RESEARCH REPORT

1. Name: Thomas Eadsforth （ID No.: SP07101 ）

2. Current affiliation: Department of Molecular Biology and Biotechnology, University of Sheffield, UK

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 for Chemical Research, Kyoto University

5. Host researcher: Professor Nobuyoshi Esaki and Professor Tatsuo Kurihara

6. Description of your current research

The main focus for my PhD concerns the development of a deeper understanding of the structure/activity relationships in imidazoleglycerol-phosphate dehydratase (IGPD). This enzyme catalyses the sixth step in the biosynthesis of histidine, the conversion of imidazoleglycerol phosphate to imidazoleacetol phosphate. In most species IGPD is expressed as a monofunctional enzyme whose 20 kDa subunit is now known to assemble to a 24-mer of 500 kDa molecular weight in the presence of certain divalent metals. However in some bacterial species including important pathogens such as *Campylobacter jejuni,* it exists as part of a multifunctional 40 kDa polypeptide that also encodes histidinol phosphatase, the enzyme catalysing the penultimate step of histidine biosynthesis, converting L-histidinol phosphate to L-histidinol. Currently, there is almost no data on the properties of these multifunctional IGPDs largely as a result of the difficulty in purifying the enzyme due to its low level abundance in the cell.

Bioinformatic analysis of the sequence of the multifunctional polypeptide guided by the structure of previously solved IGPD reveals that the majority of ligands involved in the coordination of the metal ions that are key to the assembly of the enzyme are strongly conserved in its C-terminal IGPD domain suggesting that, like the monofunctional protein, the multifunctional enzyme also assembles in the presence of divalent metals to form a 24-mer. Furthermore, the N-terminus of the IGPD domain lies on the external surface of the 24-mer allowing the N-terminal histidinol phosphatase domain of the multifunctional enzyme to be positioned surrounding an IGPD core, suggesting an assembled multifunctional IGPD would have a molecular weight in the 1000 kDa range making it one of the largest protein complexes found in the cell. The multifunctional IGPD from *E.coli* has been over-expressed in *E.coli* and a significant amount of highly active purified protein has been obtained for biochemical and structural studies. Preliminary electron microscopy analysis using negative staining indicate that the multifunctional enzyme assembles to give a highly symmetric particle whose much larger dimensions are consistent with the current view of the enzyme's assembly and domain organization. Current efforts are directed towards an analysis of the symmetry of the multifunctional enzyme using cryo-EM and in attempts to obtain crystals suitable for high resolution X-ray analysis. Determination of this structure would provide a more complete picture of this enzyme family and permit a more detailed analysis of the structure/function relationships to take place.

7. Research implementation and results under the program

Title of your research plan:

Investigations into *Shewanella livingstonensis* Ac10 Outer Membrane Protein C (OmpC) homologue and its role in cold temperature adaptation.

Description of the research activities:

The majority of the earth's biosphere is permanently below 5˚C. Many organisms, especially microorganisms, are adapted to such cold environments. Professor Esaki's group has been analyzing the cold-adaptation mechanism of a psychrophilic bacterium, *Shewanella livingstonensis* Ac10, isolated from the Antarctic Ocean. Proteome analysis of this bacterium identified approximately 30 cold-inducible proteins and work is now underway into analyzing their role in cold adaptation.

Analysis of the list of cold inducible proteins reveals that one of these proteins, *S. livingstonensis* OmpC, is a psychrophilic homologue of an outer membrane porin, which has been implicated in playing an important role in the uptake of nutrients from environments at low temperatures. Disruption of the gene coding for OmpC causes cold-sensitive growth of the bacterium. *S. livingstonensis* Ac10 produces eicosapentaenoic acid (EPA) as a component of phospholipids in the cell membrane at low temperatures, and it is suggested that EPA is important for the proper function of OmpC as the amount of OmpC is decreased in the mutant cells lacking EPA.

To date, there is little structure/function data available for *S.livingstonensis* OmpC, and all the current knowledge is derived from other species, in particular *E.coli*. It is known that the fluidity of the outer membrane is governed by the composition of fatty acids, and at lower temperatures there is an increase in the percentage of unsaturated and polyunsaturated fatty acids. *S. livingstonensis* Ac10 produces eicosapentaenoic acid (EPA) as a component of phospholipids in the cell membrane at low temperatures, and it is suggested that EPA is important for the proper function of OmpC as the amount of this protein is decreased in the mutant cells lacking EPA. This is an important hypothesis to prove, however it is difficult to do so without pure OmpC. It is hoped that synthetic liposomes can now be created to permit OmpC to be inserted across the membrane and allow its activity to be determined at a range of membrane compositions.

Current work in the laboratory has been focused on the construction of a low temperature expression system using *S.livingstonensis* Ac10 as a host. Successful identification of cold inducible expression promoter has allowed the OmpC gene to be fused to this promoter, and allowed significant levels of OmpC to be produced. After accumulating cells harboring the over expressed OmpC it was possible to harvest a highly enriched membrane envelope fraction. Following a modified protocol, it was possible to selectively solubilise the inner membrane followed by the outer membrane with several detergents. This allowed for the removal of a major proportion of cellular proteins allowing the subsequent purification outer membrane proteins to be simplified. The purification included anion exchange chromatography based on exploitation of the chemical properties and subsequent gel filtration exploited the physical properties of proteins. This resulted in a highly pure sample of protein, validating this low temperature system as a viable means of producing proteins that are thermolabile. Following subsequent analysis of the purified sample it appears that the protein is in fact another outer membrane protein, OmpF and that OmpC was not sufficiently solubilised prior to purification. Future work will now focus on identifying a detergent that will solubilise OmpC from the membrane allowing its subsequent purification. Once this has been achieved it is hoped that it will provide valuable insight into the structure and function of psychrophilic OmpC and increase our understanding of cold temperature adaptation in living organisms.

