PHENOTYPE

Oxford University Biochemical Society Journal

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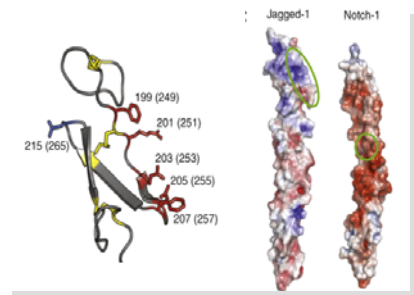
OXFORD UNIVERSITY BIOCHEMICAL SOCIETY

Contents



Welcome to PHENOTYPE!

OUBS committee

The Oxford University Biochemical Society (OUBS) is proud to present you with the first issue of the OUBS Journal: *Phenotype*. We are a student-run society and organise a wide range of events in the Department ranging from weekly seminars to Careers day for students and postdocs to an Annual Black Tie Dinner. This year we are happy to introduce our new annual event: Lecture of the Year series, which in 2008 will be given by Nobel laureate Dr Andrew Fire.

The purpose of *Phenotype* is to inform our members of the events organized by the society and to encourage discussion on issues related to science. We therefore welcome any contributions from both students and faculty. *Phenotype* will feature interviews with research heads in the Department and our guest speakers, advice for graduate students hoping for a career in academia and also student articles on any aspect of biochemistry.

Our heartfelt thanks to all those who have participated in the production of this first issue of **PHENOTYPE**. Our special thanks to Dr. Ord, Dr. Watts and Dr. Gregoriou for their special contribution

We look forward to receiving your contributions and hope that you enjoy the first of what we hope to be many issues to come.

With best wishes,
OUBS Committee

President	Marina Kolesnichenko
Secretary	Maria Demidova
Treasurer	Muhan Wang
Webmaster	Pelin Uluocak
IT Officer	Camilla Oxley
Social Secretary	Maria Carroll
'Phenotype' **Journal Editor**	Sarah Iqbal
Undergrad Representative	Alice Blachford
Postdoc Representatives	Rodrigo Reyes & Nick Anthis
Senior Member	Professor Anthony Watts

OUBS Annual Black Tie Dinner 2008
Exeter College

OUBS events for the term

Seminars take place at 4pm unless otherwise indicated.
Everyone welcome!

Monday 20th October

Venue - Large Seminar Room, New Biochemistry Building
Prof Stephen Bell
Sir William Dunn School of Pathology, Oxford
"DNA replication and cell division in the third domain of life"

Monday 27th October

Venue - Large Seminar Room, New Biochemistry Building
Dr Helle Ulrich
Clare Hall, London Research Institute, Cancer Research UK
"Regulation of DNA Damage Bypass by Ubiquitin and SUMO"

Monday 3rd November

Venue - Large Seminar Room, New Biochemistry Building
Dr Nick Brown
The Gurdon Institute, University of Cambridge

Monday 10th November

Venue - Large Seminar Room, New Biochemistry Building
Prof David Strutt
University of Sheffield

Monday 17th November

Venue - Large Seminar Room, New Biochemistry Building
Dr Lena Ström
Karolinska Institutet, Stockholm, Sweden

Monday 24th November

Venue - Large Seminar Room, New Biochemistry Building
Prof Laurence Pearl
The Institute of Cancer Research, London

Monday 8th December

Venue - Large Seminar Room, New Biochemistry Building
Prof Witold Filipowicz
Friedrich Miescher Institute, Basel, Switzerland

Wednesday 10th December

OUBS Lecture of the Year
Venue - Lecture Theatre, Medical Sciences Teaching Centre
Dr Andrew Fire (Nobel Prize in Physiology or Medicine 2006)
Stanford University School Of Medicine
"Genome surveillance mechanisms based on nucleic acid structure"

Dr Andrew Fire

Nobel Laureate
Stanford School of Medicine

OUBS is proud to present you with an enlightening talk by the 2006 Nobel Prize winner in Physiology or Medicine, Dr Andrew Fire, on 10 December 2008 at 4 pm at the Medical Sciences Teaching Centre. The talk title is "Genome surveillance mechanisms based on nucleic acid structure". This is the inaugural lecture of the annual series Lecture of the Year, given by outstanding scientists from around the world! Fabulous champagne reception to follow!

About Dr Fire's work:

The observation that injecting either sense or antisense RNA could phenocopy a knockout phenotype initially seemed like a strange nematode phenomenon. However the discovery by Andrew Fire and Craig Mello that it was mediated by a double stranded RNA molecule in a specific and catalytic manner initiated a rapid transformation of our knowledge of RNA biology, and led to methods that have revolutionised molecular biology and have promising clinical potential. Andrew Fire is continuing to work on RNA interference and small RNAs, particularly on roles in the silencing of foreign nucleic acids, and more generally in the response of the genome to the changing "genetic landscape" during development and environmental change.

Further reading:

1. Alcazar RM, Lin R, Fire AZ.

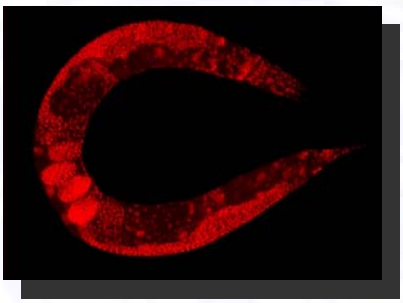
Transmission Dynamics of Heritable Silencing Induced by double-stranded RNA in Caenorhabditis elegans.
Genetics. 2008 Aug 30.

2 Haussecker D, Cao D, Huang Y, Parameswaran P, Fire AZ, Kay MA.

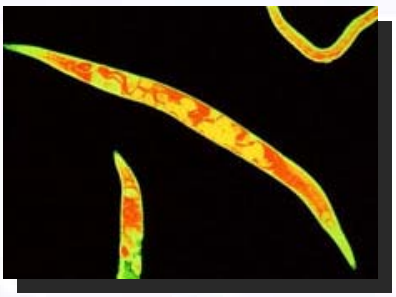
Capped small RNAs and MOV10 in human hepatitis delta virus replication.
Nat Struct Mol Biol. 2008 Jul;15(7):714-21.

3. Fire AZ.

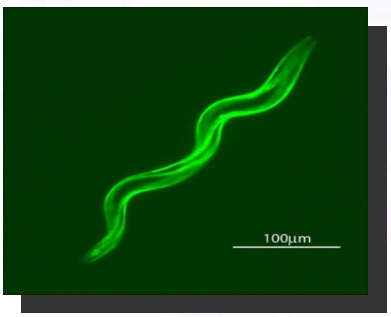
Gene silencing by double-stranded RNA (Nobel Lecture).
Angew Chem Int Ed Engl.
2007;46(37):6966-84.



