eastbio

the East of Scotland Bioscience Doctoral Training Partnership

BBSRC bioscience for the future

UK Research and Innovation

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Welcome to the EASTBIO Annual Symposium 2019

A very warm welcome to attendees at the 2019 Annual Symposium of the BBSRC-funded EASTBIO Doctoral Training Partnership. The Annual Symposium represents one of the highlights in the EASTBIO calendar.

The theme of this year's conference is 'Bioscience Research: To Biology and Beyond!' The two-day Symposium brings together guest speakers and four cohorts of our PhD students to discuss the broad range of interdisciplinary research conducted across the partnership spanning from bioscience for health to biotechnology and food security.

We hope you will enjoy the proceedings!

Dr Edgar Huitema

School of Life Sciences, University of Dundee

On behalf of the EASTBIO Management Group

& the Symposium Organising Committee

EASTBIO ANNUAL RESEARCH SYMPOSIUM: TO BIOLOGY AND BEYOND!
University of Dundee, Dalhousie Building - 13-14 June 2019

Day 1 Schedule – 13 June 2019

10:30	*Registration & coffee/tea*	The Street, School of Life Sciences - *note different venue*
11:00-11:10	**Welcome & Introduction** Chairs: Dr Edgar Huitema & student reps	Dalhousie, Lecture Theatre
11:10-11:40	**Keynote address** **Abigail L. Harris** (Strategy & Policy Officer, UKRI BBSRC) "Career and development opportunities for BBSRC students" **Chair**: Dr Edgar Huitema	Dalhousie, Lecture Theatre
11:40-12:15	**Speed-dating** **Chairs**: Amy Cooper & Meg Peyton Jones	Dalhousie, Lecture Theatre
12:15-13:00	**Poster session** Chair: Cameron Malcolm	Dalhousie, Room 1S01
13:00-14:00	*Lunch & coffee/tea*	The Street, School of Life Sciences - *note different venue*
14:00-15:45	**Student talks I: Genetic Processes & Proteins** **Professor Chris Ponting** (MRC Institute of Genetics & Molecular Medicine, University of Edinburgh) "Focus on function: From genome to base pair" **Co-chairs**: Sam Haynes & Ana Rozman	Dalhousie, Lecture Theatre
14:00-15:45	**Student talks II: Environmental Biology & Ecology** **Professor Colin Moffat** (Scottish Government, Marine Scotland) "The necessity for linking biology, chemistry and physics and including social, economic and cultural aspects when managing the human activities impacting on our seas" **Co-chair**: Rebecca Maguire	Dalhousie, Room 1F06
15:45-16:00	*Coffee/tea break*	Room 1F01, 1FO6
16:00-17:30	**Student talks III: Health and Nutrition** **Dr Andreas Kolb** (The Rowett Institute, University of Aberdeen) "Drivers of obesity and potential nutritional interventions" **Co-chair**: Gemma Fisher	Dalhousie, Lecture Theatre
16:00-17:30	**Student talks IV: Fundamental meets Synthetic Biology** **Dr Peter Murray-Rust** (Department of Chemistry, University of Cambridge) "Early career researchers and open healthcare" **Co-chairs**: Liat Adler & Alysha Knight	Dalhousie, Room 1F06
17:30	*Close of day 1* *Check-in at West Park Conference Centre & Invercarse Hotel*	West Park Conference Centre *Coach available for attendees*
19:00	*EASTBIO Dinner, followed by a Ceilidh dance*	Best Western Queens Hotel

Day 2 Schedule – 14 June 2019

9:30	*Late registration*	The Street, School of Life Sciences - *note different venue*
10:00-10:10	**Welcome & Introduction** **Chairs**: Student reps	Dalhousie, Lecture Theatre
10:10-12:40	**Student talks V: Body, Brain & Behaviour (cognitive)** **Professor Nicola Clayton FRS** (Comparative Cognition) and **Professor Clive Wilkins MMC** (Artist-in-Residence) - Department of Psychology, University of Cambridge "The Dancer remembers: The choreography of the mind and body" **Co-chairs**: Suzi Keane	Dalhousie, Lecture Theatre
10:10-12:40	**Student talks V: Body, Brain & Behaviour (general)** **Professor Gernot Riedel** (Institute of Medical Sciences, University of Aberdeen) with **Dr Carole Torsney** (Centre for Discovery, Brain Sciences, University of Edinburgh) "Sex and injury dependent nociceptor plasticity" **Co-chairs**: Amy Cooper & Kiani Jeacock	Dalhousie, Room 1F06
12:40-13:30	*Lunch & coffee/tea*	The Street, School of Life Sciences - *note different venue*
13:30-14:10	**Science Pub Quiz** **Chair**: Suzi Keane	Dalhousie, Lecture Theatre
14:10-15:30	**"Career paths, career stories"** (panel discussion) **Dr Tim George** (James Hutton, Dundee), **Dr Holly Corrigall** (GSK), **Dr Eleanor Gaunt** (Roslin, Edinburgh), **Professor Chris Ponting** (Edinburgh), **Professor Gernot Riedel** (Aberdeen), **Dr Ben Rutter** (Marks & Clerk LLP, Cambridge), **Dr David Walker** (Glasgow) **Chairs**: Courtney Aitken & Meg Peyton Jones	Dalhousie, Lecture Theatre
15:30-16:00	**Prize-giving; concluding remarks**. Close of Symposium with a drinks reception Chairs: Dr Edgar Huitema & student reps	Dalhousie, Lecture Theatre & Mezzanine level

Meet our speakers!

Professor Nicky Clayton FRS is Professor of Comparative Cognition in the Department of Psychology at the University of Cambridge, UK and Visiting Professor at the Nanging University's Institute of technology, China. She is particularly interested in the processes of thinking with and without words and comparisons between the cognitive abilities of corvids (members of the crow family) and children. She was elected a Fellow of the Royal Society (FRS) in 2010. She is also Scientist-in-Residence at Rambert (formerly Ballet Rambert), a position she has held since 2011.

Dr Holly Corrigall recently completed her PhD in Molecular Biology at the University of Aberdeen where she was studying ribosomal responses to induced translational pausing in Saccharomyces cerevisiae. As part of her PhD she undertook her PIPs placement in the Disruptive Technologies team in Biopharm Process Research (BPR) department at GlaxoSmithKline in Stevenage. Prior to her PhD, she completed her Master's in Systems and Synthetic Biology, also at the University of Aberdeen, during which she investigated DNA replication and 'on-demand' histone synthesis during S-phase in humans through both lab-work and mathematical modelling. Previous to that, she gained her BSc (Hons) in Forensic Anthropology at the University of Dundee. Since finishing her PhD she has returned to GSK in Stevenage to work in the Cell Line Development team in BPR which is responsible for the generation of clonal, stable and fully-traceable cell lines for commercial manufacture. Her role is to integrate new technologies to optimise recombinant protein expression within GSK's platform cell line.

Dr Eleanor Gaunt (Roslin Institute, University of Edinburgh) did her undergraduate in Medical Microbiology at Newcastle University (graduating in 2006), before moving to Edinburgh to undertake her PhD researching the Clinical Correlates and Epidemiology of Respiratory Viruses, completed in 2010. She did a two year postdoc in Cambridge working on rotaviruses before returning to Edinburgh for a second postdoc working with picornaviruses. She remained in Edinburgh for a third postdoc working with influenza A virus, during which time she won a Wellcome Trust/ Royal Society Sir Henry Dale Fellowship, which she took up in October 2018 to work on the molecular biology of influenza A virus.

Dr Tim George is a principal investigator at the James Hutton Institute in the middle stage of his career, with a track record that includes the publication of over 85 papers, the winning of grants with a total value in excess of £14M from a range of research funders and the generation of a growing international network. His research is focused on the role that plant genotypic and phenotypic diversity plays in controlling important biogeochemical cycles of nutrients and water in the rhizosphere soil surrounding roots. His research is undertaken at a range of scales from the cell to the field and I have taken advantage of facilities including genomics and sequencing, through plant genetic populations to long-term field trials. This research is applied in a multidisciplinary way with regular interactions with geneticists, molecular biologists, microbiologists, agronomists, statisticians and social scientists. I have established strong multidisciplinary research groups both within the James Hutton Institute, within the

SEFARI institutes in Scotland, as part of consortia within the UK and within Europe in FP7 and H2020 projects. I have also established interactions with researchers in China, Brazil, Malaysia, Australia and New Zealand. In addition, I have shown leadership in both the conceptualisation, direction and management of work packages and research deliverables in the Scottish Governments programme of research administered by RESAS.

Abigail L. Harris (Strategy & Policy Officer, UKRI BBSRC) completed her PhD on testis development in mice at the University of Oxford before moving into the world of science policy and strategy. Having completed a policy internship at the Royal Society, and after a short period working for the British Pharmacological Society, she started a role in BBSRC. Here she began by focussing on BBSRC strategy around new technologies, including bioimaging. After 6 months, she joined the Skills and Talent team and is now managing BBSRC's David Phillips and Discovery Fellowships. Her current role also focuses on BBSRC strategy and policy around early career researchers and technical careers.

Dr Andreas Kolb (The Rowett Institute, University of Aberdeen)

Andreas is a Senior Research Fellow at the Rowett Institute, University of Aberdeen. He joined the Institute after research-based roles at the University of Würzburg, Germany and Hannah Research Institute, Ayr, Scotland. His main research interest is in the area of metabolic health. His lab investigates the role of perinatal nutrition in determining life-long metabolic health consequences and the potential of phytochemicals in combatting metabolic disease.

Professor Colin Moffat (Chief Scientific Advisor Marine, Scottish Government, Marine Scotland; Robert Gordon University, School of Pharmacy and Life Sciences)

Initially studying chemistry, Colin completed a PhD in heparin biochemistry, including links to tumour angiogenesis, before joining Torry Research Station where he investigated the structure of fish lipids and their nutritional benefits. He subsequently investigated organic contaminants in the marine and terrestrial environments, pathological samples, food producing animals and food products with a specific interest in their biological effects on marine biota. Colin has specialised in methodology associated with determining the state of marine ecosystems. He lead on the production of assessments of the North-East Atlantic, including the Intermediate Assessment 2017 which utilised new indicators and targets, providing an assessment of progress towards achieving a clean, healthy and biologically diverse North-East Atlantic. Colin continues to study the movement of contaminants through trophic levels and is part of the writing team for the contaminants section of the United Nations World Ocean Assessment 2.

Dr Peter Murray-Rust

Peter Murray-Rust became lecturer in chemistry at the University of Stirling and was first warden of Andrew Stewart Hall of Residence. In 1982, he moved to Glaxo Group Research at Greenford to head Molecular Graphics, Computational Chemistry and later protein structure determination. He was Professor of Pharmacy in the University of Nottingham from 1996–2000, setting up the Virtual School of Molecular Sciences. He is now Reader Emeritus in Molecular Informatics at the University of Cambridge and Senior Research Fellow Emeritus of Churchill College, Cambridge. In 2002, he proposed an

electronic repository for unpublished chemical data called the World Wide Molecular Matrix (WWMM). He and Henry Rzepa were joint recipients of the Herman Skolnik Award of the American Chemical Society. In 2014, he was awarded a Fellowship by the Shuttleworth Foundation to develop the automated mining of science from the literature.

https://en.wikipedia.org/wiki/Peter_Murray-Rust

Professor Chris Ponting (MRC Institute of Genetics & Molecular Medicine, University of Edinburgh)
After an early career in experimental physics, Chris crossed protein science, evolutionary biology and genetics to eventually contribute leadership in international genome sequencing projects, including the landmark human project. Since then, he's been interested in mammalian long noncoding RNAs, the proportion of the human genome that is functional, sequencing DNA and RNA from the same single cell, and pinpointing single base pair changes that causally alter complex traits and diseases. For most of his career he was at the University of Oxford, but came to the University of Edinburgh in early 2016 as the Chair of Medical Bioinformatics. He has published over 340 articles, and has an h-index of 108.

Gernot Riedel is Professor of Neurosciences at the Institute of Medical Sciences at the University Of Aberdeen, where he has worked since 2006. His main research focus has been neurodegenative diseases, including the development of rodent models of neurodegenerative illnesses, such as Alzheimer's disease and Parkinson's disease. Gernot has been a local group coordinator for the British Neuroscience Association (BNA) in Aberdeen. He is also a part of the Alzheimer's research UK (ARUK) Scotland network, where he recently presented data originating from his involvement in the European Quality in Preclinical Data (EQIPD) consortium. In order to improve the drug development process, the consortium aims to tackle the root of translational issues and improve the quality of preclinical research.

