chem cam

Chemistry at Cambridge Newsletter

Autumn 2011

Solid-state NMR to **study tissues**

Looking back at the 1930s

Modelling molecular interactions

A life shaped by **Cambridge chemistry**

Yusuf Hamied finished his Cambridge PhD more than 50 years ago, and since then has built up one of India's biggest pharmaceutical companies. He tells Sarah Houlton about his Cambridge experience, his business, and why he thinks it's important to give back

You came from India to study chemistry at Cambridge in the 1950s. How did that come about?

That's a very interesting question! In March 1953, Professor Alexander Todd visited India. My father happened to be sheriff of Bombay at the time, and one of his duties was to entertain foreign dignatories who were visiting the city, including Todd. At that time, my O-level results had just come out, and my father took me to meet Todd, and showed him my O-level report card. He then asked him what the minimum requirements were to get in to Cambridge!

Todd looked at my father and me, and said, 'If we think the boy is suitable, we take him.' And my father told him that he wanted his son to go to Cambridge. At that time we did not know that Professor Todd was a fellow of Christ's College, where one of my father's uncles had studied in the 1880s, and another relative of mine had studied more recently, but he told my father that he would see to it that his son comes to Christ's. I was only 16 then, and he said I would have to wait until October 1954. And this is how I got admission to Christ's to do natural sciences – it was only because Todd visited Bombay in 1953.

How did your time at Cambridge influence what you have done in the rest of your life?

Well, I did my natural sciences tripos, and in my Part II results I was very fortunate and got a first class. By 1957, when Todd was already Sir Alexander, I went and asked him what he would advise me to do. I was close to him even during those three years of being an undergraduate – I knew his children, and I would be invited for Christmas lunch. He asked me whether I would like to do a PhD in Cambridge. I said I would love to, and he said I should come and work under him. So from 1957 to 1960 I worked under Todd at the Lensfield Road laboratory, which had just been opened. When I submitted my PhD I had not reached my 24th birthday, and I then came back to India.

My father ran a very small pharmaceutical company in Bombay, which I joined. The company, Cipla, helped raise the standards of the pharmaceutical industry in India, and took up the manufacturing of pharmaceutical raw ingredients, and encouraged other Indian companies to do the same. By the grace of God he has been very kind, and I've been very fortunate. But it all started with that meeting in 1953 between my father, myself and Lord Todd.

Was it always the plan to go back to the family business?

No – it just happened that chemistry was my best subject! I wasn't forced into the family business – it just happened that it was my line. Even today, I still do a lot of the R&D and new product developments – I really enjoy it. I looked at it almost more like a hobby than work

– I never really treated it only as a business activity, but more from a business plus humanitarian angle. Even today, 50 years, later, it's exactly the same. This is my 51st year working in the company, and the growth curve has been positive ever since 1960.

The business has clearly developed quite significantly from that small company you first went back to.

That's right. When I joined Cipla, the rupee was 5.5 to the dollar, and our sales were under a million dollars as the exchange rate then was. Now the rupee is 50 to the dollar – it's devalued by a factor of 10 over the past 50 years. But even at 50 rupees to the dollar, this year our turnover will be roughly $1.35bn. That is quite significant for a small Indian generics company that sells its products at reasonable and low prices in India and Africa.

How has the nature of the business changed since 1960?

In 1960, the Indian market was dominated by large multinational companies – 80% of the total business was in the hands of these multinationals. This was all because of the intellectual property laws and patents, which gave them a monopoly. A group of friends and I challenged this, saying that India could not afford a monopoly. It took us 12 years of fighting to get the Indian government to revise its patent laws. In the end they revised it totally in our favour, which wasn't even what we were asking for – what we wanted was a system where the scientist who innovates should be suitably rewarded, but there should be no monopoly in India. But instead they simply abolished patents.

Subsequently, the multinational companies sort of gave up in India, which was a very big mistake on their part as it allowed the Indian companies to grow, so by the turn of the century Indian companies like Cipla controlled 80% of the domestic market, and the multinationals just 20%.

They are now trying to re-enter India as the patent situation was reversed in 2005, and we are now back to how it was pre-1972. So now we are slowly seeing the multinationals increasing their domination of the Indian domestic market again. I have said openly on many platforms that what the Indian government has done is commit genocide in healthcare, and that a country like India with 1.2 billion people cannot afford a monopoly in healthcare as it leads to high prices, and people simply cannot afford the drugs. My motto has always been 'access to essential life-saving medicines at affordable prices'.

What achievements in your career have you been most proud of?

There have been three things. The first was changing the Indian patent law in 1972. The second, I have always insisted that the backbone of the pharmaceutical industry is the manufacture of active ingredients, and that is something that was virtually non-existent in India when I went back in 1960. We have really pushed this forward, and today India is regarded as the pharmacy capital of the world. The reason for this is that we manufacture these active raw materials, and this is something I started and encouraged in India, so healthcare is now self-sufficient and self-reliant in the country.

The third was that in 1990 Cipla started producing anti-AIDS drugs, and in 2001 we offered the anti-AIDS cocktail Triomune at below a dollar a day. This totally revolutionised ➢

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That's my father!

Dear Editor
A photo of Colloid Sciences for the academic year 1960-1 appeared in the Summer 2011 edition of *Chem@Cam*.

I recognised the person next to Dr Biswas (second from the left on the back row) as my late father, John Chipperfield. He went on to become a lecturer in inorganic chemistry at the University of Hull. My mother recognises the person third from the right on the front row as John Kernohan. He became a lecturer at Dundee University. I followed in my father's footsteps and did my degree and PhD in Chemistry at Cambridge (1984–90).

Ann Keep
Johnson Matthey, Royston, Herts

American colloids

Dear Editor
The page 'Colloid reminiscences' in the Summer 2011 issue of *Chem@Cam* inspired some pleasant memories. I spent 1949-50 at Colloid Science on a US National Research Council fellowship following my graduate studies at Princeton University in the US.

I was in the infrared spectroscopy group of GBBM ("boom-boom") Sutherland where I learned much about the technique of infrared dichroism for which he was a pioneer. These were in the days of rock salt optics for infrared, giving rise to some anxious times in avoiding the optics from dissolving during a basement laboratory flood.

