RESEARCH REPORT

Name: Marcus D. Phillips Affiliation (University): University of Bath	
Research Advisor: Yuji Kubo Host Institution: Saitama University	
Research Subject: Fluorescent Sensors	

1. Research Description:

The ability to detect biologically important molecules is of great interest. Synthetic sensors with the capacity to selectively detect chosen molecules and signal this presence by altering their optical signature have attracted considerable attention in recent years.

Three years ago Professor Kubo's research group reported a naphthalene-isothiouronium dyad with selectivity for the acetate anion. In this research project a boronic acid was introduced into a similar system and its selectivity examined.

It was considered that the extended receptor, with two binding sites, might provide not only considerably enhanced stability by adopting an allosteric binding motif but also more discrimination in its selectivity towards particular guest species.

2. Research Activities:

The experiments conducted were designed to determine the pK_a of the sensor, its selectivity towards potential guest species and so allow us to determine the operational parameters of the system. The sensor had been synthesized so as to permit photoinduced electron transfer (PET) to operate. The use of PET was to permit a fluorescent "Off-On" response providing information about binding events with host species.

For the structure examined the results indicated that inductive effects from the boronic acid altered the energy of the proximal isothiouronium significantly and so disrupted the PET mechanism.

3. Perspective of Research after this Program:

In collaboration with Atsushi Kobayashi a significant understanding of the designed sensor was achieved during the joint research project. Research is now focused on determining the effect of varying the spacer group between the two receptors. By increasing the separation of the two groups efficient PET activity should be observed.

4. Advisor's Remarks:

In developing chemosensor materials, effective signaling of phosphorylated saccharides in an aqueous solution remains to be a challenging target because the guest species are not only solvated strongly, but surrounding water is also competitive for intermolecular interactions between host and guest species. To overcome the phenomena, we have employed isothiouronium-boronic acid conjugated molecules in this study where the host molecule may binds phosphate/saccharide with positive cooperativity. Although Phillips has progressively challenged to tailor the molecule as a desired chemosensor material under several conditions, the positive results have not been obtained so far. However, much insight of the estimation, being based on his effort, during the JSPS summer program has become feasible for chemosensor design toward this end.

RESEARCH REPORT

Name:	Affiliation (University):
Claire Price	**University of Sheffield, UK**
Research Advisor:	**Host Institution:**
Prof. K. Taira	**A.I.S.T., Tsukuba**
Research Subject:	
Chemical Biology – Catalytic efficiency of modified ribozymes	

1. Research Description:

My PhD is concerned with the synthesis of a polyamine-uridine conjugate, with the intention of incorporating such modified RNA monomers into specific locations within a chemically synthesised RNA molecule, the Hairpin ribozyme.
The hairpin ribozyme is a small, naturally occurring RNA structure, which can self catalyse the cleavage of a phosphodiester bond within its length.
Polyamines are known to stabilize nucleic acid structures and reduce or eliminate the requirement for metal ion co-factors (eg. Mg^{2+}). This is of particular importance for the possible therapeutic uses of the hairpin ribozyme, where physiological levels of Mg^{2+} would be below that required for efficient catalysis. Once the modified polyamine-RNA conjugates are produced, the catalytic efficiency of the cleavage reaction, and the co-factor requirements of the ribozyme can be investigated.

2. Research Activities:

During my time in Japan, I worked on a related small ribozyme, the Hammerhead ribozyme. I was able to learn a variety of molecular biological and biochemical techniques. I was taught how to perform and analyse ribozyme kinetics experiments, using several mutated ribozymes, in order to assess the catalytic efficiency of the mutants. I became familiar with purification procedures such as polyacrylamide gel and agarose gel electrophoresis.
Along with the above practices, I was also introduced to RT/PCR amplification and transcription in the SELEX process in order to amplify and isolate the optimally active ribozyme.

3. Perspective of Research after this Program:

The research I carried out in Prof. Taira's laboratory was quite new to me, coming as I did from a synthetic background, however I found it very interesting and challenging. I have learnt many new skills, which will be of great help to me throughout the remainder of my PhD, and in future studies. I have very much enjoyed my time in Japan, and the experience of working in a different research area. I am grateful to the lab members for their help and advice during my stay.

4. Advisor's Remarks:

Claire has achieved a lot in the short time she has been in Japan. Although she had little experience of molecular biology when she arrived, Claire quickly became skilled in new biochemical methods and techniques, which she will find of benefit to her PhD work.
Claire worked well with other members of the group, and enjoyed her stay in Japan, as well as her research.