Dr Ben Rutter is working in the Biotechnology team as a Trainee Patent Attorney in the Cambridge office. Before joining Marks & Clerk LLP in October 2018, Ben completed his PhD at the University of Aberdeen. His research focused on elucidating the biosynthetic pathway of myriocin, a potent fungal metabolite.

Dr Magali Sivakumaran was in the first EastBio Cohort of 2008. She completed her PhD titled "Empirical and Methodological Investigations into Novelty and Familiarity as Separate Processes that Support Recognition Memory in Rats and Humans". Her research was interdisciplinary, looking at memory processing using complimentary methodologies in animal and human research and trying to bridge our knowledge of memory at differing levels of analysis. After an amazing break travelling she went on to do (and continue to do) interdisciplinary research looking at the development of episodic memory in Stirling University, in partnership with Dundee and Edinburgh University. However, following her PIPS and other life events, she decided that while she loved research she wasn't in the right field, and her heart wasn't in it fully. So she is now undertaking a degree in Midwifery with the aim of combining her love for research and caring for women, their babies and their families, and having a career as a part time midwife and part time research midwife. She is grateful for her research skills and use

them every day in a field that needs more researchers! A PhD can take you many places…often unexpected, and the traditional career path wasn't for her.

Dr Carole Torsney is a Senior Lecturer in the Centre for Discovery Brain Sciences at the University of Edinburgh. Carole Torsney received her PhD from University College London as part of the Wellcome Trust 4 year PhD programme in Neuroscience and then undertook postdoctoral training in the Department of Physiology and Cellular Biophysics at Columbia University, New York. She was then awarded a Caledonian Research Foundation Fellowship, then a Senior Academic Fellowship followed by a Lectureship at the University of Edinburgh. She is interested in studying the abnormal functioning or pathophysiology of the sensory nervous system in pain disorders, primarily using electrophysiological approaches. She is interested in exploring these questions in both sexes given there is increasing recognition of sex differences in pain sensitivity and chronic pain susceptibility but poor understanding of the underlying basis.

Dr David Walker is an Eastbio DTP alumnus who was recently awarded his PhD from the University of St Andrews. His project explored the long-term effects of early-life stress on the physiology of the ageing brain in the Japanese quail. During his PhD, David completed his PIPS working as an application scientist for Glencoe Software, who specialise in data management of scientific images. David was a student representative for his cohort throughout his studies, helped with organising two symposia, and participated in many outreach activities. David is now working as a postdoctoral research associate at the University of Glasgow researching DNA damage responses in both neural stem cells and cancer cells within the brain in response to radiotherapy and drug treatments.

Professor Clive Wilkins MMC is the Artist-in-Residence in the Department of Psychology at the University of Cambridge, a position he has held since 2012, and Visiting Professor at the Nanging University's Institute of Technology, China. Clive is a fine art painter and writer and was elected a Member of the Magician's Circle (MMC) in 2018. Clive's paintings have been frequently seen in London Mayfair art galleries. His written work has appeared in print on numerous occasions, most notably 'The Creatures in the Night', a story written and illustrated by him in 2008, and most recently 'The Moustachio Quartet'.

Student Abstracts

Theme 1: GENETIC PROCESSES AND PROTEINS

Dalhousie, Lecture Theatre, June 13TH 14:00-15:45

GUEST SPEAKER

Professor Chris Ponting (MRC Institute of Genetics & Molecular Medicine, University of Edinburgh)

Focus on function: From genome to base pair

Most of the human genome is not important: DNA changes appear not to alter cell or organismal function and are not under the scrutiny of evolutionary selection. So when we observe a molecular effect, for example that a protein binds DNA or another molecule, or its level goes up or down, it is right that we ask the F-question: is this effect Functional? This is a hard question but can be addressed using model systems such as cells or model organisms. In this talk I will start by discussing function at the Gigabase scale. Then I will zoom down in on the single base scale, explaining our recent computational studies that identify single nucleotide differences that causally alter human disease risk or traits. I will try to convince you that the 3 billion nucleotides in your genome are not all equally important.

YEAR 1 STUDENTS

Ryan Casement - University of Dundee - r.casement@dundee.ac.uk

Structure-based optimisation of fragments targeting a novel pocket on the Von Hippel-Lindau E3 Ubiquitin Ligase - Supervised by Alessio Ciulli

The Von Hippel-Lindau (VHL) complex is a Cullin-RING Ligase (CRL) for which ligands have been previously developed which can hijack the ligase for use in Proteolysis Targeting Chimeras (PROTACs) and disrupt its interaction with HIF1α. This project follows on from a fragment screen in which binders to the 'back pocket' of VHL were identified. As part of this project, a structure based medicinal chemistry optimisation is now ongoing and has so far resulted in triple digit micromolar binders, measured by surface plasmon resonance (SPR) and confirmed crystallographically.

Christine Jack - University of Aberdeen - r01cj18@abdn.ac.uk

Endocytic Trafficking of G-protein-Coupled Receptors as a Novel Regulator of Inflammation – Supervised by Dr James Hislop

Controlled inflammation is a vital process of innate protection but if inflammation becomes dysregulated it can form the basis of many chronic diseases, such as Rheumatoid Arthritis. The Formyl Peptide 2 Receptor (FPR2) has been identified as a key mediator of the endogenous anti-inflammatory response, however, the mechanisms by which the FPR2 co-ordinates this response are yet to be fully understood. By exploring the signalling and trafficking behaviour of the FPR2 we hope to establish its potential as a target for development of new anti-inflammatory treatments.

Neil Thomson - University of Dundee - njthomson@dundee.ac.uk

The role of ions in activation of GPCRs – Supervised by Dr Ulrich Zachariae, Dr Andrei Pisliakov

G-Protein Coupled Receptors (GPCRs) are the largest family of cell surface receptors and as such are the primary drug target for a variety of diseases, yet how they transmit signals remains poorly understood. A high correlation between the presence of a sodium and hydrogen ion in the GPCR, and the state of GPCR activity, suggests ions have an important role in relaying drug binding information to the cell. This computational project uses molecular dynamics simulations in conjunction with quantum chemical calculations and information theory in order to investigate the various interaction forces between ions and GPCRs.

YEAR 2 STUDENTS

Bethany Allen - University of Aberdeen - r03ba17@abdn.ac.uk

The role of innate cell PTP1B in susceptibility to fungal infection – Supervised by Dr Heather Wilson, Prof Mirela Delibegovic, Prof Gordon Brown, Dr Simon Arthur

A new class of therapeutics that inhibit the protein tyrosine-phosphatase PTP1B are currently in clinical trials for the treatment of diseases including diabetes and breast cancer. These patients are already immunocompromised, however little is known about how PTP1B inhibition influences susceptibility to fungal infection. The current project aims to investigate this question using in vitro and in vivo techniques. Myeloid-specific PTP1B knockout mice were systemically infected with Candida albicans, and were found to have increased inflammation and greater levels of pro-inflammatory cytokines in their organs than wild-type mice, indicating an exacerbated immune response. Despite this, these mice were more susceptible to infection, as evidenced by lower survival rates and greater fungal burdens in the kidneys, brain and liver. Analysis of immune cell populations in the spleen and subsequent in vitro experiments suggested an aberrant neutrophil phenotype when PTP1B is knocked out, resulting in lower reactive oxygen species production, which may explain the decreased Candida killing observed in vivo. Further infection studies are ongoing to investigate whether clinical PTP1B inhibitors recapitulate the effects observed in knockout mice, and ultimately determine whether these therapeutics may increase patient susceptibility to infection

Kyle Bennett – University of Dundee

Investigating the role of TRAF6 E3 ubiquitin ligase activity in T cells – Supervised by Professor Philip Cohen and Professor Doreen Cantrell

The tumour necrosis factor receptor-associated factors (TRAFs) are a family of signalling adaptor and scaffolding proteins, primarily functioning in developmental, homeostatic and immune signalling. The constituent family member TRAF6 is an E3 ubiquitin ligase that has long been known to transduce signals downstream of IL-1 and Toll-like receptor (TLR) families and is important in innate immune signalling. A body of work suggests significant roles for TRAF6 in the adaptive immune system, with T cell-specific TRAF6 knockouts developing an autoimmune and multi-organ inflammatory phenotype, indicating an essential role(s) for TRAF6 in T cell signalling. Knock-in mice expressing the E3 ligase-inactive TRAF6[L74H] mutant in all cells of the body have a similar inflammatory autoimmune phenotype, which develops within 16 days of birth. Suggesting an essential role for TRAF6's E3 ubiquitin ligase activity in regulating the T cell arm of the adaptive immune system and maintaining immunological tolerance. This project aims to advance our understanding of the molecular mechanisms by which TRAF6 regulates T cell biology. In particular, the project will focus on the role of the TRAF6 E3 ligase activity in CD8+ effector T cells (CTLs), a T cell subset previously reported to have intrinsic defects driven by the absence of TRAF6. I will use this model system to identify the signals that are regulated by TRAF6 and its E3 ligase activity, how the TRAF6 E3 ligase is activated or inhibited by these signals and how the TRAF6 E3 ligase regulates these processes. In particular, I will initially study the activation of TRAF6 E3 ligase and its role in IL-18 signalling in CTLs and how it may differ from IL-1 signalling in other cells, which has been studied extensively. I will also address whether TRAF6 E3 ligase activity is required in other signalling pathways in CTLs, such as IL-2 signalling and signalling downstream of the TCR. I will also use proteomic strategies to investigate the effect of loss of TRAF6 E3 ligase activity on the composition of the proteome and phosphoproteome of CD8+ T cells. The long-term goal of the project is to understand why the E3 ligase deficient TRAF6[L74H] mutant rapidly develops autoimmunity and multi-organ inflammation, and to identify components of TRAF6 signalling pathways in T cells that could be manipulated by drugs to enhance the ability of T cells to destroy cancer cells.

Ben Craske - University of Edinburgh - Benjamin.craske@ed.ac.uk - Twitter: @bcraske

Characterising the motility of human CENP-E – Supervised by Dr Julie Welburn and Professor Alison Hulme

Microtubule motor proteins play essential roles in the delivery of intracellular cargoes to their required destination within the cell. During cell division, the coordinated activities of kinesin and dynein motors are responsible for the assembly of the mitotic spindle and facilitating error-free chromosome segregation. CENP-E is a plus end directed microtubule motor and is the sole member of the human kinesin-7 subfamily. In prometaphase, CENP-E localises to the kinetochore and facilitates chromosome transport along microtubules to the spindle equator. However, the underlying mechanism by which CENP-E contributes to chromosome congression still remains controversial. Previous work has shown that full-length CENP-E purified from mitotic human cells is inactive in vitro, whilst a recombinant CENP-E motor capable of processively walking on microtubules has yet to be characterised. Thus far, we have recombinantly expressed and purified a truncated human CENP-E construct which is capable of processive, plus-end directed motility along microtubules. We have also designed and purified longer constructs which appear to be predominantly autoinhibited, potentially indicating that the stalk region may inhibit the motor domains. Using biochemical and single molecule microscopy approaches, my research aims to further characterise the properties of human CENP-E motility in vitro and determine its mode of autoregulation.

Tadhg Devlin - University of Edinburgh - tadhg.devlin@ed.ac.uk - @epigenetryps

Heterochromatin and associated proteins in Trypanosoma brucei – Supervised by Robin Allshire & Keith Matthews

The eukaryotic nucleus is classically divided into two broad categories: gene-poor heterochromatin and gene-rich euchromatin. In most model eukaryotes, heterochromatin is epigenetically defined by histone H3 lysine 9 methylation (H3K9me), and is rich in repetitive DNA sequences. Trypanosoma brucei is a kinetoplastid parasite which branched early in eukaryotic evolution, and is the causative agent of African sleeping sickness. Trypanosome histone proteins are divergent, and H3K9me is absent. As a result, the proteins and histone post-translational modifications which define heterochromatin in T. brucei are unknown. Using transcription activator-like effector (TALE) DNA-binding proteins, we are developing a system to purify proteins associated with repetitive DNA sequences, which are candidate heterochromatin regions. Results obtained thus far with telomeres provide proof-of-principle that this is a viable strategy for purifying chromatin-associated proteins in T. brucei. We are expanding the technology to further loci, and plan to identify novel factors involved in heterochromatin formation and function in T. brucei.

