

ISMB NEWS

Issue 14, Summer 2018

ISMB NEWS is a bulletin published in order to share information between the various departments involved in the Institute of Structural and Molecular Biology at UCL and Birkbeck. This includes information about events, research, new staff appointments, awards and grants.

Your comments, suggestions and contributions are welcome and will help us put together a newsletter which meets your expectations. Please email the ISMB administrator at ismb-admin@ismb.lon.ac.uk.

In this issue

WELCOME TO... FAREWELL TO... 2

IN FOCUS: ISMB PROFILES 2

Dr Anastasia Mylona

Dr Philip Robinson

RESEARCH HIGHLIGHTS 4

ISMB Featured articles and commentaries

UPDATE ON CENTRES & LABORATORIES 8

STUDENT NEWS 10

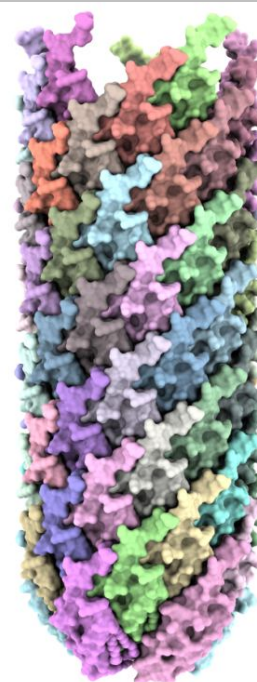
AWARDS, PRIZES & GRANTS 10

EVENT NEWS 12

2018 ISMB Symposium

ISMB Core Member Retreat

Upcoming Events



The F pilus structure determined by cryo-EM. The F pilus is an extracellular appendage elaborated by the conjugative type 4 secretion system (T4SS) encoded by the F plasmid. Conjugative T4SSs form a secretion apparatus that mediates the unidirectional transfer of plasmid DNA and other genetic elements from a donor cell to a recipient cell in a process called "bacterial conjugation". Conjugation is the main process by which antibiotic resistance genes spread from one bacterium to another. Before operating DNA transfer, T4SSs must produce a pilus through which the DNA will pass to reach out to the recipient cell. In this structure, it is shown that the pilus forms a 5-start helical array. It is made of hundreds of copies of a stoichiometric protein-lipid complex with the negatively charged lipid head groups all directed towards the pilus lumen. The pilus interior is large enough to accommodate passage of not only single-stranded DNA but also unfolded proteins.

Ref: Costa, T., Ilangoan, A., Ukleja, M., Redzej, A., Santini, J., Smith, T., Egelman, E. * and Waksman, G. (2016). Structure of the bacterial sex F pilus reveals an assembly of a stoichiometric protein-phospholipid complex. *Cell*. 166, 1436–1444

WELCOME TO... FAREWELL TO...

Welcome to Principal Investigators **Anastasia Mylona** (Birkbeck Career Development fellowship) and **Philip Robinson** (MRC CDA Research fellowship), joining the ISMB. Profiles of Anastasia and Philip can be found below.

Welcome to the following Post-Docs who recently joined ISMB lab groups:

Anais Cassaignau, **Sammy Chan** and **Alkistis Mitropoulou** (joining the John Christodoulou/Lisa Cabrita lab group), **Yu Chen** (joining Frances Brodsky's group), **Dave Hollingworth** (Bonnie Wallace's group), **Abid Javed** (Elena Orlova's group), **Aakash Mukhopadhyay** (Anthony Roberts' group), **Mauro Maiorca** and **Sony Malhotra** (Maya Topf's group), **Henry Taunt** (Saul Purton's group), **Kevin Mace**, **Yogesh Vegunta** and **Sunanda Williams** (Gabriel Waksman's group) and **Duy Khanh Phung** (Finn Werner's group).

Farewell to Principal Investigators **Filipe Cabreiro** and **Vitor Pinheiro**, who will be leaving the ISMB to take up positions at Imperial and KU Leuven, Belgium, respectively. Farewell to **Ambrose Cole**, X-ray Crystallography lab manager and welcome to **Nikos Pinotsis**, who is taking on the role. Farewell also to the following post-docs: **Amit Meir**, **Tiago Costa** (Gabriel Waksman's group), **Tom Osborne** (Jo Santini's group), **Philip Dannhauser** (Frances Brodsky's group), **Timothy Scott** (Filipe Cabreiro's group), **Carol Sheppard** (Finn Werner's group) and **Agnel Joseph** (Maya Topf's group).

IN FOCUS: ISMB PROFILES



Dr Anastasia Mylona

I started my first my independent position in January 2018, focussing on the mechanisms and the biological function of multisite phosphorylation in signalling and cancer. I obtained my PhD in biochemistry and X-ray crystallography at the European Molecular Biology Laboratory (EMBL), where I worked with Prof. Christoph Mueller on the structural characterisation of the yeast transcriptional machinery. I then obtained EMBO and CRUK postdoctoral fellowships to work at Cancer Research UK/London Research Institute (currently the Crick Institute) with Sir Richard Treisman, where I expanded my knowledge on transcription, signalling and cancer biology. During my postdoctoral years, I became interested in multisite phosphorylation and its biological role in signalling and transcription. In particular, I conceived and developed a novel multidisciplinary approach combining structural with in vivo cell biology techniques that for the first time allowed investigating mechanistically multisite phosphorylation (Mylona et al., Science 2016). Subsequently, I received a Birkbeck ISSF Career Development Award to start my independent research at the ISMB.

