

RESEARCH REPORT

1. Name: BETSCHINGER, Marie-Ann	(ID No.: SP06301)
2. Current affiliation: Department of International Business, University of Muenster, Germany	
3. Research fields and specialties: Business and Economics Humanities Social Sciences x Mathematical and Physical Sciences Chemistry Engineering Sciences Biological Sciences Agricultural Sciences Medical, Dental and Pharmaceutical Sciences Interdisciplinary and Frontier Sciences	
4. Host institution: Institute of Economic Research, Hitotsubashi University	
5. Host researcher: Professor Kyoji Fukao	
6. Description of your current research The Impact of International Trade and Investment Agreements on Foreign Direct Investment in Developing Economies The importance of developing economies as destination for foreign direct investment (FDI) has strongly increased during the last couple of years. Nevertheless, investment into these countries still often faces not only regulatory and legal investment barriers, but also an insecure business environment due to a high level of political instability deterring long-term and high profile corporate involvement. Overcoming these barriers and mitigating these risks is of large relevance for companies when conducting overseas activities. Means to achieve this is either via intra- and inter-corporate strategies or by relying upon government devices. Here, international investment and trade agreements are of large significance. Agreements most important in this context are bilateral investment treaties (BITs) and preferential trade and investment agreements (PTIAs). Although there has been a strong increase in international trade and investment agreements worldwide during the past years, there is no clear empirical evidence on their eventual relevance and the particular conditions required for attracting additional investment. One reason why convincing results have not been obtained, is, that up to now, industry- and company level differences have by large been disregarded. A further draw-back in existing studies is that the major focus has been on financial flows on a macro-level, but not on “real” activities carried out by the companies. In my research I conduct a comparative analysis of two “investor” nations, Japan and	

Germany. This permits, on the one hand, to focus on industry and firm characteristics as well as to analyse affiliate level information as employment and sales. On the other hand, bilateral characteristics can be captured. As both are large investor nations, but feature a different treaty-ratification behaviour, reasons for and effects of their differential manner of treaty ratification can be explored.

7. Research implementation and results under the program

Title of your research plan:

The Impact of International Trade and Investment Agreements on Overseas Investment Activities of Japanese MNEs in Developing Economies

Description of the research activities:

Research objectives were to obtain a detailed understanding of determinants of Japanese FDI in developing economies, the relevance of the political environment in this context, and the role of international agreements for the investment decision of Japanese companies in particular. Research activities carried out to achieve these objectives consisted of a literature and survey review, preparation of my own econometrical analysis and discussions with researchers in the field.

1) Review of literature/ official documents and surveys:

I conducted research in libraries at Hitotsubashi University, JETRO, the National Diet, the Institute of Developing Economies as well as Internet-based research. Most important findings were that Japanese research on economic partnership agreements (EPAs) and East Asian regional integration has experienced a recent “hype”, but BITs are much less researched. Looking at the literature analysing determinants of investment activities of Japanese multinationals in developing economies, the domestic institutional framework has been found to play an important role (e.g. Delios,/ Beamish 1999, Delios/ Henisz 2003, Voyer/ Beamish. 2004, Yiu/ Makino 2002), but the impact of international institutions, of which BITs and PTIAs form part, has obtained only limited attention (Umada/ Ooma 2005). Nevertheless, surveys (Japanese Bank for International Corporation (JBIC), Japanese External Trade Organization (JETRO), and Keidanren) reveal that most companies have positive expectations towards the agreements, even though only few of them actually seem to use the existent ones. But, depending upon industry, companies expect a lot from not-yet concluded agreements (in particular with Thailand and with ASEAN) and, most of all, from a China-Japan EPA. As expectations towards agreements where Japan does not form part like AFTA are high, the latter should exercise strong impact.

2) Preparation of my econometrical analysis for overseas investment activities of Japanese firms

This was the focus of my research – gathering and understanding data and revising testable hypotheses. As a result a rough econometric framework was established, data sources determined and, for Japanese sources, the latter obtained. This will allow me to start testing the hypotheses when I have returned to Germany.

Basic regression as well as conditional logit analysis will be carried out in a firm/industry panel data setting This allows capturing the impact of the agreements on the level of overseas investment activities as well as the location choice per se and mode of entry choice in particular. The analysis will be conducted for the period 1989-2004. As *dependent variable* the number of foreign affiliates, sales & employment of the latter, as well as capital stock and capital share of Japanese investors will be analysed. Toyo Keizai data on overseas activities of Japanese firms (firm level) as well RIETI data as compiled from METI survey information (industry-level) will be used. *Set-up of the equation* is going to be based on a FDI gravity equation based on the framework as established by Baltagi, Egger, Pfaffermayr (2005). I will add variables stemming from new institutional economics not only capturing the impact of the institutional environment – domestic political institutional quality and international trade and investment agreements-, but also accounting for transaction costs on an industry and firm level.

3) Discussions with researchers in the field.

Besides having very fruitful weekly meetings with my supervisor Professor Fukao, I had further discussion and was in e-mail contact with researchers in the field of the econometric analysis of foreign direct investment from different Japanese universities and institutions. I also very much appreciated discussing with fellow PhD students working in the field. My special thanks go foremost to Professor Fukao, but also to Associate Professor Ito from Senshu University, Okubo-san, HEI Geneva, Kim-san, Wei-san, and May-san from Hitotsubashi University. Furthermore, I assisted a symposium on the impact of EU enlargement on business activities of Japanese companies (organized by the Keizai Koho Center) and a RIETI workshop and symposium on “Determinants of Total Factor Productivity and Japan’s Potential Growth: An International Perspective” also highlighting the relationship between international investment and total factor productivity.

Thus, I obtained insights into existing research on the impact of the agreements on Japanese overseas investment activities and obtained necessary information and data to be able to conduct my econometric research.

8. Please add your comments (if any):

The two months in Japan were very intense and fruitful for my research, but turned out to be too short to carry out all my research ideas. Due to this fact, I will analyse material I gathered during the past two months when I will have returned to Germany and also start to conduct my econometric research there. After having conducted a comparison with German data, I will hopefully be able to come back to Japan in the near future to refine the analysis given the results from my econometrical investigations for the Japanese and German cases.

