

Precise gastight sealing for bio/chemical microchip

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1. Introduction

Recently, the use of micro-channels on microchips is catching much attention for miniaturizing and integrating bio/chemical reaction systems. The large surface area, per volume, gives high thermal conductivity to a micro-channel allowing quick and accurate temperature control of the reagents inside. In addition, its small size shortens the molecule diffusion time for fast and efficient reagent reaction. Furthermore, it requires smaller volume of reagents and reduces the waste fluid.

A micro-TAS (micro Total Analysis System) is a chemical analysis system that uses micro-channels. They are popular in immunoassay constrained by small sample sizes and they complete their tasks in very short analysis time[1]. In contrast, a system that performs chemical synthesis in a micro channel is a micro-reactor. A micro-reactor is highly efficient for thermally controlling reagents and is suitable for exothermic reaction, which requires cooling, and other reactions that need tight thermal control for putting a reagent into a specific temperature range for producing a target reagent.

Generally these microchips are manufactured by cutting grooves on substrates and covering them, however, a common problem is bonding a lid and a substrate of glass and metal with gastight sealing.

Glass is suitable material for micro-TAS's, so the researchers can visually observe the reactions[2][3]. Other transparent material, such as plastics, or silicone rubber, are also available, however, do not stand high temperature, and corrode when exposed to acid, alkali and organic solvents. In contrast, observing the reaction, perhaps, is not so important with chemical synthesis and the micro-reactor material does not need to be transparent. Therefore it should be made of metal that generally resists high temperature and pressure, and has excellent thermal conductivity. In addition, it is easy to form and is shock resistant. Some metal even resist acid, alkali, and organic solvent.

There are some method for bonding glass and

metal, diffused junction, thermal adhesion, chemical adhesion using hydrofluoric acid, however, they need high temperature, high pressure, and surface flatness in atomic order. In addition, since they are all whole surface junction, a lid could close the micro-channels covering the substrate.

To counter these problems, we propose precise bonding for not whole surface but only a local area around the micro-channels. The local bonding does not close the micro-channels and needs less heat and pressure. We employed laser welding for a metal microchip, and sintering a paste with glass flit for a glass microchip.

2. Laser welding for metal microchips

A metal microchip has to resist both high and low temperature, pressure, or stress. It also has to remain unaffected by such reagents as acid, alkali or organic solvent. Material that meet these requirement include, stainless steel, nickel, platinum, hastelloy, and inconel. We chose stainless steel for its ease of forming and low cost.

We then cut micro-channels on the surface of the stainless substrate using a fine end mill. The micro-channel size usually determines the method for machining them on stainless substrates. The channel size we needed was in the range of 200-1,000 micrometers in both width and depth. When larger, we can neglect the scale effect, however, for smaller channels, viscosity of the fluid causes flow resistance that cannot be neglected. Ferric chloride or aqua regia wet etching is also popular in cutting channels but only when the channels are 100 micrometers deep or shallower.

For the next process of covering the channels machined on the substrate, we laser welded a stainless steel plate. The specific machine we used was a Compact YAG Laser (ML-2030, MIYACHI Co., Ltd.), with a wavelength of 1064nm and a focus diameter of 500 micrometers. For finding the optimum laser output and welding conditions, we ran a preliminary test varying the laser voltage and irradiation time. Table 1 shows the results. For

welding a 0.1mm cover to a 5mm substrate, we found the optimum condition of laser output at 250-310V for 5-10msec (3.9-12.5J). Fig. 1 shows the cross-sectional view of the substrate welded with the laser output of 270V for 10msec (7.8J).

We produced a metal microchip with the processes mentioned above. Specifically, we cut 400 micrometers wide and 330 micrometers deep micro-channel, using a ball-end mill with radius 200 micrometers, on a 5mm thick SUS316L substrate. We then welded 0.1mm thick SUS316L plate on the substrate to cover the channels. A YAG laser with an output voltage of 270V and irradiation time of 10msec stopping every 400 micrometers performed the welding. Fig. 2 shows a photo of the metal microchip we produced.

We tested the welding quality by pressurizing the microchip to 220kPa, a pressure high enough pressure for general reaction, and holding the pressure for 20 minutes. A holder with inlet and outlet ports fixed the microchip in position. A fluoroplastic O-ring connected each port to a bolt with a pipe welded to it. Fig. 3 shows the pressure inside the microchip. No pressure drop was observed during this time demonstrating that the YAG laser successfully welded the microchip with gastight sealing.

