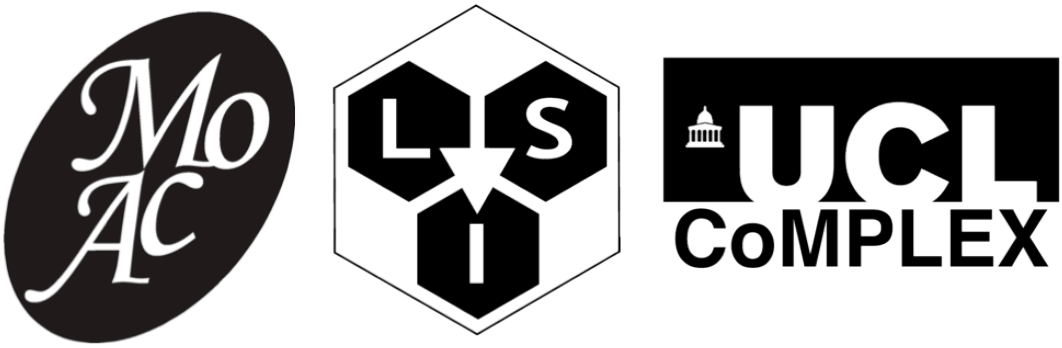
1st Edition

Conference booklet



Joint DTC Life Sciences Conference
Warwick 2012

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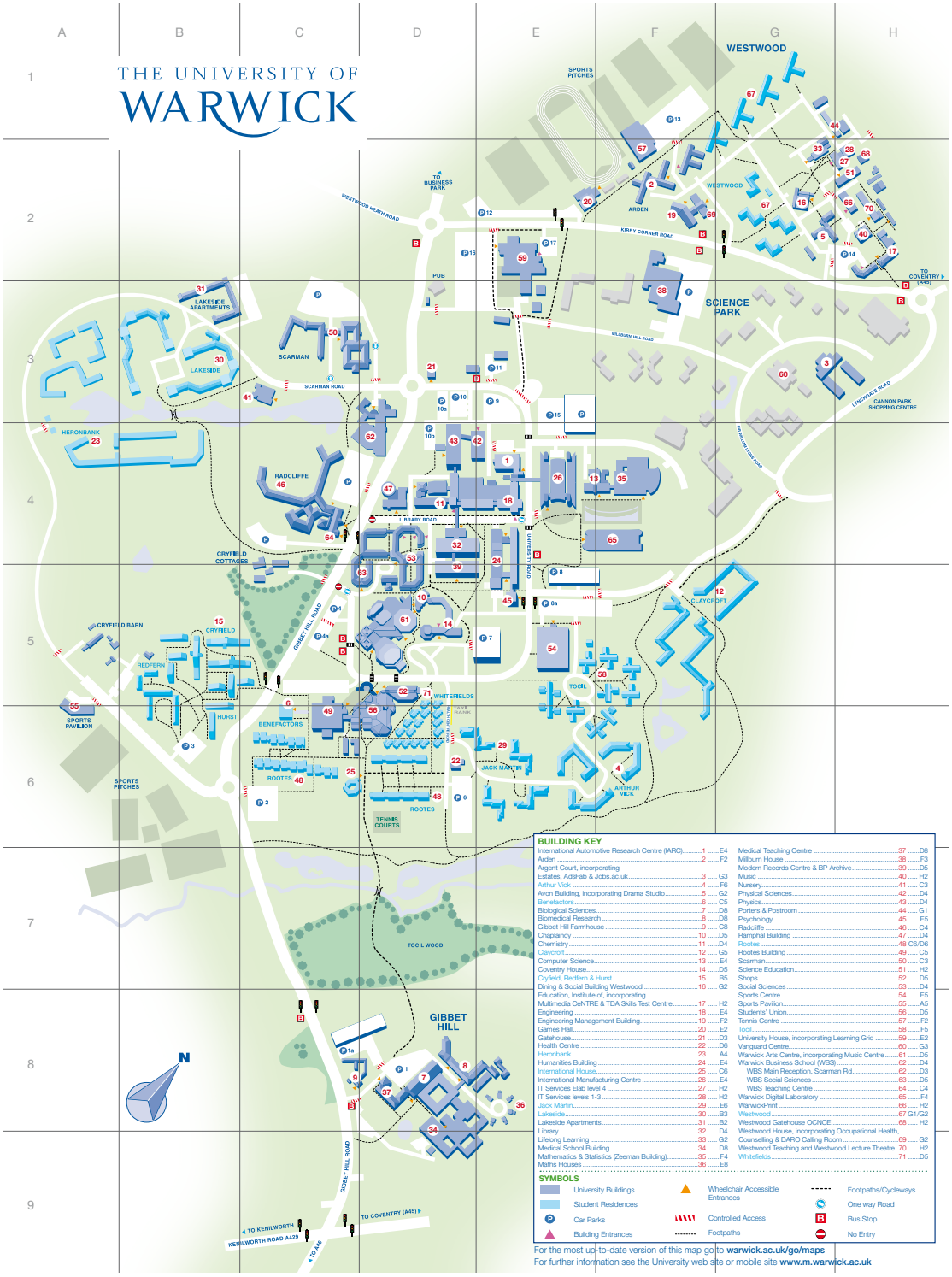
List of poster titles!

17th – 18th May 2012 A.D.



A full colour version of this booklet is available online at
http://www2.warwick.ac.uk/fac/sci/moac/news_events/dtc_conf/may2012conference/

Accommodation

On Campus.

Arden, Radcliffe and Scarman are shown on the campus map. They are all within a 10 minute walk of the MOAC dept. and the other locations used during the conference.

Off Campus.

If anyone is staying off campus, the easiest way to get here is catching the blue number 12 Travel Coventry bus from either Coventry or Leamington. These buses are fairly regular, every 10 mins from Coventry and every 30 mins from Leamington, and will drop you off at the main campus bus stop.

Locations on campus map.

Arden House	F2. 10 min walk to MOAC.
Scarman House	C3. 5 min walk to MOAC.
Radcliffe House	C4. 5 min walk to MOAC.
Main campus bus stop	C5. 2 min walk to MOAC.

Conference Locations

MOAC Department, (Coventry House, D5)
This is where the conference registration will take place from midday on the 17th May.

Chancellors' Suite, (Rootes Social Building, 2nd floor, C5)
This is where the poster session and evening meal will be held on the 17th May. The room is upstairs next to the bar in Rootes Social Building, which is just over the road from MOAC. Most delegates will be walking straight from MOAC after the talks.

Terrace Bar, (Students Union, 1st floor, D5)
The Terrace Bar will be open for us after the meal on the 17th May. This is in the Students' Union, which is next door to the Rootes Social Building.

Talk Locations

Parallel Sessions, 17th May

MOAC Seminar Room, (Coventry House, top floor, D5)
This is inside the MOAC department, and where the registration takes place on the first day.

F1.11 (Engineering Department, first floor, E4)
This is on the first floor of the engineering department, almost immediately after you enter the building. The session chair will lead people to and from this building at the beginning and end of each talks session.

Lib 2 (The Library, first floor, D4)
This is on the first floor of the library building before you actually cross the barriers into the library. The session chair will lead people to and from this building at the beginning and end of each talks session.

Plenary Lectures, 18th May

H0.52 (Humanities Building, ground floor, E4)
This is where we will start the second day, with talks from the plenary speakers.

Itinerary

Thursday 17th May

12:00 – 13:30 : Registration and lunch in MOAC dept.
13:30 – 14:45 : First parallel talks session
14:45 – 15:15 : Break for tea/coffee in MOAC dept.
15:15 – 16:30 : Second parallel talks session
16:30 – 17:00 : Break for tea/coffee in MOAC dept.
17:00 – 18:30 : Poster session in Chancellors Suite
18:30 – 20:30 : Dinner in Chancellors Suite
20:30 – Late : Terrace Bar

Friday 18th May

Tea and coffee will be available in MOAC dept. from 09:15
09:45 – 10:15 : First Plenary Lecture, H0.52
10:15 – 10:45 : Tea/coffee and conference photo in MOAC
10:45 – 11:15 : Second Plenary Lecture, H0.52
11:15 – 11:30 : Final thanks and talk and poster prizes
11:30 – 13:00 : Lunch

Plenary Lectures

Matthew Gibson: Interfacing Materials with Biology - Glycomics with Plastic Bags

Matthew Gibson is a Science City Senior Research Fellow at the University of Warwick. His research centres on the design of membrane-interacting macromolecules to aid in cryopreservation.

Kevin Warwick: The Cyborg Experiments

Kevin Warwick is Professor of Cybernetics at the University of Reading, England, where he carries out research in artificial intelligence, control, robotics and biomedical engineering.

