TCPS petri dish, PET, and PC film was prepared and the curing procedure completes the test microfluidic devices. The bond strength of nano-adhesive was tested by performing burst pressure testing. The channel was filled with water and the end of the channel closed. The inlet was attached to a water chamber pressurized with argon using a pressure regulator. The pressure was slowly increased until the channel was visibly observed to burst, leaking water out the side of the device, and the pressure at which this occurred is the reported burst pressure.

Microscopy

For the cross sectional SEM, the nano-channel samples were cryomicrotomed and the images were obtained with Environmental Scanning Electron Microscopy, (FEI/Philips XL30 FEG ESEM).

Conclusions

A novel nano-adhesive bonding process was demonstrated for creating microfluidic channels capable of withstanding pressures of higher than 50 psia. The nano-adhesive film showed strong and conformal adhesion on the substrates of complex geometries. The thickness of the nano-adhesive layer was sufficiently thin (<200 nm) so as to limit its infiltration into the microfluidic channel. Channels were successfully fabricated with this nano-adhesive film from many different organic and inorganic substrates including Si wafers, glass, quartz, PET, PC, PS, and PTFE, which clearly demonstrates that the method is fully compatible with various flexible substrates. To achieve these results, grafted iCVD PGMA was conformally coated on pre-patterned trenches and plasma deposited PAAm was applied to the flat surfaces. These individual surfaces could be stored for at least three months before sealing. Sealing was achieved by placing the coated pieces face to face and then curing at 70 °C. No blockage of the microfluidic channels by the adhesive was observed after the curing process. Hence, channels as small as 200 nm in width could be fabricated. High bonding strength of the fabricated channels was validated for at least three months. Moreover, the leftover amine and epoxide functionalities inside of the channel wall can also be utilized for further independent functionalization.[31] Epoxy groups from the sidewall of channels can be conjugated with amine compounds and amine groups at the flat side can also be separately functionalized with N-hydroxysuccinimide (NHS)-tethered compounds. Therefore, the inside of the channel can be independently modified, which potentially enables selective functionalization of the channel wall. Hence, a variety of active moieties, such as sensing molecules, electrophoretic buffers, and other active species can also be bound to the walls for specific applications.

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