Furthermore we tested the microchip by a temperature controlled reaction that mixed the reagents. The test demonstrated an exothermic reaction with acid, which is nitration of acetanilide. The local reaction temperature inside the microchip showed the good temperature controllability of the microchip.

Table 1 Results of the preliminary test varying the laser voltage and irradiation for welding a 100-micrometer cover to a 1mm substrate.

| Irradiation time voltage | 230[V] | 250 [V] | 270 [V] | 290 [V] | 310 [V] | 330 [V] |
|-----------------------------|--------|---------|---------|---------|---------|---------|
| 2.0[ms] | △ | △ | △ | △ | △ | △ |
| 5.0[ms] | △ | ○ | ○ | ○ | ○ | ○ |
| 10.0[ms] | △ | ○ | ○ | ○ | ○ | × |

- : welded successfully
- △ : not enough output for welding
- × : make a hole on the top layer

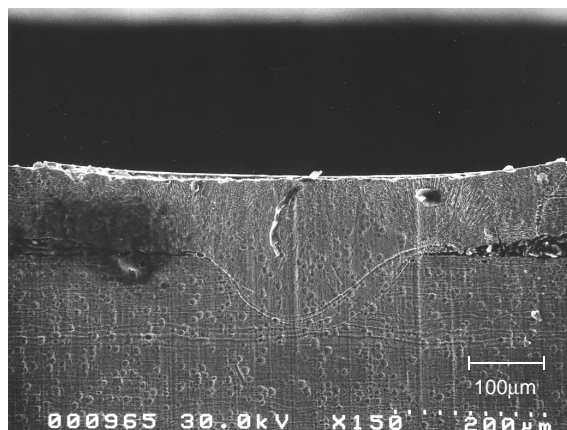


Figure 1 Cross-sectional view of the substrate welded with the laser output of 270V for 10msec (7.8J)

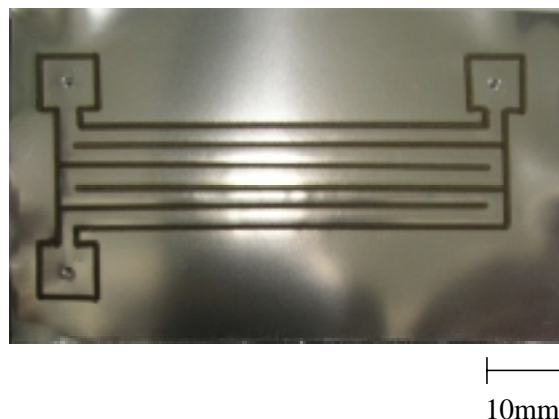


Figure 2 Photo of the laser welded metal microchip.

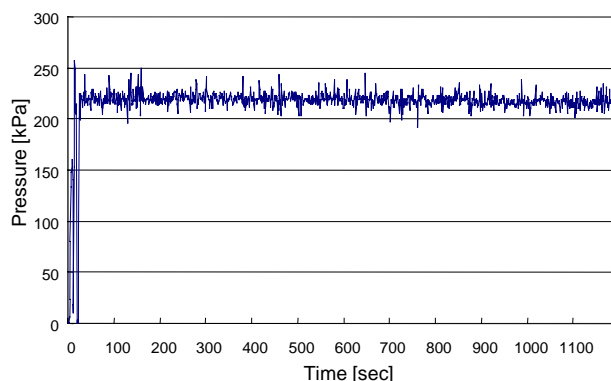


Figure 3 The pressure inside the metal microchip during pressurized to 220kPa and held for 20 minutes.

