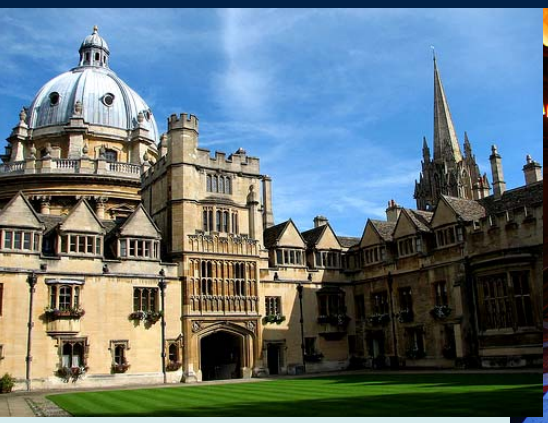
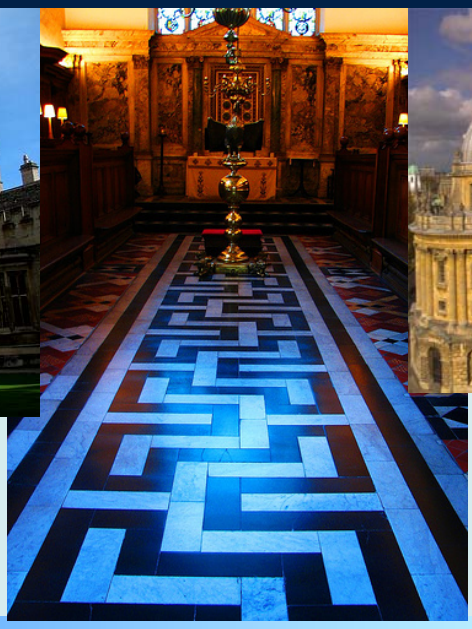
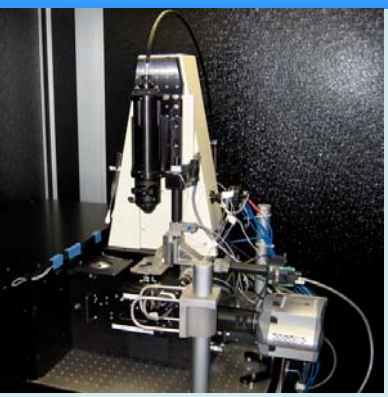
OXFORD UNIVERSITY BIOCHEMICAL SOCIETY





PHENOTYPE



ISSUE 3

TRINITY TERM'09

OUBS BLACK TIE DINNER

THE CURRENT REVOLUTION IN LIGHT MICROSCOPY

INTERVIEW WITH THE ARTISTS

OXFORD UNIVERSITY BIOCHEMICAL SOCIETY

PHENOTYPE

ISSUE 3 TRINITY TERM'09

Dear Reader,

OUBS brings to you the third issue of PHENOTYPE and the last one of this academic year. We would like to thank all of you for your valuable feedback and participation.

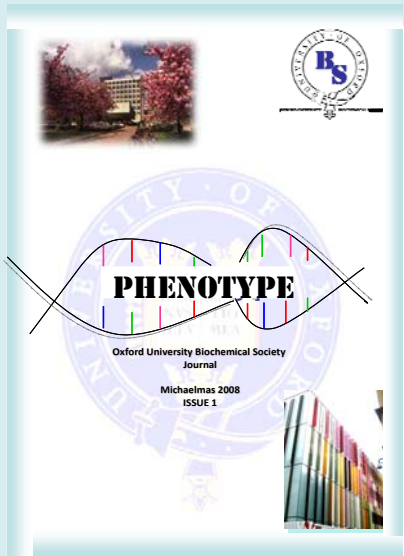
It is important that we mention those who made the third issue of PHENOTYPE possible. We would like to thank Prof Ilan Davis for his insightful and informative article on current revolution in light microscopy. We would also like to thank Prof Penny Handford for giving us a glimpse of her journey so far in 5' with, Dr Mary Gregoriou for her continued support and valuable section in our journal and last but not the least, James Halstead for sharing with us a delightful interview with the minds behind the artwork in our new building.

