FLUID DRIVE CHIPS CONTAINING MULTIPLE PUMPS AND SWITCHING VALVES FOR BIOCHEMICAL IC FAMILY

- Development of SMA 3D micro pumps and valves in leak-free polymer package -

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ABSTRACT

Versatile micro fluidic device "Biochemical IC Family" based on the concept of family IC chip-set has been proposed and developed by the authors. Several types of biochemical IC containing multiple micro fluidic devices such as reactors, concentrators and one-way valves have been developed. A luminous enzyme of firefly was synthesized by using these chips. New chips to handle chemical fluid were first fabricated successfully and basic performance was verified experimentally. Shape memory alloy (SMA) micro actuator was utilized for micro actuation.

New micro stereo lithography (Hybrid IH Process) to make 3D composite structure consisting UV polymer and other micro parts was developed and was utilized for total chip fabrication. The pump chip succeeded to flow chemical liquids through the connected chips. The switching valve chip changed reaction passes quickly. By using these biochemical IC chips, new era in where various kind of reaction system can be constructed by the chemists in their own laboratory will come.

INTRODUCTION

Authors have been conducting unique biochemical micro devices named "Biochemical IC" proposed by Ikuta et al in MEMS'94 and '96 [1,2]. This device originally named as "MIFS" (Micro Integrated Fluidic System) contains both the miniaturized chemical apparatus made of polymer and silicon circuit in one chip. Although the concept for miniaturization of chemical system on a chip seems similar to "micro-TAS" (Total analysis system), "Laboratory on the chip" and "DNA chip", the biochemical IC differs from them in various meanings.

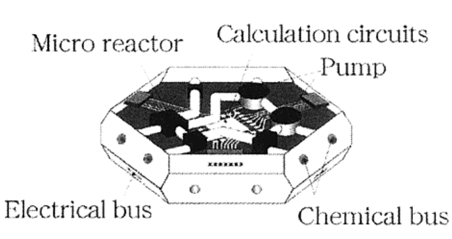
Fig.1(a) shows basic concept of our biochemical IC consisting 3D micro fluidic channel (upper part) fabricated by the IH process (micro stereo lithography) and electric parts (lower part) made by silicon process. Fig.1(b) shows modular IC concept of the biochemical LSI which satisfies more complicated capability at higher level. [3,4]

UNIQUENESS OF BIOCHEMICAL IC CHIP

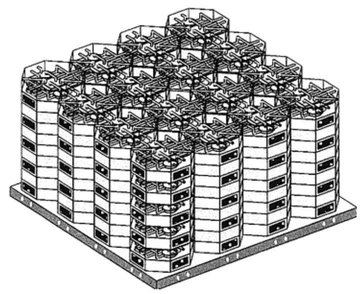
The biochemical IC has following features in comparison with other micro chemical devices.

1) Modular device architecture
2) 3D micro integrated fluidic system
3) User assemble chip set family
4) Containing micro fluid drive device
5) Versatile for various kinds of chemical reaction
6) Large scale range of flow rate and volume
7) Hybrid structure of polymer, silicon and other materials
8) Self-contained internal detector and feedback control system

This biochemical IC is based on modular IC concept similar to the today's IC/LSI family (C-MOS/TTL). Each biochemical IC chip in a disk (or cell) shape contains different functional devices such as multiple micro valves,



(a)



(b)

Fig. 1 Basic design of Biochemical IC and LSI
(a) Cellular type IC (b) Biochemical LSI

pumps, chemical condensers (concentrators) and micro reactors so on.

Another uniqueness of our approach is utilizing new 3D micro fabrication process to make a hybrid or composite structure suitable for highly integrated micro fluidic devices. Author's original IH process (micro stereo lithography) was up-graded to make composite structures consisting of UV polymer and other materials. Finally, detector concept contributes to realize cheaper disposal chip. However, it causes difficulty to miniaturize total chemical system with sensor feedback which is indispensable to implantable micro chemical devices such as DDS. Moreover, in order to miniaturize total chemical system, internal detector concept becomes more significant.

NEW FABRICATION PROCESS

Limitations of Silicon Process

The silicon process has many advantages for MEMS, although it has serious problems for micro chemical devices due to following reasons.

