Design and Manufacture of a Microfluidic Housing for a Biosensor

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May 1, 2009
Executive Summary

The objective of the Biosensor design project is to both design a microfluidic housing for a silicon biosensing chip and to create a manufacturing process for mass-producing the housing with the silicon chip inside. The project is being done for Diagnostic Biosensors, a company that creates Point-of-Use analytical systems with the goal of providing an easy, fast, and inexpensive way to diagnose personal health issues. The final product delivered to Diagnostic Biosensors at the conclusion of the project included a design for a two part microfluidic housing, a design for a set of molds to be used to create large quantities of the housing parts, and a partial manufacturing process for creating the encapsulated silicon chips.

After a significant amount of research into microfluidic design and available manufacturing technologies, the microfluidic housing was designed with the customer requirements dictated by Diagnostic Biosensors in mind. The microfluidic housing consists of two PMMA parts, an upper portion known as the microfluidic cover, and a bottom portion known as the well. The microfluidic cover is bonded directly to the silicon chip. It directs flow over the silicon chip to facilitate analyte detection and provides a means for interfacing with an external system which delivers the fluid sample being tested. The well functions to protect the silicon chip and aids in the manufacturing process. The final design of these parts was arrived at through the use of concept selection matrices which evaluated all concepts based on the degree to which they fulfilled the design requirements.

The molds used to create the housing halves were designed for use with the HEX02 hot embosser located at Louisiana State University. These molds allow for several hundred microfluidic covers and wells to be created simultaneously. In addition, the molds contain features designed for use in the manufacturing process including alignment marks and saw guides.

The manufacturing process consists of 21 individual steps which deal with molding, chip placement, alignment of the housing halves, bonding, and part separation. The manufacturing process enables several hundred silicon chips to be efficiently encapsulated in, and bonded to, the microfluidic housing.

The design was evaluated based on four major design criteria which assessed the design from a functionality standpoint and in terms of its ability to be easily manufactured. Analysis was done to ensure the microfluidic cover and well could withstand the compressive forces associated with the manufacturing process and also to ensure that the seal between the microfluidic cover and silicon chip was strong enough to withstand the internal pressure generated by fluid flow during use. From a manufacturing standpoint, analysis was done to ensure that tolerance stack would not cause any alignment issues and the molds were assessed in terms of their ability to be machined and to create high quality parts through hot embossing.

In terms of meeting the design requirements set forth at the beginning of the project, the Biosensor project can be considered a success. While a more clearly defined manufacturing process would have been desirable, time limitations associated with mold manufacturing made this impossible.
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Glossary

Analyte: Substances, typically biochemical, that are detected in an analysis.

Biosensor: A device which detects biochemical analytes (for example glucose in a blood glucose test) in biological material using some kind of a detection component.

Hot Embossing: A process by which a feature(s) is stamped into a plastic substrate under controlled temperature and pressure.

Label: A molecule or micron-sized particle that gives off a signal that is detectable by a Transducer (e.g. magnetic, fluorescent, gold).

Lab-on-a-chip: A method of taking elaborate bulky lab equipment and technology and shrinking it down to a portable, reusable device that can be used by an average individual.

Microfluidic Cover: Upper portion of the biosensor housing which controls fluid flow over the silicon sensing die and interfaces with the fluid handling system.

Microfluidic Encapsulation: Refers to the finished assembly of the Microfluidic Cover and the Well.

Point-of-Use: In this report, refers to medical devices which can be used to perform analytical tests in the field and which deliver immediate results. For example a blood glucose sensor is considered to be “Point-of-Use.”

Silicon Die: A silicon chip which contains the detection portion of the biosensor.

Transducer: Converts the signal from the label into an electrical signal that gets sent to the user interface.

Well: Lower portion of the biosensor housing which protects and supports the silicon die.
Section I - Problem Definition

1.1 Problem Scope

This project is concerned with designing, and detailing a manufacturing process for creating a mass quantity of, microfluidic devices for use in “Point-of-Use” medical devices. The microfluidic devices will eventually be made through a process which encases silicon dice between two Polymethyl-methacrylate (PMMA) sheets that have been hot embossed. The bottom sheet will contain “wells” which will provide a structure for the silicon dice to rest in. The top sheet will contain “microfluidic covers” which will protect, and provide a path through which fluid flow can be directed over, the silicon dice. The two sheets will be glued together and sawn apart to create encapsulated dice that can be incorporated into printed circuits. For the purpose of this project, the PMMA sheets, and the molds needed to make them, will be fully designed and evaluated for both feasibility in the fabrication processes selected and meeting the defined design criteria. Further, the fabrication process for creating the encapsulated dice will be documented.

1.2 Technical Review

Background

Our group is working with Diagnostic Biosensors, LLC, a company which develops products and technology for Point-of-Use analytical systems. Point-of-Use medical devices are becoming increasingly popular as they provide an easy, fast, and inexpensive way to diagnose health issues. Currently, diagnostic testing on fluid samples is done primarily in clinical labs. This process is effective, but also time and money intensive and generally needs to be carried out by a skilled lab technician. However, through the use of biosensors in Point-of-Use medical devices, we can effectively create a “lab-on-a-chip.” This lab-on-a-chip provides results quickly, inexpensively, and without the need for a skilled technician. It is also portable and has potential applications ranging from use by soldiers in combat to doctors making house calls to remote locations.
In some Point-of-Use sensors, such as the one our design will be used in, the biosensor portion of the device is interchangeable, as it becomes contaminated after each use. Examples of applications of these sensors include checking blood glucose levels and even diagnosing liver disease [1].