As we come to the end of the first year of PHENOTYPE we would like to invite suggestions and ideas for the next issues so that we can take this to the next level. The purpose of this journal is to inform our members of the events organised by the society and to encourage discussion on issues related to science. We therefore welcome any contributions from both students and faculty.

We hope to see many of you at OUBS Annual Black Tie Dinner on 3rd July.

We wish you a lovely summer!

Regards,
OUBS Team
2008-09



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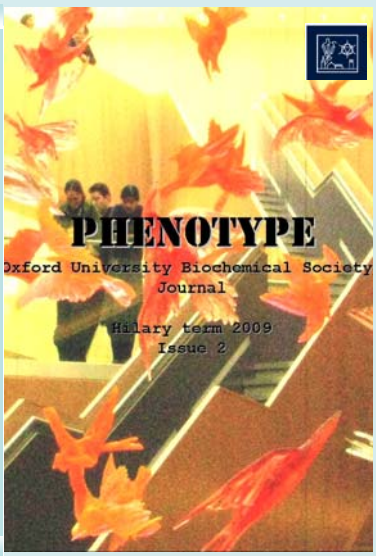
Michaelmas'08



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OXFORD UNIVERSITY BIOCHEMICAL SOCIETY

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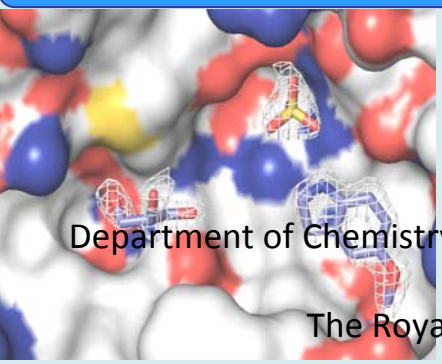


Monday 18th May

Prof Chris Abell

Department of Chemistry, University of Cambridge, Co-founder of Astex Therapeutics

"Fragments and Droplets"

The Royal Society of Chemistry Seminar (www.rsc.org)

Monday 1st June

Dr Florian Brueckner

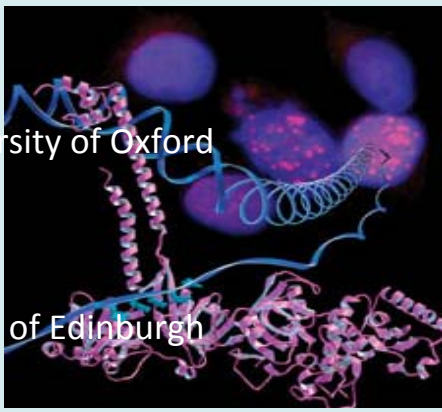
Imperial College Diamond Light Source, Oxfordshire

"A movie of the RNA polymerase II nucleotide addition cycle"

Monday 8th June

Dr Fumiko Esashi

Weatherall Institute of Molecular Medicine, University of Oxford



BRAC2

Coding-Sequence Determinants of Gene Expression in Escherichia coli

Monday 15th June

Prof David Tollervey

Wellcome Trust Centre for Cell Biology, University of Edinburgh

Monday 27th June

Dr Maitreya Dunham

University of Washington, Seattle

"Genomic analysis of experimental evolution in yeast"

Sponsored by The Genetics Society (www.genetics.org.uk)

Friday, 3rd July

OUBS Annual Black Tie Dinner

Brasenose college

All the seminars will take place in the Seminar room of the New Biochemistry building at 4 pm

OUBS ANNUAL BLACK TIE DINNER

The OUBS Annual Black Tie Dinner will be held at Brasenose College on Friday 3rd July 2009. This year, we will be hosting Professor Fotis Kafatos from Imperial College London. After studying Zoology at Cornell University, Kafatos went on to Harvard to become the youngest full professor at the age of 29.

He founded the Crete's Institute of Molecular Biology and Biotechnology and in 1993, he returned to Europe to direct the European Molecular Biology Laboratory (EMBL). Now based at Imperial College London, Kafatos is world renowned for his work in Malaria-causing mosquitoes and also for supporting and improving research opportunities for promising young scientists.