Norman Sheppard was in the group, and subsequently joined the Cambridge chemistry department. A good friend was the late Maurice D'Hont who went on to head the chemistry division of the Belgian Atomic Energy Program where I subsequently visited him at Mol and had the pleasure of joining him in a helicopter ride to the Belgian World's Fair. Another good memory was joining Maurice in the motorcycle side car of the able laboratory technician, Tom Robinson, for some sailing in the Norfolk Broads. Tom subsequently married Swedish student Britta Davidsonn and joined her in Sweden, where my wife and visited them sometime later.

GBBM left for the US during my stay to head a group at the University of Michigan, which my college classmate Sam Krimm joined, and subsequently became a professor of biophysics at Michigan.

Impressive lectures were those of Dirac, Hoyle, and Leonard – ones about (whom students said he had great portential) as well as philosophy lectures by Bertrand Russell. I returned to the University of Massachusetts in Amherst, MA where I made good use of my newly learned skills, and later helped found its polymer science and engineering programme, which acquired leadership in its field.

Thus Cambridge Colloid Science played an important role in nucleating many endeavors, and served an important role in inspiring many mentioned in the current article, including the late Fred Eirich with whom I maintained contact at Brooklyn Polytechnic, and Geoffrey Gee, a pioneer in colloid science and rubber studies.

Dick Stein
University of Massachusetts, Amherst, US

CUAS hero

Dear Editor
I have just read the *Chem@Cam* Summer 11 e-publication and noted, with interest, the article in the Alumni section relating to Kenneth Campbell VC.

While at Clare College, Campbell was very much a member of Cambridge University Air Squadron during Oct 1937-39. We also have on record that his tutor was Mr H Thirkill.

John Jarvis
Wg Cdr Retd, CUAS Adjutant

eChem@Cam

Chem@Cam is now being sent out by email to those who have asked for a pdf version rather than a hard copy in the mail.

If you would like to swap your paper magazine for an e-version, then please send an email with the subject line 'eChem@Cam' to jsh49@cam.ac.uk, and we'll start to send you the mag electronically from the next issue. Don't forget to tell us your postal address so we can check that the correct person is being removed from the mailing list for the paper magazine.

If you're not sure what it will look like, you can check out e-back issues on the newly redesigned department website, www.ch.cam.ac.uk

Don't worry if you still want to receive a paper copy – we'll continue to print and mail the magazine for the foreseeable future, so you won't miss out!

chem@cam
Chemistry at Cambridge Newsletter

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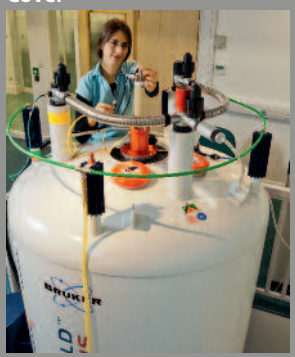


Elodie Salager, a postdoc in Clare Grey's group, using the NMR machine in the Todd-Hamied lab

Photograph:
Nathan Pitt & Caroline Hancox

This newsletter is published three times a year by the University of Cambridge Chemistry Department. Opinions are not necessarily those of the editor, the department, or the university.

Editor-in-Chief: Steve Ley
Editor: Sarah Houlton
Photographers:
Nathan Pitt, Caroline Hancox
Editorial Board:
Brian Crysell, Bill Jones, Jonathan Goodman, Rosemary Ley, Jeremy Sanders

Address:
Chem@Cam, Department of Chemistry, University of Cambridge, Lensfield Road Cambridge CB2 1EW
Phone: 01223 763865
email: news@ch.cam.ac.uk
website: www.ch.cam.ac.uk

Elan funds drug discovery centre

A new centre dedicated to research into innovative therapies for Alzheimer's and Parkinson's diseases is being established in the department. The Irish-headquartered pharmaceutical company Elan will invest $10 million over the first five years of the initial 10 year collaboration.

The Cambridge–Elan Centre for Research Innovation and Drug Discovery will provide an interdisciplinary environment to enable translational research. The aim is to discover novel compounds that can alter the behaviour of proteins associated with neurodegenerative disorders that can be developed into new treatments.

Work on understanding the fundamental molecular origins of these neurogenerative disorders has been ongoing in Cambridge for more than a decade, and Elan has a long-standing interest in neurodegenerative diseases. As well as looking for novel compounds the aim is for the centre to characterise the fundamental physico-chemical mechanisms by which they alter the behaviour of proteins associated with neurodegenerative disorders.

Chris Dobson, Michele Vendruscolo and Tuomas Knowles are all involved in the centre. 'The department, and indeed the University, are very keen on the venture, and on the opportunities that exist to build on it for the future,' Chris says.

'The process of bringing together researchers at Cambridge and at Elan has already created novel insights and opportunities in drug discovery,' he adds. 'The new centre builds on the successes of this initial interaction to establish a long-term relationship to lead to novel and effective therapies for the most debilitating, costly and rapidly proliferating diseases in the modern world.'

Chris: establishing a long-term relationship to work on these disease areas

■ In other news, Chris Dobson has been elected as a Fellow of the Academia Europaea. Founded in 1988, it has more than 2000 members from the physical sciences, biological sciences, medicine, mathematics, humanities, social sciences, economics and law. He's in good company – of 19 current UK members working in chemistry, almost half have a Cambridge chemistry connection.

Photos: Nathan Pitt

November is named lecturer season, and pictured above are the BP, Linnett and Melville lecturers, all of whom visited the department that month. From the top: Jean-Marie Tarascon of the University of Picardie in France gave the BP lectures, including a talk on Li-ion technology, its state-of-the-art and materials issues. Next is Linnett Lecturer Peter Wolynes of Rice University in the US, who gave four lectures on his work on a wide variety of uses of a statistical description of the energy landscape across biology, chemistry and physics. Finally, the Melville Lecturer was Geoffrey Coates of Cornell University, also in the US. He spoke about the development of new routes to benign polymeric materials.

ERC funding adds 500 core computer

A new computer is now up and running, providing David Wales' group with a 500 core computer cluster server to carry out calculations of how molecules and bulk systems self-organise.

Photo: Nathan Pitt

David's new computer will run complex calculations on how systems self-organise

Funded by the European Research Council, the computer will allow the group to implement novel computational methods based on the analysis of the potential energy landscape. These will be used in a wide range of applications, from materials chemistry to more biological projects.