8. Please add your comments (if any):

Whilst my studies to date have allowed me to work with several large macromolecular assemblies and provided me with the opportunity to acquire skills in a wide range of molecular biological, structural, biochemical and biophysical techniques thus far I have not had an opportunity to work on membrane proteins. The research on OmpC has provided me with a marvellous opportunity to work on a membrane protein for the first time and to develop a new set of skills that will complement those I have experienced to date. I believe that these skills will be invaluable for my continuing career development and future research. Finally I believe that the experience of working in a Japanese laboratory has not only broadened my scientific horizons but has also provided me with a unique opportunity to experience a new culture.

RESEARCH REPORT

1. Name: Ewan Galbraith （ID No.: SP07102）

2. Current affiliation: University of Bath

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: Kyushu University

5. Host researcher: Associate Professor Kazuki Sada

6. Description of your current research

The design and synthesis of optical, primarily fluorescent, chemosensors for anions. Synthesis and electrochemical analysis of boronic acid dendrimers and boron-based redox active species for use in electrochemical recognition systems in biphasic conditions. Oxygen bridged di-Boron compounds as potential fluorescent biological markers and sensors.

7. Research implementation and results under the program

Title of your research plan:

The Combined Utilization of Fluorescent Fluoride Sensors and Super-Swelling Polyelectrolyte Gels in Non-Polar Solvent.

Description of the research activities:

Polyelectrolyte gels that swell to over 100 times their weight in low polarity solvents have been previously synthesized within the group using tetraphenylborate as the anionic component. Conversion of the easily prepared bromide salt of the cationic monomer to the unstable fluoride salt was achieved. Polymerization with dodecyl acrylate and ethylene glycol dimethacrylate as the cross-linker was achieved via irradiation at 350nm using Mucher's Ketone as a radical photoinitiator. The four step synthesis of a novel P.E.T chemosensor for fluoride anion was completed, one unusual aspect being a C_8 alkyl chain to aid solubility in non-polar media. In a solution of this sensor in chloroform, swelling of the gel successfully occurred. Swelling factor calculations and further swelling experiments are ongoing.

Cationic component of existing gels are tetraalkylammonium derivatives. A more lipophilic alternative may be the utilization of phosphazene bases. Synthesis of a novel P_1 phosphazene base incorporating a styrene unit was completed to allow inclusion into the polymer matrix.

RESEARCH REPORT

1. Name: Nina Grant （ID No.: SP07103 ）

2. Current affiliation: University College London, University of London

3. Research fields and specialties:

Humanities XSocial Sciences Mathematical and Physical Sciences
Chemistry Engineering Sciences Biological Sciences
Agricultural Sciences Medical, Dental and Pharmaceutical Sciences
Interdisciplinary and Frontier Sciences

4. Host institution: Kurume University

5. Host researcher: Professor Akira Tsuda

6. Description of your current research

At UCL, we have just completed an initial study investigating links between positive affect and health. This study recruited 100 full time female members of staff of UCL, aged 18-65 and of various socio-economic status. We took biological and psychological measures across two separate 24-hour periods, one on a weekday and one on a weekend day (Friday – Saturday). Each 24-hour study period began around 5pm, when participants finished work. The two study days were identical in format. For biological outcomes, we measured salivary cortisol at 7 time points (1700, bedtime, waking, waking plus 30 mins, 1000, 1200 and 1500). Participants also wore a solid-state heart rate monitor which provided a measure of heart rate variability, energy expenditure and sleep quality. Height and weight measures were taken for calculation of BMI (body mass index). Psychological measures included state and trait measures of well-being, such as standardized self-report questionnaires and also the Day Reconstruction Method. Other factors were also measured, including work strain, financial stress, hostility, and social networks. Data collection has recently been completed, so during the next few months we will begin to analyse this data.

7. Research implementation and results under the program

Title of your research plan:

Positive well-being and health: A cross-cultural comparison

Description of the research activities:

The purpose of my research trip was to set up a study to investigate links between positive affect and health in a Japanese population. Initially this involved submitting applications to the ethics board at my host university and working with suggestions from the board so that the study was passed. I then finalized the measures to be used for the Japanese sample and arranged for translations to be carried out. In many cases we made alterations to our UK protocol to take account of cultural factors. For instance, we reduced the length of the questionnaire to make it more convenient to complete. This process took up some time, during which I made plans for recruiting participants and worked with Japanese colleagues to arrange this. We began collecting data one month into the program, which was much quicker than we had anticipated. We have now had 20 participants complete the research and have recently begun to recruit more from another campus. I have set up databases for each of the measures and have entered all the data so far collected.

Whilst setting up the study, I also spent some time in the lab learning how to perform cortisol assays. In the UK, we send our samples away to be assayed so this was a valuable skill to learn. I have completed the assays for all the samples currently collected, however, at the present time we do not have enough data to begin to look at any results.

The study will continue until we have collected a minimum of 50 participants, with a view to collecting 100. I will be in close contact with the team of researchers in Japan that I have been working with this summer. We hope that this study will be a precursor to a larger scale collaborative project in the future. I plan to return to Kurume later this year to continue working on this project.

RESEARCH REPORT

1. Name: Simon Horne （ID No: SP07104 ）

2. Current affiliation:

University of Newcastle upon Tyne, Newcastle upon Tyne, NE1 7RU, ENGLAND

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: Kyushu University

5. Host researcher: Professor Shiraishi Fumihide

6. Description of your current research

Competition from emerging markets and tougher environmental constraints are fuelling the demand for cleaner and more efficient processes in the chemical and allied industries. Poor process understanding, scale up problems, and ineffective use of system information are key issues in today's industrial sector. Therefore alternative approaches for the modelling, design, and analysis of processes must be considered.

