INTEGRATED POLYMETHYLMETHACRYLATE - POLYDIMETHYLSILOXANE DEVICES FOR MICROFLUIDIC APPLICATIONS

by

Rahul Subhash Sonkul

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Rahul Subhash Sonkul

This thesis has been read by each member of the following supervisory committee and by majority vote has been found to be satisfactory.

08/19/2009 _____

08/19/2009 _____
Daniel Adams

08/19/2009 _____
K. Larry DeVries

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I have read the thesis of Rahul Subhash Sonkul in its final form and have found that (1) its format, citations, and bibliographic style are consistent and acceptable; (2) its illustrative materials including figures, tables, and charts are in place; and (3) the final manuscript is satisfactory to the supervisory committee and is ready for submission to The Graduate School.

Date

isory Committee

Approved for the Major Department

Tim Ameel
Chair/Dean

Approved for the Graduate Council

Charles A. Wight
Dean of The Graduate School

ABSTRACT

Polymeric materials are widely used in manufacturing of microfluidic devices, and polydimethylsiloxane (PDMS) is a commonly used polymeric material in research laboratories due to its potential for rapid prototyping. However, PDMS is less desirable for mass production applications as it requires considerable processing time. With the development of micro/nano imprinting techniques, microfluidic structures can also be rapidly imprinted on other polymers such as Poly(methyl methacrylate) (PMMA) and polycarbonate using molding technologies. Even though PMMA is the material of preference for our application--a nanoporous membrane-based RNA extraction system--a PDMS membrane is an integral part for the functioning of pneumatically actuated valves and pumps. Since there is no well-established method that exists for bonding PDMS to PMMA, an attempt has been made in this thesis to increase the functionality of PMMA microfluidic parts.

The work can be classified into two main categories: manufacturing of hot embossed plastic parts and development of bonding technology for PDMS and PMMA. To prepare the PMMA parts, a hot embossing template of brass is designed and manufactured for imprinting the microfluidic parts. Functional silanes such as Amino-Propyl-Tri-Ethoxy-Silane and Bis-Tri-Methoxy-Silyl-Propyl-Amine are used to obtain an irreversible chemical bond between PMMA and PDMS, which cannot be achieved effectively with existing bonding practices such as glow discharge and thin layer PDMS adhesive.

The silane bonding method requires tight control of a number of variables to obtain a leak proof bond. Increased microscopic scratches on the PMMA substrate results in more surface area for bonding, which in turn helps in increasing the bond strength. A small variation in the proportion of adhesion promoters used for bonding varies the bond strength considerably. The application of pressure, curing time and cleanliness of surfaces also plays an important role in bonding. Short beam shear strength tests and leak tests were performed repeatedly to check the strength and quality of the bond, which are found to exceed the requirements based on the operating conditions of the microfluidic chip.

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CHAPTER 1

INTRODUCTION

The microelectromechanical system (MEMS) field has seen significant research and development with a huge market potential in the last two decades. A variety of MEMS-based devices are used in automobile, electronics, aerospace, semiconductor, and biomedical applications [1-3]. The devices include pressure sensors, accelerometers, sensors, pumps and valves for fluid flow control. The micromachined silicon-based pressure sensor is considered to be the very first and most successful commercial application of the MEMS technology as of now [4].The investment in MEMS-based products has gone up from few million to several billion dollars in the last two decades [5]. The microfluidic applications of MEMS technology came into existence in the early 90s, though a few products were present in late 80s as well [6]. These microfluidic devices are used for fluid flow analysis, chemical, biological and medical applications [7-9]. In addition, microfluidic devices also find application in the semiconductor processing industry [10]. Biomedical applications are the most researched among the above mentioned applications of microfluidic devices.

MEMS-based product demand is increasing at a considerable rate and most of the future growth is expected in case of the MEMS-based microfluidic disposable devices, which are currently in their early stage of development [11]. Use of MEMS technology in nonconventional energy storage systems such as nuclear micro- batteries, micro-fuel cells

and micro-super capacitors are increasing at an unprecedented rate [12]. Though applications involving DNA detection systems and other microscale genetic analysis devices are being commercialized now, the neuroscience and neural instruments are still in the development stage, which also has a huge future market [13]. The overall market for the MEMS products was $8 billion in 2005. It is expected to increase to $40 billion by 2015 [11].

The importance of biomedical instrumentation has increased to a great extent in recent years, which has led to growth in the use of microfluidic devices [14]. Some of the notable examples are (i) real-time feedback obtained from the MEMS-based devices to simplify surgical tasks and to reduce the risk for doctors and surgeons [15]; (ii) DNA extraction, RNA extraction, drug delivery, cancer diagnosis and dialysis equipment [16-17]; (iii) microfluidic drug delivery systems designed to deliver precise quantities of drug at specified locations and at the required time [14].

MEMS-based microfluidic systems possess unique attributes such as small size, reduced dead volumes when using expensive liquids or gases and very short analysis times [18-19]. The low volume of the reagents used during analysis produces a low amount of waste, which in turn leads to lower environmental impact. The testing devices are disposable in most applications and require no reprocessing and recalibration. Certainly the overall operational cost of the microfluidic systems comes down to a great extent, which should make these devices more popular. The microfluidic systems can be easily coupled with sensing devices, which help in effective analog or digital control of the system. The functionality of the microfluidic systems is improved with the absence of moving parts in some systems. This attribute also eliminates typical errors involved due

to the friction and inertia of moving parts. Other systems show no deviation in the system response in harsh environments [20]. All of these advantages result in increased life cycles for microfluidic systems, which is not typical for a mechanical system.

In spite of the considerable development in the MEMS field, packaging remains the most common concern in any MEMS-based system. In some cases, the interface required with the environment for sensing, actuation or fluid flow makes the packaging task more difficult. On the other hand, some applications require complete isolation from outside exposure [21]. Interconnection and leakage prevention are important concerns in microfluidic systems. Packaging typically dominates the total system cost, which alone may cost more than 75% or more of the total cost of the system [22]. More precise and faster packaging techniques will help to bring down the total cost of MEMS-based systems and will open the market for new MEMS products [23].

Materials for Microfluidic Devices

Polydimethylsiloxane (PDMS)

The materials used in the fabrication of microfluidic chips range from different polymers to glass to silicon. The most commonly used polymeric material in research laboratories is PDMS. PDMS has a number of advantages over the other polymeric materials such as ease in handling, no requirement of clean room facilities and low processing time for small scale manufacturing [24]. However, the processing time required for the PDMS is comparatively longer than the other polymeric materials such as PMMA and polycarbonates (PC). Hence it is less desirable for the mass production of disposable devices.

Pyrex Glass

Pyrex glass wafers can also be used for patterning and assembling of microfluidic channels [25].Microstructure patterning on a pyrex glass wafer can be done using RIE or micro tool machining processes. In micro tool machining process, wafers are patterned with a tool tip in presence of NaOH. Spark assisted chemical etching at the tool tip patterns microstructure on a glass surface. A wire electrodischarge grinding machine is used for determining the tool tip path [26].

Silicon

Silicon (Si) is the most important material in the development of MEMS technology. It was the very first material used in the design of a MEMS based pressure sensor. There are many techniques available to generate any kind of fluid channels on silicon wafers. Microfluidic channel dimensions from a few millimeters to several nanometers can be manufactured on silicon wafers. Silicon, however, has its limitations when it is considered as a possible material in the fabrication of microfluidic chips. A common concern using the silicon is that it requires clean room facilities, which add a huge cost in the development of any microfluidic chip [27]. Additionally, it requires a separate mask design for any new pattern and a series of operations such as lithography, etching, etc. All these processes require a long time in any development activity and this makes silicon an incompatible material for rapid prototyping of microfluidic chips. Also the brittle crystal properties of silicon do not easily accommodate moving parts in the microfluidic system [28].

