

RESEARCH REPORT

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| 1. Name: Roman BARTNIK | (ID No.: SP05301) |
| 2. Current affiliation: Research Associate Institute of East Asian Studies / Japanese Economic Studies University of Duisburg-Essen, Lotharstr. 65, 47048 Duisburg, Germany. | |
| 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: Hitotsubashi University Graduate School of Economics 186-8601 Kunitachi Tokyo | |
| 5. Host researcher: Prof. Hiroyuki Okamuro | |
| 6. Description of your current research Internationalization of research and development is a recent and broad trend in the high-tech industries. Within this main trend, the growing importance of supply-side factors for the multinationals' R&D investment is much discussed in the literature. Especially access to local knowledge bases is growing in importance in knowledge intensive industries such as pharmaceuticals or electronics. Linked to the aspired benefits of such access however, are problems of re-integrating local knowledge in the global organizational network of the multinational corporation. Division of labour in knowledge intensive processes leads to specific problems of coordination and incentive setting. The related trade-offs between local and global integration are of strong interest to organizational scientists. On a background of growing technological complexity, namely the further blurring of traditional boundaries between the natural sciences, growing dynamics pushed by increasing codification and the diffusion of information technologies as well as tight time constraints, innovation in high-tech industries is a fascinating field to study sectoral, organizational and national influences on the division of labour. While these questions have been intensely discussed however, empirical comparative evidence especially on the team level interactions in Japanese and German companies is still rare. Comparing structures between these two countries seems especially interesting due to specific institutional features distinguishing Japanese and German companies from Anglo-Saxon forms of organization. My research project aims to contribute to this | |

discussion by comparing international R&D organization in different organizational and sectoral settings between Japanese and German companies.

7. Research implementation and results under the program

Title of your research plan:

International R&D organization. The situation of German multinationals in the Japanese pharma market.

Description of the research activities:

During my two months at Tokyo Hitotsubashi University I have conducted semi-structured exploratory interviews with major Japanese and German companies in R&D intensive industries (mainly chemical and pharmaceutical industries). These interviews served two main purposes: firstly as a pre-test to study dynamics of headquarter-affiliate interaction in a specific industry setting before proceeding with inter-industry comparisons. Secondly to establish contacts with management from major Japanese and German companies as early as possible in order to negotiate broad empirical access for the subsequent German – Japanese comparison of international R&D organizations. Questions asked during the interviews focused on the exchange and integration of R&D related information and knowledge. In this, the organization of external and internal linkages (e.g.: alliances and foreign affiliates), especially the degree of codification vs. tacitness are the common focus of interest. In addition to the interviews, contact to researchers in the field and industry associations was established.

Firstly, interviews were conducted with four of the biggest Japanese pharmaceutical companies. Results show that the degree of internationalization especially of basic research is distinctly smaller in the Japanese companies and the integration of research groups in international projects is less pronounced. I will aim to use the personal connection made during these interviews to complement this analysis of management structures with first-hand knowledge from the project level by interviewing researchers and R&D managers in several locations, based on the contact to the Corporate Communication departments, and assurance of further assistance by the managers.

Secondly, I conducted interviews with top management (CEO and divisional manager level) of six German affiliates from the pharmaceutical and chemical industry. Results showed that basic research is a strong and growing motivation of the siting decision for these companies, as opposed to the more traditional development functions. Scientists and managers in these companies are strongly integrated in global R&D projects, interacting with colleagues from headquarters and other locations on multiple levels and on a daily basis. To assist in the study, the

contacts in the German affiliates promised to provide both reference to experts at company headquarters, further interviews with project members and managers, and in two cases possibilities for participant observation in the further course of my research project next year.

While the small sample only allows for tentative conclusions, the structure and intensity of interaction seems to be coupled to industry-related features of the research process, namely the degree of result codification, task-interconnectedness and the degree of affiliate's status as a center of excellence in the corporate structure. Additionally, doubt was cast on three rather common practices in quantitative research on innovation processes: separation of research on company-internal knowledge transfer between company units and company-external transfers such as alliance settings seems questionable when the focus is on the transfer and not on the formal structure of the transfer arrangement. The boundary between internal and external exchanges might be negligible in tight alliance settings and common points between foreign direct investments in R&D locations and alliances seem to call for an integrated analysis. Conversely, it became apparent during the interviews that strong divergences between research and development processes and within the cluster often lumped together as "high-tech" industries seem to warrant careful controls and conceptual justification before analyzing them on an aggregate level.

These findings, contacts and hypotheses will provide the basis for this more extended empirical study I aim to conduct next year in Japan, comparing international R&D organization in German and Japanese companies. To test the generated hypotheses, different sectors will be studied and larger numbers of companies in each sector and country compared by a combination of further interviews and statistical analysis.

A review of Japanese literature in the area of interest described above (see point 6) in will be one of the results of this research stay. A paper and presentation at the Euro-Asia Management Studies Association (EAMSA) conference in Frankfurt a.d.O. and a presentation at the European International Business Academy (EIBA) conference in Oslo the same month will present the analysis of the interviews conducted during the JSPS research stay to the scientific community. In these contributions, a specific focus will be laid on the situation and R&D organization of German multinationals in the Japanese pharmaceutical market.

8. Please add your comments (if any):

I had a very interesting and stimulating time at Hitotsubashi University and found both my supervisor and my colleagues to be very friendly, helpful and supportive. I will strive to use the connections gained here during workshops and presentations to further enhance Japanese – German dialogue in management science and economics. I would also like to

use this short stay as a preparation for a longer research experience in Japan.

9. Advisor's remarks (if any):

During his stay in Japan, Mr. Bartnik was very active in making contacts with and doing interviews with Japanese and German firms. I expect him to develop his research successfully on the basis of the research experience in Japan. I find his research topic very interesting and will continue to support his efforts in the future.