A biosensor is the heart of any Point-of-Use medical device and is the portion which actually senses and processes the concentration of an analyte within a fluid sample. Biosensors consist of five major components: a sample handling system, a sensitive biological element, a label, a detector element, and electronics and signal processing to display the output in a meaningful manner. A fluid sample first enters the device and travels through the sample handling system which delivers the sample to the sensitive biological element. A label is then attached to the desired analyte (i.e. glucose, etc.) which then flows over, and becomes attached to, the detector element. This detector element is connected via electrical traces to the signal processing portion of the biosensor, where the analyte concentration is determined and output to a graphical user interface (GUI).

In the biosensors created by Diagnostic Biosensors, the sensitive biological element, label, and detector element portions of the biosensor are all contained within a very small (~6mm long, 1.5mm wide) silicon die. The focus of our project is on designing a structure which encapsulates this silicon die, providing a path for fluid flow over, and protection for, the die. In addition, a manufacturing process for mass producing the encapsulated dice will be designed.

**Prior Art**

This section contains an overview of the existing technology and methods which are relevant to our design. It will focus on technologies and processes relevant to the creation of our design specifically (an encapsulation for the silicon die), rather than on Point-of-Use sensors in general.

The technologies and processes presented here can be grouped into two categories: those dealing with the design of the device with respect to functionality, and those dealing with manufacturing the device.
Device Design Technologies

With respect to the design of the device, two major things were considered. The first was whether the device should be single layer or multilayer. The second was control of fluid flow through the device. Both of these considerations are explored in detail below.

Single vs. Multilayer Design

In our design, a fluid sample travels through the device and is then directed through a chamber which contains a silicon die. This chamber is made of PMMA and can be constructed in two ways. The first is what is known as single layer design. In this type of design, one single piece of PMMA is used to create the entire part. This works well for structures with simple geometries, but is not a viable option when part geometry becomes complex, due to manufacturing limitations. When structure geometry becomes complex, multilayer design, which is often employed in rapid prototyping of microfluidic devices, is the method of choice [3]. Multilayer design uses slices of polymeric material which are stacked and bonded together in order to create the desired geometry. Figure 1 illustrates this point.

As seen in the figure, the multilayer design has a more complex T-shaped fluid passage. This design would be impossible to make as one piece by normal manufacturing methods such as injection molding or hot embossing because the recesses in the shape would make releasing the part impossible. Looking at the multilayer design, it can be seen how use of multiple bonded layers enables the creation of the structure.

Figure 1 - Single vs. Multilayer Design
There are many situations in which a more complex design requiring multilayer construction needs to be employed, but one of the most common is for crossing fluid streams. When it is desired to physically make two separate streams of fluid cross without mixing, one channel carrying fluid needs to pass over the other stream (like a bridge). In order to do this, multilayer design is implemented.

**Control of Fluid Flow**

Fluid flow over the silicon die is critical in our design. Without proper control of this flow, the results of the sensing may not be accurate. There are many ways in which fluid flows can be controlled, but some of the more popular methods include forcing the flow through channels, using other streams of fluid to force the fluid into a desired location, and focusing flow electrostatically or electrokinetically.

One of the simplest ways to control flow is simply to force it through a desired flow channel. For example, in Figure 1, the multilayer design incorporates a T-shaped passage way, which could be used to force fluid to flow in a T-shape. Fluid can be made to flow in nearly any shape and nearly any path using this method.

Using other fluid streams to force fluid to do what you want is another method of flow control called “fluidic focusing.” In our design, it was specified by our project advisor that two fluid inlet ports would be used in order to facilitate flow control. This is done by using the second stream to force the first stream to the bottom of the fluidic chamber in order to better facilitate sensing, which is done on the silicon chip which forms the bottom of the fluidic chamber.

A third method for controlling flow is to electrokinetically focus the flow. In this method, a sample flow is “electrokinetically pre-focused into a narrow stream and guided to the desired outlet port by means of a simple control voltage model” [4]. Using this technique, one or more sample streams can be guided to desired outlet ports without the use of a valve.
There were four major issues that needed to be addressed in the design of the manufacturing process. First was the process for molding the two sheets of PMMA which contain the upper and lower halves of the encapsulation. Second was the method for aligning the two sheets of PMMA. Third was a method for bonding the two PMMA sheets together. And last was a method for cutting the sheets apart to produce the finished products, which are individual encapsulated silicon dice.

Molding

Molding of the two sheets of PMMA (one containing wells, the other fluidic covers) will be done through a process known as hot embossing. It was specified by the project sponsor, Diagnostic Biosensors, at the outset of the project that this would be the method employed. This method was selected because it provides the ability to mass manufacture parts, is inexpensive, fast, works well for micro scale parts, and had been used successfully by Diagnostic Biosensors in the past.