Champagne Reception commences at 7.00pm
Dinner in Brasenose College Hall
After Dinner drinks in the newly refurbished Brasenose College Bar Come join us on the Friday 3rd July 2009!

We hope to see you there!

LAST YEAR'S DINNER

"This has been a great evening, thank you so much!"
~ Professor Christopher Leaver

"I'm glad to be back!"
~Professor David Sherratt

"The OUBS dinner was a great success!"
~ Dr.Michael Carroll, Dow AgroSciences

OXFORD UNIVERSITY BIOCHEMICAL SOCIETY

PHENOTYPE

5' WITH...

PROF. PENNY HANDFORD

Prof. Penny Handford has been Tutor in Biochemistry since October 1998; before that she was a Royal Society University Research Fellow in the Sir William Dunn School of Pathology, University of Oxford. Her main research interests are the molecular basis of human disease, specifically genetic diseases such as Marfan syndrome, retinitis pigmentosa, age-related macular degeneration and CADASIL that may be caused by mutations which affect the calcium binding epidermal growth factor-like domain.

Q. When did you realise that you wanted to be a scientist?

P: Probably in the 1st year at my local comprehensive school. Mr. Jenkins (Biology) and Mr. Dowson (Chemistry) were two of the better teachers and in those days you could make class Chemistry quite exciting with lots of explosions and noxious fumes. Mr. Jenkins was brave enough to take us on a couple of field trips to the Sicily Isles to study flora and fauna. At 6th form college, I realised I liked the biochemical bits of biology best and opted to do Physiology and Biochemistry at Southampton University

Q. If you were not a biochemist, what would you be...

P:I wouldn't mind swapping jobs with David Attenborough-but that is still science. I always liked History at school so perhaps a historian of some sort.

Q. Your favourite book..

Pictures of Perfection by Reginald Hill

Q. If you are not in the lab you are...

P: Transporting teenage children to cricket matches or horse-riding. I like to ride at weekends when I can.

Q. Worst disaster in the lab...

Touch wood- we haven't yet had a real disaster in the lab. My own personal disaster was as a 3rd year project student at university, I spent two weeks autoradiographing a 3H-gel using a piece of cardboard rather than a piece of X-ray film. When I came to hand-develop the "film" it just went soggy in the developer and fell apart ! My excuse was that I wasn't allowed to use any darkroom light when opening the film, so I extracted a cardboard divider instead of the real thing. I made myself scarce for the next couple of weeks.

"It is of huge importance- being in the right place at the right time when a field starts to take off."

Q. What has been the most important moment of your career so far?

P: Getting my Royal Society Research Fellowship to work on fibrillin and Marfan syndrome.

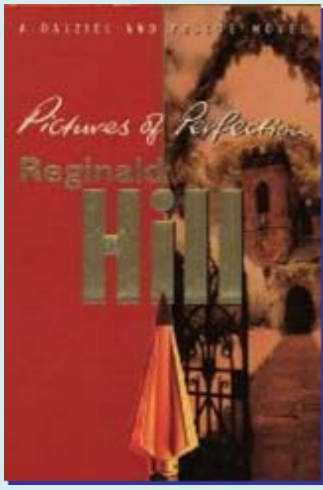
Q. In your view, what is the importance of luck in research?

P: It is of huge importance- being in the right place at the right time when a field starts to take off. I was a post-doc in George Brownlee's group in the Dunn School when Iain Campbell was developing NMR methods to study protein modules. I just hooked up with Martin Baron in

5' WITH...

PROF. PENNY HANDFORD

IDCs group and applied the methods to study molecular mechanisms underlying haemophilia B and more latterly Marfan syndrome.



Q. Describe your personality in four words.

P: quiet, tenacious, direct, critical

Q. One human trait you hate

P: Arrogance

"The answers lie in the detail"

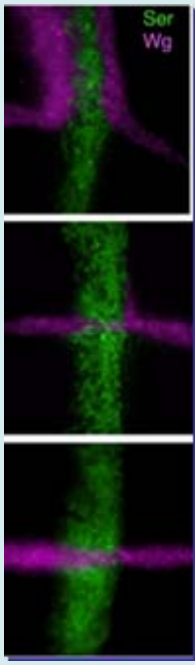
Q. Favourite vacation spot

P: Saussignac in SW France

Q. Best advice you ever received

P: "Only research in areas that you are really interested in", and "the answers lie in the detail". Following my degree, my PhD supervisor told me that things could only go downhill from then on!