The research vision of my lab is to understand the mechanism and functional role of multisite phosphorylation in physiology and disease. The activity of cells is controlled by signalling pathways, which ensure that cells and tissues function properly. Protein phosphorylation is an important post-translational protein modification and a major regulatory mechanism of cellular signalling. Deregulation of phosphorylation pathways commonly underlies disease aetiology. Proteins often get phosphorylated not only at one but at multiple sites by a single protein kinase. Multisite phosphorylation is a key regulatory mechanism in many cellular processes, and has been suggested to provide a precise tool to generate complex functional outputs from single kinase signalling input. However, to date essentially all

studies have focused on single phosphorylation events, because multisite phosphorylation was impossible to study, due to the absence of a suitable methodology. I have developed a novel multidisciplinary methodology pipeline combining structural (time-resolved NMR, X-ray crystallography), biochemical and in vivo cell biology experimental strategies, which we will apply to study the mechanism and functional role of multisite phosphorylation in tumorigenesis. Phosphorylation of a target protein at multiple sites acts as a code and governs interactions with protein partners. These phosphorylation-dependent interactions determine how a protein behaves and how it shapes a specific cellular function. The ultimate goal of our research is to understand how multisite phosphorylation controls the activity of transcriptional regulators and how it can alter the architecture of signalling pathways in diseases like cancer, which may pave the way for novel treatments.

[Research interests and publications: <http://dev.ismb.lon.ac.uk/anastasia-mylona/>]

[email: a.mylona@mail.cryst.bbk.ac.uk]

Dr Anastasia Mylona

Dr Philip Robinson

My research group investigates the structure, mechanism and biology of the SWI/SNF-family of chromatin remodelling complexes. We strive to understand the molecular basis of SWI/SNF's ATP-dependent chromatin remodelling activity, the architecture of its multiple subunits, details of its interaction with nucleosomes and the molecular determinants of SWI/SNF recruitment to target gene promoters. To address these questions we use a multi-disciplinary approach that combines biochemical and biophysical analyses with structural biology techniques (X-ray crystallography and cryo-EM), advanced mass spectrometry and computational modelling.

Chromatin remodelling complexes are large multi-subunit molecular machines that are required in all eukaryotes to overcome the barrier presented by the tight packaging of DNA into nucleosomes. By harnessing the energy released from ATP hydrolysis to mobilise target nucleosomes, these machines provide DNA access to the factors responsible for transcription, DNA repair, replication and recombination. In yeast, the SWI/SNF complex primarily stimulates transcription from inducible target genes whereas in higher eukaryotes SWI/SNF complexes also play a fundamental role in the establishment of tissue- and developmental stage-specific transcriptional programs and function as an important global tumour suppressor. Mutations affecting human SWI/SNF subunits are found in a staggering 20% of all human tumours. Through high-resolution structural studies we therefore hope to lay the foundations for the development of chemotherapeutics targeting mutant human SWI/SNF.

I graduated from the University of Nottingham with a degree in Biochemistry and Genetics in 2001, and moved to the MRC Laboratory of Molecular Biology to perform my graduate studies. Working with Dr. Daniela Rhodes I developed a novel in vitro method for the assembly of long, regularized nucleosome arrays, which were used to study the structure of compact chromatin fibres and the effects of histone PTMs on chromatin compaction. I next moved to the lab of Roger Kornberg at Stanford University to



study the structure of the transcription initiation machinery, with a particular focus on the structure and role of the 1MDa Mediator complex. There, I employed a multidisciplinary approach to solve a number of multi-subunit transcription complexes, which have helped to shed light on the mechanism of transcriptional pre-initiation complex formation at gene promoters.

[Research interests and publications: www.labrobinson.com]

[email: p.robinson@mail.cryst.bbk.ac.uk]