I wish to thank JSPS for making this stay here in Japan possible and Professor Fukao for his very constructive and very kind support. Special thanks also goes to Moriyama-san for organizing my stay at Hitotsubashi University and making it such a wonderful and unforgettable experience.

9. Advisor's remarks (if any):

This JSPS program is very well organized. The student, Ms. Betschinger is a very talented and motivated person. I enjoyed supervising such a good student.

RESEARCH REPORT

1. Name: GUTCH, Harold W.	(ID No.: SP06302)
2. Current affiliation: University of Regensburg	
3. Research fields and specialties: Humanities Social Sciences Mathematical and Physical Sciences Chemistry Engineering Sciences Biological Sciences Agricultural Sciences Medical, Dental and Pharmaceutical Sciences X Interdisciplinary and Frontier Sciences	
4. Host institution: Tokyo University of Agriculture and Technology	
5. Host researcher: Associate Prof. TANAKA, Toshihisa, Ph.D	
6. Description of your current research	
<p>BSS (Blind Source Separation) is the task of recovering a set of source signals S from observed recordings X, where the recordings are given by a linear mixing of the sources (so $X = AS$ for some matrix A). A is usually assumed to be (pseudo-)invertible, otherwise obviously no perfect recovery is possible. If X and S are of the same size, and the components of S are independent, this task is called ICA (Independent Component Analysis). In this case A (and hence S) can be recovered uniquely, up to the obvious indeterminacies scaling and order, and efficient algorithms performing this recovery are available.</p> <p>Our work focuses on the theoretical aspects, however signal processing, and ICA as a single step in a processing filter chain has many real world applications, and many such can be found in quite different fields such as audio and image processing, financial data analysis, telecommunications, bioinformatics and biomedical data analysis. Examples of this include analyzing functional magnetic resonance imaging (fMRI) scans with the goal of recovering the underlying signals. In this case we try to identify parts of the brain that are related to a given task in a non-intrusive way, i.e. by merely measuring activity on the scalp.</p> <p>However, the main problem with ICA is that it cannot be known in advance if the true source signals really are mutually independent, and ICA algorithms actually do not work anymore in such a case, as can be shown with toy data. We call the task of separating such linear mixtures of sources, where some dependencies within the sources exist, ISA (Independent Subspace Analysis). Experiments with toy data have given good evidence that extensions of classical ICA algorithms can be used here.</p>	

Our main focus currently is the development of a general ISA model, in which any given signal can be analyzed. After precisely defining the ISA model in which the goal is to group dependent signals “as well as possible”, this mainly consists of two parts. First, it has to be shown that within this framework, the ISA of any signal actually is unique (existence of ISA is obvious), and second, the correctness of the extensions of the above mentioned algorithms has to be proven within this model – or, alternatively, the algorithms have to be enhanced.

7. Research implementation and results under the program

Title of your research plan:

Decomposing Random Vectors into Groups of Variable Blocksize

Description of the research activities:

As noted above, the extension of ICA to ISA consists of two separate parts. During my stay at TUAT, my work was focused on the theoretical aspect of the extension, that is, proof of the uniqueness of ISA for any given random variable. Here the first major step would be proof of the uniqueness of ISA for a signal that consists of two independent groups. From this the step towards general ISA for any number of groups will be fairly easy.

Another aspect of my research activity at TUAT consisted of work on problems where both Prof. Tanaka's group and our group – or more specifically, me during my stay – could contribute to the solution.

As for the first point, I was able to prove uniqueness of ISA for a signal consisting of two independent groups. My first proof was finished after roughly half the time of the stay at TUAT, however that proof contained an error, which I did not find at first, and I then spent some additional time trying to correct it until I realized that it was not possible to simply fix the error and be done with it. After starting from the beginning again, after a few days I was at a point where the final steps seemed not to be so hard anymore, however it took me until my last week at TUAT to finally finish my work.

As for the second point, collaborations with Prof. Tanaka's group, we quickly found problems where we could work together, however as pointed out above, work on my primary focus took longer than expected, so that we unfortunately were unable to do actual work together. However, we plan on continuing the established link between our two work groups and approaching the problems we can focus on together in the future, after the end of my stay in Japan.

8. Please add your comments (if any):

Unfortunately mathematical work often consists of just trying something and if it does not work, disregarding the approach, so it is not easy to estimate the quality and length of work in advance. Therefore I am glad that I still managed to reach my goal during the last week of my stay in Japan.

I thank everybody in Prof. Tanaka's work group for the academic freedom I was given, everybody at JSPS and DAAD for the help and supporting this stay, and everybody else who contributed to my great time in Japan, both from an academic point of view and from a personal point of view in the time I spent outside of the university getting to know life (as a foreign researcher) in Japan.

9. Advisor's remarks (if any):

His mathematical work successfully linked with the problem of blind deconvolution which our group have struggled. Unfortunately, we could not have time enough to give a solution to this problem due to his short stay; however, I believe that this stay is a nice start point for our further collaboration.

RESEARCH REPORT

1. Name: Matthias Hofmann	(ID No.: SP06303)
2. Current affiliation: Dept. of Dermatology and Venerology J.W. Goethe University, 60590 Frankfurt/Main, Germany	
3. Research fields and specialties: Humanities Social Sciences Mathematical and Physical Sciences Chemistry Engineering Sciences X Biological Sciences Agricultural Sciences Medical, Dental and Pharmaceutical Sciences Interdisciplinary and Frontier Sciences	
4. Host institution: Dept. of Dermatology, Ehime University School of Medicine Shitsukawa, Toon-shi, Ehime 791-0295, Japan	
5. Host researcher: Prof. Dr. Koji Hashimoto / Dr. Satoshi Hirakawa	
6. Description of your current research High tumour interstitial fluid pressure (TIFP) is a characteristic of most solid tumours. Clinically, TIFP is described as a physical parameter that hampers the uptake of anti-tumour drugs into tumour tissue and thus lack of therapeutic effects. My current working program was started under the frame of a Marie Curie fellowship at the Dept. of Biomedicine, Section of Physiology at the University of Bergen (Norway). The primary topic is the investigation of the effect of increased plasma colloid osmotic pressure (COP) on TIFP in a xenograft tumour model using Rowett nude rats. I argue the hypothesis that the injection of colloid osmotic fluids (e.g. serum albumin) will enhance the transport of potential cytostatics into the tumour. This would augment the efficacy of chemotherapy. Experiments are now continued at my home institute with the focus on the uptake of fluorescent macromolecules. Furthermore, it is known that the rare distribution of lymphatics in solid tumours is one of the main reasons for enhanced TIFP (Heldin <i>et al. Nat Cancer Rev</i> , 2004). In general, every tumour cell line shows a different TIFP value. Yet, it has not been investigated if tumours with reduced TIFP values might have a more dense lymphatic network in contrast to tumours with higher TIFP values. The stay at my japanese host institute is focussed on immunohistochemical staining of lymphatic vessels in tumour tissue to adress this specific question.	