Q. What has been your biggest mistake or regret?



P: Don't have any regrets- I have been lucky enough to be able to keep researching in the areas that interest me. I'm sure I have made loads of mistakes, but none that have stopped me doing what I want to.

Q. Favourite classical experiment?

P: I wish I had been the person to develop PCR technology using a thermostable polymerase!

Q. How do you imagine biochemistry research will change in the next twenty years?

P: More integration with Mathematicians and Physicists.

OXFORD UNIVERSITY BIOCHEMICAL SOCIETY

PHENOTYPE

SEEING IS BELIEVING: THE CURRENT REVOLUTION IN LIGHT MICROSCOPY

By Prof. Ilan Davis

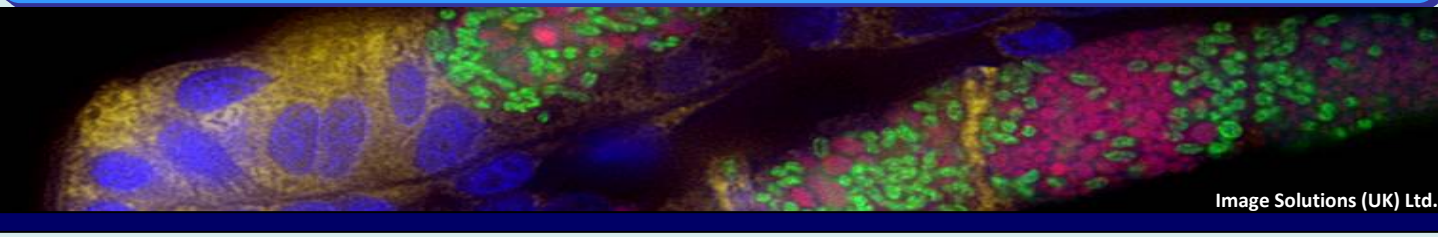


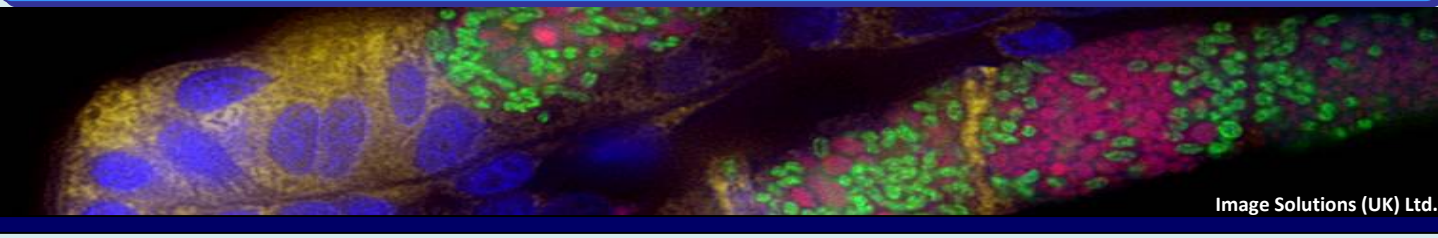
Image Solutions (UK) Ltd.

The 2008 Nobel prize in Chemistry was awarded to Tsien, Chalfie and Shimomura for their discovery and development of the green fluorescent protein, GFP. This follows a long line of Nobel prizes awarded to discoveries that have advanced microscopy, as imaging has played such a pivotal role in biological and medical sciences. Other more recent developments in microscopy methods involve four kinds of activities: specimen preparation, probe development, improvements in instrumentation and post acquisition analysis of the images. **The current revolution in light microscopy involves advances on all four fronts**, but perhaps the most headline grabbing improvements have been the emergence of new instruments allowing increased precision or resolution and improved single molecule imaging. Ever since the first powerful compound microscopes were built, the resolution of light microscopy was essentially limited by diffraction of light, by well understood phenomena in optics, to about half the wavelength of light used (250nm for green light). Remarkably, in the last few years this "fundamental resolution limit" of light microscopy has been overcome in a number of independent ways. These collectively have been referred to as "super-resolution" methods, although they depend on a variety of principles that have been around in the physical sciences for many years and at least in some cases, it is more correct to refer to them as providing improvements in precision of imaging rather than resolution.