RESEARCH REPORT

Name: Ruth Goodridge
Affiliation (University): The University of Leeds, U.K.

Research Advisor: Professor Chikara Ohtsuki
Host Institution: Nara Institute of Science and Technology (NAIST)

Research Subject: Estimation of the bioactivity of a glass-ceramic fabricated via a selective laser sintering process.

Research Description:

Research is being carried out at the University of Leeds, UK to assess the feasibility of using the layer manufacturing technique, Selective laser sintering (SLS), to produce bioactive glass-ceramic implants for use in bone replacement applications. SLS is an attractive process for this application as it offers the potential to manufacture custom-made implants. For the past 3 years, the ability to process a calcium phosphate glass-ceramic material using SLS and the optimisation of the mechanical properties of the produced part has been the main area of research. However now that the successful production of these parts by SLS has been demonstrated, the biocompatibility and bioactivity of the samples needed to be assessed. Japan is leading research into the assessment of synthetic materials ability to directly bond to bone, and therefore it was desirable to seek the expertise of the biomaterials laboratory at NAIST to carry out these experiments.

Research Activities:

Both *in vitro* and *in vivo* studies were performed during my stay at NAIST. The bioactivity of laser sintered and conventionally cast samples were assessed by soaking the samples for various time periods in a simulated body fluid (SBF), with an ion composition similar to human blood plasma. After each immersion period, the surfaces of the samples were characterised by thin film XRD and SEM/EDX in order to detect any apatite formation. Changes in element concentrations of SBF due to exposure of the specimens were determined by ICP emission spectroscopy. These were compared to Bioglass®, a known bioactive material, and a commercial non-bioactive glass. An *in vivo* experiment, involving implantation of the material into rabbit tibia, was also performed.

Perspective of Research after this Program:

The results from this work indicated that the currently used material has lower affinity to bone tissue than originally thought, and hence highlighted the need to rethink the material presently used with the selective laser sintering process. These findings have provided important information that will be included in my PhD thesis and will influence the future direction of work in Leeds. A collaboration between Leeds University and NAIST is being pursued, to bring together the expertise of the two departments. Thanks to the helpfulness and patience of the staff and students at NAIST, I have learnt several new techniques that will be very useful for future work. In addition to scientific research, the programme has given me an insight into the Japanese way of life both in and out of the laboratory, and has provided me with many new contacts and friends.

Advisor's Remarks:

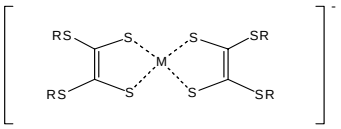
Ms. Ruth D. Goodridge worked very hard on her research project about evaluation of biocompatibility of the glass-ceramics in the system SiO_2-Al_2O_3-P_2O_5-CaO-CaF_2, during her stay on JSPS programme. She carried out many experiments including implantation of her materials in rabbit tibia as well as examination of surface structure of the materials under a physiological condition. In her experiment she also learnt to operate the facilities such as a scanning electron microscopy, inductively coupled plasma emission spectroscopy, and so on. All the works on the research by her were excellent, and she helped my students, too. These experience and data obtained in my laboratory may help her to complete her Ph. D. thesis, and support her research career.

RESEARCH REPORT

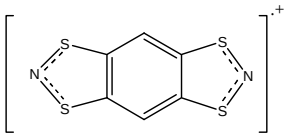
Name:	**Affiliation (University):**
Sarah S. Staniland	The university of Edinburgh (UK)
Research Advisor:	**Host Institution:**
Prof. Kunio Awaga	Nagoya University, (Advanced Materials)
Research Subject:	
Sulphur based salts for new magnetic materials	

1. Research Description:

Metal dithiolene complexes have been studied extensively for there ability to make new conducting and magnetic materials. More recently, new, paramagnetic, organic molecules have been synthesized using heteroatoms (such as S & N) and conjugated systems to give them interesting magnetic characteristics. The dithiolene anion and organic cation (radical) can be co-crystallised to form a new magnetic salt, and there magnetic properties studied.