Microstructure Molding Methods

Laser Cutting

In laser micromachining, a fluidic structure is cut on a thin plastic or metallic sheet using lasers, or it can be used to make molds for PMMA structures using hot embossing. In this case, the structure is used as a mold to repetitively produce PDMS microfluidic parts [29]. In another approach the laser cut channels are glued to a metallic support and then used as a hot embossing mold to imprint channels on PMMA or polycarbonate sheets as shown in Figure 1. The drawback of this method is that it cannot be used at higher pressures and temperatures. This mold does not last long since the channels are not an integral part of the rigid mold.

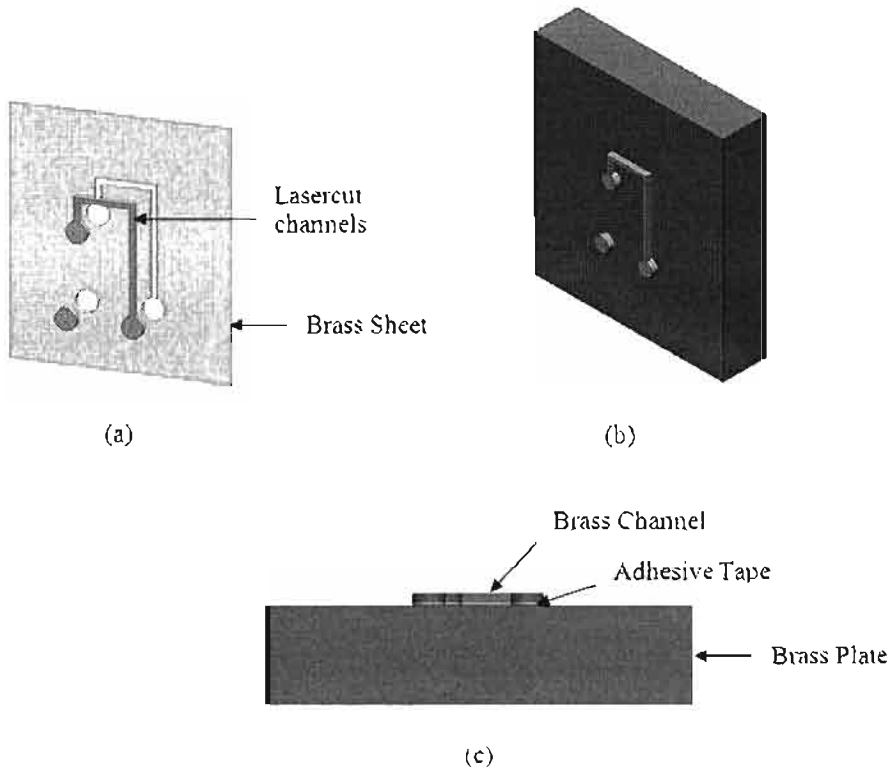

Figure 1 Hot embossing stamp made from the laser cut channels. Kapton adhesive tape is used to bond brass channels to a thick brass plate

Xurography

Microfluidic channels on PDMS can be imprinted with the use of a technique called soft lithography. Xurography is a technique for making inexpensive molds, which uses a single side adhesive tape (Scotchcal Tape) as a mold material [30]. The microstructures are cut using a plotter and stuck to any plane surface that can be used as a mold. Structured microfluidic PDMS parts can be easily bonded to each other since only oxygen plasma or corona treatment is required to activate the surface for bonding. Even Xurography is a rapid prototyping method but may not be useful for mass production of microfluidic devices. The molds made using this technique do not last long.

Lithography

In another method a polymeric master replication technique is used for the mass production of PDMS devices [31]. This can be considered as a two-stage mold manufacturing technique. In this technique, a glass slide is negatively patterned using a wet etching method. The glass slide is then used to replicate the microscale patterns on a number of PMMA sheets using hot embossing and these PMMA parts are used as molds to produce PDMS devices subsequently.

Alternatively a PDMS mold can also be used as an embossing tool to imprint the microchannels on a PMMA sheet. In this method, a negative photoresist SU-8 is used to create the structures on a silicon mold. These primary molds are used to make PDMS parts and finally the PDMS parts are used as an embossing die for the PMMA parts. The PMMA parts are heated in vacuum above the glass transition temperature in contact with the PDMS structures. The glass transition temperature of PDMS is much higher than the PMMA, so it does not melt, but it does initially deform before regaining its shape in the

liquid PMMA nearby. An applied vacuum pushes PMMA against the PDMS, hence the fluidic structures are replicated on PMMA parts [32]. The soft tool material and increased cycle time reduce the mold life considerably. The drawback of this method is that it is valid only when a few parts are needed.

Electron Beam Lithography

This method used for the manufacturing of disposable microfluidic devices is based on electron beam lithography. Patterns are fabricated on a silicon mold using a combination of electron beam lithography and reactive ion etching [33]. The silicon mold developed using the above technique can produce the channels in submicrometer to nanometer range and the mold can be used to hot emboss a number of parts.

Bonding Techniques

Thermal Bonding

Thermal bonding is a highly developed and well established method available for bonding similar polymeric materials. This method allows an irreversible bond when both the mating parts are heated above the glass transition temperature in the presence of high pressure. Typically the microfluidic structures on PMMA are obtained using the hot embossing process. These hot embossed parts are then exposed to oxygen plasma for a short period of time in order to make the bonding surfaces hydrophilic [33]. Finally the mating parts are kept in contact with each other at glass transition temperature and at a pressure of 100 bar as shown in Figure 2 to obtain a thermal bond between them. The applied pressure and temperature are inversely proportional in this bonding process.

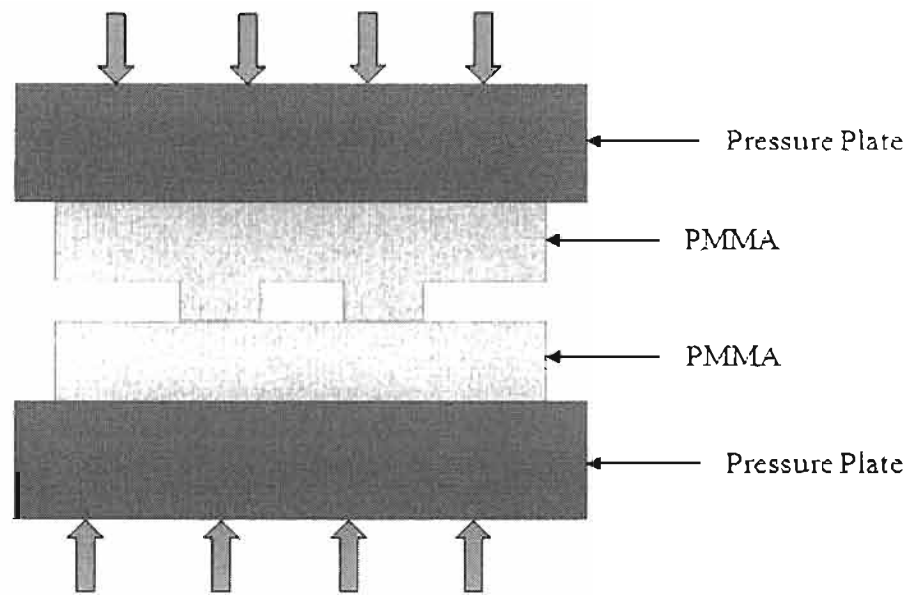

Figure 2 Schematic representation of thermal bonding process.

Ultrasonic Bonding

Ultrasonic bonding is a solid phase bonding process in which one or both of the mating parts are softened by the application of ultrasonic energy [34]. The ultrasonic energy applied to the metal creates dislocations in the part causing higher density and mobility with a reduction in the shear stress required for plastic deformation. The compressive load applied pushes contaminants out leaving a very clean contact surface. The heat generated during the scrubbing of two clean surfaces helps the diffusion at contact area to facilitate bonding.

Glass-PDMS-Glass Bonding

This is a two-stage bonding process in which the microfluidic structures are patterned on a glass slide using SU-8 or AZ9260 photoresist and PDMS. First, the photoresist is applied on the glass slide and UV light is exposed through the patterned chrome mask [35]. In the next step, PDMS is spin coated on the photoresist coated glass slide. An RIE etch is done to remove the excess PDMS layer until it can be lifted off and the remaining photoresist is dissolved using acetone. The outer surface of the PDMS is then exposed to oxygen plasma, which makes it hydrophilic and leaving dangling negative OH silanol groups. Finally, the structure is sandwiched with the other glass slide to create a permanent bond as shown in Figure 3.