The process of hot embossing starts with the creation of a mold. This mold can be made out of a variety of materials, but brass is commonly used because it is easy to machine and has favorable thermal conduction properties. The size of the mold can vary, but must be compatible with the particular hot embossing machine being used. For our design, a hot embossing machine located at Louisiana State University will be used. This machine accepts 5 inch diameter circular molds which are attached to the machine by 6 bolts. In order to accommodate these bolts, 6 through holes must be machined into the brass mold. The creation of features in the mold is done through a process known as micro milling. The micro milling process is exactly like that used to mill out large molds, but on a smaller scale. It begins with the creation of a computer model of the desired mold. This model is then converted into a series of cuts and passes which can be sent to a computerized milling machine which creates the actual mold. Once the mold has been created, the parts are ready to be hot embossed.
Hot embossing is a process by which a design is “embossed” into a polymeric sheet, PMMA in our case. This embossing is done by heating the mold to just above the glass transition temperature of the plastic and then, under a complete vacuum, pressing the mold insert into the polymer under a defined time, temperature and force which are dependent on the mold shape and type of polymer [2] (see Figure 2). The displacement versus temperature curve is mainly defined by the Young’s modulus of the material being embossed, which changes as a function of temperature [5]. Doing this under a vacuum ensures that no air becomes trapped in the plastic, creating bubbles. When working on a micro scale, even small air bubbles in the plastic could destroy the parts.

![Figure 2 - Hot Embossing Schematic (Source: Gurung Thesis)](image)

**Alignment**

One of the most critical steps in the manufacturing of our design is the alignment of the two sheets of PMMA for assembly. If not precisely aligned (within 50 microns), the fluidic covers and wells may not interface properly, resulting in a defective part.

Two widely used methods exist for precisely aligning micro scale parts. The first is building physical alignment features into the molds. The second is creating some kind of feature in the mold which can be used to optically align the parts.

Physical alignment features can be built into the individual parts themselves, or into areas of the mold which do not contain parts. These are referred to as individual and overall alignment features, respectively. They are simply features which interface with a corresponding feature on the other mold. For example, one popular overall alignment feature is a ball and groove joint.
In this joint, one mold contains dimples which fit into corresponding grooves on the other mold, thereby aligning the two molds (see Figure 3).

![Figure 3 - Ball and Groove Joint (source: Gurung Thesis, edited by author)](image)

One of the drawbacks to physical alignment features is the difficulty and expense involved in machining them into a mold.

Optical alignment is done by machining the same shape into both of the molds at two locations, and then using an alignment microscope to line the shapes up. One commonly used shape is a simple cross as seen in Figure 4.

![Figure 4 – Typical Optical alignment features (Source: [6] UofM Nano Fabrication Center)](image)

The University of Minnesota Nano Fabrication Lab contains an MA-BA-6 backside alignment microscope which could be used in the alignment the two PMMA sheets for our project. This microscope contains two cameras spaced approximately 50mm apart which will be used to align the features on each of the PMMA sheets to within 2 microns. Figure 5 shows where alignment marks should be located.
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Figure 5 - Setup of MA-BA-6 Alignment Microscope (Source: [6] UofM Nano Fabrication Center)

**Bonding**

Our design requires that the fluidic cover be bonded and sealed to the silicon chip and that the silicon chip be bonded to the well. With this in mind, two commonly used bonding processes in industry today were explored: bonding with epoxy and plasma bonding.

Bonding using an ultraviolet (UV) epoxy was the first design explored. It was recommended by our project sponsor that we research Loctite® UV epoxies, as they had been used successfully by him in the past for similar applications. The properties and common applications of Loctite® 3921™ appeared to fit well with the type of design we are creating, so its properties in particular were researched. From its data sheet we see that Loctite® 3921™ remains in a viscous state until it is exposed to ultraviolet light at a wavelength of approximately 365 nm. The cure time of the epoxy is dependent on thickness, but for our application should take less than 10 seconds. In addition, Loctite® 3921™ is inexpensive to buy, easy to apply, and has the ability to bond different material types, including PMMA and glass (which for our design, we approximate the silicon chip as being) and is “suitable for use in the assembly of disposable medical devices” [7].
The bond strength for PMMA to glass is given as 3.9 N/mm² and for PMMA to PMMA is 7.7 N/mm². This information is useful for evaluating the design.

Plasma bonding is another method which can be used to bond microfluidic devices made from polymeric materials (generally PDMS) to glass. In plasma bonding, both the glass and the polymeric material to which the glass will be bonded are placed inside of a stream of plasma for approximately one minute. The device is then placed in contact with the glass, causing a seal between the two to form. This must be done within approximately one minute of removing the polymer and the glass from the plasma stream for bonding to occur properly. Because it involves exposing the glass to a plasma stream, any sensitive structures or material on the glass could be damaged or destroyed. For example, in our design the silicon chip contains sensitive biological material. Mass-manufacturing parts with this method could also be difficult [8].

**Part Separation**

The last step in the manufacturing process of the encapsulated silicon dice is to cut apart the finished assembly of PMMA sheets (the bottom sheet containing wells and the top sheet fluidic covers) and silicon dice, thereby creating individual encapsulated dice. The method used to cut apart the sheets needs to be accurate enough to cut inside of a 200 micron gap so as not destroy any of the encapsulated dice. Two methods for cutting apart the encapsulated dice were explored: sawing and laser cutting.