Gemma Fisher - University of St Andrews - gf33@st-andrews.ac.uk

Mechanism and Engineering of Cold-Adapted ATP-phosphoribosyltransferase. – Supervised by Dr Rafael da Silva & Prof Rebecca M J Goss

The aim of my research is to elucidate the mechanism of ATP-phosphoribosyltransferase (ATPPRT) from Psychrobacter arcticus in order to generate opportunities for protein engineering. ATPPRT is the first and flux-controlling enzyme of the histidine biosynthetic pathway. ATPPRT is an octamer composed of two distinct subunits: HisG, which is catalytic, and HisZ, which is regulatory. HisZ allosterically activates HisG but also mediates histidine feedback inhibition. The goal of this project is the development of an ATPPRT suitable for industrial application free from histidine feedback inhibition. Steady-State kinetics, isothermal titration calorimetry and differential scanning fluorimetry have been employed to propose a kinetic mechanism for this enzyme. Furthermore, the rate-limiting steps of the catalytic cycle for the activated and non-activated HisG were uncovered by a combinatorial approach of

viscosity studies, pre-steady-state kinetics and by exchanging the divalent metal at the enzyme active-site from which it was determined that HisZ shifts the rate-limiting step. Current work includes using site-directed mutagenesis to understand the complex allosteric regulation/activation by HisZ. We have demonstrated by 31P-NMR that ADP is a substrate for PaATPPRT and characterised the steady-state kinetic parameters of this reaction. We are investigating a histidine biosynthetic strategy commencing from ADP.

Susi Keane - University of Edinburgh - s1778856@sms.ed.ac.uk

Dissecting the proviral functions of Jmjd6 in influenza A virus infection – Supervised by Prof. Paul Digard, Dr Christine Tait-Burkard

Jumonji domain containing protein 6 (Jmjd6) is a highly conserved nuclear protein with a variety of functions in transcriptional regulation. Previous work has shown that siRNA knockdown of Jmjd6 in the human lung epithelial cells resulted in reduced expression of viral proteins and RNA following influenza A virus (IAV) infection. Additionally, Jmjd6 knockdown A549 cells appeared to have increased secretion of IFNα/β in response to IAV infection, as well as increased expression of the interferon stimulated gene Mx1 and phosphorylation of IRF3 compared to wild type A549 cells expressing Jmjd6. These preliminary data suggested a link between Jmjd6 and the innate immune response.This project aimed to dissect this apparent proviral role of Jmjd6 in the innate immune response to IAV. In the process of this investigation alternative knockdown techniques and CRISPR-Cas9 edited Jmjd6 deficient cells were developed. In these cell systems, the inhibition of viral replication was not seen. Additionally, enhanced IFN responses are only seen with the original siRNA knockdown system. These findings suggest that the previously posited proviral role of Jmjd6 was due to experimental an artefact.

Felicity Macdonald - University of Edinburgh - s1211093@ed.ac.uk

Determining the mechanism and impact of HB-EGF-derived EGFR signalling in CD4+ T cells – Supervised by Dr Dietmar Zaiss and Professor Simon Arthur

Along with a critical role in growth and development, recent research has shown that the Epidermal Growth Factor receptor (EGFR) plays a key role in immunity. Cells of the adaptive immune system, such as CD4+ T cells, are one cell type that upregulate the expression of this receptor after activation in lymphoid organs. HB-EGF is the highest affinity ligand for the EGFR and after binding to the receptor elicits a downstream signalling response that appears to dictate the differentiation capacity of these T cells. This differentiation then determines how the cells can react during an immune response. My PhD project is to elucidate the role and downstream mechanism of HB-EGF-derived EGFR signalling in CD4+ T cells.

Samantha Jacqueline Mpaulo - University of Aberdeen - s.mpaulo@abdn.ac.uk

Orthogonal DNA Double-Strand Break Formation during Meiosis – Supervised by Dr Alexander Lorenz and Dr Adele Marston

Meiosis is critical to the success of sexual reproduction. It not only ensures genetic continuity from one generation to the next, but can also enhance the genetic diversity among members of a species. An integral aspect of meiosis is the programmed formation of DNA double-strand breaks (DSBs), which occur with a higher frequency at specific sites across the genome, known as hotspots. Following DSB

induction, these breaks are repaired by meiotic recombination preferentially using the homologous chromosome as the template. The repair can result in either crossover or non-crossover products, both of which may be associated with a gene conversion event. Only crossover events establish connections between the parental chromosomes. These represent sites of reciprocal exchange between parental chromosomes, and are essential for correct meiotic nuclear divisions.

To better understand the regulatory mechanisms that underpin various aspects of meiotic recombination (DSB formation and repair type), I investigate how manipulating DSB delivery influences repair outcome. I achieve this by combining a meiotically expressed CRISPR/Cas9-system with a genetic recombination assay, in fission yeast. This enables me to induce DSBs independent of the meiotic DSB formation machinery, which will provide novel insight into the mechanisms driving certain types of repair outcome.

Meg Peyton Jones - University of Edinburgh - meg.peytonjones@ed.ac.uk

Investigating the localisation mechanisms and roles of distinct cohesin pools along the chromosome in eukaryotes – Supervised by Adele Marston, Alex Lorenz

Chromosome structure and behaviour varies dynamically throughout the cell cycle. Cohesin, a ring shaped protein complex, is loaded onto chromosomes and performs a number of critical roles in their regulation. Best known for holding sister chromatids together from S phase until their separation in anaphase, it also functions in loop extrusion, in enabling recombination events in meiosis, in facilitating DNA replication and repair, and in setting up the correct orientation of kinetochores during cell division. Cohesin is not distributed randomly along chromosomes, but is rather enriched at specific locations. The highest density is found at centromeres and heterochromatin. As of yet, it is unclear how cohesin localises to these regions, and how these distinct cohesin pools contribute to the roles cohesin plays. My project seeks to explore these questions, using Schizosaccharomyces pombe as a model system.

Charlotte Scoynes – University of Edinburgh - s1736553@ed.ac.uk

Understanding the role of RNA interference in the pathogenic yeast Cryptococcus neoformans – Supervised by Dr Elizabeth Bayne

RNA interference (RNAi) is a mechanism of controlling gene expression through targeted short interfering RNA fragments of 21-25nt. This occurs through an evolutionarily conserved mechanism involving a Dicer protein which cleaves dsRNA into siRNA duplexes, and an Argonaute protein in an RNA-induced silencing complex (RISC) which binds the siRNA duplexes, and uses one of the two siRNA strands to guide the complex to its complementary target mRNA. Upon targeting the mRNA, the mechanism of silencing can vary from the recruitment of chromatin modifiers, to blocking translation. In Schizosaccharomyces pombe, RNAi silences target genes through the recruitment of Clr4, a histone methyltransferase which lays down the epigenetic silencing mark H3K9me3. However, the mechanism of silencing is unknown in the pathogenic yeast Cryptococcus neoformans, which uses RNAi as a method of genome protection against transposons. In C. neoformans JEC21 genome, multiple copies of some RNAi components are present, including two Dicer and two Argonaute proteins, with neither copies completely redundant although no functional differences are known. Using deletion mutants of the main RNAi components in C. neoformans JEC21, I have performed chromatin immunoprecipitation (ChIP) to determine if, similarly to S. pombe, the RNAi machinery silences targets through H3K9 methylation.

YEAR 3 STUDENTS

Imogen Johnston-Menzies - University of Edinburgh

Investigating the differential virulence of Salmonella enterica serovars in livestock animals using quantitative proteomics – Supervised by Jo Stevens and Prerna Vohra

Salmonella enterica is a bacterial pathogen with a worldwide association with animal and human disease. Livestock species such as cattle and pigs serve as hosts for interestingly host-adapted Salmonella serovars where the outcome of infection is dependent on host-serovar specificity. In pigs, an important example of adaptation is S. enterica serovar Choleraesuis, a serovar adapted to cause systemic typhoid-like disease in pigs but enteritis in cattle. S. Choleraesuis and S. Typhimurium – which causes self-limiting diarrhoea in a wide range of hosts – both use type III secretion systems (T3SS) as critical virulence factors. The T3SS has been previously hypothesised to strongly impact Salmonella host-adaptation. We have characterised the secretomes of two strains of well-defined virulence in pigs – S. Typhimurium ST4/74 and S. Choleraesuis SCSA50 – using label-free quantitative proteomics. Our main finding was that not only does the repertoire of secreted T3SS proteins differ between ST4/74 and SCSA50, but the amount of protein secreted is also significantly different. Validation by immunoblotting and RT-qPCR has confirmed this result and we are now investigating the regulation of the T3SS in these strains at the transcriptional level, with the ultimate goal of clarifying links between protein secretion, host-adaptation, and the zoonotic potential of Salmonella serovars.

YEAR 3 PIPS TALKS

Joshua L Wort – University of St Andrews - jw277@st-andrews.ac.uk

PIPS talk – Supervised by Dr Bela E. Bode

Implementation of national genomic medicine programmes is becoming increasingly common, and in recent years many large-scale initiatives have emerged that engender the changing attitudes and approaches to healthcare. Scotland is well positioned internationally to embrace genomic medicine. In this project, strategies for implementation of genomic medicine in Australia, Estonia, Israel, The Netherlands, New Zealand, Sweden and the wider UK are discussed in relation to the Scottish landscape. In particular, themes and issues that are critically evaluated include: initiative funding, leadership and delivery model, relevant infrastructure, models of consent, research, development and industry-facing activity, patient and public interaction and engagement and digital health. It is hoped that the outcome of this work will inform the chosen strategy employed by Scottish government for national implementation of genomic medicine in the future.

Theme 2: ENVIRONMENTAL BIOLOGY AND ECOLOGY

Dalhousie, Room 1F06, June 13th 14:00-15:45

GUEST SPEAKERS

Professor Colin Moffat

- Chief Scientific Advisor Marine, Scottish Government, Marine Scotland, Marine Laboratory, 375 Victoria Road, Aberdeen AB11 9DB
- Robert Gordon University, School of Pharmacy and Life Sciences, Garthdee Road, Aberdeen, AB10 7QB

The necessity for linking biology, chemistry and physics and including social, economic and cultural aspects when managing the human activities impacting on our seas

Our vision in Scotland is for 'clean, healthy, safe, productive, biologically diverse marine and coastal environments, managed to meet the long-term needs of people and nature'. As human activities (and thus pressures) continue, they will have an impact, some local to the activity, some remote from the activity. Ultimately the overall environmental impact is a consequence of anthropogenically forced changes in the chemistry, physics and biology – they are inextricably linked. However, in attempting to manage the environmental changes, through managing the associated human activities, the social, economic and cultural aspects must not be ignored. Balancing all these aspects is complex, but essential if Scotland is to deliver its marine vision.

YEAR 1 STUDENTS

Liat Adler - University of Edinburgh - Liat.Adler@ed.ac.uk

Incorporating components of the carbon dioxide concentration mechanism from Chlamydomonas reinhardtii into higher plants – Supervised by Alistair McCormick

Photosynthesis is a key target for genetic enhancement for producing crops with improved yields. Our approach for enhancing photosynthesis is to incorporate components from an algal carbon dioxide concentration mechanism into C3 plants. My current work is focused on characterising candidate proteins for bicarbonate pumps and rubisco aggregation in plants.

Amy Cooper - University of Aberdeen - r03ac18@abdn.ac.uk - Twitter @_doe_a_deer

Elucidating the honey bee immune response and pathogen transmission at the Varroa mite feeding site – Supervised by Dr Alan Bowman, Dr Ewan Campbell and Professor Tom Freeman

The European honey bee (Apis mellifera) has a vital role in agriculture and food security due to its pollination services, however it is unfortunately undergoing a major health crisis. The ectoparasitic Varroa mite continuously feeds from the same site on the honey bee, creating an open wound and transmitting pathogens such as the Deformed Wing Virus. By focusing on this site and using various techniques to investigate honey bee gene expression and DWV activity I hope to build a more accurate picture of what is happening within this complex relationship.

Margarita Kalamara - University of Dundee - m.kalamara@dundee.ac.uk

Using microfluidics to study Bacillus subtilis biofilm formation on plant roots – Supervised by Prof. Nicola Stanley-Wall and Prof. Cait MacPhee

Biofilms are social communities of bacteria which are widespread in nature and are of medical, industrial and agricultural importance. The model organism Bacillus subtilis is used in agriculture as a biocontrol agent, a property that requires biofilm formation on the roots. The aim of the project is to use a microfluidic system and confocal microscopy to study biofilm formation by diverse soil isolates of B. subtilis on the roots of Arabidopsis thaliana.