Although obtaining design equations that describe reactor system dynamics is an essential part of modelling continuous industrial process, determining such models from chemical and physical knowledge can be difficult due to complex and unknown dynamic behaviour. In such case, creating a reactor system model in terms of power-law form could be advantageous.

This work regards a unique hybrid modelling technique that quickly and efficiently determines design equations in a steady-state reactor system where the underlying chemical reaction network is entirely or partially unknown. The technique named *a simplified hybrid power-law system method* (SHPL-system method) is conceptually similar to S-system representation in Biochemical Systems Theory (BST) by describing reaction terms in power-law form, however along with other changes, the reactor operation and reaction terms are separated to form a hybrid structured model.

The methodology is outlined, and then a demonstration with regard to a CSTR system with an unknown chemical reaction network is given. This technique can be used to identify rate and power-law constants from steady-state reaction data, showing the structural advantage of SHPL over S-system representation. Due to limited space, only a brief description of the SHPL theory is given by consideration of 'power-law representation' accuracy, with respect to the etherification of ethanol and oleic acid in a Continuous Stirred Tank Reactor (CSTR) system.

Keywords: Hybrid power-law modelling, CSTR, BST, unknown chemical reaction network, accuracy

7. Research implementation and results under the program

Title of your research plan:

Modelling of Chemical Reactors with Unknown Reaction Networks by a Simplified Hybrid Power-Law System Method

Simplified Hybrid Power-Law Modelling (SHPL)

One can consider a Hybrid Model to be conceptually comprised of two parts, a function associated with well understood dynamic behaviour, often described by a first principles model, and that of a function describing unknown behaviour, often in practice using neural networks. This concept is represented by the following:

$$\frac{dx_i}{dt} = \bar{f}_i(x) + f_i\ (x)$$

where $\bar{f}_i(x)$ represents known model terms, i.e. terms that describe the known behaviour of the ith state x_i of the system, and $f_i(x)$ represents the respective unknown terms within the ODE.

In this work, we consider a continuous stirred tank reactor (CSTR) system, of which the behaviours of the process design variables such as flowrates, reactor volumes and inlet species concentrations are well understood. The dynamics of a liquid phase, isothermal, well mixed, constant volume CSTR can be described by a set of ODEs in the form

$$\frac{dx_i}{dt} = \frac{F}{V}(x_{i,in} - x_i) + R_i \equiv \frac{F}{V}(x_{i,in} - x_i) + f_i(x)$$

where F is the inlet (and outlet) flow rate, V is the reactor volume, x_i represent the respective species concentrations at a specified instant and the $x_{i,in}$ represents the species inlet concentrations. The first term of each component balance describes a net inflow rate involving the difference between the inflow and outflow concentrations of each species. The R_i terms are considered to describe the changes in species concentrations due to chemical reactions. The set of functions which describe R_i are unlikely to be known unless detailed chemical mechanism and kinetic studies have been undertaken. Therefore R_i can be replaced with the more generalised term for an unknown function f_i(x).

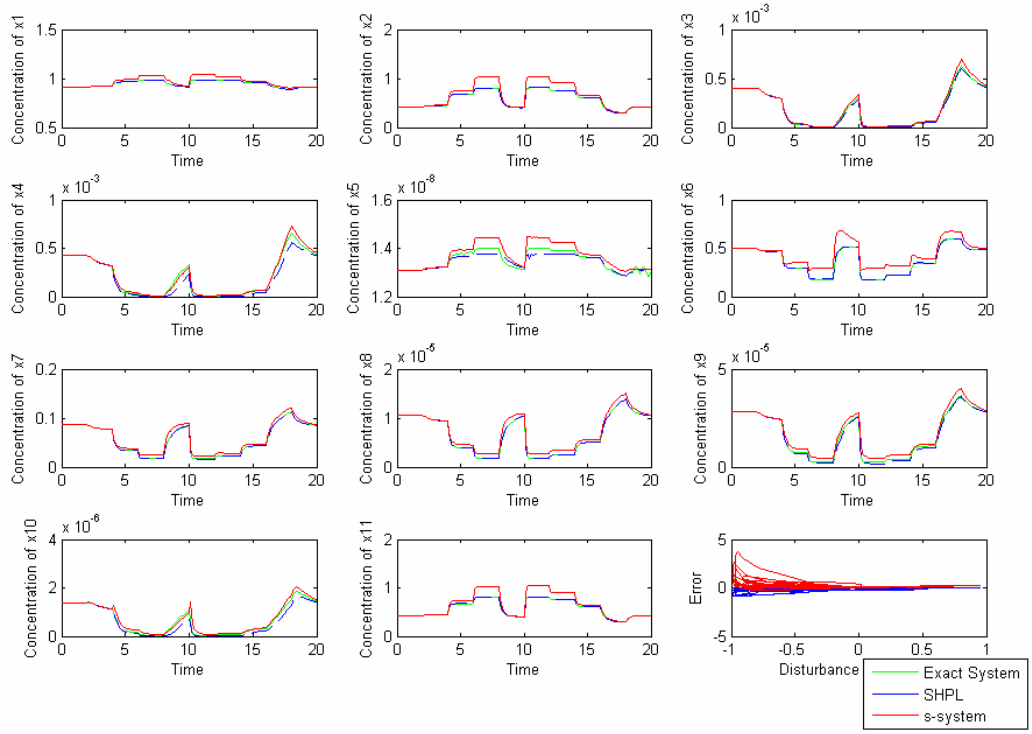
Often f_i(x) can be determined via an approach method such as neural networks (Hugget et al., 1999). However there are fundamental problems relating to the violation of mass conservation laws and thermodynamic principles (Olivares 2004) which give rise to unrealistic predictions. Therefore, a power law approximation is considered here for the modelling of f_i(x) which is beneficial due to the physically interoperable. The equation which represents the SHPL approach is therefore