'Rates, mechanisms and pathways will be characterised for systems ranging from soft and condensed matter, through atomic and molecular clusters, to proteins and nucleic acids,' David explains. 'Structure prediction is another key aspect of this research programme, with a particular emphasis on proteins associated with variable pathogens, such as the influenza virus.'

He is working with numerous collaborators on these projects, including colleagues in the chemistry, physics and zoology departments here in Cambridge. Installing the computer itself was a significant project, and Catherine Pitt from the computer officers' team carried out the vast majority of the work.

Challenging chemistry

The first Cambridge Chemistry Challenge was a resounding success. The brainchild of Peter Wothers, the internet-based challenge was open to anyone of any age from anywhere in the world. It was designed to stretch students' science knowledge, providing puzzles that made them think.

When the monthly online competition finished at the end of June, Year 12 students in the UK who had done well in the challenge sat a written exam, set by teachers and university chemists.

More than 3000 students in 250 schools across the country took part, and the best performers were presented with their 'Chemistry Challenge' awards at a reception at the House of Commons in November by Cambridge MP – and department alumnus – Julian Huppert.

One of the award-winning students was Alexander Moore, who's studying Cambridge Pre-U chemistry at Winchester College. 'I really enjoyed the competition,' he says. 'The questions required you to think outside the box, and apply other skills like maths. I thought I'd done well, but was surprised to find out I'd achieved one of the top marks in the country!'

Peter was really pleased the competition was such a success. 'It's fantastic to see it strike a chord with so many students,' he says.

'At school, students are taught the facts, but here they have to apply knowledge of other subjects and think creatively – these are exactly the kind of skills that are needed for university. It's therefore useful for students wanting to go on to study chemistry at undergraduate level because it gives them that competitive edge.

As well as support from the department, the challenge had the backing of University of Cambridge International Examinations (UCIE), and OCR, Oxford, Cambridge and RSA Examinations. 'I'm delighted that this competition has proved to be so successful, engaging and inspiring thousands of students around the world,' says UCIE chief executive Ann Puntis. 'These are our young chemists of the future. Through participating in the challenge, they demonstrate an interest in chemistry that goes beyond the classroom, preparing them for success at university and beyond.'

Pictured (l-r) are Julian Huppert, Peter Wothers, Alexander Moore and Andrew Wolters, a chemistry teacher at Winchester College

The challenge was such a success that it's going to be back in 2012. The first online challenge will be available at a minute past midnight on Sunday 1 January – go to www.C3L6.org to find out more.

ERC advanced grant awarded to Dominic

Photo: Nathan Pitt

Dominic: funding granted over the next five years

Dominic Wright has been awarded an advanced grant from the European Research Council. The five-year grant will support his work on non-classical main group chemistry, supramolecular chemistry and catalysis.

The ERC distributes scientific funding across Europe under the EU's 7th Research Framework Programme. Advanced grants are given to established researchers with a recent track-record that identifies them as scientific leaders, carrying out groundbreaking or unconventional research at the frontiers of their field.

The grant will fund Dominic's work on p-block elements. He will be looking at the fundamental and practical applications of these elements in supramolecular chemistry – chemistry that is typically the domain of carbon chemistry – and catalysis, the classical domain of transition metals.

The programme has two major components, which span the non-metallic and metallic areas of the p-block. The first component involves the development of systematic approaches for building macromolecular inorganic systems, and their application in host-guest chemistry, gas storage and chemistry.

The second part of the programme looks at applications of p-block metals in both stoichiometric and catalytic bond-forming reactions. This would provide cheaper alternatives to precious metal catalysts in the synthesis of both small molecules and polymers.

Peter's ACS prize

Emeritus reader Peter Murray-Rust has won the 2012 Herman Skolnik award, presented by the American Chemical Society's Division of Chemical Information.

Peter was recognised, along with his long-time collaborator Henry Rzepa of Imperial College, for their continued efforts to advance the field of chemical informatics, particularly in electronic and online forms. The citation also mentions the standards they created to facilitate science, and their promotion of new ways to collaborate and exchange chemical data.

Their work has led to a dramatic improvement in the ways in which molecular data are embedded in published scientific articles, preserving chemical identifiers, and facilitating both indexing and searching online. It has had a huge impact in chemical document analysis, chemistry on the internet, and in creating a viable strategy for making electronic chemistry information as widely accessible and usable as possible in the information age.

The prize consists of a $3,000 honorarium and a plaque. Peter and Henry will also present an award symposium at the ACS National Meeting in Philadelphia in autumn 2012.

Photo: Nathan Pitt

Bill Jones (left) officially handed over the reins as head of department to Daan Frankel at the beginning of October – and received a suitably liquid thank you in return!

Inaugural climate meeting

In the autumn, the department hosted the first seminar series for the Cambridge Centre for Climate Science, or CCfCS. The centre is a joint venture between the university and the British Antarctic Survey (BAS) to promote research and other activities in climate science at both institutions.

Several university departments are involved in the centre. As well as chemistry, it includes scientists from the departments of applied mathematics and theoretical physics, earth sciences, geography and plant sciences.

For the kick-off seminar, John Pyle gave a talk on the latest findings of the Intergovernmental Panel on Climate Change, or IPCC, in the context of physical climate science.

'This was a tremendously well attended seminar,' says Alex Archibald, who's one of the scientific coordinators of CCfCS. 'The aim is to continue to hold regular seminars to showcase the strength and depth of climate science being performed within the university.'

John Pyle spoke about the IPCC's latest findings at the meeting

Photo: Nathan Pitt

Shankar caught on camera

Photo: Nathan Pitt

Left: Shankar gets a grilling by a reporter for the TV news; below, with Nagaratna

A recent publication in the journal *Nature Chemistry* from Shankar Balasubramanian's group attracted a lot of media interest. He was even filmed in the lab for regional BBC and ITV news, with plenty of other media coverage in the national press, and various international publications.

The work was led by a PhD student, Nagaratna Hegde, who has now graduated and returned to her native India. 'She was interested in the anticancer properties of a complex thiazole-peptide natural product, thiostrepton,' Shankar says. 'This molecule has been known for many years to have antibiotic activity through its interaction with bacterial ribosomes, and more recently it was discovered that it also has anticancer properties.'