Wild-type *C. elegans* hermaphrodite stained to highlight the nuclei of all cells (Credit: *PLoS Biol* **3**(1): e30)



RNA interference was first discovered by Andrew Fire and Craig Mello through their work on *C. elegans* worms, shown above. (Credit: James King-Holmes / Science Photo Library)



C. elegans roller expressing myo3p-GFP fusion. (Copyright Freddie Partridge, 2005)

4. Valouev A, Ichikawa J, Tonthat T, Stuart J, Ranade S, Peckham H, Zeng K, Malek JA, Costa G, McKernan K, Sidow A, Fire A, Johnson SM.

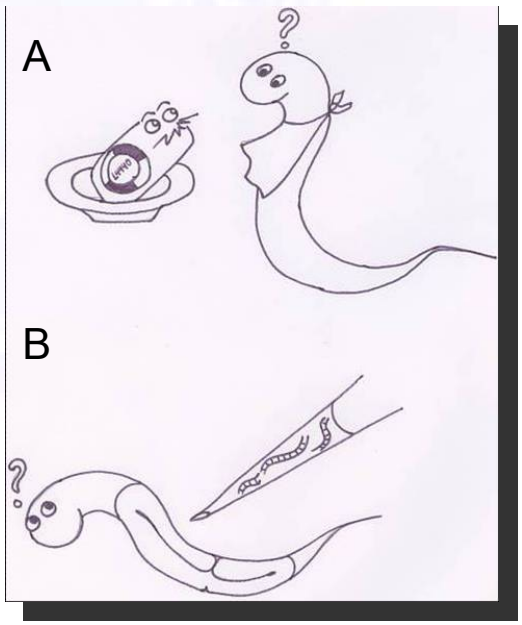
A high-resolution, nucleosome position map of C. elegans reveals a lack of universal sequence-dictated positioning.
Genome Res. 2008 Jul;18(7):1051-63.

5. Subramanian S, Lui WO, Lee CH, Espinosa I, Nielsen TO, Heinrich MC, Corless CL, Fire AZ, van de Rijn M.

MicroRNA expression signature of human sarcomas.
Oncogene. 2008 Mar 27;27(14):2015-26.

6.Pak J, Fire A.

Distinct populations of primary and secondary effectors during RNAi in C. elegans.
Science. 2007 Jan 12;315(5809):241-4.



RNA interference in *C. elegans* can be done via **A.** feeding or **B.** microinjection (Copyright Maria Demidova 2005)

OXFORD UNIVERSITY BIOCHEMICAL SOCIETY

Research highlights

Recent research highlights from the Department

A key motivation for our forthcoming move into new accommodation is to facilitate interactions between the disparate groups and areas in the department. Paralleling this in a sense, a series of recent papers highlight how analyses of molecular interactions and recognition mechanisms, at different levels, are central to much of the work in our Department.

Notch receptors, together with various ligands such as Serrate, are important for development across the metazoa. The binding of the ligand can cause both activating and inhibitory effects, and this aspect has been addressed in a paper **(Cordle, J.** *et al, Nat. Struct. Mol. Biol.)* from the Handford lab. Impressively crossing disciplinary boundaries, this paper used a combination of *in vitro* analysis of protein binding, X-ray crystallography and NMR to identify the interface between the ligand and receptor. Mutation of key residues showed that this interface is important for both activating and inhibitory effects of Notch and Serrate in the *Drosophila* wing.

Glycosylation of Notch is key for its function, and recognition of sugars is a common theme for many developmentally important proteins. A collaboration between the Campbell and Russ labs has solved the structure of the rhamnose-binding lectin domain from the rather enigmatic synaptic function gene latrophilin-1, the target of the black widow spider toxin, and homologous to a domain in the axonal guidance protein Slit **(Vakonakis, I.** *et al, Structure).* The NMR structure shows that the carbohydrate binds to an exposed pocket in the domain. However key residues in this pocket are not conserved. This leads the authors to the perhaps surprising conclusion that the domain is more likely to recognise non-carbohydrate ligands.

Recognition of carbohydrates is definitely important for non-self recognition in the innate immune system. Genetic analysis of immunity in *Drosophila* has had great success, most notably the discovery of the Toll receptor. The Ligoxygakis group have complimented their genetic research with a biochemical analysis of the way in which three proteins, GNBP1, PGRP-SA, and PGRP-SD synergistically recognise components of bacterial cell wall hence triggering an immune response **(Wang, L.** *et al, Proc. Natl. Acad. Sci. USA)*.

Improper interaction between proteins, causing aggregation, is the primary event in many diseases. Understanding what triggers aggregation may therefore be important therapeutically. Whilst many of us are content to think about genes, the sequence of proteins, or perhaps common post-translational modifications, the Wentworth lab suggest in a recent paper **(Scheinost, J.C.** *et al, Angew. Chemie. Intl. Ed. Engl.)* that the non-enzymatic adduction of the *seco*-sterol atheronal-B to lysine-16 of amyloid beta induces fibrilisation. The very "non-genetic" nature of this effect could plausibly contribute to the sporadic (non-hereditary) nature of the majority of cases of Alzheimer's disease.

No discussion of molecular interactions at this time could omit the recent growth in network biology. Whilst classical biochemists might despair at the sweeping claims of the systems biologists and mutter about their lack of ability to even define the field, we should perhaps remember that scientific revolutions are by their very nature hard to judge. New paradigms become established (according to Max Planck) not by convincing their opponents but as new generation of scientists grow up familiar with their ideas. It will be interesting to see how the biochemists and systems biologists "break out" together in the new building. I conclude with an example of systems biology from our own Béla Novák and colleagues **(Sabouri-Ghomi** *et al, J. Theor. Biol.)*. What could be more traditionally biochemical than the Michaelis-Menten equation? The authors show that, with careful analysis, the equations of enzyme kinetics can be applied to protein interaction networks, and use this to make predictions about the types of networks, and the key parameters, required to generate types of irreversible switches. This type of analysis makes us think about the assumptions implicit in a traditional biochemical model of arrows smoothly linking molecules and shows that there is complexity even in a simple switch.

Graduate matters

By Dr Mary Gregoriou
Director of Graduate Studies
Department of Biochemistry

Q. Are there any student representatives in the department and how do I contact them?

A. *Students in Biochemistry are represented on the Medical Sciences Division's Joint consultative Committee (JCC) by Christoph Loenarz and Ben Lee (http://www.bioch.ox.ac.uk/aspsite/index.asp?pageid=512). Ben and Christoph also serve on the Teaching, Safety, Graduate Advisors and Graduate Studies departmental committees.*

Q. What deadlines I should know about as a first year student?

A. *First Year postgraduates (CDB Programme students will be advised separately by their programme)*

30 October 2008: By this date you are expected to have arranged and held a formal meeting with your supervisor in which you agree a provisional working title of your research, your research aims and objectives for the next 6 months, research and skills training. Record important decisions from this meeting using the Initial Meeting Form provided (http://www.bioch.ox.ac.uk/aspsite/index.asp?pageid=364), and ask your supervisor to sign it. Arrange to meet your advisor who will need to read discuss and countersign your form. A copy of the signed form should be sent to the DGS for your file.

