

# **Report on Visit to MESA+ Institute for Nanotechnology of University of Twente by International Training Program**

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This report describes the research activity during the long-term research program in International Training Program of Young Researchers sponsored by Japan Society for the Promotion of Science. I visited MESA+ Institute of University of Twente in the Netherlands from January 8th to March 8th, 2012, by the program for incubating young researchers on plasma nanotechnology materials and device processing conducted by Plasma Nanotechnology Research Center in Nagoya University. I report on the life, the research environment and my research progress in MESA+ Institute.

## **1. Life and research environment of Twente University**

University of Twente is located in Enschede, in the eastern district of the Netherlands. The campus has a lot of buildings for education and research, a sports gym, a hotel, student accommodations, a supermarket, and so on. The campus is surrounded by greenery, and has beautiful scenery. In the university, there are a lot of institutes such as MESA+ institute for Nanotechnology, MIRA institute for biomedical technology and technical medicine and IMPACT institute for energy and resources.

The MESA+ institute is one of the largest nanotechnology institutes in the world. It plays an important role in development of the field of nanotechnology as a principal institute of NanoNed, Holland's government project. In the institute, there are many researchers from various fields such as physics, electronic engineering and chemistry. They are carrying out research and development regarding nano technology.

I engaged in research in BIOS group of MESA+ institute, where technologies related to the microfluidic device called Lab-on-a-Chip (LOC) are investigated. The BIOS group, directed by Professor van den Berg, aim at understanding of nanofluidics and nanosensing, developing new micro- and nano-technologies for LOC systems, and demonstrating the

potential of LOC applications. BIOS group has around 50 members. Professor van den Berg and 5 scientific staffs direct their own different research projects with several postdoctoral fellows and Ph. D. students.

There are three major differences between BIOS group and Japanese research group. The first one is existence of the technical staffs. BIOS group has five technical staffs. They manage reagents and equipments in the laboratory, fabricate experimental tools and advise about experimental methods. By supporting of the technical staffs with matured knowledge, the research efficiency and feasibility seemed to increase. The second one is the number of the postdoctoral fellows and Ph. D. students. In the group, there are 8 postdoctoral fellows, 19 Ph. D. students while there are only 5 master students and 1 undergraduate student. Therefore, research activities are conducted by the postdoctoral fellows and Ph. D. students, and the atmosphere of the laboratory is active. Master and undergraduate students intensively investigate their own projects with the postdoctoral fellows' and doctoral students' support. In the student room, I often found that they discuss with other students and the supervisor. The third one is their work style. All members begin their work by 9 o'clock and finish the work by 18 o'clock, and they go home sooner after working. By following their work style, I learned importance of switching on and off, and of planning the schedule of the day. By the time limitation of research, I became extremely conscious how to rationalize my experiments every day.

## **2. Research progress**

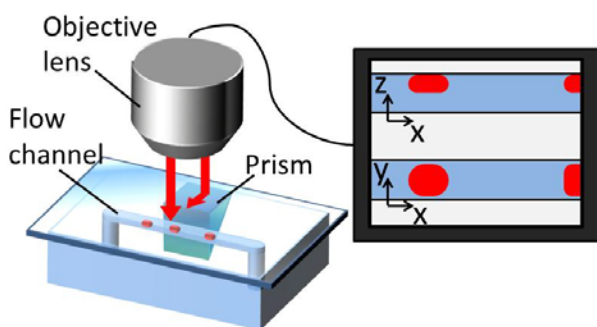
In the program in BIOS group, I tried to develop the novel microscopic observation chip with embedded small optics.

### **Introduction**

Recently, microfluidic systems which integrate micrometer-sized flow channels in a small substrate are

becoming an important technology in various fields such as organic synthesis, biotechnology and chemical analysis. The advantages of the integrated system are miniaturization of apparatuses, reduction of sample amounts, efficient chemical process, and so on. Microfluid sometimes shows a strange behavior compared with bulk fluid. Therefore, observation and understanding of the microfluid is one of the most important research problems in the research field. Most previous reports use microscopic observation, fluorescence microscopic observation and particle image velocimetry. However, it is difficult for these methods to observe the microfluid in three dimensions and/or in real-time.

In this research, I tried to develop a novel microscopic observation chip with small optics for three dimension and real-time observation of microfluid. Specifically, I tried to develop the microfluidic system with embedded prism which can be used for simultaneous observation of top and lateral views of a microchannel by using a microscope objective lens (Figure 1).