$$\frac{dx_i}{dt} = \frac{F}{V}(x_{i,in} - x_i) + \alpha_i(\prod_{j=1}^{n} x_j^{a_{ij}}) - \beta_i(\prod_{j=1}^{n} x_j^{b_{ij}}) + \varepsilon_i$$

where the power law structured parameters α and β are pseudo rate constants and a_{ij} and b_{ij} are pseudo kinetic orders and ε_i corresponds to model prediction error, at time t. The SHPL method is primarily an engineering approach to determination of design equations for steady state reactor systems where the underlying reaction kinetics is unknown or not well understood.

SHPL Modelling of the Enzymatic Esterficication of Ethanol and Oleic Acid in an isothermal CSTR

The SHPL model is derived from steady state data along with the standard S-system technique for the esterification reaction, and compared to the original mathematical form. Dynamic responses of the identified models within a CSTR are shown below under fluctuating feedrate conditions between 0.5 – 3 m^3/s:



where $x_1 \ldots x_{11}$ are species associated with the reaction and concentration is in mol/m^3

The calculated results clearly show that the SHPL model adequately represents the chemical system even though no knowledge of the underlying network is available, showing significantly less relative error when compared to the S-systems technique. The success of SHPL is primarily based on obtaining good experimental data, including concentration data for each reactive species, and an optimisation method capable of satisfactorily identifying the SHPL parameters.

8. Comment: *A research paper with regard to this work will be submitted for publishing shortly, where results and concepts are described in more detail.*

References

Oliveira, R. (2004) Combining first principles modelling and artificial neural networks: a general framework. *Computers and Chemical Engineering*, **28**, 755–766.

Hugget, A., Sébastin P., and Nadeau J.P. (1999) Global optimization of a dryer by using neural networks and genetic algorithms *AIChE J.*, **45**, 6, 1227.

RESEARCH REPORT

1. Name: Kerry J. Knox （ID No.: SP07105）

2. Current affiliation: University of Bristol

3. Research fields and specialties:

Humanities Social Sciences X Mathematical and Physical Sciences
X Chemistry Engineering Sciences Biological Sciences
Agricultural Sciences Medical, Dental and Pharmaceutical Sciences
Interdisciplinary and Frontier Sciences

4. Host institution: Hokkaido University

5. Host researcher: Professor Noboru Kitamura

6. Description of your current research

Aerosols are small solid or liquid particles dispersed in a gas medium. They play a key role in numerous scientific disciplines, including drug delivery development and atmospheric chemistry. Aerosols have an important impact on atmospheric composition and climate due to their interactions with light and involvement in chemical reactions. However, while the effects of greenhouse gases on climate are increasingly well understood, the effects of aerosols in the atmosphere are not [1]. 'Optical tweezers' is an experimental technique in which an intense beam of light is used to isolate individual small particles [2]. The patterns of light scattered by a droplet can be analysed to determine its radius with high precision, allowing the evolving size to be tracked as its environment changes [3]. Information on droplet composition may also be extracted.

A wide range of properties has been explored at the University of Bristol using this approach, including the absorption of light by a droplet and the fluorescence from a dye present in the droplet.

1. *Climate Change 2007 - Summary for Policymakers*, Intergovernmental Panel on Climate Change
2. Ashkin A, *Phys. Rev. Lett.,* 1970, **24**, 156
3. Sayer R M, Gatherer R D B, Gilham R J J and Reid J P, *Phys. Chem. Chem. Phys.,* 2003, **5**, 3732

7. Research implementation and results under the program

Title of your research plan

The optical manipulation and characterisation of aerosol particles:
Polymerisation in optically-trapped aerosol droplets

Description of the research activities:

The aim of this work was to initiate and monitor polymerisation processes in an optically-tweezed aerosol droplet. Polymerisation of aerosol droplets is of interest because the behaviour of organic constituents in liquid aerosol droplets may involve polymerization processes, affecting their chemical and physical properties and influencing their roles in the atmosphere. Polymerisation in single droplets has previously been studied using electrostatic trapping techniques [4]. Polymerisation of optically-trapped aerosol droplets is more challenging as the droplet compositions which can be used are restricted to those which can be readily nebulised. Optical tweezers have many advantages however, for example the ability to confine and control multiple droplets [5]. Therefore despite the challenges it was ambitiously attempted to initiate polymerisation in an optically-trapped, monomer-loaded droplet. Several approaches to polymerisation have been investigated.

The first involved photochemical initiation of polymerisation. A suitable monomer/initiator/cross-linker combination for initiation using 488 nm continuous wave illumination was optimised. This involved finding a solution which will polymerise in the bulk phase but which can also be nebulised. The optimised solution was 1.4 M monomer (acrylamide) in an aqueous solution of sodium chloride saturated with initiator (2-Hydroxy-4′-(2-hydroxyethoxy)-2-methylpropiophenone) and cross-linker (N,N'-methylene bis(acrylamide)). Pulsed laser illumination was also used in order to increase the photon density within the droplets. Several important factors have been investigated but photochemically-initiated polymerisation of an optically-trapped droplet was not achieved.

The second approach involved thermal activation via internal droplet heating achieved by illumination with, and consequent absorption of, 1064 nm light. Potassium persulphate was used as a thermally-activated polymerisation initiator. This initiator is activated above 35^{o}C and it is feasible that a trapped droplet

illuminated with 1064 nm light reaches this temperature [6]. Polymerisation did not occur, however, demonstrating that the droplet does not reach 35^{o}C.