Sawing is the first method for part separation we explored and has been used successfully in the past to cut apart PMMA structures [9]. With this method, the PMMA/silicon die assembly is attached via double sided tape of known thickness to a cutting platform. This tape will hold the encapsulated dice in place once they have been separated from the rest of the sheet and will also allow for the saw to cut all the way through the PMMA and into the tape. Next the saw is lined up, turned on, and the pass is made. This process is repeated until all of the encapsulated dice have been cut apart [10].

Laser cutting is another method which is currently being used to cut PMMA structures.
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The quality of the cut produced by laser cutting is one of the biggest issues to consider because the PMMA is a plastic, which easily deforms under high temperature. However, by determining the correct laser power and cutting velocity, laser cutting can achieve very accurate results. Using a CO2 laser to cut PMMA, accuracies of 0.12 to 0.37mm have been achieved [11].

1.3 Design Requirements

A successful design is one which meets all of the design requirements. These requirements must be able to be quantified and evaluated at the end of the design process. Important requirements that were identified as necessary for the biosensor design to be successful are itemized below in Table 1.

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<th>Importance</th>
<th>Evaluation Method</th>
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<td>1</td>
<td>Alignment of all parts must be accurate to within 50 microns</td>
<td>If not properly aligned, the fluidic cover may not interface properly with the chip well and/or flow from the fluid ports may not pass over the sensing portion of the silicon chip</td>
<td>Tolerance analysis of the part dimensions and the optical alignment process will be performed</td>
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<tr>
<td>2</td>
<td>Needs to withstand estimated assembly pressure of 1MPa</td>
<td>Forces during the assembly process must not damage the product</td>
<td>AN ANSYS simulation will be used to evaluate the product for robustness</td>
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<td>3</td>
<td>The seal between the lip of the microfluidic cover and the silicon die must withstand the pressure created by fluid flow through the chamber</td>
<td>To ensure that the device is able to handle normal operating pressures and will not break or leak</td>
<td>CFX analysis to determine fluid pressure and analysis of the bond between the lip of the microfluidic cover and die</td>
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<td>4</td>
<td>Mold design must be suitable for micro-milling and hot embossing</td>
<td>If the design of the mold is not suitable for milling and hot embossing it is useless</td>
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Section II – Design Description

2.1 Summary of the Design

Our design can be broken into three major portions: a plastic housing for a silicon die, two molds used to make upper and lower halves of the housing and a manufacturing process for encapsulating the silicon die in the housing.

The plastic housing (known as the microfluidic encapsulation) for the silicon die consists of a separate lower and upper half, respectively known as the well and microfluidic cover. The lower half (well) protects and holds the silicon die while the upper half (microfluidic cover) creates a chamber through which fluid can flow over the silicon die.

The second portion of the design is two brass molds which are used to mass-manufacture PMMA sheets which contain large quantities of the two halves of the microfluidic encapsulation. In addition to containing the upper and lower halves of the microfluidic encapsulation, the molds also contain features which aid in manufacturing.

The final portion of the design is a manufacturing process for creating individual encapsulated silicon die from the PMMA sheets. This process involves placement of the die, alignment of the components, bonding of the components and cutting free the individual encapsulated die.

2.2 Detailed Description

Functional Block Diagram
Functional Description

Microfluidic Encapsulation

The microfluidic encapsulation for the silicon die has three main functions: it controls the fluid flow over the silicon die, protects the die, and provides a means for interfacing with the fluid handling system. It consists of two components, the microfluidic cover and the well. The silicon die is not a component of the microfluidic encapsulation and is only shown in Figure 6 so that it can be easily seen how the die fits into the encapsulation.

Figure 6 - Microfluidic Encapsulation

Figure 7 gives a general overview of how the microfluidic encapsulation works.
Figure 7 - Overview of How the Microfluidic Encapsulation Works

As seen in the figure, fluid flows into the microfluidic cover on one end through an inlet (the design actually consists of two inlet ports, discussed later), passes through a chamber created when the microfluidic cover is bonded with the silicon die, and finally exits through an outlet on the other side. Inside of the chamber, the sample is exposed to biomaterial printed on the silicon die which attaches labels to the desired analyte. These labels are then attracted by small sensing elements embedded in the silicon, which convert the concentration of labels into an electrical signal. This electrical signal is then transferred through traces in the silicon to external electronics and signal processing.

Each half of the microfluidic encapsulation, the well and the microfluidic cover, were designed with two things in mind: functionality and easy manufacturability.

**Well**

The shape of the well (Figure 8) – a simple box – was designed with easy manufacturability and the adage that the simplest design is usually the best in mind. The length and width of the inside of the well were chosen to be slightly larger than the dimensions of the silicon die. The thickness of the walls was chosen to be thin enough to minimize material use while still being structurally sound. The depth of the well was selected so that there was enough space to hold a layer of glue and the silicon die and finally to have the lip on the microfluidic cover rest just below the top edge of the well.
Figure 8 - Well Detail

The top surface of the length wise edge of the well (1) is angled in, towards the center of the well, at 15° in order to interface properly with the fluidic cover. 15° is also a common angle for the bottom of milling tools, making machining the mold for the part easier and less expensive.