Alysha Knight - University of Aberdeen - a.knight.18@abdn.ac.uk

The roots of soil and food security – Supervised by Professor Paul Hallett, Dr Gareth Norton, Dr Tim George

The presence of the rhizosphere and its significance to plant productivity is well researched, however less is known about the drivers that cause its physical formation and how soil management strategies and specific crop traits impact this. This project aims to understand the mechanisms behind how crop roots interact with the rhizosphere to extract nutrients and change the physical and chemical properties of the soil. We hope eventually to establish how we may manipulate root: soil interactions to increase

arable agricultural productivity and sustainability (e.g. reducing fertiliser usage, relieving soil compaction, increasing the nutritious quality of crops).

Hannah A Lawther – University of St Andrews - hl87@st-andrews.ac.uk

Pipeline for Discovery and Diversification of Novel, Bioactive Marine Natural Products – Supervised by Professor Rebecca Goss, Professor Stephen Gillespie, and Dr Gordon Florence

By using a combination of genome mining and molecular biology, new or novel biosynthetic gene clusters are being targeted to be carried through to heterologous expression so the resulting product can be identified and its bioactivity established. By identifying the genes responsible for certain modifications, known biosynthetic gene clusters can potentially be modified to tailor natural products to have chemical handles, thus generating suites of analogues.

YEAR 2 STUDENTS

Kerry Leslie - University of St. Andrews - kl97@st-andrews.ac.uk or Kerry.leslie@hutton.ac.uk

Core effectors and host targets of plant parasitic nematodes – Supervised by Dr Sebastian Eves-van den Akker, Dr Sophie Mantelin and Prof. John Jones

Plant parasitic nematodes infect many major food crops worldwide, causing damage globally valued at approximately 80 billion U.S. dollars per year. Some nematodes form a feeding site called a syncytium in the roots of their host. Relatively little is known about how nematodes initiate and maintain these feeding structures. However, specialised proteins and small molecules, known as effectors, secreted into the plant by the pathogen, are thought to play critical roles in these processes. It is important to establish a greater understanding of the role of effectors in syncytium formation and maintenance alongside host invasion by the nematode. Exploiting the genomic and transcriptomic data available from four syncytium-forming species; G. rostochiensis, G. pallida, R. reniformis & N. abberans, I have identified a series of candidate core effectors conserved in syncytia-forming nematodes. A subset of three of these core effectors (Gr20E03, GrGLAND11 and GrGLAND15) of unknown function are being studied in more detail. Two of these, GrGLAND11 and GrGLAND15 localised to the actin cytoskeleton when expressed as fusions with fluorescent proteins. Yeast two-hybrid has identified a predicted arginine N-methyltransferase as a potential interacting host protein of GrGLAND11. I am currently investigating the role of this interaction in more detail.

Michael McDonald - University of Edinburgh - s1472380@sms.ed.ac.uk

Isolation and characterisation of methanogenic consortia from conventional and extreme environment to optimise sustainable biogas production – Supervised by Dr Andrew Free and Professor Rosalind Allen

My research focuses predominantly on the methanogenic Archaea and the microbial ecology of extreme environments, with a particular interest in low pH environments. Once largely ignored due to the thought that such areas were too hostile to prove habitable, we now know these environments are untapped resources in regard to their unusual microbial diversities and the potential applications of these extremophilic microbial consortia. My work aims to utilise such sites as a source for microorganisms with relevance to sustainable biofuel production. By using sediment microbial communities from both acidic and conventional pH freshwater sites in Scotland, my PhD so far has explored carbon degradation from complex polymers to methane through the action of methanogens, along with their bacterial partners. To this end, my work aims to explore the diversity/function ecological relationships in methanogenic communities in nature, their resilience in bioreactors and their ability to enhance biogas production. Additionally, I am interested more broadly in the use of novel techniques to study extremophiles through both culture based and molecular approaches to gain a greater insight into the taxonomy and function of microorganisms from the rare biosphere.

Beth Moore - University of Aberdeen - b.moore.17@abdn.ac.uk, @BethLilyMoore

Understanding the biogeography of an insecticide resistant crop pest with a complex lifecycle – Supervised by Dr Lesley Lancaster, Fiona Highet, Dr Ewan Campbell, Gaynor Malloch, Dr Jon Pickup

Understanding the factors contributing to the shifts of species is key, especially when it comes to commercially important species that require management, such as crop pests. Sitobion avenae, the grain aphid, is a widespread insect pest of grains across the UK. It has an interesting lifecycle, seasonally altering its reproduction. In summer female aphids give birth to live clonal offspring creating a rapid population boom of clonal lineages, but come winter they produce male and female offspring which mate to make cold-resistant eggs. However climate change is causing more clones to survive winter as the temperatures required to trigger the switch to sexual reproduction are not being reached. This leads to interesting fluctuating patterns of clonal diversity across the UK as well as the persistence of insecticide resistance clones. My project is using combination of field work, sequencing and a long term data on aphid populations to investigate the factors driving these patterns.

Zak Towle – University of Edinburgh - zak.towle@ed.ac.uk

Enhancing the Enzymatic Degradation of Lignin – Supervised by Louise Horsfall, David Clarke, Nick Westwood

Lignin is the one of the most abundant biopolymers on the planet, formed via the oxidative crosslinking of three phenylpropanoid monomers. This oxidative free radical crosslinking gives rise to lignin's inherently random and recalcitrant heteropolymer structure. There is a vast array of lignins produced by both the biofuel and paper industries, with both sectors often burning lignin to fuel their industrial processes. Although the burning of lignin provides an easy and cheap means of disposing of waste, it is both harmful to the environment and a suboptimal use of a potentially valuable feedstock. Ligninolytic enzymes offer a potential solution to degrade this complex polymer into useful chemicals often derived from petrochemicals. These enzymes can be found in most types of organisms, although the most industrially relevant are often derived from fungi and include enzymes such as laccases and

peroxidases – which catalyse the oxidative depolymerisation of lignin. To enhance lignin degradation, these enzymes will be used to degrade lignin and lignin model compounds, with the subsequent breakdown products analysed via techniques such as FT-ICR MS. Moreover, HSQC NMR will be used to guide pre-treatment of lignin to generate a simpler substrate for enzymatic degradation.

Jamie C. Weir – University of Edinburgh - Jamie.Weir@ed.ac.uk

The effects of temperature and habitat on phenological variation in the abundance of spring-feeding Lepidoptera – Supervised by Dr Albert Phillimore

Many species use climate as a cue to time stages in their life history, and the synchrony of important interspecific interactions (e.g. a predator coinciding rearing its offspring with the maximum availability of a prey species) can be mediated by a shared response to specific climatic conditions. However, climate change has the potential to negatively impact species in such synchronised interactions where either exhibits a quantitatively distinct plastic response to particular environmental variation – for example, although the larvae of many moths (Lepidoptera) which feed in early spring in temperate woodlands appear to time their egg hatch date with budburst of their host trees, egg hatch and budburst date advance by different degrees with increased temperature, disrupting any pre-existing synchrony. In order to better understand the effects of climate change on synchronised interspecific interactions, this project considers the under-studied relationship between the phenology of spring-feeding moth larvae and their host-plants, how fitness and rates of development vary across host-plant species, and the implications of this for the scale of Lepidopteran adaptation to host-plant phenology.

Tara Wight – University of Edinburgh - tara.wight@ed.ac.uk

Enhancing plant resilience via mechanically induced stress-priming: a solution for sustainable agricultural development – Supervised by Dr Naomi Nakayama

The detrimental effects of climate change pose a huge threat to crop production, and significant increases in yield are required to meet the needs of our growing population. In Japan, mechanical conditioning is effectively used to improve the resilience and yield of wheat and barley. Mechanical stimulation leads to changes in plant growth and development, and has been shown to improve general stress resilience. The model plant Arabidopsis thaliana was used to investigate the effect of repeated mechanical stress on plant growth and gene expression. The potential agricultural benefits of mechanical stress treatment were then investigated using the East African crop plant Eragrostis tef (tef). Preliminary results suggest that this treatment reduces root lodging and increases the number of tillers per plant, potentially leading to increased yield and resilience to adverse weather. Future work will include investigating the molecular response to mechanical stress in tef and working with farmers in Ethiopia to develop treatment protocols suitable for application in the field.

YEAR 3 STUDENTS

Michael Gallagher - University of Edinburgh - M.Gallagher-10@sms.ed.ac.uk

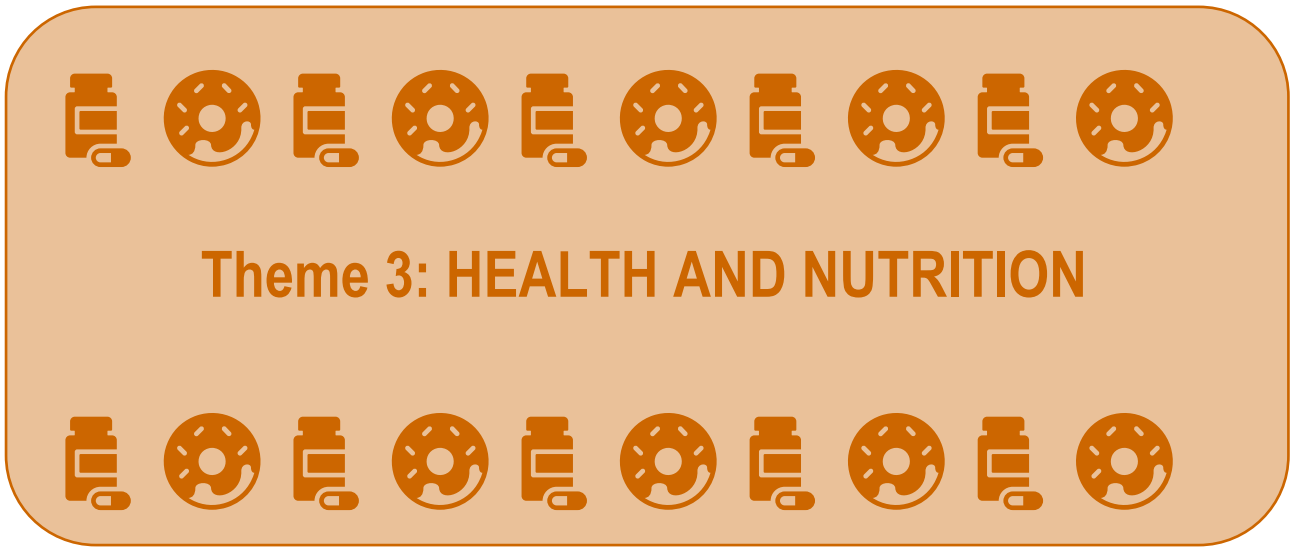
New approaches to characterise viral diseases in Atlantic salmon – Supervised by Iveta Matejusova and Daniel J. Macqueen

Global farmed production of salmonid fishes is worth >£8 billion annually, accounting for ~15% of total traded farmed fish. However, a major bottleneck limiting growth of this industry is loss caused by infectious viral diseases, which can have devastating economic impacts, with few effective therapeutics or preventative vaccines available. Salmonid alphavirus (SAV) is the causative agent of pancreas disease in Atlantic salmon. This virus currently has six subtypes recognized, which are thought to be somewhat geographically structured, and have varying pathogenicities. This presentation reports my investigations into the usefulness of current-generation sequencing technologies to achieve accurate characterization of SAV subtype-diversity within a population of both farmed and wild fishes. Long-range PCR and targeted sequence capture have been performed before sequencing using the MinION and Illumina NextSeq platforms, respectively. These approaches have enabled us to recover full-length genomes with ultra-deep coverage which in turn allow us to detect co-circulating strains in a population at relatively low frequencies. This study aims to better understand viral evolution, phylogeography and population dynamics. We hope that application of such data within the aquaculture industry will ultimately help control the spread of devastating diseases and contribute to economic and food security.

