July 2006

ibdg newsletter

www.ibdg.org.uk

Inorganic Biochemistry Discussion Group
affiliated to:
The Royal Society of Chemistry (Dalton Division) & The British Biophysical Society

In This Issue:-

Message from the Chair

Welcome to the summer issue of the IBDG newsletter where, amongst other things, we describe our recent meetings and report on future plans.

I would like to start by congratulating the winners of our inaugural award for outstanding achievements by a young scientist in the field of inorganic biochemistry. We had an impressive field of candidates, which gave the committee cause for cheer as to the future of the subject in the UK. After much discussion we unanimously agreed that the award should be shared between Dr Judy Hirst (MRC Dunn Human Nutritional Unit) for her application of voltammetric methods to study redox active centres in proteins and Dr Vasily Oganesyan (University of East Anglia) for his development of theory, analysis and computer simulation methods for advanced spectroscopic methods with application in the study of metal centres in proteins. Dr. Oganesyan gave his award presentation in April at the RSC Electron Spin Resonance Group International Meeting in Edinburgh; Dr. Hirst will speak at our very own January 2007 IBDG meeting. I congratulate them both and look forward to a similarly outstanding field for the 2008 award.

Since the last newsletter we have had a very successful January meeting at Queen Mary, University of London. A full report is included in this issue, but I would particularly like to thank Prof. Peter Heathcote and Dr. John Viles who coordinated the scientific and local programmes. The meeting was scientifically exciting and financially successful due to good attendance and successful sponsorship. One feature of this meeting was that some speakers were given extra time to incorporate "advanced tutorial" aspects of their techniques, specifically aimed at postgraduate students. BBSRC funded the students to attend and these presentations were very successful. The committee is keen to expand on this work, hopefully leading to the development of a special techniques workshop in

inorganic biochemistry - with more than a nod to the incomparable course that Bob Crichton has run successfully many times at Louvain-la-Neuve. Watch this space for more details (or contact me directly if you have ideas as to how you would like this to progress).

Next January, our annual meeting will see us returning to Imperial College, London. Dave Dexter has coordinated an exciting collaboration between IBDG, the European Iron Club, Special Parkinson's Research Interest Group (SPRING) and the Parkinson's Disease Society UK more details of which can be found below. After a number of chemistry focussed meetings, I welcome this return to a forum highlighting medical aspects of inorganic biochemistry. Such an approach has resulted in many successful meetings in the past and I hope that many of you will attend; the chemistry will not be watered down and there should be lots of exciting, applied research on show.

Finally, for those of you who are not already aware the Chemical Biology Forum (CBF) exists to bring together all RSC interests at the interface of the chemical sciences and the biosciences. Emma Raven (IBDG committee member) was recently appointed to the CBF executive. It is likely that this grouping will be hosting a series of major biennial conferences from 2008. Up-to-date news on all our activities (and especially meetings) can be found on our web pages:- **www.ibdg.org.uk**

Chris Cooper (Chair IBDG) ccooper@essex.ac.uk

January 2007 IBDG Meeting

'Mechanisms of Iron Induced Neurodegeneration: A Focus on Parkinson's Disease' **– is the subject of the 2007 IBDG annual meeting to be held on 5th and 6th January at Imperial College London, South Kensington Campus.** The meeting is being organised by IBDG, European Iron Club, Special Parkinson's Research Interest Group (SPRING) and Parkinson's Disease Society UK. Speakers will include:-

Prof J Porter (UK)	Prof A Shanzer (Isreal)
Dr J Hirst (UK)	Prof M Wilson (UK)
Prof R Crichton (Belgium)	Prof J Conner (USA)
Dr D Dexter (UK)	Prof T Rouault (USA)
Prof H Schipper (Canada)	Prof M Youdhim (Israel)
Prof P Jenner (UK)	

and poster sessions will be held each day.

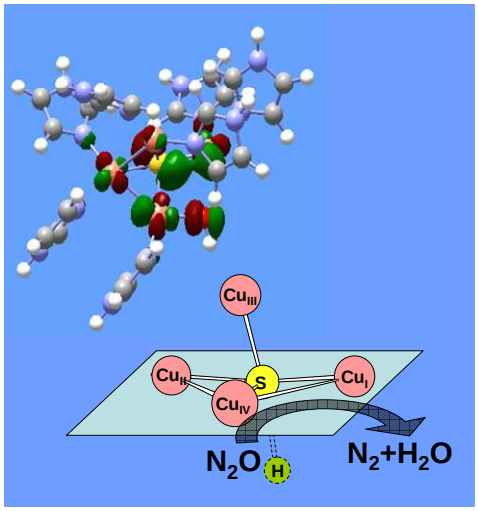
The full program, registration forms and poster guidelines will be available from:-
http://www.parkinsonstissuebank.org.uk/

Further details or informal enquiries should be directed by e-mail to pdbank@imperial.ac.uk.