Parallel Session 1: Modelling

Lib 2

Session 1 **Chair: Daniel Turner**

Talk 1: **Daniel Pearce**
Moving and staying together: the role of visual projection in flocking animals
Talk 2: **Sang Young Noh**
Interactions of Patchy Membranes with Nanoparticles
Talk 3: **Fintan Nagle**
Photorealistic avatars
Talk 4: **Melissa Maczka**
Investigating how neuromodulations alter neurovascular coupling using information-theoretic generative embedding

Session 2 **Chair: Richard Snowdon**

Talk 1: **Vince Hall**
Globular protein structures from Circular Dichroism using a neural network
Talk 2: **Callum Dickson**
Computational study of drug-membrane interactions
Talk 3: **Anthony Nash**
Molecular dynamics of receptor tyrosine kinase transmembrane protein domain
Talk 4: **Nikolas Burkoff**
Protein Structure Prediction and Energy Landscape Exploration

Parallel Session 2: Chemical Biology and Instrumentation

MOAC Seminar Room

Session 1 **Chair: Vicky Marlow**

Talk 1: **Andrew Soulby**
Determining structural changes with deamidation of native state gas phase proteins using FTICR-MS and ion mobility mass spectrometry.
Talk 2: **Christopher Douse**
Regulation and Dynamics of the *Plasmodium* Cell Invasion Motor: Insights from NMR
Talk 3: **Anna Haslop**
Development of 18F-labelled phosphonium cations as PET imaging agents of the mitochondrial function during apoptosis
Talk 4: **Sean Warren**
FLIM-FRET imaging of cell signalling in chemotaxis

Session 2 **Chair: Kate Meadows**

Talk 1: **Amy Hippard**
Peptide-based inhibitors for synaptojanin-1 and PTPMT1
Talk 2: **Doug Kelly**
Towards high throughput FLIM: instrument development and applications
Talk 3: **Verity Stafford**
Development of new molecules and affinity tags that interact selectively with G-quadruplex DNA
Talk 4: **Michelle Cheung**
EVV 2DIR Spectroscopy: A Novel Tool to Investigate Protein Phosphorylation and Charge Effects

Parallel Session 3: Genetics and Cell Biology
F1.11

Session 1 **Chair: John Blood**

Talk 1: **Jack Heal**
HIV-1 protease: the rigidity perspective
Talk 2: **James Sudlow**
Design of Inhibitors for p97-cofactor Binding and High-Throughput Assay Development
Talk 3: **Ciara McCarthy**
Expression of genes regulating mitochondrial fusion and fission in human adipose tissue are influenced by adiposity and bariatric surgery
Talk 4: **Chung-Ho Lau**
Probing PI3K signalling dependent Tumour Metabolism using NMR metabolomics

Session 2 **Chair: Michael Chow**

Talk 1: **Robert Deller**
Peptidomimetic approaches to mimicking antifreeze protein function
Talk 2: **Ed Harry**
High Temporal Resolution Tracking of Kinetochores and Spindle Poles in Mitotic HeLa Cells
Talk 3: **Fairuzeta Ja'afar**
Mechanisms of Microbubble Interactions with Activated versus Non-Activated Vasculature
Talk 4: **Beata Klejevskaja-Borrie**
Structural and functional characterization of potential G-quadruplex motifs from the proximal promoter of GATA4 gene
Talk 5: **David Paterson**
The Phospholipid Interactions of Antimicrobial Peptides

Peptide-Based Inhibitors for Synaptojanin-1 and PTPMT1

Amy Hippard[1]

Supervisors: Dr. Ed Tate[1] and Dr. Rudiger Woscholski[1]

[1] *Department of Chemistry, Imperial College London, Institute of Chemical Biology*

Phosphoinositides (PIs) are an important group of phospholipids, involved in cell signalling and membrane trafficking. Maintaining the correct distribution of phosphoinositides within cells is essential and many diseases, including cancer, diabetes, Alzheimer's disease and Down Syndrome, have been directly linked to perturbations in the network of kinases of phosphatases which mediate the intracellular conversions between different types of phosphoinositides.

Synaptojanin-1 is a polyphosphoinositide phosphatase. It is enriched at the pre-synaptic membrane and catalyses the dephosphorylation of the phosphoinositide $PI(4,5)P_2$. This process is known to be essential for the function of the synaptic vesicle cycle, and synaptojanin has been highlighted as a potential drug target for Alzheimer's Disease and Down Syndrome.

PTPMT1 is classed as part of the protein tyrosine phosphatase superfamily but, as with similar enzymes like PTEN, its primary substrate is a phosphoinositide. PTPMT1 is localised exclusively to the mitochondrion and dephosphorylates the phosphoinositide PI(5)P, as well as phosphatidylglycerol phosphate. The activity of PTPMT1 mediates mitochondrial ATP synthesis and analysis of PTPMT1 is of interest as a potential drug target for pancreatic cancer and type II diabetes.

This talk will focus on the development of peptide-based inhibitors for both synaptojanin-1 and PTPMT1.

Determining structural changes with deamidation of native state gas phase proteins using FTICR-MS and ion mobility mass spectrometry.

Andrew Soulby[1,2]

Supervisors: Peter B O'Connor[1], James H Scrivens[2],
[1]*Department of Chemistry, University of Warwick, Coventry, UK.*
[2]*Department of Biological Sciences, University of Warwick, Coventry, UK.*

The post translational modification of proteins occurs continuously in vivo and can result in changes of protein structure that alter functionality with potential health implications. Here, ion mobility, topdown HDX- ECD and infra red absorption dependant unfolding-ECD are used to assess the structural changes of native state gas phase Calmodulin and Beta-2-microglobulin following post translational modification. Briefly, proteins were deamidated (conversion of Asparagine to Aspartic Acid or Iso-Asp via amine group removal and water addition) in NaOH at a pH of 9 overnight before being desalted, purified and resuspended in 10mM Ammonium Acetate. The previously mentioned mass spectrometry methods were then carried out using nanospray alongside non deamidated controls. Deamidation was selected as a modification primarily because it occurs frequently with protein aging in vivo and also because it involves the conversion of an uncharged residue (Asn) to a negatively charged one (Asp) making it more likely for the modification to have an impact on local and global structure. Ion mobility is a robust method for this type of study and results from the topdown FTICRMS methods will be compared with this data to assess the extra structural information they can provide over solely utilising ion mobility.

Development of ^{18}F-labelled phosphonium cations as PET imaging agents of the mitochondrial function during apoptosis

Anna Haslop[1]

Supervisors: Nicholas Long[2], Christophe Plisson[3], Antony Gee[4]

[1] *Imperial College, Department of Chemistry, London and GSK*

[2] *Imperial College, Department of Chemistry, London*

[3] *Imanova Ltd, Hammersmith Hospital, London*

[4] *King's College, Division of Imaging Sciences, St. Thomas' Hospital, London*

The discovery that mitochondria are involved in the early stages of apoptosis has opened a whole new area for researchers to target.[1] The depletion of the mitochondrial inner membrane potential is found to be an initial step and a point of no return for apoptosis. Compounds such as lipophilic cations that are selectively taken-up into the mitochondria owing to this potential lend themselves to biomolecular imaging. Previous literature reports state that phosphonium salts have shown this dependency but are limited due to poor radiochemical yields or complex multi-steps syntheses.[2] The aim of this work was to efficiently synthesise a library of radiolabelled phosphonium cations via 'Click' chemistry and analyse their suitability to act as imaging probes for apoptosis by measuring their selective and membrane potential dependent uptake into the mitochondria. Phosphonium salts bearing a fluorine-labelled 1,2,3-triazole moiety were prepared via the 'Click' reaction between [^{18}F] fluoroethyl azide and phosphonium salts bearing terminal alkynes. The ^{18}F labelled azide was prepared on an Advion MinuteMan microfluidic platform and purified by distillation prior to coupling with the alkyne precursors. The chain length between the phosphorus center and the triazole, and the functional groups on the phenyl rings were varied in order to investigate the effect on the reaction rates, the lipophilicity of the compound and the ability to be selectively taken up into the mitochondria.

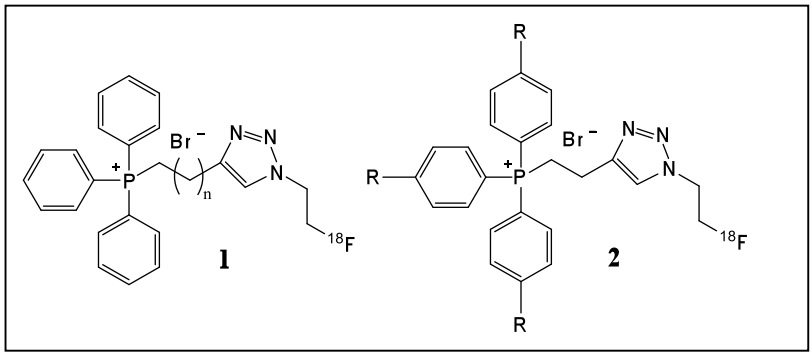


Fig.1. Structures of ^{18}F labelled phosphonium cations

[1] V. Rostovtsev, K. Sharpless, L. Green, V. Fokin, *Angewandte Chemie-International Edition,* 2002, **41**, 2596-2599.

[2] V. Ravert and I Madar, *Journal of Labelled Compounds and Radiopharmaceuticals*, 2004, **47**, 469-476.

Molecular dynamics of receptor tyrosine kinase transmembrane protein domain

Anthony Nash[1]

Supervisors: Dr. Rebecca Notman[2], Dr. Ann Dixon[3]
[1]*MOAC, University of Warwick*
[2]*Department of Chemistry with the Centre for Scientific Computing, University of Warwick*
[3]*Chemical Biology, Department of Chemistry, University of Warwick*

Approximately 33% of the human genome encodes helical transmembrane (membrane spanning) proteins (TM proteins). Yet despite being abundant in nature and the crucial role they play in cell function, revealing the protein's structure and function continues to prove problematic. Receptor tyrosine kinases play an important role in cell proliferation. A single hydrophobic to hydrophilic mutation to their TM amino-acid sequence alters the behaviour (see Fig. 1) and has been linked to certain cancers. Using Molecular Dynamics (MD) we have started to investigate how a single amino-acid mutation in the TM domain of an RTK affects its ability to function correctly. We present preliminary atomistic and coarse-grained results of the structural characteristics between wildtype and oncogenic single peptides and dimers.