Solvent Assisted PMMA-PDMS-PMMA Bonding

Solvent assisted PMMA-PDMS-PMMA bonding is used to obtain a bond between two different polymeric materials. A PDMS membrane can be sandwiched between two PMMA substrates by using this method. This technique of obtaining an irreversible bond is similar to the technique developed in this thesis work. Acetonitrile is used for the surface functionalization of PMMA and PDMS film is compressed against it [36]. Similarly the other PMMA part is bonded to the PDMS film to obtain the entire structure.

Microwave Welding

Microwave welding can be used to bond two microfluidic channel parts. Bonding of the PMMA substrates takes place due to localized heating at the interface. Microwave energy of 300 W is applied for 15 sec during the bonding process which melts and bonds the PMMA at interface [37]. The temperature variation is observed from 40^0C to 350^0C

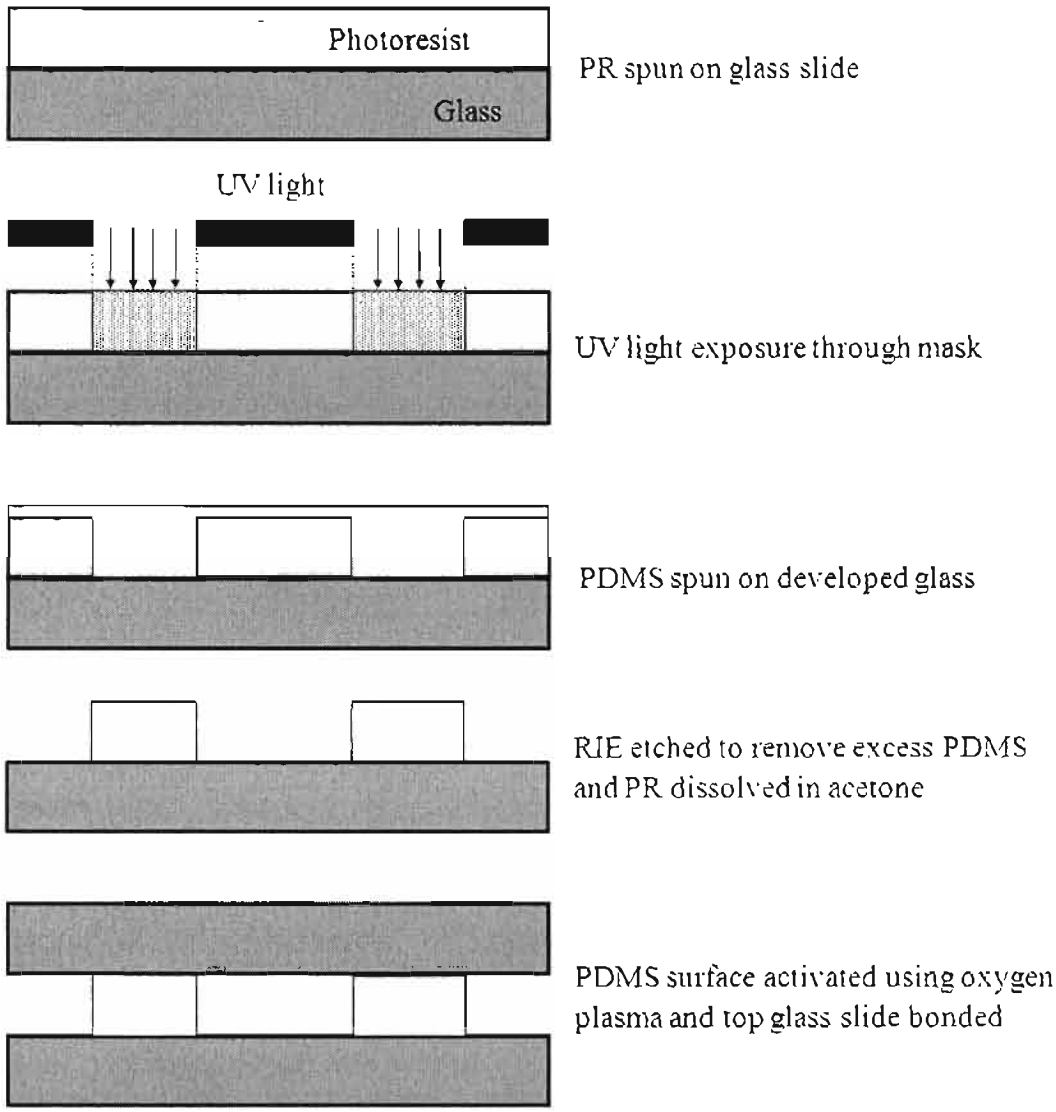

Figure 3 Schematic representation of the steps involved in glass-PDMS-glass bonding.

at the interface which is much higher than the glass transition temperature of PMMA. Since the microwave energy is applied for a very short time, no large deformations are observed at the channel structures.

Motivation

Significant progress has been made in the microfluidics field. However, cost effective manufacturing of disposable microfluidic devices still remains a common concern.

In this thesis work methods for combining the functionality of PDMS with the ease of manufacture of PMMA are developed and presented. In particular, the high flexibility and gas permeation capabilities of PDMS are desired, but making devices completely out of PDMS is expensive and the manufacturing process is relatively slow due to the long curing times of PDMS. PMMA can be hot embossed or injection molded, but has limited flexibility and is limited in terms of gas permeation (which is usually a desirable property). To gain the advantage of both materials, a method to bond components made of each material separately needed to be developed. Specifically, we developed a method for bonding PDMS membranes across PMMA microfluidic structures. The existing bonding techniques available work poorly for the manufacturing of integrated PDMS-PMMA devices and there remains major room for improvement. Therefore a new bonding technique is developed for the effective bonding of PDMS to PMMA that gives irreversible covalent bonds between the two different polymeric materials.

Scope of Work and Significance

This project focuses on attaching PDMS membranes to PMMA based microfluidic devices. To accomplish this, a CNC machined hot embossing die made out of brass was

used to make dozens of PMMA parts (and could be used to make thousands or even millions), and PDMS was bonded to the PMMA parts. A PDMS membrane used in the PMMA-based microfluidic device increases the device functionality and makes a move forward in the development of integrated microfluidic devices. Also, the bonding technique can effectively be used in the packaging of MEMS-based sensors where PDMS can be used as a cushioning material. Dead end channel tests and the short beam shear tests were performed on the PMMA-PDMS-PMMA integrated devices and the bond strength was found to be far superior to existing bonding methods. The biocompatibility of the polymeric materials makes them very useful for medical applications. Sudden variation in the working environment does not affect the device functionality and it can be used for the remote applications also.

Chapter Outlines

The thesis work is organized as follows. The first chapter states the importance of MEMS microfluidics. It also mentions the statistics of the vast growing MEMS industry and the potential research areas for the MEMS-based microfluidic systems. Later, it describes the materials used for the manufacturing of disposable devices, methods of manufacturing of hot embossing dies, and bonding and packaging methods. This chapter also summarizes difficulties encountered in the cost effective manufacturing of disposable devices. The second chapter describes the steps involved in the fabrication of microfluidic devices. This chapter describes the brass hot embossing die manufacturing, hot embossing of PMMA wafers and the PMMA-PDMS-PMMA bonding procedure. The third chapter is a paper that is in preparation for publication and describes the main

results for the thesis work. It also describes in detail the newly developed PMMA-PDMS-PMMA bonding method. This chapter also describes the experimental procedure in detail to measure the bond strength of the PMMA-PDMS-PMMA bonding technique and a dead end channel test to find leakage in the system. The last chapter is a summary of findings and potential future work related to this research field.