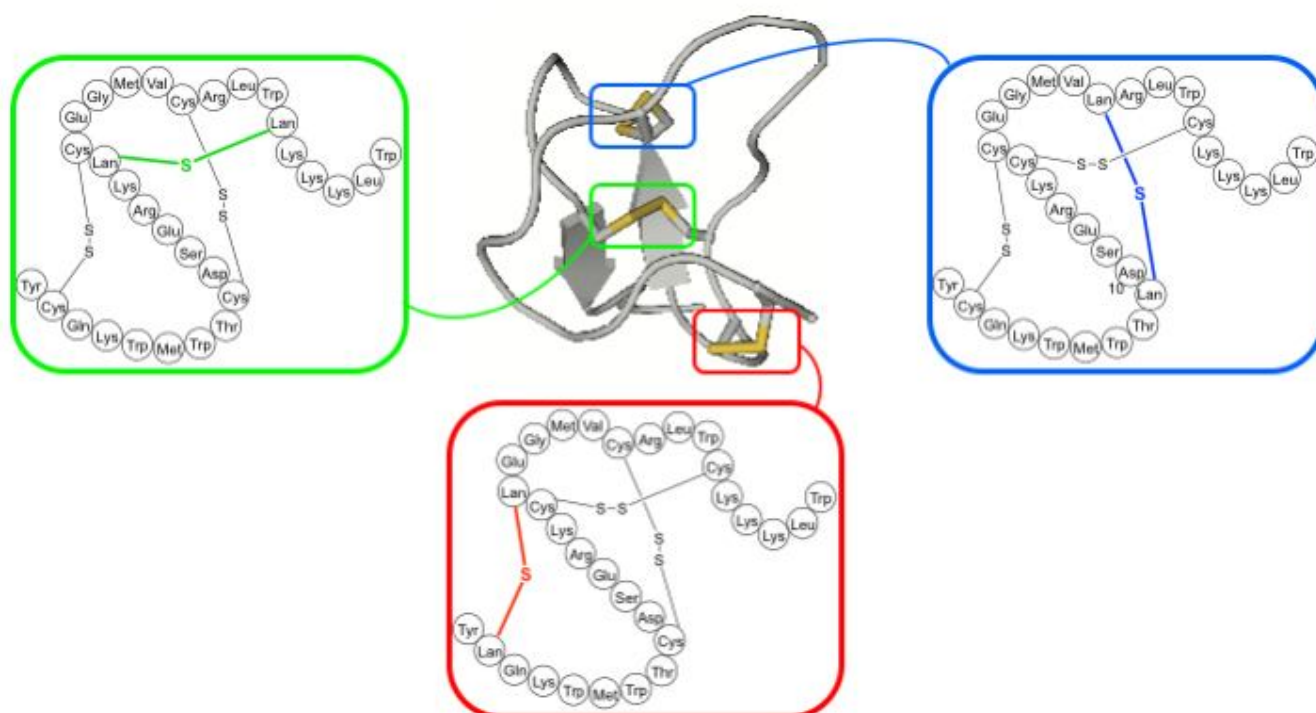
Dr Philip Robinson

RESEARCH HIGHLIGHTS

A chemical and structural biology study of the role of disulphide bridges in the tarantula toxin ProTx-II

Spider peptide toxins have recently received much attention as selective and potent sodium channel blockers. These naturally occurring peptides have multiple cysteine residues and contain intricate disulphide bonding patterns that are crucial for their biological activity. The tarantula toxin ProTx-II is a 30-amino acid peptide with three disulphide bonds. Previous work indicated that it adopts an inhibitory cystine knot (ICK) structure, with cystine bridges in an 1-4, 2-5, 3-6 pattern. ProTx-II has been the subject of considerable research interest recently as a possible lead for the treatment of chronic nociceptive pain. It has the highest known potency against the Na_v1.7 sodium ion channel, which is found predominantly in the peripheral nervous system, and has 100-fold greater selectivity for this ion channel compared with other Na_v subtypes.