5 December 2008: Seminar reports to be submitted to Advisors.

13 March 2009: Seminar reports to be submitted to Advisors.

30 March 2009: By this date you are expected to have arranged and held your second formal Meeting with Supervisors and Advisors.

20 & 21 April 2009: Biochemistry Department Annual Retreat: Research presentations etc

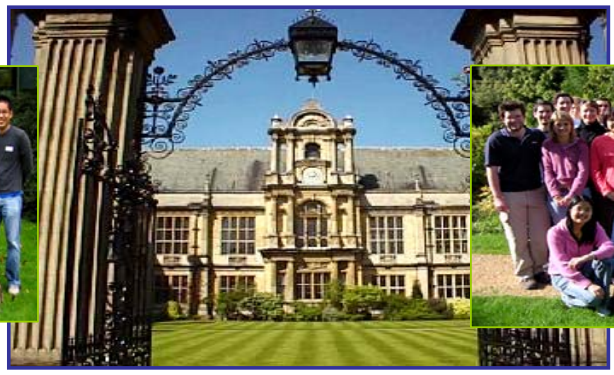
22 & 23 April 2009: Scientific Writing and Presentation Skills Course.

30 May 2009: MSc by Research, DPhil (3 or 4-year), BBSRC Programmes Submit a GSO2MSD form to the DGS for approval of assessors. GSO2MSD can be downloaded from http://www.admin.ox.ac.uk/gso/forms/. Complete Parts I, II and III and get signatures from your current supervisor, the DGS and your College, and return the form to the DGS who will seek assessors reports and Board approvals. Wellcome Trust Structural Biology students starting on 1/10/2008 should do this by 10 October 2010.

19 June 2009: Seminar reports to be submitted to Advisors.

17 July 2009: Submit your Research Report to two transfer to DPhil status assessors. Your transfer to DPhil status interview will be set by your assessors or your programme committee.

Biochemistry graduates 2005-06

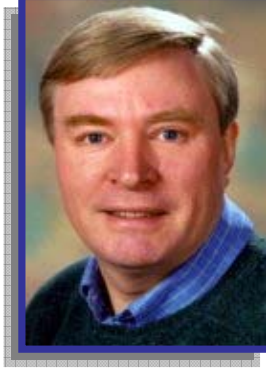


Examination Schools, High street

Biochemistry graduates 2006-07

5' with. . .

An exclusive interview with Professor Anthony Watts,
Department of Biochemistry
University of Oxford



Prof Watts' research group is working on resolving structural details of membrane peptides and proteins at high resolution. He is the Director of Biological Solid State NMR Facility at Rutherford Appleton Laboratory, Biological Managing Editor of European Biophysics Journal, Chairman of British Biophysical Society and a member of Bionanotechnology IRC.

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

At a very early age, maybe at 10 years old. At 11 years old I had a chemistry set and at 14 had built a linear induction motor. I was an avid amateur radio enthusiast for 4 years; developing photos and tracking satellites were also hobbies as a teenager.

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

Probably a surgeon or pilot, but teaching and researching science is much more varied, rewarding and exciting.

Q. *Your favourite book...*

I enjoy most genres except romances and always have one or two books on the go. A favourite is just too difficult to answer.

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

Travelling to scientific meetings to give talks, although more recently I have been taking a few short vacations before or after meetings, usually hiking and chilling out in a remote place. DIY is also a hobby and I like undertaking major projects; more recent ones include a complete kitchen refit, building an oak staircase and I am happy tackling plumbing and electrical work. Woodworking is also a schoolboy skill I like to keep up, but I get no joy from gardening.

Q. *Worst disaster in the lab...*

We've had two incidents with centrifuges, one when the rotor disintegrated at high speed. But when our 800MHz magnet quenched, blowing the base plate out, the pressure from the 300 litres of liquid helium being released as gas ripped up all the vinyl flooring and it stuck on the ceilings and walls. It took over a year to get the magnet back to field.

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

Being selected as only one of two European graduate students to attend a NATO 3 week biomembrane teaching course at Yale in 1973, just after the "fluid-mosaic" model of a biomembrane was published by Jon Singer and Gareth Nicholson. There was such a buzz with so much seminal work being published and discussed, and the students had an opportunity to get involved and interact with the giants of the field. It was probably then that I became passionate about science and decided to stick with it as a career.

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

"Luck" or "serendipity" is vital. If all the results were predictable, research gets boring. Unfortunately in today's climate of assessments, productivity and target driven research, the opportunity for inquisitive, "blue skies" research is all but disappearing. As Fermi said "If the result confirms the hypothesis, then you've made a measurement. If the result is contrary to the hypothesis, then you've made a discovery".

Q. *Any memorable lucky findings?*

Many, but one of the best in the early 1980s was observing diamagnetic anisotropy in membranes which orients them in a high magnetic field. This was rejected by 4 journals but is now established and well accepted even though our paper was never published since the referees would not believe it, and one said the effect was "laughable" – I have kept the review to remind me to have faith in one's work, even though peer review can be cruel.

Q *Describe your personality in five words.*

Fundamentally optimistic but with realism.

Q. *One human trait you hate.*

Arrogance.

Q. *Favourite vacation spot.*

A hot desert or wilderness such as Anza Borrego or Death Valley, but Tulum and Cuzco are also really enchanting places.

Q. *Best advice you ever received.*

I have both had and given lots of advice, but I do like some of the sayings of Enrico Fermi. For example, "Never be first; try to be second", which he is quoted as saying after having his b-decay paper turned down by *Nature* because "it contained speculations which were too remote from reality", and a well quoted one, but usually out of context, "Whatever nature has in store for mankind, unpleasant as it may be, men must accept, for ignorance is never better than knowledge". From a more literary character "The secret to success in life is to make your vocation your vacation" (Mark Twain) which is highly appropriate for anyone who enjoys their job, as I do.

Q. *What has been your biggest mistake or regret?*

In common with many people when trying to establish a career, especially in science, not spending enough time with the children, but maybe being a grandfather in December will give me a chance to make amends.