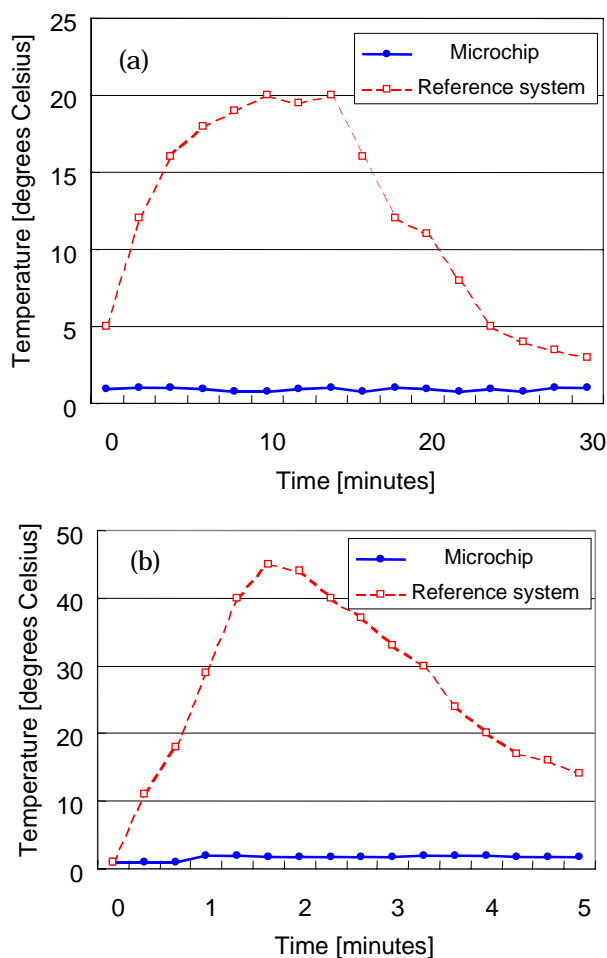


Figure 4 Temperature transition during (a) 30 minutes reaction, and (b) 5 minutes reaction.

The reaction proceeded as follows: First, 10 grams of acetanilide were dissolved in 30ml of sulfuric acid, and 12ml of nitric acid were added into the solution. For producing the target reagent p-nitroacetanilide, the microchip had to hold the reaction temperature at 15 degrees Celsius or less. Adding pure water to the mixture recrystallized the p-nitroacetanilide which was then separated by filtering. Syringe pumps fed the sulfuric acid solution of acetanilide, and the nitric acid. Thermocouples were attached to where the junction was for measuring the reaction temperature.

Fig. 4-(a) shows the temperature transition during a 30 minutes reaction of the two reagents, and Fig. 4-(b), that when we forced the reaction to complete in 5 minutes. We also took a reference measurement of the same reaction inside a much

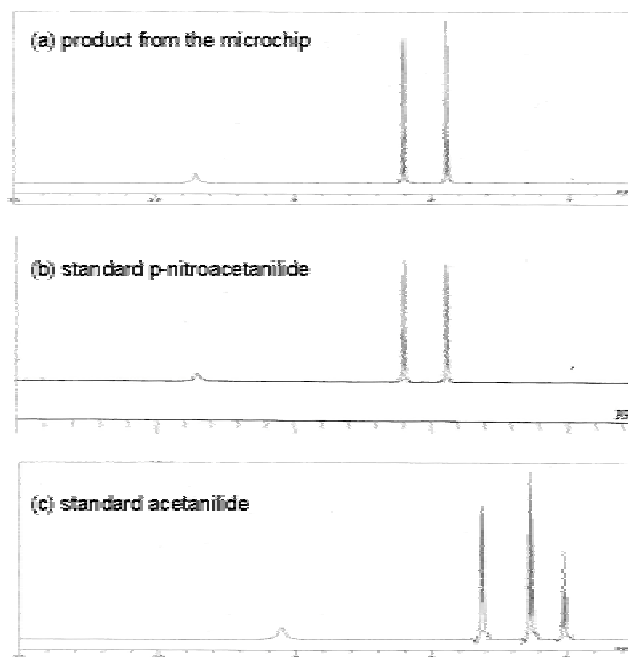


Figure 5 Analysis results of the composition of (a) the product from the microchip, (b) standard p-nitroacetanilide and (c) acetanilide using nuclear magnetic resonance.

larger beaker. Both graphs show that the reaction temperature values were kept at 3 degrees Celsius or less inside the microchip, whereas it went up to 20-45 degrees in the reference system.

We next analyzed the composition of the product from the microchip using nuclear magnetic resonance (NMR). Fig. 5-(a) shows the analysis results, and Fig. 5-(b) and Fig 5-(c) show the composition for standard p-nitroacetanilide and acetanilide. Comparing the peaks in the charts reveals that the microchip produced the required amount of p-nitroacetanilide without any residual. This test confirmed that the microchip succeeded in mixing and letting the reagents react while controlling its temperature.