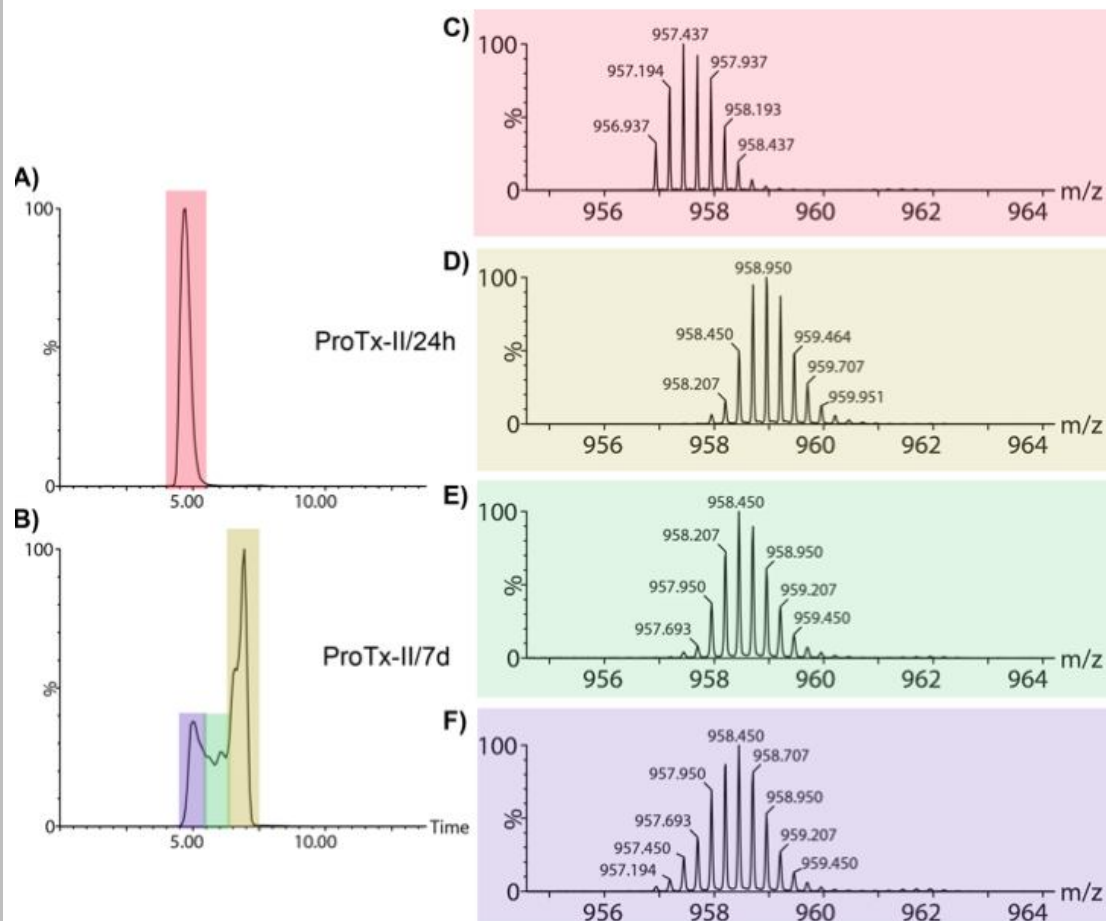
The biological properties of this toxin are crucially dependent on the structural constraints dictated by the cystine bridging pattern, and the peptide is therefore susceptible to reduction of the disulphide bridge *in vivo*, reducing both potency and half-life. In this work, we wanted to establish whether we could replace individual disulphide bridges in ProTx-II with thioether bridges. As these cannot be reduced *in vivo*, our hypothesis was that this would lead to greater structural stability. We have previously developed automated solid-phase synthesis methods for preparing thioether-bridged peptides, using a thioether-bridged diamino diacid, lanthionine, with orthogonal protecting groups on the different amino and carboxylic acid groups that can be selectively removed to allow regioselective cyclisation. Using this methodology, we synthesised three ProTx-II analogues with individual cystine bridges replaced by thioether bridges.



[Figure 1] Thioether-bridged analogues of ProTx-II

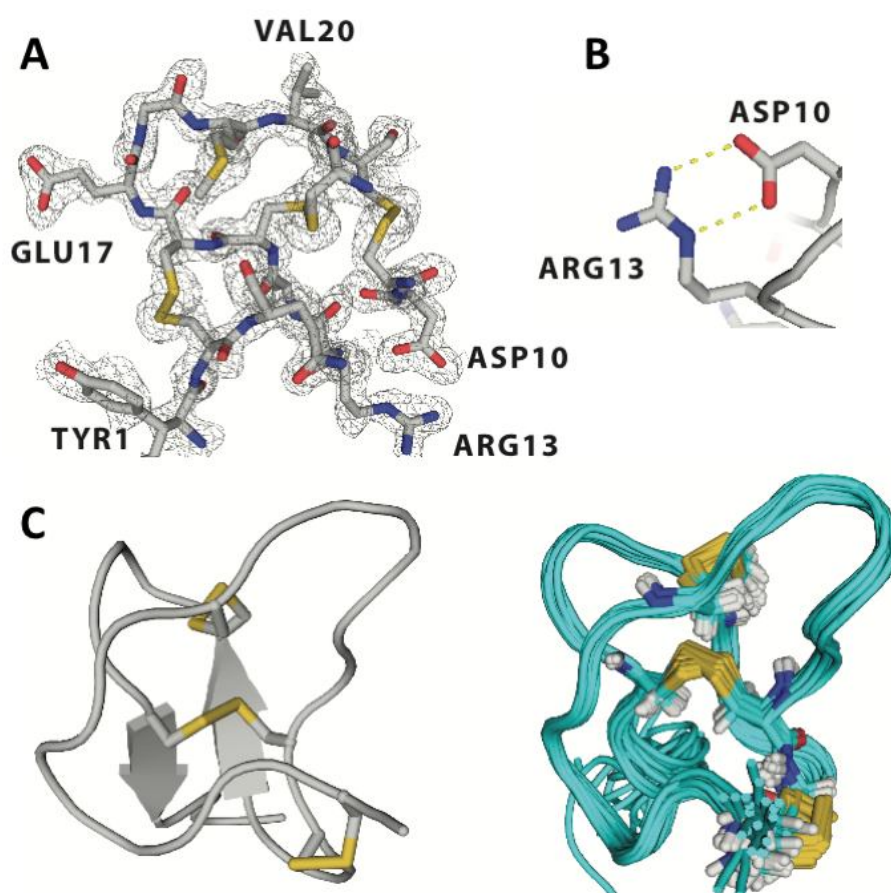
It turns out that the thioether bridge is not a good replacement for the cystine bridges in ProTx-II, as all three of these peptides were inactive against an *in vitro* Na_v1.7 patch clamp assay. As part of this assay, we had synthesised the native linear peptide sequence and carried out oxidative folding/disulphide bond formation in order to have the wild type structure as a control. We used two different methods reported in the literature to carry out the oxidative folding, and were surprised to learn that only one of these methods gave us a biologically active peptide. We probed this by ion mobility-mass spectrometry (IM-MS), which can be used to separate peptides with the same sequence but which adopt different conformations.