Glue expansion slots (2) are intended to allow excess glue in the bottom of the well escape when the silicon die is pressed in during the manufacturing process.

Microfluidic Cover

Figure 9 shows the microfluidic cover upside down in order to more clearly point out important features. The design of the cover was largely based on making manufacture and assembly of the finished encapsulated die as easy as possible. There are no recesses in the design, making single layer molding possible, and all features have an aspect ratio of less than 3:1 throughout the design, which is significantly less than the maximum 5:1 ratio for hot embossing.
The bottom surface of the length wise edge of the cover (1) is angled out, away from the center, at 15° in order to interface properly with the well and facilitate easy machining.

The lip (2) is the portion of the microfluidic cover which actually makes contact with the silicon die. It is bonded to the silicon die via medical grade UV curable glue (Loctite® 3921™) and creates a seal around the fluid chamber (5). Its width was dictated by the smallest bit that could be used in the micro-milling process (0.255mm). The lip sticks out slightly farther than the bottom surface of the fluidic cover so that it is the only thing which makes contact with the die and so that it may be easily dipped in Loctite® 3921™ during the manufacturing process. The slightly rounded shape of the lip has several functions. First, it helps to minimize glue flow into unwanted areas of the silicon die when the two are brought in contact, as would occur if the lip were flat. Second, glue being pulled down by gravity will tend to follow the curved surface towards the contact point, helping to ensure a glue seal is formed. Last, the rounded shape is a common tip for milling bits, which makes machining the mold less complicated.
The fluid chamber (5) allows the fluid being analyzed to flow over the sensing portion of the silicon die. Its dimensions and location are chosen so that it rests perfectly on top of the sensing nodes on the die.

Fluid inlet and outlet ports ((3) and (4), respectively) allow the microfluidic cover to be connected to the fluid handling system. They provide a passage through the top of the microfluidic cover which allows fluid to flow from external micro tubes into the chamber and then out the other side. The outer most of the two fluid inlet ports is the port through which the fluid being tested will actually flow into the chamber. A secondary fluid stream flows in the inner most of the two inlet ports. The fluid stream from this port is there to push the first stream (the actual sample) down to the bottom of the chamber near the sensors in the hope that it will facilitate more accurate sensing. The fluid flowing out the two outlet ports is a mixture of the sample fluid and the secondary fluid stream.

**Brass Molds**

The brass molds are used to create a mass quantity of each half of the microfluidic encapsulation as well as features which aid in the manufacturing of the assembled encapsulated dice. They were designed for use in the HEX02 hot embosser located at Louisiana State University and to be machined by C-Axis, a company specializing in micromilling. The upper mold contains negatives of the microfluidic cover and the lower mold contains negatives of the well. The location of the microfluidic covers and wells on the upper and lower molds match so
that later, during the manufacturing process, the two PMMA sheets can simply be aligned and bonded together. This eliminates having to bond each microfluidic cover to each well individually

**Upper Mold**

![Figure 11 - Upper Mold and Details](image)

The upper mold (Figure 11) contains 176 negatives of the microfluidic cover (5). It can be seen in Figure 11 that extra space exists on the mold which could be used for creating more covers. This was attempted, however due to problems encountered generating a CAD file of that size, we had to settle for the current design. Further discussion on this can be found in the “Next Steps” section.

The rest of the features present within the mold are either necessary for, or aid in, manufacturing.

Six 3.18mm diameter through holes with a 5.08mm diameter counter bore were placed around the outside of the mold (4). These holes were designed to attach, via 6 M3 bolts, the mold to a HEX02 hot embosser.
The microfluidic covers are placed in groups of two and are connected by a channel (3) to other groups of two covers. This channel will create a PMMA connection between the pairs of covers, and was designed to hold all of the parts together once they have been ejected from the mold.

The five “plus sign” marks (2) are alignment markings. These marks were designed for use with the MA-BA-6 alignment tool, located at the University of Minnesota Nano Fabrication Center (NFC). Corresponding marks on the lower mold will allow for a molded PMMA sheet of microfluidic covers to be precisely aligned (within 2 microns) with a molded PMMA sheet of wells.

Saw guide marks (1) were also built into the mold. These marks will be used in the final step of the manufacturing process when the now bonded PMMA sheets are cut apart using the NFC Disco wafer saw, creating individual encapsulated die.

**Lower Mold**

![Lower Mold and Details](image)

The lower mold (Figure 12) contains the same features as the upper mold, the only difference being that it contains well molds instead of microfluidic cover molds and it also contains small channels for glue expansion (1). During the manufacturing process, glue is placed in the wells
and the silicon dice are then depressed into the wells. Any excess glue travels out of the well through the glue expansion slots and into the glue expansion channel. Because of the relative simplicity of the well design in comparison with the microfluidic cover design, no problems were encountered in creating a CAD model and so the number of wells was maximized on the mold.

**Manufacturing Process**

This section details a manufacturing process for creating individual encapsulated silicon die.

Some of the steps in the process are complex and were not able to be fully designed due to the time limitations associated with this project.