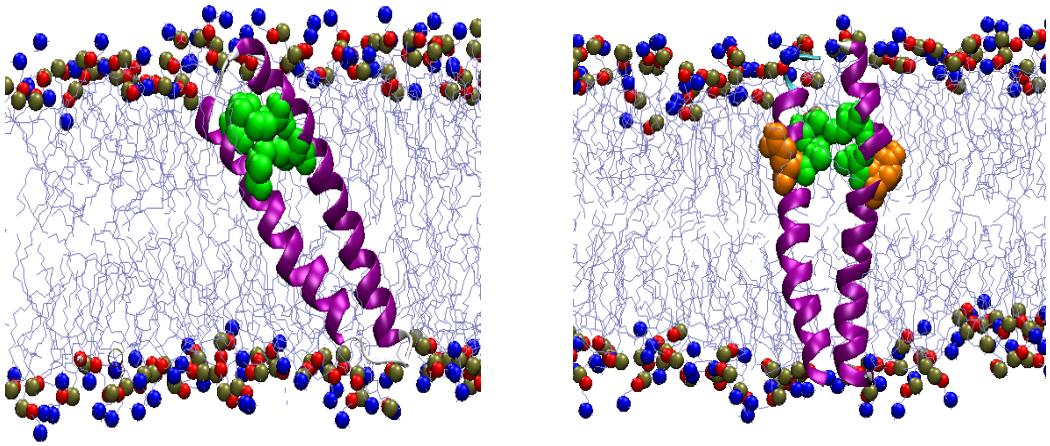


Fig.1 Left: Wild type TM dimer, *Right:* Oncogenic TM dimer. With the inclusion of the oncogenic residue, the structural dynamics differ considerably. Green space-filling spheres represent IxxxV interfacial motif, and orange space-filling spheres represent the hydrophilic substitution. Water has been omitted for clarity.

Structural and functional characterization of potential G-quadruplex motifs from the proximal promoter of GATA4 gene

Beata Klejevskaja-Borrie[1]

Supervisors: Prof. R. Vilar [2], Dr L. Ying[3], Prof. M.D. Schneider[3]

[1] *Institute of Chemical Biology, Imperial College London*

[2] *Department of Chemistry, Imperial College London*

[3] *National Lung & Heart Institute, Imperial College London*

Metabolically active DNA can in addition to its well known left-handed double helix structure (B-DNA) adopt alternative conformations which could potentially play an important role in many gene regulatory processes. One such non-canonical DNA structure is G-quadruplex, which forms from guanine-rich DNA sequences due to the ability of guanines to form tetrads by hydrogen bonding of Watson-Crick and Hoogsten faces. Bioinformatics studies have shown that potential G-quadruplex DNA sequences (PQSs) are distributed non-randomly in eukaryotic and prokaryotic genomes and are co-localized with gene regulatory elements[1]. Over 40% of human gene promoters contain at least one PQS which suggests that G-quadruplexes are of biological importance[2]. The focus of my project is structural and functional characterization of G-quadruplex motifs from the proximal promoter region of *GATA4* gene. GATA4 is a zinc-finger transcription factor important in the activation of many genes[3]. It was chosen as an attractive target due to its critical involvement in cardiac development as well as healthy cardiomyocyte maintenance and survival in adult heart [4]. Proximal promoter region of *GATA4* gene contains several conserved quadruplex motifs which could potentially be important regulators of *GATA4* expression [5]. We have recently confirmed the formation of a stable intramolecular *GATA4* quadruplex structure *in vitro* by circular dichroism (CD) spectroscopy and gel electrophoresis. Mutations of the GATA4 quadruplex motif (I-II) lead to downregulation of gene expression as determined by luciferase assay in HEK293T cells. This suggests that formation of G-quadruplex structure in the proximal *GATA4* promoter could aid activation of gene expression by enhancing the binding of Sp-1 transcription factor.

[1] Z. Du, Y. Zhao and N. Li, *Nucleic Acids Research*, 2009, 1-15

[2] J.L. Huppert, and S. Balasubramanian, *Nucleic Acids Research,* 2007*,* **35**, 406-413

[3] R.J.Arceci, *et al. Molecular and Cellular Biology*, 1993, **13**, 2235-2246.

[4] A.Holtzinger, and T.Evands, *Development* , 2005, **132**, 4005-4014.

[5] Y.Ohara, et al. Biol.Pharm.Bull., 2006 , **29**, 410-419.

Computational study of drug-membrane interactions

Callum Dickson[1]

Supervisors: Ian R. Gould,[1] Lula Rosso,[2] Antony D. Gee[3]

[1] *Department of Chemistry and Institute of Chemical Biology, Imperial College London, South Kensington, SW7 2AZ, United Kingdom.*

[2] *Department of Neuroscience, Imperial College London, South Kensington, SW7 2AZ, United Kingdom.*

[3] *Division of Imaging Sciences, King's College London, St Thomas' Hospital, London, SE1 7EH, United Kingdom.*

The molecular dynamics simulation of lipid bilayers allows the atomistic study of the structure and dynamics of a model cell membrane. The mixing of lipid types and introduction of cholesterol allows a more realistic cell membrane composition to be achieved.

Such a model may then be used to study drug-membrane interactions via potential of mean force calculations. These calculations reveal the free energy profile of a drug passing through such a membrane. Ultimately we hope to study the non-specific binding of drugs, specifically positron emission tomography (PET) radiotracers, to cell membranes using such methods. If a predictor of non-specific binding can be identified then this may greatly accelerate the discovery and development of new PET radiotracers.

Regulation and Dynamics of the *Plasmodium* Cell Invasion Motor: Insights from NMR

Christopher H. Douse[1]

Supervisors: Ed Tate[1,2], Ernesto Cota[1,3] and Tony Holder[4]

[1]*Institute of Chemical Biology, Imperial College London, SW7 2AZ, U.K.*
[2]*Department of Chemistry, Imperial College London, SW7 2AZ, U.K.*
[3]*Division of Molecular Biosciences, Imperial College London, SW7 2AZ, U.K.*
[4]*Division of Parasitology, MRC National Institute of Medical Research, London, NW7 1AA, U.K.*

A key event in the complex life cycle of *Plasmodium* spp., the protozoan parasites that cause malaria, is the invasion of erythrocytes by blood stages known as merozoites. The motive force required for this process is provided by a dedicated actomyosin motor consisting of an unusual myosin (MyoA) that is part of a multi-protein assembly making up the biomolecular invasion machinery. One of these proteins is Myosin Tail Interacting Protein (MTIP), which links the motor to the inner membrane of the merozoite [1].

The MTIP/MyoA complex can be reconstituted *in vitro* using peptides mimicking the C-terminal tail of MyoA [2,3], and since inhibition of the interaction *in vivo* should stall invasion and disrupt the parasitic life cycle, it has been identified as a target for the development of novel antimalarials and chemical genetic tools [3].

In this talk I will describe the application of NMR spectroscopy and other biophysical techniques in studying the MyoA binding domain of MTIP from *Plasmodium falciparum* (Fig. 1, below). In particular, I will show how these experiments have informed inhibitor development and enabled us to extract structure-function relationships concerning the regulation and dynamics of this pathologically relevant system [4].

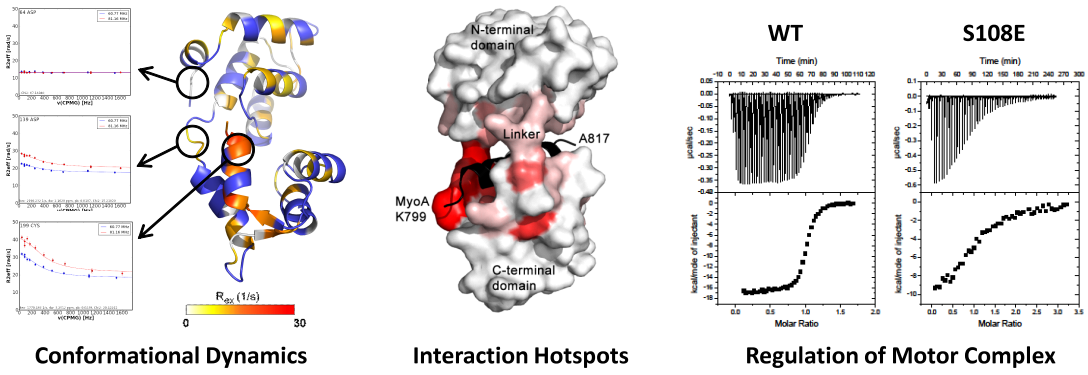


Fig. 1. Biophysical analysis of MTIP/MyoA using NMR, Crystallography and ITC

[1] J. L. Green *et al. Journal of Molecular Biology,* 2006, **355**, 933-941.
[2] J. Bosch *et al. PNAS USA,* 2006, **103**, 4832-4837.
[3] J. C. Thomas *et al. Molecular Biosystems*, 2010, **6**, 494-498.
[4] C. H. Douse *et al.,* 2012 (submitted)

Probing PI3K signalling dependent Tumour Metabolism using NMR metabolomics

Chung-Ho Lau[1]

Supervisors: Hector C Keun[1], Eric W-F Lam[2], Rudiger Woscholski[3]

[1] *Biomolecular Medicine, Department of Surgery and Cancer, Faculty of Medicine, Sir Alexander Fleming Building, Imperial College London, London, SW7 2AZ, U.K.*
[2] *Cancer Research-UK Laboratory, Department of Surgery and Cancer, Imperial College London, Hammersmith Campus, Du Cane Road, London W12 0NN, UK*
[3] *Institute of Chemical Biology and Department of Chemistry, Imperial College London, Exhibition Road, London SW7 2AZ, U.K.*

Metabolic reprogramming is a critical hallmark of cancer diseases, with Warburg effect being the best known example, and in recent years there has been a resurging interest in identifying small molecule biomarkers using high throughput metabolomic platforms as the importance of environmental risk factors is increasingly recognised. NMR technique has proven to be a particular popular approach in monitoring metabolite profiles as analysis can be performed on numerous sample types, ranging from cell lysates to human biofluids with minimal sample preparation required.