1) 3D micro fluidic channel is not available
2) Internal chemical reaction cannot be observed
3) Making hybrid (or composite) structure with other parts is difficult
4) Mixing is difficult
5) Leak free packaging is difficult

The silicon process such as surface micro machining and etching cannot fabricate real three dimensional structure even though deep x-ray lithograph can make tall structure with high aspect ratio. Flat and two dimensional fine channels bring difficulties of both high density integration and mixing chemicals. Since the viscosity affects dominant in the micro scale due to " scale effect ", it is hard to realize perfect mixing in the shallow well or channel made of silicon process. Great effort to solve mixing problem have been made for these years. It can be eliminated easily if the well has more three dimensional shape such as cubic.

Transparency of material also becomes more important for micro chemical devices. Because it is deeply demanded to see internal chemical reactions for various kinds of chemical analyses.

In order to solve above issues due to conventional process, systematic researches described in later sections have been conducted.

Composit Structure Using Hybrid IH Process

Unlike silicon process, the IH process (micro stereo lithography) uses variety of UV curable polymers to create 3D micro structure. Most of UV polymer is transparent for visible right over 380[nm] wave length. The transparency of material plays significant roles in case of micro chemical devices to monitor internal chemical reactions by using optical method.[4]

Following merits of IH process for micro chemical devices have been verified.

1) Transparent micro device
2) Complicated 3D micro structure
3) No packaging is required
4) Freely movable micro mechanism
5) Hybrid (composite) structure made of polymer and other materials

The new technique to make a hybrid structure is applicable to both micro and macro stereo lithography. This "Hybrid structure" means composite structure combined UV polymer with any other solid parts such as electronic parts. The MIFS and biochemical IC chip are the typical example.

Fig. 2 shows the sequence of Hybrid IH process. The other micro parts such as ultrafiltration membrane and silicon rubber are inserted during polymer solidification process as shown in Fig.2(2). The unsolidified liquid UV polymer can be washed out by rinsing. Finally, a small vacancy around the filtration membrane or silicon rubber is produced.

Since no additional bonding process is needed, the chip packaging without any leakage can be made easily. The packaging difficulty and leakage problem can be eliminated completely. This unique method to produce hybrid structure is not possible by using any other micro fabrication process.

Above mentioned process can expand design flexibility for various kinds of micro chemical devices in where many electronic and mechanical parts are combined effectively.

PASSIVE BIOCHEMICAL IC CHIPS

Prototype of Passive Chip-Set

Fig.3 shows the basic concept of total micro chemical system constructed by the biochemical IC chip family. The first upper layer cell is the "connector chip" to connect each channel with tube in multiple way. The second layer is the "pump chip" with micro pumps to flow liquid

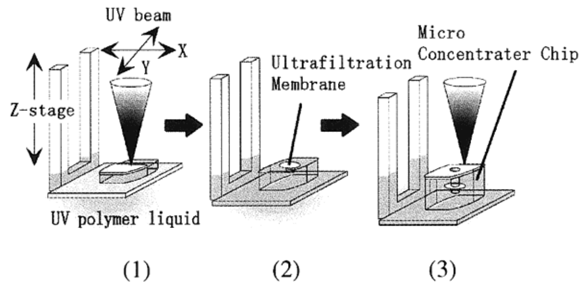


Fig.2 New fabrication process of hybrid micro chip using Micro stereo lithography (Hybrid IH process)
(1) pre-solidification process
(2) inserting process
(3) post- solidification process

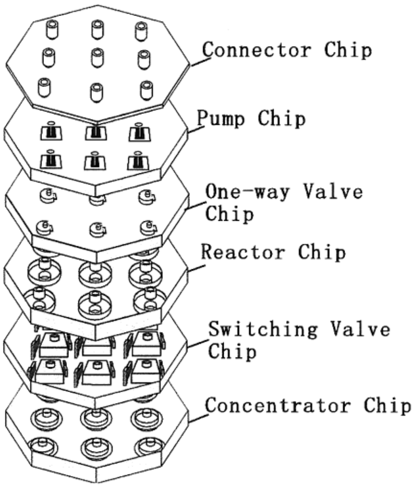
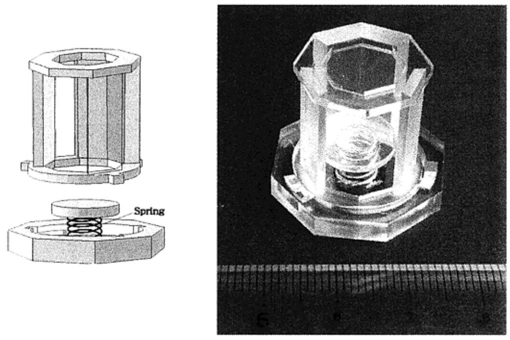