RESEARCH REPORT

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| 1. Name: Alexandra Brintrup | (ID No.: SP05302) |
| 2. Current affiliation: Cranfield University, School of Industrial and Manufacturing Science, Cranfield, Bedfordshire MK43 0AL, UK | |
| 3. Research fields and specialties: <div>Humanities Social Sciences Mathematical and Physical Sciences</div> <div>Chemistry Engineering Sciences Biological Sciences</div> <div>Agricultural Sciences Medical, Dental and Pharmaceutical Sciences</div> <div>X Interdisciplinary and Frontier Sciences</div> | |
| 4. Host institution: Kyushu University | |
| 5. Host researcher: Prof. Hideyuki Takagi | |
| 6. Description of your current research <p>In addition to multiple “quantitative” criteria that industrial design optimization problems typically involve, multiple “qualitative” criteria might also come into question during the lifecycle of design. These kinds of criteria are highly subjective and are hard to quantify or clearly specify in order to satisfy a large audience. A typical industrial problem may involve criteria of different nature and these criteria may have complex relations with each other. A recent answer to aid this complex problem solving procedure is Multiple Objective Optimization (MOO), which seeks to identify multiple solutions to a given optimization problem at each optimization run, where each solution in the solution set offers a different blend of qualitative or quantitative criteria satisfaction. A soft computing technique, Evolutionary Computation (EC), offers an ideal platform to practice MOO since it can optimize solutions simultaneously and achieve a set of solutions in a single run. Our current research aims at proposing and developing a set of soft computing based methods to handle multi-objective design optimization problems encountered in industry where objectives are both qualitative and quantitative in nature. The Interactive Multiple Objective Design Optimization (IMODO) framework is a first step attempt to give the industry a powerful tool to deal with such complex decision making patterns, and to help define and identify optimum designs faster.</p> | |

7. Research implementation and results under the program

(As much as possible, describe the contents and results of your research in a manner that is easily understandable to a non-specialist in your field.):

Title of your research plan:

Multi-objective Design Optimization using Parallel IEC

Description of the research activities:

The JSPS summer project was devoted to develop and test a particular method for carrying out evolutionary multi-objective optimization. The method employed a parallel interactive genetic algorithm (IPGA) that sought to optimize objectives of different nature in separate island populations. Each island population of solutions to the given design problem was evaluated by a different fitness function, which measured the fulfillment of one design criteria. The qualitative criteria island is the one where the solution evaluation is outsourced to the human user. The separation of criteria with this procedure resulted in better utilization of the time spent by the user to evaluate solutions, since the computer could evaluate a larger number of solutions on different criteria islands much faster. The elite solution sets were transferred between the criteria islands, in order to aid the user understand the relations between different design criteria and reach a compromise decision within the solution landscape.

The approach was compared with previously developed methods during the course of the research, including the INSGA (Interactive Non-dominating Sorting Genetic Algorithm) and the ISqGA (Interactive Sequential Genetic Algorithm). The INSGA employed a pareto front ranking technique whereas the ISqGA employed a sequential approach to satisfy varying criteria. Sign and Wilcoxon tests compared the average qualitative and quantitative fitness convergence of the 3 platforms, and indicated that the IPGA is significantly advantageous over ISqGA and the INSGA.

On the other hand, the IPGA that has been used for testing involved a pseudo user fitness evaluation function. User evaluation in real life can be quite noisy and show inconsistency. Therefore more tests are needed to analyze the complete affects of migration between islands and on user decision making with real test subjects.

9. Advisor's remarks (if any):

She introduced a new approach after our discussion and compared it with her previous works though experimental evaluation. The progress of designing experiment, programming, and conducting experiment for two months was quite reasonable. The experimental results look good enough to present at a conference, which delights me. We are planning to make a conference paper after additional experiments. Good job!

RESEARCH REPORT

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| 1. Name: Dana Duevelmeyer | (ID No.: SP05303) |
| 2. Current affiliation: Chemnitz University of Technology | |
| 3. Research fields and specialties: <div style="display: flex; flex-wrap: wrap; padding: 5px;"> <div style="width: 33%;">Humanities</div> <div style="width: 33%;">Social Sciences</div> <div style="width: 33%;">x Mathematical and Physical Sciences</div> <div style="width: 33%;">Chemistry</div> <div style="width: 33%;">Engineering Sciences</div> <div style="width: 33%;">Biological Sciences</div> <div style="width: 33%;">Agricultural Sciences</div> <div style="width: 33%;">Medical, Dental and Pharmaceutical Sciences</div> <div style="width: 33%;">Interdisciplinary and Frontier Sciences</div> </div> | |
| 4. Host institution: Graduate School of Mathematical Sciences, The University of Tokyo | |
| 5. Host researcher: Prof. Masahiro Yamamoto | |
| 6. Description of your current research <p>In my present work imbedded in the work of the group of Prof. Hofmann I am going to study more analytically the theoretical properties of the inverse problem of parameter identification in the specific jump diffusion model</p> $dS_t = S_t((\mu - \lambda v)dt + \sigma dW_t) + S_t - dN_t^c.$ <p>We are particularly interested in stable solvability of the inverse problem. Therefore we analyze properties of the forward operator of this inverse problem which maps the five parameters determining this model to the density function of return distribution. We have proven that this forward operator is continuous. Furthermore we have isolated the parameters which cause non-injectivity of the forward operator and hence we have proven the injectivity of the forward operator over a restricted domain. We have demonstrated that there is an asymptotical non-injectivity which causes instability problems whenever the jump intensity increases and the jump heights decay simultaneously. We have shown that the inverse problem is stably solvable, provided that the domain of the forward operator is restricted in a specific manner so that techniques of compact sets can be exploited. Unfortunately, there occur some instability effects by solving the least squares problem numerically even if the noise level δ is very small. These ill-posedness phenomena are caused by an ill-conditioned extremal problem which we obtain after discretization. To obtain stable approximate solutions of the estimation problem, we use a multi-parameter regularization approach, where a least-squares fitting of empirical densities is superposed by a quadratic penalty term of fitted semi-invariants with weights. The little number of required weights is controlled by a discrepancy principle. For the realization of this control, we propose and justify fixed point iteration.</p> | |

7. Research implementation and results under the program

(As much as possible, describe the contents and results of your research in a manner that is easily understandable to a non-specialist in your field.):

Title of your research plan:

Description of the research activities:

In order to compute an optimal solution

$$\mathbf{p}_{opt}^\delta \in D = \{\mathbf{p} \in \mathbb{R}^5 : \sigma > 0, \lambda \geq 0, \sigma_Y \geq 0\}$$

of the regularized problem in an efficient manner, we search for a saddle point of the non-linear in general non-convex optimization problem

$$L(\mathbf{p}, \alpha) = \|\mathbf{A}(\mathbf{p}) - \mathbf{z}^\delta\|^2 + \sum_{k=1}^l \alpha_k \left(|s_k(\mathbf{p}) - s_k^\delta|^2 - \delta_k^2 \right) \rightarrow \min_{(\mathbf{p}, \alpha) \in D \times \mathbb{R}_+^l}.$$