In this project we aim to exploit NMR to better understand how PI3K signalling status impacts on tumour cell metabolism using chemical inhibitors of the pathway in cell culture models. The data we acquired so far with PI3K inhibitor LY294002 and mTOR inhibitor Rapamycin from two breast cell lines indicates metabolic responses, including in glycolysis and choline metabolism, can potentially be used to identify pathway inhibitor activity and/or responses from PI3K dependent genetic intervention.

Expression of genes regulating mitochondrial fusion and fission in human adipose tissue are influenced by adiposity and bariatric surgery

Ciara McCarthy[1]

Supervisors: Philip G. McTernan[2] and Gyanendra Tripathi[2]
[1]*MOAC Doctoral Training Centre, University of Warwick*
[2]*Warwick Medical School, University of Warwick*

Mitochondria are essential for synthesising ATP required for cellular metabolism. In response to changes in their cellular environment, mitochondria are able to alter their morphology and abundance through the balance of "fusion" and "fission" events. The aim of this study was to profile the expression of mitochondrial genes in the abdominal subcutaneous (AbSc) adipose tissue (AT) of lean, obese and Type 2 Diabetes Mellitus (T2DM) individuals and determine if bariatric surgery could modulate this gene expression.

Methods: AbSc AT from 12 Caucasian women, aged 38-60 yrs with T2DM and BMI >35 kg/m2, who underwent restrictive or malabsorptive bariatric surgery was collected at the time of surgery and 30 days post-surgery by biopsy. AbSc AT from two control groups of non-diabetic females was also included in the study; overweight/obese: n=11 with BMI>27.5 kg/m2, aged 35-60 and lean, n=6 with BMI<25.0 kg/m2 aged 40-50. Expression of genes was measured by qRT-PCR.

Results: Overweight/obese individuals had a higher expression profile of both fission (*DRP1*; 3 fold and *Fis1* 1.3 fold) and fusion genes (*MFN2*; 1.5 fold, *OPA1*; 7 fold and *FOXC2*; 2 fold) compared to lean (n=11, $p<0.05$). With the exception of *DRP1* and *FOXC2* (2 fold higher and lower respectively), pre-bariatric T2DM subjects had a gene expression profile similar to that of lean individuals. Following bariatric surgery, expression of both fusion (*FOXC2*, *MFN2* and *OPA1*) and fission genes (*DRP1* and *FIS1*) (n=12, $p<0.05$) significantly increased.

Conclusions: This study highlights differences in the expression profile of genes regulating mitochondrial fusion and fission in AT between lean, obese and T2DM individuals. Expression of both genes regulating fusion and fission processes were higher in AT of obese compared to lean subjects. Following bariatric surgery, the expression of these genes was up-regulated in the AT. Future studies examining the effects of 15% weight-loss are planned.

Moving and Staying Together: The Role of Visual Projection in Flocking Animals

Daniel Pearce[1]

Supervisors:Matthew Turner[2], Kevin Moffat[3]
[1]*MOAC dept., Department of Physics, University of Warwick.*
[2]*Complexity Science, Department of Physics, University of Warwick.*
[3]*Department of Biology, University of Warwick*

Swarming is a behavioural phenomenon observed throughout the animal kingdom; flocking in birds, swarming in insects, shoaling in fish and herding in mammals. Most previous attempts at understanding this phenomenon postulate that members of a swarm allign their velocity with those of their immediate neighbours'. Such *local models* seem plausible, mainly on the grounds that it is unfeasible for an individual to follow the positions and velocities of all other members of an arbitrarily large swarm. We analyse instead the possible role of a biologically plausible *global* measurement of the swarm in which each individual observes a *projection* of the swarm. A simple class of candidate models arises naturally. We analyse these in 2D and show that they appear qualitatively compatible with experimental data. In particular the following features arise naturally: (i) anisotropic inter-bird orientational correlations (ii) super-diffusive information transfer across the swarm (iii) advanced efficiency at detecting a predator. All three of these features are observed in large flocks of starlings [1][2]. Finally our model suggests a mechanism for swarms to self-select a particular density at which the swarm is *marginally opaque*. This corresponds to a non-trivial relationship between the number of individuals in a swarm and its size. Our model therefore makes several experimentally testable predictions.

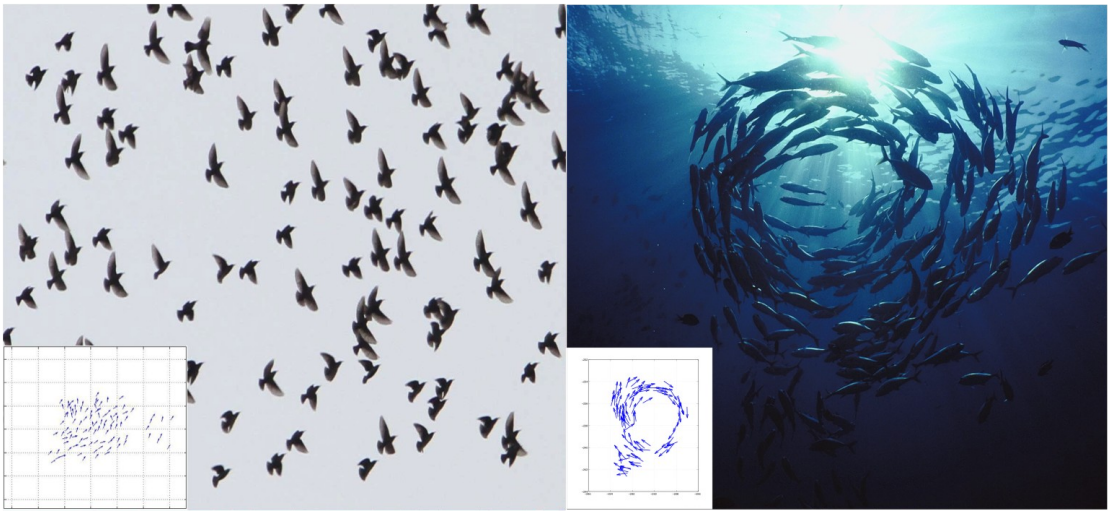


Fig.1. Distinct examples of collective animal behavour and how they can be simulated using the same algorithms (inset).

[1] Ballerini, M. *et al*. *Anim. Behav*. 2012, **76**, 201.
[2] Pitcher, T. *Anim. Behav*. 1983, **31**, 611.

The Phospholipid Interactions of Antimicrobial Peptides

David Paterson[1]

Supervisors: Professor Jon Cooper[1], Dr. Manlio Tassieri[1]

[1]*Department of Biomedical Engineering, University of Glasgow.*

Drug-resistant bacterial strains are one of the greatest challenges facing medicine; they are the leading cause of mortality from infectious agents in the developed world, killing more people annually than HIV/AIDS[1]. To combat these "superbugs", the perfect antibiotic must be highly potent, selective between prokaryotic and eukaryotic cells and immune to drug-resistance mechanisms. Members of the linear, cationic antimicrobial peptide (AMP) family display all these characteristics[2], yet their development as antibiotics has been hindered, by the lack of understanding of the peptide-lipid interactions that govern their mechanism of action. AMPs form membrane-spanning toroidal pores, composed of aggregates of lipids and peptide molecules (fig. 1), causing cell death by dissipation of chemical gradients and leakage of intracellular contents[3]. Prokaryotic and eukaryotic cellular membranes show characteristic compositional differences, which some AMPs exploit to selectively target bacterial cells, while others are non-specific and lyse both mammalian and bacterial cells. Understanding this selectivity mechanism will inform the design of potent new antibiotics, using natural AMPs as a starting point. To establish the criteria for selectivity, we will use biomimetic giant unilamellar vesicles (GUVs) as artificial biomimetic membrane systems (fig. 1), presenting a close facsimile to *in-vivo* membranes. We have developed a microfluidic platform for the investigation of AMP interactions with GUVs, where GUVs are manufactured on-chip, before being trapped within a microfabricated array (fig. 1). Using the precise control of fluid flow offered by microfluidics, we will expose the GUVs to AMPs, using fluorescent techniques to investigate the AMP-lipid interactions leading to pore formation.

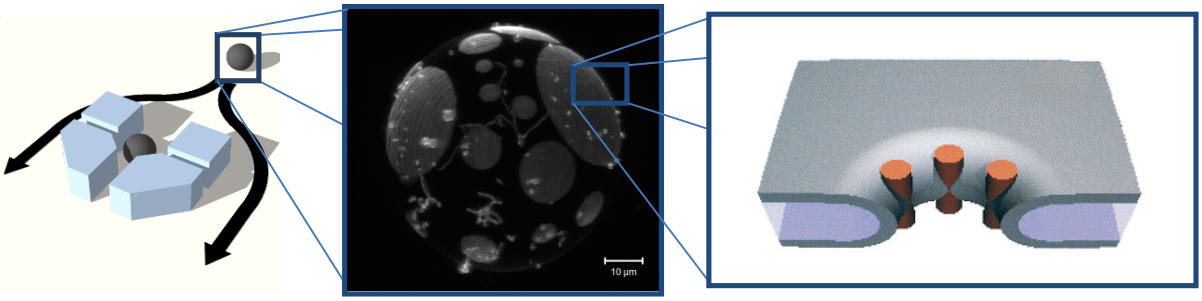


Figure 1: (left) single microfabricated GUV trap; *(centre)* 3D rendered image of biomimetic GUV obtained by confocal microscopy, with domains enriched with fluorescently tagged lipids clearly visible, representative of the lipid rafts found in-vivo; *(right)* diagram of toroidal pore, lined with both peptide (red) and lipid molecules (blue).