This revealed that one method of oxidative folding gave an ensemble of mis-folded peptides in which only two of the possible three cystine linkages had been formed, whereas the other method, which used a redox buffer that allowed cystine bridges to break and re-form during the folding, gave a single folded species with three cystine bridges which was the biologically active form.



[Figure 2] IM-MS shows a single peak for the correctly folded, biologically active peptide, but a series of peaks for the incorrectly folded peptides resulting from aerial oxidation of the linear precursor sequence.

To confirm the disulphide bond connectivity of the biologically active ProTx-II, we investigated its structure by X-ray crystallography. The structures of spider venom peptides have generally been studied by NMR; growing suitable crystals for X-ray crystallography is notoriously difficult for peptides of 30-35 amino acids, and no X-ray crystal structures of isolated ICK peptides had previously been reported. We solved the structure to atomic resolution (0.99 Å). The disulphide bonds can be clearly resolved in the electron density, with the expected disulphide bond arrangement (1-4, 2-5, 3-6), together with a largely rigid and hydrophobic central core and more conformationally labile C and N-termini. It corroborates many features of the previously published structure solved by NMR (PDB ID: 2N9T) and provides conclusive proof that the biologically active form of ProTx-II adopts the ICK fold.



[Figure 3] Comparison of the X-ray and NMR structures of ProTx-II show similar overall structure with both adopting the ICK fold. Additional hydrogen bonding consistent with a β -hairpin between residues 19 and 27 is observed in the X-ray structure.

Prof Alethea Tabor

Ref: *The role of disulfide bond replacements in analogues of the tarantula toxin ProTx-II and their effects on inhibition of the voltage-gated sodium ion channel Na_v1.7*

Wright, Z. V. F., McCarthy, S., Dickman, R., Reyes, F. E., Sanchez-Martinez, S., Cryar, A., Kilford, I., Hall, A., Takle, A. K., Topf, M., Gonen, T., Thalassinou, K., Tabor, A. B. (2017)

J Am Chem Soc, 139, 13063 – 13075

ISMB Featured Articles and Commentaries

Commentaries are available on the following publications on the ISMB news webpage (<http://www.ismb.lon.ac.uk/news.html>)

Local cellular neighbourhood controls proliferation in cell competition

Bove, A., Gradeci, D., Fujita, Y., Banerjee, S., Charras, G., Lowe, A.R.

Molecular Biology of the Cell (2017) 28: 3215-3228

A Liquid to Solid Phase Transition Underlying Pathological Huntingtin Exon1 Aggregation

Peskett, T. R., Rau, F., O'Driscoll, J., Patani, R., Lowe, A. R., Saibil, H. R.

Cell Biology (2018) Volume 70, ISSUE 4, P588-601.e6

This paper was also referred to in an article entitled 'Breakthrough Brings Hope in Diluting Huntington's' in the London Evening Standard on 29th June 2018.

In February the BBSRC published a case study about arsenic sensors developed by Prof Joanne Santini, which can be read at the following link:

<https://bbsrc.ukri.org/documents/simple-arsenic-sensor-could-save-lives/>

In January, ongoing research led by the Dr Sanjib Bhakta with Prof Simon Gibbons of the UCL School of Pharmacy into the potential role of Persian shallots in the fight against antibiotic resistance in cases of tuberculosis featured in an article on BBC News: <https://www.bbc.co.uk/news/health-42751095>

UPDATE ON RESEARCH CENTRES & LABORATORIES

ISMB EM lab takes delivery of its Krios

As recognised by the award of the 2017 Nobel Prize in Chemistry, cryo-electron microscopy (EM) is a powerful technique for undertaking studies of fine cellular structures, viruses and macromolecular complexes. The Wellcome Trust funded state-of-the-art, 300 kV cryo-EM was delivered to the ISMB at the end of April, 2018. The grant for the ThermoFisher (formerly FEI) Krios microscope was awarded to Prof Helen Saibil, Prof Maya Topf, Dr Giulia Zanetti, Prof Elena Orlova, Prof Carolyn Moores, Prof Mark Marsh, Prof Gregory Towers, Dr Anthony Roberts, Dr Alan Cheung and Prof Gabriel Waksman.



Above: Delivery of the Krios microscope on 24th April 2018



Above: The constructed Krios microscope in the EM laboratory

Prior to the microscope's delivery, the Krios takes ~8 weeks to build and several months more to test and set up. We expect data collection to begin at the end of the summer. Users who have samples ready for high resolution data collection will be trained to use automated data collection software. Training dates will be circulated via the EM group.