The numerical computation of such saddle-point can be performed by the iteration

$$\mathbf{p}^{(j)} := \mathbf{p}_{\alpha^{(j)}}^\delta \quad (j = 0, 1, \dots);$$

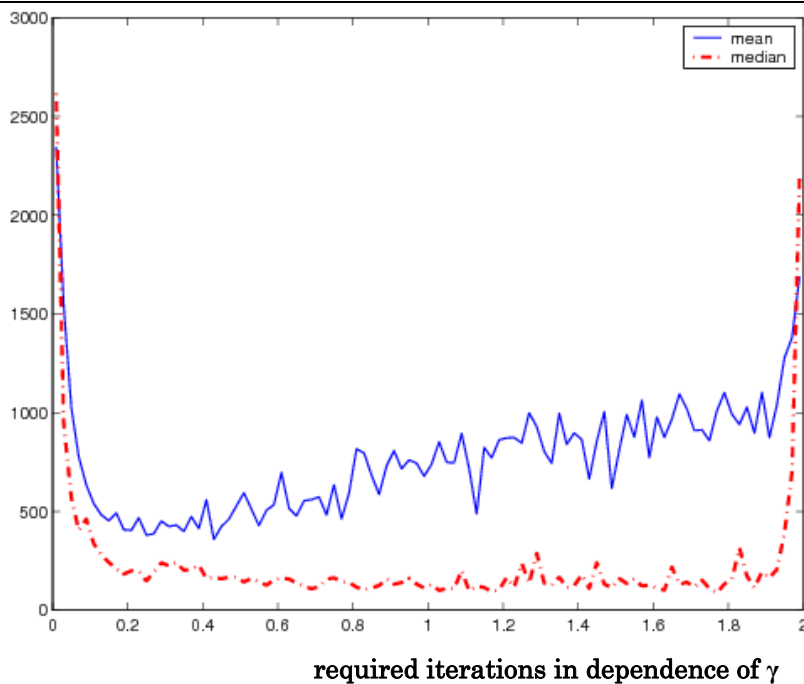
$$\alpha_k^{(j+1)} := \alpha_k^{(j)} \max \left\{ \frac{|s_k(\mathbf{p}^{(j)}) - s_k^\delta|^2}{\delta_k^2}, \varepsilon \right\} \quad (j = 0, 1, \dots; k = 1, \dots, l).$$

The multi-parameter algorithm, however, can be improved by a modification based on exponent variation for an arbitrary positive chosen γ

$$\alpha_k^{(j+1)} = \alpha_k^{(j)} \max \left\{ \frac{|s_k(\mathbf{p}^{(j)}) - s_k^\delta|^\gamma}{\delta_k^\gamma}, \varepsilon \right\} \quad (j = 0, 1, \dots; k = 1, \dots, l).$$

I prepared an extensive numerical case study to analyze the impact of γ and found out that the value γ strongly influences the number of required iterations.

For very small γ the required number of iterations also grows such that an intermediate interval (see figure), for example γ in interval $[0.2, 1.5]$, can be recommended for use in this iteration process to improve the efficiency of the algorithm.



Besides I had the opportunity to study some recent paper of Prof. Hofmann and Prof. Yamamoto to convergences rates for Tikhonov regularization based on some smoothness conditions and approximate source conditions.

8. Please add your comments (if any):

I would like to thank Prof. Yamamoto and his research group for kind hospitality. They provided me an insight into Japanese culture so that time I stayed at the University of Tokyo has been very enjoyable. I am grateful for the fruitful discussions with Prof. Yamamoto about inverse problems in general and particularly about reducing the total amount of computation in the parameter identification problem. Thanks to JSPS for giving me this opportunity.

9. Advisor's remarks (if any): Dr Dana Duevelmeyer has mainly studied mathematical analyses and numerical methods for applied inverse problems, especially the parameter identification in jump diffusion processes which model realistic stochastic behaviour of prices of stocks. Throughout her whole stay, she has kept daily academic contacts with me and other members of my group (2 JSPS postdocs, 6 graduate students at Graduate School of Mathematical Sciences of the University of Tokyo, 4 engaged members for a commissioned research project on inverse heat problems with the Nippon Steel Co.) and we have organized weekly seminars here which have offered occasions for exchanging their recent results and discussing.

Since the main objectives of my group are very matching with her speciality, I am confident that such contacts should be useful for her and us. Moreover she discussed several inverse problems also with my other visitors e.g., Professor Y C Hon from the City University of Hong Kong who studies related stock market problems. By those meetings, I can greatly expect that in the near future we may be able to develop joint projects. I would like to add that she is very interested in Japanese cultures also and I believe that her stay should be very useful for her understanding "Japan" generally.

