JSPS Core-to-Core Program
FY2011 Implementation Plan (Project No. : 20002)

Research Theme International Core Research Center for Micro/Nano Chemistry
Duration of Project 2010/4/1 – 2013/3/31 (36 months)
Core Institution in Japan (Co-Chair) School of Engineering, The University of Tokyo
(Takehiko Kitamori)

Implementing Organizations

○ **Japan**

Japan	Core Institution	School of Engineering, The University of Tokyo	
	Co-Chair (name and title)	Takehiko Kitamori, Professor	
	Cooperating Institutions	Kyoto University Nagoya university Waseda University Japan Women's University	Number of Cooperating Institutions 4

○ **Partner Countries**

	Core Institution	Uppsala University, Sweden	
	Co-Chair (name and title)	Ulf Landegren, Professor	
	Cooperating Institutions	Lund University Royal Institute of Technology	Number of Cooperating Institutions 2

	Core Institution	University of South Australia, Australia	
	Co-Chair (name and title)	John Ralston, Professor	
	Cooperating Institutions		Number of Cooperating Institutions 0

	Core Institution	IBM Watson research Center, USA	
	Co-Chair (name and title)	Tze-Chiang Chen, Fellow & Vice President, Science & Technology	
	Cooperating Institutions		Number of Cooperating Institutions
			0

	Core Institution	Nangyang Technological University, Singapore	
	Co-Chair (name and title)	Ai-Qun Liu, Associate Professor	
	Cooperating Institutions		Number of Cooperating Institutions
			0

	Core Institution	Swiss Federal Institute of Technology Zurich, Switzerland	
	Co-Chair (name and title)	Petra Dittrich, Assistant Professor	
	Cooperating Institutions		Number of Cooperating Institutions
			0

Objectives of Research Exchange (including the five years after the project finishes)

Recently, many researchers investigate micro and nano chemistry which integrate various chemical functions (experimental rooms) into a ~cm size glass substrate. In this situation, we have pioneered our original methodology and fundamental technology, and we are highly evaluated. However, this field needs combination of various fields and technologies. For example, single molecule detection needs combination of detection and miniaturization, and microfluidics is based on surface chemistry and fluid dynamics. These combinations are really important for both fundamental research and application.

Therefore, we will construct strong collaborations with Rudbeck laboratory in Uppsala University and Ian Wark institution in the University of South Australia, and establish a worldwide core for frontier micro and nano chemistry combining single molecule engineering and surface chemistry for both fundamental research and application.

(1) Collaborations on combination of our methodology and each partner institution's technology such as single molecule engineering and surface chemistry
(2) Construction of single molecule analysis systems and application to medical and biological field
(3) Education of next generation young researchers who can cross several fields such as chemistry, physics and biology

As described above, we will establish a core of micro/nano chemistry to contribute Japanese industry, and educate young researchers to promote next generation science and technology.

Results to the present

① Promotion of collaboration research

Single DNA analysis is required for various fields such as bacteria detection and medical diagnosis. Prof. Landegren et al. in Uppsala University developed RCA (Rolling Circle Amplification) method which can detect single DNA as fluorescent dots. By using this methid, single DNA detection can be realized. However, detection limit of RCA in bulk scale is low (0.1%) because molecules move around. So, we propose to integrate RCA in microchip using beads immobilized with primer DNA. By using a microchip and beads, products can be confined in microchannel and so, low concentration sample can be measured. To realize this, immobilization of primer DNA on beads by collaborating with South Australia University and also integration of RCA in microchip are required.

· Collaboration with South Australia

By exploiting surface chemistry technology of Prof. Ralston in Ian Wark institution, primers were immobilized in beads, and the immobilization was confirmed by hybridization of complementary fluorescent probes to the primers.

This result was submitted to a journal (Priest et al. Angew. Chem. Int. Ed., submitted) and accepted in international conference, μTAS (2 papers). Moreover, regarding this result, Prof. Kitamori became a collaborator of large project in Australia.