Our new microscope was celebrated as part of the biennial ISMB Symposium in June 2018. As part of the Symposium, the annual Rosalind Franklin lecture was given by internationally renowned cryo-EM expert Professor Eva Nogales on June 18th (<http://www.bbk.ac.uk/science/about-us/events/science-week/>), followed by a ThermoFisher-sponsored drinks reception.

The new microscope will provide cutting-edge, high throughput performance for analysis of single particles and cellular assemblies. We anticipate it will have a transformative impact on the ISMB EM lab – building on our accumulated expertise, the facility will enhance our support to scientists in ISMB who seeking to address important research questions using cryo-EM.

Prof Carolyn Moores

STUDENT NEWS

Congratulations to Emma Elliston and Stephen McCarthy who won prizes for best talk and best poster respectively at the 2018 ISMB Postgraduate Symposium on 11-12 June 2018.

Congratulations to Jennifer Stiens, Yiannis Galdadas and Trishant Umrekar, who were each awarded prizes at the ISMB Symposium for their contributions to the 'live blogging a Scientific Conference' competition on the #ISMBLondon2018 twitter feed.

Congratulations to Faiza Javaid from Vijay Chudasam's group, who recently had two publications accepted:

Bahou, C., Richards, D. A., Maruani, A., Love, E. A., Javaid, F., Caddick, S., Baker, J. R., Chudasama, V. *Highly homogeneous antibody modification through optimisation of the synthesis and conjugation of functionalised dibromopyridazinediones* Org. Biomol. Chem., 2018, 16, 1359-1366

Fernandez, M., Javaid, F., Chudasama, V. *Advances in targeting the folate receptor in the treatment/imaging of cancers* Chem. Sci., 2018, 9, 790-810

Congratulations to former Wellcome Trust programme student Chris Earl, whose thesis research was published in April in Nucleic Acids Research. Chris graduated from the PhD programme last October, and now works at the Francis Crick Institute with Neil McDonald:

A structurally conserved motif in γ -herpesvirus uracil-DNA glycosylases elicits duplex nucleotide-flipping

Earl, C., Bagn  ris, C., Zeman, K., Cole, A., Barrett, T., Savva, R.

Nucleic Acids Res. 2018 May 4;46(8):4286-4300. Doi: 10.1093/nar/gky217

Congratulations to another former Wellcome Trust Programme programme student Benjy Lichman, who has recently taken up a lectureship in Plant Biology at York University.

Josh Bullock, former BBSRC LIDo programme student with Maya Topf and Kostas Thalassinou has had two papers accepted as first-author papers:

Modeling Protein Complexes Using Restraints from Crosslinking Mass Spectrometry

Bullock, J., Neeladri Sen, N., Thalassinou, K., Topf, M.

Bioinformatics, published 24 May 2018

Jwalk and MNXL web server: model validation using restraints from crosslinking mass spectrometry

Bullock, J. M. A., Thalassinou, K., Topf, M.

Bioinformatics, published 7 May 2018

AWARDS, PRIZES & GRANTS

Congratulations to Dr Sanjib Bhakta on being awarded the inaugural Rishi Bankim Chandra Memorial Award, in recognition of his significant contributions to the field of global infectious diseases research.

Congratulations to Dr Filipe Cabreiro on being a recipient of EMBO's Young Investigator Award for 2017.

<http://www.embo.org/news/press-releases/2017/embo-welcomes-28-new-young-investigators>

Congratulations also to Prof Frances Brodsky, who was elected as Member of EMBO at the same time.

Finally - Dr Irilenia Nobeli was awarded a ticket to Oxford Nanopore's London conference (worth around £1000) in May 2018 by winning their Haiku competition. Congratulations Irilenia! Her winning entry read:

"Counting syllables

to tell tales of transcript tails

London is Calling"

EVENT NEWS

Recently Awarded Grants

Funding Body	Awardee/s	Details
The Academy of Medical Sciences (AMS)	Dr Giulia Zanetti	£100,000 awarded for the project, <i>Visualising the role of TANGO1 in COPII-mediated procollagen transport by cryo-EM</i> , to run for 2 years from May 2018.
Wellcome Trust	Dr Konstantinos Thalassinou	£705,137 awarded for the project, <i>Timestamping Integrative Approach to Understand Secondary Envelopment of Human Cytomegalovirus</i> , to run for 5 years from April 2018.
Biotechnology and Biological Sciences Research Council (BBSRC)	Prof Saul Purton	£462,698 awarded for the project, <i>Redesign of the chloroplast genome - towards a synthetic organelle</i> , to run for 3 years from July 2018.
BBSRC	Prof Christine Orengo	£621,215 awarded for the project, <i>Increasing the Coverage and Accuracy of CATH for Comparative Genomics and Variant Interpretation</i> , to run for 4 years from July 2018
BBSRC	Prof Elena Orlova	£347,873 awarded for the project, <i>Structure and biochemical mechanism of DNA replication initiation machines</i> , until January 2021.
Pioneer Hi-Bred International Inc.	Prof Helen Saibil	£480,628 awarded for the project, <i>To generate high resolution structures of proteins in membrane associated and/or soluble oligomeric states using CryoEM</i> , until the end of October 2020.
Wellcome Trust	Prof Maya Topf	£653,371 awarded for the project, <i>Timestamping integrative approach to understand secondary envelopment of human cytomegalovirus</i> , from April 2018 for 5 years.
BBSRC	Prof Bonnie Wallace	£736,056 awarded for the project, <i>Bioinformatics Resources for Circular Dichroism Spectroscopy and Structural Biology: Operation, Enhancement, Curation, and New Developments</i> , from 2018-2022.