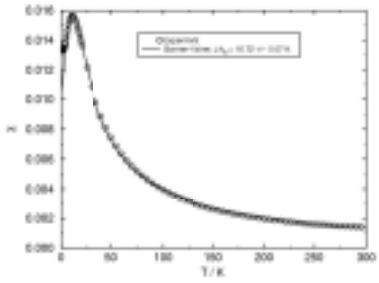
A metal dithiolene



An organic, paramagnetic, radical cation (BBDTA)

2. Research Activities:

My group in Edinburgh specializes in the synthesis and study of the dithiolene complexes. Prof. Awaga and his lab have synthesized many new organic radical cations. Previous collaborations have meant that I had already received one of the cations from Prof. Awaga and worked on it in Edinburgh. Here in Nagoya I got the chance to co-crystallize new cations with some dithiolenes that I brought out with me, as well as trying new methods to crystallize complexes. I achieved this for the salts $[Cu(mnt)_2]BDTA_2$ and used the x-ray crystallographic equipment to determine the crystal structure. I also obtained crystals of $[Ni(dmit)_2]BDTA$ & $[Ni(dmit)_2]BBDTA$ and am awaiting crystal data. I used the SQUID to measure the magnetic properties and the EPR to look at specific locations of the unpaired electrons, at various temperatures. I then mathematically modeled the magnetism from the data and found the copper complex to be a near perfect 1D magnetic chain. Other crystallizations are underway involving cations such as TTTA.



Magnetic susceptibility of $[Cu(mnt)_2]BDTA_2$

3. Perspective of Research after this Program:

This program has definitely given my PhD a real boost with the production of crystals and crystal structures. I have found everyone in the lab very helpful and eager to explain and demonstrate equipment and techniques, and what was especially appreciated was the effort to speak English to me. Everyone in the group also made me feel very welcome in the university as we always went to lunch together, as well as outside the university, when they would take me into Nagoya for festivals and outings. I thoroughly enjoyed working in a chemistry lab in Japan and found it very productive, in the sense of personal work achieved and collaborative discussions.

4. Advisor's Remarks:

Ms. Sarah Staniland has obtained fruitful results during her stay in my lab, after her earnest research. She succeeded in the crystal growths of new compounds composed of her ditiolene-complex anions and our thiazyl-radical cations, by testing various conditions for crystallization. The obtained structures and the magnetic properties are so interesting that they would attract much interest of the chemists in the field of molecule-based electric and magnetic materials. I hope that her achievement here will be a good boost for her PhD work. Besides the chemistry, I appreciate her international friendship: her friendly attitudes made everyone here more positive and more international.

RESEARCH REPORT

Name:	Affiliation (University):
Jennifer Gibson	**University of Bristol, UK**
Research Advisor:	**Host Institution:**
Prof Koichi Narasaka	**University of Tokyo**
Research Subject:	
Electrophillic Amination of Arenes using Oxime Derivatives	

1. Research Description:

Recently the Narasaka group published the use of oxime derivatives as electrophillic aminating reagents. This involves the unusual S_N2 type attack of nucleophiles onto the sp^2 nitrogen of oxime derivatives **1** to form the imine **2** and subsequent hydrolysis to give the amine **3** (Figure 1.1).[1]

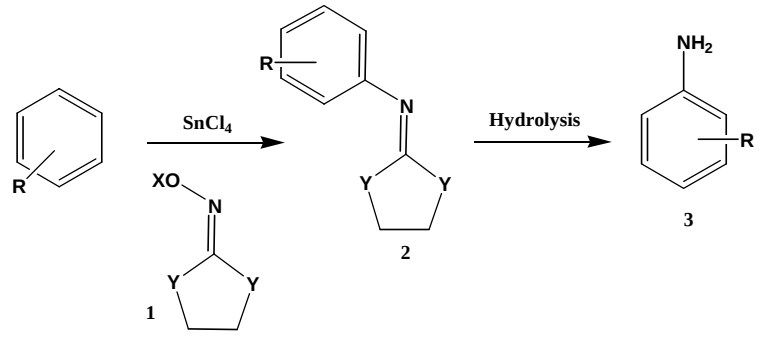
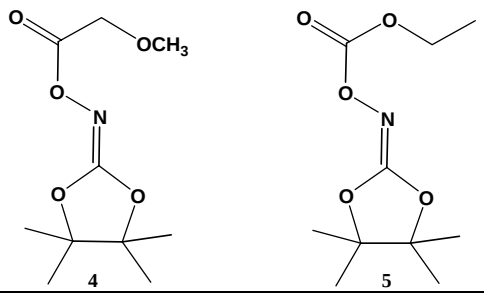


Figure 1.1: Electrophillic amination using oxime derivatives.[1]

1. Baldovini, N., Kitamura, M., Narasaka, K.; *Chem. Lett.,* 2003, **32**, (6), 548-549.

2. Research Activities:

My research activities involved the preparation and screening of the carbonate derivatives **4** and **5** as electrophillic aminating reagents. Under a variety of conditions the oxime **4** proved to be a far less efficient electrophillic aminating reagent. A competing methoxyacetylation reaction of the aryl moiety was involved. More positively, after screening a variety of conditions the electrophillic amination of 1,3-dimethoxybenzene and 1,3,5-trimethoxybenzene was achieved with CF_3COOH and **5**. The resulting arylamines were easily obtained by treatment with sodium carbonate (aq.)



