Report on Visit to University of Twente, The Netherlands by International Training Program

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This report describes my research activities and working experience on International Training Program (ITP) by Japan Society for the Promotion of Science at BIOS Lab on a Chip group, MESA+ Institute, University of Twente, The Netherlands for the period 12 October, 2010 through 10 December, 2010.

1. Enschede and University of Twente

Enschede is a main city of the Twente region, located in the east of the province of Overijssel, and the city has an estimated population of 150,000. Its economy was traditionally characterized by mainly textile production, and also machine industry and metalworking industry, but after a significant period of transition in 80s, the region has been able to develop itself as a "technology valley", founded on the presence of University of Twente and a growing number of high tech industries of the field in electronics. In the city center, besides department stores and banks, there is the Rijksmuseum Twenthe, which is famous for remarkable collection of 17th and 18th-century art works, and the official stadium of FC Twente, a football club playing in the highest football league in the Netherlands. In addition, because Enschede is near the German border, it has a close relationship economically and culturally with Germany.

Figure 1. The Saturday market.

Many people from Germany visit the market held in the city center on every Saturday and from Enschede station, there is a local train connection served by the German national railway company.

University of Twente (UT) is a national university located in the northwest of Enschede. This university was founded in 1961 and now has 9,000 students and 3,300 faculty and staff. The motto of UT is "The entrepreneurial university." The unique teaching programs of UT aimed at commercialization of technology encourage and assist entrepreneurs to start new companies, and more than 700 successful spin-off companies have been generated from the university. Also, UT is the only full campus university in the Netherlands. On the campus, there are all kinds of facilities including sports facilities, bars, cafeterias, a medical center, a supermarket, a hairdresser, and dormitories for students and faculties, as well as research and educational facilities.

Figure 2. The cafeteria on the campus.

2. BIOS - Lab on a Chip group

On this program, I was working at BIOS – Lab on a chip group chaired by Professor Albert van den Berg in MESA+ Institute. The BIOS group is doing the research and

development of Lab-on-a Chip systems, including many complex sample preparation steps and multiplexed detection on a single substrate fabricated by semiconductor fabrication techniques. Their core competence is found in micro/nanofluidics, micro/nanofabrication, and electrical measurement techniques, and the group is considered as one of the pioneering groups in this field. In the BIOS group, there are currently 45 members, including 5 scientific staffs, 8 postdocs, 5 technical staffs, 16 PhD students, 7 master students, and so on. Several research groups are organized by about 5~6 postdocs and students under each scientific staff. I got the impression that the communication within each research group was well-balanced as they have meetings frequently. And also, I felt that the technical staffs play an important role on research. Besides setup/fix of microscopes and a range of devices, their work is including safety management in laboratories, making order-made tools to fabricate microchip devices, and giving an advice on experiment.

The BIOS group owns more than 5 lab rooms, such as Assembly room, Microscope room, Chemical lab, Main lab, Bio lab, and so on. The building Carré where the group is located has just been completed in this June. The laboratories are very clean and hold many types of equipment. And I felt that the safety rules in the laboratories are very thorough. It is required to have a safety introduction from technicians in order to use laboratories.

Figure 3. Building "Carré".

During my stay, I had a chance to visit the cleanroom of MESA+ Institute, which is completed this year as well. It is a national cleanroom of the Netherlands and fully equipped with state-of-the-art etching equipment, mask aligners, dedicated chemical benches for every type of photoresist.

Figure 4. Assembly room.

3. The process of research

Recently, there is a growing interest for highly controlled manipulation of micro-sized droplets by using microfluidic device. For example, droplet arrays produced by splitting a single-droplet array, synthesis of CdS nanoparticles utilizing droplet fusion and sorting of droplets by size have been demonstrated.

My research theme on this program was "Manipulation of droplets utilizing the principle of hydrodynamic filtration (HDF)." The basic mechanism of HDF is shown in Figure 5 (a). At a microchannel bifurcation, the width of the flow region entering into the branch channel, w_1, determines the minimum size of particles that do not flow into the branch channel. Namely, the particles with radius lager than w_1 would never flow in the side channel. And this technique can be employed for multistep exchange of continuous phase.

By applying the concept of HDF to manipulate of droplets, the droplet-based molecule separation system based on the hydrophobicity differences or the system to synthesize multilayer emulsions via multistep chemical treatment (Fig.

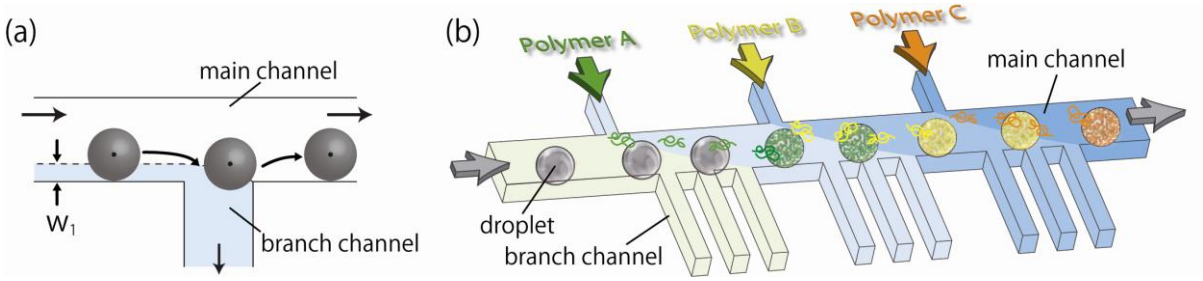

Figure 5. Schematic diagrams showing the particle behavior at a branch point of a main channel (a), and the system to synthesize multilayer emulsions using the principle of HDF (b).