RESEARCH REPORT

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| 1. Name: Grundmann, Oliver | (ID No.: SP05305) | | | | | | | | | | | | |
| 2. Current affiliation: Research group Dr. Veronika Butterweck, Department of Pharmaceutics, University of Florida, U.S.A | | | | | | | | | | | | | |
| 3. Research fields and specialties: <table style="width: 100%; margin-top: 5px;"> <tr> <td style="width: 33%;">Humanities</td> <td style="width: 33%;">Social Sciences</td> <td style="width: 33%;">Mathematical and Physical Sciences</td> </tr> <tr> <td>Chemistry</td> <td>Engineering Sciences</td> <td>Biological Sciences</td> </tr> <tr> <td>Agricultural Sciences</td> <td style="text-align: center;">X</td> <td>Medical, Dental and Pharmaceutical Sciences</td> </tr> <tr> <td colspan="3">Interdisciplinary and Frontier Sciences</td> </tr> </table> | | Humanities | Social Sciences | Mathematical and Physical Sciences | Chemistry | Engineering Sciences | Biological Sciences | Agricultural Sciences | X | Medical, Dental and Pharmaceutical Sciences | Interdisciplinary and Frontier Sciences | | |
| Humanities | Social Sciences | Mathematical and Physical Sciences | | | | | | | | | | | |
| Chemistry | Engineering Sciences | Biological Sciences | | | | | | | | | | | |
| Agricultural Sciences | X | Medical, Dental and Pharmaceutical Sciences | | | | | | | | | | | |
| Interdisciplinary and Frontier Sciences | | | | | | | | | | | | | |
| 4. Host institution: Department of Nutrition, University of Tokushima | | | | | | | | | | | | | |
| 5. Host researcher: Prof. Junji Terao | | | | | | | | | | | | | |
| 6. Description of your current research <div style="margin-top: 10px;"> <p>1. The first presumption to be verified states an anxiolytic effect of <i>Apocynum venetum</i> (Dogbane Leaf). In order to confirm this hypothesis, an in vivo mouse experiment has been conducted. A well established animal model for assessing drugs with anxiolytic activity is the elevated plus maze (EPM). The outcome of this experiment is currently presented on various international conferences.</p> <p>2. Recent investigations have shown that <i>Apocynum venetum</i> does not induce CYP 3A4 or P-glycoprotein. However, binding and transport of various compounds of <i>Apocynum venetum</i> would be of great interest for further studies. Although the CNS-active compounds of <i>Apocynum venetum</i> are still unknown, flavonoides and apocynines are most likely to show anti-depressant and anxiolytic activities. The absorption from the intestinal epithelium of compounds has a great influence on their pharmacological activity. As a model to study cell interaction and epithelial transport under controlled conditions in vitro, the human colon carcinoma cell line, CACO-2, which shows morphological and biochemical similarity to normal intestinal enterocytes, can be used. Also the influence of <i>Apocynum venetum</i> as a food supplement for the treatment of in vitro cell stress symptoms can be evaluated. This project corresponds with the research interests of Prof. Junji Terao, Department of Food Function, University of Tokushima, Japan.</p> <p>3. Many drugs with an antioxidant activity are supposed to have an anti-cancer effect. <i>Apocynum venetum</i> contains several compounds (e.g. flavonoides, phenol glycosides) that are known to have a protective influence. Several experiments to confirm this hypothesis are planned for 2006.</p> </div> | | | | | | | | | | | | | |

4. A clinical phase I study is planned for 2006. To confirm the results in animals regarding the interaction potential of AV with P-glycoprotein and CYP 3A4, healthy subjects are given midazolam (metabolized over CYP 3A4) and digoxin (uptake over P-glycoprotein), and study the effects of a co-administered AV extract compared to placebo. This is to transfer the animal results on humans. These results will be published shortly after.

5. In addition to these main goals, the search for the active compounds of Dogbane leaf are under investigation in cooperation with the University of Muenster, Germany.

7. Research implementation and results under the program

(As much as possible, describe the contents and results of your research in a manner that is easily understandable to a non-specialist in your field.):

Title of your research plan:

Transport studies of *Apocynum venetum* L. in a CACO-2 model

Description of the research activities:

The first goal was to learn about the techniques involved in cell cultivation. Prof. Murota is an experienced researcher on the field of cell cultures and introduced me to the working conditions with CACO-2 cells and the protocol of the transport studies. At the same time the development of the analytical technique for the quantification of compounds necessitated the compilation of standard curves. The analytical system used was a chromatographic HPLC system with an electrochemical detector. Each transport study had time points at 1, 2, 4, and 6 hours at which the samples were taken and the cells were destroyed to evaluate the concentration of compounds inside the cells. Due to metabolism inside the cell, half of the samples had to be pre-treated with a retrenching enzyme to quantify the metabolic fate of the administered compounds.

The results suggest an influence of yet unknown compounds of the plant extract on the uptake and metabolism of main components of the plant, which contribute to the pharmacological activities. However, the study showed, that structural features may contribute to a different metabolism, such as different sugars linked to the flavonoid main structure. It is known that sugars influence the uptake and metabolism of a compound as the body wants to metabolize substances to more water-soluble metabolites to be excreted by the kidneys. In addition, the absorption and metabolism of proposed active compounds seems to be altered by macromolecular structures such as tannins.

This study also confirmed, that not the actual plant compounds analyzed are the pharmacological active compounds, but mainly metabolites contribute to the activity. Further studies both focusing on influencing factors of uptake and metabolism and pharmacological active compounds will be conducted following this first experiments.

Besides the main focus of my own research, another goal was the implementation of an animal model focusing on antidepressant activities of administered compounds. The TST (tail suspension test) is a widely used screening test to search for antidepressant activity. This mouse model was finally instituted and is now used to screen for antidepressant activity of certain compounds, mixtures, or plant extracts.

8. Please add your comments (if any):

My thanks are directed to Prof. Terao, Prof. Murota, and Dr. Sakakibara, who provided me with all the help and advice I needed and gave me a lot of opportunities to experience Japanese every-day life. I also would like to thank all the students of the department for their help, support, and patience in communicating with me. Thanks to Prof. Butterweck, my supervisor, who was always supportive of the idea to visit Japan. And of course thanks to all the JSPS and DAAD employees who worked hard to make the stay as comfortable as possible for the fellows. Thanks for the great opportunity and invaluable experiences I made during my stay!

9. Advisor's remarks (if any):

Mr. Grundmann studied eagerly. He has a good personality and had a good communication with my staff and students.