7. Research implementation and results under the program

Title of your research plan:

Impact of the density of lymphatics on the tumour interstitial fluid pressure in solid epithelial tumours

Description of the research activities:

Main focus of my research work was to investigate the distribution of lymphatic vessels in two different tumour entities 1) A431 (squamous epithelial vulva carcinoma) and 2) A549 (lung epithelial carcinoma) which differ in their tumour interstitial fluid pressure (TIFP) values. Solid epithelial tumours of A431 cells show a high TIFP (over 10 mmHg) while tumours derived from A549 cells exhibits a lower TIFP (ca. 5mmHg).

Immunohistochemical staining was the method of choice to investigate the distribution of lymphatics in tumour tissue sections of paraffin-embedded or frozen tumour tissue sections. To stain specifically lymphatic vessels I used antibodies derived against podoplanin. Podoplanin is a transmembrane glycoprotein that is highly expressed in lymphatic endothelial cells.

Paraffin-embedded tumour sections were incubated with podoplanin antibody after being rehydrated. This was followed by the incubation with fluorescent-linked secondary antibodies to make the podoplanin positive regions visible. Freshly frozen and in Tissue Tek-embedded tumours were sectioned using a microtome, thus fixed with cold acetone and methanol. For lymphatic staining the podoplanin antibody was used, too. Additionally, frozen sections were double-stained against CD31 to highlight the distribution of blood vessels.

To investigate potential molecular mechanisms which can result in a different lymphatic distribution as seen in both tumours I examined the expression of VEGF-A (vascular endothelial growth factor) and VEGF-C. Both growth factors play a crucial role in lymphangiogenesis. Experiments resulted in a strong VEGF-A mRNA and protein expression in A431 tumours while A549 tumours showed a lack of those growth factors. Furthermore, RT-PCR analysis of A431 tumour tissue showed an enhanced expression of human hypoxia-inducible factor-1 α (HIF-1 α), which regulates the supply of blood to tissues through its effects on the VEGF expression.

In conclusion, my experiments showed that the lymphatic distribution between two epithelial tumour entities (A431 and A549) can differ strongly. Intratumoural lymphatics were solely found in A431 tumours, while A549 tumours lack intratumoural lymphatic vessels. Immunohistochemical findings were corroborated

by molecular biological data. A431 tumours highlighted a strong HIF-1 α and VEGF-A expression assuming a strong molecular induction signal for lymphangiogenesis. Whereas A549 tumours showed no expression of these transcription and growth factors. Interestingly no expression of VEGF-C was observed in A431 tumours at the current stage of development. Therefore, the A431 tumour might be a good “biological” model to study the effects of VEGF-A on lymphangiogenesis without the interfering effects of VEGF-C.

Finally, my study displayed that the lymphatic system showed no impact on the TIFP in the examined tumours. Therefore, the role of lymphatics on the TIFP might be overestimated in the current literature. Additionally, a future anti-lymphatic therapy would not affect the TIFP and could be proposed to reduce the risk of metastasis in cancer patients.

8. Please add your comments (if any):

At first, I want to thank Prof. Hashimoto and Dr. Hirakawa who provided me with all their help, scientific advice and giving me the possibility to join their group. I would like to thank my colleagues Dr. Dai, Ms Tan, Ms Tsuda, Ms Wan and Dr. Yan for their great help.

Finally, I would like to thank Prof. Ninomiya for his invitation to visit his group at the Dept. of Molecular Biology and Biochemistry at Okayama University. It was a pleasure for me to present my data and to have a lot of fruitful talks with the members of his group (Prof. Oohashi, Prof. Yonezawa, Prof. Hirohata, Prof. Ohtsuka) and the affiliated students.

Thanks to JSPS for giving me the opportunity to have a great insight into Japanese research and daily life.

9. Advisor's remarks (if any):

Mr. Matthias Hofmann, a well-motivated scientist, has promoted a specific project of the lymphatic system particularly focusing on TIFP in certain environments. Although new blood vessel formation during tumour development has been clearly addressed so far, little is known about tumour-associated lymphatic vessel growth and its potential role in tissue fluid drainage of physiological requirements. However, Mr. Hofmann clearly identified a molecular mechanism of tumour lymphangiogenesis focusing on VEGF family members. Furthermore, this pathologic lymphatic vessel growth surprisingly fails to reduce TIFP values, suggesting that tumour lymphangiogenesis develops as an independent manner from physiological conditions. Therefore, this novel finding may further support tumour lymphangiogenesis as a therapeutic target for prevention of metastasis in accordance with the clinical relevance of cancer research.

RESEARCH REPORT

1. Name: Jäger, Heide	(ID No.: SP06304)
2. Current affiliation: MIRIAD, Manchester Metropolitan University, UK	
3. Research fields and specialties: Humanities <u>Social Sciences</u> Mathematical and Physical Sciences Chemistry Engineering Sciences Biological Sciences Agricultural Sciences Medical, Dental and Pharmaceutical Sciences Interdisciplinary and Frontier Sciences	
4. Host institution: Kyoto University, Japan, Department of Architecture and Architectural Engineering	
5. Host researcher: Prof. Teruyuki Monnai	
6. Description of your current research <p>I currently do research in the field of architectural anthropology. The PhD thesis “<i>Resonance of the roji- inscribing memory through walking the urban backstreets</i>” is concerned with the narrative nature of the daily activities taking place in the urban backstreet. The research will investigate the importance of the urban backstreet (example of the Japanese roji) within the urban fabric, and consider the ways in which the history and ambitions of the local community become meaningful entwined in that space. The backstreet type roji is chosen to embody the relation between collective memory and place-making.</p> <p>Two address the relationship of the dynamic activities in the roji and inscribed past and present, the PhD research and the following fieldwork in 2007 will be based on two approaches: (1) spatial-historical and (2) participant observation. The first approach will focus on the spatial evolution of the urban place of the roji in connection to the urban fabric of the Japanese city as a way of connecting the theoretical analysis to the field research. The second approach will concentrate on the social evolution of the roji, through utilising tools and methods from ethnographic research.</p> <p>The current research approach argues that the urban backstreet is here seen as a locus of historical and cultural knowledge regarding the personal encounters between people’s spatial routine of walking and experiencing a small, enclosed urban place. Accordingly, the main research question will focus on the grasping and understanding of the potential of the roji as space which is acquired, experienced and named through the way their inhabitants access and behave within its physical boundaries.</p>	