5 (b)) would be constructed.

In this study, I aimed to examine the droplet generation and the one step exchange of the continuous phase.

1st Week: My supervisor, Dr. Lingling Shui, introduced their group and lab rooms. And we had discussions about my research project and checked the chemicals and equipments I would use.

2nd Week: I fabricated devices. The device was made of polydimethylsiloxane (PDMS), silicon-based elastomer, and a glass slide. I used the mold which had been fabricated in advance in Japan. PDMS replica was bonded with a glass slide via oxygen plasma treatment. The microchannel design is shown in Figure 6. I used a flow-focusing device to generate droplets and it had a narrow orifice with a width of 10 μm.

3rd Week: I advanced the preparation of experiment and read some papers about droplet generation/manipulation.

4-6th Week: I examined if the droplets were actually generated in my microchannel network and observed the droplet behavior in the downstream. The aqueous phase containing Tween 80 (a nonionic surfactant) as the continuous phase and Fluorinert FC-40 as the dispersed phase were introduced from Inlet 1 and Inlet 2, respectively,

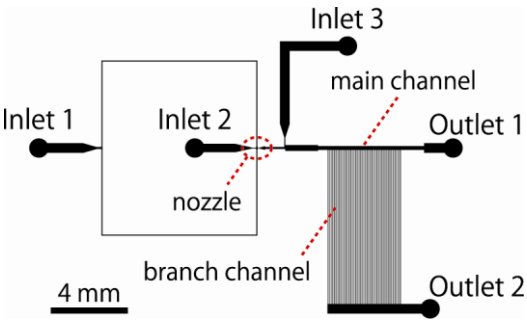

Figure 6. Microchannel design.

by using a syringe pump, while the Inlet 3, which is for exchange of the continuous phase, was closed. By controlling the flow rates (the continuous phase: 0.5 ~ 1.5 μL/min, the dispersed phase: 0.01 ~ 0.1 μL/min), droplets with diameters from 20 to 40 μm were stably generated. And at the branch points in the downstream, it was observed that the generated droplets stably flowed in the main channel without entering into the branch channels.

7-8th Week: I examined the exchange of the continuous phase by introducing sodium fluorescein solution from Outlet 3. As shown in Figure 7, it was observed that the first continuous phase was gradually exchanged to the second continuous phase. For the future work, I am planning to design a new microchannel design for multistep exchange of continuous phases and to apply this system to further practical applications.

4. Life at BIOS group

At BIOS group, scientific staffs, postdocs, and PhD students have their rooms of 3 ~ 4 people, and master students have their own desks in the student room. And I had a desk in the student room, too. The students are very friendly and kindly helped me a lot. In University of Twente, the master's program is two-years. Master students have lectures in the first year, and in the next year, they work on their master's degree research at research groups. Also, it seems that relatively many students do an internship at universities or research institutes in foreign countries during their master's program, compared to in Japan. It was very interesting for me to hear from them about their experience of internship.

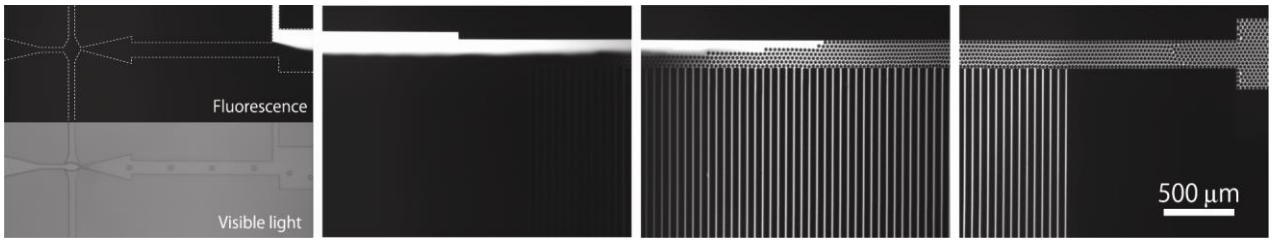

Figure 7. Microscopic images of generation of droplets and the flow in the microchannel. The volumetric flow rates from Inlet 1, 2, and 3 were 0.8, 0.025, 1.0 µL/min, respectively.

On every Monday, I joined the group meeting. 2 ~ 3 postdocs / PhD students have presentations of their research progress and introduction of related papers per one meeting. A lively discussion was made in every meeting. The meeting is held in English because there are many members from foreign countries, such as India, Pakistan, China, Germany, and so on.

In addition to research, I had many opportunities to join the group activities, such as birthday parties of the members, group lunch, which is held once a month, and group dinner. In December, there is a traditional winter festival, Saint Nicholas, in the Netherlands and Belgium. I celebrated Saint Nicholas day and played a dice game with the lab members and that was very good experiment to come in touch Dutch cultures.

5. Acknowledgment

Through this program, I could attain the new knowledge and technique of my research field, and also have many experiences to come in touch with foreign countries. Although I had been worried that I could do research in a foreign country communicating in English before I left Japan, I could make my stay very valuable thanks to the support by Professor van den Berg, Dr. Lingling Shui, and the all members of BIOS group. I would like to keep in touch with the people who I met during my stay in the Netherlands and have a chance to exchange our research progress in any conferences.

Finally, I would like to greatly appreciate the support of ITP staffs, the people of MESA+ Institute, and Assistant Professor Noritada Kaji of Nagoya University.