Confocal microscopes depend on shinning a laser spot on the specimen and scanning it across the specimen to produce an image. The resolution of this method is limited, amongst other things, by the size of the confocal spot, which in turn is limited by diffraction limits of light. The first super-resolution method is a confocal method developed by Prof. Stephan Hell at Max Planck, Göttingen. It depends on a trick by which you can prevent fluorescent molecules that reside in the outer region of a laser spot from emitting light. This is achieved by using a ring-shaped second laser that causes a phenomenon known as Stimulated Emission Depletion (STED). A STED instrument can now be bought commercially from Leica, but has the drawbacks of not being applicable to all fluorescent dyes, requiring specialized lasers and loosing a lot of light in the process of STED. But the "resolution" improvement is very impressive in XY. STED can be improved further in the Z direction using two opposing objectives, known as 4Pi, but this approach has proven difficult to implement.

Structured Illumination (SI) is an alternative method for achieving "super-resolution". It is a wide-field based method, which means that the entire specimen is illuminated at the same time. Instead of scanning a small laser spot across the specimen, structured illumination involves shinning a fine striped pattern on the specimen. The resulting image is then acquired at multiple angles and phases to build up a composite image that has twice the resolution

SEEING IS BELIEVING: THE CURRENT REVOLUTION IN LIGHT MICROSCOPY



in XY and Z, after processing. SI works because small features in the specimen, that are below the diffraction limit of a conventional microscope, creating an interference pattern that that is larger than the diffraction limit and can be used to calculate the appearance of the original feature by processing the data. SI is available this year as a commercial product as part of the OMX microscope, developed by Prof. John Sedat at UCSF. Although more modest than STED in its increased resolution, SI can be used with most fluorescent dyes and conventional light sources. It does require a bright specimen that is relatively resistant to bleaching and has been shown to be usable for live cell imaging. The OMX microscope is also capable of conventional fast multidimensional wide-field imaging and has excellent sensitivity in 4 simultaneous wavelengths of light.

The third resolution breaking set of methods is in fact more correctly a trick allowing a very high precision determination of the location of individual molecules in a relatively dense field of overlapping molecules. These methods have been developed by a number of investigators in parallel and given various exotic acronyms, from STORM to FIONA. The best known of these is Photo-activation Light Microscopy (PALM), developed by two, at that time unemployed, physicists Prof. Eric Betsiz and Prof. Herrald Hess in collaboration with a Cell Biologist, Prof. Jennifer Lippincott-Schwartz. Using a photo-activatable GFP, PALM relies on activating only a small number of non-overlapping molecules in a dense field and then capturing their fluorescence and calculating their position with a precision of approximately 10-20nm. Through repeated rounds of further activation and capturing, an image of all the molecules in the field can be assembled with such pin point precision. PALM uses relatively simple hardware, so will have a wide applicability. A more recent variation of this method, Interferometric PALM (iPALM) was developed by Prof. Herrald Hess, in which interferometric methods are used to image the molecules at 5nm precision in the Z axis. Like 4Pi, iPALM involves the use of two apposing objectives, so is technically very difficult to build and use.

While it is very easy in hindsight to appreciate why the seminal work on GFP deserves a Nobel prize, it is much harder to predict which if any of the current emerging "super-resolution" methodologies will lead to the most important breakthroughs in the future. Nevertheless, it is clear that the pace of development of new microscopy methods and instruments has been truly breathtaking in the past few years and our ability to visualize molecules in cells is currently being revolutionized.