1. The two brass molds will be sent to LSU for use in the HEX02 hot embosser.
2. LSU will create two PMMA sheets using the hot embosser. One sheet (known as the top sheet) contains microfluidic covers; the other (bottom sheet) contains wells.
3. A thin layer of excess PMMA will be ground off of the top and bottom sheets using a disc grinder located at LSU to expose the alignment features on each sheet and to open up the fluid ports in the microfluidic covers on the top sheet.
4. The two PMMA sheets will be sent back to Diagnostic Biosensors.
5. Using a glue printer, Loctite® 3921™ UV curable glue will be place into the center of each of the wells on the bottom sheet.
6. Through a process which has not yet been developed, a silicon die will be placed in the center of each chip well.
7. Using the MA-BA-6 alignment microscope at the University of Minnesota Nano Fabrication Center and the alignment features built into each PMMA sheet, the bottom and top sheets will be aligned so that each well has a microfluidic cover located directly above it.
8. The top and bottom sheets will then be slowly brought together, causing the lip of the chamber in the microfluidic cover to contact the silicon die in each well and push them down. Excess adhesive will flow out of the glue expansion slots in the wells. The sheets will continue to be brought together until the microfluidic covers and wells come into contact. At this point the silicon dice will be at their desired depth.
9. The top sheet will be carefully removed from the wells in order to not disturb the now placed silicon dice.
10. UV light is then shone onto the bottom sheet for at least 60 seconds, curing the UV glue in the wells and cementing the silicon dice in place.
11. A biomaterial printer will then be used to place a desired biomaterial on each of the now secured silicon die in the wells. The type of biomaterial used is dependent on what analyte is being sensed.
12. A sheet of glass will be prepared with at least a 6 inch diameter circle of Loctite® 3921™ at a known thickness of 50 microns. Producing this thickness will be achieved through a process which has not yet been determined.
13. The top sheet will then be placed onto the sheet of glue, thereby coating the lip on each microfluidic cover with the desired amount of glue.
14. The top and bottom sheets will again be placed into the alignment microscope, aligned, and brought together.
15. Each glue covered lip in the microfluidic covers of the top sheet will then be in contact with each silicon die in the wells.
16. UV light will be applied to the sheets for at least 60 seconds, thereby curing the glue and cementing each lip to each die, creating a seal around the fluid chamber.
17. The now assembled top and bottom sheets will be carefully removed from the alignment microscope.
18. The assembly will be placed on a sheet of double sided tape of known thickness, the other side of which will be attached to a mounting plate.
19. The mounting plate will be placed onto the disco wafer saw at the University of Minnesota NFC.
20. The saw will be aligned with the saw guide marks and will make passes down each row of encapsulated die until they have all been separated.
21. The end result will be hundreds of individual fully encapsulated silicon die.

2.3 Additional Uses

Two portions of the design in particular may have additional uses. The first is the general design of the microfluidic cover. Though it is designed to fit over the sensing portion of a specific silicon die, with minor alterations to the shape of the chamber it could be used with other designs as well. This is particularly useful to Diagnostic Biosensors because they have several die designs. The second portion of the design that may have additional uses is our manufacturing process. With minor alterations, this process could be applied to other microfluidic devices to achieve inexpensive, fast and easy mass-manufacturing.
Section III – Evaluation

3.1 Evaluation Plan

Four major design requirements needed to be evaluated. The first was to ensure the alignment of all parts was accurate to within 50 microns. Because a prototype was not actually built, a detailed tolerance analysis was done on the design to ensure that tolerance stack would not cause greater than 50 microns of misalignment. The second requirement was that the microfluidic encapsulation needed to withstand an estimated assembly pressure of 1 MPa. This was evaluated using an ANSYS simulation and validated with a rough hand calculation. The third was that the seal between the microfluidic cover and the silicon die must withstand the fluid pressure generated during use. A flow simulation was first performed to evaluate the maximum pressure within the chamber during fluid flow. This pressure was then used to validate that the seal between the cover and the die was in fact strong enough. The last design criteria that needed to be met was that the upper and lower mold design must be manufacturable. This was validated by ensuring that our design met design criteria set forth by the company doing the mold milling (C-Axis) and Louisiana State University, who will do the hot embossing. Also, quotes were obtained from C-Axis and LSU, signifying that the molds were producible and suitable for creating hot embossed parts.

3.2 Evaluation Results

This section contains a condensed version of the analysis performed on the design. For detailed reports, see Volume II, Section III – Evaluation Supporting Documents.

Alignment

In order to ensure that all the parts will be aligned properly, careful tolerance analysis had to be performed. Tolerance analysis is used because each part has some dimensional uncertainty associated with it. These uncertainties are given in a range of the desired dimension. This
uncertainty affects the size of each part, and in turn will affect the accuracy of aligning the fluid ports. If the chip well was designed to be too small for a larger silicon chip the silicon chip would not be able to fit into the chip well. By doing tolerance analysis, it allows a 95% confidence level that all of the parts will be in contact with one another, that they will all fit together, and the fluid ports would be aligned to within fifty microns.