RESEARCH REPORT

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| 1. Name: Ms Sara Maria KRANZ | (ID No.: SP05307) |
| 2. Current affiliation: Research Assistant to Prof Dr Jochen Taupitz at the Institute for Medical Law of the Universities of Heidelberg and Mannheim (IMGB); PhD student to Prof Dr Michael Ronellenfitsch at the Faculty of Law of the University of Tuebingen | |
| 3. Research fields and specialties: Social Sciences (Specialities: European Law& European Politics) | |
| 4. Host institution: National Institute of Science and Technology Policy/Ministry of Education and Sciences (NISTEP/MEXT), 2 nd policy-oriented group 2-5-1 Marunouchi, 100-0005 Tokyo | |
| 5. Host researcher: Yasushi Makiyama, MD | |
| 6. Description of your current research | |
| <p><i>“Biomedicine in European Law. Competences of the European Legislator”</i> is my current research focus and is at the same time the theme of my doctoral thesis. Legislation for biomedical research and issues as well as the political and ethical questions in biomedicine, biotechnology and genetic engineering in Europe and abroad come along with the controversial questions of the competences of the European Legislator in this field. The global dimension of biomedicine and the broad national, European and international debates indicate a badly needed analysis of the possibilities for setting up common rules on a European level, which would be legally binding for all member states. The importance of regulating biomedical issues also on the <i>international level</i> become apparent considering the latest developments in therapeutic cloning research: Recently, at August 3, 2005 researchers at the Seoul National University have reported about their success in cloning the first dog, which could become a useful animal research tool for research into human health. In May 2005, the same researchers have created nearly a dozen new lines of human ES cells by SCNT method, which is a tenfold increase of success rate in cloning human cells in nearly one year.</p> <p>Beside the necessity of balancing biomedical technology with the controversial aspects of human dignity, the right to life and the freedom of research, it is also increasingly important to scrutinize the economic values and the legal questions of the “commercialization of the human being”, and to develop common European provisions for a strong biomedical and pharmaceutical market system compared to the Asian and the US market. The EC-Treaty and the Draft Contract of the European Constitution provide several rules for the European Legislator in order to regulate biomedical issues, e.g. the Common Internal Market (Art.95 EC-Treaty), Public Health Policy (Art.152 EC-Treaty), the rules for Science and Technology Policy (Art.163ff. EC-Treaty) as well as the provisions of the Charter of Fundamental Rights of the Union, Part II of the EU Draft Constitution (particularly Art.II-63). The Convention on Biomedicine of the Council of Europe and different international Conventions will also play a leading role on the Union’s level, even if these Conventions are legally not binding. One of the main open questions, which need to be clarified in this context is, whether a (cloned) embryo, germ cells, ES-cells, human tissues and organs are “goods” according to Art.23 EC-Treaty.</p> | |

7. Research implementation and results under the program

Japan has taken a leading position in biomedical sciences and spearheads the questions of legislation in biomedicine and the controversial ethical and societal discussions among all Asian countries. Thus, analyzing Japanese biomedical law is especially suited for legal comparison with European biomedical law.

I. Legal subjects and main legal aspects for the analysis of Japanese biomedical law

The “anchor” for the analysis has been the

- Japanese Constitution, especially Art.13 (keiji no songen)
- Human Cloning Act (HCA)
- “Guidelines for Handling of a Specified Embryo” as well as the “Guidelines for Derivation and Utilization of Human Embryonic Stem Cells”
- other related Acts and Guidelines within this context, e.g. the Eugenic Protection Law, the Maternal Protection Law, the abortion rules within the Criminal Act (Art.212ff.), the law of torts and damages (Art. 721, 886 Civil Law Act), the Organ Transplantation Act, the guidelines of the medical doctors associations and of the JFSG (Japanese Society for Obstetrics and Gynaecology)
- some important reports from the MEXT, the MHLW and the Council for S&T, especially the report of the Committee on Bioethics of the Council for S&T from July 2004 about the legal handling of therapeutic cloning and the production of fertilized eggs for fertility treatment research in two new Guidelines.

The main legal questions, which have been analyzed:

- 1.) the legal term “**human dignity**” and its legal definition in Japan in comparison to Art.13 of the Constitution (“the respect for the individual” – *keiji no songen*) and to the westernized definition of “human dignity”/“*Menschenwuerde*”
- 2.) the “**status of the embryo**” and the “**beginning of life**”: is the embryo a “human being” in Japan and protected by “human dignity”? When does life begin?
- 3.) the rights of the individual within the concept of “**common welfare**” (Art.11, 13 JC)
- 4.) the system of setting “**Administrative Guidelines**” instead of “Acts”
- 5.) the **historical, religious and ethical background** (“Kant versus Buddha”; Monotheism versus plurality of philosophies, religions and ethics)

II. Results

Ad 1., 5.) As the term “human dignity” is an *imported* term from the West and doesn’t exist in Japanese Constitution and Law, a widespread **ignorance, nescience and lack of knowledge what human life and human dignity constitutes in the context of biomedicine** has to be noticed. Thus, there doesn’t exist any positive or negative definition of the “human embryo” and its legal and constitutional protection, of the “beginning of life” or of the limits for academic freedom, neither in the legal, nor in the ethical field. **Art.13** (“*keiji no songen*”- principle) is not applicable in this context, since this principle has to be considered in a more narrow sense and is therefore rather related to the “social rights for human beings”, i.e. the guarantee of a happy life, the right to work, the right of personal autonomy, the right to property et al. Some Jurists (Prof Ida et al.) and the Council for S&T - influenced by western thinking - have made some attempts to create a concept of “human dignity” in a **general manner** as well as for **case-by-case** use. According to this, human dignity has to be considered as a more comprehensive and abstract legal term, which embraces the “respect for human life” and the “value of human

life” in a general manner; all human beings have their own identity and should be respected and be treated equally because of their “*dignity*” - which is quit close to the principle of the “protection of human rights”. In the case of **reproductive cloning**, this group has defined **4 elements**, which compose “human dignity” only in the case of reproductive cloning: The instrumentalization of the human being, the presetting of genetic particularity, the violation of the individuality and the confusion of the societal and family order. These elements have finally launched the total ban on reproductive cloning within the HCA (“*Transfer-Prohibition of cloned embryos*”), which bans all kinds of human reproductive cloning, and also special types of hybrids and chimeras (**Art.3 of the HCA**). Case-by-case definitions seems to become widely accepted among the Jurists and the government and could be a convenient solution to overcome the ignorance of the internationally acknowledged term “human dignity”. This handling is absolutely different from most of the Western Law and Biolaw: The Constitutional systems in most of the European countries, especially in Germany, are bound on the philosophy of the “**humanism**”, the **philosophy of Kant** and the **Catholicism Dogma** and determine the beginning of human life and the absolute protection of human beings with the *union of sperm and egg* (=embryo). Beside international Declarations, like the Universal Declaration of Human Rights (Art. 1:“all human beings are born free and equal in dignity and rights”), the “Objektformel” of Kant - “a human being is a purpose of itself and may not be degraded to a mere object” – has become the main objective of the German Constitution: “The human dignity is indefeasible” (Art.1). In Japan however, the “**holistic approach**” and the **plurality of religions and ethics** has generated the fact, that “nobody understands the principle of human dignity as that human beings should be granted dignity because of the differing status of human beings and animals in the system of existence”, Prof Shimazono stresses.