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CHAPTER 2

FABRICATION

Material Selection

Most polymeric materials are biocompatible or can be modified to be biocompatible. Therefore it is an important category of materials used for microfluidic devices and their use is continuously increasing in medical applications. These materials involve PMMA, polycarbonate, and PDMS. To avoid sample contamination from one run to another run, microfluidic devices used in most of the biomedical applications are made disposable [1]. The advantage of using polymeric materials in the fabrication of microfluidic chips is that the parts can be produced at considerably less cost compared to silicon or glass, in addition to chemical stability and biocompatibility. Currently PDMS cannot be used in commercial applications because of the time required in manufacturing these devices. PMMA and polycarbonates are widely used in the mass production of disposable microfluidic devices. The various techniques used in the production of microfluidic devices are laser micromachining, micro-injection molding, laser ablation, lithography and hot embossing. Hot embossing can be considered as the most cost effective method since it takes a few minutes to produce the hot embossed parts and also it does not require any clean room facility for the mold manufacturing.

Hot Embossing

In this work, a hot embossing die (stamp) is designed that has the patterns for a microfluidic system and silica filter housing on it. A 4" stamp contains one set of microfluidic parts and three sets of silica filter parts. Brass is selected as the material for the hot embossing stamp because of its easy machinability. A three-dimensional SolidWorks sketch is used as an input for the FeatureCAM software, which generates the program for the CNC machine. The FeatureCAM software itself decides all the tools, speeds and feeds to suit the design requirements.

This hot embossing stamp is then used by EV Group at their manufacturing facility and they decide the baseline process parameters such as temperatures and pressures required during the bonding cycle. A semiautomated wafer bonding system is used for the hot embossing as shown in Figure 4. Also optical microscopy is used to check the variation in imprints on PMMA substrates at different process parameters.

Figure 4 Semiautomated wafer bonding system is used for the hot embossing of PMMA parts

Once the imprinted PMMA wafers were received back in Utah, they were diced using a DISCO dicing saw at the University of Utah microfabrication facility. Diced part images are shown in Figure 5. The jig saw is also used for dicing some of the wafers. It has been found that the jig saw diced part edges are uneven and rough.

A detailed discussion of number of steps involved in hot embossing from stamp design to dicing of PMMA parts is included in Chapter 3.

PMMA-PDMS-PMMA Bonding

Bonding of microfluidic parts is considered to be an important and critical step in the complete production cycle of microfluidic chips. Solvent assisted PMMA-PDMS-PMMA bonding techniques are the only methods that can be used in this project among all the methods discussed in Chapter 1, because it allows bonding of a PDMS membrane to PMMA part. In this method, paraffin wax is used as a sacrificial material to prevent the flow of bonding reagents into the channel cavities. Pumps and mixer cavities present in the microfluidic chip do not allow use of sacrificial layers in them. Sacrificial materials cannot be easily removed from the pump and valve cavities once the bonding is done.

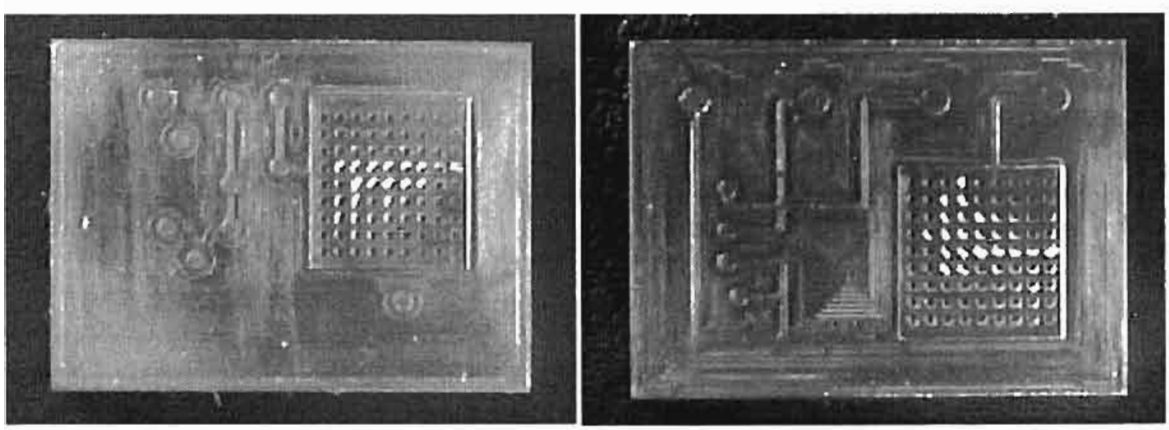

Figure 5 Microfluidic parts diced using Disco dicing saw

Therefore this technique does not work well for our microfluidic chip application. A new bonding technique for the bonding of different polymeric materials is developed in this thesis. The complete bonding cycle is discussed in detail in Chapter 3. In general, the silanes such as APTES and BTMSPA are used for surface functionalization. The use of silanes and corona treatment makes the PMMA surface hydrophilic leaving OH- for surface groups for covalent bonding. Similarly the corona treatment performed on the PDMS membrane makes it hydrophilic and allows for an irreversible bond between PDMS and PMMA. The bonded part is clamped between 2" clamps to obtain complete bonding at the contact surface and it also helps in removing voids present at the contact area.

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CHAPTER 3

INTEGRATED PMMA - PDMS DEVICES FOR MICROFLUIDIC APPLICATIONS

Abstract

Polymeric materials are widely used in manufacturing of microfluidic devices, and polydimethylsiloxane (PDMS) is a commonly used polymeric material in research laboratories due to its potential for rapid prototyping. However, PDMS is typically considered less desirable for mass production applications as PDMS requires considerable processing time. Using micro/nano imprinting techniques, microfluidic structures can also be rapidly imprinted in other polymers such as poly(methyl methacrylate) (PMMA) and polycarbonate using molding technologies. Even though PMMA is the preferred material for our application--a nanoporous membrane-based RNA extraction system--a PDMS membrane is required for the functioning of pneumatically actuated valves and pumps. Since there is no well-established method for bonding PDMS to PMMA, this paper presents a method to bond PDMS to PMMA and thereby increase the potential functionality of PMMA microfluidic parts.

The work can be separated into two sections: manufacturing of the hot embossed PMMA parts and development of a bonding technology for PDMS and PMMA. In the first section, we describe a brass hot embossing template that is designed and manufactured for imprinting the microfluidic parts. In the second part, functional silanes

such as AminoPropylTriEthoxySilane (APTES) and Bis(TriMethoxySilylPropyl)Amine (BTMSPA) are used to obtain an irreversible chemical bond between PMMA and PDMS, which cannot be achieved effectively with existing bonding practices such as glow discharge or PDMS overmolding.

The proposed bonding method was found to be quite successful, but the method requires tight control of a number of variables to obtain a leak proof bond. Adding microscopic scratches to the PMMA substrate results in more surface area for bonding, which in turn helps increase the bond strength, but this can also increase the likelihood of leaks through the microscratches. A small variation in the proportion of adhesion promoters used for bonding varies the bond strength considerably. The application of pressure, curing time and cleanliness on the surfaces also plays an important role in the bond strength. Short beam shear strength tests and leak tests were performed repeatedly to check the strength and quality of the bond, which are found to exceed the requirements needed for most microfluidic devices.

Introduction

The use of microfluidic devices in various applications has increased tremendously over the last several years and this increase is expected to continue in the future. These microfluidic devices are used in a variety of applications including: fluid flow analysis, sensing, chemical, biological, and medical applications [1-3]. On the commercial side, inexpensive, disposable biomedical devices are in great demand due to the miniature size of the devices, the limited consumption of expensive liquids or gases, and the typically short time required to perform various analyses [4-6]. Since polymeric materials are

typically biocompatible and limited surface treatment is required prior to their use, these materials are widely used for the manufacturing of disposable devices. PDMS, because of its simple processing, flexibility, transparency, generally inert character, and ability to replicate any shape, is a preferred material among the polymeric materials for rapid prototyping. However, the cost and manufacturing time for producing PDMS devices limits the usage of PDMS in mass production. Alternate polymeric materials such as PMMA or polycarbonate can be easily used in mass production of microfluidic devices, as they are thermoplastics that can be readily embossed or injection molded.

