Research Article

A Method for Manufacturing Flexible Microfluidic Chip Based on Soluble Material

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In this paper, a novel method for manufacturing flexible microfluidic chips without bonding process is proposed, which combines 3D printing technology and material dissolution technology. The manufacturing process of the microfluidic chip is as follows: a soluble HIPS mold with a preset shape is manufactured by 3D printing and placed in a molten PDMS solution for solidification. Soak in the limonene material to dissolve the mold and form a microchannel in the cured PDMS. Experimental studies have shown that the temperature and concentration of the limonene solution have an important effect on the dissolution rate. A 0.62 cm³ HIPS mold has the fastest dissolution rate at 100°C and 50% concentration. The proposed method provided a new idea for fabricating flexible microfluidic chip. Compared to bonding process, it has the characteristics of not relying on complicated processing conditions and low manufacturing cost.

1. Introduction

The microfluidic chip is originally called the “laboratory on a chip.” It is a microplatform through the microchannel, pump, valve, liquid reservoir, electrode, and other different structures in the microscale environment to complete microprocessing or microexperiment. In recent years, it has developed into a new research field of biology, chemistry, medicine, fluid, electronics, materials, machinery, and other disciplines. With the wide application of microfluidic chips, various manufacturing methods have been proposed [1, 2].

With the emergence of cutting-edge processing technology, there have been major breakthroughs in the preparation of microfluidic chips. A method utilizing PMMA and ABS solvent was adopted to manufacture a chip with well microchannel integrity [3]. Improperly, the optical transparency of the chip is insufficient. Consequently, chips with higher optical transparency can be obtained based on the micromilling processing method [4]. But despite all that, this method will produce burrs on the surface of the microchannel. For instance, a solvent processing laser etching microchannel technology for fabricating a microfluidic chip was employed to

improve the quality of the chip microchannel [5]. Nonetheless, extra special bonding glue is required in the production process. Subsequently, a GATP thermocompression process was presented to obtain a microfluidic chip with no bonding glue [6]. Insufficiency, in the production process, the process steps are complex and cannot be produced on a large scale. Fortunately, in order to facilitate the large-scale production of chips, micromicrochannels are utilized based on the traditional 3D printing-fused deposition molding method. That method eliminated tedious processing steps and postprocessing [7]. Unfortunately, the flow passage with a single configuration cannot produce a complicated flow microchannels. Correspondingly, the production of chips is based on ceramic plate printing—PDMS pouring method, which was able to manufacture micromicrochannels with complex configurations [8]. Inadequacy, the microchannel production process is demanding. Significantly, 3D printing mold—PDMS pouring technology effectively reduces the manufacturing process requirements of complex structure microchannels [9]. However, the chip preparation is time-consuming. Especially, a belt-adhesive laser cutting and sealing integrated TLCSI chip is developed [10]. This method completing the bonding in

FIGURE 1: Manufacturing method schematic diagram. (a) Soluble 3D printing mold; (b) principle of limonene dissolution; (c) limonene dissolution process; (d) chip fabrication process.

the meantime during the laser cutting process shortened production time. Ultimately, the final curing strength of the chip is unsatisfactory.

This paper presents a new microfluidic chip fabrication process. The 3D printing technology and limonene dissolution technology are applied to manufacture a microfluidic chip. And then, the influences of the temperature and the concentration on the solution velocity are discussed. Furthermore, the mixing experiment is implemented. Finally, the summing-up is concluded.

2. Materials and Methods

2.1. Materials and Instruments. HIPS and ABS were purchased from Flashforge, China. Sylgard 184 silicone elastomer and curing agent were purchased from Dongguan Sanbang New Material Technology, China. 3D printer (Flame, Flashforge) is employed to print pouring mold and microchannel mold with the material of HIPS and ABS (Flashforge, China). Limonene solutions (Flashforge, China) are adopted to fabricate a microfluidic chip with the material of the PDMS. Injection pump (LSP02-2B, Longerpump) is utilized to implement mixing experiment. The cross-section of the micromicrochannel is observed based on an inverted fluorescence microscope (OLYMPUS IX73, Japanese).

Figure 1 shows a method of manufacturing a flexible microfluidic chip. Figure 1(a) shows the process of the soluble 3D printing mold. As shown in Figure 1(b), limonene solutions are utilized to dissolve the microchannel mold

and then form an empty microchannel in PDMS microfluidic chip. HIPS and limonene are mixed to form a homogeneous mixture through molecular diffusion.

2.2. Fabrication of the Microfluidic Chip. The manufacturing process of PDMS microfluidic chip with the empty T microchannel is shown in Figure 2. The specific production process and related matters for attention are shown in Table 1.