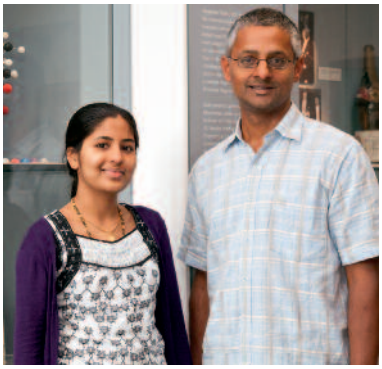


Photo: Caroline Hancox

Nagaratna made chemical derivatives of the natural product to establish which parts of its chemical structure were essential for its biological activity against breast cancer cells. She then used a tagged derivative to identify the protein targets. These included a transcription factor called FoxM1, which is already known to be a driver of a number of different cancer types, including breast cancers.

'She then elucidated the biophysical details of the thiostrrepton-FoxM1 interaction which led to a proposed mechanism of action in the cell,' Shankar adds. 'Thiostrepton is also known to act via inhibition of the proteasome, so it clearly has multiple modes of action which may, interestingly, prove to be synergistic.

'Nagaratna's work now enables us to elucidate the effects of targeting FOXM1 protein and may well inspire the design or discovery of new drug-like molecules that act via this mechanism. The work is particularly exciting for us, since directly drugging transcription factors has generally been considered to be a very challenging, if near impossible, approach to intervene with biology.'

Another prize for Jonathan

Jonathan Nitschke has won the Cram Lehn Pedersen prize for 2012. This prize is sponsored by the RSC journal *ChemComm*, and recognises significant, original and independent work in supramolecular chemistry by emerging investigators.

The prize is named in honour of the winners of the 1987 Nobel Prize in Chemistry, Donald Cram, Jean-Marie Lehn and Charles Pedersen, which was awarded for the development and use of molecules with structure-specific interactions of high selectivity.

Appropriately, Jonathan won for his pioneering work in container molecules, functional materials and dynamic ligand chemistry.

'I'm incredibly honoured to receive this prize, which reflects most of all on the hard work, talent and creativity of my scientific co-workers, past and present,' Jonathan says. 'It's a great pleasure to be part of the vibrant international community of supramolecular chemists.'

As well as receiving a £2000 cheque, Jonathan will be travelling to New Zealand in January 2012 to give his award lecture at the 7th International Symposium on Macrocyclic and Supramolecular Chemistry at the University of Otago.

Todd-Hamied Laboratory opened

Photos: Nathan Pitt

The new Todd-Hamied Laboratory was officially opened in August. Refurbished with the generous assistance of Yusuf Hamied, and named in honour of his supervisor and mentor Lord Todd, the lab is home to Geoffrey Moorhouse Gibson professor Clare Grey's group.

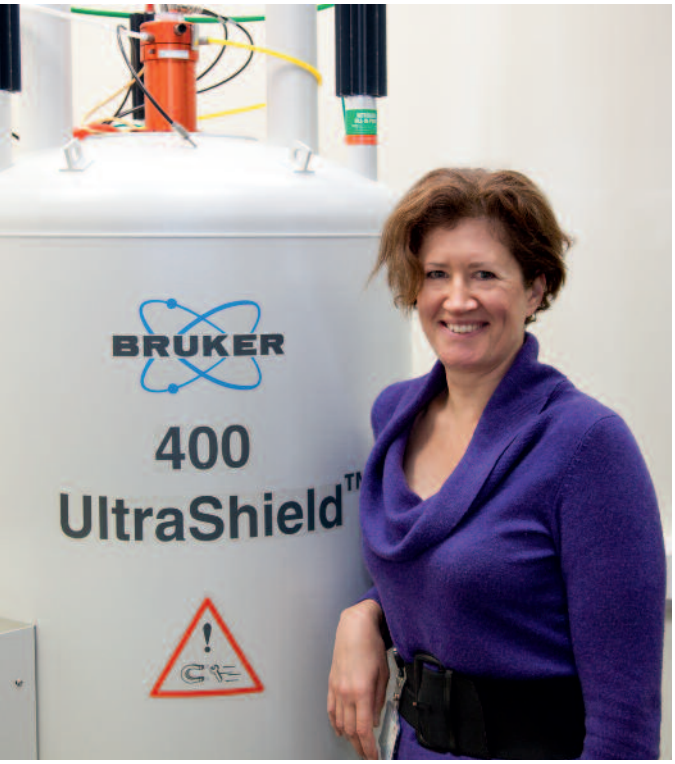
The shiny new space represents a significant transformation – and a lot of time, work and effort. This area of the basement used to be home to Alfie Maddock whose work on radiochemistry left it heavily contaminated with radioactive protactinium, and before any refurbishment could take place the whole area had to be decontaminated.

The official opening also featured several talks. Clare spoke on her work on using NMR spectroscopy to aid the design of the next generation of batteries and fuel cells.

Also speaking were Melinda Duer, who gave a presentation about her work on solid state NMR of tissues, this issue's cover star Elodie Salager, with a talk about NMR crystallography, and Christopher Pickard of UCL, who spoke about his work on structure prediction and NMR shift calculations from first principles.

Pictured clockwise, from above: Yusuf unveils the plaque; Clare's talk; Bill Jones does the introductions; Clare shows Yusuf the lab; and Yusuf poses with his wife Farida at the entrance to the new lab

Tissue studies by NMR



Photos: Caroline Hancox

Increasingly complex systems can now be studied by solid state NMR, and Melinda Duer is using it to look at important biological processes in real tissue

Recent developments in solid state NMR technology have enabled increasingly complicated systems to be studied. Signal-to-noise ratios and resolution have both improved dramatically, and Melinda Duer is now starting to unravel some complex biological processes.

'Although the advances in solid state NMR have been largely incremental technology improvements, they have made a huge difference,' she says. 'In the past we thought it might be theoretically possible to get quantitative structures from heterogeneous, non-crystalline samples. Now, it is actually possible.' Yet it's still not straightforward – the spectra remain complex, and the signals from the site of interest need to be picked out.

Much of Melinda's current work focuses on collagen. 'It's an elongated triple helical protein that self-organises in parallel fibres,' she says. 'Specific crosslinks form between the fibres, so although it's not crystalline and has no strong 3D order, there is sufficient local order for NMR structure determination.'