For moderate volumes hot embossing is a cost effective method for imprinting microchannels on polymeric substrates [7]. A template for hot embossing can be manufactured from quartz [7], nickel, silicon [8], epoxy resin [9], PDMS [10] and other materials. Since quartz and silicon are brittle materials, molds made from these materials have limited life and in some cases these materials do not last for more than five hot embossed parts [9]. Epoxy resin is more durable than the glass or silicon materials, but it has a low glass transition temperature (i.e., 180^0C), which limits the use of epoxy resin molds at higher temperatures. In this paper we have used a brass substrate as a template material for hot embossing because it is robust and easy to machine. The brass template is capable of producing several thousand hot embossed parts without sacrificing device functionality. Other techniques available for manufacturing hot embossing molds are photolithography and etching [8], laser micromachining [11], laser ablation [12], anodic aluminum oxide processing with electroforming [13], and nickel electroplating [9]. However, all these processes require microfabrication and clean room facilities resulting in considerable costs for manufacturing when compared to brass hot embossing molds.

An alternative mold manufacturing method that eliminates the microfabrication and clean room costs is CNC machining, which can easily pattern fluidic channels down to about 100 μm dimensions on a brass plate. CNC machining is not capable of producing channels in the nanometer range, but close tolerances can be achieved on fluidic channels whose dimensions are about 100 μm. All the channel dimensions of the microfluidic parts used in this paper are in the range of 100 to 300 μm (channel width and depth), and are generated using an accurately machined brass template for hot embossing.

The sequence of operations involved in modern microfluidic devices - for example, a chip designed to take a sample from cell lysis to RNA extraction on a single biochip - makes the chip design very complex. These complex devices include onboard valving and pumping at multiple locations. A PDMS membrane can be used for opening and closing of valves and it also acts as a diaphragm in pump operation [14] for many microfluidic devices made in PDMS. The requirement of an elastic membrane for the operation of pumps and valves makes the PDMS (or similar elastomers) an important material in what might otherwise be a PMMA-based microfluidic system, and necessitates a PDMS-PMMA bonding technique.

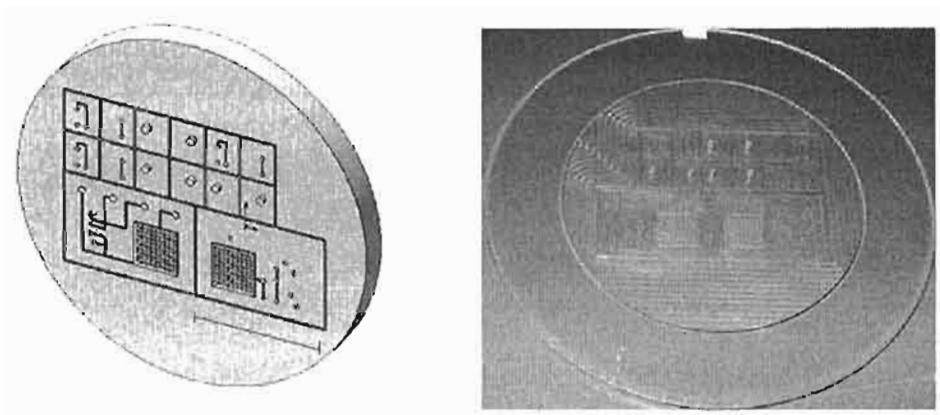
PMMA-PMMA bonds can be achieved with microwave bonding [15], thermal bonding in water [16] and vacuum assisted thermal bonding [17], but these bonding methodologies do not work when using dissimilar polymeric materials such as PMMA and PDMS. A PMMA-PDMS-PMMA bond can be obtained by directly spin coating PDMS on a PMMA substrate and allowing it to cure for several hours [18]. Limitations of using such an approach are: the PDMS membrane cannot be transferred from one surface to another without tearing, the bond is not completely irreversible and the bond is

not strong enough to withstand high pressures. A bond between PMMA-PDMS can be obtained by applying high pressures at room temperature, but reported data seems to be insufficient to gauge the effectiveness of the technique [19]. Recently a low temperature surface functionalization method using air plasma and acid hydrolysis was reported to improve the bonding between PMMA and PDMS [20]. A PDMS membrane was spun on one of the mating microfluidic parts, which had only the valve ports and no channels, but our microfluidic system has channels on both of the mating parts and this technique cannot be used for many applications. Another group reported the surface pretreatment of PMMA using silanes to create an irreversible bond between PMMA and PDMS [21]. The functional silanes (APTES, BisTriEthoxySilylEthane (BTESE) and BTMSPA) were used for surface functionalization. In this paper, a mixture of APTES and BTMSPA diluted in isopropanol is used for the surface pretreatment of the PMMA substrate. The bonding between PDMS and PMMA is facilitated by the availability of silicon-carbon bonds due to the presence of adhesion promoters. A surface corona discharge treatment was also performed on both polymeric materials (PMMA and PDMS) to assist in the creation of covalent bonds between each polymeric surface. The present work differs from the previous reports as it (i) uses only APTES and BTMSPA as the adhesion promoter, (ii) includes sanding of the substrates to create microscratches which increase the surface area for bonding, (iii) includes extensive characterization, and (iv) applies the bonding of not just a PDMS membrane but also of PDMS manifolds to PMMA successfully.

Fabrication

Hot Embossing

A conventional CNC machine (VF-E, HAAS Automation Inc. CA) was used to manufacture a hot embossing stamp containing some representative microfluidic structures, including pumps and valves. A three-dimensional sketch drawn in SolidWorks 2007 SP4.0 (SolidWorks 2007 SP4.0, Dassault Systemes, USA) was used as an input for the FeatureCAM software (FeatureCAM 2008, Delcam,USA) which directly generates the tool path for a CNC machine and also decides the other machining parameters. Close tolerances of 300±3 μm are achieved using CNC machining. Brass was selected (12.5 mm thick) as a stamp material because of its easy machinabilty and low cost. This template made from the brass material as shown in Figure 6 (a) was used for imprinting microchannels into 2 mm thick PMMA substrates [Figure 6 (b)].



(a) (b)

Figure 6 Drawing of the brass template and image of the actual hot embossed wafer (a) Drawing of the brass template that shows microchannels, membrane cavities and pump architecture for the microfluidic chip. Scale bar is 36 mm. (b) Image of the actual hot embossed wafer.

Hot embossing was performed at EV group (Tempe, AZ). The EVG520IS semi-automated wafer bonding system was used for imprinting the microchannels on PMMA. A contact force of 10 kN was applied for imprinting the channels. A DISCO programmable dicing saw (DAD 641, DISCO Corp. Japan) was used to cut the imprinted microfluidic parts from the PMMA wafer. A diamond-coated blade (NBC-Z 2050, DISCO Corp. Japan) rotates at high speed to induce a smooth cut. A 1 mm drill bit was used to make input and output holes at various valve locations and render the parts ready for bonding.

PMMA-PDMS-PMMA Bonding

The PMMA-PDMS bonding technique required multiple steps as shown in Figure 7. First, the PMMA substrates have certain machining and registration marks which were also transferred from the template. These marks were removed by uniform polishing of the microfluidic parts on smooth polish paper (600 grit size).

Functional silanes such as BTMSPA (82985-35-1, Gelest Inc. PA) and APTES (13822-56-5, Gelest Inc. PA) were used to enable bonding of the PMMA substrates to the PDMS membrane. A mixture of APTES and BTMSPA was prepared in isopropanol in 1: 1: 20 proportions, respectively. In order to mix the contents properly in isopropanol, the mixture was centrifuged (C1301P-ISC, ISC Bio Express, Korea) for 10 s at 30000 rpm. This solution was carefully spread on the PMMA substrates using a pipette tip. Prior to the APTES/BTMSPA application, the microchannels and pump cavity were covered with a single side adhesive tape (Scotchcal, 3M, MN) as shown in Figure 8.