Finally thermal activation was sought via externally heating of a droplet using temperature-controlled equipment. Preliminary results indicate that polymerisation may have occurred, determined by Raman spectroscopy and imaging techniques. Once confirmed this should result in a joint paper being submitted for publication.

4. Widmann J F and Davis E J, *Colloid and Polymer Science,* 1996, **274**, 525
5. Fällman E and Axner O, *Appl. Opt.,* 1997, **36**, 2107
6. Carls J C, Moncivais G and Brock J R, *Appl. Opt.,* 1990, **29**, 2913

8. Please add your comments (if any):

I am very grateful to Professor Kitamura for accepting my application, for providing guidance during my project and for making my stay in Sapporo so enjoyable. I would like to thank Dr. Ishizaka and Suzuki-san very much for their tremendous help in the lab. I would also like to thank the entire group for their friendly company and for helping me with all sorts of problems! I have been highly impressed by this research group and feel extremely lucky to have spent time with them learning their way of working. I have had a wonderful summer in Sapporo. Many thanks to JSPS for organising and running this very worthwhile programme.

9. Advisor's remarks (if any):

I appreciate very much for her contributions to Raman spectroscopy of laser trapped aerosols and our experiments in my lab have advanced greatly during her stay. Our collaborations in Sapporo have opened opportunities to pursue new experimental studies on aerosols and I strongly hope to continue research collaboration with her and her group in Bristol.

RESEARCH REPORT

1. Name: Jessica Langer （ID No.: SP07106）

2. Current affiliation: Royal Holloway, University of London

3. Research fields and specialties:

X Humanities 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: Meiji Gakuin University

5. Host researcher: Professor Ayako SAITO

6. Description of your current research

At present, my research has two main strands. One is the working out of an effective theoretical basis for my study of science fiction and postcolonialism: it has been my argument that applying postcolonial concepts to science fiction texts, analyzing certain postcolonial texts using concepts identified with the genre of science fiction, and studying those texts in which the authorial context is postcolonial and the generic context is science fictional strengthens both fields, lending an important specific ethical context to science fiction and including more potentiality in the field of postcolonial studies. The other strand is a more general focus on Japanese cinema and other media and culture, as they relate to aspects of postcolonial theory and the specifics of Japan's struggle with its history and identity in the face of imperialism. Japan's post-colonial identity is unique among both formerly colonial and formerly colonized nation-states due to its modern history as both colonizer and colonized, and has therefore been an especially interesting and fruitful site of inquiry.

The chapter I am currently writing, and for which I came to Japan to do research, is on Japanese science fiction and postcolonialism. In this chapter, I aim both to situate Japan within the wider discursive contexts of both postcolonial studies and East Asian area studies, and also to look at the ways in which the genre of science fiction has been reflective of Japan's postcolonial (and post-colonial) situation.

7. Research implementation and results under the program

Title of your research plan:

Beyond Gojira and Gundam: Japanese Science Fiction and Postcolonialism

Description of the research activities:

In Japan, I have been able to consult many Japanese-language books that have not been published in England. In particular, a new encyclopedia on Japanese SF film was published in 2006, and it has been helpful to my research. I have also had the opportunity to search through several libraries for resources, including the Waseda University film library, the National Film Centre library, the Meiji Gakuin University library (including the vast and excellent library of rare films held by the Department of Film at Meigaku), and the Japan Foundation library in Roppongi. In doing so, I have been able to consult many rare and out-of-print sources including older copies of the literary journal *Sekai SF zenshuu*, out-of-print Kodansha English Library translations of Hoshi Shin'ichi's and Tsutsui Yasutaka's stories, and early issues of *Kinema junpo* including special publications by the journal.

Most significantly, in the course of my research I have discovered several pre-war science fiction films, and I will have the opportunity to see one of them at the National Film Centre. The NFC holds the only copy in existence of the pre-war SF film *Kaidenpa senritsu* (1939), and some of the only existing stills from the lost film *Kaidenpa satsujin kousen* (1936), both of which I have arranged to see on 24 August.

The research budget provided by the JSPS has allowed me to hire a research assistant to help me in translating difficult materials, which has enabled me to work with plenty of Japanese-language sources. In particular, this has allowed me to work with Tsutsui Yasutaka's story "Betonamu kanko kousha", which is important to my thesis; with my RA's help, I am working on a full translation of the story. Through this, as well as using Japanese in my daily life in Tokyo, my Japanese language skills have improved enormously.

I will be staying until 2 September in Japan in order to go to Worldcon 2007, a major science fiction convention that is being held in Japan this summer for the first time in

its history. Whilst there, I have arranged to meet with many luminaries of the Japanese SF field, including Takayuki Tatsumi and Kotani Mari. These meetings will benefit my research and will foster academic connections between the UK and Japan.

8. Please add your comments (if any):

I am incredibly grateful to the JSPS for the opportunity to do this research. There is no way I would have been able to consult all of these sources, which are essential for my research project, had I not come to Japan. I am also very grateful to my advisor, Professor Saito, for all of her generous assistance.