The pore formation kinetics in GUVs can established, by detecting the release of enclosed fluorescent markers[4][5]. The effect of membrane composition on AMP activity provides data on the lipid interactions underpinning the mechanism of action. The effects of AMP binding on existing lipidic domains are determined by confocal microscopy; disruption of *in-vivo* lipid-rafts could be a secondary affect contributing to the antibacterial action of these peptides.

Fluorescent analysis of single biomimetic GUVs, within a microfluidic device, is a novel platform for the study of AMP-lipid interactions. Data gathered using this method could potentially inform the rational design of new antibiotics, significantly impacting the field of drug discovery.

[1] F. R. DeLeo and H. F. Chambers *The Journal of Clinical Investigation* 2009 **119** (9) 2464 – 2474.
[2] G. N. Tew *et al*. *Biochimica et Biophysica Acta* 2006 **1758** 1387 – 1392.
[3] L. Yang *et al*. *Biophysical Journal* 2001 **81** 1475 – 1485.
[4] E. E. Ambroggio *et al. Biophysical Journal* 2005 **89** 1874 – 1881.
[5] Y. Tamba, H. Ariyama, V. Levadny and M. Yamazaki *J. Phys. Chem* 2010 **114** 12018 – 12026.

Towards high throughput FLIM: instrument development and applications

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Fluorescence lifetime imaging (FLIM) is a potentially powerful tool in the life sciences with a diverse range of applications, including detection of protein-protein interactions by Förster Resonance Energy Transfer (FRET)[1] and measurement of local environment parameters of endogeneous fluorescent proteins[2]. A fully automated plate reading FLIM microscope facilitates greater throughput, allowing users to gain more data per condition, and more conditions per experiment. Furthermore, building such an instrument from the ground up allows a great degree of flexibility, especially in the implementation of customised software which can be developed in close partnership with users.

A variety of biological systems are being examined using the instrument, within several different collaborations. A summary of results will be presented to showcase the versatility of the instrument in addressing biological problems.

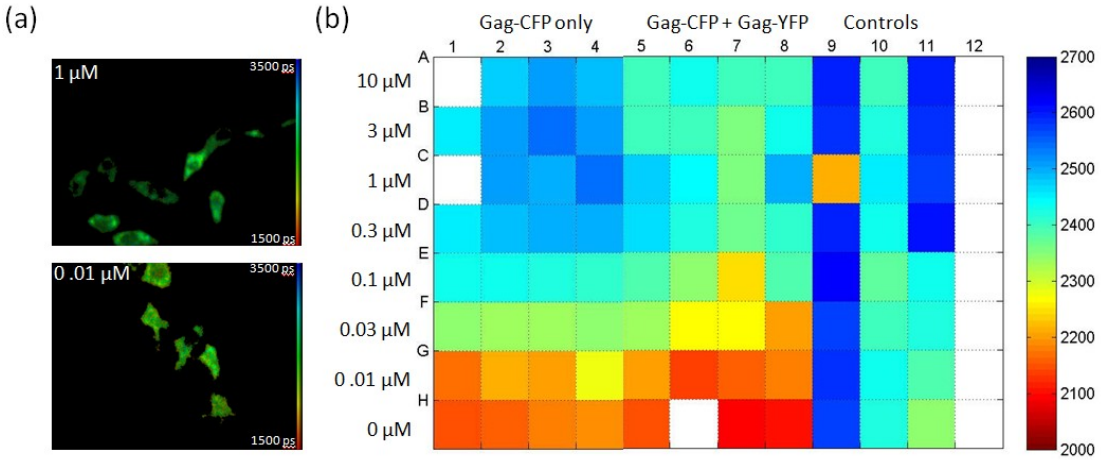

Fig.1. (a) Fluorescence lifetime images and (b) a fluorescence lifetime plate map showing changes in lifetime due to FRET between Gag-eCFP and Gag-YFP constructs involved in virus-like particle formation upon treatment with NMT inhibitor.

[1] S. Kumar *et al.*, *ChemPhysChem,* 2011, **02** (03), 609-626.

[2] J.-S. Yu *et al.*, *J.Biomed. Optics,* 2011, **16** (03), 036008.

High Temporal Resolution Tracking of Kinetochores and Spindle Poles in Mitotic HeLa Cells

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During mammalian cell division duplicated chromosomes must align along the spindle equator, there they undergo periodic-like motion between the two halves of the mitotic spindle. These movements are driven by the kinetochore (KT) which assembles on each sister chromatid and forms a dynamic linkage to the plus-end of spindle microtubules. To investigate the nature of chromosome dynamics we previously established a KT tracking assay [1], where KTs were automatically tracked and classified in 4D movies (20 x 0.5 microns in Z and 41 x 7.5 sec in t (5 min total)) of HeLa cells expressing eGFP-CENPA as a KT marker. Although our previous assay gave new insights into KT dynamics through global statistics [1] it did not give trajectories of sufficient temporal resolution to allow for more detailed classification e.g. attachment state or allow direct modelling of oscillations. Here we describe a next-generation KT tracking assay that provides unprecedented spaciotemporal resolution of both KT and spindle pole (SP) dynamics by using the same computational methods on cells that also express eGFP-Centrin as a SP marker. Using fast spinning disk confocal microscopy we have been able to achieve a temporal resolution of 2 sec per frame for 5 min without any severe photobleaching or affecting mitotic progression. Each frame consists of 25 x 0.5 microns in Z. Our latest data reveal how the mitotic spindle has a damping system to allow normal KT movements. Moreover, we can observe KTs in multiple distinct movement states including "oscillation" and "stall" phases. We are currently using these datasets to build new mathematical models of KT dynamics.

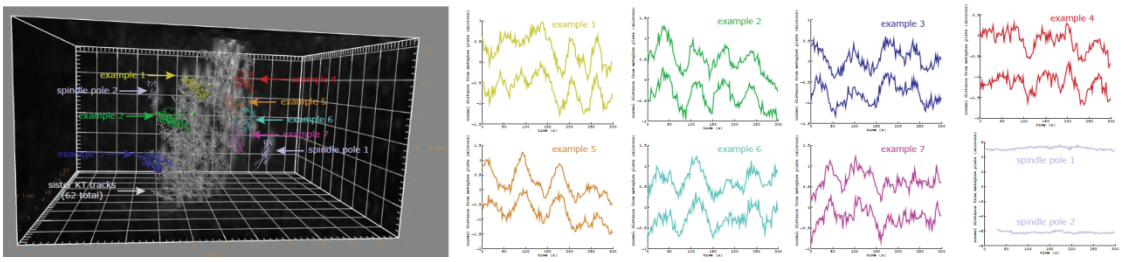

Fig. 1. Tracking results overlaid with a raw frame. Seven kinetochore pair example trajectories plus the spindle pole trajectories are shown (as normal distance from the metaphase plate over time).

[1] K. Jaqaman *et al. J. Cell Biol*, 2010, **188** (5), 665–679

Mechanisms of Microbubble Interactions with Activated versus Non-Activated Vasculature

Fairuzeta Ja'afar[1,2]

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Microbubbles (MBs) are ultrasound contrast agents, comprising of small (typically 2-3 μm in diameter) gas voids, stabilised by a biocompatible shell, usually made up of a lipid monolayer, protein or polymer, and suspended in aqueous dispersions (see Fig. 1). Their clinical use is widely established, reflected by the availability of commercial MB agents. However, it has been found that commercial MBs, although non-targeted, stick to sites of inflammation, causing them to persist in the vasculature.[1] Whereas a number of potential initiators and mechanism(s) have been proposed as suitable explanations for this non-targeted MB retention in the vasculature, much uncertainty remains about how these vascular cues influence their behaviour.[2][3] In this study, we evaluated the binding differentials of various commercial MBs (SonoVue™, Optison™ and Definity™/Luminity™) and the experimental agent BR38, with a model inflamed (activated) and normal (non-activated) vasculature *in vitro*. We employed human umbilical vein endothelial cells (HUVECs) and observed MB binding using brightfield microscopy under physiological flow conditions. We then examined the role of MB surface charge on HUVECs/MBs binding affinities using a combination of laser Doppler velocimetry (LDV) and phase analysis light scattering (PALS) on a Zetasizer Nano Z. We found a 3-fold and 1-fold approximate increase in the number densities of Optison™ and SonoVue™ MBs adherent respectively, on activated versus non-activated HUVECs ($p<0.05$), indicating a surface component to non-targeted MB binding to HUVECs. We found no correlation between MB surface charge and binding affinity. However, we feel that current use of LDV/PALS is unsuitable for MB surface charge characterisation.