7. Research implementation and results under the program

Title of your research plan:

In situ in the street: approach interaction research methods to capture day-to-day activities in the Japanese Urban backalley roji

Description of the research activities:

To address the main research question and the direct relationship between a spatial and social understanding of the back alley, the researcher examined during the Research stay in Japan, **firstly** two interaction research methods: (1) Cultural Probing (Gaver, 1999) and (2) the RSVP Cycles (Halprin, 1982). Whereas Cultural Probing is a method developed to elicit inspirational messages from people, here the students, to capture moments in urban space (in sketches, photographs), the RSVP Cycles is a methodology which presents 4 key aspects of understanding/ capturing movements (in e.g. personal maps).

Secondly, applying the research methods in a fieldwork setting, allowed the participants to develop an improved perspective to observe the narrow backstreet roji, its context and daily activities. For the conducting of the research in Japan, the researcher engaged students of the Kyoto University, Department of Architecture, Laboratory of Prof. Teruyuki Monnai, which took part in the fieldwork and workshop. Through choosing three areas in the urban realm of Kyoto which were suitable for the size of the research stay, the methods were in a **first phase of fieldwork** practically applied.

The case studies were chosen because of their direct relation to the traditional urban fabric of Kyoto and the assumption that they offer a spatial and social authentic roji setting. The criteria for choosing the representative cases were developed in the stage of preparation according to meetings and gathered historical and recent documents.

In a first meeting with Ms. Misato Oku from the Kyoto-shi Keikan Machizukuri Center, the fieldwork team acquired a first insight and into the urban history and the background/ current situation of urban backalleys in Kyoto. In a second meeting, Ms. Oku made it possible to meet Dr. Kenji Kanbayashi who observed the rojis of Kyoto in an extensive research. These meetings offered the team a unique chance to acquire a more deeper and understanding of the roji setting in Kyoto. After a first evaluation of the gathered data/documents, the actual fieldwork was prepared and a catalogue of criteria developed which should allow us to observe the roji according to an empirical approach which combines spatial and social analysis.

Each participant functioned during the fieldwork as a kind of agent, applying both methods and gathering/ collecting a personal data set in form of visual and textual material like sketches, photographs, short interviews and fieldnotes.

In the final step of Analysis, the participants assembled and analysed their data according to a personally chosen, empirical approach and produced so a '*collective*

document' of the urban space roji. The documentation "Roji Research" can be seen as a preliminary, collaborative result in the further process of the PhD research and fieldwork. The conducting of the workshop was aimed to engage participants of different backgrounds to offer a preliminary, collaborative fieldwork study which combined empirical and creative work.



Mainly, this research stay in Japan wanted to offer an insight in the fact that we experience the city through the small events and personal memories which are most time connected to a certain street or alley. And the variety of the student backgrounds and the related interesting empirical approaches (like e.g. form, texture, history or soundscape) showed us how divers we can grasp and understand the potential of the roji. This roji-documentation is in this sense a qualitative piece of research and an active form of argumentation combining empirical and creative analysis.

In the further process of the PhD research it is therefore the aim to deepen this understanding and to develop an integral approach analysing the back alley roji according to a set of specific criteria. Whereas a first set of criteria will be developed according to the spatial evolution of the urban place of the roji, the second part will focus on the social evolution of the roji through utilising tools and methods from ethnographic research such as field notes, personal mapping, informal interviews and visual sources, as photographs and video-recording.

9. Advisor's remarks (if any):

I am very interested in Ms. Jäger's approach to urban backalley rojis from the viewpoint of architectural anthropology. Her roji research is deeply related to our research topic, *Semiotic Study on the Design of Architectural and Urban Space*. She has surveyed various rojis in Kyoto with my laboratory students and analysed not only formal properties but also social and cultural meanings of the roji. The results of this research are compiled in a beautiful booklet "Roji Research", and it is possible to find many cues to design good living environments.

Ms. Jäger will develop more profound analysis of rojis for her PhD research based on the "Roji Research" in Kyoto. I hope our collaborative research will continue in the future.

RESEARCH REPORT

1. Name: Arnim Jenett	(ID No.: SP06305)
2. Current affiliation: Lehrstuhl fuer Genetik und Neurobiologie, Bayerische Julius-Maximilians Universtitaet Wuerzburg, Germany	
3. Research fields and specialties: Humanities Social Sciences Mathematical and Physical Sciences Chemistry Engineering Sciences X Biological Sciences Agricultural Sciences Medical, Dental and Pharmaceutical Sciences Interdisciplinary and Frontier Sciences	
4. Host institution: Institute of Molecular and Cellular Biosciences, Center of Bioinformatics, University of Tokyo	
5. Host researcher: Dr. Kei Ito,	
6. Description of your current research The Virtual Insect Brain Protocol by A. Jenett, Johannes E. Schindelin and M. Heisenberg. Our project deals with a general, largely unsolved problem in the life sciences: the quantification of shape. The study case here is the brain of the fly <i>Drosophila melanogaster</i> . Working with the fly, the brain scientist needs to compare the brains of different specimens of one strain, as well as the brains of different strains. Such quantitative comparisons are crucial for structure-function mapping, for investigating neuronal plasticity, for understanding the significance of genes on brain and behavior, and for the exploitation of gene expression patterns in the brain. So far, comparisons had to rely on the eye and imagination of the trained scientist. In the last years we build the Virtual Insect Brain (VIB) protocol, a new software tool for the standardization and comparison of morphological data obtained by confocal microscopy. In essence, the VIB Protocol enables untrained users to fuse multiple data sets in a common coordinate system. Our current aim is to gain as many collaborators as possible for the usage of the VIB protocol. Normalizing their data to a common coordinate system generated by our software will enhance the comparison of neuroanatomical data gained in the contributing Labs and therefore it will facilitate their collaboration.	