RESEARCH REPORT

1. Name: Christopher Lee Millington （ID No.: SP07107 ）

2. Current affiliation: University of Sheffield England

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: Tokyo institute of Technology

5. Host researcher: Prof. Akio Takenaka

6. Description of your current research

My research is based around the organic synthesis of modified non-natural DNA. I currently have 4 different collaborations involving modified DNA synthesis, however the general theme could be said to be; using modified DNA to investigate DNA repair mechanisms. DNA is constantly being damaged within the body, not just by toxic chemicals from the outside world but also by many chemicals produced within the body. However the body also has many differing repair mechanism for dealing with the many types of DNA damages that can arise. This area of research also relates to cancer research, since damage to particular areas within DNA code can lead to cancer. One particular repair mechanism which we are interested in involves only one protein, Alkyl Guanine Transferase (AGT). AGT repairs alkylation damage at the O6 position of guanine. AGT is found in high levels in some forms of cancer, however many existing cancer treatments work by alkylating DNA to damage it, thereby killing the cell. The presence of high levels of AGT within the cancer cells counteracts many cancer drug therapies. Therefore deactivation of AGT is an active area of cancer therapy research. The compounds we have made so far are based on existing drugs in Phase II clinical trails but incorporated into DNA. Results show that they are much more potent then there counterparts, but this is only *in vitro* (within a test tube, not inside a living organism).

7. Research implementation and results under the program

Title of your research plan:

Crystallization and structure determination of modified DNA designed for anti-sense DNA therapy.

Description of the research activities:

Previous research lead to the development of a modified cytosine base that is capable of increasing the melting temperature of double stranded DNA by 4 degrees Celsius per modification. Modified DNA bases are of interest in the area of anti-sense DNA therapy. The basic idea is to control the synthesis of any protein by targeting messenger RNA (mRNA) for degradation. Within the cell exists an enzyme called RNaseH which degrades RND-DNA duplexes. Therefore if a sequence of DNA which is complementary to the mRNA sequence is introduced into the cell it should be broken down by RNaseH and stop protein synthesis. However the duplexes formed between natural DNA and RNA are not stable enough to be considered applicable as a drug therapy. Therefore much research has gone into the area of using modified DNA to increase the strength of the interaction with the mRNA complementary strand. The modification developed within my research group was designed to work by increasing base stacking interactions in the duplexes. To investigate this further we are interested in acquiring a crystal structure of a DNA duplex containing the modified cytosine base.

However I am a chemist, not a crystallographer. The first part of my project was only a practice in the ways of a crystallographer. Hence I used the common introductory experiment of crystallizing the protein lysozyme. Firstly I purified the protein using polyacrylamide gel electrophoresis (PAGE). This is a common technique but one which was new to me. Then I made a crystallization plate and waited for the crystals to grow. After about a week I had some crystals. From hear you have to take daily pictures of the crystals and measure there size to make sure there still not growing. After this I selected the conditions within which the best crystals grew and made more crystal plates based around this condition; basically this is optimization of the crystallization condition. Once these crystals had grown I selected the best ones and used the X-ray analyses machine to collect diffraction data on the crystals. Loading the crystals onto the machine is a very tricky procedure and many of them broke during this process. After this I tried to solve the crystal structure but it proved that the data I collected was of to low a quality, this was most probably due to crystal damage. After this I tried crystallization of a natural DNA duplex as DNA crystallization is generally considered harder then with proteins; since DNA crystallizes in a narrower range of conditions. I was successful in crystallizing DNA and I was able to solve the crystal structure also. However the computer software used to do this is Linux operating system based, so first I had to learn how to use this. Now I was ready to start the actual experiment of my project, but the time was already close to the end. So far I have completed the synthesis and purification of the modified DNA sample and made a crystal plate, but however we have no crystals, therefore varying conditions need to be explored in the future. The worked will be carried on by one of the existing lab members on my departure.

8. Please add your comments (if any):

I am very grateful to Akio Takenaka and all his lab members for accepting me through the JSPS course and there constant help and support.

RESEARCH REPORT

1. Name: Helen Moor （ID No.: SP07108）

2. Current affiliation: Queen's University Belfast

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: The University of Tokyo

5. Host researcher: Professor Yasuhiro Iwasawa

6. Description of your current research

My PhD research is based upon the development of in-situ ATR-IR (Attenuated Total Reflection Infra-red) for the characterization of a range of different catalyst materials. Thus far, my work has focused on developing and optimizing a laminar flow-through reactor, which can be positioned in the ATR system to allow the collection of IR spectra in-situ, as the reactants are passed through the cell over a catalyst layer in the ATR system. Recently the performance of this flow-through reactor and the IR instrument has been assessed by replicating experiments previously carried out by other research groups concerning the characteristic adsorption of CO to the surface of a palladium catalyst. These experiments confirmed the reactor design and instrument were performing satisfactorily, and more recently the system has been used to investigate the reaction mechanism of the hydrogenation of ketoisophorone.

Future work includes further developing the flow through cell to allow for mixing of the reactants, and the aim is eventually to scale the system up to batch scale.

7. Research implementation and results under the program

Title of your research plan:

"The Characterisation of a Range of Alumina Based Silver de-NOx Catalysts Using in-situ Solid State NMR"

Description of the research activities:

My research at the University of Tokyo has focused on the characterization of a range of different silver-based alumina catalysts using solid state ^{109} Ag NMR with the aim to understanding how the catalyst behaves during the de-NOx reaction both with and without added hydrogen, which has been found to significantly enhance the performance of the catalyst.

NMR spectra have been collected and interpreted for all three different weight percent fresh catalyst samples. The sample of interest, 2 wt% silver on alumina, was then subject to a range of different oxidizing and reducing environments in order to determine what effect these environments had on the silver atoms. The results of these experiments were encouraging in that we could see changes in the Ag environments after different gas treatments. Initially there had been some concern that 2 wt% would be too low a concentration of silver considering the low abundance of ^{109} Ag to record good quality spectra, however this did not prove to be the case although long acquisition times were needed.