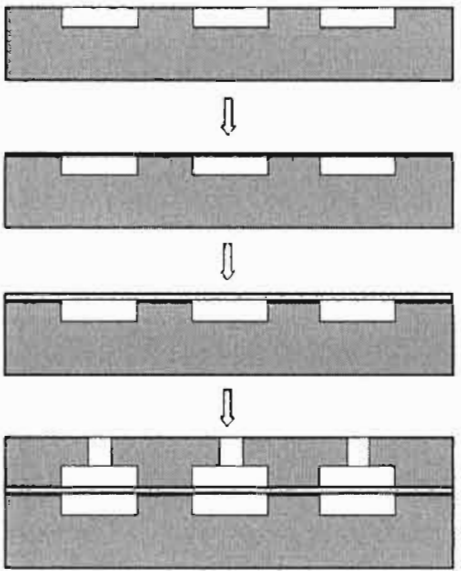


Figure 7 Schematic diagram of fabrication steps involved in PMMA-PDMS bonding. The single side adhesive tape used for this work was a Scotchcal tape that was used to prevent the seepage of the adhesion promoter solution in the channel area. The absence of the adhesion promoter in the channel area prevents unwanted sticking of PDMS membrane to the channel walls and thus prevents channel blockage. The thickness of the PDMS membrane was 65 μm.

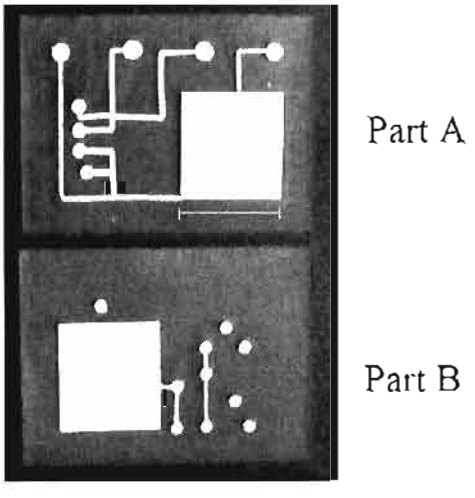
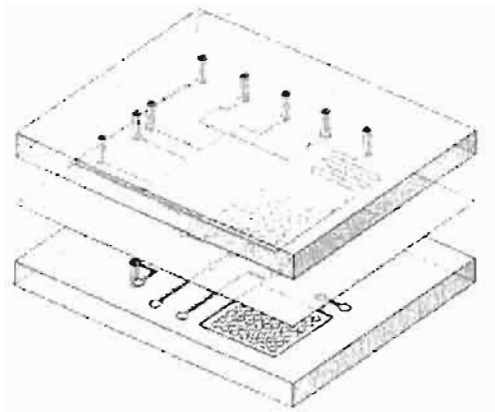
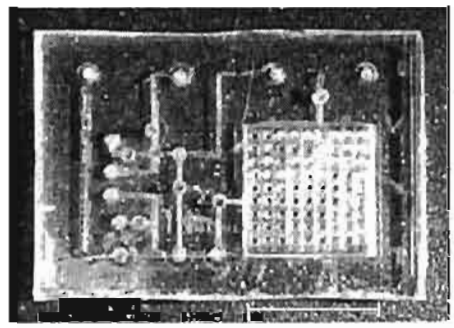


Figure 8 Picture of the tape mask used to prevent unwanted silane seepage inside the microstructures. The silane-based adhesion promoter was applied on the dark areas of the image. Scale bar is 12 mm.

This tape was cut using a knife plotter (FC 5100-75, Graphtec America, Inc. USA) in order to prevent unwanted seepage into the microchannels and pump cavity. The applied layer of silane solution was allowed to cure for 15 to 20 minutes at room temperature. The PMMA substrates were covered with a petri dish to avoid unwanted contamination with foreign particles and dust. A PDMS (Sylgard 184, Dow Corning Corp. MI) membrane was spin coated (WS-4004-GNPP/LITE, Laurel Tech Corp. PA) at 2000 rpm for 30 s inside a petri dish whose surface was covered with a backing of rubylith tape (300 Gauge, Ulano Corp, NY). This membrane was allowed to cure in an incubator (American Scientific Products) at 65^0 C for 30 minutes. After complete curing of the silane solution, the PMMA substrates and the PDMS membrane surface was treated with a corona glow discharge (LM4243-05, Enercon Industries Corp. WI) and then bonded together. The substrates to be bonded were pressed between two glass slides with the help of 2" spring clamps. The purpose of using glass slides was to maintain uniform pressure across the entire bond area. The substrate in contact with the membrane was allowed to cure for 1 hour in an incubator at 65^0 C. After partial curing, a similar procedure was repeated for bonding the other PMMA substrate to the same PDMS membrane. The entire assembly was again clamped between two glass slides using the 2" spring clamps and cured in the incubator for 14 to 16 hours at 65^0 C to complete the curing and bonding process. A schematic diagram and actual PMMA-PDMS-PMMA bonded parts are shown in Figure 9 (a) and (b).



(a)



(b)

Figure 9 Top and bottom microfluidic part with membrane sandwiched between them. (a) Three-dimensional sketch of PMMA substrates with microstructures imprinted and PDMS membrane sandwiched between them. The diagram shows microchannels, diaphragm pump, fluidic ports and pneumatic/vacuum interfaces. (b) Image of the actual microfluidic part. Scale bar is 12 mm.

Experiments

Short Beam Shear Tests

Short beam shear strength tests (ASTM D 2344/D 2344 M) were performed to determine the bond strength between the PDMS-PMMA interfaces using an Instron 4303 machine. This test is valid for specimens up to 6 mm thick with flat or curved surfaces [24]. The combination of a PDMS membrane between two PMMA substrates was assumed to be a polymer matrix composite material with three laminates. The specimens used for these particular tests were PMMA pieces (24mm x 18.4mm x 2.1mm) without any microstructures on them. The test composites were prepared with the same bonding procedure as explained in the previous section. A schematic diagram for the test setup is shown in Figure 10.

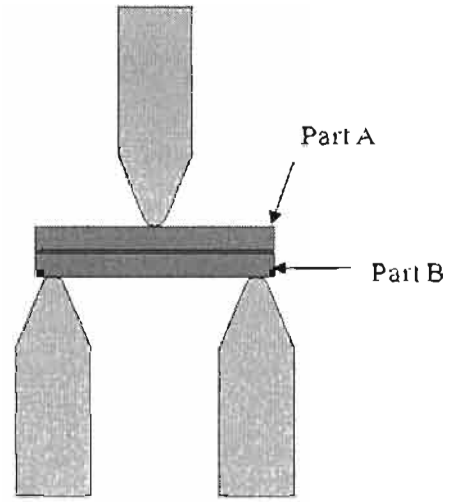


Figure 10 Schematic diagram of short beam shear strength test setup. The distance between the bottom supports is 4 times the total thickness of the test specimen. The load center was located at the center of test specimen.

A 5 kN load cell with a loading nose was used to apply the load on each specimen at the midpoint, and the ends were rested on two supports on either side that allow lateral motion during loading. The load cell moves vertically downward at a speed of 1 mm/min.. The load was continually applied until the specimen fails under shear or in tension. Failure modes in the tests were closely observed in order to accurately interpret the test data.

Leakage Tests

Unwanted leakage of fluid is a constant problem in microfluidic systems. Though the tensile or shear strength of the bond may be high, even small leaks can ruin a microfluidic system. Therefore, tests were performed on the PMMA substrates with the desired microstructures to determine at what pressures leaks would develop. Even though the actual working pressure to be used in the microfluidic system is only 35 kPa, the

bonding strength was checked repeatedly by applying pressures as high as 250 kPa on these devices. Cycle times were also extended by 5 minutes (i.e., from 15 minutes to 20 minutes) beyond that used in normal microfluidic systems in order to check the system performance for the worst case scenario. In addition, leak tests were performed at 450 kPa on dead end channel specimens using devices fabricated using the same bonding procedure. A color dye mixed in water was flowed into the dead end channels at pressures as high as 450 kPa for a certain time period to check for leakage in the microfluidic system. Note that the dead end channels are able to fill as the PDMS is gas permeable and the air bubbles escape through the membrane [25].