Luke Woodford - University of St Andrews - lw86@st-andrews.ac.uk - Twitter: @doomeddrone

Healthy Honey Bees – analysis of the deformed wing virus population to assess rational Varroa control - Supervised by David J Evans (U of St Andrews), Alan Bowman (U of Aberdeen)

Abstract – Varroa destructor is an ectoparasitic mite which causes serious losses of honey bee colonies globally. The mite acts as a vector for a range of pathogenic viruses, most important of which is Deformed Wing Virus (DWV). Overwintering colony losses, accounting for 25-50% of annual losses, are associated with high levels of Varroa-DWV infestation. Effective miticides are available to improve colony health. However, treatment is rarely coordinated or used rationally, meaning controls are not implemented to maximise their efficacy and mite infestations continue to persist. This study uses coordinated treatment of Varroa in a geographically isolated environment (the Isle of Arran, Scotland). The aim is to show that rational, coordinated treatment is beneficial, using known characteristics of the DWV virus population as an indicator of colony health. A high level of a near-clonal virus population indicates poor colony health, whilst low levels of a diverse population of DWV is characteristic of healthy colonies with low/no Varroa levels in the colonies. Sampling and virus analysis were conducted before and after treatments of the ~55 colonies with changes in virus diversity quantified by next generation sequencing analysis. This study will inform our development of Varroa control strategies for UK beekeepers.



Theme 3: HEALTH AND NUTRITION

Dalhousie, Lecture Theatre, June 13th 16:00-17:30

GUEST SPEAKERS

Dr Andreas Kolb (The Rowett Institute, University of Aberdeen)

Drivers of obesity and potential nutritional interventions

YEAR 1 STUDENTS

Maggie Hicks - University of Edinburgh - m.a.hicks@sms.ed.ac.uk

Wearable 3D printed biosensors for non-invasive health monitoring through sweat – Supervised by Dr Baojun Wang

Non-invasive monitoring of biomarkers has many health applications such as monitoring long term conditions, response to medications and in diagnostics and also allows monitoring outside of a medical setting. Currently most non-invasive monitoring uses wearable sweat sensors with electrochemical detection which gives sensitive detection of a wide range of biomarkers, but these face challenges from sensor drift affecting accuracy, a high initial cost of sensor production and the stability of the protein-based recognition elements. The aim of this project is to develop a 3D printed biomaterial containing DNA based sensors for lactate, cortisol, sodium and potassium as a proof-of-principle low cost method for producing wearable biosensors which are more stable for long term sensing applications.

Maria Kouridaki – University of Edinburgh - mariakour96@gmail.com

Design, synthesis and biophysical evaluation of novel tri-vector cyclophilin ligands – Supervised by Dr Julien Michel, Prof Alison Hulme

Cyclophilins (Cyps) are a major family of drug targets that are challenging to prosecute with small molecules because the shallow nature and high degree of conservation of the active site across human isoforms offers limited opportunities for potent and selective inhibition. Aim of this project is to design and synthesize novel tri-vector ligands that bind to a third unprecedented pocket within the active site of the enzyme in order to achieve selectivity among the different isozymes, based on validated data from molecular dynamics simulations and free energy calculations. Then the synthesized ligands are going to be evaluated through biophysical assays as for their affinity, potency and selectivity.

David Lewis - University of Edinburgh - d.a.lewis-1@sms.ed.ac.uk

Establishing a method for proteomics analysis of proliferating CD8+ T cells – Supervised by Dr.Tony Ly, Prof. Doreen Cantrell, and Prof. Rose Zamoyska

CD8 T cells are an important population of lymphocytes which have a role in controlling viral infection and stemming tumour growth, however the processes governing their proliferation and differentiation are still under debate. Proteomics provides as with an ubiased method to quantify protein content within a population of cells and track how it changes at specific time points. Using FACS sorting on key cell cycle markers, it will be possible to separate unsynchronised proliferating T cells by cell cycle stage and compare the proteomes, thereby observing which processes increase or decrease as they go through the cycle, providing new insight into the mechanisms which govern CD8 T cell proliferation following antigen recognition

Kieron Lucas - University of Dundee - k.y.lucas@dundee.ac.uk

Structural and functional characterisation of the streptococcal rhamnose-polysaccharide regulating and translocating enzymes, GacF and GacE – Supervised by Dr Helge Dorfmueller and Professor Mike Ferguson

Streptococcus pyogenes (S. pyogenes) is a Gram-positive, clinically relevant, human exclusive pathogen capable of causing diseases ranging from mild to severe. Approximately 500,000 deaths per annum can be attributed to severe S. pyogenes infections and no vaccine currently exists to prevent these debilitating diseases. S. pyogenes is commonly referred to as Group A Streptococcus (GAS) due to the prominent cell wall carbohydrate it possesses, the Group A Carbohydrate (GAC). GAC is composed of an alternating α-1-2 α-1-3 polyrhamnose backbone that is decorated on the α-1-2-rhamnose with an immune-dominant β-1,3-linked-N-acetylglucosamine (GlcNAc) unit. My post-graduate studies will focus on two of the GAC biosynthesis proteins, GacF and GacE. Techniques such as structural biology will be performed in order to characterise the active sites of these proteins in an apo / substrate bound state. Biochemical analyses coupled with high resolution mass spectrometry will also be utilised in order to fully characterise the molecular capping entity.

YEAR 2 STUDENTS

Matilda Cederblad - University of Aberdeen - m.cederblad@abdn.ac.uk

Electrophysiological Assessment of Visual Processing after Brain Injury / Spatial attention and awareness in multi-sensory integration – Supervised by Professor Arash Sahraie, Dr Søren Andersen, Dr Mary-Joan MacLeod

The redundant target effect (RTE) refers to the observation that subjects produce faster responses in a detection paradigm if they are presented with multiple sensory stimuli in comparison to a single presentation. This speeding of reaction time to multiple stimuli is known as redundancy gain. To investigate the role of awareness in RTE we attenuated healthy observers' subjective experience of subthreshold stimuli by using Continuous Flash Suppression (CFS) technique. Across multiple experiments, we demonstrated that the magnitude of redundancy gain was correlated with the level of subjective awareness of the stimuli, higher subjective awareness of unimodal stimulation was associated with larger redundancy gains. Research on audio-visual interactions of stimuli suppressed from visual awareness by CFS has pointed towards a relationship between audio-visual spatial congruency and degree of visual awareness. In two experiments we have investigated the relationship between both the incidence of aware responses and reaction times to either visual, auditory or combined audio/visual stimuli. Furthermore, we manipulated spatial attention by instructing the participants to attend to multiple or a single spatial location. Preliminary results suggest that addition of an auditory signal, co-occurring in both space and time to the onset of masked visual target lead to higher incidence of reported awareness.

Jordan Mitchell - University of Edinburgh - jordan.mitchell@ed.ac.uk

Development of multi-parametric tests for the diagnosis of feline tuberculosis – Supervised by Professors Danièlle Gunn-Moore and Jayne Hope

Tuberculosis (TB) is an increasingly recognised disease of cats in the UK, with ~1% of all feline biopsy samples submitted to diagnostic laboratories showing changes consistent with mycobacterial disease. The most commonly isolated organisms were Mycobacterium (M.) microti (19%) and M. bovis (15%), responsible for causing TB.To ascertain the zoonotic risk and appropriately treat cases, it is essential to rapidly obtain an accurate diagnosis and identify the causative organism. Current methodologies have their limitations: most biopsy samples are negative on Ziehl-Neelsen staining for acid-fast bacilli, culture fails in 50% of cases, the interferon-gamma release assay cannot speciate non-tuberculous mycobacteria and PCR is limited for non-human applications. From a bank of formalin-fixed paraffin embedded biopsies, this project aims to better describe the histopathological and immunohistochemical features seen in cases of feline TB and to investigate whether there are differences between M. microti and M. bovis infections. Remnant blood and serum samples will be investigated to characterise the humoral response to mycobacterial infections, with the aim of developing a rapid, in-house antibody-detection test kit for use by vets in clinical practice to identify cases of TB at an earlier stage.

Olivia Watt – University of Aberdeen - o.watt@abdn.ac.uk - Twitter: oliviawatt15

Genetic Determinants of Plant Bioactive Production: Informing Crop Breeding for Health – Supervised by Prof Wendy Russell, Dr Kelly Houston, Dr Robbie Waugh, Dr Charles Bestwick

Barley is a crop currently underutilised as a human food source, with only 2% of UK-grown crops being used directly for food. Extensive literature indicates that consumption of wholegrains reduces the risk of health disorders such as cancer, heart disease and type 2 diabetes. There is strong evidence that the health benefits are attributable to fibre. This includes a registered health claim for beta-glucan, a soluble fibre found in oats and barley known to lower cholesterol. An elite barley line known to be high in beta-glucan was analysed and shown to also be a rich source of micronutrients and non-nutrient phytochemicals, compared to commercially available barley products. These phytochemicals are of significant interest due to their potential to reduce inflammation. A human nutrition study has been designed and undertaken to assess the bioavailability of phytochemicals upon consumption and any bioactive metabolites produced, which was previously unknown.

YEAR 3 STUDENTS

Rosie Barraclough - University of Edinburgh - s1677276@sms.ed.ac.uk

Use of advanced technology to enhance monitoring of dairy cow health and welfare – Supervised by A. I. Macrae, M. H. Haskell, and R. Boyce.

The objective of this study was to use automated behavioural monitoring under commercial farm conditions to describe the behaviour of dairy cattle in late gestation, to quantify any behavioural differences between primiparous and multiparous cows, and to quantify any behavioral differences between assisted and unassisted calvings. A triaxial accelerometer (IceQube; IceRobotics Ltd., Scotland) was fitted to the leg of dairy cattle to automatically collect lying time, step count, total motion, and the total number of standing and lying bouts (postural transitions). Data were summarized into -2h and -24h periods and were analysed using mixed-effect models. In the 4 days prior to calving, there

was a statistically significant difference in the behavior of primiparous cows compared to multiparous cows; on average, primiparous cows lay down 2.8h/d less, had 9.1 more postural transitions/d, had 172 more steps/d, and total motion was greater by 14%. There was no difference in the behaviour of assisted and non-assisted cows on the day of calving or within the last 4 days prior to calving, however assisted cows had 16.5% more postural transitions on the day of calving compared to non-assisted cows. These findings indicate that the number of postural transitions could be used as an indicator of animals that are experiencing calving difficulty, and parity should be considered when predicting the day of calving.

Juan Carlos Entizne – University of Dundee - e.entizne@dundee.ac.uk

StRTD: A high-quality transcriptome annotation for Double-Monoploid Solanum tuberosum – Supervised by Prof. John Brown, Dr Runxuan Zhang

Changes in the transcriptome are the basis of phenotypic responses of eukaryotic organisms to environmental or developmental cues. Re-programming of the transcriptome occurs at the transcriptional and post-transcriptional levels and includes, in particular, alternative splicing (AS). RNA-sequencing (RNA-seq) is used to quantify genome-wide transcriptional and AS changes. The accuracy of differential expression (DE) and differential alternative splicing (DAS) analysis depends on the accuracy of quantification of transcripts by alignment-free programs (Salmon, Kallisto). These require a complete, diverse and high-quality Reference Transcript Dataset (RTD). Based on the work done for the development of a high-quality annotation for Arabidopsis (AtRTD2) (Zhang et al., 2017), we are developing a general computational pipeline to generate high-quality transcriptome annotations from existing annotations and available RNA-seq data. We applied our pipeline to generate a novel high-quality transcriptome annotation for the double-monoploid (DM) potato line Solanum tuberosum (StRTD). StRTD has increased diversity of non-redundant, non-chimeric and non-fragmentary, transcripts compared to the current potato transcriptome (Potato Genome Sequencing Consortium). It has been used to analyse a time-course of infection of DM by late blight and investigate NMD. Given the importance of the assembly of high-quality reference annotations for the accurate expression/AS analysis of RNA-seq datasets, this pipeline will represent a valuable tool for plant scientists. For many plants, genome sequences are limited and transcriptomes are incomplete or non-existent. The pipeline allows RTDs to be generated for plant/crop species with genome sequences using RNA-seq data and to enhance expression/AS analysis.

Jessica Powell – University of Edinburgh - jessica.powell@roslin.ed.ac.uk

Profiling epigenetic landscapes across immune cell types of European and African cattle breeds – Supervised by Liam Morrison, James Prendergast and Tim Connelley

Selective pressures imposed by the local environment and its array of pathogens has caused diversification of cattle subspecies. While European taurine cattle have been the focus of bovine research, the genetic and epigenetic basis underpinning European and African subspecies diversity is poorly defined. Epigenetics is known to play an important role in the regulation of gene expression, and hence influence important traits including disease resistance. However, the tools and reference resources to study the cattle epigenome are almost entirely lacking. In this project, pipelines to map DNA methylation, chromatin accessibility and transcriptional landscapes have been developed and applied to seven immune cell types in Holstein-Friesian cattle. Clustering of cell types based on their DNA methylation and transcriptional profiles has revealed good concordance between datasets. In addition, differential chromatin accessibility analysis has revealed regions with a cell-type specific

chromatin state. Application of these pipelines to two African cattle breeds will provide valuable insights into divergent regulatory sites linked to breed-specific advantageous traits, such as disease resistance. The exploitation of such heritable traits provides the potential to improve cattle productivity in both Africa and Europe.