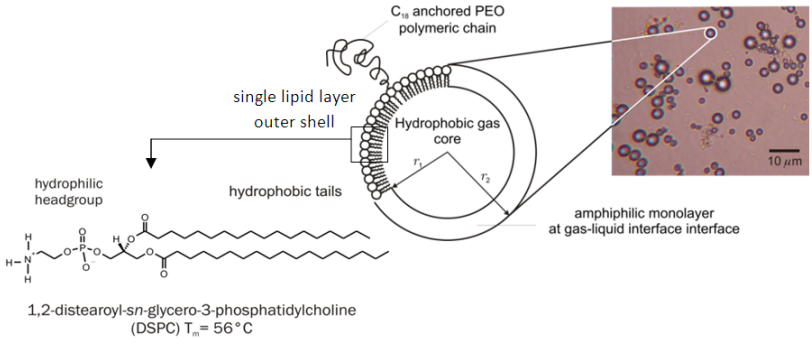

Fig.1. Typical microbubble construct: Hydrophobic gas core encapsulated by a lipid monolayer suspended in aqueous dispersion.

[1] D.R.Owen, J.Shalhoub, S.Miller, T.Gauthier et.al., *Radiology*, 2010, **02** (255), 638-644.
[2] J.R.Lindner, M.P.Coggins, S.Kaul et.al., *Circulation*, 2000, **101**, 668-675.
[3] N.G. Fisher, J.P.Christiansen, A. Klibanov et.al., *Journal of the American College of Cardiology*, 2002, **40** (4), 811-819.

Photorealistic Avatars

Fintan Nagle[1]

Supervisors:Alan Johnston[2], Peter McOwan[3],
[1]*UCL CoMPLEX*
[2]*First Supervisor affilitaion 1, First Supervisor affilitaion 2*
[3]*UCL*
[4]*Queen Mary UoL*

As well as recognising static facial expression, the human brain is very good at processing dynamic expressions such as the smile of a good friend. But how is dynamic expression processed differently from static expression, and what neural and functional commonalities do the two processes share? My research attempts to measure recognition based solely on dynamic expression. This is done by taking a portrait video clip of one person and projecting their facial motion on to a photorealistic avatar (as if the avatar were copying their motions). Recognition power on clips of celebrities will then be evaluated. My poster and talk will mainly cover the technology behind the expression transfer procedure. We work using the multidimensional face space paradigm, with principal component analysis for data compression.

Fig.1. Generated images with various degrees of caricaturing.

HIV-1 protease: the rigidity perspective

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Supervisors: Stephen Wells[2], Robert Freedman[3], Rudolf Römer[2]

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[3]*Department of Life Sciences, University of Warwick*

HIV-1 protease is a key drug target due to its role in the life-cycle of the HIV-1 virus. There are more than 200 high resolution (≤ 2 Å) X-ray crystal structures of the enzyme in complex with a variety of ligands. We have carried out a broad study of these structures using the rigidity analysis software FIRST. This approach allows us to make inferences about the effect of ligand binding upon the rigidity of the protein. The protease inhibitors currently used as part of antiretroviral treatments can be split into two categories, which may offer an explanation for the efficacy of particular combination therapies.

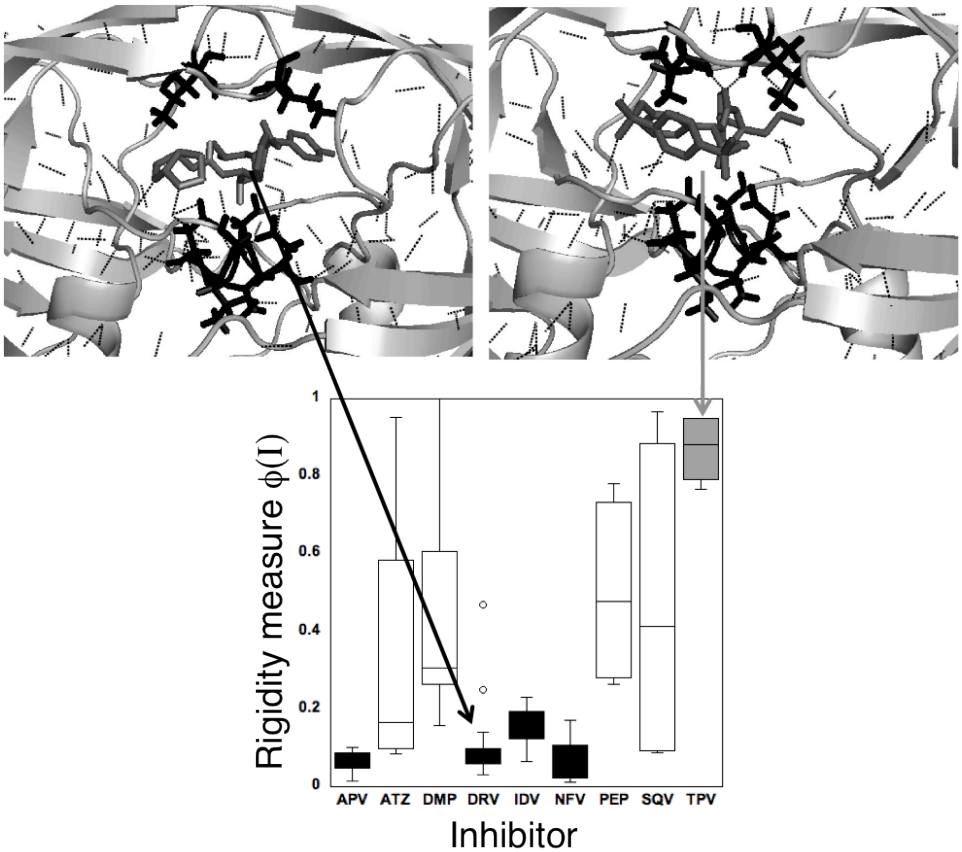

Fig.1. Structures crystallised with the inhibitor Darunavir have consistently low values of Φ(I), which measures the impact of the inhibitor upon the rigidity of the flaps. Contrastingly, structures crystallised with Tipranavir have consistently high values of Φ(I).

Design of Inhibitors for p97-cofactor Binding and High-Throughput Assay Development

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p97 is a highly abundant protein in human cells and is essential for many forms of life. It's putative mechanism of action is the binding various cofactors and subsequent transfer of energy from ATP hydrolysis, through the cofactor, to substrate proteins. It is the binding to these cofactors, predominantly through the p97 N-terminal domain, that mediates the many functions of p97 (Fig 1) [1][2]. The subsequent unfolding or degradation of the substrate proteins is known to regulate a diverse number of processes. The malfunction of p97 in many of these processes has been linked to a range of diseases including Alzheimer's disease, Huntington's disease, Cancer and Cystic Fibrosis [3]. However not all of the processes in which p97 takes place are known and the exact function and mode of action of this protein is still under debate.

To supplement the genetics studies currently underway, exogenous ligands will be designed to interfere with p97-cofactor binding with the effect of these ligands being studied *in vivo*. This is known as chemical genetics. Furthermore, p97 inhibition is thought to be a valid approach to treating a number of the diseases mentioned above.

Analysis of the "hot-spot" interactions between p97 N-domain and the UBX-domain on p47, one of the adaptors of p97, has allowed the design of a range of novel inhibitors of p97-cofactor binding. [1]

The design and development of a high throughput *in vitro* assay based on Förster Resonance Energy Transfer (FRET) is currently on-going.

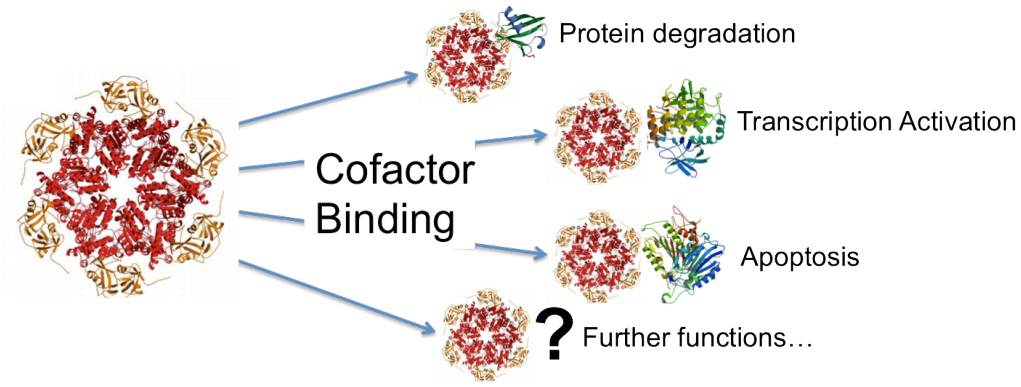

Fig.1. The binding of p97 to various cofactors mediates its various cellular functions.

[1] Q. Wang, *et al. Journal of Structural Biology* 2004, **146**, 44.
[2] R. M. Dai, *et al. The Journal of biological chemistry* 1998, **273**, 3562.
[3] N. Vij, *et al. Journal of Cellular and Molecular Medicine* 2008, **12**, 2511.

Investigating how neuromodulations alter neurovascular coupling using information-theoretic generative embedding

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[2]*Doctoral Training Centre, University of Oxford*
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The majority of cognitive psychology studies use blood oxygen level dependent (BOLD) functional magnetic resonance imaging (fMRI) to image brain function as it is non-invasive and boasts high temporal resolution. However, the BOLD signal reflects the hemodynamic response to the neuronal activity we are interested in and their coupling (neurovascular coupling), especially during neuromodulation (pathological or pharmacological), is not well understood. This lack of understanding may mean that in some cases the models of neurovascular coupling used to estimate neuronal activity from BOLD signals are incorrect, resulting in incorrect brain regions being identified as significantly activated or deactivated in response to a stimulus.