· Collaboration with Uppsala University

By using primer immobilized beads prepared in the method described above, RCA processes were integrated into a microchip by applying our methodology of micro/nano chemical systems as shown in Figure 1. As a result, detection rate was highly improved compared with conventional PCR tubes (90 times), and detection of ultra small number of DNA molecules was realized (zmol(10^{-21} mol)). Also, by using this method, detection of practical genome samples were realized.

These results are accepted in a journal as a co-author paper (Sato et al. Lab Chip, in press) and two papers were in preparation (Xi et al. Anal. Chem., in preparation) (Wakabayashi et al. Lab Chip, in preparation). Furthermore, 5 papers were accepted in an international conference (μTAS) (accept rate: under 60%). One of them was nominated for a poster award from 500 presentations (Tachihara et al., Proc. MicroTAS (2008)).

Based on these results, Sato (Lecturer) moved from our group to Japan Women's University as an Associate Professor and had an independent laboratory, and she got NEDO project for young researchers (Total 50 million yen).

Now, we are constructing a novel single molecule analysis system integrating capturing of DNA and protein and single molecule detection which is the original goal by developing the established technology. If this is realized, very sensitive and rapid analysis become possible and expected to contribute to medical and biological fields.

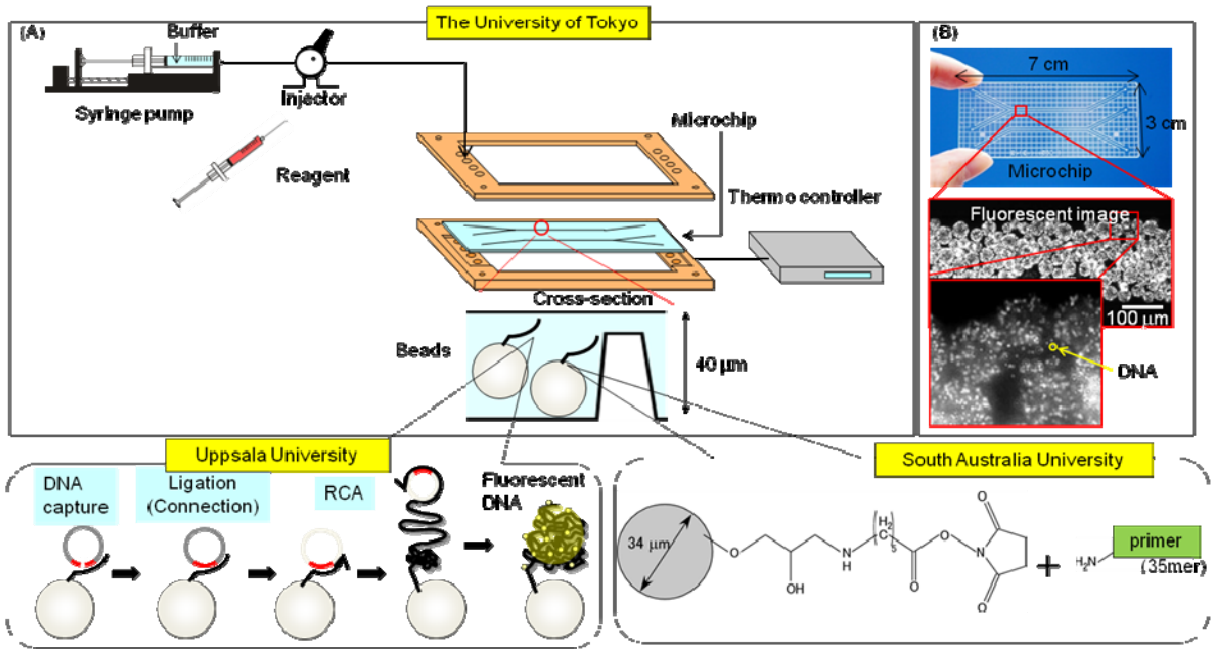

Figure 1 (A)DNA detection method in a microchip. (B)Microchip and microchannel fluorescent image

② Education of young researchers

To improve English communication skill, our group use English for presentation and discussion in seminars. Owing to such activity, 2 young researchers in our group received awards in international conferences. Moreover, we hold joint seminars in Sweden and Australia every year, and held a 3 countries' symposium in Japan in March, 2010. Through such exchanging, the number of young researchers' travel to abroad became twice compared with that before this program started.