Results and Discussion

Hot Embossing operation

Several dozen PMMA parts were manufactured using hot embossing and the brass mold. Various tests were performed on the PMMA substrates to determine the baseline process parameters. The template was tested for its replicability on a 2 mm thick PMMA substrate by using a contact force of 5 kN to 10 kN and maintaining the die temperature at 130^0 C. It was observed that the tests performed at the 10 kN contact force give a much better background surface finish than that at 5 kN. It should also be noted that the 5 kN force for hot embossing results in considerable feature variations between the PMMA substrate and the template. In addition, the gates and cross sections appear more accurate at a contact force of 10 kN.

PMMA-PDMS-PMMA Bonding

Bonding of PMMA to PDMS was the most challenging part of this work, and there were several challenges that needed to be overcome to allow the success of the bonding technique. First, it is very difficult to transfer a PDMS membrane that is spin coated on a flat surface to a PMMA substrate without forming any air pockets under the bonded membrane. Therefore, the membrane was spin coated on a backing of a rubylith tape fixed inside a petridish. After bonding the exposed side of the membrane to the PMMA substrate, the rubylith backing was easily be removed from the other side of the membrane without any tearing. Second, to eliminate machining marks, sanding was required on the substrate, which creates microscopic scratches on the PMMA substrate. These microscopic scratches increase the overall surface area on the PMMA substrate available for bonding and in turn increase the bond strength. Third, the determination of the curing time after bonding was also a major unknown for this technique. After creating 15 replicates, it was observed that a curing time of 16 to 18 hours at a temperature of 65^0 C gives a uniform, strong bond between PMMA and PDMS. This curing time is adequate for our application requirements, though the bonding time is an important concern for this method as it requires significantly more time than any other existing bonding methods. Finally, the cleanliness of the work environment is a major factor and affects the bond quality considerably. The presence of any dirt or dust on the bonding surface causes the bond quality to deteriorate.

Short Beam Shear Test

Typically, short beam shear tests (SBST) are designed to test the shear strength of polymer matrix composite materials. SBSTs are used to determine the short beam shear strength of high modulus fiber reinforced composite materials. Therefore the test specimens made up of two PMMA substrates with a PDMS membrane sandwiched between them as shown in Figure 11 (a) and (b) can be considered as a symmetric laminate composite material. Shear force is the dominant loading in this test, but the substrate may also fail due to the internal stresses in other modes such as tension or compression.

In the first test, a 1kN load cell was used and the next two tests were performed using a 5 kN load cell which moves at a speed of 1 mm/min. Two test specimens failed just after a 1 kN load and the third specimen failed at 0.8 kN. The displacements of the specimen at failures are 0.94 mm, 1.01 mm and 1.38 mm respectively. In all three tests

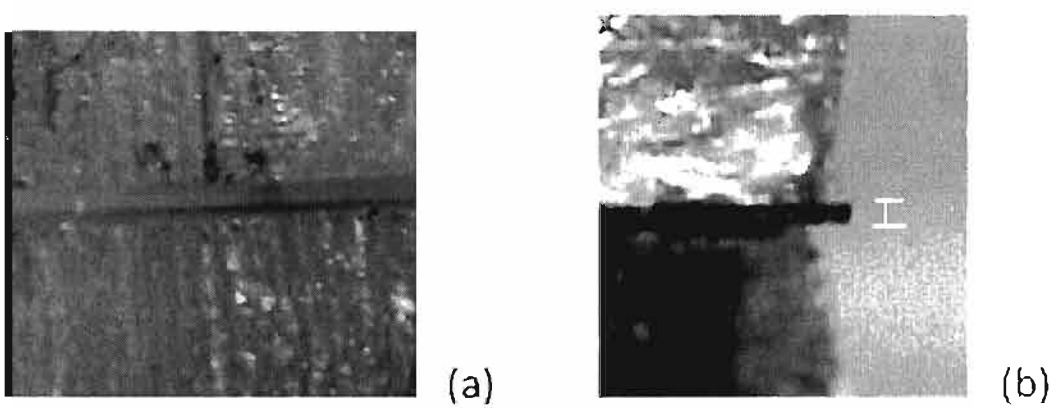


Figure 11 Optical images of the PMMA-PDMS-PMMA part before and after shear test (a) Optical image of the PMMA-PDMS-PMMA interface before the shear test (b) Optical image the PMMA-PDMS-PMMA interface after the shear test. It should be noted that these pictures are not taken from the same location on the test specimen. The image after the shear tests shows an intact PMMA-PDMS-PMMA bond even with fractured PMMA substrates. No delamination of the PDMS membrane or twisting of from PMMA substrates was observed after the short beam shear test.

conducted for this experiment, part B as mentioned in Figure 10 failed in tension, followed by part A under compression. Figure 12 shows the failure loads for three different tests.

The formula used for calculating the maximum shear stress at the center is

$$\tau = \frac{3}{4}\frac{P}{b.h}$$

where P is the applied load, b is the width of the specimen, h is the height of the specimen, and τ is the shear stress in the specimen.

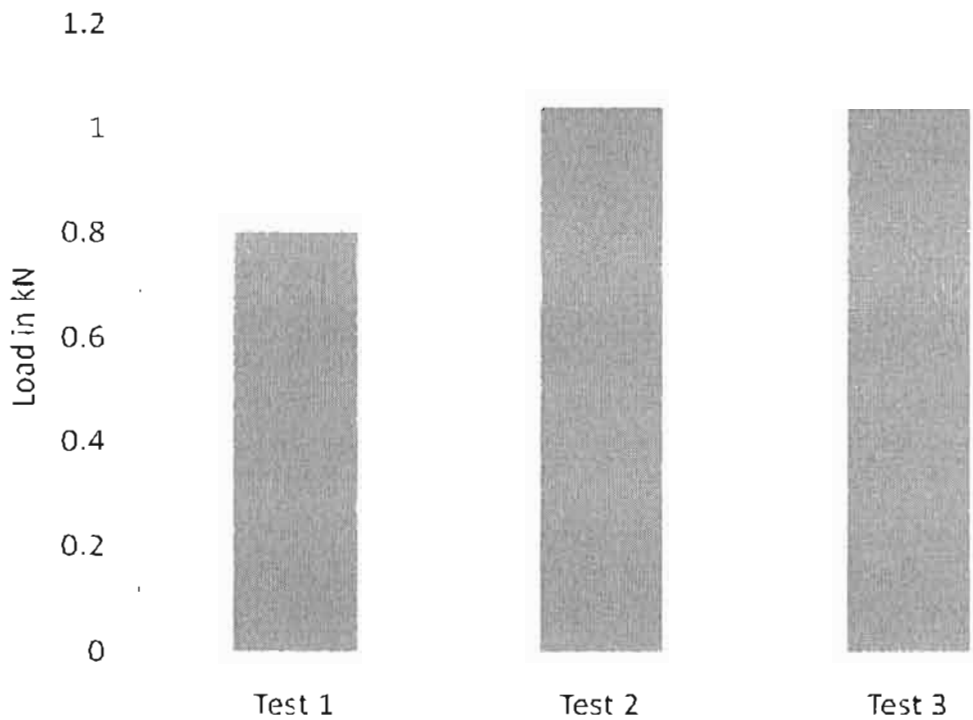


Figure 12 The plot shows failure loads for three different short beam shear tests. First, the test was carried out with a 1 KN load cell and the specimen failed at 0.8 KN. The later tests were carried out at 5 KN as the failure load was approaching the 1 KN load cell value for the first test. Test 2 and Test 3 are examples of these tests and show near-identical failure characteristics with failure loads of 1.04 KN and 1.04 KN, respectively.

Tensile failure occurred when the shear stress was 9.85 MPa and there was no shear failure observed in any of the test specimens. This indicates that the bond strength of the joint in shear is greater than 9.85 MPa, and that is why the specimen failed in tension before the bond failure due to shear. The laminates get twisted in plane in the case of shear failure, but it was not observed during or after the test. If the PMMA is assumed to be a brittle material, then from a Mohr's circle diagram [see Figure 13] it can be concluded that the tensile strength of the bond is 9.85 MPa and the shear strength is at least 9.85 MPa.