3. Paste sintering for glass microchip

Direct glass junction needs high pressure and high temperature about 800-1400 degrees. Otherwise it needs dangerous process with hydrofluoric acid. Thus, we employed sintering process of a paste with glass flit which needs lower temperature, less pressure and no hydrofluoric acid. In addition, controlling the thickness of the paste layer can skip

the glass grooving process including complicated mask process.

Fig. 6 shows the bonding process of the glass microchip. We first put a channel-shaped polyimide film as a core on a 1 mm thick substrate. We then put a glass flit paste on the substrate along the channel core using a precise dispenser. Next, we put another 1 mm thick glass plate on the substrate and sintered them at 580 degrees for 1 hour. The core which is 500 micrometers wide and 150 micrometers thick decomposed during the sintering. The glass flit has a particle size of 50nm-2 μ m and a deformation temperature of 475 degrees.

Fig. 7 shows the sintered microchip. We measured the channel width and depth, and the bonding strength of the microchip. The result shows that the channel size was in the range of 460-540 micrometers in width and 140-160 micrometers in depth. It means that sintering process made a channel size error of 8% from the lost core. The bonding strength against tensile stress was 1.2 MPa, enough pressure for the general reaction. However, micro cracks, which causes leakage, were found on the sintered paste. They seemed to be produced when the solvent in the paste vaporized. Sintering the paste in vacuum for degasification will defeat this problem.

4. Conclusion

We developed two bonding method for metal and glass microchips. YAG laser successfully welded a SUS316L plate over the micro-channels to cover them. The welding quality was tested by pressurizing the microchip and holding the pressure. Our metal microchip performed well in nitration of an acetanilide. Paste sintering achieved glass bonding. We put glass flit paste along a polyimide core using precise dispenser. Sintered for 1 hour at 580 degrees, the glass microchip has a bonding strength of 1.2MP, however, it has a channel size error of 8%, and micro cracks on the sintered paste. The future work is to optimize the sintering conditions for bonding without cracks.

References

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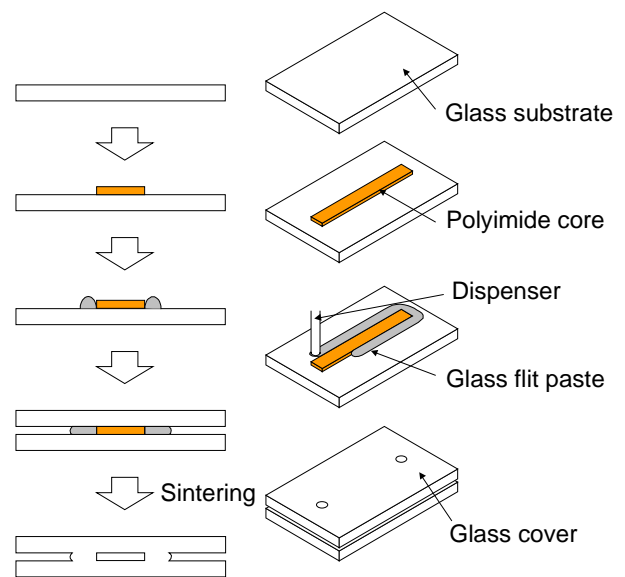


Figure 6 Configuration of the bonding process of the glass microchip by sintering glass flit paste.

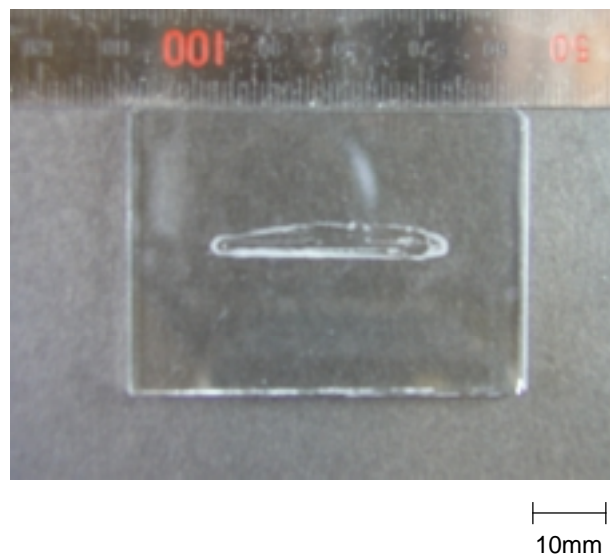


Figure 7 Glass microchip sintered for 1 hour at 580 degrees.