Fig.3 Concept of Biochemical IC Chip-set family



(a) (b)

Fig.4 Folder Unit for Biochemical IC
(a) Basic design (b) Prototype unit

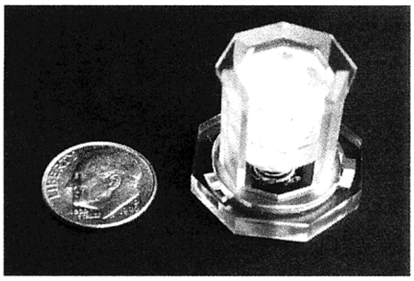
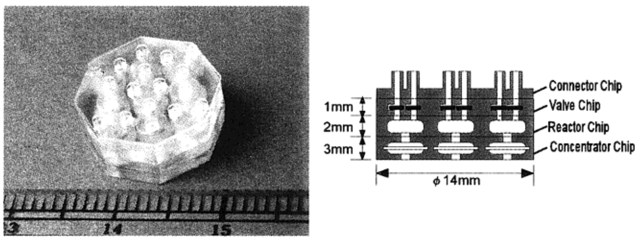
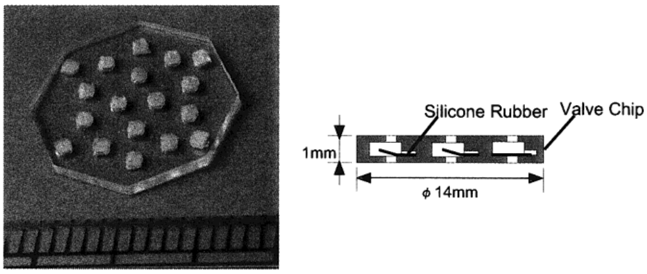


Fig.5 Folder Unit with Biochemical IC Chips



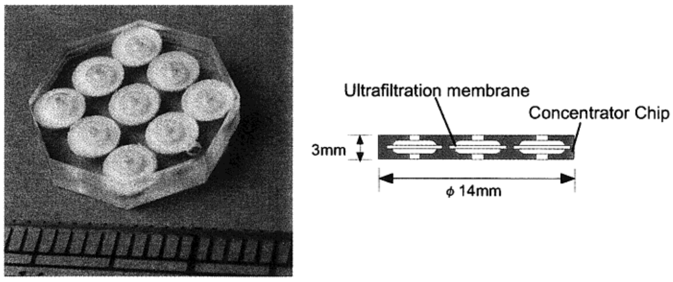
(a) (b)

Fig.6 Prototypes of Passive Chip-set
(a) prototype chips (b) cross section of four chips



(a) (b)

Fig.7 Valve chip with nine micro one-way valves
(a) prototype chip (b) internal structure



(a) (b)

Fig.8 Concentrator chip with nine micro concentrators
(a) prototype chip (b) internal structure

actively. The third layer is the "valve chip" consists of multiple one-way valves. The forth layer is the "reactor chip" contains multiple reactors. The fifth layer is the "switching valve chip" to control flow line actively. The sixth layer is the "concentrator chip" contains multiple condensers.

The present size of each chip is 14 x 14 and the thickness is from one to three [mm].

Fig.4 shows the folder unit to stack up the biochemical IC chips. Thin silicon rubber films are sandwiched between two chips. All of the chips are held tightly by spring force to prevent fluid leakage as shown in Fig.5. This pressure is adjustable by changing spring stiffness according to application.

Fig.6(a) is the prototyped biochemical IC chips and cross sectional view of each layer is shown in Fig.6(b). Total height is about 3 [mm].

Fig.7(a) shows the prototype of the one-way valves chip and Fig.7(b) shows the cross section. Each micro valve consists of silicon rubber valve in the micro chamber with one inlet and one outlet. The size of the valve is 3[mm] in diameter. One valve chip has nine micro valves at this model.

Fig.8(a) is the concentrator chip containing nine micro concentrators. As shown in Fig.8(b), a ultrafiltration membrane can filter chemicals depending on the molecular size. Total size of the each micro concentrator is much smaller than previous version of micro concentrator reported in MEMS'99 by the authors.[5]

Both of valve and concentrator chip are fabricated by hybrid micro stereo lithography. The ultrafiltration membrane to filter various chemicals in the difference of molecular size is inserted during layer by layer UV polymer solidification process.