③ Presentations

To exchange research result, our group is active for conference and paper presentations. During 2 years of this program, the number of published papers is 34, the number of presentations in international and conferences is 61. Especially, the number of presentations in µTAS conferences is 18 in both 2008 and 2009, which is outstanding and the same number as that of one country (e.g. 20 presentations. from France). We also invited several researchers from partner countries. Results and collected information are open in this program's home page (http://park.itc.u-tokyo.ac.jp/kitamori/project/).

④ Additional effects

Regarding this program, some of the members received awards and promoted. For example, our group received 7 awards including 2 international awards such as IBM Faculty Award (Prof. kitamori). Also, many of the members promoted. For example, a researcher invited from Sweden (Dr. Renberg) promoted and became Associate Professor in KTH. In international collaboration systems, we renewed an international exchanging agreement with the University of South Australia, and constructed a joint laboratory in Ian Wark institution. This is very important for a core of international exchange with Asia, Oceania and Europe. Regarding collaborations with Sweden, we also renewed an international exchanging agreement Uppsala and Lund University. Furthermore, Prof. Landegren was authorized as a fellow in the University of Tokyo. As described above, we obtained results larger than the original aim and constructed the basis for the next program.

Summary of FY 2011 Exchange Plan

Joint Research

Based on the single molecule detection method in the previous program, we will develop single cell analysis system on micro/nano chemical chip. The objective is to open a new field by collaborating with other fileds' top researchers: Prof. Ulf Landegren in Uppsala University in Sweden (Medicalbio), Prof. Ralston in the University of South Australia, Australia (Surface chemistry) and Dr. Chen in IBM (IT, MEMS), and the same fields' young researchers, and to construct a young researcher growth network by exchanging with the same fields' young researchers: Prof. Liu in Nangyang Technological University, Singapore and Prof. Dittrich in Switzerland. We summarize and combine the research below and develop single cell analysis devices toward medicine such as ES or iPS cell analysis and CTC (Circulating Tumor Cell) analysis systems.

We plan collaborations with 2 institutions that are continuous from the previous program as the followings. Uppsala University will optimize single molecule detection method and realize single molecule detection from very small sample such as single cells. South Australia University will develop surface modification in extended-nano channels and verify liquid properties there.

We plan collaborations with new 3 institutions that joined from this year. IBM will develop molecule or ion detection method using nanowire. This method will be applied to monitoring off secreted molecule detection from single cells. Nangyang technological University will develop specific cells (such as CTC) detection method by measuring diffractive index of cells. Swiss Federal Institute of Technology Zurich will develop methods for capture and detection simulation using artificial cells made of vesicles.

We will dispatch students or post-docs to Uppsala University and University of South Australia for about 2 weeks/person. Also, we will dispatch to IBM, Nangyang Technological University or Swiss Federal Institute of Technology Zurich to obtain experimental skills. Moreover, we will accept young researchers from each contries for about 1 week/person to initiate our technology.

Seminar

We will hold joint seminars in every country to present each research progress and discussion. In both of Japanese and partner countries' sides, most of attendees are young researchers including cooperating institutions.

Researcher Exchanges

To report collaboration research above, we will join and present in the following international conferences: The 14th International Conference on Miniaturized Systems for Chemistry and Life Sciences (μTAS2010, Groningen, Netherland) which is the largest conference in this field, The 10th International Symposium on Microchemistry and Microsystems (ISMM2010, Hon Kong, China), The 6th International Chemical Congress of Pacific Basin Societies (PACIFICHEM2010, Honolulu, HI, USA), and in the following largest domestic conferences: The 21st Society for Chemistry and Micro-Nano Systems (21CHEMINAS, Tokyo) and 22nd CHEMINAS, Nagoya.