The requirements of aligning the fluid ports to within fifty microns, and that all of the pieces fit together depended upon the dimensions of the chip well. These dimensions were defined based on tolerance analysis. The machining done on the brass molds and the silicon chip dimensions both have uncertainties associated with them. When placing the silicon chip into the chip well these two uncertainties depend on each other and can be added together:

\[ U_{total} = \sqrt{U_1^2 + U_2^2 + \ldots + U_n^2}. \]

Once the total uncertainty is found the chip dimensions can be calculated. After these dimensions are found the glue depth can be determined and more importantly the maximum alignment error can be found. This error would be found by placing the silicon chip in the corner of the chip well which would be the furthest possible position away from the fluidic ports on the fluidic cover.

After the analysis is done each minimum dimension for the chip well is found along with the final design dimensions shown in Table 2. The minimum dimension was found so that if the actual design dimension was larger the silicon pieces would be able to fit into the chip well.

<table>
<thead>
<tr>
<th>Table 2 - Actual Vs. Minimum Chip Well Dimensions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimum (microns)</td>
</tr>
<tr>
<td>-------------------</td>
</tr>
<tr>
<td>1475</td>
</tr>
<tr>
<td>Final Design (microns)</td>
</tr>
</tbody>
</table>
Using the values of the width and length the farthest that the silicon chip can be misaligned is 122 microns if it was placed in the corner of the chip well. Assuming that the silicon die can be placed in the center of the well, the maximum alignment error that can be caused by the parts uncertainty is 8.2 microns.

In the worst case scenario the maximum alignment would be off by 122 microns. This value is significantly larger than the desired displacement of fifty microns; however, this value represents the worst case scenario. The majority of the parts will be aligned much more accurately, even if they were placed in the corner of the chip well.

Assuming that the die is placed in the center of the well, the maximum alignment error is only 8.2 microns. This value is much smaller than the required maximum of fifty microns and even in the ideal range of less than ten microns.

The process of placing the silicon dice into the wells is quite vital. If the process is accurate in placing the dice towards the center of the well, the fluidic ports should always be within fifty microns of their desired location.

**Structural Integrity**

During assembly of the molded PMMA sheets, they are exposed to a significant amount of pressure in order to ensure the sheets are sufficiently bonded together. In this process, the pressure is applied to the top of the assembly (on the microfluidic cover) and is transferred to the well through its side walls. In order to ensure that the side walls of this well can withstand the assembly pressure they will be exposed to, hand calculations as well as ANSYS simulations of the situation were carried out to avoid buckling or localized yielding of the plastic material.

Based on experimental results gathered by 3M, the observed “finger pressure” an individual can apply ranges from 0.03 to 0.1 Mpa. By using a design pressure of ten times this value and applying 1 Mpa over the surface of a single microfluidic cover (and therefore 0.5 Mpa over each well wall) the design can be evaluated for strength. The critical force that can be applied to a column before buckling occurs is given by the following equation:
This can then be solved for the thickness of the wall (h) in terms of the load applied, the height of the wall, and the modulus of elasticity of the material:

\[ h = \sqrt{\frac{48PL^2}{\pi^2 E}}. \]

Based on the design criteria and a modulus of 3.2 Gpa the minimum thickness that can be used and avoid buckling is 0.0083 milimeters (8.3 micrometers).

Modeling this in ANSYS, a uniform pressure was applied to the top surface of the microfluidic encapsulation with the bottom surface of the well fixed in all directions, the deflection and Von-Mises stress in the walls and microfluidic cover were determined. The simulations were done with a wall thickness of 100 micrometers rather than 8.3 micrometers. This is to make machining the mold to create this component possible. During this simulation, the silicon die was removed since the maximum observed deflection with the die was 0.3 micrometers. This case is then a true worst case scenario. The maximum deflection observed in any design was seen was at the center of the microfluidic cover with a magnitude of 25 micrometers. Finally, with a maximum yield stress of 72 Mpa the microfluidic encapsulation observes a maximum stress of 37 Mpa.

Based on this analysis, evidence suggests that this encapsulation will not fail under the loading conditions expected during the assembly process.

**Seal Analysis**

During normal operation, the chamber of the encapsulated die will be under pressure due to fluid flow. In order to ensure that the seal between the lip of the microfluidic cover and the silicon die was strong enough to withstand this pressure, an analysis was done to first estimate the pressure which would be generated in the chamber and second to find the strength of the bond between the lip and the die. To accomplish this, a CFX simulation of the fluid flow to
obtain the pressure within the chamber and hand calculations of the normal and shear forces at the seal were performed.

The results of these analyses were a maximum fluid pressure of $1.7905 \times 10^5$ Pa inside the chamber, which translated to a force of 0.394N. The strength of the bond between the lip and the silicon die when bonded with Loctite® 3921™ UV curable glue was estimated to be 8.88N. This means that the seal between the microfluidic cover and the die can withstand up to 22 times more pressure in the chamber.

Based on this analysis, evidence suggests the design will not fail under the design pressure.

**Ability to Manufacture**

The final critical design requirement for the project is that the mold inserts to be used in the hot embossing machine can both be made and are suitable for the hot embossing process. This required communication with both C-Axis who will be doing the machining, as well as Louisiana State University CAMD which will be doing the hot embossing. The requirements that were gathered are shown in Table 3 and Table 4.