7. Research implementation and results under the program

Title of your research plan:

The Virtual Insect Brain Protocol: creating and comparing standardized neuroanatomy.

Description of the research activities:

- **Standardization and reconstruction of single cell stainings in the optic lobe of *Drosophila melanogaster***

In collaboration with Kazunori Shinomiya I was able to enhance the functionality of the VIB protocol during my stay at the Ito-Lab remarkably. Initially constructed for the standardization of rather large structures like brain areas the protocol currently can also be used for the standardization of single cell stainings. A 3D-reconstruction of the standardized shape of the stained neurons was gained using the neuro-tracer module written by Schmidt et al. (NeuroImage 2004). Thereby the analysis of the fine structure and potential interactions of the stained cells could be facilitated. This approach is a very good start for a close collaboration with the Ito-Lab and will be carried on in future.

- **Development of an unbiased template selection procedure**

For standardizing neuroanatomy a template data set is needed. It provides the common coordinate system for the procedure. Therefore it must be the one with the most normal neuroanatomy out of the group of specimens a standard brain is computed on. Hitherto the selection of the Template is carried out by an iterative process starting with an initial Template selection by the user. This approach is afflicted by the bias of the user. Due to unavoidable variations in the staining and/or data acquisition even trained users tend to select rather the nicest specimen than the most normal one. To enable an unbiased selection of the Template even by untrained users I developed a procedure which automatically defines the specimen with the most normal neuroanatomy during my stay.

- **Proliferation of the VIB protocol**

The VIB protocol is build to enable the comparisons of neuroanatomy between specimens as well as between different Laboratories. Therefore our interest is to win as many collaborators as possible. During my stay at Japan I was able to build up several contacts to leading scientists in the field of insect neurobiology:

- Prof. Arikawa	Sokendai	Hayama
- Prof. Sasaki	Tamagawa University	Machida
- Prof. Kubo	University of Tokyo	Tokyo
- Prof. Furukubo-Tokunaga	University of Tsukuba	Tsukuba
- Prof. Mizunami	Tohoku University	Sendai
- Prof. Yamamoto	Tohoku University	Sendai
- Prof. Kanzaki	University of Tokyo	Tokyo

The interaction with my hosts was throughout positive and collaboration could be directly initiated in 50% of the visited Labs. Most of the other Labs also indicated interest in working with the VIB protocol. Therefore my travel in Japan led to great success. Additionally I was able to gather many interesting and important comments for the further development of the VIB protocol during the discussions with the members of the visited Labs..

- Development of an Internet-based query-tool for neuroanatomical databases

While creating large amounts of anatomical data during the process of standardization the need for a search engine for neuroanatomic data bases arose. The first approaches in building such a tool directly on the basis of MySQL and php failed due to the complexity of the problem. Talking to T. Kazawa from the Kanzaki-Lab I finally found a way to implement such a tool as planned. Progressing fairly quick I expect to have the planned tool implemented by the end of the year.

8. Please add your comments (if any):

Many thanks to the JSPS which gave me the great opportunity of this stay. Especially the framework program including language crash course and home stay at a Japanese family in the first week is very precious because it allows the fellows gently to acclimate to the foreign environment and get rid of their jet lags. Maybe the ending convention could be a little longer, because I bet, there will be much to tell each other.

RESEARCH REPORT

1. Name: Christoph Schmidt	(ID No.: SP06306)
2. Current affiliation: University of Edinburgh	
3. Research fields and specialties: Humanities Social Sciences Mathematical and Physical Sciences Chemistry Engineering Sciences X Biological Sciences Agricultural Sciences Medical, Dental and Pharmaceutical Sciences Interdisciplinary and Frontier Sciences	
4. Host institution: Graduate School of Supramolecular Biology, Yokohama City University	
5. Host researcher: Professor Yoshifumi Nishimura	
6. Description of your current research <p>High-field Nuclear Magnetic Resonance (NMR) (500 to 800 MHz) and other biophysical tools are used to study the structure and dynamics of proteins in solution. Research activities are multidisciplinary and extend from molecular biology and mutagenesis through protein purification and characterisation, to the structure determination at atomic resolution using biomolecular NMR. Of principal interest are the regulators of the complement cascade which form a part of the innate immune system. The innate immune system acts as the first line of immune defense in humans and other higher mammals.</p> <p>The plasma protein factor H (150 kDa) regulates the activity of the alternative pathway of the complement cascade. Deficiencies in factor H function lead to under-regulation of this pathway, resulting in diseases associated with permanent complement activation (e.g. glomerulonephritis, chronic haemolytic uremic syndrome or age-related macular degeneration).</p> <p>The 20 complement control protein (CCP) modules of factor H are joined by linking sequences that vary in length, with the longest linkers occurring in the central portion of the molecule.</p> <p>The five factor H linkers of CCP10-CCP14 consist of six, seven or eight residues. The largest numbers of linker residues occur on either side of CCP13, which is the smallest CCP module known. The coincidence of the relatively small CCP module of 13 with the higher number of linkers in the central part of factor H is likely to reflect some unique architectural features. To explore the structural details of this portion of factor H, the following constructs have been expressed in yeast expression system (<i>Pichia pastoris</i>): fH-11; fH-11-14; fH-12; fH-12-13; fH~13; fH-12-14 and fH-13-14.</p>	

NMR spectroscopy and other biophysical methods are being employed to develop a precise understanding of the arrangement of modules in this central portion of factor H. The module pair fH-12-13 - joined by a linker of eight residues - has been used in initial high-field multidimensional NMR studies and produces very high quality spectra.

7. Research implementation and results under the program

Title of your research plan:

BIOPHYSICAL STUDIES OF THE DNA-BINDING DOMAIN OF THE BACTERIAL PURINE REPRESSOR

Description of the research activities:

The purine repressor (PurR) regulates bacterial genes which encode enzymes for purine biosynthesis. Amongst other functions, purines are needed to form two of the four essential DNA bases. PurR consists of two domains, an N-terminal DNA-binding domain (DBD) and a C-terminal co-repressor domain. Two 3-dimensional high resolution protein structures of PurR are already available. The solution structure of the DBD of PurR has been determined in its free state while the crystal structure of whole PurR has been determined bound to its cognate DNA sequence. Structural differences in alpha-helical content let to the conclusion that a dimer form of the DBD of PurR is essential for its specificity in DNA binding. Therefore a mutant of the PurR DBD was made in order to obtain a dimer form with specific DNA binding.