Leak Tests

Prevention of leakage in microfluidic systems is always a challenging task, especially when the fluid lines are not completely sealed for the valve operation and disparate materials such as PMMA and PDMS are involved in one single unit. Therefore, leak testing is a major criterion for proper testing of such systems. The microfluidic system being tested here has a high number of valves in a very small area and opening and

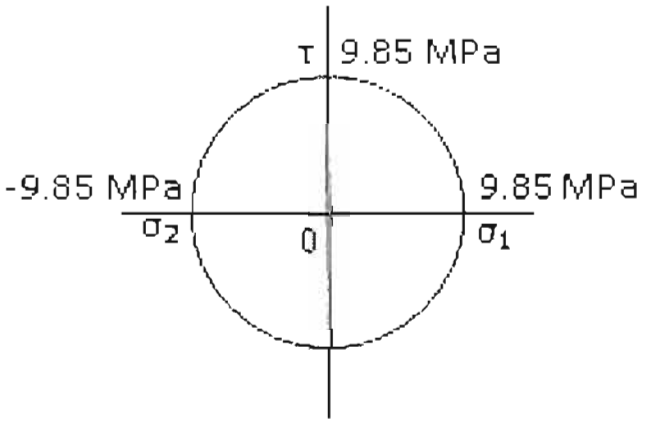


Figure 13 Mohr's Circle showing the failure of bond at 9.85 MPa in tension and in compression. It can be concluded from the Mohr's Circle that the shear strength of the bond is same (i.e., 9.85 MPa) in case of pure shear loading.

closing of valves takes place by applying vacuum and pressure to the PDMS membrane. This renders the valve locations a potential leakage spot. System performance was checked at as high as 250 kPa pressure, though the actual pressure required for the system operation is only 35 kPa. No bond rupture or delamination of PDMS from PMMA substrates was observed. No leakage was observed in the test specimen when the flow tests were carried out after applying the high pressure. Also, the valve and pump operation was very smooth at this high operating pressure.

Dead end channel tests performed at 520 kPa showed no delamination of the PDMS membrane and no leakage was observed during the testing. The microfluidic system could have sustained higher pressures, but the number of joints present in the fluidic line such as connectors and reducers did not allow applying pressure beyond 520 kPa. Overall, the bond strength of PDMS-PMMA is comparable to the bond strength of PDMS composite tape and glass [22-23] as shown in Figure 14.

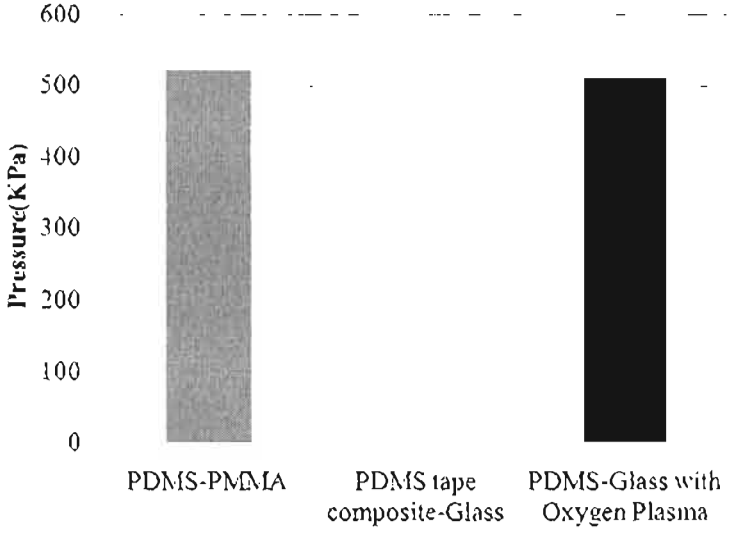


Figure 14 Bond strength comparison of PDMS-PMMA bond with the PDMS composite tape-Glass and PDMS tape-Glass (oxygen plasma). Dead end channel tests are used to check the bond strengths of the various joints. PDMS-PMMA bond strength falls between the PDMS composite tape-Glass and oxygen plasma bonded PDMS tape-Glass.

Conclusion

A method for bonding PDMS membranes to PMMA microfluidic substrates was demonstrated and shown to have bond strengths more than sufficient for typical microfluidic system operation. This technique allows the combination of inexpensive PMMA parts fabricated using hot embossing and PDMS membranes, which allow the creation of complex pumps and valves. The technique developed to obtain PMMA-PDMS interface bonding can be easily used in the fabrication of disposable detection and extraction devices required in biomedical applications. Surface pretreatment using the silanes gives covalent bonding at the PMMA-PDMS interface, which is difficult to achieve using other methods. The maximum temperature to which PMMA substrates were exposed during the complete bonding cycle is 65°C, which is well below the glass transition temperature of PMMA (i.e., 105°C). This prevents the deformation of hot embossed microfluidic channels. Microscopic scratches created by surface polishing on PMMA result in strong bonding at the cost of reducing transparency. Short beam shear tests were performed to check the shear and tensile strength of the PMMA-PDMS bond interface and it has been found that the bond strength in tension and shear is at least double that for existing bonding methods. Also dead end channel tests were performed to verify that no leaking occurs in working devices. Thus, the bonding method can be effectively used in the future for other similar applications where the microfluidic system demands a relatively high operating pressure. The bond obtained using the surface functionalization gives a higher bond strength than bonding facilitated using other adhesion promoters such as acetonitrile [26]. The functional silanes (APTES and

BTMSPA) used for the PMMA surface treatment are biocompatible and can be used for microfluidic devices used in medical applications.

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CHAPTER 4

CONCLUSION

The thesis work demonstrated a cost effective method for the manufacturing of hot embossing die without the use of any clean room facilities. The manufacturing method of brass hot embossing stamping die can easily be applied for the other materials such as steel, aluminum and platinum. This microstructure imprinting method is much simple and rapid than the conventional imprinting methods used for silicon wafer stamp. The bonding method developed for PMMA-PDMS bonding helps to easily incorporate a PDMS membrane between two PMMA microfluidic parts. This may lead to opening up of new market for the microfluidic devices where pumps and mixers are incorporated on a single microfluidic chip that is made of different materials.

The temperature is always a concern in during the bonding process of any polymeric devices. The thermal bonding method requires at least glass transition temperature during the bonding. However, the PMMA-PDMS bonding method developed in this thesis is performed at 65°C which is well below the glass transition temperature (Tg) of PMMA (i.e., 105°C) . This helps to prevent unwanted deformation of the microstructures while bonding.

Short beam shear tests performed on the PMMA-PDMS parts showed that the bond strength in shear and tension is atleast double than the existing bonding methods. It can

be concluded from the high pressure dead end channel tests that the bonding method can easily work for high pressure microfluidic devices.

Future Work

A hot embossing die designed in this thesis work has all the fluidic structures in the micrometer or millimeter range. The nanostructure stamping dies cannot be machined by the CNC machines. There is a wide scope for the development of patterning methods used for the die manufacturing. Also, the CNC machine has its limitation for higher aspect ratio structures.

An effort has to be put to apply this bonding technique towards thermoplastics, polycarbonates, acrylic and glass since these materials are widely used in the manufacturing of disposable devices. Another potential area for the future work is addressing interfacing these devices. Since these materials have hard crystal structures, the interfacing devices such as barb fittings and tubes do not easily fit into these devices and require additional layer of PDMS at the interface. The time required for the bonding is an important issue in related to this thesis work. A curing agent has to be investigated that can be mixed and applied to the PMMA surface in addition to the functional silanes. This will help in reducing the production time drastically.

We have developed our own PDMS membrane transfer technique which is not a standard procedure in a typically bonding operation. An easier way needs to be invented to transfer cured PDMS membranes on to the PMMA substrate, which will avoid formation of voids on the bonding surface. The presence of voids on the contacting

surfaces reduces the bond strength drastically and also makes the joint susceptible to unwanted leakage in microfluidic chips.