This is the key to the success of NMR in biological systems – it can be used where there is local order, even if overall the system is fairly chaotic, as long as it is not too flexible, and the atoms 'see' the same environment. There might be a million molecules within a fibrous collagen bundle, but as the motifs repeat across the whole bundle, each equivalent carbon in every molecule is in a similar environment.

'As far as we know, no-one has ever tried to look at a solid protein structure in the solid tissue where it was made, resides and functions,' Melinda explains. 'You need ^{13}C enrichment to see a signal, and then you need quite a lot of the molecule to get a decent signal. But as most NMR work is done on samples with 1% ^{13}C, we worked out that if we could create 10mg of strongly enriched material, we might succeed.'

Solid state NMR relies on the magnetic behaviour of spinning atoms which interact through space, and studying these interactions gives an insight into their structural arrangement. 'We can use these properties in various ways, such as two-dimensional correlation spectra where the magnetisation is transferred from one spinning carbon atom to another, so we can see which atoms are near each other,' she says.

'If the interaction is very small, which it often is, it has to be amplified, and this is where NMR technology has really moved on recently. You can even use the intervening protons to transfer the magnetic interaction. If two carbon atoms are, say, 8Å apart, that's too far to see a direct interaction, but as the carbon interacts with a nearby proton, which then interacts with the next proton, and so on until it reaches the other carbon atom, we can "walk" the interaction across the molecule and see the overall interaction.'

STRUCTURAL CONSTRAINTS

Measuring maybe 10 different forms of interaction and putting them all together generates a list of structural constraints, and ultimately only one picture of the structure can fit them all. 'It's the same basic idea as solution NMR – just a bit more complicated!' she says.

Melinda works with a very talented technician, Rakesh Rajan, in the bone biology group headed by Roger Brooks at Addenbrookes, where there are cell culture facilities. Rakesh has been able to create enriched collagen in a way no-one has ever managed before. 'He waded through 80 years of literature to find papers about using tissue culture in bone, cartilage and so on, took what he thought were the best elements of each one, put them all together in one protocol, and tried it out,' she says. 'It worked first time – we couldn't believe it! While it only made about 7mg, it gave really sharp, well resolved spectra. And it wasn't a fluke – every time he repeated the culture, it worked.'

A single cell culture flask can now generate 10mg of enriched extracellular collagen matrix. This gives sufficient signal for a whole range of 2D, 3D and even 4D NMR experiments, and they have started doing the same type of structural determinations that have been commonplace for a decade with crystallised, purified proteins produced by bacterial expression or peptide synthesis.

REAL WORLD MATERIAL

Importantly, material generated via cell culture is closer to 'real world' material than crystallised proteins, which are not glycosylated – they do not have sugar molecules attached to the protein chains. 'Synthesised proteins are potentially very different from native mammalian proteins, as most are glycosylated in the real tissues,' Melinda says. 'The hydrogen bonding potential of the sugar can affect the rate of protein folding, the shapes they fold into, and what enzymes and other molecules can bind to it.

'Material made by bacterial expression or peptide synthesis will only ever give you a crude estimate of structure in a real tissue. Even if you could make collagen in a peptide synthesiser or express it bacterially, much of the rest of the structure is also created after the protein chain is formed, so cannot come out of a peptide synthesiser. The only way to look at collagen truly as it functions in a tissue is to look at collagen made in a tissue.'

By adding different ^{13}C enriched materials to the cell culture, they have started to collect together structural constraints that will help them determine a structural model for the cell adhesion process in collagen. Collagen is best known for its role as a structural scaffold, but they are focusing the way it signals to cells and encourages them to differentiate in a particular way, in collaboration with Richard Farndale's group in biochemistry.

'The first step is cell adhesion, and then various crucial integrin molecules involved in cell signalling bind to it,' Melinda says. 'We want to look at cell adhesion sequences, and see how they change when, for example, there is

excess sugar around, and in various different diseases, as well as when there is wear and tear. If the collagen matrix that forms in tissue culture is damaged or partially degraded, what happens?'

Perhaps the most interesting observation thus far is the glycosylation patterns on the collagen. 'We know that collagen is glycosylated in some way, and we also knew from our earlier work on bone that the mineral in bone is pressed up against some kind of sugar – but we couldn't work out what kind of sugar it was, or where it was.'

SERENDIPITOUS SUCCESS

As is so often the case in science, the answer arrived serendipitously. 'We had run out of labelled glycine for cell culture, but we did have some ^{13}C enriched glucose we'd been using for other things, so we tried using that in the cell culture,' she says. 'We hoped it would be metabolised by the cells to give us general ^{13}C enrichment. This worked to an extent – we saw some enriched serine and glycine – but to our surprise we also saw the sugar itself in the spectra.

'At first, we thought it must be left-over glucose that hadn't been washed off, but whatever cell culture conditions we tried, we always got exactly the same material out at the end. It wasn't random or accidental – it was actually there, as part of the collagen matrix, ordered and packed in exactly the same way, and we could see how it interacted with the matrix's protein parts.'

They are still working out the exact structure, but the signals are the same as those previously seen in bone when sugars were close to the mineral. This would make sense if it is coating the collagen in some way. 'We're still determining the structural model for the cell adhesion site, but these results are really interesting as no-one has seen these sugar interactions before,' she says.

More recently, the group has developed a 'heavy mouse' where all the tissues are heavily $^{13}C/^{15}N$ enriched, and that is allowing them for the first time to start looking at protein structures in real tissues.

Her work isn't only of theoretical interest, however – it may give an insight into what's going on in a variety of different diseases. One example Melinda is working on is alkaptonuria, a rare condition where a person cannot make the enzyme which carries out the final stage of the metabolism of tyrosine. The tyrosine byproduct homogentisic acid accumulates in the blood, and is deposited in collagenous tissues. Eventually, it polymerises to form a black 'goo' that remains within the tissue, and destroys it.

'Homogentisic acid is akin to sugar, with a hydrophobic and a hydrophilic part,' she says. 'However, its hydrophobic part is much more hydrophobic than that in sugar, and makes up a bigger proportion of the molecule. Its natural place in the body is therefore sitting up against collagen, where it replaces the sugar as the interactions are stronger, and it stays there as it is not particularly soluble.' As the body ages, tissue turnover rate reduces and collagen is replaced less frequently, the acid gradually builds up to a point where its packing density is sufficient to trigger spontaneous polymerisation.