Within the JSPS summer program this mutant DBD of PurR was be expressed as a single- (¹⁵N isotope enriched) and double-labeled (= ¹⁵N and ¹³C isotope enriched) mutant using bacterial *E. coli* expression system. The purified monomer forms were dimerised and cleaned up. The resulting purified dimer form was used to submit it and its specific DNA complex to a set of biophysical tools as well as to continue the NMR characterization.

For protein expression of single- and double-labeled PurR-DBD two three liter fermentations were performed with the addition of the appropriate labels, respectively. The labeled proteins were extracted from the *E. coli* cells using a standard sonication method. Consecutively, with an ion-exchange chromatography and gel filtration chromatography clean protein was obtain within two purification steps. This pure monomeric protein was submitted to dimerisation conditions.

Gel filtration chromatography was applied after dimerisation to clean the dimer form from monomeric remnants. Parts of the dimer form were complexed with its cognate DNA.

Using Fluorescence Intercalating Displacement (FID) the binding constant of the Dimer to its cognate DNA could be determined.

Circular Dichroism (CD) spectroscopy revealed an elevated content of alpha helix in the DNA bound form of the dimeric protein.

Several 1D (dimensional), 2D and 3D Nuclear Magnetic Resonance (NMR) experiments were performed with the protein in the free and DNA-bound state. Strong shifting of the resonance signals between free and DNA-bound protein states support the findings obtained from CD spectroscopy.

8. Please add your comments (if any):

The experience gained during this research project conducted in Prof Nishimura's lab is very valuable for me. Not only could I deepen my general knowledge about DNA binding proteins and the technique of NMR, but also have I been introduced to a range of biophysical techniques not used in my current PhD project. Therefore, I would like to express my sincere thanks to Prof. Nishimura for hosting my JSPS summer stay as well as for providing me with a very interesting research topic! Moreover, I would like to thank the PhD students Mrs. Ishizu and Mr. Morita a lot for their patience in instructing me during the numerously conducted experiments!

RESEARCH REPORT

1. Name: Thomas Schmidt	(ID No.: SP06307)
2. Current affiliation: Friedrich-Schiller-Universität Jena Otto-Schott-Institut für Glaschemie	
3. Research fields and specialties: Humanities Social Sciences Mathematical and Physical Sciences Chemistry X Engineering Sciences Biological Sciences Agricultural Sciences Medical, Dental and Pharmaceutical Sciences Interdisciplinary and Frontier Sciences	
4. Host institution: Nagoya Institute of Technology	
5. Host researcher: Professor Toshihiro Kasuga	
6. Description of your current research <p>Proton conductive surfaces and interfaces on glass are of big interest in Technology. Silica glass has special surface properties that are useful for a wide range of applications. Focusing on membranes sintered of silica microspheres applications aimed on are electroosmotic pumps, fuel-cells, and catalysts. Basis for these membranes are SiO₂ microspheres produced by means of sol-gel-technology. The membranes can be conditioned to enhance properties of surface allocation and protonconductivity. The present research engages green body preparation and sintering parameters for crack free membrane production as well as observing property changes during sinter process.</p>	

7. Research implementation and results under the program

Title of your research plan:

Preparation of new membrane structures from monodisperse SiO₂ microspheres

subtitle:

Characterisation of Microsphere- and Membrane Properties

Description of the research activities:

Membranes sintered from Silica micro spheres have the capability to be proton conductive. The untreated micro spheres produced by Sol-Gel process show OH-groups in FTIR spectra. However being heat treated the associated peaks could only be determined up to temperatures of 400°C (2h). Sintering temperatures higher than 1000°C cause the OH-peaks to disappear. For applications of proton conducting membranes the OH-groups have to be reintroduced. For this reason 1100°C, 2h heat-treated samples were treated with acid (HF) as well as basic (NaOH) agents. Positive results could be detected in FTIR spectra of NaOH-treated samples. Peaks could be determined associated to OH-groups after treating 1g sample for 2h with 10ml NaOH (0,01mol/l). Particle size measurements show that referring only on particle size analyzing devices could lead to results that strongly differ from the real powder properties. A comparison of results from SEM-micrographs interpretation by graphic software and data obtained from particle size measurement device shows significant deviations in mean diameter value, standard deviation and size distribution as well as other values. Concluding SEM offers a more precise but extensive method for measuring the microsphere size. As consequence of the conducted experiments several new questions arise concerning the influence of reagents and contained impurities, the conditioning of membrane surfaces for strong proton conductivity and about resistance against chemical dissociation processes. Experiments have to be conducted answering those questions.

9. Advisor's remarks (if any):

It was shown that further discussion should be needed for preparation of proton conducting film derived from SiO₂ spheres. Especially, it is very important to control the nano-sized pores and the composition of the spheres. These problems are expected to be resolved by further work after this program.

RESEARCH REPORT

1. Name: Michael SPERBER	(ID No.: SP06308)
2. Current affiliation: Brandenburg Technical University, Cottbus	
3. Research fields and specialties: Humanities X Social Sciences Mathematical and Physical Sciences Chemistry Engineering Sciences Biological Sciences Agricultural Sciences Medical, Dental and Pharmaceutical Sciences Interdisciplinary and Frontier Sciences	
4. Host institution: Tohoku Culture Research Center, Yamagata	
5. Host researcher: Dipl.-Ing. Kyoko IIDA; Prof. Norio AKASAKA	
6. Description of your current research At present I am finishing my thesis “Changes in the culture of learning in peripheral regions – with a special consideration of the contradictory field of cooperative administration, committed citizenship and innovative milieu in Lower Lusatia”. Lower Lusatia was a mining region until the political change in East Germany in 1989. This region has now severe development problems, including brain-drain and self-abandonment of those people who stay. This phenomenon could be explained as acquired helplessness in reaction of a collectively experienced life-event and several unsuccessful trials to develop a new identity (meaning structure). I concentrate on the relationship between regional development and the introduction of new action-guiding conceivabilities. Particularly the idea of place, values and the point of view determine, how people develop a place (Ipsen). That’s why I am interested in the theory of “Poetic Places”. Since I work across disciplinary borders (as planner, political and social scientist) and since I engage with peripheral regions, I am especially interested in the topic, how new (innovative) ideas can be introduced and diffused in a region with structural ruptures and (mental) blockades in development. As result of my research in Tohoku I made an appointment with Kyoko Iida to elaborate a cooperative paper, dealing with following subjects: <ul style="list-style-type: none">• description and comparison of one peripheral region in East Germany and one rural region in Tohoku• description of the economic, social and mental situation and the problems in both regions	

- description of people's self-images, visions and identities
- description of one or two typical innovative projects for each region
- analysis how the projects (and proposed identities) contribute to the development of the region.