Prof. Ilan Davis
Wellcome Trust Senior Fellow and Chair of Cell Biology,
Department of Biochemistry,
University of Oxford

OXFORD UNIVERSITY BIOCHEMICAL SOCIETY

PHENOTYPE

ART AND SCIENCE

As a stranger to modern art, James Halstead meets two of the minds behind the artwork in our new building and tries to find out what links lie between art and science…

"Sometimes it feels as though everything is connected" Michael Dye

It was clear from the beginning that the artistic side of science was an important component in the design of New Biochemistry Building even before it was built. The designer's sketches were futuristic with daring colour schemes and the 'Salt Bridges' contemporary art project described a number of imaginative concepts in the making. Indeed there was a lot of interest surrounding the prospective pieces as senior scientists and celebrated artists sat down to discuss a new kind of collaboration.

So, as someone who rarely comes in contact with contemporary art, it was pretty exciting to see it all come together around me. When I finally moved into the building the artwork was as interesting and salient as anticipated, though I was intrigued about the narrative behind the work. Were their inspirations biological? Why did they employ particular mediums? Why is artwork important in the workplace? So in order to get some perspective on this, I decided to do some experimental interviews with some of the artists behind our New Building to try to uncover the inspiration behind their works and the roles they feel they may serve in a science department.

Tim Head's Light Cycle shows 256 irregularly spaced 45mm diameter round pixels set onto a wall surface that change colour and intensity in a cycle that is repeated indefinitely. The cycle employs some irregular elements that generate unpredictable variations. It is perhaps not surprising that this randomising element piece has its founding in biology. Tim draws parallels between this approach to making art and the **"general approach in the department to investigating and speculating on the behaviour of organic material in particular environments".** The Light Cycle is strangely entrancing and brings to mind some of the imaging and modelling that goes on in the building. Biology is being revolutionised by computers and I ask if Tim's choice of medium appears reflect this. He says that "over the last ten years [his] work has made direct use of the computer, speculating on the elusive and contrary nature of the digital medium and its unsettled relationship to the physical world and to ourselves". As the artist in residence for Structural Bioinformatics and Computational Biochemistry Unit, Tim's piece seems very much at home in the science that surrounds it.

OXFORD UNIVERSITY BIOCHEMICAL SOCIETY

PHENOTYPE

ART AND SCIENCE

Tim Head: Light Cycle

Peter Fraser, the photographer in residence for the construction of the New Building describes his coming to the project warmly. "At the time of being commissioned I was unable to state clearly my intentions for my work at the site, not least because for most of my career I have had to begin to work in order to discover what the work itself wants to be".

Peter Fraser: Photography (2006)

I explain that this fear of having no set goal is perhaps common to both artists and first year DPhil students alike. Peter cites a near-death experience in the Sahara desert, and the kindness offered him in his recovery, as turning point in his career and that his work at Oxford "is the purest expression of my [this] experience to date". Walking around the Department after hearing this I start to feel like the photography does have a descriptive side to it. I'll never understand Peter's experience, but perhaps the demolition of old structures and the construction of a new building hold special significance for him. I decide against asking him this; perhaps it is possible to analyse something too much.

For a truly interesting perspective on art in science I was lucky enough to chat to **Michael Dye**, a post-doctoral molecular biologist and avid artist. Michael's works have been published on the front cover of EMBO journal on two occasions and one of his pieces permanently displayed in the Dunn School of Pathology. Michael uses the more classical medium of oil painting though refers to modern painters such as Hodgkin as inspiration. Like Tim Head he finds biology a "tremendous source of inspiration". It is interesting to hear him talk about **"the unbelievable complexity of life processes"** and how his work attempts to reflect on that. Indeed the title of one of Michael's pieces, "Sometimes it feels as though everything is connected", feels like an appropriate emblem for molecular biology as whole.

Artwork seems to be becoming more and more common in the academic workplace, but what role does it serve? Tim Head believes that a valuable purpose of art is to "expose [us] to other ways of thinking and that seeing ideas represented in another form (in this case visual)

ART AND SCIENCE

helps to shift perspectives in the workplace". Michael Dye had some attractive thoughts on the subject, suggesting that art about science by scientists could be encouraged in the workplace by scientific departments. Though it may take a leap of confidence to display your own artwork in front of your colleagues, if space were provided for artistic efforts then such pieces may really add to the charm and creative feel of a building.