Ad 2.) Referring to the Council of S&T, Prof Ida et al. the embryo is not a human being yet and not a thing neither, but a “***germ of human life***”, i.e. the early beginning of human life; This position is located between the concept in most of the western countries and the extreme positions of Peter Singer and others, who define the embryo as a mere cell cluster or lump.

In spite of this definition one has to underline, that neither the ***beginning*** of life (embryo and fetus), nor the ***end*** of life (“brain death” versus “heart death”) is clearly defined in Japanese Law, since these items appears to be often ignored within the public and the government. The discussions have been started much later than in the West, don’t proceed effectively or are confused; the discussions on Organ Transplants or on genetically modified organisms (GMO) at present are prominent examples. Nevertheless, the “germ”-definition has generated the legal principle, that the ***beginning of life, i.e. the embryo, should not be created for other purposes than for reproduction*** (=“ART”-embryo); this principle is widely accepted within the research community, the public and among most of the Jurists.

However, this principle is opposed to the technology of **therapeutic cloning** and **production of human fertilized eggs** for clinical and research practices, since an embryo needs to be destroyed for that techniques. From a legal point of view, the solution for the ongoing discussions concerning the permit of therapeutic cloning for basic research and the production of fertilized eggs for clinical use in new Guidelines (based on Art.4 of the HCA) might be the determination of this principle with **two exceptions**: First, for supernumerous frozen embryos, which are left from artificial fertility treatment (=ART-embryos) - with the consent of the parents (sic!) –, and second, for therapeutic cloning (=“SCNT”-embryo), since this technology is an artificial process without any fertilization of human egg and with the purpose of healing sick people and research of latent diseases, like Alzheimer, Parkinson and Diabetes. Whether the “***utago-no***”-case, in which the Supreme Court has been laid down stricter legal conditions for “personal

rights”, could be used in similar cases, in which the personal rights of the patient or donor have been injured, needs to be investigated case-by-case.

Ad 3) The individual interest is legally considered as part of the common interest, since the individual is part of the community and needs therefore be protected by governmental power. Nevertheless, one has to notice, that “life style” has been changed since 40 years and has generated a process of increase of individual value and a kind of “individualism” with great influences on the whole social system in Japan. Hence, the concepts of “common welfare” and “individual value” tend *in practice* towards the Western concept of “individualism”.

Ad 4) Setting Guidelines and not Acts in order “to regulate” biomedical research (at present: Guidelines for “Derivation and Utilization of human ES cells, for “The Handling of “Specified Embryos”; soon also for “Therapeutic cloning”, and “Production of Fertilized Eggs for Fertility Treatment Research”) is *absolutely* contrary to the legal handling in Western countries in these kinds of sensitive and controversial issues. Nevertheless, in Japan, Administrative Guidelines are a common and ordinary type of regulation, since they are an effective, flexible and speedy tool with lower resources costs for the handling of the rapid developments in biotech and biomed. In addition, neither the government nor the scientists are interested in a highly regulated S&T sector, since they want to provide S&T research as much as legally and ethically possible. Most of the Guidelines in general can therefore be defined as a result of a “political negotiation process” between both parties and the public. In addition, neither the silent majority (=the public), nor the vocal minority (=researchers) appears to trust in the parliament and the parliamentarians’ knowledge in these highly complicated legal and ethical issues. However, regulating biomedical issues *exclusively* in Administrative Guidelines is intransparent, opposed to the Constitution and should therefore be reconsidered.

Title of your research plan:

“What’s up with Japanese biomedical law”?

Description of the research activities:

Use of Literature:

- toshokan, Waseda University and NISTEP/Dr. Makiyama
- toshokan, Todai

Interviews with:

- Prof Ryuichi IDA, Law School, Kyoto University
- Prof Michiko ISHII, Law School, Meiji-University, Tokyo
- Prof Shiro ISHII, Professor for Legal History, former Vice President of Todai and of the
- Prof Saku MACHINO, Law School, Sophia-University, Tokyo
- Prof Susumo SHIMAZONO, Faculty of Letters, Todai
- Prof Fumio TOKOTANI, OSIPP, and Prof Motomu Shimoda, Graduate School of Medicine, Osaka University
- Prof Michitaro URAKAWA, Prof Waishiro IWASHI, Prof Katsunori KAI, Law School, Waseda University
- Prof Mikihiro WADA, Law School, Hosei University, Tokyo
- Prof Yutaka HISHIYAMA, Nihon Gakujutu Kaigi, Former Director for the Bioethics and Biosafety Office, MEXT

- Prof Norio NAKATSUJI, Director and Professor, Institute for Frontier Medical Science, Kyoto University
- Dr Shinichi NISHIKAWA, Group Director, CDB, RIKEN-Center, Kobe/Port Island
- Dr Nikolaus MUELLER, Director Managing, Nihon Schering K.K., Osaka
- Ms. Yoko URYUHARA, Product Manager, Transplantation & Immunology Business Unit, Novartis Pharma K.K., Tokyo

Trips to:

- CDB, RIKEN-Center, Kobe/Port Island
- Kyoto University
- Nihon Schering K.K, Osaka
- University of Osaka

8. Please add your comments (if any): The time in Tokyo was fantastic and eventful and I gained lots of experiences: both in my research field and in the culture and daily life in Japan. I will miss this time and it was not the last time to come to Japan, that's for sure! Nevertheless, the partly noticed ignorance and the informal and intransparent handling of issues also in daily and "ordinary" matters, is sometimes quit difficult to follow and to accept as a person, who is affected by European culture.