Eevi Savola - University of Edinburgh - E.A.K.Savola@sms.ed.ac.uk, @EeviSavola

Genetic and environmental variation in the effect of dietary restriction on life-history trade-offs and ageing in Drosophila – Supervised by Dr Craig Walling, Dr Pedro Vale

Dietary restriction (DR), limiting the overall calorie content of food or certain nutrients, limits reproduction and extends lifespan. However, some studies have suggested genetic and environmental variation in the response to DR Additionally, recent evolutionary theory has suggested that the response to DR of lifespan extension is a laboratory artefact. In more stressful conditions, DR will not extend lifespan. To study how developmental diet affects larval development time, adult life-history traits, and survival from infection, we reared eggs from an outbred population of Drosophila melanogaster on five protein restriction diets by altering the carbohydrate to protein ratio of the food. A subset of flies were challenged with bacteria, injured or had no treatment as adults. Adults were kept on standard laboratory fly food. Aspects of both larval and adult life-history traits were measured. Development time was shorter with higher protein diets. Larval DR affected early-life reproduction. Across treatments, larval DR did not extend lifespan. These results provide information on how developmental diet alters the relationship between various life-history traits and response to infection as adults.

YEAR 3 PIPS TALKS

Kate Mathers - University of Dundee - k.mathers@dundee.ac.uk

Secretion, mode of action and utilisation of a new anti-bacterial toxin – Supervised by Dr Sarah Coulthurst

PIPS: World Health Organisation Country Office, Turkey

Working on the Refugee Health Programme, I learnt about the different areas of work that are involved in delivering healthcare to the Syrian refugee population in Turkey. One role of the Country Office is to secure continued funding from donors such as the EU Trust Fund and foreign governments. I helped to compile progress reports detailing how agreed targets were being met under current funding agreements. I also took minutes for working group meetings with other UN agencies and local NGOs, who shared their recent achievements, current issues and ongoing projects. These meetings ensure that the various organisations work together to co-ordinate their responses to the needs of the refugee population. During my PIPS, I helped to draft a report on the results of a recent health status questionnaire of over 4000 refugee households. These results provide a vital source of information for identifying gaps in current services, covering a broad range of topics including living conditions, use of health services and risk factors for non-communicable diseases. Overall, my PIPS provided a fantastic insight into many roles of the WHO and their provision of healthcare to the Syrian refugee population.

Charlotte Woolley - University of Edinburgh - s1576473@sms.ed.ac.uk

Designing Muttley: FreeAgent's statistical sidekick for sales (PIPS project) – Supervised by Dylan Clements, Ian Handel, Mark Bronsvoort, Jeff Schoenebeck (PhD supervisors), Dave Evans (PIPS supervisor)

During my PIPS (Professional Internship for PhD Students) I worked in the data science team at FreeAgent: an accountancy software company. The primary aim of my PIPS project was to improve the efficiency of the sales team by predicting the future success of potential customers. I cleaned and joined together several different types of data including historical customer surveys, website analytics, official company status, geographical information and metrics of activity within FreeAgent and modelled success (defined as having added clients to FreeAgent) using logistic regression, from which we identified several different predictive variables. We prioritised sensitivity over specificity because we considered that customers that were falsely predicted to be unsuccessful would be more costly to the company than customers falsely predicted to be successful. Therefore, a receiver operating characteristic (ROC) curve was created to visualise all potential prediction cut-offs and a threshold was chosen to maximise sensitivity. After optimisation, the model performed with 93.33% (80.43%, 97.83%) sensitivity and 48.48% (24.14%, 67.61%) specificity. It was thus named 'Muttley' and implemented as an interactive tool into Salesforce so that further data could be collected and the model could be updated and improved whilst guiding the decision making of the sales team.

Theme 4: FUNDAMENTAL MEETS SYNTHETIC BIOLOGY

Dalhousie, Room 1F06, June 13th 16:00-17:30

GUEST SPEAKERS

Dr Peter Murray-Rust (Department of Chemistry, University of Cambridge)

Early career researchers and open healthcare

See the following links:

- https://www.slideshare.net/petermurrayrust/early-career-reseachers-and-open-healthcare
- https://twitter.com/LoganCorina/status/986485254075699200

YEAR 1 STUDENTS

Kiani Jeacock – University of Edinburgh - s1831167@ed.ac.uk - Twitter: @kianijeacock

Understanding the role of post-translational modification in age-related protein aggregation – Supervised by Dr David Clarke, Dr Tilo Kunath, Dr Mathew Horrocks

Parkinson's disease (PD) is the second most common neurodegenerative disorder; however a lack of comprehensive diagnostic tools means patients are frequently diagnosed at a late stage in the disease. Various proteoforms of alpha-synuclein (αSyn) have been linked to the aetiology of PD and some may represent ideal candidate biomarkers to enable earlier disease diagnosis. Our research involves using multiple mass spectrometry techniques to probe the structural and functional properties of these various proteoforms to identify species that demonstrate a potential role in early PD pathology, and may therefore be suitable as biomarkers.

Alice Scarpa - University of Aberdeen - r06as18@abdn.ac.uk

Improving the forecast and management of biodiversity through machine learning and artificial intelligence – Supervised by Prof Justin Travis, Dr Wei Pang

Management strategies that can effectively address uncertainty within an ecosystem have become increasingly important. Within ecosystem management issues, how to stop the spread of an invasive species is a topic of particular interest and is the focus of this project. Here we develop an adaptive management system to optimally control a pest in order to maximise the survival of the endemic species.

Eugene Shrimpton-Phoenix – University of St Andrews - esp1@st-andrews.ac.uk

Computational Enzyme Redesign – Supervised by Michael Buehl & John Mitchell

Use of a combination of Quantum-mechanical and Newtonian methods to computationally model the reactivity of a polyethylene-terephthalate (PET) degrading enzyme. The immediate aim of this project is to identify the reaction mechanism of this enzyme by exploring its potential energy surface (PES). A further aim is to identify 'hot-spots' in the enzyme where single-point amino acid substitutions that may prove beneficial to the enzyme's activity.

Rosie Spencer - University of Aberdeen - r.spencer.18@abdn.ac.uk

Genome editing and modelling to understand the biogenesis and function of a novel anti-parasitic drug target – Supervised by Dr Jonathan Pettitt, Dr Berndt Müller, Dr Ekkehard Ullner, Dr Judith Sleeman

Abstract: Spliced leader trans-splicing is essential for nematode gene expression, but the mechanism by which it is achieved is poorly understood. We are investigating the key RNA and protein components in spliced leader trans-splicing using C. elegans as a model system. Our ultimate goal is to exploit these components as targets for the development of new therapeutics to treat nematode parasitic infections of humans, animals and plants.

YEAR 2 STUDENTS

Aron Ferenczi – University of Edinburgh - s1238047@ed.ac.uk

Developing and utilizing a transgene-free genome editing toolbox for the production of high value pigments in unicellular photosynthetic organisms – Supervised by Dr Attila Molnar

We've developed the most efficient gene editing protocol to date in the model green alga Chlamydomonas reinhardtii using CRISPR and DNA repair templates. We're excited that this technique may be cross-species applicable and thus enabling genetic engineering for the algal biotech sector.

Becky Smith – University of Edinburgh - r.h.smith@ed.ac.uk – Twitter: @BeckyGenomics

Advanced bioinformatics tools and pipelines for the next-generation of microbiome analysis – Supervised by Dr Mick Watson (The Roslin Institute) and Dr Alan Walker (The Rowett Institute)

Bridging the gap between genetics and microbiology lies metagenomics; which uses next generation sequencing data and combines it with other disciplines to gain additional information from environmental samples. The testing of tools used on metagenomics data can be difficult, it is impossible to see the full picture from sequencing data alone. Effective evaluation of metagenomic data analysis, often through bioinformatics tools, either relies on in vitro mock communities of known composition, or in silico simulated metagenomics data. Taxonomic classification aims to place taxa, or a living organism, into the phylogenetic tree of life. Here, the tool InsilicoSeq is used to generate ground-truth metagenomics data (Gourlé, Karlsson-Lindsjö, Hayer, & Bongcam-Rudloff, 2019). This study uses a customised reference database consisting of all taxonomy used to generate the simulated metagenome, is used to benchmark the classification tool Kraken2. Taxonomic classification is done using the customised database, the 'standard' kraken2 database, and the 'miniKraken2' database. Classification rates were comparable between the standard and mini databases, and highest with the customised ground-truth database. This demonstrates the influence of reference database choice and composition on taxonomic classification, particularly for environments which are under-represented.

Agata Wawszczyk - University of Edinburgh - s1235039@ed.ac.uk

Translational regulation of bacterial micro-injection system – Supervised by Prof. David Gally, Dr Sander Granneman

Enterohaemorrhagic Escherichia coli (EHEC) is a food-borne pathogen associated with outbreaks of bloody diarrhoea and haemolytic uremic syndrome. It is commonly found colonizing cattle in which it sustains asymptomatic infections. A critical virulence factor of EHEC is its ability to attach and efface the intestinal epithelium, which is dependent on production of Type 3 Secretion System (T3SS), a molecular syringe encoded on Locus of Enterocyte-Effacement (LEE). Expression of T3SS seems to be

staged with a checkpoint after production of the basal apparatus and before expression of the syringe's 'needle'. LEE-encoded protein SepL has been shown to control this translational switch. However, little is known about the SepL regulation, there is an evidence that conformation of the sepL encoding mRNA determines its translation. We hypothesize that interaction between LEE-encoded protein/s and the mRNA is necessary to achieve the mRNA conformation permissive for translation. Examination of sepL-GFP fusions expression in basal apparatus deletion backgrounds provided evidence for involvement of LEE-encoded basal apparatus components in translational regulation of SepL. Additionally, chemical probing using selective 2'-hydroxyl acylation analysed by primer extension (SHAPE), suggested that sepL mRNA secondary structure is a likely inhibitory factor in SepL expression. Ongoing work focuses on characterisation of mechanisms underlying proposed interactions.

YEAR 3 STUDENTS

Grant Gale – University of Edinburgh - grant.gale@ed.ac.uk - Twitter @Cyanosaurus_rex

Generating new molecular tools to manipulate phycobiliprotein yields in cyanobacteria – Supervised by Alistair McCormick, Baojun Wang

Cyanobacteria can synthesise complex molecules utilising light and fixed carbon dioxide making them a promising platform for the renewable production of biochemicals. Genetic tools have been developed to advance metabolic engineering in cyanobacteria to levels commensurate with other model cell factories. Available tools do not conform to any cloning standard thus are difficult to share. CyanoGate is a GoldenGate system we have developed based on the Phytobrick syntax that includes a suite of new genetic tools. I present components of Cyanogate, including 36 promoters, chromosomal integration or self-replication vectors, and CRISPR interference for gene repression characterised in the model cyanobacterium Synechocystis sp. PCC 6803.

Isobel McLachlan - University of Edinburgh - s1203028@sms.ed.ac.uk

Dynamic Modelling of Foot and Mouth Disease in Endemic Areas – Supervised by Mark Bronsvoort (UoE), Ian Handel (UoE), Glenn Marion (BioSS), Ian McKendrick (BioSS)

Foot and mouth disease (FMD) burden disproportionally affects Africa where the disease is considered endemic. Smallholder livestock keepers experience significant losses, but disease dynamics and mechanisms underlying persistence at the herd level and beyond are still poorly understood. We address this knowledge gap using stochastic, compartmental modelling to explore FMD dynamics of individual herds within an endemic setting. Our model structure is of the form susceptible-exposed-infectious-recovered-carrier. Results suggests repeated introduction of virus from out-with the herd is required for long-term viral persistence. Presence of immune individuals within the herd reduces the chance that new disease exposures will result in a significant secondary outbreak. This gives rise to a period of reduced risk which increases with initial outbreak size and slower population turn-over. Whilst inclusion of a carrier state increases viral persistence (although not indefinitely) other measures of herd level disease dynamics are similar to the model without carriers. Changing serotype dominance has been reported to contribute to perceived persistence in endemic regions. Our predicted duration of the reduced risk supports different strains of FMD virus resulting in the observed yearly herd-level outbreaks.