IBDG Award Winners

IBDG's inaugural Young Investigator's Award was shared by Dr Judy Hirst (MRC, Cambridge) and Dr Vasily Oganesyan (UEA, Norwich).

Judy's award recognised her contributions to the development of voltammetric methods for studying redox proteins. Her award lecture will be presented at IBDG's January 2007 meeting and some of her work will feature in the Autumn Newsletter. Vasily's award recognised his development of novel theory and computational methods for simulating the spectroscopic properties of metalloproteins and model compounds. He delivered his award lecture 'Advanced spectroscopic methods in bioinorganic chemistry: a theoretical insight' at the 39th Annual ESR International Meeting in Edinburgh earlier this year. As Vasily explained, a wide range of spectroscopies are routinely applied to the study metal centres of biological importance but it can be challenging to understand the molecular origins of the spectra. This is particularly true when examining sites with multiple metal ions in close proximity. Such centres can, in theory at least, exist in a range of oxidation states. An example is the Cu_4S centre 'Cu_Z' of nitrous oxide reductase. This could access five oxidation states, two of which are predicted to be detectable by perpendicular mode electron paramagnetic resonance (EPR) spectroscopy. Vasily's methods demonstrated that the $[Cu_4S]^{3+}$ oxidation state accounts for the Cu_Z EPR of nitrous oxide reductase. In addition, he found that the S and Cu ions carrying the greatest electron density lie in a plane which may represent the catalytic 'core' that is engaged when reducing N_2O to N_2.



Vasily's work has developed from degrees in physics and biophysics. These were gained from Moscow State University and Institute of Molecular Biology where he first encountered magnetic CD (MCD) under the tutelage of Prof. Yuri Sharonov and developed a fascination with the challenges for theoretical modelling of complementary spectral information. The result was a move to Prof. Andrew Thomson's laboratory at UEA, Norwich where Vasily is now an EPSRC Advanced Fellow. Many of Vasily's current projects focus on developing general methods for the interpretation of multi-frequency pulsed EPR spectroscopy, a development stimulated by the recently established 'Henry Wellcome Laboratory of Biological Chemistry at UEA' that houses a new generation Bruker pulsed EPR instrument. Vasily is particularly keen to establish methods that allow spin 'probes' to be used to elucidate the structure, organisation and motion of proteins and amorphous polymers. He feels that such methods will lead to applications in a broad range of complex molecular systems ranging from liquid crystals to protein complexes and that he hopes will eventually be applicable to intra-cellular studies.

John Reglinski (left) presents Vasily with his award.

Vasily Oganesyan was talking to Julea Butt.

Professor RJP Williams – A Profile

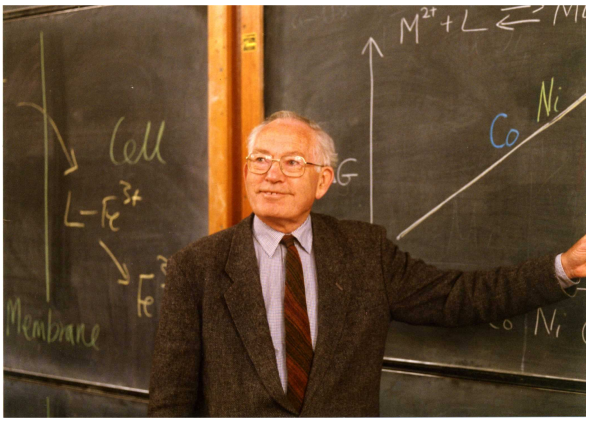
This year Professor Robert J P Williams FRS – known affectionately as 'Bob' or 'RJP' – celebrates his 80th birthday. It is a landmark for Emeritus Professor of Inorganic Chemistry at Oxford University who is the father of bioinorganic chemistry. In his 80th year, he looks back on his career.