7. Research implementation and results under the program

Title of your research plan:

~~Peripheral regions: problems and development approaches~~ (planned)

"Poetic places – an intercultural perspective" (almost finished article, 15 pages)

Description of the research activities:

The time of my research in Yamagata was divided in (more or less) two different overlapping periods. The first 3 weeks (June 21- beginning of July) provided me personal orientation. I received an overview in the field of research at Tohoku Culture Research Center, I got to know the approaches of research, the kind of questioning and discussing. I became familiar with Japanese style of working and decision making. I have to admit, that this process of becoming familiar in the "new culture" was not always easy. But how challenging it was sometimes, it was intensive and an enriching life experience as well. I found, that almost all members of the "Institute" were idealists (in their activities of promoting Tohoku Region) – the way I prefer to work in Lusatia Region (East Germany). Thus a cordial sympathy arose to "my group".

The second period began in my second week, when I concretised my research topic for my time in Yamagata. The dialogues with "my colleagues", especially with Mrs. Iida made clear to me, that one European approach, the theory of poetic places (Detlev Ipsen), was received with great interest at Tohoku Culture Research Center. But many colleagues told to me, that they have some problems to understand the details of the theory, e.g. terms like "(regional) identity" or "Lebenswelt". But also the philosophical background (e.g. Habermas' Theory of communicative action) should be better explained. I'd got the opportunity to become involved in their research more deeply, if I would focus the intended article on the intercultural perspective of poetic places theory.

I preferred to do a bi-directional work. On the one hand it was easy for me to explain the appropriate parts of European philosophical ideas and

(cultural) history - and the practical work of Detlev Ipsen. (I worked together with him once). On the other hand I also wanted get to know the Japanese conceivabilities more intensely. I decided to interview the staff as experts of designing and/or analysing Japanese poetic places and to join their book project of poetic places with an article. (Additionally I accompanied Mrs. Iida to her field research in Yamagata Prefecture.)

The result of my is this article, comparing Japanese & European conceivabilities about promoting a region by poetic places and describing (inter)cultural - philosophical background of poetic places' theory.

The article explicates, that the atmospherical and sense-intending sentiment and the processuality is the intercultural link of poetic places between Western and Japanese. The difference is, that in European philosophy "spatial mind-image" (Raumbild) is connected with disputatious moral concepts, but Japanese spatial mind-images preferably refer to generally accepted moral concepts. This difference is caused by the different way, how individuality and meaning is constructed in Japanese and Western culture. Nevertheless the approach of poetic places works in Japan too, if cultural differences in interacting and communicating are considered.

8. Please add your comments (if any):

I count myself lucky, that Kyoko Iida supported me outstandingly and obligingly in all cases, e.g. in making the appointments and translating the real difficult topics. I thank the members of Tohoku Culture Research Center for the cordial hospitality and for the open minded & helpful support. I also thank all my interview partners for their openness and empathy with my request.

RESEARCH REPORT

1. Name: Albert H. Vette	(ID No.: SP06309)
2. Current affiliation: Institute of Biomaterials and Biomedical Engineering University of Toronto, Canada	
3. Research fields and specialties: Humanities Social Sciences Mathematical and Physical Sciences Chemistry X Engineering Sciences Biological Sciences Agricultural Sciences X Medical, Dental and Pharmaceutical Sciences Interdisciplinary and Frontier Sciences	
4. Host institution: National Rehabilitation Center for the Disabled, Tokorozawa, Japan	
5. Host researcher: Dr. Kimitaka Nakazawa	
6. Description of your current research <p>The overall goal of my research at the Institute of Biomaterials and Biomedical Engineering (University of Toronto) is to (1) determine the physiological control strategy (<i>motor control</i>) and (2) characterize the resulting biomechanical mechanisms (<i>muscle actuation</i>) that are responsible for stabilizing the human body during upright stance. The gained knowledge will assist in explaining physiological phenomena such as the source of body sway during upright stance. Moreover, it will allow us to identify the neural and biomechanical deficiencies that are responsible for loss of balance in the elderly.</p> <p>In order to accomplish the first task, the control strategy in question is expected to compensate for: (1) a long neurological time delay between sensory information acquisition and motor command delivery, which represents a significant destabilization factor; (2) nonlinear muscle activation patterns; and (3) closed-chain dynamics that are present during bipedal stance (two feet on the ground). By means of systematic simulations, which implemented classical control theory theorems as well as electromyogram (<i>EMG</i>) and center of mass (<i>COM</i>) recordings from healthy individuals, we have identified a control strategy that is capable of stabilizing the body in a physiological manner. Using these theoretical results, we furthermore conducted an experimental study that evaluated our control system in a subject with spinal cord injury.</p> <p>The second task of characterizing the responsible biomechanical mechanisms will be accomplished by: (1) studying the contribution of each calf muscle for stabilizing the human body during upright stance; and (2) investigating whether our control strategy is capable of eliciting these biomechanical mechanisms. The first part of this task was</p>	

completed during my research experience in Japan (*see below*).

We have also studied the cause of spontaneous body sway as well as characteristic differences between body sway of young and elderly people during standing. This is an important issue since a larger sway fluctuation as seen in elderly individuals has been related to falling and its serious consequences. Our preliminary findings show that a smaller sway size in young individuals is related to a more effective sensory use of their body's velocity information.