3. **Perspective of Research after this Program:**

Being involved in the JSPS scheme has been an invaluable experience. It has provided me with not only with the opportunity to do research within an excellent chemistry group, but also to learn about the Japanese culture. I have fully enjoyed my time here and I owe the Narasaka group my thanks for all their kindness and enthusiasm during my stay. I hope the work carried out over the last few months will lead to some further interesting research.

4. **Advisor's Remarks:**

In these 2 months, Miss Jennifer Gibson has been concentrated in her research work in my group and made great innovation on the 2 essential problems on the electrophillic amination with oximes, such as the preparation of the starting materials 4 and 5 and the activation of these oximes for arene substitution. These findings are the key issues to develop a new method for the direct amination of arenes, which has still remained as an unsolved problem in the organic chemistry. Based on these discoveries, we will be able to establish an efficient method of the amination of aromatic compounds in the near future. I found these her contributions are achieved really due to her excellent understanding on key points of research works and enthusiasm in organic chemistry, and also she has made a good influence to my students. I am very grateful to her for joining in my group, though it is such a short visit.

Only the problem for her life in Japan is that she doesn't like any fish cooking even western styles. I hope, in the next visit to Japan, she will improve herself to be able to enjoy a variety of Japanese cuisines, which is one of the good ways to understand mutual cultures.

RESEARCH REPORT

Name: Richard Dawson Affiliation (University): Bristol University (UK)	
Research Advisor: Professor K. Takara **Host Institution: Disaster Prevention Research Institute, Kyoto University**	
Research Subject: Flood risk modelling	

1. Research Description:

My research is currently focused on the field of flood risk modelling. Recently in the UK I have been involved in generating flood risk assessment methodologies and creating flood risk maps of England and Wales. These maps have to consider predicting the frequency of river flooding or coastal storm surges, the likelihood that the existing flood defence system will be overwhelmed, the extent and depth of flooding and the resulting consequences.

My research at Bristol University has until recently focused on floodplain flow modelling and the assessing the likelihood of flood defence failure.

2. Research Activities:

The research activities of Professor Takara's group in Kyoto University complimented my previous work perfectly. The area of flood risk modelling that I am least familiar with, Hydrology (which involves the prediction of river flows), is the main expertise of the lab in which I am based.

Soon after arriving in Japan, Professor Takara invited me to attend the IUGG conference in Sapporo with his laboratory. This provided an excellent opportunity to communicate with some of the international leaders in Hydrology and obtain a broad perspective of the state of the art in Japan and the rest of the world. I am very grateful to the Professor for this marvellous opportunity.

I have also learnt about the research that is being done in Professor Takara's host laboratory. The international nature of this research meant that I was able to associate with both researchers from Japan and many other countries in the world. I have also been able to learn about the differences between Japanese and British flood problems – and how the two countries adapt their respective flood fighting strategies accordingly.

3. Perspective of Research after this Program:

My research in Japan has enabled me to gain a good grounding in Hydrology – an area of flood risk modelling in which I had only limited experience before my arrival. This experience will enable me to return to Bristol University with a useful contribution towards my current research project. I look forward to continuing contact and further collaboration with Professor Takara and the Disaster Prevention Research Institute at Kyoto University. I wish him and his laboratory all the best in their future research.

I have very much enjoyed my stay as a member of Professor Takara's laboratory, but I also consider myself very lucky to have been based in Kyoto; a beautiful city with a long heritage. I was also able to visit many other cities in Japan, allowing me to gain a real flavour of Japanese life and culture.

Finally, I would like to thank the JSPS for their support and funding and providing me with this fantastic opportunity to further my research in Japan.

4．**Advisor's Remarks:**

Participating in the JSPS Summer Program at my laboratory (Flood Disaster Research section) in Disaster Prevention Research Institute, Kyoto University, for about six weeks, Mr. Richard Dawson has gained some aspects of river management policies in Japan as well as in Asia and Pacific Region. I believe he communicated with various scholars and visitors here and exchanged different ideas about hydrology, water resources, *etc*.