RESEARCH REPORT

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|---|-------------------|
| 1. Name: Claudia E. Lehmann | (ID No.: SP05308) |
| 2. Current affiliation: University Medical Center Hamburg-Eppendorf, Department of Medical Psychology | |
| 3. Research fields and specialties: <div style="display: flex; flex-wrap: wrap; padding: 5px;"> <div style="width: 33%;">Humanities</div> <div style="width: 33%;">Social Sciences</div> <div style="width: 33%;">Mathematical and Physical Sciences</div> <div style="width: 33%;">Chemistry</div> <div style="width: 33%;">Engineering Sciences</div> <div style="width: 33%;">Biological Sciences</div> <div style="width: 33%;">Agricultural Sciences</div> <div style="width: 33%;">Medical, Dental and Pharmaceutical Sciences</div> <div style="width: 33%;">X Interdisciplinary and Frontier Sciences</div> </div> | |
| 4. Host institution: National Cancer Center, Research Institute East, Psycho-Oncology Division | |
| 5. Host researcher: Yosuke Uchitomi, MD, PhD | |
| 6. Description of your current research <p>In Germany I work as a scientific researcher in the fields of psycho-oncology and medical rehabilitation. Psycho-Oncology deals with psychological and social factors in the development and course of cancer. Its knowledge is used systematically in prevention, treatment and rehabilitation of cancer. Medical rehabilitation is an important part in the treatment of chronic diseases such as cancer. Its main subject is not the disease itself but the consequences of it (e.g. functioning disabilities). Currently I am involved in a multi-center study focusing on the evaluation of out-patient and in-patient cancer rehabilitation. Besides, I am writing my dissertation on the need for rehabilitation and psychosocial care of cancer patients with a focus on patients` characteristics (e. g. psychiatric co-morbidity, daily hassles, coping with the illness).</p> <p>Furthermore, our research group is currently planning an international study, focusing on the epidemiology of psychiatric disorders, the need for psychosocial treatment and the barriers of health care utilization in cancer patients. It is planned to include European, Asian and American countries and to start the project in Japan and Germany involving more countries after design and methods have been decided.</p> | |
| 7. Research implementation and results under the program (As much as possible, describe the contents and results of your research in a manner that is easily understandable to a non-specialist in your field.): <p>Title of your research plan:</p> <p>The association between psychiatric co-morbidity and cultural characteristics in patients with cancer</p> <p>Description of the research activities:</p> <p>Starting the cross-cultural comparison study in Japan and Germany was the main aim of my stay in Japan. According to this my research activities at the Psycho-Oncology Division, National Cancer Center Research Institute East (NCCRIE), focused on the concrete definition of the Japanese-German study protocol (core questions, sample characteristics and study design). At first the research topics were defined. For the association between psychiatric co-morbidity and cultural characteristics in cancer patients is a very broad and unspecified subject area we decided to focus on communication, particularly patients` communication preferences regarding the physicians` breaking bad news. "Bad news" can be defined as any information that negatively changes a person`s view of his/her</p> | |

future¹. With regard to cancer bad news usually contain information about recurrence, failure of treatment or palliative prognosis. It was shown that the physician's style of communicating bad news has an effect on patients' distress, adjustment and his/her level of anxiety and depression². Hence, during recent years studies on patients' preferences regarding physician's disclosure of bad news^{3,4} have been conducted and guidelines as well as communication trainings for physicians have been developed^{5,6}. Despite of these efforts there is to be mentioned that (1) most of the research studies include Anglo- American and Australian samples. Accordingly it remains unclear to which extent the results found in those studies can be transferred to patients or physicians from other cultures such as Asian or European cultures. (2) Most of the guidelines base rather on experts' opinions than on patients' preferences. Besides, although there are hints that people from Western and Eastern countries differ regarding attitudes and behaviour there are few studies focusing on cultural differences in the medical context⁷.

At the Psycho-Oncology Division, NCCRIE, a preliminary study focusing on this topic has been conducted⁸ followed by the development of a 70-item questionnaire measuring patients' preference for physicians' communication style. In a further research study⁹ this questionnaire had been validated and analyses were conducted regarding preferences and the related factors (e.g. anxiety, depression, socio-demographic data). Over 500 cancer patients were investigated and by comparing the results with an American study¹⁰ differences in preferences of patients with different cultural backgrounds are revealed. Hence, communication preferences are of international interest and we will focus on this topic in our cross-cultural project. Generously I got the permission to use the Japanese data (n>500) for our study so it was decided to use the same instruments (measuring e.g. anxiety, depression, social support). Except two questionnaires assessment instruments are internationally known questionnaires. So the next important task of my work was the translation and back-translation of these two instruments. After that I worked on the defining of concrete hypotheses. It can be suggested that Japanese and German cancer patients differ in communication preferences regarding the physician's use of euphemisms and the term "cancer", discussing life expectancy and physician's consideration of family members.

Overall, the main objectives of my research stay in Japan were achieved: The study protocol is completed, core questions are defined and the data assessment in Germany can start after my return.

In addition to these research activities during my stay at the Psycho-Oncology Division I participated in all scientific activities and so I learnt very much of Japanese psycho-oncological research. This also included the participation in the Joint Congress of the Japanese Society of Palliative Care and the Japanese Society of Psycho-Oncology as well as the opportunity to stay at the University of Hiroshima, at a hospital in Okayama and at the Chiba Cancer Center. In all of these institutions I had the chance to experience research and clinical work and to broaden my knowledge about Japanese palliative care and cancer rehabilitation.

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literature. *Annals of Oncology* 16: 1005-1053; 2005.

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8. Fujimori M, Akechi T, Akizuki N et al.: Good communication with patients receiving bad news about cancer in Japan. *Psycho-Oncology* (in press); 2004.

9. Fujimori M, Akechi T, Morita T et al.: Preferences of cancer patients in Japan regarding the disclosure of bad news. (in prep.); 2005.

10. Parker P, Baile WF, de Moor L et al.: Breaking bad news about cancer: Patients preferences for communication. *Journal of Clinical Oncology* 19: 2049-2056; 2001.

8. Please add your comments (if any):

I would like to thank Dr Uchitomi for being my host supervisor during my stay in Japan, for his valuable support and for providing many new learning experiences. I would like to thank all of his co-workers in the Psycho-Oncology Division, National Cancer Center Research Institute East (especially Dr Fujimori, Dr Inagaki, Dr Akizuki and Miss Katayama), for their assistance with research activities as well as with daily life. I would also like to thank Dr Kato and his staff of the Kato-Naika Hospital, Okayama, and Prof Yamawaki and Prof Okamura and their co-workers of the University of Hiroshima, for giving me the opportunity to visit their institutions and for their kind support.

9. Advisor's remarks (if any):

I would like to thank this Program director for having an opportunity to have an excellent researcher to be a potential leader in the field of Psycho-Oncology. I had a very good time to exchange recent findings and to discuss on many research plans with an enthusiastic, cooperative, but modest researcher.