I report an information-theoretic generative embedding framework for quantifying changes in the relationships of neuronal activity and hemodynamics under different neuromodulations. Generative embedding involves drawing on available knowledge of the physical processes generating a timeseries in order to decrease its dimensions to a set of mechanistically interpretable parameters, which are then embedded in sophisticated statistics such as information-theoretic measures of dependence. Principles from information theory were chosen to interrogate the effects of different neuromodulations on neurovascular coupling because they provide a comprehensive and model-free way to analyse relationships. Namely, the mutual information between the generative parameters of a neural imaging timeseries and the different neuromodulations under which those timeseries were acquired quantifies the extent to which the biophysical processes generating the timeseries are different under the different neuromodulations. The maximal information coefficient extends this analysis to quantify the differences in the strengths of the couplings of the generative parameters of concurrently acquired signals of neuronal activity and hemodynamics under the different neuromodulations in an equitable way. In doing this, conclusions can be drawn about the susceptibility of the couplings of neuronal and hemodynamic processes to the different neuromodulations, irrespective of what those couplings are.

EVV 2DIR Spectroscopy: A Novel Tool to Investigate Protein Phosphorylation and Charge Effects

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Supervisors: Prof David Klug[1,2], Dr David Mann[1]

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2 The Institute of Cancer Research, Chester Beatty Laboratories, 237 Fulham Road, London SW3 6JB, UK

Protein phosphorylation is the most widespread and arguably the most important type of PTM. [1] The phosphorylation of one or more proteins of cells often regulates protein-protein interactions that in turn regulate most aspects of cellular physiology. Thus, in order to understand how different cell processes are controlled, it is necessary to learn how phosphorylation events are regulated.

The novel Electron-Vibration-Vibration Two-Dimensional InfraRed (EVV 2DIR) technique is a non-linear spectroscopic method that measures the vibrational coupling spectrum in a way analogous to the measurement of spin couplings by 2D NMR methods. This qualified protein fingerprinting strategy also has the ability to provide protein structural information and also detect intermolecular interactions, which is useful for studying protein-protein and protein-ligand interactions. The EVV 2DIR technique can provide added value over established proteomic methods in the study of post-translational modifications, specifically the absolute quantification of phosphorylation levels, something difficult to achieve with mass spectrometry.

Small tyrosine-containing peptides have demonstrated a linear dependence of cross-peak intensity on tyrosine phosphorylation. Further investigation with phosphorylated serine and threonine analogues have revealed that the linear dependence could be due to the charge on the phosphate group.

[1] *P*. Picotti, B. Bodenmiller, L. N. Mueller, B. Domon, R. Aebersold, *Cell,* 2009, **138**, 795 - 806

Protein Structure Prediction and Energy Landscape Exploration

Nikolas Burkoff[1]

Supervisor: David Wild[1]

[1]*Warwick Systems Biology*

In this talk I will be describing the method we have developed to predict protein structure. Our method involves two separate stages: firstly, the prediction of protein secondary structure and beta-sheet contacts and secondly, incorporating this information into a coarse-grained physical model to fold the protein [1].

I will also be describing how our coarse-grained model can be used, in conjunction with nested sampling, to explore the energy landscapes of protein folding simulations [2]. Nested sampling is a Bayesian sampling technique developed to explore probability distributions localized in an exponentially small area of the parameter space [3]. The algorithm provides both posterior samples and an estimate of the evidence (marginal likelihood) of the model. A topological analysis of the posterior samples can be performed to produce energy landscape charts, which give a high-level description of the potential energy surface for the protein folding simulations. These charts provide qualitative insights into both the folding process and the nature of the model and force field used, see Fig. 1. The nested sampling algorithm also provides an efficient way to calculate free energies and the expectation value of thermodynamic observables at any temperature, through a simple post processing of the output.

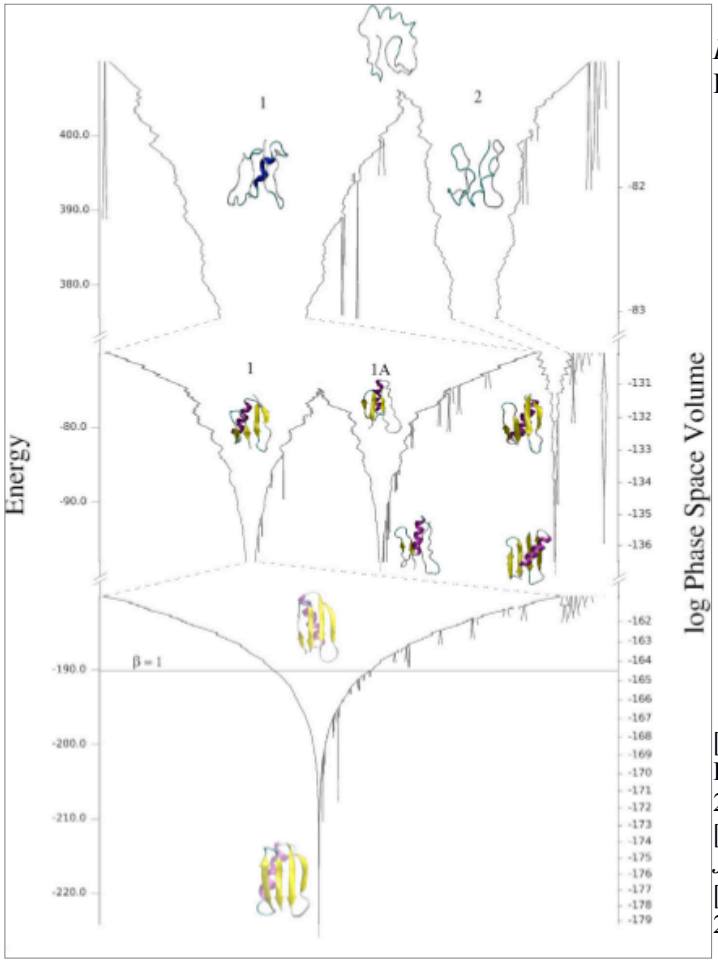

Fig.1. The energy landscape of Protein G [2].

[1] A. A. Podtelezhnikov, and D. L. Wild. *Source Code Biol. Med.* 2008 **3**, 12.

[2] N. S. Burkoff *et al. Biophysical Journal,* 2012, **102**, 878-86

[3] J. Skilling, *J. Bayesian Anal.* 2006 **1**, 833-860.

Peptidomimetic Approaches to Mimicking Antifreeze Protein Function.

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Supervisors:Matt. I. Gibson[2], Daniel. Mitchell[3] & Manu.Vatish[3]

[1]*Molecular Organisation and Assembly of Cells Doctoral Training Centre, University of Warwick, Coventry, CV4 7 AL, UK.*
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There is a real need for improvements in the cryopreservation of biological materials. Ice recrystallisation during freeze/thawing of cells is a major contributor to cell damage during cryopreservation. Current techniques often use vitrifying cryoprotectants at high concentrations that require rapid freeze and thawing rates. High concentrations of vitrifying cryoprotectants also make it difficult for rapid removal post-thawing and therefore have serious limitations in a clinical setting.

Antifreeze(glyco) proteins (AFGPs) are a naturally occurring class of proteins found in cold-acclimatised species that have a simple polymeric structure[1]. AFGPs display a strong recrystallisation inhibition (RI) activity. Previous work has demonstrated their application as cryoprotectants is limited due to their secondary effect of dynamic ice shaping (DIS) that increases cell damage[2]. Furthermore it is unviable to isolate AFGPs from primary sources in appreciable amounts and expression in recombinant systems has had limited success so far.

We have developed several biocompatible peptidomimetic molecules which have comparable RI activity to AFGPs without significant DIS effects and are investigating their use as low concentration cryoprotectants in numerous cell types. Future work will continue to explore the link between RI and cryopreservation allowing the targeted design of improved peptidomimetic molecules.

[1] M.I.Gibson., *Polym. Chem,* 2010, **1**, 1141-1152.

[2] J.F Carpenter and T.N. Hansen., *Proc. Nat. Acad. Sci* , 1992, **89**, 8953-8957.

Interactions of Patchy Membranes with Nanoparticles

Sang Young Noh[1]

Supervisors: Rebecca Notman[2], David Cheung[2], Stephan Bonn[3]
[1]*MOAC Doctoral Training Centre, University of Warwick*
[2]*Centre for Scientific Computing, University of Warwick*
[3]*Department of Chemistry, University of Warwick*

The self-assembly of colloidal particles shows a promising route to constructing highly ordered novel materials. Recent scientific literature has identified the formation of self- assembled "Janus" vesicle in a mixture of neutral and anionic amphiphiles, induced by insertion of a metal cation [1]. This suggests that self-assembly in a system of mixed charge is possible and thermodynamically stable. We are primarily interested in inducing this kind of self-assembly in a amphiphilic bilayer using nanoparticles, with the aim of extrapolating this concept to in practical uses such as drug delivery. We are currently modelling syn- thetic polymer bilayers in water using course-grained molecular dynamics with the LAMMPS molecular dynamics simulator. Initial work focused on the assembly and characterisation of single-component polymers with respect to the length of the hydrophilic head group. As a result of this we showed that the model surfactant polyoxyethylene (C12E2) forms sta- ble bilayers and identified this as a candidate for further study. To incorporate a mixture of species we have modified the interaction strength between half of the polymers and the remaining polyoxyethylenes to 90%, 75% and 50% of the interaction energy between two polyoxyethylene molecules, and we are investigating the phase separation as a function of this attractive interaction. The modified polymers are designed to be simple mimics of per- fluorocarbons and it is planned to extend this work by developing coarse-grained parameters for the perfluorocabons. This will enable us to make comparisons with a parallel experi-mental programme. Currently we are modelling the insertion of a gold nanoparticle into these mixed bilayers with the aim of simulating nanoparticle-induced phase separation. We designed the course-grained (CG) interactions between a polyoxyethylene and 1nm, 1.5 nm and 2 nm radius gold nanoparticles [2]. The trajectory of the nanoparticle going through a polyoxyethylene bilayer has been studied using steered molecular dynamics and umbrella sampling methods. The next step is to design a ligand functionalised nanoparticle with an ionic and neutral ligand as it would be in an experimental environment.