Grants applications – upcoming deadlines

Funding body	Funding opportunities	Deadlines
BBSRC	Responsive Mode Research Grants	25 September 2018, 16.00
EPSRC	Fellowships	Applications for Post-Doctoral, Early Career and Established Career Fellowships are welcomed at any time.
Wellcome Trust	Investigator Awards	12 November 2018, 17.00
Wellcome Trust	Seed Awards	2 October 2018, 17.00

2018 ISMB Symposium - report

The sixth biennial ISMB research symposium was held in mid-June 2018 in the Clore Management Centre at Birkbeck. It featured a total of 10 first-class scientific talks over the two afternoons of Monday 17th and Tuesday 18th June; for the first time, it took place during Birkbeck's annual Science Week and included the Rosalind Franklin lecture. This annual lecture by a woman who is distinguished in one of the science disciplines represented at Birkbeck is part of the college's commitment to the Athena SWAN equality initiative.

Gabriel Waksman, who has been the ISMB's director since it was founded in 2003, introduced the symposium by drawing delegates' attention to the latest piece of state-of-the-art research apparatus to arrive in the ISMB: a new Titan Krios electron microscope, powerful enough to obtain atomic-resolution images of large molecular complexes. To mark this, many of the researchers chosen to speak were expert proponents of this technique.

The symposium was divided into four sections, each covering a different research area: computational and chemical biology; structural biology; biophysics and proteomics; and biochemistry and cell biology. First to speak in the computational and chemical biology section was an old friend of the Bloomsbury colleges, Professor Sir Tom Blundell. He had succeeded J.D. Bernal as Professor of Crystallography at Birkbeck in 1976, remaining there until his move to the University of Cambridge in 1996. His lecture was a 'tour de force' covering over half a century's research in computational chemistry, structural biology and drug discovery in academia and industry. In 1999, he founded a successful drug discovery company, Astex, and the company's first drug, ribociclib, has recently been licensed for advanced breast cancer. In his academic work, too, he has always studied proteins implicated in disease, from insulin in the 1960s through HIV protease in the 1980s to DNA repair proteins that are important cancer targets today.

The next speaker, Birte Höcker from the University of Bayreuth in Germany, described work in her lab to design a protein with a specific fold. The fold chosen, the 'TIM-barrel', has a concentric double barrel structure with two very similar halves, suggesting that it evolved through gene duplication. Höcker described combining part of a gene for a TIM-barrel with a gene for a protein that resembles the half-structure to produce an artificial protein she termed a 'hopeful monster'. She also described a collaborative project in which a TIM-barrel structure was built 'from scratch' for the first time: this has been a design goal for structural and computational biologists since 1986.

The first speaker in the structural biology section took delegates even further back in the history of his discipline, and of Birkbeck, than Blundell. Ken Holmes, who has spent most of his career at the Max Planck Institute for Medical Research in Heidelberg, Germany, studied for his PhD at Birkbeck with JD Bernal and Rosalind Franklin. He described his work with Franklin on the structure of the tobacco mosaic virus, showed photographs of the archaic-looking equipment on which this pioneering work was performed, and movingly described the bravery and determination shown by Franklin in the months before her premature death from cancer in 1958. Philip Robinson, who joined the ISMB only a few months ago, then described elegant studies of protein complexes involved in initiating the process of gene transcription using electron microscopy and obtained during his postdoctoral work with Nobel laureate Roger Kornberg in the University of Stanford, California.

The final talk on the first day was the Rosalind Franklin lecture, given by electron microscopist Eva Nogales from the University of California in Berkeley, USA. She began by paying tribute to the 'inspiration' of another world-leading female electron microscopist, Birkbeck's own Helen Saibil. Her talk focused on structures of protein complexes involved in gene regulation, including a large gene expression 'switch' known as polycomb repressive complex 2 (PRC2). As disrupting the function of this complex can lead to uncontrolled cell division, a hallmark of cancer, it shows promise as a cancer drug target.

Tuesday's lectures began with the section on biophysics and proteomics, and with another speaker

from California: Stanford University's Jody Puglisi. He turned delegates' attention to the second process involved in gene expression: protein synthesis. This is catalysed by a large 'molecular machine', the ribosome: it is a dynamic one in which the ribosome subunits rotate around each other as each amino acid is added to the growing protein chain. Puglisi's group uses a fluorescence-based technique to monitor this process, one molecule at a time, and can see antibiotics disrupt the synthesis cycles like grains of sand in an ordinary machine.