'We have been working with a group at Liverpool University and have made big strides in understanding why it affects tissues the way it does,' she says. 'Doing something about it is another matter entirely! As collagen is naturally hydrophobic, if it were able to get these molecules out of the collagen we think it might spontaneously repair, at least to some extent.

'It's a dreadful disease, and it's emotionally tough, not least because I'm working with a chemist who has it, and had to take early retirement as a result. However, the project is really exciting and I've never experienced anything like the way we all work together – I'm working with groups in London, Liverpool, the US and France, and there's no competitive edge, we all just want to find a cure.'

HARDENED ARTERIES

Another important disease area she's working on is cardiovascular disease, which follows on from her long-standing work on bone, after a chance meeting with Addenbrookes British Heart Foundation fellow Cathy Shanahan – now a professor at Kings College London – at a conference. 'She asked me if I realised the mineral that forms inside blood vessels when they harden is pathologically the same as bone,' Melinda says. 'While I did, I hadn't much thought about it as the general view was that it was a random flushing out of calcium phosphate from blood serum.

'But Cathy was fairly sure it formed in a controlled way in response to injury or infection. She gave us some samples of calcified human arteries that were so furred up there was no blood flow, and when we ran solid state NMR spectra on them we saw small amounts of collagen plus massive sugar signals – exactly the same thing we had seen in bone – and other smaller signals from citrate and protein, again very similar to bone. This gives a very strong indication that it's formed the same controlled process that happens in bone.'

This is perhaps unsurprising, she suggests, as biology tends not to create wholly new processes unless it really needs to. The two groups are now collaborating, with a grant from the British Heart Foundation, to look more closely at the way blood vessels calcify. Arteries, essentially, have three layers, and calcification of the medial layer – the centre of the tissue – is characteristic of people with diabetes and renal failure, as well as general ageing. In the intimal layer, the internal surface of the artery, calcification occurs around lipid deposits, but these deposits might be present for 20 years without calcification, before it suddenly hardens.

'We looked at what triggers the two processes, and it turns out to be the sugar!' Melinda says. 'Over time, both the intimal and medial layers collect sugar, and diabetic and renal failure patients collect sugar faster than others, and this seems to be the prerequisite for mineralization to start – it's the same in both layers.

'The presence of lipids disrupts the collagen layers, allowing the sugars to enter. It's still early days, but our initial results are really interesting. It's all been possible because of the improvements to solid state NMR – there's a folklore around that it's only possible to carry out experiments on enriched, synthesised proteins, but nowadays cell cultures are good enough that you can work with real tissues, which gives a much better picture of what's really going on.'

Left to right: Wendy Lau, Karin Muller, Jeremy Skepper (one of her collaborators), Rakesh Rajan, Matt Mason (another collaborator), Melinda, Dave Reid, Cristina Elliott-Garcia, Erika Davies, Wing Ying Chow, Dominique Bihan (collaborator)

Photos: Nathan Pitt

Melinda Duer

CV

Born: Hertfordshire; grew up in Australia and Cornwall

Status: Husband Neil Piercy works in IT, designing mobile base stations

Education: Studied chemistry as an undergraduate here at Cambridge, followed by a PhD in theoretical inorganic chemistry with Malcolm Gerloch.

Career: After her PhD, she moved into solid state NMR, at first as a temporary lecturer, and is still here, having been promoted to reader in 2011.

Interests: She competes in triathlon and does a lot of cycling and mountain biking and is currently planning a cycling trip across Bhutan. She also enjoys painting.

Did you know? She wrote her first NMR book in an old long house in the middle of Bodmin Moor, Cornwall. The house had no electricity, no running water and was a 45 min walk from the nearest road. She had a horse for transport, so she could get her computer batteries charged up each day at the local pub.

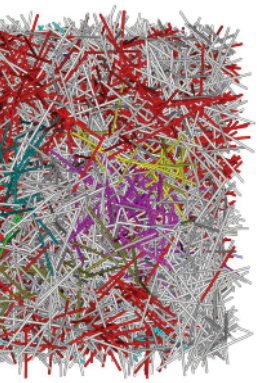
Less is more in calculations

Modelling molecules requires making simplifications.Mark Miller is looking at complex systems by reducing the number of variables

Many molecules and materials are far too complicated for computational chemists to create models that include every single possible parameter. That's why Mark Miller's calculations look at complex systems using simple models, enabling him to see the bigger picture without getting overwhelmed by the details. If the system is simplified correctly, the results are surprisingly true to life.

'The approach is pretty coarse grained,' he explains. 'I always start off from a description that throws away a lot of detail. For example, I've done some work on proteins, and even if you consider each amino acid as a single "blob" representing all of its atoms, simulations can still give interesting information.'

The protein folding problem is a good example. 'To understand the biological function of a particular protein, it is very useful to be able to predict the precise structure that a particular sequence of amino acids will fold into, but another intriguing question is how is a protein able to fold up in the first place? What is the difference between a sequence that can fold, and one that can't? And, given all the things that might go wrong, why does folding ever work? You can ask questions like this without having to go into atomistic detail, and you probably get a better generic understanding of it by throwing away some of the detail.'



He's recently looked at how the folding and binding of proteins to a substrate can be influenced by disordered polymer chains around the binding site. Not all proteins are fully structured in solution, often gaining better defined structure only when they bind to their target substrate. But what influence do other nearby components have on the process?

'The model we used was almost shockingly simple,' he says. 'The model protein was made up of beads – each representing an amino acid – on the sites of a cubic lattice, with the chain between them remaining fully flexible but restricted to joining adjacent sites. The disordered polymer additions were treated as chains of occupied sites on the lattice, without any energetic interactions – producing a purely entropic effect where the chains get in the way of the folding and binding.

'We found that if the model protein tries to fold in solution and then bind, it has a lot more trouble getting past any steric hindrance that's localised around its binding partner, whereas if it folds cooperatively as it binds with the substrate, the free energy barrier lower. We might be able to use this effect to control the rate of binding and unbinding in artificial self-assembling systems.'