Q. *Favourite classical experiment?*

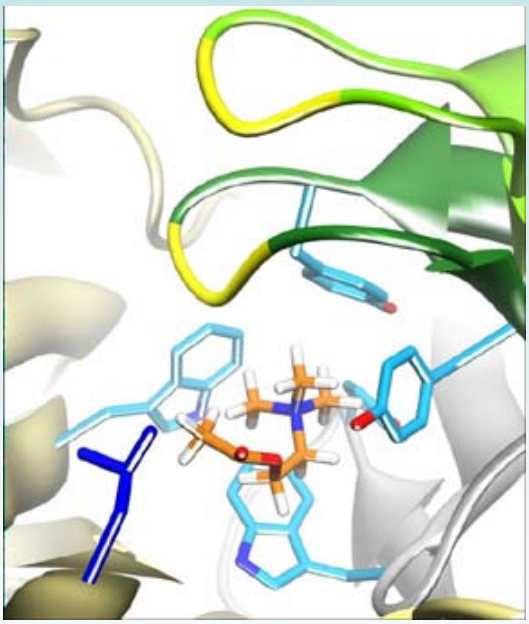
This has to be the work of the great experimentalist Michael Faraday, who had no understanding of mathematics or theory. After 5 years of Government directed work at the Royal Institution to improve optics for economic benefit in instrument production he discovered, within months, electromagnetic induction which was wholly unappreciated by his paymasters. When asked what use it would be to mankind, Faraday replied that he was not sure, but Government would tax any benefits if they did arise.

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

Understanding and using biology will be the next major focus for wealth creation and the well-being of Mankind in the world over the next 20 years. In terms of what research will be done and how, I suspect that the trend we are seeing in computer-management of very large data sets and data mining, along with systems-like approaches, will dominate. Minimal experimental data will provide sufficient information that we shall be able to predict biomolecular structures and function for all cellular activity and at all levels of complexity. All genes will be sequenced, and many methods will be robot sized. Single molecule crystallography and NMR will be routine and sensitivity enhancements will be made in all experimentation, if indeed this still goes on. Human health care will be individualized through drug and gene matching, and metabolic disorders will be a thing of the past because of biochemical research. Many new drugs based on biopharmaceuticals will be available and synthesized

biologically. We will understand much better how the brain works, and may even be able to create living cells at will and maybe even different types of life based on elements other than carbon. Environmentally, bacteria will be used to reprocess waste safely, and GM crops will be the norm. A major worry will be longevity and an ever-expanding population, and how to maintain a quality of life for everyone. As now, the major hurdles to advances will be political and worries from a highly vocal minority of uninformed extremists.

Most prominently, I foresee young scientists having the option to go to Asia (anywhere east of the Arab states) rather than stay in the West for a post doc, or even a tenured job. This is because there is a shift taking place from the dominance of the West in science to the East, with an incredible investment being made with a view to protecting their potential future wealth creation and global position for several generations to come, with a major emphasis in health care area and biological sciences. Well funded (with money generated from oil and manufacturing revenues) and committed scientists, many of whom have been trained in the West and then repatriated, are being established in labs with superb technical and infrastructure support, and a light touch in regulation and administration which is unheard of in the West. This is a great opportunity for anyone wanting to travel for science



The cation- p interaction of acetyl choline, a major brain neurotransmitter, and the ligand gated, nicotinic acetyl choline receptor has been resolved using solid state NMR, giving an insight into the binding mechanism and the residues surrounding the site. (Watts, 2005, Nature Reviews Drug Discovery *, 4, 555-568*

"Biochemistry- the evolving Department"

By Dr. Margery Ord

I feel very old having been invited to write about earlier moves of the Biochemistry department, set up by Council in November 1920. Originally Biochemistry did not have a building of its own, but was allocated space in "Old" Physiology.

By 1935 Professor Peters, who had taken up his post in 1923, was already applying to Hebdomadal Council for more space for teaching and research. This first expansion of the department created four more research labs, and enlargement of the practical classroom. But this expansion soon proved insufficient. Professor Svedberg, who developed the first ultracentrifuge, offered Peters the loan of such an instrument- which would need special housing and more funds! These were duly found, largely through the continuing generosity of the Rockefeller Foundation, and following the appointment of John Philpot as OC of the instrument, and Sandy Ogston emerging as the pioneering Lecturer (in those days Demonstrator) in "physical biochemistry". Molecular Biophysics could be said to have arisen in Oxford Biochemistry before WW2.

A Readership in Microbiology was created in 1944 for Donald Woods who arrived in the department in 1945. The growth of his research team and the post WW2 expansion of biochemistry (and science generally) in Oxford created considerable pressure on space. In WW2 concrete huts had frequently been erected to provide accommodation for many essential services. Such a hut was put up for

Peters' Building (LHS) and Old Physiology (Sherrington Building, RHS) Surveyours' hut in front

Woods' group, roughly on the area later occupied by the Krebs tower, and soon after Krebs' arrival in 1954 his MRC unit in Cell Metabolism also had an urgent need for accommodation. Two more huts were duly erected on the space now occupied by the canteen area for the current builders.

In the early 1950s Physiology moved across the road to its present site, and for a short while Krebs' unit and visitors could colonise "old physiology". Lloyd Stocken and I were able to utilise a room in the attic of old physiology where we could do autoradiography, and other rooms in its basement which were cool, where we could run chromatography columns to separate nucleotides (State of the Art method at the time).

Krebs had been awarded his Nobel prize when he was still at Sheffield, but the Rockefeller Foundation agreed to transfer the grant they were giving him to Oxford to enable the Tower block to be built. The University also agreed to fund the current Microbiology building to house Woods and his group. Woods was responsible for most of this building's design. The FHS Biochemistry had been established in 1949, with a 4th year in which a practical project, usually in a research group, was a major component - as was extensive practical laboratory work for the first 3 years (11am-5pm 4-5 days/week, usually with a break for lunch, for c. 2.5 terms/year) An undergraduate teaching laboratory had been included in the Woods building. Practical instruction in microbiological techniques has been a continuing element in the undergraduate course. The black Microbiology laboratory was completed in 1960.

Next, plans started to build the Tower (Krebs) block. The University appointed Mr Ward as architect and three senior members of staff, Drs Cecil, Parsons and Stocken, were responsible

Before World War II: the 'Old' Department from the East (note tennis courts to the east)