RESEARCH REPORT

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|---|---|---|-------------------------------------|--|---|------------------------------------|--|--|--|--|--|---|--|--|
| 1. Name: | Philipp Michel | (ID No.: SP05309) | | | | | | | | | | | | |
| 2. Current affiliation: | The Robotics Institute, Carnegie Mellon University 5000 Forbes Ave, Pittsburgh, PA 15213, USA | | | | | | | | | | | | | |
| 3. Research fields and specialties: | <table><tr><td><input type="checkbox"/> Humanities</td><td><input type="checkbox"/> Social Sciences</td><td><input type="checkbox"/> Mathematical and Physical Sciences</td></tr><tr><td><input type="checkbox"/> Chemistry</td><td><input checked="" type="checkbox"/> Engineering Sciences</td><td><input type="checkbox"/> Biological Sciences</td></tr><tr><td><input type="checkbox"/> Agricultural Sciences</td><td colspan="2"><input type="checkbox"/> Medical, Dental and Pharmaceutical Sciences</td></tr><tr><td colspan="3"><input checked="" type="checkbox"/> Interdisciplinary and Frontier Sciences</td></tr></table> | | <input type="checkbox"/> Humanities | <input type="checkbox"/> Social Sciences | <input type="checkbox"/> Mathematical and Physical Sciences | <input type="checkbox"/> Chemistry | <input checked="" type="checkbox"/> Engineering Sciences | <input type="checkbox"/> Biological Sciences | <input type="checkbox"/> Agricultural Sciences | <input type="checkbox"/> Medical, Dental and Pharmaceutical Sciences | | <input checked="" type="checkbox"/> Interdisciplinary and Frontier Sciences | | |
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| <input checked="" type="checkbox"/> Interdisciplinary and Frontier Sciences | | | | | | | | | | | | | | |
| 4. Host institution: | Digital Human Research Center National Institute of Advanced Industrial Science and Technology (AIST) | | | | | | | | | | | | | |
| 5. Host researcher: | Dr. Satoshi Kagami | | | | | | | | | | | | | |
| 6. Description of your current research | <p>I work with humanoid robots, focusing on the intersection of computer vision and motion planning. My aim is to equip humanoids with some of the perception skills needed to autonomously navigate, manipulate and interact in everyday human environments. This includes biped walking, obstacle avoidance, object localization & grasping, tracking and interacting with people, etc.</p> <p>At Carnegie Mellon, we have recently been working with a Honda ASIMO humanoid robot, using vision techniques to locate and track objects moving dynamically in the robot's vicinity during a walking sequence. By integrating such sensory information with a planner operating at the level of footsteps and capable of efficient dynamic re-planning, we have enabled ASIMO to autonomously traverse obstacle filled, unpredictably changing environments, explicitly making use of the robot's biped walking abilities to step over obstacles.</p> <p>The goal for my summer stay at the AIST Digital Human Research Center was to investigate perception algorithms for the HRP-2 humanoid platform and expand my previous research to work for more general robot navigation scenarios.</p> | | | | | | | | | | | | | |

7. Research implementation and results under the program

(As much as possible, describe the contents and results of your research in a manner that is easily understandable to a non-specialist in your field.):

Title of your research plan:

Perception and Environment Reconstruction on the HRP-2 Humanoid Robot

Description of the research activities:

At the Digital Human Research Center, I have been working with Dr. Satoshi Kagami and Dr. Koichi Nishiwaki to perform real-time, on-body environment reconstruction for the HRP-2 humanoid using both 2D and 3D sensor data. The goal is to efficiently generate representations of the humanoid's surroundings which can subsequently be used to find obstacle-free walking paths, to decide whether a certain area is safe to step onto, to localize objects of interest for grasping and manipulation, etc.

For the 2D case, I used a calibrated camera mounted on the robot's head together with a motion capture system to generate a global map of the floor area as if viewed from a fixed virtual camera looking straight down onto the environment. Knowing both intrinsic and extrinsic camera parameters (from calibration and localization using motion capture, respectively) allows the full camera projection matrix to be recovered, essentially yielding all knowledge about how scene points are projected onto the camera image. Given the assumption that obstacles on the floor are planar, this allows a direct mapping between image coordinates and ground plane coordinates, called a *homography*, to be established. Using the homography, incoming camera images can be warped onto the ground plane and integrated over time to yield a constantly updating map of the floor area and associated obstacles in the environment. The camera essentially acts like a "flashlight", shining out certain areas of the floor as HRP-2 walks or looks around, and updating the corresponding parts of the environment map.

I also employed the recently developed CSEM SwissRanger sensor to perform three-dimensional environment reconstruction. The sensor provides distance measurements for each one of its 124x160 pixels by measuring the time-of-flight of infrared light emitted by an array of LEDs. Being in the early stages of development, the sensor ships in an uncalibrated state, and does not yield reliable distance measurements. After calibrating the sensor to correct for lens distortion and measurement inaccuracy, I again employed motion capture to yield the precise location and orientation of the sensor in the environment. This information together with the sensor measurements allows the full 3D position in world coordinates of each scene point in the field of view of the sensor to be reconstructed. Mounting the SwissRanger on HRP-2's hand allows the robot to scan its environment, thus enabling 3D environment maps to be generated in real-time. These can subsequently be used

for obstacle avoidance, object localization or to detect the height of elevated floor areas, such as stairs, for the robot to step onto.

Together with my host researchers and two other JSPS summer fellows, we integrated our research on perception, planning and action on the HRP-2 platform, enabling it to navigate autonomously among obstacles and actively manipulate its environment.

A more complete overview of my research in form of a poster can be found here:

<http://www.cs.cmu.edu/~pmichel/publications/Michel-DHRCResearch2005.pdf>

8. Please add your comments (if any):

I had an amazing time during my stay in Tokyo and at AIST. I was given the unique opportunity to work with some of the most advanced humanoid robots in the world. Moreover, I felt like an integral part of an incredible community of researchers whose guidance and friendship were truly invaluable. My hosts and the students in the lab created a supportive and fun work environment. I hope to continue the productive scientific collaboration started this summer and return to the lab in the future.

Outside of work, I was able to explore Tokyo with Japanese friends, visit fellow JSPS students around Japan and go on a trip with my entire lab. I continue to be fascinated by Japan and its culture, language and people and am now highly motivated to continue studying Japanese when I return to the US.

I wholeheartedly recommend the JSPS Summer Program to anyone wanting to pursue cutting edge research and at the same time immerse themselves in an incredible culture.