Bob Williams' interest in bioinorganic chemistry started in 1943. 'It's a long time ago!' he quips. As for many people, his interest in the subject was spawned at school. On a forestry camp holiday from his local Grammar School he noticed that after the trees were felled chemicals were added to the soil – but not just the normal nitrogen, phosphorus, potassium mixture that you would expect in a fertilizer, but borate as well. Bob realised that the plant biologists had noticed what no chemist had: that plants require a large number of elements for growth. His ambition – which in the end turned into his life's quest – was to establish why some elements were used in biology and some others were not. His intention on arrival as an undergraduate at Oxford University was to answer this question. 'But Oxford University did not allow chemistry students to do biology!' he laughs. It was the first of a number of barriers that he has had to overcome before chemistry as a discipline really embraced biological problems.

What does he remember of his Oxford undergraduate days? 'It was a very tough course,' he says, 'and there was no syllabus at all!' I wonder what QAA would make of that? 'The tutors made no effort at all to train you for the exam,' he says, 'they trained you to understand chemistry, and included as much mathematics as possible in doing so. Because of this, we had no idea what was going to be asked in the exams – you could be asked anything at all at the examiner's whim'.

During his Part II studies at Oxford with Harry Irving, he discovered that dithizone bound different metal ions with different affinities – and established the now universally accepted Irving-Williams series (remember that this was before he had even obtained a B.A.). This is just one of several new areas that Bob has created, but he is modest about this achievement: 'Some people get lucky in their lives, and I got lucky', he says. It became clear much later on that the Irving-Williams series was relevant in biology too.

After a postdoctoral spell in Uppsala, Sweden, developing 'gradient elution analysis' (ideally for proteins) – another area that everyone now uses routinely – he returned to Oxford in 1951 as a junior research fellow. During these early years, he spent many hours looking around for ways to tackle larger biological molecules, an area of science that was not viewed as likely to be particularly productive for him. 'When I told Sir Hans Krebs that I was going to work on metal ions in biology he told me that it was a complete waste of time and that all the metal ions were merely impurities'. But although the role of metals in biology had not been widely accepted at this time, he was fortunate, he says, to have been given great freedom to pursue his ideas in the Inorganic Chemistry Laboratory at Oxford. 'The ICL was a dumping ground for misfits', he declares, 'so I fitted in very neatly!'.



His career through the 1960s, 1970s and 1980s led him from heme chemistry and vitamin B12, to NMR of paramagnetic proteins, protein structure determination by NMR and through to minerals in biology. Early model chemistry about redox energies and electron transfer led him to propose

in 1961 that energised proton gradients drive ATP formation in cells. During this time, he was one a only a handful of people that realised that protein structures were more mobile than the protein crystallographers believed, and he carried out many fundamental experiments to establish whether it was possible to do protein structures in solution. One well-tested idea is that the fold energy of a protein around a metal ion can create a special constrained state – an 'entatic state' – of enhanced functional value. Just recently, Bob has been writing on the use of heavy metal isotopes in kinetics of metal ion uptake. In 1990, approaching retirement, he embarked upon a series of now famous textbooks with J J R Fraústo da Silva. The first of these – *The Biological Chemistry of the Elements* – is now in its second edition and summarises Bob's view on metals in biological systems. In his lastest book, entitled *The Chemistry of Evolution*, Bob puts forward new ideas that argue that there is an underlying chemical basis to evolution. Interesting? Of course. Controversial? Certainly. But we all know that Bob's never been afraid to put controversial new ideas forward and see where they end up.

For those younger people who have not witnessed Bob's contributions first hand, it really is no exaggeration to say that he spawned a whole new discipline in UK chemistry. He's seen so many former students and postdocs move to distinguished academic positions of their own (several of them FRS themselves), that it would be too difficult to try to mention them all. 'I would forget someone important and they would get very annoyed with me' he chuckles. So what is the secret of his success? 'I've been very lucky', he tells me, 'but you do need more than luck. You need to be able to recognise when something falls in your lap – so you need to be looking for the 'fallout' as much as for anything else'.

But what impresses you most about Bob is the sheer wealth of knowledge that he has across such a wide spectrum of science. Even at the age of 80, he's as fresh as a daisy - a veritable font of ideas. He can talk about chemistry, biology, evolution, cell biology, biochemistry and physics and convince you that they are all connected. He's what the research councils like to call 'multidisciplinary': but of course he was wearing a multidisciplinary hat long before hats like that came into fashion. In fact, it took him a long time to persuade the department at Oxford that he could teach a biology course for chemists. 'They told me there was no room in the timetable!', he says, ' so I went to a friend of mine in the Zoology Department and taught it out of hours there!' Now, of course, every chemistry department in the country has some element of bioinorganic represented within their degree courses.