Such extremely coarse-grained models do have their disadvantages – notably the inability to make quantitative predictions about a particular protein, as the models are protein-like polymers with the key physical ingredients of a protein, rather than any specific protein. 'You can, however, predict qualitative effects and their relative magnitude, which indicates whether something is likely to work or not,' he says.

'It's also possible to refine models to be a little more detailed. For example, you can take the model off the lattice and represent the protein as a tube, where the thickness captures the volume of the backbone and sidegroups and the stiffness the backbone's flexibility. The other essential ingredient is hydrogen bonds. With these basic properties, you can already get alpha helices, beta sheets and other features of folded proteins. It's still very coarse grained, but it's a matter of choosing the right level of detail for the question you want answering.'

He's applying his previous experience in colloids, where it's rarely necessary to look at molecules individually, and throwing away a lot of detail can still leave you with a realistic description of what's going on. The simplest colloids to model are just hard spheres, like billiard balls, that neither attract nor repel each other but cannot overlap. Amazingly, even such simple particles have a first-order phase transition from a crystal to a liquid. However, if you dissolve polymers in a suspension of hard spheres, the polymers effectively push the spheres together. The spheres then appear to attract each other. The strength of this attraction can be controlled by altering the concentration of the polymer, and the range of the attraction by changing the polymer size.

Photo: Nathan Pitt

The image on the left is a snapshot of Mark's carbon nanotube model, with the biggest connected clusters coloured in. The red cluster spans the entire system, and would conduct electricity

'Unlike atoms, you can influence the forces between colloids, enabling particles and materials with specific properties to be devised, such as lightweight materials that conduct electricity,' he says. 'Electricity could be conducted by a low-density network of long, thin carbon nanotubes. We looked at how this network might form computationally and how, by adding other components to the suspension the nanotubes were encouraged to join up. We threw away as much detail as possible – the nanotubes became rigid cylindrical objects, and hard spheres induced the attraction – and studied how the two differently shaped objects in the mixture interacted, and how the overall structure was affected.'

The whole idea, he says, is to distil things as far as possible to their essence, and then work out which physical ingredients are important, and which can safely be ignored without losing the phenomenon you are interested in. 'Starting off with a very simple model is a good idea, even if it is not directly applicable to the ultimate problem' he says. 'You often find that "simple" models don't behave as simply as you thought, but once you understand what's going on at a basic level you can add more detail and complexity in an intelligent way.'

CV Mark Miller

Born: Gibraltar, to Maltese parents. Moved to the UK at the age of 3, and grew up in Leicestershire.

Education: Natural sciences at Cambridge, followed by a PhD with David Wales here in the department.

Career: He moved to the University of Washington in Seattle, US for a postdoc with Bill Reinhardt, and then Amsterdam to work with Daan Frenkel. He then returned here as a junior research fellow at Churchill, and then an EPSRC advanced fellowship. He's still at Churchill, as director of studies for chemistry.

Interests: Classical music – he sings and plays piano and organ, but is doing more conducting these days. He recently conducted a symphony for the first time – Tchaikovsky's 2nd with The Orchestra on the Hill.

Did you know? Not content with being *Chem@Cam*'s Autumn 2010 cover star, Mark has been pictured in a rather different publication, too – *Style* magazine. He was posing with a Marilyn Monroe impersonator at Churchill's 50th anniversary ball, and the snap was taken by Gavin Bateman, husband of our receptionist Sheila. 'I only found out about it when a colleague spotted it in the magazine on a plane!' he says. Sadly, this time he was relegated from the cover to the back page – by Kylie Minogue…

A spider for all molecules...

ChemSpider
The free chemical database

A new extension to the IDBS's E-WorkBook – the electronic lab notebook (ELN) we use here in the department – makes it easy for chemists to send novel structures to the ChemSpider database.

ChemSpider, which can be found at www.chemspider.com and is owned by the Royal Society of Chemistry, is a free chemical structure database on the internet that provides fast text and structure search access to more than 26 million structures from hundreds of data sources.

Aileen Day at the RSC (who also happens to be married to Graeme Day here in chemistry) has developed a plug-in that allows a user to click on a structure or reaction in the ELN that they wish to make public, and it will automatically send the structures to ChemSpider. The structure can then be found by chemists from all over the world who search the database – a simple and effective way to publicise work.

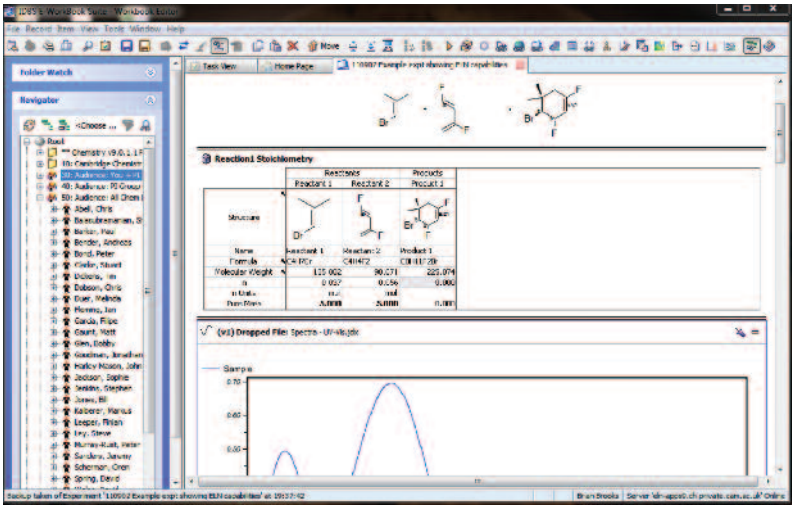
The new plug-in was developed in collaboration with IDBS, and with additional guidance from Brian Brooks, Tim Dickens, Bobby Glen and Steve Ley in the department.