Experimental Verifications of Basic Performances

The protein synthesis and concentration by the family of biochemical IC chips are verified by several experiments.

In order to verify biochemical concentration ability, a synthetic protein "Luciferase" (photo protein of firefly) is used.

To simplify experiment, Luciferase assay system (Promega) and YM30 (MILLIPORE) as an ultrafiltration membrane were used. The assay reagents consist of luciferase, luciferin, ATP and so on. The synthesis reaction was made in the micro reactors. One-way valves prevent inverse flow from the reactors during chemical reaction.

As shown in Fig.9, a bright luminous was observed from the concentration chamber and correspondent voltage from the photo diode is provided successfully. The time response according to the increase of concentration is indicated in Fig.10. The measured concentrate rate data demonstrates that larger than 10 times high concentrate solution can be obtained at the present time. This rate is sufficient for various biochemical reactions.

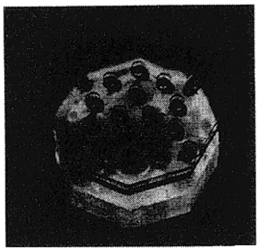


Fig.9 Luminous from micro concentrator chip

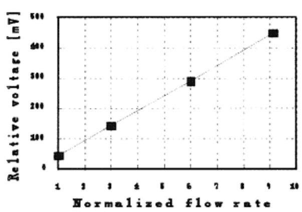


Fig.10 Experimental result of concentration rate

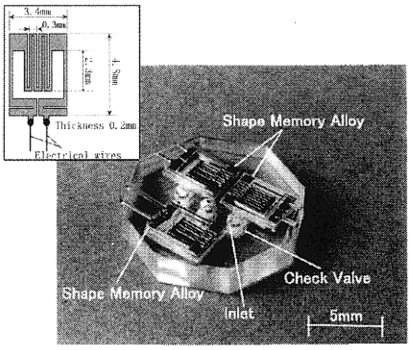


Fig.11 Prototype of the micropump chip

ACTIVE BIOCHEMICAL IC CHIPS

Prototype of Active Chip-set

Active devices such as pump and active switching valve were designed and fabricated successfully.

Micro pump chip

The cold-rolled TiNi SMA alloy sheets (t=0.2[mm]) were cut by YAG laser and annealed at 672K for 30 min. for memorizing shape. The maximum displacement for pumping is 0.3 [mm] and the maximum force is 370 gf. The size of micro pump chip is 14 x 14 x 3.0 [mm] and it contains three micro pumps. Since the Hybrid IH process fabricated total chip, no additional bonding process is required. Each pump designs are reciprocating pumps, consisting of two check valves, a deformable chamber and a SMA actuator. (Fig.11)

Fig.12 shows the schematic diagram of pumping sequence. The fluid is forced to flow out through the outlet valve, when the pump chamber contracts and the fluid is drawn in through the inlet valve, when the chamber expands. In other words, the actuator cycles the volume of the pump chamber, while the check valves ensure unidirectional flow through the chamber. Each pump rates for water are on the order of 10 micro liter/min. (Fig.13) This pump rates is quite enough because the volume of micro reactor is three micro liter.

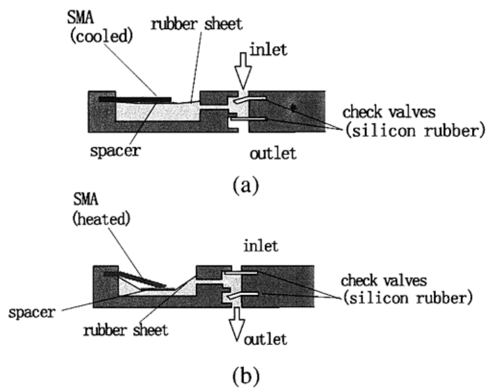
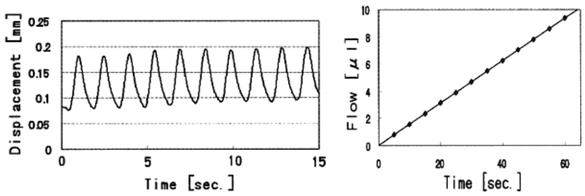


Fig.12 Operation principle of micropump
(a) suction condition (b) discharge condition



(a) (b)

Fig.13 Experimental result of the micropump
(a) dynamical displacement of SMA actuator
(b) pump rate