3. Results and Discussion

3.1. The Dissolution Rate of HIPS. Figure 3(a) shows the relationship between the dissolution rate and time at different temperatures. The higher the temperature, the faster the dissolution rate. It only takes 30 minutes for the mold to dissolve completely at 100°C. The dissolution rate of the mold reaches the maximum when the concentration of limonene is 50%, as shown in Figure 3(b).

With the deepening of research, we found that the principle of similar compatibility can explain the above phenomenon. Similar miscibility principle is appropriate for HIPS and limonene, owing to a common property of non-polar. The relationship between dissolution rate, concentration, and temperature can be explained by Equation (1).

$$\Delta G_m = \Delta H_m - T\Delta S_m, \quad (1)$$

where ΔG_m is the mixing free energy of high impact polystyrene (HIPS) and cinene solution, ΔH_m is the enthalpy of

FIGURE 2: Preparation of microfluidic chip.

TABLE 1: Manufacturing steps and parameters.

Steps	The production process	Specific methods and parameters
Step 1	Printing the ABS framework	3D printing technology is employed to fabricate the ABS framework with the size of 6 * 5 * 5 cm.
Step 2	Printing the HIPS mold and casting the PDMS	3D printing technology is utilized to manufacture the HIPS mold with the length of 0.8 cm and the cross-section size of 200 μm * 200 μm . The PDMS solution is poured with a thickness of 0.3 mm and cured at 80 degrees.
Step 3	Placing the HIPS microchannel mold	The HIPS mold is placed on the PDMS surface. Heat curing is carried out with the temperature of 80 degrees and the time of 20 minutes.
Step 4	Casting and curing	The PDMS solution is poured with a thickness of 0.3 mm and cured at 80 degrees.
Step 5	Punching the holes	The holes with diameter of 2 mm are punched in the chip.
Step 6	Dissolving the microchannel mold in limonene solvent	The dissolving time is 30 minutes with the temperature of 100°C and the limonene concentration of 50%.
Step 7	Completing the chip	The microfluidic chip with an empty T microchannel is fabricated.

mixing of HIPS and limonene, ΔS_m is the mixing entropy of HIPS and limonene, and T is the dissolution temperature. When the value of ΔG_m is less than zero, the dissolution process of HIPS is implemented spontaneously. As the ΔG_m gradually decreases, the dissolution rate of HIPS in the solution gradually increases. As shown in Figure 4, with the increase of temperature, ΔG_m gradually decreases, which means that the dissolution rate gradually increases.

According to free energy Equation (1), for the given parameters including ΔS_m of 12.84 and ΔH_m of 0.00081, ΔS_m value is through Equation (2). ΔH_m value is through Hildebrand Equation (3). The specific parameters are shown in Table 2.

$$\Delta S_m = -R(n_1 \ln \phi_1 + n_2 \ln \phi_2), \quad (2)$$

where R is the entropy coefficient, n_1 is the number of moles of HIPS material, n_2 is the number of moles of limonene material, Φ_1 is the solvent volume fraction, and Φ_2 is the solute volume fraction. Finally, ΔS_m value is 12.84. According to Hildebrand Equation (3), the details are as follows:

$$\Delta H_m = V_M \phi_1 \phi_2 (\delta_1 - \delta_2)^2, \quad (3)$$

where V_M is the molar mixing volume 20.00032, Φ_1 is the solvent volume fraction, Φ_2 is the solute volume fraction, and δ is the solubility parameter. Figure 5 reveals the influence of the solubility difference on the mixing enthalpy ΔH_m . The value of the ΔH_m depends on the solubility parameter difference with the expression of $\delta_1 - \delta_2$. According to the theory, the smaller the solubility parameter difference is, the shorter the time is.

FIGURE 3: The relationship between the HIPS mold dissolution rate and the parameters of the limonene solution. (a) Effect of water bath temperature on dissolution rate. (b) The mold dissolution rate changes with the concentration of the limonene solution. (c) Dissolution rate curve under optimal parameters. (d) Overall dissolving effect of HIPS mold.

Concretely, the value of the solubility parameters of the HIPS material is 9.1. It can be obtained that the minimum mixing enthalpy is corresponding to the concentration of 50%, the second one is the concentration of 30%, and the last one is the concentration of 100%. That result is simultaneously verified from the experiment results demonstrated in Figure 3(b).

During the experiment, it was found that HIPS swelling phenomenon occurred during the dissolution process. Figure 6 shows the HIPS swelling phenomenon. During the swelling process, the overall volume of the HIPS mold increases by 10% to 30%.