7. Research implementation and results under the program

Title of your research plan:

Active Torque Contribution of Each Calf Muscle for Stabilizing the Human Body during Upright Stance

Description of the research activities:

Background: For standing humans, the body's COM is maintained at a variable distance in front of the ankle joints. Consequently, gravity acts on the body to topple it forward. Since passive torque components due to intrinsic mechanical properties of the joints, i.e., stiffness and viscosity, are too low to oppose this toppling effect, three calf muscles need to be actively modulated by the central nervous system to stabilize the body during upright stance: (1) the soleus (*SOL*), (2) the medial head of the gastrocnemius (*MG*), and (3) the lateral head of the gastrocnemius (*LG*) muscle. While *SOL* has been shown to have a tonic EMG profile during standing, *MG* has phasic characteristics. Additionally, *SOL* shows the highest average activity and *MG* the highest correlation with body sway among the three muscles.

Objectives: (1) To identify each muscle's torque contribution during upright stance as well as during isometric voluntary contractions. (2) To isolate the torque components during standing that are due to intrinsic mechanical properties of the joints (*passive components*) and due to centrally controlled muscle modulation (*active components*).

Methods I – Experiments: In order to accomplish these tasks, two experiments were performed: (1) Measurement of EMG activity, ankle torque and COM fluctuation during upright stance. (2) Measurement of EMG activity and ankle torque fluctuation during the execution of isometric torque tasks (e.g. impulses and sinusoids). Both experiments were performed by 14 subjects (age: 25 to 44) who had no medical history with respect to neurological or biomechanical disorders.

Methods II – Analysis: Since muscle tissue has been shown to have second order, low-pass filter characteristics, the *Direct Optimization Method* was used to identify two sets of second order transfer functions for *SOL*, *MG*, and *LG* during (1)

isometric torque execution and (2) upright stance. These transfer functions were then used to determine each muscle's torque contribution as well as active and passive torque components during upright stance.

Result I – Torque contribution of each muscle: The findings of the performed study suggest that SOL is the dominant force generator during upright stance. MG on the other hand is mostly responsible for active torque modulation that correlates with the COM fluctuation. In some subjects, however, MG had the potential to additionally support a fatiguing SOL by means of tonic force generation. Finally, LG was shown to be only active during phases of fatigue or a more extreme COM location in front of the ankle joints. This result agrees with previous reports that LG is a muscle that is mainly used during walking and running.

Result II – Isolation of active and passive torque components: We found a distinct relationship between the passive torque component and the COM fluctuation. As such, the passive torque component that opposes the toppling effect of gravity increases and decreases during forward and backward sway, respectively.

Conclusion: The results will allow us to identify the calf muscle that is most adequate for functional electrical stimulation, potentially enabling individuals with paraplegia to perform daily activities while standing.

8. Please add your comments (if any):

The facilities as well as the equipment that I got involved with at the National Rehabilitation Center for the Disabled (Tokorozawa) were very impressive. I had the opportunity to get to know new experimental devices, learn about novel methodologies and techniques, and benefit extremely from the Japanese researchers' expertise. There is no doubt that my stay in Japan was of great academic value for me. As such, I would like to thank JSPS, DAAD and my host researcher, Dr. Kimitaka Nakazawa, for this unique and unforgettable experience.

RESEARCH REPORT

1. Name: Christian Vogel	(ID No.: SP06310)
2. Current affiliation: University of Duisburg-Essen	
3. Research fields and specialties: Humanities Social Sciences Mathematical and Physical Sciences X Chemistry Engineering Sciences Biological Sciences Agricultural Sciences Medical, Dental and Pharmaceutical Sciences Interdisciplinary and Frontier Sciences	
4. Host institution: Kwansei-Gakuin University	
5. Host researcher: Prof. Yukihiro Ozaki	
6. Description of your current research <p>In my research the biodegradable polymers, poly(3-hydroxybutyrate) (PHB) and its copolymer, poly(3-hydroxybutyrate-co-3-hydroxyhexanoate) P(HB-co-HHx) have been investigated by different physico-chemical methods (TGA/DSC-FTIR, FTIR imaging and Rheo-optical FTIR) with the aim of better understanding their thermal and mechanical properties and to improve their processing conditions.</p> <p>For thermogravimetric analysis coupled with FTIR spectroscopy (TGA/FTIR) a polymer sample is heated beyond the decomposition temperature and the weight loss of the polymer is recorded. Simultaneously, the gaseous decomposition products are measured by gas-phase mid-IR spectroscopy. Thus, a detailed picture on the thermal decomposition of the investigated poly(hydroxyalkanoate) (PHA) in the respective environment (nitrogen or oxygen) can be obtained.</p> <p>The technique of imaging mid-infrared spectroscopy with a focal-plane array detector is applied to blends of poly(hydroxyalkanoates) with other synthetic polymers in order to study phase separation phenomena as a function of composition.</p> <p>Rheo-optical Fourier-Transform IR (FTIR) spectroscopy is a technique where a polymer sample is subjected to a mechanical treatment (e.g. elongation or elongation/recovery cycles) and simultaneously investigated by mid-IR spectroscopy with polarized radiation. This method is applied to study the effects of mechanical deformation and relaxation on the orientation of selected PHA's and PHA blends.</p>	

7. Research implementation and results under the program

Title of your research plan:

Analysis of IR-spectroscopy data by chemometric methods and temperature-dependent IR-measurements of ultrathin biodegradable polymer films.

Description of the research activities:

I took my thermal and spectroscopic data (thermogravimetry coupled by IR, rheo-optical IR and FTIR Imaging) from Germany to Japan and undertook analysis using two chemometric methods: two-dimensional (2D) correlation and perturbation-correlation moving-window two-dimensional (PCMW2D) correlation spectroscopy. 2D correlation is a formal but very versatile approach to analysing a set of spectroscopic data collected for a system under some type of external perturbation. Perturbation-Correlation Moving-Window 2D Correlation has the advantage that a spectrum can be plotted between a spectral and a perturbation variable axis, which easily deliver information about the change of spectral intensity at perturbation direction. By these methods the decomposition process PHB under oxygen could be identified. Also other interesting information about the thermal and mechanical properties of the polymers was found from the IR-spectra.

In addition, I worked with ultrathin biodegradable polymer films (thickness between 1 - 100 nm). These polymer films were prepared by spin coating on a gold substrate and were then investigated using reflection-absorption-IR-spectroscopy (RAS) in combination with a variable temperature cell. This has provided information about the melting behavior of thin films and possible differences that have affected the bulk sample.