His work has been recognised publicly by many different awards over the years: included in his medal collection are three from The Royal Society of Chemistry, three from the Biochemical Society and four from International Science Societies. What has he enjoyed most about his academic career? Two things, he thinks. First, the sheer satisfaction of achieving something meaningful and seeing other people recognise that. 'You enjoy your work more when that happens because it adds colour to your work,' he says. Second, the students he has taught. 'They've been a fantastic bunch,' he says, 'just to give them half a lead and watch them find something that you could not have found yourself is hugely rewarding. It's like children in a family producing something that the father could not'.

But this ability of Bob's to set people off into uncharted territory has been one of his great strengths, of course. His commentary on the subject is so incisive that he is able, quite literally, to create whole new projects from a conversation in the corridor. The Inorganic Biochemistry community owe Bob a huge debt. He's been an inspirational, influential and hugely successful ambassador for our subject for longer than most of us remember. We wish him all the very best on his 80th birthday.

RJP Williams was talking to Emma Raven

Meeting Report

Metals and Radicals in Biology: Spectroscopic Insights

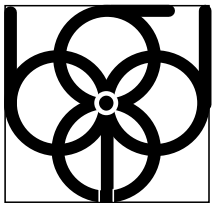
January 2006; and as cold Siberian winds whistle across the UK the promise of a nice warm beverage upon arrival is a welcoming thought. This year the IBDG discussion forum took place at Queen Mary's College, University of London in an event hosted jointly with the Electron Spin Resonance (ESR) Group. The meeting focussed on the application of advanced spectroscopic methodologies, notably EPR and MCD spectroscopies, as tools to probe free radical and transition metal centres in proteins.

A quick glance through the conference program reveals an interesting selection of poster abstracts – I know which ones I'll be looking at! The lectures are essentially split into two different formats. The first are tutorial lectures intended to communicate a basic understanding of the advanced spectroscopic techniques, together with an example of its application, to a wider audience. The second are research lectures where current ideas and results are presented and put open to a reasonable length of discussion.
Day one saw Robert Bittl (Berlin) open with a tutorial lecture on the application and uses of high field and high frequency ESR spectroscopy. Specific examples were presented showing how this technique could be used towards understanding protein-cofactor interactions. One such memorable example involved the flavin cofactor of the LOV2 domain of Phototropin. This was followed by two additional research lectures, both concerned with the application of high field and high frequency ESR, which made the earlier tutorial lecture essential listening. These were followed by award-winning presentations from two younger scientists. Emily Flashman (Oxford) discussed the characterisation of the 2-oxoglutarate Fe-dependent oxygenases and their role in the hypoxic response and Dariush Hinderberger (Zurich) described ESR results that probe the nature of the Ni-alkyl bond in methyl-coenzyme M reductase. Poster presenters advertised their science in one-minute presentations that were followed by ample time for poster viewing before the conference dinner and bed.

Day two saw Steve Rigby open with a tutorial lecture on the application and uses of both continuous and pulsed ENDOR spectroscopy. Additional tutorial lectures by Fraser MacMillian (Frankfurt) and Andrew Thomson (UEA) highlighted the use and application of 2D ESR spectroscopy and MCD spectroscopy, respectively. Again research lectures utilizing these techniques made the tutorial lectures essential listening. The conference finally drew to a close with the presentation of prizes for the best poster and talks by young emerging scientists. In summary, the conference provided a useful insight into the advanced spectroscopic techniques now available together with an idea of how they can be used towards the study of metals and radicals within biological systems.
Dr Jason Crack, UEA (Poster Prize Winner)

IBDG Committee

Prof Chris Cooper (Chair, Biophysical Society Representative), Dept. of Biological Sciences, University of Essex, **Dr John Reglinski** (Vice-chair) Dept. of Pure and Applied Chemistry, University of Strathclyde, **Dr Julea Butt** (Secretary, Newsletter editor) School of Chemical Sciences and Pharmacy, University of East Anglia, **Dr Jon McMaster** (Meetings Secretary) School of Chemistry, University of Nottingham, **Dr Dave Evans** (Treasurer), Dept. of Biological Chemistry, John Innes Centre, Norwich , **Dr Kate Brown** (Imperial College, London), **Dr Rob Evans** (King's College, London), **Dr Emma Raven** (Leicester), **Dr John Viles** (Queen Mary, London).



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NEW MEMBERS 2006

Only applicable for members who do not pay *via* the RSC

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