Figure 7(a) shows the entire dissolution process of the HIPS mold in the limonene solution. During the first 20 minutes, swelling phenomenon occurs as the limonene solvent comes into contact with the HIPS material. In 20 to 40 minutes, the swelling phenomenon ends and the volume of HIPS remains unchanged. After 40 minutes, the dissolution process begins, and the HIPS mold is completely

dissolved in 80 minutes. Figure 7(b) shows the HIPS swelling rate in 20 minutes, and the fitting formula of swelling rate is obtained.

$$Y = 0.00054X + 0.0083, \quad (4)$$

where Y is the volume of HIPS material and X is the swelling time. Finally, the optimal solution parameters are obtained as shown in Figure 3. It was found that limonene solution with 50% concentration in 100°C water bath had the best dissolution effect, and the channel could be dissolved in 25 min. And dissolving effect is shown in Figure 3(d).

Figure 8(a) shows the microscopic diagram of the channel before HIPS dissolution, while Figures 8(b)–8(d) are the microscopic diagrams of the channel formed after dissolution. Among them, the channel width is 200 μm and the height is 100 μm. The 3D printing accuracy is 200 μm, and

FIGURE 4: Effect of temperature on dissolution time.

TABLE 2: The specific parameters.

ΔG_m (KT)	ΔS_m (J/K)	ΔH_m (J/K)	Φ_1 (cm/ml)	Φ_2 (cm/ml)	R (constant)	V_M (cm ³)	n_1 (mol)	n_2 (mol)
-321	12.84	0.00081	1	0.000016	8.310	20.00032	0.019	0.14

FIGURE 5: The relationship between the mixing enthalpy ΔH_m and other parameters.

the channel accuracy can be guaranteed to remain in 200 μm by dissolution, due to the good scalability of PDMS.

The channel production method adopted in this paper is limonene dissolved HIPS mold method, that is, limonene dissolved HIPS material to finally get the molding channel, without vacuum environment or high temperature equipment for processing. The mold was made using 3D printing technology. The 3D printer used in this paper can achieve

FIGURE 6: HIPS swelling phenomenon.

FIGURE 7: HIPS state changes during the manufacturing process.

FIGURE 8: Comparison of mold and forming groove mirror.

the highest precision of $200\mu\text{m}$. Table 3 shows the die and final channel dimensions.

3.2. Comparison of Bonding Methods of Different Materials.

The main fabrication methods of microfluidic chip were summarized. Table 4 lists several chip manufacturing methods for different materials, which have corresponding adding processes and processing equipment. It is worth noting that the production method in the table requires high equipment, and the processing steps are complex. Glass-silicon wafer material was fabricated based on photoresist film bonding [11]. The microchannel is etched optically with a lithography machine. The final chip is fabricated based on the bonding method. However, this method leads to insufficient chip strength. For this use of glass-glass material chip production [12], chemical vapor deposition was developed. Plasma etching machine etches microchannels in the glass and then bonds them under high temperature and pressure conditions, resulting in higher chip strength. Unfortunately, the conditions for the bonding temperature are strict. In contrast to this, PMMA-PMMA material is based on high temperature hot-press bonding [13]. Hot press for chip bonding can reduce the manufacturing temperature. There is a fly in the ointment; its bond synthesis power is low. Fortunately, PDMS-glass was adopted. For adhesion after surface modification [14], the success rate of chip preparation is improved. It is worth noting that the surface modification requires special gas, which is dangerous to some extent. In view of the above several chip fabrication methods, all require a three-step process to complete chip production. In this paper, the chip can be prepared in only 2 steps. The microchannel preparation is through the dissolution method, which has the advantages of high yield and high chip strength.

TABLE 3: Accuracy comparison between HIPS die and forming channel.

Accuracy of the channel	Length	Wide	High
Print the finished channel mold	205	201	50
Dissolve to complete the channel	200	200	49

The main fabrication methods of microfluidic chips are reviewed. Table 5 lists three chip fabrication methods for different materials, each of which has a corresponding addition process and processing equipment. It is worth noting that the production methods in the table have high equipment requirements and complex processing steps. PDMS was prepared based on sugar templating approach [15]. The PDMS material is vacuumized by vacuum device, then heated, and finally dissolved to produce the chip. However, this approach is cumbersome. Remarkably, a lost-wax casting method was used to fabricate channels [16]. The preparation of the channel by melting wax material needs to be dissolved at high temperature, so it is easy to leave residue in the channel. The final channel is of poor quality. Given both of these methods, a three-step process is required to complete the chip. In this paper, only two steps are needed to fabricate the chip. The microchannel preparation method is prepared by dissolution method, which has the advantages of high yield and high chip strength.