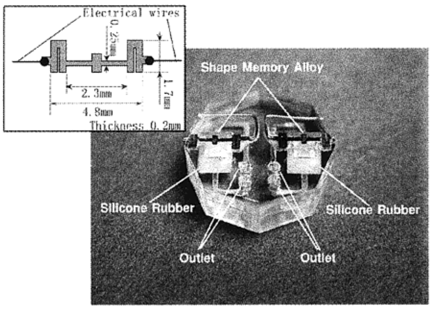
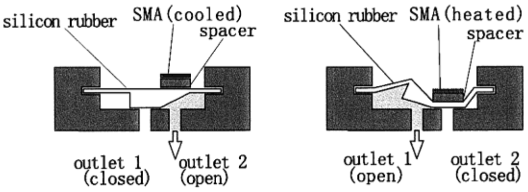


Fig.14 Prototype of the micro switching valve chip



(a) (b)

Fig.15 Operation principle of the micro switching valve
(a) normally condition (b) switching condition

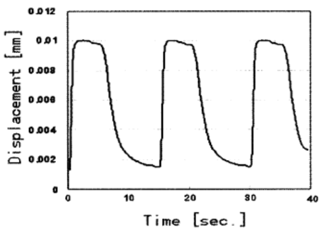


Fig.16 Response time of the micro switching valve
(Switching time: approximately 0.5 sec.)

Switching valve chip

The switching valve chip to select direction of flow dynamically was fabricated, which are actuated by two SMA micro actuators as shown in Fig.14. This valve design is one inlet-two outlet connection valve, consisting of two silicon rubbers as a valve and SMA actuators. The chip size is 14 x 14 x 4 [mm]. This chip was also fabricated by using hybrid IH process.

Fig.15 shows operation principle of one valve. The outlet 2 opens while SMA is cooled and the outlet 1 opens while SMA is heated to push down silicon rubber valve.

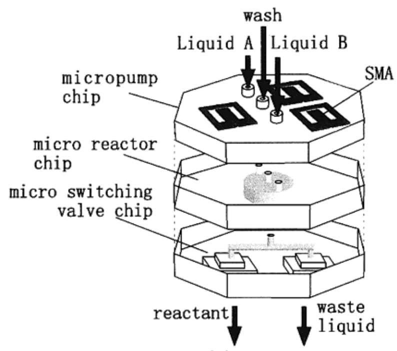
The response of the switching valve was measured as shown in Fig.16. The switching time in active phase was better than 0.5 [sec] and the response time of opposite way in passive phase was about 2 [sec]. This delay was caused by the slow cooling rate of SMA. This result satisfies practical use, because intermittent operation is major.

Experimental Verifications of Active behavior

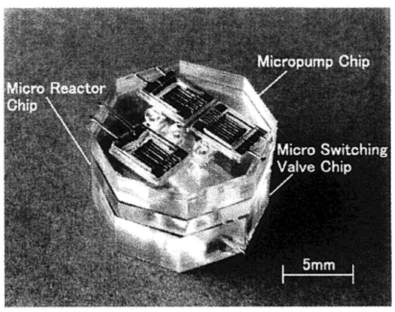
By using above three types of biochemical IC chips as shown in Fig.17, several experiments were done.
1) The liquid A and B are flowed by the pump chip and mixed. 2) After mixing and reaction is finished, reactant is flowed through outlet. 3)Water for washing is introduced into reactor and wasted through another outlet through the valve chip.

The biochemical IC chips with above active fluid drive chips are demonstrated by the experiments. By using three types of chemical chips, a simple experiments of neutralized reaction using sodium hydroxide and phenolphthalein was done. Fig.17 shows the schematic design of the biochemical IC chips with above active fluid drive chips. The first upper layer cell is the micro pump chip to flow sodium hydroxide through the inlet. The second layer is the micro reactor chip. The third layer is the micro switching valve chip to switch to another outlet. Silicone rubbers were put between each chip to connect biochemical IC chips and the biochemical IC chips were under pressure not to leak out.

Fig.18 is the sequential photographs for demonstration while the neutralized reaction is proceeding in transparent biochemical IC chips. First, phenolphthalein was introduced into the micro reactor through the inlet by the injection and filled .Secondly, sodium hydroxide was flowed though another inlet by the micro pump and mixed in micro reactor as shown in Fig.18(b). Thirdly, the micro pump was keeping on flowing sodium hydroxide and reactant was flowed through the left outlet. The left outlet of the micro switching valve chip is in a normally open condition. Finally, another outlet was switched by the micro switching valve chip. Reactant was flowed through switched outlet by the micro pump as shown in Fig.18(d). These procedure is the essential unit for various kind of reactions.