It was apparent after talking to the artists that appreciation of the science in their art is a large consideration for them, both as a source of inspiration and as a medium. When I thought about it a little bit, I realised that as scientists the converse is also true: we can all appreciate the art in our science at times. Elegant arguments and classic experiments often have an artistic ring to them, and nothing can open up a complicated model like a lucid figure or movie. Indeed, a dash of theatrical showmanship can grab even the most tired seminar audience. Perhaps the link between art and science runs deeper than I had previously thought.

Tim Head is an internationally recognised artist and was the artist in residence for Structural Bioinformatics and Computational Biochemistry Unit (www.timhead.net).

Peter Fraser was appointed as the photography resident for the building project. Peter has recently published in the photography journal Photoworks (2009 Issue 12; http://www.photoworksuk.org/). Newly commissioned work produced in Wales will be exhibited and published by Ffotogallery, Cardiff, in September 2009 (www.peterfraser.net).

Michael Dye is a post-doctoral researcher in the Sir William Dunn School of Pathology in Nicholas Proudfoot's group with diverse interests in the arts. Michael's paintings have been published on the front cover of EMBO journal and one is displayed in the Dunn School.

James Halstead is a first year DPhil in Biochemistry

OXFORD UNIVERSITY BIOCHEMICAL SOCIETY

PHENOTYPE

GRADUATE MATTERS

By Dr Mary Gregoriou, Director of Graduate Studies

How much time should a student allow for writing their DPhil thesis?

In the UK, funding bodies require PhD students to submit their theses within four calendar years from starting their degree course. Since about 2000, the four-year PhD was introduced in the UK to provide financial and mentoring support for all four years of the PhD, supporting courses, opportunities for lab rotations, and non-lab-based learning of soft skills. The intention was to help students acquire the necessary knowledge and understanding of their field, choose their research questions and manage submission of their thesis within four years whilst supported financially for four years.

How long it takes to write a thesis depends on the student (organisational and writing skills), the type of projects attempted, the amount of work accomplished and the resources available (time and funding). Being well organised helps enormously, so it is advisable to keep clear records of hypotheses, rationales, aims, objectives, experiments, preparations, materials and methods, results, tables, figures, legends, references, and conclusions. These should be organised in lab books with tables of contents, and electronically. This work as well as critical evaluation of the literature should be done daily-weekly during the experimental phase of the PhD.

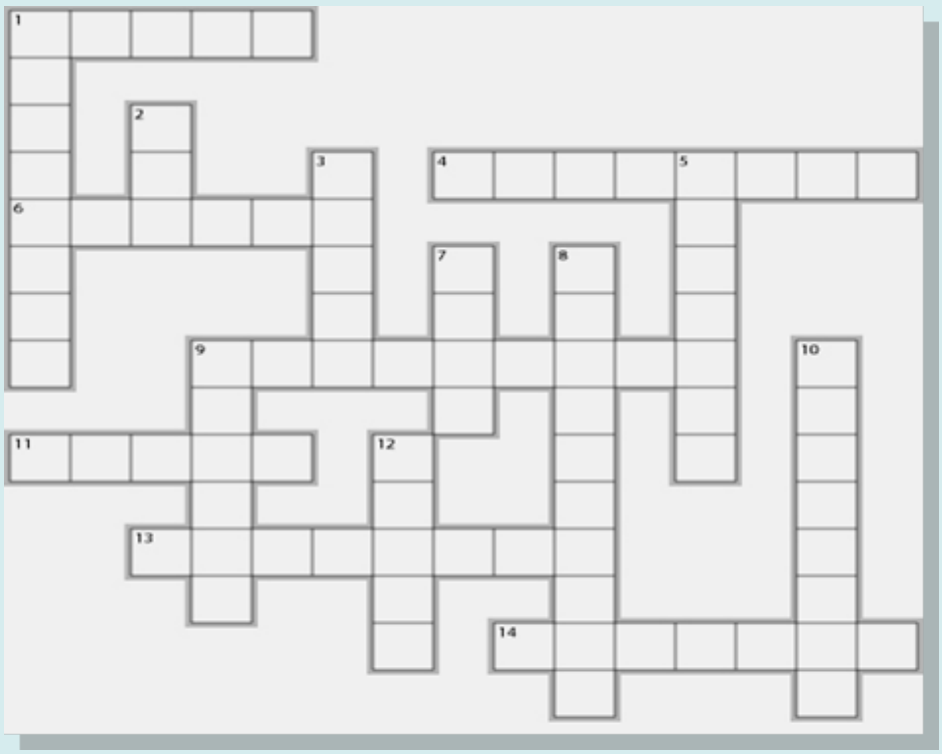
It would probably take most students who are skilful in scientific writing six - eight weeks to produce a complete first draft of their thesis and another four weeks to make re-arrangements and corrections if necessary (excluding drawings, tables legends). Two-four weeks of waiting for feedback from supervisors should be allowed. Supervisors will need to make time to read drafts carefully and return with comments, and may happen to have additional pressing priorities when your draft is completed. So in total 3 months, for preparation of the manuscript, plus 3 weeks to physically produce bind and deliver the thesis to the University is a reasonable time to allow.