Since Kyoto has many cultural heritages and places to visit, he also enjoyed his off time around Kyoto and also learned something about Japanese culture, history and so forth. I am very much delighted to have received such an active young researcher in my laboratory, which was stimulating to our activities. I wish for Richard’s future success and will keep in touch with him to develop further cooperation between Japan and UK. Thanks for the support of JSPS.

RESEARCH REPORT

Name:	**Affiliation (University):**
Andrew Ingham	School of Pharmacy, University of London.
Research Advisor:	**Host Institution:**
Professor Inaba	Chiba University

Research Subject:

DSC analysis of protein for protection during lyophilization.

1. Research Description:

My work focuses on the freeze dried storage of macromolecules. This typically includes particles from 4nm - 20μm.

Freeze dryings main potential advantage is that it can transform liquids to solids without exposing a sensitive drug (protein, plasmid, complex) to conventional drying stresses. The cost of storage at room temperature is the main economic benefit but also allows transport without the refrigeration chain. An implication for medicine transport in underprivileged countries is a very important secondary bonus.

2. Research Activities:

The effect of eleven different enzymes on the point of crystallization and melting of the lyo-protectant Sucrose have been looked at with conventional and high sensitivity DSC.

In order to determine any sequence relationship a bioinformatics approach was used to screen large numbers of potential sequences for correlation with tabulated data.

3. Perspective of Research after this Program:

Data collected here moves the project into the analysis stage. The large volume of data means many hypotheses will be tested against it and conclusions used to improve process control of the freeze dryer.

The international program focuses you on your work with many new views forcing you to review long standing views on a specific subject this is never a bad thing.

Further information on this work as well as software and methodology can be found at www.eatcha.com

4. Advisor's Remarks:

A. Ingham has made a lot of measurements using both conventional and high sensitivity DSC. The compiled data will contribute to make a significant progress for estimating the enzymes stability.

RESEARCH REPORT

Name: **Luke Carrivick**	**Affiliation (University): University of Bristol, UK**
Research Advisor: **Prof Nigel Collier**	**Host Institution: National Institute of Informatics**
Research Subject: **Medical Informatics – Diagnosis of Lung Disease from CT images.**	

1. Research Description:

Each year in the UK alone there are more than one hundred and fifty thousand deaths from lung disease. With earlier diagnosis, the standard of living of some of the patients could be greatly improved. Computed Tomography scans are becoming an increasing popular method of medical imaging. The technique is a relatively safe and non-invasive way of producing detailed and accurate internal images of the body. The subject of my PhD research is to provide techniques that can be used to automate diagnosis of disease and facilitate more rapid diagnosis by Radiologists.

Specifically I am interested abstract mathematical representation of medical knowledge with can be used to provide a reasoning tool from which an automatic diagnosis can take place. To populate such a system we have a set of examples from which to learn. The raw data is in the form of a collection of high-resolution CT images along with free text reports written by expert radiologists.

2. Research Activities:

Professor Colliers' group at the NII specializes in linguistics, particularly in the natural language processing of biological texts. They were able to direct me in how best to convert free text radiology reports into a structured form. From this I will now be able proceed to the next stage of my research.

During my stay I was also fortunate enough to visit Prof. MINATOS' Biomedical Imaging and Informatics group at Nara Institute of Science and Technology. Here I gave a short talk that resulted is some very useful and original discussion about my work. It also gave me good understanding of the machinery and methods that are used to produce the data with which I work.

3. Perspective of Research after this Program:

Automatic medical diagnosis is a complex and challenging field that requires the combination of many techniques from a broad range of fields. As a multidisciplinary problem it is very important to always be aware of all aspects of the problem. So, for me the most rewarding aspect of my short JSPS fellowship has not been the concrete research results, but the opportunity it has given me to present and discuss my work to a wide range of people from different backgrounds. This has forced me to reexamine some of the more fundamental aspects of my work that I had previously taken for granted. Consequently I have gained many new ideas and new perspective that will no doubt hold me in good stead for my future research.

I have greatly enjoyed my time in Japan and would seriously consider returning again should an opportunity arise.

4. **Advisor's Remarks:**

We were very happy to have hosted Luke during his stay in Japan. During his time with us we held fruitful discussions to exchange information regarding his research on medical report analysis for lung disease diagnosis and our project on information extraction from molecular biology documents. Luke regularly attended our project group meetings, contributing to the discussions, and also held individual discussions with me and our project members throughout his stay. Towards the end of his stay in Japan we arranged for him to visit the Minato Lab at NAIST for discussions related to medical image analysis. I hope that Luke was able to gain a new perspective on his research and to develop his ideas further as a result of his time with us.