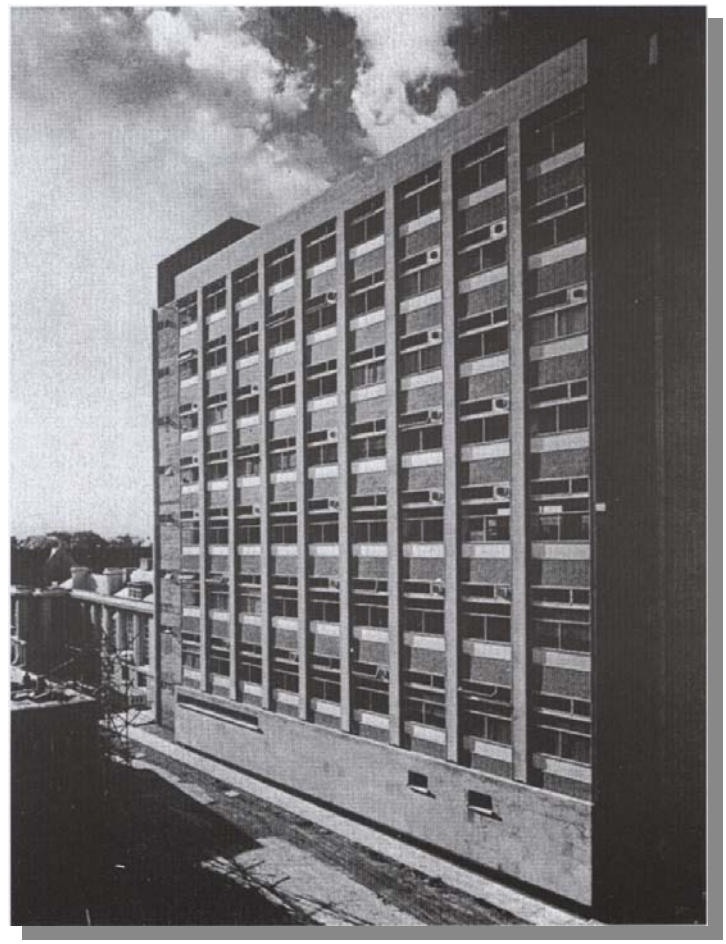
Front door of 'Old' Department (note Peters' car at the left of the car-park)

Back door to the 'Old' Department (Peters' Building) with the Krebs huts to the East

within Ward's design for allocating space over the 7 floors and basement. Teaching laboratories were allocated to the 1st, 2nd and 3rd floors, a generously spaced library went onto the 7th floor, and an adjacent cafeteria, both with splendid views north and south. It was noteworthy that the Professor retained his old office in the Peters building, which had a little space too for his secretary (now PA) and his own pretty adequate laboratory. But now, Krebs' MRC unit could get together on the 4th floor. Unsurprisingly Drs Cecil, Parsons, and Stocken chose the spaces they wanted in the new building, Stocken (and I) very happily going onto the 6th floor, facing South, and Parsons and Cecil facing north. All the University lecturers had the same areas, comprising a lab, an adjacent not too small office and an instrument room which commonly then contained balances, and at least one spectrophotometer. The lecturers had freedom to put the benches into their labs as they wished but the position of the sinks and fume cupboards (then standard) were fixed. There was also more space at the east ends for larger scale equipment like centrifuges or Geiger counters. In 1963 when the Tower block was opened, there were only two female University lecturers. Unsurprisingly male facilities were included on the 6th floor!

I don't remember that actually moving was too tiresome - but of course it seemed that at first we had much less space. In fact we had our own area for experiments and in the same lab, for a graduate student, and our other lab for the other graduate students (usually there were 2 or 3 graduate students, a 4th year doing his/her project and one or two visiting post-docs.) Over the years from 1963 when the Tower block was opened, until 1979 when Stocken retired, we and Dennis Parsons colonised the 3rd, south facing lab on the 6th floor, which also had an office which housed our secretary (then a common addition to research groups- no computers yet) and, in the adjoining little room the amino-acid analyser and our assistant who ran it (for us very happily going onto the 6th floor, facing South, and Parsons and Cecil facing north.

Health and Safety rules were less obtrusive than they appear to be today. Our group always had coffee together in one of the labs and at Christmas a major meal created by us "on the premises". In the earlier Peters building, the whole department had met for tea in the (physiology)



The 'New' Krebs Tower building at the time of its completion (c.1963);

library, a habit which continued until the canteen was created on the 7th floor, and smaller (scientific?!) discussions there became more difficult. Also of course there was the paternoster lift, continuous, not dangerous to normal individuals, and supported by the still existing lift to carry equipment and disabled visitors. The paternoster was a very popular attraction for child visitors at the W/Es. Another contrast to to-day's position was the ease with which people could go easily from department to department. Even during WW2 when secret work was going on in various science area sites, access was easy - though "loose talk costs lives" was a widespread wartime saying.

Professor Porter succeeded Krebs in 1967. He took over Krebs' space easily but soon space and money had again become an issue. Porter's interests in the structure of proteins, especially immunoglobulins, stimulated his excitement in the work opening up in physical chemistry with Rex Richards' introduction of NMR techniques. A vigorous interdepartmental group soon emerged to which Porter offered such space to

house the magnets as he could squeeze out, and he went ahead successfully to get money from the MRC and the University to put up the Rex Richards building. And there were other pressures developing too. Largely due to Krebs, chairs were created in both Molecular Biophysics and Genetics. The first holder of the Biophysics chair, David Phillips, had to be accommodated in Zoology, and Professors Bodmer and John Edwards were squeezed into "old physiology" and its little available laboratory space. Two further changes were to take place, both greatly reducing potential overcrowding of the Tower block. Professor Dwek's study of glycosylation had attracted substantial money from Monsanto so that the Porter building, which initially also housed part of Plant Sciences, could be erected still quite close to the main department. Also, by the 1990s the amount of practical work in the FHS syllabus had been substantially reduced. Firstly what had been the lab for 2nd year Biochemists on the first floor of the Tower building could be changed to provide "classical" lab space for Cathy Pears and Lynne Cox. Then the 2nd floor where UGs had another year of practical work, was partly converted into offices, and finally the third floor teaching lab now houses Penny Handford's and Louis Mahadevan's groups. When the old Biochemistry building went, so did the last of the classical classroom laboratories. Practical work for UGs now occurs in Zoology.

From when the Tower block opened in 1963 numbers of undergraduates reading Biochemistry rose steadily from the 3 admitted in 1949 to 85 $\pm$ 5 from the 1990s. These could be accommodated in the two ground floor lecture theatres in the Tower and in the larger theatre shared between old Physiology and Biochemistry, which was regularly used for seminars and special lectures. Now for larger theatres the department has to negotiate with Medical Sciences, Physiology or Zoology to use one of their theatres. There are very few sites in Oxford which have large enough theatres to house plenary lectures for international meetings.

One very important development, probably not getting underway here (apart from the structural groups who were "in at the start") until the 1990s was the increasing use of, and dependency on, computers - and the Net in which to search out and report new observations and interpretations - causing the departmental library to be closed - and Systems Biology to get underway on the 7th floor. Indeed computing, and its need for IT staff and really efficient and economic electrical services, including air-conditioning, has largely determined the need for a new building. I don't remember that the various moves made over the past 50+ years were too traumatic. I hope this will be true too in 2008 but am willing to bet that we will not have seen the last of either the structural or organisational changes. Biological systems evolve!