[1] D. A. Christian *et al.Nature Materials*, 2009, **8**, 843-849.
[2] H. Heinz *et al. J. Phys. Chem. C*, 2008, **112***,* 17281-17290.

FLIM-FRET imaging of cell signalling in chemotaxis

Sean Warren[1]

Supervisors:Prof. Paul French[2], Dr. Matilda Katan[3], Dr. Christopher Dunsby[2], Prof Mark Neil[2]

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2 Photonics Group, Department of Physics, Imperial College London, London SW7 2AZ
3 Department of Structural and Molecular Biology, University College London, WC1E 6BT

Cell motility plays an important role in development, immune response and metastasis. Several classes of signalling molecules including enzymes involved in turnover and modification of phosphoinositides (PtdIns) [1] and components of signalling networks controlling Rho GTP-ases [2] play key roles in these processes. Fluorescence lifetime imaging (FLIM) of Förster resonant energy transfer (FRET) based biosensors has emerged as a powerful tool for studying the spatial and temporal activation of proteins involved in signalling processes in live cells.

We demonstrate a system for timelapse FLIM-FRET biosensor imaging of cells in the presence of a gradient of the chemoattractant PDGF created by perfusion from a micropipette. We use a Nipkow spinning disk system combined with a gated optical intensifier to capture time resolved fluorescence images in ~5-10 seconds with low photobleaching.

In particular we have imaged Rac1 activation and IP3 concentration using modified versions of the FLAIR [3] and LIBRA [4] sensors respectively optimised for FLIM and show their localised distributions in response to a directional stimulus.

To analyse the FLIM data we have developed a new package for global analysis of time and polarisation resolved datasets. We employ a modified variable projection algorithm based on the approach of Goulb et. al. [5] to allow efficient global analysis of large (~100s images) datasets with relatively modest CPU and memory requirements. We apply corrections for incomplete decays, and instrument response functions (IRF) collected with a reference dye rather than a true scatter IRF. We demonstrate that this allows two separate lifetimes to be resolved in highly photon limited FRET data with low gate numbers and the fractional contribution at each pixel to be determined.

[1] Kolsch, V., Charest, P. G., and Firtel, R. A. (2008) J Cell Sci 121, 551-559
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[3] Kraynov, V.S., Chamberlain, C., Bokoch, G.M., Schwartz, M.A., Slabaugh, S., Hahn, K.M. (2000) Scuence 209(5490), 333-337
[4] Tanimura, A., Nezu, A., Morita, T., Turner, R.J., Tojyo, Y. (2004) J Biol Chem. 279(37), 38095-38098.
[5] Golub, G, Pereyra, V, (2003) Inverse Problems 19(2), R1-R26

Development of new molecules and affinity tags that interact selectively with G-quadruplex DNA

Verity Stafford[1,2]

Supervisors: Professor Ramon Vilar[1], Dr David Mann[2]

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Over the past few years, G-quadruplex DNA has been established as a potential target for anti-cancer drugs. Stabilisation of quadruplex DNA in the telomeric region is thought to inhibit telomerase, an enzyme overexpressed in cancerous cells and related to cell proliferation[1]. Furthermore the formation of quadruplexes in the promoter region of certain oncogenes (such as c-myc) is thought to play an important role in regulating their expression[2]. Therefore the development of small molecules with the ability to interact selectively with quadruplex DNA is receiving increasing attention. In particular metal complexes provide a novel approach for targeting quadruplex DNA[3,4].

A family of metal complexes have been prepared possessing a terpyridine core capable of π-π stacking with quadruplex DNA and a cyclen based side arm to provide additional interactions with the loop, grooves and phosphate backbone. Different metals were used to synthesise di-metal complexes, both homo- and hetero- metallic in nature. By chelating different metals to the terpyridine and cyclen modalities, different parts of the quadruplex scaffold were favourably targeted. Metal complex-DNA interactions were studied using a number of well established biophysical techniques: Fluorescence Intercalator Displacement assay, UV-vis and Circular Dichroism spectroscopy. Several of the compounds were found to bind with high affinity for quadruplex DNA.

In addition, a family of metal salphen complexes attached to solid supports have been prepared. These affinity beads have been successfully used to mediate the selective isolation of labelled G-quadruplex DNA when in competition with duplex DNA. The complexes displayed different levels of affinity and selectivity depending on the metal(II) ion used. Current work is aimed at using the affinity beads have to isolate Htelo DNA in the presence of varying amounts of cell lysates (U2OS cancerous cells).

[1]. N. W. Kim, M. A. Piatyszek, K. R. Prowse, C. B. Harley, M. D. West, P. L. Ho, G. M. Coviello, W. E. Wright, S. L. Weinrich and J. W. Shay, *Science*, (1994), **266**, 2011-2015.

[2]. A. Rangan, O. Y. Fedoroff and L. H. Hurley, *J. Biol. Chem.*, (2001), **276**, 4640-4646.

[3]. S. N. Georgiades, N. H. Abd Karim, K. Suntharalingam and R. Vilar, *Angew. Chem. Int. Ed.*, (2010), **49**, 4020

[4]. K. Suntharalingam, D. Gupta, P. J. Sanz Miguel, B. Lippert and R. Vilar, *Chem. Eur. J.*, (2010), **16**, 3613

Globular protein structures from Circular Dichroism using a neural network

Vincent Hall[1]

Supervisors: Alison Rodger[2], Evor Hines[3]

[1]*Vincent Hall MOAC, Chemistry, Engineering, University of Warwick*
[2]*MOAC, Chemistry, University of Warwick*
[3]*Engineering, University of Warwick*

Circular dichroism (CD) spectroscopy can be used for quick, easy-to-obtain data to determine the secondary structures of proteins, probe their interactions with their environment, and to aid drug discovery. Circular dichroism uses circularly polarised light to excite atoms in the proteins, they then emit light at specific wavelengths. Proteins absorb left- and right-circularly polarised light differently; this provides information about the protein secondary structure. However, the interpretation of the spectra, which are plots of absorbance of light against wavelength, can be difficult, requiring an expert. To make this much easier, software packages have been developed to recognise patterns in the data and give secondary structure estimates, see Fig. 1. This talk looks at 'SSNN', a newly developed self-organising map (SOM) [1] neural network written by the authors. It is currently in the testing and optimising stage – being compared with similar programs for finding protein secondary structure, including the code written by the authors of [2]. SSNN predicts structures of globular proteins, currently no programs can predict secondary structure for trans-membrane proteins or peptides; it should be easy to adapt SSNN to this task given a good data set, due to the neural network nature of the software, which is highly adaptable. Another extension of the SOM would be to combine data from different methods such as infrared and Raman spectroscopies with CD, to get a more complete view of the protein or chiral molecule in question.

keywords: Circular Dichroism, Self Organising Map, K2d, protein secondary structure, intelligent systems

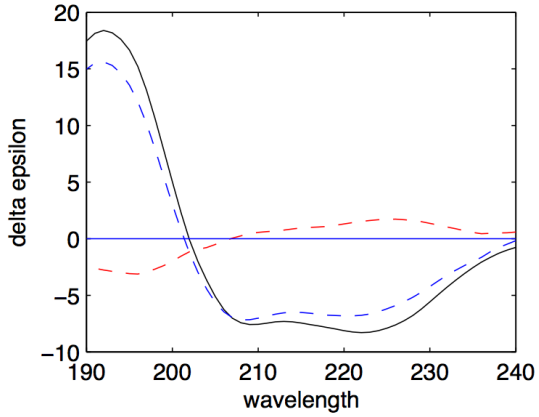

Fig.1. Example plot of myoglobin, real in black, predicted by SSNN in blue, error in red.

[1] T. Kohonen, *Biological Cybernetics,* 1982, **43**, 59-69
[2] M. Andrade. *et al., Protein Engineering, 1993* **6**, 4 383-390

Poster Presentations

1. Alex Savell
Aberration Correction in Super-Resolving 3D-STED Microscopy of Lymphocyte Interactions

2. Andrea Dimitracopoulos
Modelling microtubule-cortex interactions to understand the role of cell geometry in spindle morphogenesis

3. Andy Bell
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4. Audrey Plaquin-Chan
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5. Ben Miles
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6. Ben Fitton
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7. Cameron Fyfe
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8. Caroline Montgomery
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9. Claire Dow
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10. Charlotte Strandkvist
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11. Chris McDonald
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12. Chrissie Waddington
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13. Emmanouil Protonotarios
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14. Federico Garza de Leon
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15. Fintan Nagle
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19. Janine Symonds
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25. Matthew Thomas
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26. Michael Epstein
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29. Nitipol Srimongkolpithak
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38. Sarah-Jane Richards
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39. Snezhana Akpunarlieva
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40. Sonja Lehtinen
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41. Steve Norton
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44. Tharindi Hapuarachchi
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48. William Pitchford
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