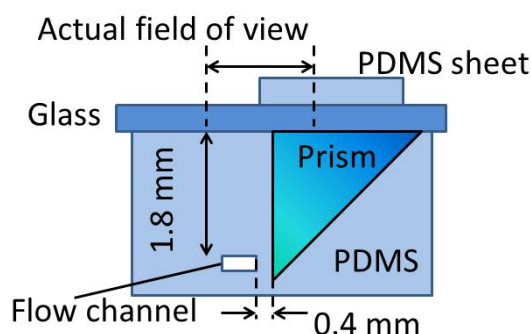


**Figure 1** Conception of the chip with embedded prism for three dimensional observation.

### Design of micro chip

In order to observe top and lateral views of a microchannel by a microscope lens, the flow channel and the prism have to be put in the actual field of view of the microscope. In this research, I conceived the chip design shown in Figure 2. The width of the channel is 300  $\mu\text{m}$ , and the height is 80  $\mu\text{m}$ . A right angle prism having a base length of 2 mm was chose for easy handling. An objective lens having a magnification of 5 was chose by considering the microchip size and the actual view field (2.5 mm  $\times$  3.8 mm). By setting the right angle prism 400- $\mu\text{m}$ -away from

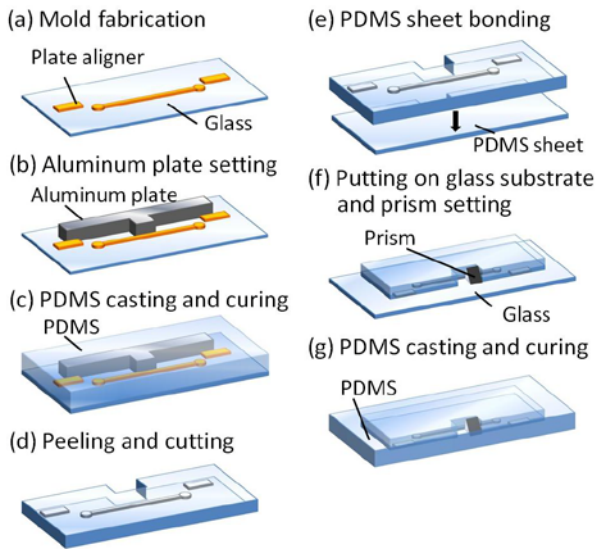
the flow channel and 1.8-mm-away from the glass substrate, I expect that the top and lateral views of the flow channel can be observed simultaneously. In this design, the lateral view is observed through the prism, and the light path length disagrees with that of the top view. In order to compensate the difference, a PDMS sheet is put on the glass substrate.



**Figure 2** Design of the chip with embedded prism for three dimensional observation.

### Fabrication of chip

The microchip was fabricated by using a soft lithographic method with polydimethylsiloxane (PDMS). The fabrication process is illustrated in Figure 3. The mold is made of negative thick photoresist (KMPR-1035) and has a pattern for the flow channel and the structure for aligning the aluminum plate (Figure 3a). In order to place the prism just 400- $\mu\text{m}$ -away from the flow channel, indent was fabricated by using the aluminum plate (Figure 3b). After setting the aluminum plate, liquid prepolymer of PDMS was casted and polymerized (Figure 3c). The PDMS was peeled off (Figure 3d). The PDMS sheet was bonded to a 1.8-mm-thick flat PDMS sheet by a plasma bonding method (Figure 3e). The bonded sheet was set on a glass plate and a prism was set into the indent (Figure 3f). After that, liquid prepolymer of PDMS was casted again and polymerized (Figure 3g).