Future work will include carrying out the de-NOx reaction both with and without added hydrogen, then analyzing the catalyst post-reaction and comparing this to both the fresh catalyst and the spectra obtained under the different oxidizing and reducing environments in order to understand how the silver behaves during the reaction and hopefully gain more understanding into how the added hydrogen improves the performance of the catalyst so significantly.

8. Please add your comments (if any):

I have very much enjoyed my time in Japan and at The University of Tokyo and found it an invaluable experience.

9. Advisor's remarks (if any):

Ms. Helen Moor, coming from Queen's University Belfast, is a very smart and top class student. She has performed very important experiments on exploring the genesis of de-NOx catalysis of Ag/Al_2O_3, particularly the promotional effect of coexisting H_2 by means of solid state NMR. The results that Ms. Moor found in Iwasawa's lab placed the foundation of future collaboration between Iwasawa group at the University of Tokyo and Hardacre group at Queen's University Belfast on the important topic of Ag catalysis. Further, Ms. Moor has positive attitude and enthusiasm for touching and communicating with different culture and history. The presence of Ms. Moor has evidently influenced the students as well as postdocs and members of my laboratory positively. Everybody of my laboratory welcomes Ms. Helen Moor, who has brought with her excellent program and occasion to interact with foreign students. The JSPS program is significant for both the visiting student and the members of the hosting laboratory.

RESEARCH REPORT

1. Name: Graham Newton （ID No.: SP07109）

2. Current affiliation: University of Glasgow

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

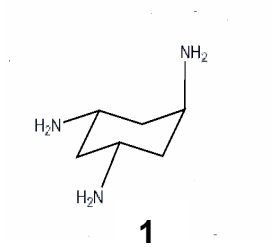
4. Host institution: University of Tsukuba

5. Host researcher: Professor Hiroki Oshio

6. Description of your current research

The focus of my PhD is based around three main areas: The synthesis of new multidentate ligands; the formation of polynuclear metal and mixed-metal clusters based on these ligands; and their analysis by cryospray mass spectrometry (CSMS).

The ligand which has formed the basis for the bulk of my research has been primarily the aliphatic triamine *cis,trans*-1,3,5-triaminocyclohexane (*trans*-tach **(1)**).



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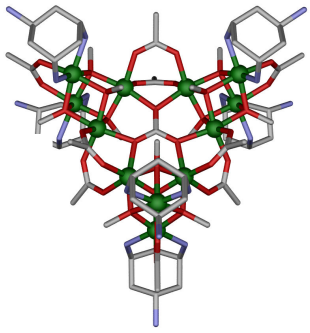

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Studies of the complexation behaviour of **1** have yielded a number of highly interesting results. Using **1** a range of high nuclearity clusters have been crystallised including a family of iso-structural nickel and cobalt clusters (**2**) comprising twelve metal ions. The family consists of the full series of mixed metal $\{Ni_{12-n}Co_n\}$ clusters (n = 1 – 11). All have been solved crystallographically and can be further elucidated using CSMS. This use of CSMS is the first example of the technique being used successfully with high nuclearity Ni^{II} and Co^{II} complexes to show intact clusters in solution.

7. Research implementation and results under the program

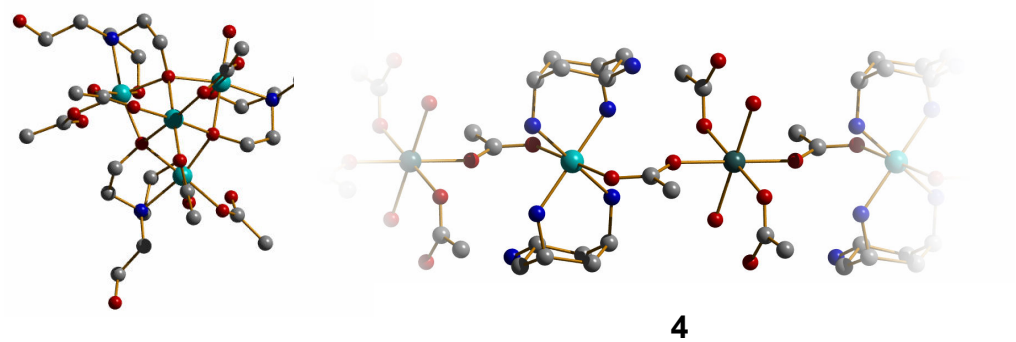
Title of your research plan:

The generation of new metal and mixed metal coordination clusters with interesting magnetic properties

Description of the research activities:

The premise for the research was to generate new interesting metal clusters from known building blocks and to utilize the facilities available to conduct full physical property measurements on some clusters synthesized over the course of my PhD. Both aspects proved fruitful, with particularly the formation of new materials giving very encouraging results.

New clusters formed include an asymmetric Ni tetrahedron **3** with triethanolamine as a ligand, and a new mixed metal Mn^{II} and Ni^{II} chain material **4**.



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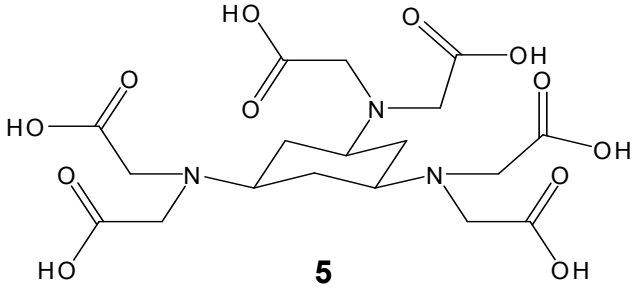
The Ni_4 cluster **3** is interesting as it is an example of an asymmetric material based on very simple building blocks. Neither material has been fully analysed as to its physi **3** roperties as yet, but **4** in particular could be of great interest. It constitutes the 4[th] in a series of mixed metal clusters based on Ni^{II} which have been shown to exhibit ferromagnetic coupling between metal centres. In simpler terms, this represents the directionality of magnetism on the atomic level. If something is ferromagnetically coupled, that means it has an overall direction of magnetic spin (i.e. north-south) and as such can be potentially be classed as a magnet. Further analysis will elucidate this result and determine the importance of this cluster.