Petra Schwill from the Max Planck Institute of Biochemistry in Martinsried, Germany has an ambitious goal: to build a simplistic model cell from non-living parts. She set out the minimal criteria for life, which include self-organisation and reproduction, and described a set of bacterial proteins that control how those cells divide. Some proteins assemble into a ring structure in the centre of the dividing cells, while others suppress ring formation elsewhere in the cells so division occurs correctly. She is building an assembly of these proteins as a step towards 'a minimal [artificial] cell that can actually divide'.

The final section, on biochemistry and cell biology, began with a lecture from Andrea Musacchio from the Max Planck Institute of Molecular Physiology in Dortmund, Germany. Sticking with the theme of cell division, he described structural studies of a ring-shaped protein complex termed the kinetochore that forms at the centre of the dividing chromosomes - the chromatids - during eukaryotic cell division. This binds chromatid pairs to the mitotic spindle in the centre of the cell before they are pulled apart as the cell divides. Musacchio described the structures of several parts of this large complex before suggesting that the spindle-kinetochore interaction acts as a 'checkpoint' so division will only occur if the chromatids are properly assembled. A second ISMB speaker, Anthony Roberts, then presented elegant structural studies of a motor protein called dynein-2 that carries molecular 'cargo' from the tips of cilia into the cell body.

Friedrich Forster from the University of Utrecht in the Netherlands gave the final presentation. His group uses a form of electron microscopy known as cryo-electron tomography to visualise structures of proteins in place inside living cells. The examples that he chose to highlight were ribosomes bound to the membranes of the endoplasmic reticulum (ER): these synthesise proteins that will end up in membranes or secreted from the cell. The ribosome binds to the ER-translocon complex, which was resolved in the native membrane. The structure of the native ER translocon provides important insights into the transfer of freshly-synthesized proteins into the membrane and how sugar molecules attach to many of them.

The next ISMB symposium will be due to take place in June 2020. A full report of the symposium is available on the new ISMB website at <http://www.ismb.lon.ac.uk/biennial-symposium/>

Dr Clare Sansom





ISMB academic staff retreat at Kew Gardens

In the midst of the summer heat on 19th July about 25 ISMB members from UCL and Birkbeck College embarked on the pursuit of both relaxation and inspiration in Royal Kew Gardens afar from the toils of their laboratories and offices. Good company and fine food, in the peaceful and idyllic environment of the botanical gardens ensured that the trip was an instant success.

The academic components of this trip included three short presentations from eminent Kew Gardens scientists describing their work on plant genomics and wood analysis & identification.

Importantly, everybody participated happily and loudly in a team building exercise aimed at strengthening unorthodox communication with the goal of building a throne with balloons and Sellotape whilst blindfolded. Rather funny, and not as easy as it sounds. Michael's team won, mostly by cheating ;-).



The rest of the time was spent strolling through the tropical conservatories and the gardens, along the 'tree top' walk looking at flowers and trees, birds and bees and butterflies... We ended the day in the late afternoon with coffee and cake and drinks discussing important, and less important, issues before embarking on the trip home. All agreed: our mission was accomplished!



Prof Finn Werner

Upcoming Events

ISMB Seminars	The 2018/19 term one ISMB seminar series , <i>Mischievous Microbes</i> , will begin on 26th September 2018 , taking place on Wednesdays in the Gavin de Beer Lecture Theatre, UCL Anatomy Building, until 12 th December. Details are announced by email and on the following page of the ISMB website: http://www.ismb.lon.ac.uk/seminar/
ISMB Friday Wraps	A new programme of ISMB Friday Wraps will begin on 12th October 2018 . The meetings will continue to take place with the timings trialled last term, ie. with the two half hour talks taking place from 15.00-16.00 in Room B62, followed by refreshments from 16.00 in B64 each Friday at Birkbeck. Details are announced by email and on the following page of the ISMB website: http://www.ismb.lon.ac.uk/fridaywrap
2018/19 London Structural Biology Club (LSBC) meetings	There will three meetings of the LSBC in 2018/19, on dates to be confirmed in November, March and June, which will be announced by email. Subscription to the LSBC mailing list is via the following link: https://bbk.us17.list-manage.com/subscribe?u=9c3884bf770242d8a9025c8df&id=32f1b9bfe4
London Metabolism Club (LMC)	The LMC is a cross-London network for promoting basic and applied research on cellular metabolism in health and disease, with the aim to increase collaboration between different academic groups and discuss the most recent advances in metabolic research. Its 2 nd meeting will take place on Monday 17th September from 17.00-20.00 in the JZ Young Lecture Theatre, UCL Anatomy Building, Gower St, London WC1E 6XA. The event is free, but attendees are asked to register at the following link so that the catering can be planned accordingly. Further details about the meeting are also available via the link. https://www.eventbrite.co.uk/e/london-metabolism-club-autumn-2018-meeting-tickets-48367739210?utm_term=eventurl_text

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Please email items of news to the ISMB Administrator (Andrew Service): **ismb-admin@ismb.lon.ac.uk**