Guillermo Serrano Nájera - University of Dundee - gserranonajera@dundee.ac.uk

Trendy Genes: Automatic hypothesis generation for drug discovery – Supervised by Daniel Crowther

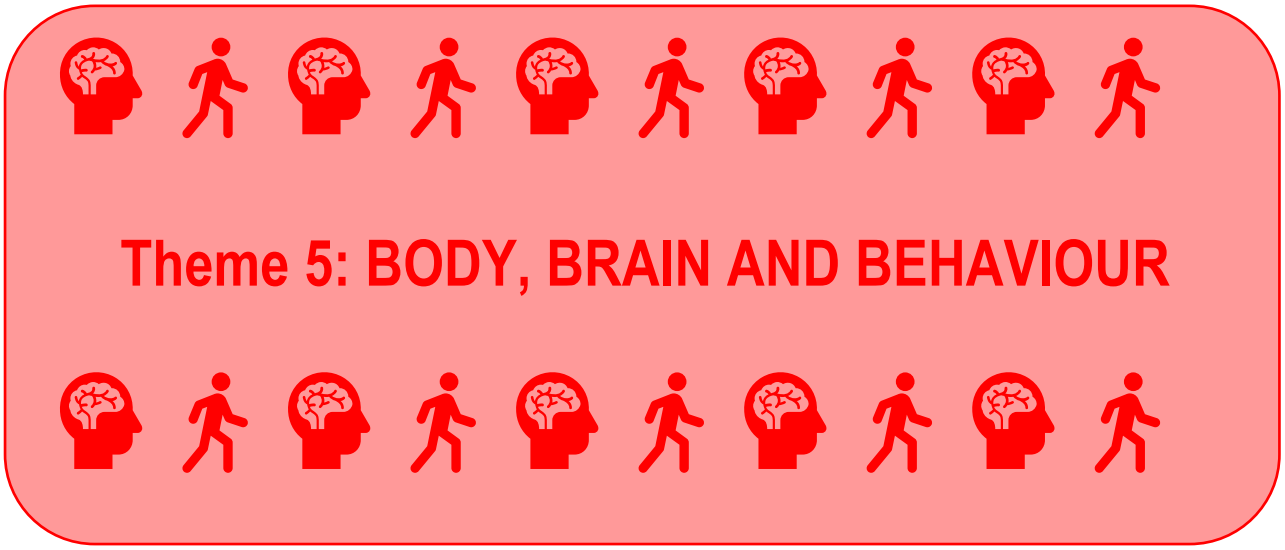
AI-assisted drug discovery has been proved to speed up the development of new pharmaceutical agents given a protein target. Nevertheless, target identification remains as the first bottleneck to overcome. Traditionally, target identification has been carried out by individual scientists using the available literature and local expertise. However, the increasing publication rates hamper both, the maintenance of an overview and the identification of new trends. Here we propose a new pipeline for high-quality hypothesis generation in drug discovery through the automatic analysis of the literature. Every paper in PubMed was unambiguously associated with a gene or disease using a novel procedure based on cocitations networks and machine learning. Subsequently, recurrent neural networks were trained to predict the publication dynamics of every gene. Thus, a gene is trendy if it presents more publications or citations than expected. In order to understand why a gene is trendy, communities in the citation networks along with automatic topic detection routines were used to extract essential information from groups of publications. Finally, we identified common features among papers of interest for the pharmaceutical industry to assess which trendy genes are potential targets. We expect this pipeline to be useful for funding agencies and biotech companies in addition to offer new ways to explore the literature for individual researches.

YEAR 3 PIPS TALKS

Charlotte Repton – University of Edinburgh - charlotte.repton@ed.ac.uk

Outsiders: Land Settlement in Scotland after WWI (PIPS) – Supervised by Jane Brown, NRS Maps and Plans

After WWI, unemployment was high (especially for ex-soldiers) and farming production low. One perceived reason for the agricultural decline was the movement of rural people into the cities and emigrating abroad. Throughout the 1920s, the Scottish government set about solving these problems via the Land Settlement scheme, in which large estates were broken up for landholdings (farms) of small to intermediate size. These landholdings had fixed rents, provided generous loans for equipment and stock, and were marketed to ex-servicemen in particular. However, the actual success of the schemes has not been assessed until now. I examine the sociological and agricultural impact of the schemes, and ask: 1) Did landholdings increase farming output? 2) Did landholdings decrease unemployment, especially amongst soldiers? and 3) Did the landholding schemes bring more people to the Scottish countryside?



Session 1: Dalhousie, Lecture Theatre, June 14th 10:10-12:00 – With Prof Nicola Clayton and Mr Clive Wilkins

Session 2: Dalhousie 1F06, June 14th 10:10-12:00 – With Prof Gernot Riedel and Dr Carole Torsney

GUEST SPEAKERS

GROUP I: COGNITIVE SCIENCE BRANCH

Nicola Clayton (Professor of Comparative Cognition) FRS & Clive Wilkins (Artist-in-Residence) MMC

The dancer remembers: The choreography of the mind and body

In this presentation we will explore the complex relationship between memory and experience from the inside and the outside. The stories we tell ourselves influence the way we see and the way we remember. We imagine we see everything but we seldom do. We think we remember the diversity of the world around us but cognitive roadblocks in our thinking constrain the process. When all is said and done all we are left with is a two- dimensional approximation of the complexity of the reality around us. This may be why we think the future will be more like the present than it ever will be.

For further information please visit The Captured Thought - https://thecapturedthought.com.

Further reading:

- Clayton, N. S. & Wilkins, C. A. P. (2018). Seven Myths of Memory. *Behavioural Processes*, 152, 3-9.
- Clayton, N. S. & Wilkins, C. A. P. (2017). The Creative Navigator's Compass: Memory and Perception~ and how we know which way we are facing. *The Psychologist* 35, 10-14.
- Clayton, N. S. & Wilkins, C. (2017). Memory, Mental Time Travel and the Moustachio Quartet. *Royal Society Interface Focus* 30, 22-26.
- Laland, K., Wilkins C. A. P. & Clayton, N. S. (2015). The Evolution of Dance. *Current Biology* 26, R5-9.

Joint publications

- Clayton, N. S. & Wilkins, C. A. P. (2012). Imagination: The Secret Landscape. Being Human. http://www.beinghuman.org/article/imagination-secret-landscape
- Laland, K., Wilkins C. A. P. & Clayton, N. S. (2015). The Evolution of Dance. Current Biology 26, R5-9.
- Clayton, N. S. & Wilkins, C. A. P. (2016). Big Picture: Art is the process of memory. The Psychologist 29, 15-16.
- Clayton, N. S. & Wilkins, C. A. P. (2017). The Creative Navigator's Compass: Memory and Perception~ and how we know which way we are facing. The Psychologist 35, 10-14.
- Clayton, N. S. & Wilkins, C. A. P. (2018). Memory, Mental Time Travel and the Moustachio Quartet. Royal Society Interface Focus 30, 22-26.
- Clayton, N. S. & Wilkins, C. A. P. (2018). Seven Myths of Memory. Behavioural Processes, 152, 3-9.

Group I – Students presenting:

- Courtney Bernadette Ann Aitken
- Veronika Ambrozova
- Matt Colligan
- Jacob Ridley John Francis
- Karina Kangur
- Rebecca Maguire
- Joseph Moore
- Ana Rozman
- Randeep Samra
- Aikaterini Zafeiri

GROUP II: GENERAL NEUROSCIENCE AND PHYSIOLOGY BRANCH

Profeessor Gernot Riedel, Institute of Medical Sciences, University of Aberdeen

Dr Carole Torsney (Centre for Discovery, Brain Sciences, University of Edinburgh)

Sex and injury dependent nociceptor plasticity

Group II – Students presenting:

- Grace Bailey
- Sarah Blincko
- Jason Nicol Clark
- Jessica-Lily Harvey-Cox
- Kerry Leslie
- Cameron Malcolm
- Fiona Jane Ramage
- Daniela Schnitzler
- Holly Woodward

YEAR 1 STUDENTS

Veronika Ambrozova – University of St Andrews - va26@st-andrews.ac.uk

Network analysis of lateral entorhinal-hippocampal circuits for episodic memory – Supervised by Dr James Ainge, Dr Emma Wood

My project aims to examine the neural mechanisms underlying memory encoding and retrieval. It investigates the role of lateral entorhinal-hippocampal circuits in these processes by combining behavioural measures together with genetic and molecular techniques.

Grace Bailey – University of Edinburgh - s1798029@ed.ac.uk

Epigenetic control of nuclear chromatin architecture during cardiomyocyte development – Supervised by Sari Pennings and Colin Semple

Shortly after birth, cardiomyocytes become non-proliferative which means that injury to cardiac tissue in later life can be fatal. Specialised heterochromatin found around the centromere is essential for proper mitosis. My project will investigate changes in chromatin architecture during mouse cardiomyocyte development and explore the impact on mitotic potential of these cells.

Jason Clark - University of Aberdeen - j.clark.18@abdn.ac.uk

Application of computational-driven design of function-directed ligands for selective retinoic acid receptor binding – Supervised by Professor Peter McCaffery, Professor Peter Coveney, Professor Andrew Whiting, Dr Iain Greig

Abstract: Understanding the function of retinoic acid (RA) and the process of retinoic acid receptor (RAR) ligand binding are vital in progressing research into the potential therapeutic role of retinoids in neurodegenerative diseases. This project aims to utilize computationally-enhanced design and modelling techniques to develop selective RAR ligands, which will be used to develop quantitative structure-activity relationships and understand the mechanisms of RAR activation. These ligands will be tested biologically to identify unique genomic and non-genomic activity which feeds back into the design process in a systems biological approach, aiming to produce ligands which optimally trigger specific RAR pathways and allow for genomic and non-genomic triggers to be distinguished.

Matt Colligan - University of Edinburgh - matt.colligan@ed.ac.uk - duguidlab.com

Neural circuits underlying visuomotor integration during forelimb reaching – Supervised by Ian Duguid

In order to interact with our environment we use visual information to guide our movements. To understand how the brain integrates visual and motor information, I will record cell population activity in candidate visuomotor areas of the mouse brain during a forelimb reaching task. Combined with brain area-specific inactivation experiments, I will attempt to characterise the functional connectivity within neural networks that process visual information for the guidance of movement.

Cameron Malcolm - University of Aberdeen - r02cm18@abdn.ac.uk

Uncovering the pharmacology of a novel receptor target for age-related macular degeneration – Supervised by Dr Fiona Murray

Age-related macular degeneration (AMD), the leading cause of blindness in the industrialised world, is characterised by degeneration of the retinal pigment epithelial (RPE) cells. The orphan G-protein coupled receptor GPR75 is highly expressed in RPE cells and multiple single nucleotide polymorphisms affecting GPR75 have been identified in AMD sufferers. This project aims to uncover the pharmacology of GPR75 and elucidate its function in relation to AMD pathology.

Ana Rozman - University of Aberdeen - a.rozman.18@abdn.ac.uk Twitter @AnaRozman2

Neural mechanisms of colour appearance across the lifespan – Supervised by Dr Jasna Martinovic and Dr Ines Jentzsch

Age related changes to the structures involved in human colour vision are subject to many age related changes, implying appearance of colour would change as a subsequence of healthy ageing. This however does not seem to be the case due to compensation for losses by cortical mechanisms. Our project aims to characterise these mechanisms for the first time using a combination of psychophysical and electroencephalographic (EEG) methods.

Holly Woodward - University of Edinburgh

How do sex hormones regulate the function of arteries and valves? – Supervised by Vicky MacRae, Patrick Hadoke

Aortic stenosis is caused by mechanical injury, inflammation, fibrosis, and sometimes calcification, although the mechanism behind calcification is unknown, partly due to a lack of sufficient animal models. We are developing a model, by inserting a guidewire into the left ventricle of C57BL/6J mice and rotating it up to twenty times across the aortic valve then taking serial ultrasound scans to determine cardiac and aortic function. Although development of this model is still undergoing, if successful, this model could be used in research addressing mechanisms and possible pharmaceutical treatments of calcific valve disease.