Part of the research plan was to investigate another ligand, *cis,cis*-1,3,5-triaminocyclohexane-*N,N,N',N',N'',N''*-hexaacetic acid (hact **(5)**).



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Many coordination attempts were carried out under solvothermal conditions (i.e. high pressure and temperature), an area of specific expertise in the Oshio group. As a result of this no crystal structures have been discovered as yet, but encouraging signs of complexation can be seen and further work will build on this.

8. Please add your comments (if any):

My time in the Oshio lab and Japan in general has been something I will always look back on as a great experience. The combination of meeting some great scientists, both on the JSPS program and in the work place in Japan has been incredibly valuable both in terms of knowledge gained and friendships made.

I'd like to thank the British Council, JSPS, Professor Oshio and all my lab mates and new friends for making it such a great summer.

9. Advisor's remarks (if any):

Mr. Graham Newton has spent two months in our lab, and he worked very hard and prepared a couple of new compounds, one of which is a promising candidate for a new family of single chain magnet. I am sure that he had very good experiences in doing new chemistry and in touching Japanese way of life and thinking that he has never experienced before. I certainly conclude that this exchange program was very successful and is the start of collaboration with Prof. Lee's group in Univ. of Glasgow where Mr. Graham Newton came from. I thank Mr. Graham Newton for his coming to Japan and also thank JSPS program for giving him this opportunity.

RESEARCH REPORT

1. Name: Richard Threlfall （ID No.: SP07110）

2. Current affiliation: University of Liverpool, United Kingdom

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: Graduate School of Frontier Sciences, University of Tokyo

5. Host researcher: Associate Professor Takeshi Wada

6. Description of your current research

Current research within the Cosstick group is focused on chemical modification of oligonucleotides, such as DNA and RNA, with a view to their application as novel antisense or antigene therapies. Recently, it has been established that peptides derived from the modified DNA building block thymidine form secondary structure in solution, that is, have an ordered conformation due to intramolecular interactions. This is a significant step towards developing these protein/DNA hybrid molecules into a workable and useful application.

Oligomers of the modified thymidines have been produced by standard, manual solid-phase peptide synthesis. Although this process is easy to perform, it is relatively time consuming and laborious compared with automated solid-phase DNA/RNA synthesis. Also, purification of the final product from both of these techniques is usually performed by High Performance Liquid Chromatography (HPLC) which is also expensive, time consuming and not a particularly scalable procedure.

As well as developing the synthesis and applications of these modified oligonucleotides it is desired that alongside this a method of large-scale synthesis with minimal purification can be generated which can be applied to both modified and conventional peptides. This is where fluorous technology may be applicable.

7. Research implementation and results under the program

Title of your research plan:

Fluorous Dendrons and the Future of Purification-Free Synthesis

Description of the research activities:

It has been established that highly fluorinated dendrons are compatible with natural amino acids such as glycine and could be applied to peptide synthesis for short chain peptides. Initial attempts to couple a modified thymidine amino acid residue directly to highly fluorinated groups proved challenging, probably due to the great difference in solubility between the fluorous groups and the DNA derived amino acid. It is also thought that the relative size and bulk of both molecules had a detrimental effect. Both heavy and light fluorous technologies, that is, the use of large dendrons for solution-phase extractive purification and tag molecules with a smaller percentage of fluorine for use with chromatography on fluorous silica gels respectively, were equally unsuccessful. However, although the direct coupling strategy was not fruitful, it was postulated that the introduction of a natural amino acid residue to act as a linker between the dendron and the modified thymidine would provide a solution.

This indeed proved to be the case and application of heavy fluorous technology with the natural amino acid glycine proved to be high yielding, efficient and convenient. The highly fluorinated dendron and N-protected amino acid were condensed at the carboxylic acid terminus using novel phosphorous-based coupling reagents developed by the Wada group. This reaction and the following deprotection of the amino acid both progressed smoothly and rapidly. The ease with which the reaction proceeded is encouraging and demonstrates that it should be possible to construct oligomers with several further residues. After solvent extraction with fluorous solvents, no purification of either product was required and this is a significant achievement in solution-phase peptide synthesis.

The addition of the modified thymidine residue was a little less efficient than the first condensation with glycine and this is likely to also be a steric effect but with a reduced consequence due to the presence of the glycine linker. The reaction proceeded to approximately 75 % completion after 24 hours at room temperature. Significantly, fluorous extractive purification was still possible leading to recovery of both product and unreacted starting material in the fluorous phase, indicating that recycling of unused materials should also be possible. The length of oligomer it is possible to build until fluorous extraction is no longer possible is a point that will be investigated further as part of a collaborative effort, as will procedures for cleavage of peptides from the fluorous supports.

8. Please add your comments (if any):

I would like to thank JSPS for the opportunity to come out to Japan on the summer programme. I would also like to express my gratitude to Associate Professor Takeshi Wada and his research group for all their kind help, assistance and encouragement and for making my time in Japan so enjoyable.

9. Advisor's remarks (if any):

Richard Threlfall from the University of Liverpool enthusiastically carried out the experiments for JSPS summer program in our laboratory. In the beginning, it was very difficult to get his desired compounds, but finally, he succeeded in achieving some reactions as he described above. I hope he will continue and complete a series of his reactions in Liverpool. This work is a collaborative project between the Cosstick group and our group and hopefully, we will be able to produce a joint publication in near future.