**Table 3 – CAMD/LSU Requirements**

<table>
<thead>
<tr>
<th>Requirement</th>
<th>Specification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vertical Wall Draft</td>
<td>3° preferred</td>
</tr>
<tr>
<td>Aspect Ratio of Standing Features</td>
<td>Less than 5:1</td>
</tr>
<tr>
<td>Mold Insert Dimensions</td>
<td>119.075mm Diameter</td>
</tr>
<tr>
<td></td>
<td>111.125mm Diameter BC for 6 x M3 bolts evenly spaced with counter bore</td>
</tr>
<tr>
<td></td>
<td>7.925mm thick</td>
</tr>
<tr>
<td>Mold Insert Material</td>
<td>Brass</td>
</tr>
</tbody>
</table>
Table 4 - C-Axis requirements

<table>
<thead>
<tr>
<th>Requirement</th>
<th>Specification</th>
</tr>
</thead>
<tbody>
<tr>
<td>File Transfer Format</td>
<td>IGES</td>
</tr>
<tr>
<td>Tolerance</td>
<td>12.7μm is easy, 2.54μm possible but expensive</td>
</tr>
<tr>
<td>Smallest Tool</td>
<td>0.254mm end mill</td>
</tr>
<tr>
<td>Aspect Ratio of Cutting Depth</td>
<td>Less than 3:1</td>
</tr>
<tr>
<td>Bottom Features</td>
<td>Rounded preferred over angled</td>
</tr>
</tbody>
</table>

With these requirements in mind, the design was finalized and reviewed by the design team to ensure that all requirements were met. When the requirement about the smallest tool size was found to be violated, changes to the lip design took place to increase its size as well as change its geometry from an angled edge to a rounded one. This eases manufacturing as well as ensures the desired glue control abilities between the microfluidic cover and the silicon sensor.

Finally, the solid models of the molds were sent to C-Axis for quote and CAMD/LSU for approval. Due to the work done prior to sending these files, no further iterations were required and a quote was obtained and approval gained for the mold designs.

### 3.3 Discussion

#### Design Strengths

The design of the microfluidic encapsulation is robust. It has the ability to survive large assembly, manufacturing, and in the field forces without breaking or being damaged. The design also allows for greater flow rates, and therefore pressures, to be present inside of the encapsulated die than will ever be seen in application. The pressure can increase approximately 22 fold from the application pressure without the chip seal failing. If the outer seal between the
microfluidic cover and well do break the inner seal between the fluidic cover and silicon die are still strong enough to support the encapsulated die without the biosensor failing during use.

In addition to its robustness, the design allows for the encapsulated dice to be mass-manufactured. This is essential, as Diagnostic Biosensors is a business and must be able to quickly and inexpensively manufacture products to be profitable.

**Design Weaknesses**

As with any manufacturing process, especially on a micro scale, the design is prone to manufacturing defects and failures. If a failure occurs in any one of the many manufacturing steps, the final product may be defective. One of the biggest risks in the manufacturing process is a defective microfluidic cover or well in a mold causing the two PMMA sheets to not fit together properly.

Another weakness with the current design is that the number of microfluidic covers on the upper brass mold is not maximized due to limitations with the CAD package used to create the mold.

Finally, the manufacturing procedure is untested, and as with most prototype designs, it is likely that problems will be encountered. It is expected, however, that any problems that arise will be relatively minor and will be fixable.

**Next Steps**

The first step that should be taken is to have the upper and lower molds machined. Before doing this, it may be desired to add additional saw alignment marks to the molds and to research methods for creating a CAD model for the top mold which has the number of microfluidic encapsulations maximized. From this point, the molds should be sent to LSU for use in hot embossing the upper and lower PMMA sheets. The sheets should be carefully inspected for defects or other problems before continuing on.
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Once the hot embossed PMMA sheets have been found satisfactory, the manufacturing process laid out in this report should be implemented. To do this, several of the manufacturing steps will need to be worked out. The first is the placement of the silicon dice into the wells. The process for doing this should be efficient and accurate. Poor accuracy could cause the microfluidic cover alignment to be outside of the 50 micron tolerance specification. The second step is creation of a process for dipping the sheet of microfluidic covers in glue of a specified thickness. To create a layer of glue of known thickness, one solution may be to place a material of known thickness (scotch tape may work) onto a glass plate, cover the plate in glue, and then to squeegee off the excess glue.

Next, a method for aligning and bonding the encapsulated dice with other previously designed subcomponents of the completed biosensor needs to be designed.

Finally, the design should be tested by assembling a prototype encapsulated die and running fluid through it under pressure to ensure that no leaks or other problems occur.
References


http://www.iop.org/EJ/abstract/0960-1317/15/6/002

http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6TFC-4GX6HX3-1&_user=10&_rdoc=1&_fmt=&_orig=search&_sort=d&view=c&_acct=C000050221&_version=1&_urlVersion=0&_userid=10&md5=9bc327f23fb50393f3379452f9bde903

http://www.jo-mt.de/cps/rde/xbcr/SID-26EE34DB-0B3DE49D/mikrotechnik_1/Polymer_Microfluidic.pdf


http://tds.loctite.com/tds5/docs/3921-EN.pdf


http://hal.archives-ouvertes.fr/docs/00/25/32/31/PDF/ajp-jp4199404C7170.pdf

[10] Disco Wafer Saw Standard Operating Procedure, University of Minnesota NFC.
http://www.nfc.umn.edu/equipment/sop/sop_saw.pdf