(a)



(b)

Fig.17 Biochemical IC chip family with
micro fluidic control devices
(a) prototype design (b) prototype chip

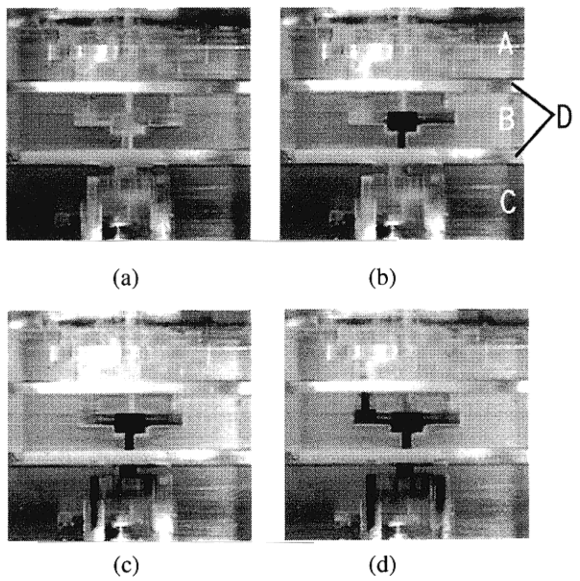


Fig.18 Sequential photographs of neutralized reaction
A : micro pump chip B: micro reactor chip
C: micro switching valve chip D: silicone rubber
(a) before neutralized reaction
(b) after neutralized reaction
(c) flow through left outlet
(d) after switching to another outlet

CONCLUSIONS

The Biochemical IC chips family were fabricated by using hybrid micro stereo lithography technique newly developed by authors. Following are basic features of this research.

1) New process using IH process (micro stereo lithography) to make various 3D micro fluidic components was developed and applied to both multi-concentrator and multi-valve chip.
2) Multiple micro fluidic devices were fabricated successfully in high through put in comparison with silicon process
3) Experimental verification as passive biochemical IC chip such as ultrafiltration, reaction and one-way valve were made
4) Total micro chemical system is easily constructed by connecting each IC chips
5) Transparency of UV polymer was extremely useful to see internal status of biochemical reaction in the IC chip
6) Feasibility of the IC family concept for micro chemical system was demonstrated by these prototypes
7) Leak-free Packaging was verified
9) Dead space in the micro channel can be minimized by stacking thin disk type chip with multiple reaction channels.
10) Active chip such as micro pump and micro concentrator chip were fabricated and basic performance were verified experimentally.

Various diameter of each channel between one [mm] and one [mm] can be fabricated by using several kinds of IH process now. [6]

The style of both chemical experiment and development will be changed drastically by realizing our biochemical IC chips in near future. These devices must contribute to not only biomedical applications but also basic science.

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REFERENCES

[1] K.Ikuta, K.Hirowatari, T.Ogata, "Three Dimensional Micro Integrated Fluid Systems Fabricated by Micro Stereo Lithography", Proc. of IEEE International Workshop on Micro Electro Mechanical System (MEMS'94), pp.1-6, (1994)
[2] K.Ikuta, T.Ogata, M. Tsuboi, S. Kojima, "Development of Mass- Productive Micro Stereo Lithography (Mass-IH Process)", Proc. of IEEE International Workshop on Micro Electro Mechanical System (MEMS'96), pp.301-306, (1996)
[3] K. Ikuta, "3D Micro Integrated Fluid System toward Living LSI -Challenge for Artificial Cellular Device-,"Artificial Life, MIT Press, pp.17-23, (1996)
[4] K.Ikuta, S.Maruo, Y.Fukaya, T.Fujisawa, "Biochemical IC chip toward cell free DNA protein synthesis,"Proc. of the IEEE International Workshop on Micro Electro Mechanical Systems (MEMS98), pp.131-136, (1998)
[5] K.Ikuta, S.Maruo, T.Fujisawa, A.Yamada, "Micro Concentrator with Opto-sense Micro Reactor for Biochemical IC Chip family", Proc. of the IEEE International Workshop on Micro Electro Mechanical Systems (MEMS'99), pp.376-381,(1999)
[6] S. Maruo and K. Ikuta, "Two-photon three-dimensional microfabrication for the production of movable mechanism with 0.5 micrometer resolution," Proc. of 10th International Conference on Solid-State Sensors and Actuators (Transducers '99), 1232-1235 (1999).