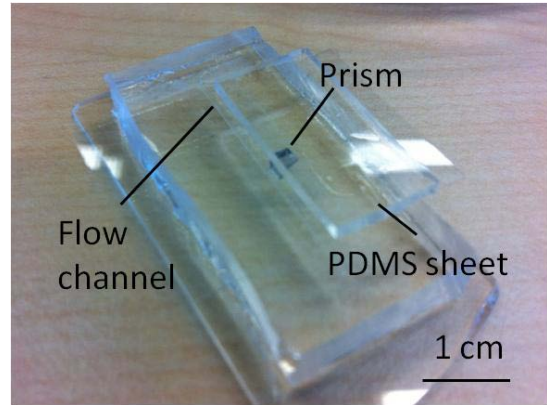


**Figure 3** Chip fabrication process. In order to place the prism only 400  $\mu\text{m}$  away from flow channel, indent was fabricated by using the aluminum plate (b). In order to place the flow channel 1.8 mm away from glass plate, the fabricated PDMS sheet was bonded to 1.8-mm-thick PDMS sheet (e). After setting the bonded PDMS sheet on the glass plate and putting the prism into the indent, liquid prepolymer of PDMS was casted and polymerized

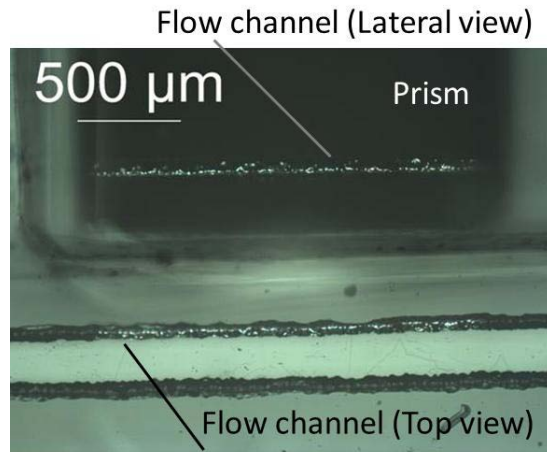
### Results and Discussions

The chip is shown in Figure 4. The microfluidic system integrated with the flow channel and the prism was successfully fabricated. The thickness of a PDMS sheet for the light path length compensation was set to 1.1 mm, which was calculated from the numerical aperture of objective lens (0.15), the light path length difference, and reflective indices of PDMS and the prism. The 1.1-mm-thick PDMS sheet was put on the glass substrate at the head of prism. Thus, the top and the lateral views of the channel were observed simultaneously, as shown in Figure 5. Since the prism was placed very close to the fluidic channel, the leakage from the channel to the prism should be verified. In order to verify the problem, fluorescent aqueous solution was flowed into the fluidic channel, and no leakage was observed as shown in Figure 6.

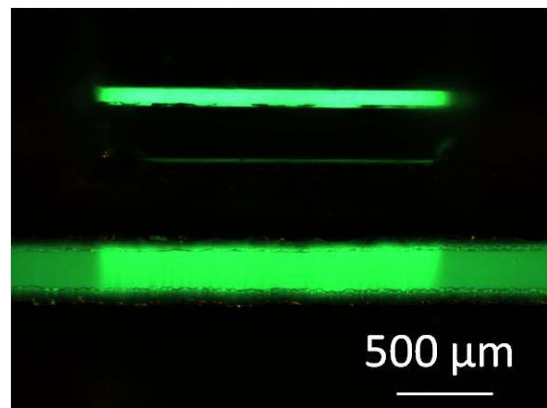
Thus, I successfully developed the novel microscopic observation chip with embedded prism for three dimension and real-time observation of the microfluidic channel. Hence, I will apply the developed chip for particle image velocimetry (PIV) and discuss the applicability of the novel technique.



**Figure 4** Fabricated micro chip. A fluidic channel and a prism were integrated in the microchip.



**Figure 5.** Microscopic image of micro channel. The fluidic channel was observed by using a 5x objective lens. Top and lateral views of the micro channel were simultaneously observed.



**Figure 6.** Fluorescence image of micro channel. The fluidic channel was observed by using a 5x objective lens. In the top view of the micro channel, stronger fluorescent was observed in the area near prism than other part because of double excitation beam exposed from objective lens and prism.

In this program, by studying leading-edge nanotechnology and biotechnology, I learned various knowledge related to my research field. Furthermore, by discussing and investigating with researchers from various countries, my communication skill has been improved very much. During my stay in the Netherlands, I discussed not only with the members of BIOS group, but also with people in the student accommodation on climate, culture, politics, economy, and so on. I could know foreign cultures and got a new understanding on my own culture. I convince that the knowledge and the experience acquired through the program will be very helpful for my research carrier.

I acknowledge Professor Toyoda, Professor Baba, and Professor Tokeshi of Nagoya University, for giving me this precious opportunity. I sincerely appreciate Professor van den Berg, Professor Carlen and Professor le Gac, and the members of University of Twente for their support.