New Biochemistry building, 2008

Margery G. Ord did her PhD in London with Robert Thompson in the late 1940s on the distribution of acetyl and butyrul cholinesterases in human and rodent tissues, an area of research stimulated by the development of nerve gases in Germany. In 1951, she came to Oxford to work with Lloyd A. Stocken on the biological effects of ionising radiation which were now of general concern following the development of the atomic bomb. In the 1970s, together with Stocken and Ian Walker, she was examining structural and metabolic aspects of nucleohistones. Changes in histone phosphorylation led Stocken and Ord to look at cell-cycle related biochemical changes in sea-urchin eggs, liver and lymphocytes, studies later pursued on yeasts in Microbiology under Prof Paul Nurse. Margery was a Departmental Demonstrator from 1954 to 1959 and then a University Lecturer in Biochemistry and Tutorial Fellow at Lady Margaret Hall until 1988, when she was succeeded by Dr Garry Brown. Upon retirement, Margery has taken a keen interest in the history of the Department and has co-authored a number of books on the subject with colleague Stocken including the latest "The Oxford Biochemistry Department 1920-2006". A limited number of copies are available from OUBS on request (courtesy of Margery).

"The Harwell Connection"

By Sarah Field

The Mary Lyon Center, This revolutionary mouse house houses animals used at Harwell and by other research groups including several European consortia. Mary Lyon herself can often be seen at the unit seminars and student symposia at the MGU at Harwell.

Twenty one miles from the dreaming spires of Oxford, not far from the majestic towers of Didcot power station and nestled beside the Rutherford Appleton Laboratory lies a small collection of buildings. This is the home of the MRC Mammalian Genetics Unit (MGU). Most MGU students are members of Oxford University and many are affiliated to the Department of Biochemistry. We are rarely seen in the department, however, dazed and confused Harwell students occasionally venture into the Oxford science park to attend a seminar or meet with their Oxford supervisors. When I saw the recent call for articles for this new magazine, I thought it would be the perfect platform to give the rest of Biochemistry a little insight into the world of Biochemistry students based at the MGU.

As a rule students with the MGU are members of Wolfson College and most of us live in Oxford, which is great as it allows us to take part in college life. However, the downside to living in Oxford is the commute; each morning intrepid MGU students have to do battle with the dreaded A34. We brave the 40 minute drive, dodging lorries and murderous car transporters in order to get into work. The Harwell site is somewhat isolated, so setting up an experiment and popping out to the shops or home for lunch is just not an option; there are no shops and home is another terrifying drive away. An integral part of daily life at Harwell is meeting up in the small cramped tea room for coffee and lunch. On special occasions we decamp to one of the pubs in the surrounding countryside. One of the most valuable skills in the armoury of a Harwell student is the ability to invent a reason for such an excursion almost weekly. The upside of our relative isolation is that the student body gets on very well and there is little inter-lab rivalry, the small research groups (typically 4 to 6 people) all cooperate extensively with each other. There is a unique community atmosphere at Harwell which is rare in larger research establishments.

The research interests of groups at Harwell range from bioinformatics to metabolism, deafness through to neuroscience, developmental biology and genomic imprinting; all supported by the Mary Lyon Centre (MLC). This sweeping, super-clean, state of the art mouse facility is just a stone's throw from our labs and is home to a variety of services which support the work of Harwell based scientists as well as those from other centres across Europe. The overarching mission of the site is to generate mouse models for human disease, using chemical (ENU) mutagenesis and the powerful phenotyping pipelines that the MLC has to offer. Many groups within the MGU maintain strong links with groups from various departments in Oxford and further a field.

After another hard day's work at the coal face of phenotype driven genetic research, the students of the MGU return to the run the gauntlet of the A34 once more, battling through traffic jams and lorry fires to reach Oxford and home.

Look out for Harwell students at the D.Phil student seminars and poster sessions in the coming terms.

For more information, visit: http://www.har.mrc.ac.uk/

Sarah Field is a Biochemistry student, just about to embark on the third year of her D.Phil at the Mammalian Genetics Unit based at MRC Harwell. She started work at Harwell in 2005 and spent her first year working in 3 separate labs, as part of a new MRC funded 4-year PhD programme. She chose to do her D.Phil project in the Molecular embryology group and is currently working on a mouse mutant which displays defects in the specification of the left-right axis. She is a member of Wolfson college and has been very involved in the boat-club.

Why your BMI is all down to your genes?

By Alice Blachford

Recent research has found evidence for genes that will revolutionise our understanding of body weight and control of appetite. It is hoped this may lead to more effective treatments to halt the potential obesity epidemic.

For many years a genetic link with obesity has been observed in twin and adoption studies, demonstrating genes play important roles in the likelihood of developing obesity within a particular environment. Certainly, single mutations have been demonstrated to cause rare forms of severe obesity, for example mutation within the *ob* gene causing leptin deficiency. However, until recently genes that increase risk of common obesity were relatively unknown. What is known is that common obesity does not have a single genetic source but rather increased risk of obesity is caused by combinatorial effects of multiple genes as well as diet and exercise.

Recently, genetic polymorphisms within three separate genes have been identified as pertaining to higher BMI values. Interestingly, these genes are not involved in mechanisms of fat storage but rather in global regulation of appetite and satiety.

In his latest paper published in *Nature* Professor Froguel of Imperial College combines data collected in studies conducted in several European countries of genotypes obtained from obese and lean Caucasian individuals. This demonstrates that single nucleotide polymorphisms (SNPs) at specific regions along the PCSK1 gene significantly increase the risk of obesity.

PCSK1 encodes a prohormone convertase enzyme that is involved in the production of the fully functional forms of the hormones insulin, glucagon and melanocortin. The active forms of insulin and glucagon are essential for the correct uptake of glucose from the bloodstream and deficiencies in their production may help to understand the observation that obese individuals have a tendency to be hypoglycaemic following meals. The exact effect of the convertase deficiency is not fully understood, however it must not completely prevent insulin synthesis as the samples do not include sufferers of type 1 diabetes. Rather the effects of the convertase on insulin and glucagon synthesis must be more subtle.

Melanocortin is normally released in the pituitary of the brain during food consumption to give a feeling of fullness and deficiencies in production of this protein may explain the tendencies for obese individuals to overeat. Other studies have identified SNPs within the melanocortin receptor gene MC4R with increased risk of obesity.

This demonstration that obesity can be caused by defects in the global hormonal system is echoed by previous studies that identify specific polymorphisms within genes as increasing BMI. A previous study published by Professor Froguel identified mutations within a single region of the FTO (fat mass and obesity) gene that are associated with increased waist circumference and subcutaneous fat deposits. Crucially possession of this gene increases risk of childhood obesity in children from the age of seven. The protein product of the FTO gene demonstrates highest expression within the brain, indicating it may also influence appetite and behaviour towards food.

These recent studies will revolutionise current thought about the causes of common obesity and open up a new avenue for future research. Figures released by the Department for Health this year estimate one quarter of adults and one fifth of children under the age of 16 are obese. Left unchecked, in 2050 60% of men and 50% of women will be clinically obese. Obesity in children could rise to one quarter. This year the number of prescriptions for obesity drugs passed one million. However this research suggests education to improve our attitude towards food may be more effective, especially in children.