3.3. Chip Mixing Experiment. Figure 9 shows the mixing performance test of 3D microfluidic prototype based on soluble HIPS. Concentration tests were carried out on different positions of A, B, and C in the same channel. The results in Figure 9(a) show that the new manufacturing method can achieve a mixed effect functionally. The experiment process is as follows: deionized water and blue ink are utilized to implement the mixing experiment with the fluid velocity of

TABLE 4: Comparison of different microfabrication methods.

Chip material	Production methods	Manufacturing conditions	Main manufacturing equipment	Important technological process
Glass-silicon wafer	Lithography Lamination adhesive	Vacuum	Lithography 3 steps	Optical lithography Bonding
Glass-glass	Chemical vapor deposition	High pressure Elevated temperature	Plasma etching machine 3 steps	Chemical etching Bonding
PMMA-PMMA	Elevated temperature hot pressing	Elevated temperature and high pressure	Hot press 3 steps	Etching Elevated temperature bonding
PDMS-glass (PDMS)	The surface modification Adhesion	Room temperature High pressure	Plasma cleaning machine 3 steps	Chemical etching The surface modification bonding
PDMS	3D printing Dissolve	Room temperature	3D printer 3 steps	Dissolve No bonding

TABLE 5: Comparison of different microfabrication methods.

Chip material	Production methods	Manufacturing conditions	Important technological process	The channel dimension (μm)
PDMS	Sugar templating approach	Vacuum Convection heating Freezing Hydrolysis	Vacuum Heating Hydrolysis	300-500
Hard wax resin	Micro lost-wax casting	High pressure Elevated temperature	High temperature heating	300
PDMS	3D printing Dissolve	Room temperature	Dissolve No bonding	200

FIGURE 9: Mixing performance test of 3D microfluidic prototype based on soluble HIPS. (a) The change trend of the concentration index at different positions over time during the mixing process; (b) principle of mixed experiment; (c) microscopic microchannel diagram of different positions.

1.730 mm/m. To investigate the mixing index, the concentration Equation (4) is introduced as follows [17–20]:

$$Y = 357.28661 - 2.50297X + 0.00437X^2, \quad (5)$$

where X is the grey value and Y is the concentration, respectively, specifically through bringing grey value of grey value X into the above equation.

$$I_N = 1 - \frac{1}{50\%}(Y \times 100\% - 50\%). \quad (6)$$

I_N is the mixing index. It is well known that the larger the mixing index is, the better the mixing effect is. It can be seen from Figure 5 position A that with the increase of the time, the mixing index increases 0 from 0.796 to 0.841. Furthermore, the growth rate of the mixing index increases obviously, when the time exceeds 30 s. That is due to the increase of the microchannel length. As a consequence, the chip fabricated through this paper's method is practical.

4. Concluding Remarks

This paper proposes a new method, without bonding process, for manufacturing integrated microfluidic chips with 3D printing and limonene dissolution technology. Experiments were carried out to verify the influence of limonene on the dissolution of the microchannel under different conditions. Finally, a hybrid experiment was performed on the fabricated chip. Conclusion is as follows:

- (A) Free energy theory can explain the influence of temperature on the dissolution rate. In this paper, the dissolution experiment was conducted at room temperature, 60°C, and 100°C in 3 sets of water bath temperatures. The best water bath temperature was 100°C
- (B) The study found that the smaller the concentration difference between HIPS and limonene solution, the more significant the dissolution rate. Under 100°C water bath heating conditions, 30%, 50%, and 100% concentrations of limonene solvents were prepared for channel dissolution experiments. It was found that the dissolution times at the three concentrations were 70 min, 60 min, and 80 min, and the dissolution rate was the fastest at 50% concentration
- (C) The expansion of HIPS mold at the beginning of dissolution was found, in the HIPS material dissolution process, because HIPS materials and limonene solution diffusion capacity are different. And large molecular chains in HIPS materials are entangled with each other, and for high intermolecular forces, the limonene molecules will first infiltrate between the HIPS molecules, which weakens HIPS molecular interaction force, causes volume expansion, and produces swelling phenomenon

- (D) On the T-chip made in this article, a mixing experiment of two liquids was carried out. Verify the effectiveness of the chip. Finally, the concentration mixing index of the chip is as high as 0.547

The integrated chip manufacturing method proposed in this paper realizes efficient and convenient production and processing of microfluidic chips. It has the advantage of being able to manufacture complex microchannels without chip bonding and contribute to the improvement of chip production efficiency.

Data Availability

Some or all data, models, or code that support the findings of this study are available from the corresponding author upon reasonable request (list items).

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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