If you are not able to take three-four months to write your thesis, you may need to divide your time each day/week between reading, writing and doing experiments or analysing results, in which case you should start writing as soon as a project is finished and not later than 6 months before your funding support runs out. Multitasking seems attractive, as it is often unclear when experiments should stop for thesis writing to begin.

CROSSWORD

"Members of the Biochemistry Department: past and present"

Do you think you know your department well, try your wits at this crossword. Send your answers to oubs@bioch.ox.ac.uk by 4th July 2009. The winner will be drawn out of a hat and gets £10 worth of book vouchers! SAM HUGHES was the winner of the last crossword!!



Across

1.An extremely dedicated lecturer, for whom his students have set up the Facebook appreciation society. (5)
4.Devised the Southern blotting technique (Lasker Award 2005). (8)
6.Human geneticist behind the Channel 4 series "Faces of Britain", examining the genetic make-up of the British population. (6)
9.Member of the famous family, his uncle was Boris, the Noble Prize winning novelist. (9)
11.The first Whitley Professor of Biochemistry at Oxford. (5)
13.Discovered DNA fingerprinting (Lasker Award 2005). (8)
14.The current Whitley Professor of Biochemistry. (7)

Down

1.Winner of the 1976 Nobel Prize for his identification of the Hepatitis B virus. (8)
2.Honourary Fellow of Lady Margaret Hall and co-author of the book "The Oxford Biochemistry Department 1920-2006". (3)
3.Discovered the citric acid cycle (Nobel Prize 1953). (5)
5.Famous for *C. elegans* sex determination studies. (7)
7.Glycobiology Institute member, who founded Oxford GlycoSciences Ltd. (4)
8.Second Professor of Microbiology at Oxford, who used bacteria to carry out pioneering studies of developmental phenomena. (10)
9.Determined the chemical structure of an antibody (Nobel Prize 1972). (6)
10.Current Guinness Professor of Microbiology. (8)
12.Shared the Nobel Prize in 2001 with Tim Hunt and Lee Hartwell for their discoveries of key regulators of the cell cycle. (5)

Prof Margaret Heck (University of Edinburgh) pictured here after her seminar with Anjana and Prof Ilan Davis, 23 February 2009.

Dr Fumiko Esashi (Weatherall Institute of Molecular Medicine, Oxford) met with Prof David Sherratt during her visit to the Department, 8 June 2009

Lunch after the Careers Day 2009, 11 February.
Dr Richard Capper, Oxford Gene Technology, Prof Jane Mellor, Dr Barry McGuinness

Dinner with Prof Harvey McMahon, OUBS speaker on 19 January 2009.
Pelin Uluocak, Gamze Camdere, Harvery McMahon

Prof Chris Abell (University of Cambridge) with OUBS committee members, Sarah Iqbal and David Yadin, 18 May 2009.

Prof Tom Strachan visiting the Department on 9 June 2009 to give a talk "Abnormal cohesin regulation and developmental malformation", pictured with DPhil student Andi Pauli

OUBS would like to thank the sponsors for their support