Alice Blachford is a fourth year undergraduate student of Biochemistry, doing her part II project in Dr Furger's lab at the moment, studying the components of 3'end formation of mRNA in C.elegans.

Bringing Academia and Blogging Closer Together

by Nick Anthis

Nick's blog: http://scienceblogs.com/scientificactivist/

Given that there are over 112 million blogs on the internet, there is a pretty good chance that you regularly read at least one blog, have your own blog, or know someone who does. I have maintained my own blog (http://scienceblogs.com/scientificactivist/) since January 2006, and it is just one of thousands of blogs written at least partially about science. Some of these science blogs (like mine) are written by graduate students. Some are written by more senior scientists. Others are written by science journalists or by people in other science-related professions. A blog is really just a website with regularly updated and chronologically organized material, but additional features—such as the ability of readers to comment on material—create a more informal, collaborative, and conversational atmosphere. This can be a particularly powerful tool for communication when you have scientists writing about their and others' science in such an environment.

Over a year ago, I joined two other science bloggers—Shelley Batts and Tara Smith—in setting out to write a definitive account of this phenomenon and to argue for the value of the science blog. In order to do this, we drew from the collective experience of our fellow science bloggers, far and wide, asking how blogging had affected their work, their careers, and their lives--both positively and negatively. The results were astounding. Beyond just being able to communicate science as never before, we heard from scientists who had started new collaborations, enhanced their scientific work, advanced their careers, and had been offered a whole array of new and unique experiences and opportunities in part or in full due to their blogs. In fact, the stories we heard were so compelling that instead of just communicating them we asked ourselves another question: why has this phenomenon gone so underreported and unappreciated within academic circles? And, more pointedly, how can we most effectively communicate this potential to an academic audience, in hopes of catalyzing even more of these wonderful successes?

We gave our best effort at addressing this gulf between academia and the blogosphere, and the result was recently published in *PLoS Biology*. In our paper, we address various instances of efforts to bring academia and blogging closer together, and we offer a series of suggestions for how academic institutions—and loggers—might carry this forward to the next level. We believe that when bloggers and academic institutions work together, the results can be mutually beneficial for both parties, and can be carried out in a way that advances the institution's mission without destroying the independence that makes the blogosphere so powerful. By no means are we saying that all science bloggers would want to be more closely associated with an academic institution—far from it, in fact—but we suggest how this might be accomplished when deemed desirable.

And, when would that be? An academic institution might benefit from a blog when that blog promotes work coming out of that institution, for example. More powerfully, though, blogs have the potential to initiate lively and far-reaching conversations, opening new lanes of communication between scientists, and occasionally sparking fruitful collaborations. Blogs also allow scientists to engage directly with the general public, thus contributing to the public

understanding of science—one of the many facets of a university's mission. Academic institutions are in a unique position to nurture these phenomena, and by bringing academically-oriented bloggers together under an academic umbrella, institutions can lend credibility and offer a new hub for these dynamic conversations. And, hopefully, by embracing a culture more favourable to blogging and by making sure the necessary tools are readily accessible, such institutions can bring more scientists (and especially more senior scientists) into the blogging world.

A notable example of how academic institutions can work more closely with blogs comes from Stanford University, where one individual—Ian Hsu—has been charged with creating a central directory of blogs written by students, faculty, and staff of the university. Over 150 blogs are already indexed in the Stanford Blog Directory (http://blog.stanford.edu/), and that number is sure to continue to grow. Such university-wide initiatives are rare, though, and much more common are blogs and blog networks associated with individual institutions within a university. One example from close to home is the Oxford Internet Institute (http://www.oii.ox.ac.uk/). Some universities have also instituted official blogs to publicize their own research, as the University of Oxford has with the Oxford Science Blog (http://www.ox.ac.uk/media/science_blog/).

While many science blogs written primarily about academic subjects could easily be embraced by academic institutions, the same cannot be said for others that include a substantial amount of material on politics, religion, and other non-academic subjects. Unfortunately the latter category is probably larger than the former. In fact, the most popular science blog on the internet—Pharyngula (http://scienceblogs.com/pharyngula/)—which boasts over 1.5 million visors each month, devotes much more space to arguing against creationism than to writing about the author's area of academic interest—developmental biology. Such a valuable resource need not be discounted in full, however, as tools are available to identify only those blog entries of academic interest. The technology and expertise to do this is already available in the blogosphere, so only a little bit of outreach would be required for an academic institution to harness the potential of these sometimes-science bloggers.

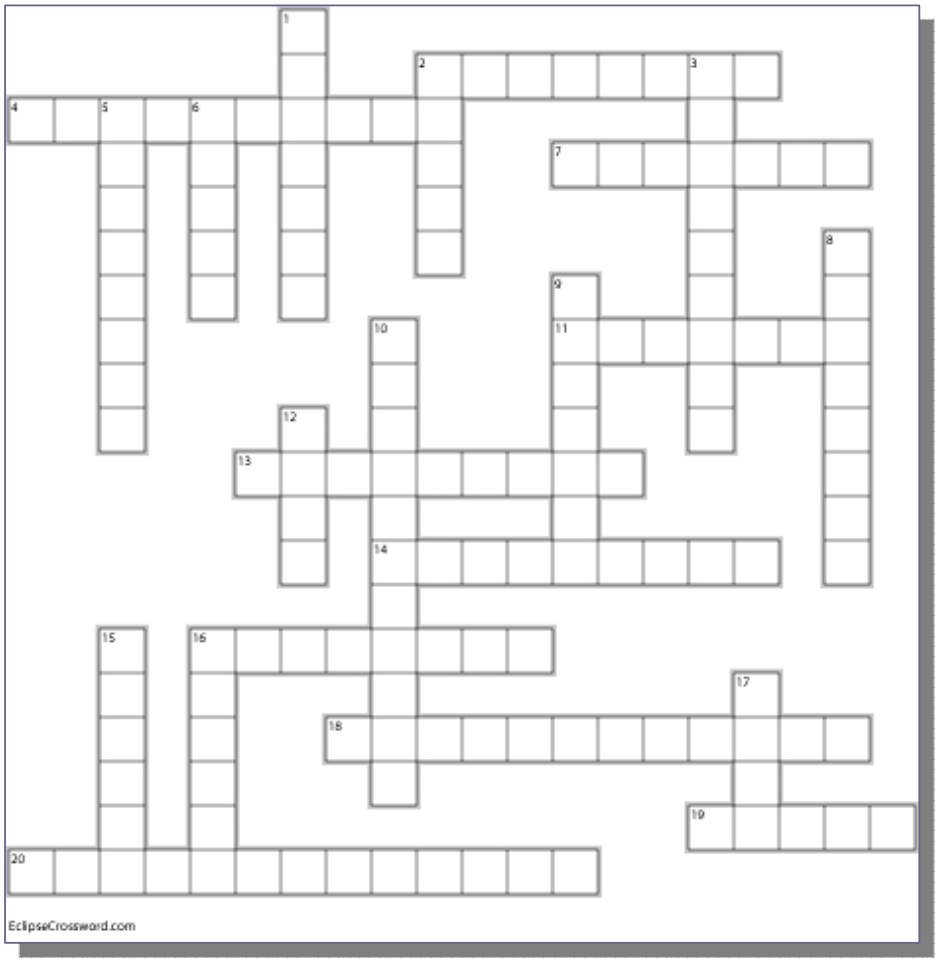
The blogosphere is a wild and untamed place, with seemingly as much misinformation available as accurate information. However, there are more than a few gems in the rough, particularly among science bloggers. Academic institutions should pay attention to this phenomenon and consider how they might more directly engage with these bloggers—for mutual benefit. Such activities could bring new individuals into the fray and could lead to many more success stories. As my co-authors and I conclude our paper, "by initiating frank and open-minded conversations about shared goals, blogs and institutions can work together to advance the quality and scope of the ongoing global conversation about science we all participate in and depend upon." It would be a shame to not act on such great potential.