YEAR 2 STUDENTS

Courtney Aitken - University of St Andrews - cbaa@st-andrews.ac.uk - Twitter: @courtneyaitkenx

Neurophysiological markers of memory error monitoring across the lifespan – Supervised by Dr Akira O'Connor, Dr Ines Jentzsch

Memory decision-making can occasionally fragment and lead to experiences that indicate conflict in our memory systems. For example, in the experience of déjà vu, there is a mismatch between two concurrent mental evaluations; an inappropriate assessment of familiarity and an objective evaluation of unfamiliarity. Déjà vu experiences are not marked by any outward behavioural change, so we often rely on self-reports of the experience to study it. Self-report data has demonstrated that people in their young adulthood (aged around 18-25) experience déjà vu most often with the incidence declining through adulthood thereafter. This mirrors what we know about conflict monitoring performance and neurophysiological markers (of conflict monitoring) more generally. Young adults tend to perform better on behavioural measures of error detection and show stronger neurophysiological responses to conflict or lapses in error detection. Therefore, the aim of my project is to investigate déjà vu and its relationship with previously unexplored neurophysiological correlates of conflict monitoring across the lifespan.

Sarah Blincko - University of St. Andrews - sb336@st-andrews.ac.uk

Exploring Regeneration in Amphioxus using Lineage Tracing Techniques – Supervised by Dr Ildikó Somorjai

Amphioxus are marine invertebrates and are the most basal living member of the phylum Chordata. This basal position is of significance, since the amphioxus genome is simpler than the human genome as amphioxus have not undergone the two rounds of whole genome duplication that occur later in evolution. In addition, amphioxus possess a high regenerative capacity, particularly in the postanal tail. Considering characteristic chordate structures, such as a notochord and neural tube, are found in amphioxus, understanding their regenerative ability can help us improve processes like wound healing in humans, for example.

So far, amphioxus tail regeneration has been characterised morphologically. However, little is known about which signalling pathways are involved, the role they play, and which cells are responsible for producing the regenerate. We have developed a lineage-tracing technique using a lipophilic fluorescent dye which will allow us to follow the migration of cells, in order to learn more about the plasticity of different cell types. Our initial findings have implied that neural tube cells are responsible for producing only the neural tube in the regenerate, but further work is needed to understand if other cells contribute to this regenerated structure, such as stem cells.

Jacob Francis – University of St Andrews - jrjf2@st-andrews.ac.uk

Developing a network-based understanding of Drosophila larvae locomotion using computational neuroscience and live imaging of neural activity – Supervised by Dr Stefan Pulver, Dr Anne Smith

Understanding how neural networks implement behavioural decision-making is a fundamental goal of neuroscience. Through observation of Drosophila larval locomotion, we have identified what appear to be attempts at peristaltic waves. These events, termed ‘attempted waves’, have qualitative similarities to normal peristaltic waves but differ temporally and spatially compared to normal larval behaviour. Furthermore, these events have been also found in the isolated central nervous system. We identify a strong phenotype of an association between attempted forward waves (posterior based event) and anterior based events, elucidating to a possible interplay between two or more rhythm generating kernels. Through in-depth analysis of these events and observing locomotion as a whole, we are able to infer functional architecture relating to larval locomotion. We provide several testable hypotheses in

the form of a model for neural network architecture in the context of locomotion.

Joe Moore - University of Edinburgh - joe.moore@ed.ac.uk

Network analysis of entorhinal-hippocampal circuits for spatial cognition and memory – Supervised by Emma Wood, James Ainge

Memories of environments are important for navigation and remembering events (what happened where). Formation of these memories requires sensory information about the outside world, such as local or contextual cues and visual landmarks. The hippocampus and entorhinal cortex play key roles in this process, but functions of the specific neural circuits are unknown. Previous data showed that place cells in the hippocampus were less likely to use information about global visual landmarks when the medial entorhinal cortex was lesioned. These experiments test the hypothesis that this information enters the hippocampus via the layer 2 stellate cells of the medial entorhinal cortex. This cell population was selectively deactivated in transgenic mice using a virus that caused expression of tetanus light chain toxin. These mice were then assessed on use of global landmarks, based on behavioural and electrophysiological measurements, compared to control mice. Behavioural tasks included testing of object-location association recognition memory, and electrophysiology experiments involved recording changes in activity of hippocampal place cells with various environmental cue manipulations.

Fiona Ramage - University of Dundee – F.J.Ramage@dundee.ac.uk – Twitter: FJRamage

Mechanisms behind the short-term effects of high-fat-sugar and ketogenic diets on cognition– Supervised by Dr Ros Langston (UoD), Prof Lynda Williams (UoA) and Prof Jerry Lambert (UoD)

High-fat and high-sugar Western diets have long been known to negatively impact metabolic health. It has now been shown that their consumption can have severe consequences for brain function. While many different mechanisms have been proposed for diet-induced brain changes, none are fully characterised. Little is known about the very short-term versus longer term effects of these diets on the brain, or the relative importance of dietary carbohydrate in mediating the negative effects of high-fat diets. We are currently conducting systematic reviews of proposed mechanisms for high-fat diet-induced brain changes in mice and rats, which will form the basis for later in vivo studies. The aim of our in vivo experiments is to measure short-term peripheral and central changes induced by high-fat and ketogenic diets and to define their mechanisms. We fed adult mice a high-fat-sugar diet (HFD) or a ketogenic (high-fat zero carbohydrate) diet, which had differential effects on peripheral physiology. EchoMRI revealed that HFD-fed mice gained body weight and fat mass after 3 days on diet, whereas KD-fed mice did not. KD-fed mice had increased blood ketones and slightly decreased blood glucose after 6 days on diet, which HFD-fed mice did not. We are using in situ hybridisation and mass spectrometry to analyse brain samples from these mice, to determine the short-term effects of HFD and KD. Gene markers of inflammation (SerpinA3N), neuronal plasticity (CRMP2 and BDNF), and hormone signalling (insulin, leptin, and ghrelin receptor), as well as by products of metabolism (advanced glycation end products (AGEs) and ceramides) will be quantified.

Aikaterini Zafeiri - University of Aberdeen - r01az17@abdn.ac.uk

Mechanisms via which the human fetus is at risk from over-the-counter analgesics – Supervised by Professor Paul A. Fowler (University of Aberdeen), Dr David C. Hay (University of Edinburgh), Dr Rod T. Mitchell (University of Edinburgh), Dr Mairi Maclean (University of Aberdeen)

The use of over-the counter medications during pregnancy is widespread, especially for analgesic compounds (e.g. paracetamol, ibuprofen). The dose and frequency of use of these drugs is difficult to regulate, and there are associations between in-utero analgesics exposure and increased risk of congenital defects in the offspring. While the human foetal liver has been shown by our group and others to be active in the late first/second trimester, very little is known about the actual mechanisms involved in uptake, metabolism/biotransformation and clearance of medicines and their metabolites. The aim of this project is to explore the effects of common over-the-counter analgesics on the human fetus, provide basic mechanistic understanding of these effects, as well as information on the responses of the foetal liver to those analgesics and their metabolites. Our unique human foetal tissue collection, allowed for analysis of RNA-sequencing data and in-vitro liver systems for the determination of gene and protein pathways involved in metabolism and clearance of medications at different stages during gestation. This analysis also compared results between male and female foetuses, as well as adult normal function. In the longer term such data would be useful in designing analgesics that could be used by pregnant women without posing serious risks to the developing human fetus.

YEAR 3 STUDENTS

Scott Dillon - University of Edinburgh - s1542732@sms.ed.ac.uk; @dillonbonebi

Characterisation of the intimate relationship between collagen and mineral during skeletal biomineralisation – Supervised by Prof. Colin Farquharson and Dr Fabio Nudelman

Bone mineralization is orchestrated by osteoblasts which secrete matrix vesicles (MVs) 100-300nm in diameter into a collagenous connective tissue scaffold. MVs provide a localised concentration of calcium and inorganic phosphate (Pi) ions to facilitate mineral nucleation, however the mechanism by which intravesicular Pi generation is achieved is currently unclear. Phosphatases are essential in promoting biomineralization through liberation of Pi from biological molecules. The phosphatase PHOSPHO1 is a critical effector of this process postnatally however its role during embryonic development, along with its relationship with established phosphatases such as tissue non-specific alkaline phosphatase (TNAP), has yet to be fully elucidated. I have used a range of cellular/molecular biology methodologies and bioimaging techniques to characterise the phenotype of the Phospho1 knock-out (Phospho1-/-) during the very first steps of skeletal development in the embryo. PHOSPHO1 co-localised with TNAP at distinct patches at the membranes of mineralising cells, while both genes were upregulated over skeletal development. Mineralisation is severely delayed in Phospho1-/- embryos which demonstrate a much slower rate of mineral formation. At the nanostructural level, Phospho1-/- animals exhibited generalized hypomineralisation and an accumulation of mineral-deficient MVs.

Karina Kangur - University of Aberdeen

Perception of Material and Texture in Vision and Action / The influence of visuohaptic experiences on visual and haptic perception of material properties – Supervised by Dr Constanze Hesse & Prof Julie Harris

Previous literature suggests that humans perform in a statistically optimal way when estimating material roughness using both vision and/or touch. If both modalities receive conflicting information, the perceptual system combines the estimates from each modality where the resulting percept has shown to reflect an almost perfect average estimate of the two. Currently, we have a limited understanding of the relationship between the perceptual estimation of material roughness and the visuomotor system, and its effect on the temporal kinematic parameters. While previous studies have primarily focussed on participants' roughness perception in manual exploration tasks, we wanted to explore whether and how experiencing visuohaptic conflicts change the estimation of object roughness during more natural object interactions (i.e., grasping). In a series of experiments, our aim is to address these research questions by using behavioural 3D motion-tracking in reaching and grasping tasks; and roughness estimation in perceptual tasks involving textures that have been manipulated in their spatial density. These experiments will allow us to gain insight into how material roughness influences visuohaptic perception of surfaces, and how this information is processed in the brain.

Keywords: Human neuroscience, Psychophysics, Vision, Action

James MacLeod - University of St Andrews

Optogenetic Dissection of Locomotor Networks in Larval Drosophila melanogaster – Supervised by Dr Stefan Pulver

Dopaminergic modulation of the exploratory headsweep motor pattern in Drosophila melanogaster larvae MacLeod J[1], Pulver SR[1] [1]School of Psychology and Neuroscience, University of St Andrews, United Kingdom

Drosophila larvae navigate by moving along chemical, light and temperature gradients. This is achieved by alternating between straight runs and exploratory headsweeps whereby the animal moves its head and olfactory organs left and right before reorienting to direct subsequent runs up or down sensory gradients. Previous work suggests that exploratory headsweeps may be produced by a dedicated central oscillator, subject to neuromodulation. Here, we explore how the biogenic amine dopamine influences the production of headsweep motor patterns. We used optogenetic and pharmacological manipulations of dopamine signalling in vivo and in vitro and observed the effects on the headsweep motor program. We found increased dopamine signalling to strongly inhibit headsweeps, and inhibition of dopamine signalling to promote headsweeps. To uncover neurons underlying the phenotype, electrophysiological recordings of motorneuron activity were carried out while optically imaging calcium dynamics in dopaminergic neurons. A high proportion of dopaminergic cells showed rhythmic activity that was correlated with fictive behaviours, including a number of TH-expressing neurons phase-locked to headsweep dynamics. These data suggest a role for dopamine in the modulation of the headsweep motor pattern and suggest a previously unknown role of dopaminergic signalling in the production of directed movement.

YEAR 3 PIPS TALKS

Christina Brown - University of Edinburgh - s0901786@sms.ed.ac.uk

A Science Policy internship at the Scottish Government – working with the Tobacco Control Team - PhD supervisor – Professor Matthew Nolan - PIPS supervisors - Morris Fraser and James Niven

The Tobacco Control policy team at The Scottish Government collaborate with experts in academia and health organisations in order to determine what policies will help reduce the number of smokers in Scotland. My role was to assist in research for various topics and observe the process from published academic papers to strategies to be commissioned by government. To assert the relationship between smoking and weight gain, I wrote a literature review citing many physiological and psychological mechanisms for the cause, as well as possible interventions for policy making. However my main project was focused on e-cigarettes – their safety and possible use as cessation tools. Succinct reports were written to highlight research and interventions that would help aid new government strategies – e-cigarettes in relation to mental health, pregnancy, cessation and inequalities for example. This was aided by speaking to many stakeholders in tobacco research: academics, NHS Scotland, NHS Boards, ASH Scotland, Cancer Research UK, retailers and government ministers. The research was applied to the new five-year action plan on Tobacco control, 'Raising Scotland's Tobacco Free Generation' and was published in June 2018.

Disclaimer: Every effort has been made to ensure that the information contained within this booklet is correct at the time of publication. Updates on the EASTBIO Symposium programme and details are published on our EASTBIO website, at http://www.eastscotbiodtp.ac.uk/eastbio-symposium-2019.