Shelley A. Batts, Nicholas J. Anthis, Tara C. Smith (2008). Advancing Science through Conversations: Bridging the Gap between Blogs and the Academy *PLoS Biology*, **6 (9)**

Nick Anthis is a DPhil student in the Department of Biochemistry, studying protein NMR. He is an at large member of the OUBS committee, and served as treasurer from 2006-2008. Nick writes a blog on science and politics called The Scientific Activist, which can be found at http://scienceblogs.com/scientificactivist/";

Crossword
"Nobel Prizes 1901-2007"

It is that time of year again! As the Nobel Prizes were announced in October and 'Nobel fever' once again takes over the world, what better time to test your current knowledge of all things Nobel? Give this crossword a go and send your answers to oubs@bioch.ox.ac.uk by 1st November 2008. The winner will be drawn out of a hat and gets £10 worth of book vouchers! Look out for the answers in next term's issue of Phenotype.

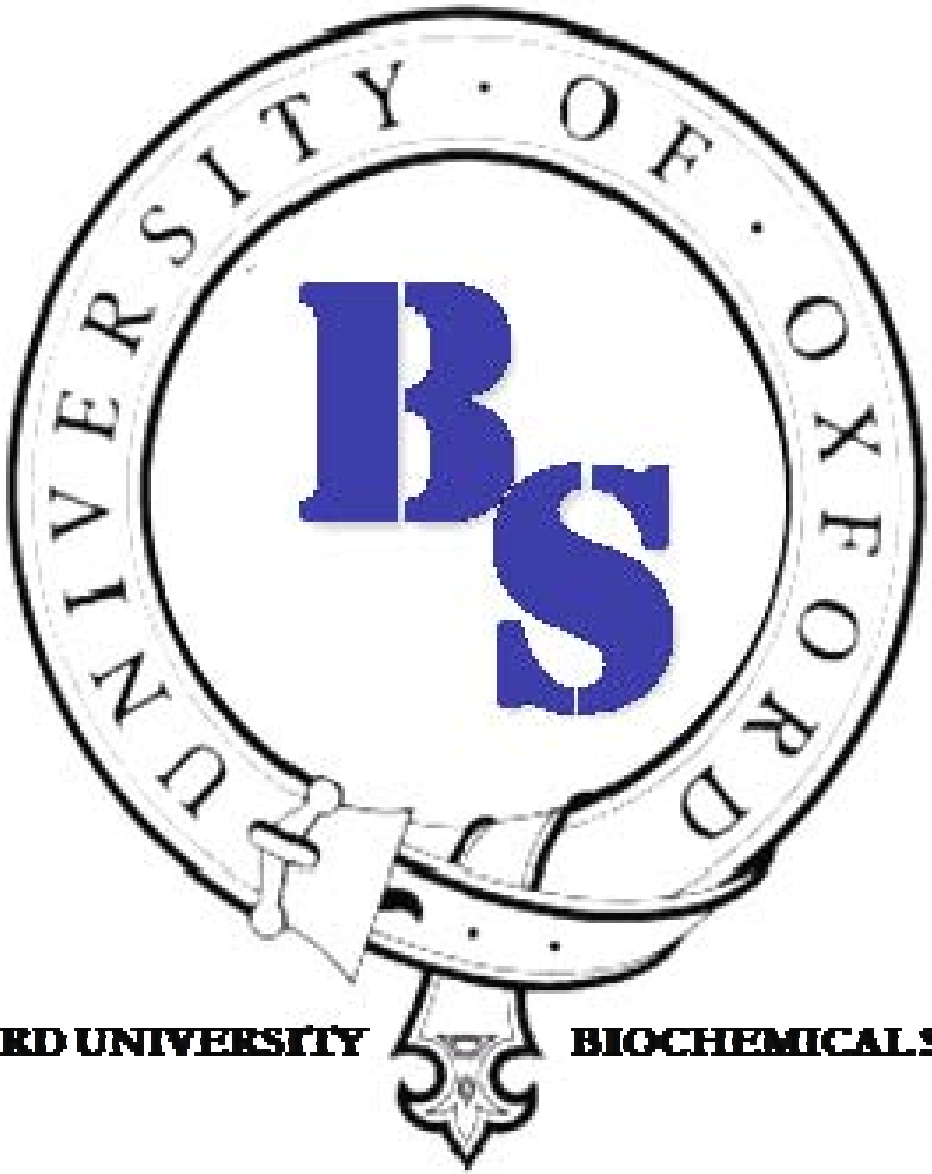


Across

2. Invention Alfred Nobel is famous for. (8)
4. The only woman to win twice. (5, 5)
7. "Surely You're Joking, Mr _____!" (7)
11. The last woman to win the Chemistry Prize. (7)
13. Forced to decline a Literature Prize. (9)
14. Prize category not stipulated in Nobel's will. (9)
16. The most recent Oxford-educated winner. (8)
18. Literature laureate who died in 2008. (12)
19. First Oxford winner. (8)
20. Youngest winner. (8, 5)

Down

1. The only person to win Chemistry and Peace Prizes. (7)
2. Date of the award ceremony is the anniversary of Nobel's ____. (5)
3. Brothers Jan and Nikolaas (Nico) won in 1969 and 1973 respectively. (9)
5. Winner of most Prizes. (3, 5)
6. The most recent British laureate, based in Cardiff. (5)
8. Swedish engraver who designed the Physics, Chemistry and Physiology medals. (8)
9. "Nobel Alley" University. (7)
10. Peace medal inscription: "For the peace and _____ of men". (11)
12. Inspiration behind "The Beautiful Mind". (4)
15. Marie Curie's hometown. (6)
16. Declined a Literature Prize. (6)
17. City where Peace Prize is awarded. (4)



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