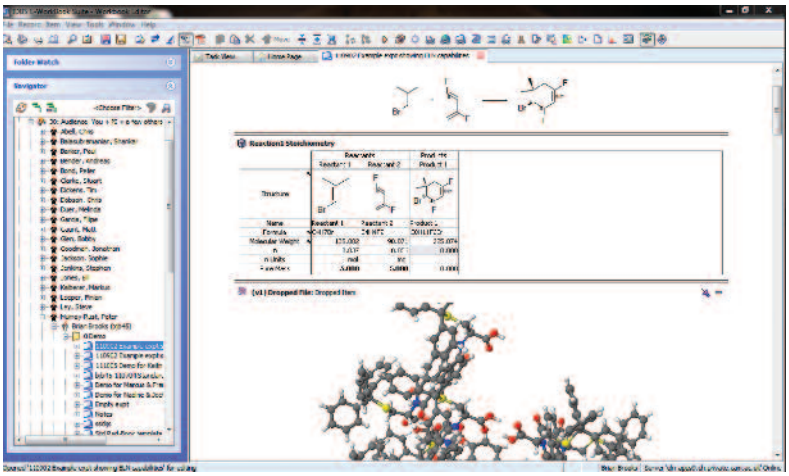
At present, only the chemical structure is passed to ChemSpider. Future versions will allow entire chemical reaction schemess to be published, plus supporting data such as spectra and reaction yields.

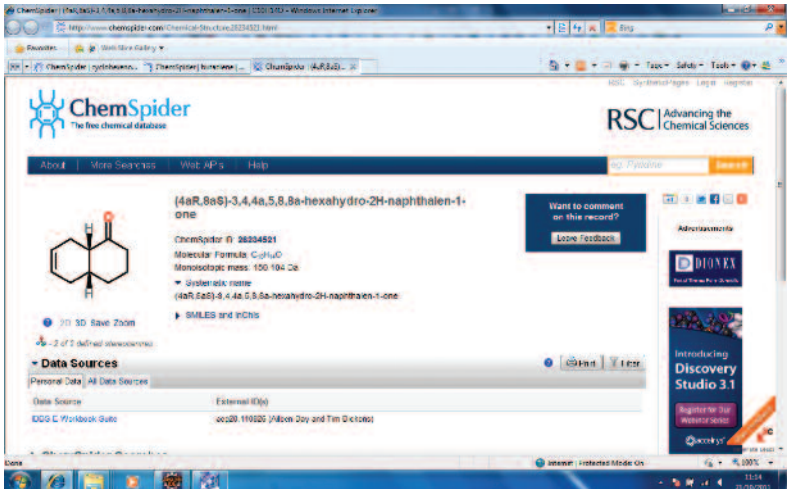
The extension also allows searches of ChemSpider to be launched easily from within the ELN. Any structure in the ELN can be used as the search criteria, and the results are returned in an internet browser.

Bobby Glen thinks the plug-in will prove very useful. 'Much of the chemistry that is carried out is lost – it is simply not published and languishes in forgotten lab notebooks,' he says. 'Capturing novel molecules soon after synthesis on a searchable database like ChemSpider is now an effortless process directly from the ELN, which will greatly encourage sharing of compounds, synthetic methods and all the associated data. It's instant messaging for chemists.'

It has also been welcomed by Antony Williams, vice president of strategic development at the RSC. 'The ability to now publish compound data from the IDBS ELN directly to ChemSpider offers a path to direct exposure of novel chemistry as well as the chemist doing the work,' he says. 'This public compound registration capability is the first move towards ultimately exposing synthetic methods and associated experimental data to the community. Our vision is coming to fruition through this collaboration.'







Screenshots of a reaction in the ELN and (bottom) how a molecule appears on ChemSpider

All existing ELN users will be emailed with instructions of how to obtain and use the extension.

Important note: *always confirm with your PI if you want to publish a molecule on ChemSpider before it has been published in a journal!*

Memories of 1930s Cambridge

At 93, Peter Plesch must be one of our oldest readers. He studied here in the late 1930s, and these are some of his memories of that time

One great advantage of the British scientific tradition is that the supervision and teaching in the laboratories has always been in the hands of at least moderately senior members of the staff, in contrast to the custom prevailing on the Continent, where what is there regarded as a tiresome chore is mostly left to junior. Thus it was that I came into contact with some of the most distinguished chemists of the day.

Amongst them was a saturnine Welshman, A.E. Moelwyn-Hughes, who became influential through his rigorous, somewhat forbidding, textbooks on various aspects of physical chemistry. He created the maxim: 'The true physical chemist blows his own [glass] apparatus and solves his own equations', a guideline which I attempted to follow.

Another of the notable physical chemists was G.B.B.M. Sutherland. He was suspected of being co-author of a famous book of the 1930s, 'The Nightclimbers of Cambridge'. This was an account of the climbing routes across the roofs of the colleges and other buildings, well illustrated with spectacular photographs.

Since my copy went astray and the book is very rare now, I cannot confirm that it was there that I saw a photograph of Sutherland, dressed in a ballet skirt, making a fifth figure on one of the unoccupied pedestals of the balustrade on the Wren Library at Trinity. He was one of the founders of the science of infra-red spectroscopy, a most distinguished scientist, became Sir Gordon Sutherland, and Master of Emmanuel College. I met him again, decades later, as a fellow collector of Chinese antiquities.

The romantic streak in me manifests itself through my attraction to the mysterious, the un-understood, and consequently that which is suspect to the establishment. In the 1930s, colloid science still had such a stigma and that is why it attracted me. Wilhelm Ostwald, one of its founders, called it the world of neglected dimensions. It was a great credit to the University of Cambridge that it accepted a grant towards the foundation of a department of colloid science, despite opposition from some conventional and traditional members of the faculty, especially the organic chemists.

The first head of this department was Eric Rideal, a man of wide scientific experience, full of ideas, open-minded and enterprising. By the middle of the decade, he had assembled an unusually talented crew – even by Cambridge standards – which included many refugees from Europe. I decided I would much prefer to spend the 'long vacation term', a period of six weeks in midsummer, working as a volunteer research assistant in that laboratory, rather than take the very dull course in organic analysis which was recommended for the weaker students like myself. I obtained the requisite permission from my tutor to come up for the long vacation term, and as an historian he was not too concerned about just what chemistry I would be doing.

I then approached Jack Schulman in the colloid science department, asking whether he could find me some research job as a volunteer in his group during the long vacation term. He appealed to me, because of his imaginative lecturing and his debonair appearance, not unlike Clark Gable, and I often met him at parties and the theatre, usually with a pretty girl by his side. His special appeal for me was that he seemed to be the only don who took me seriously, and who showed some interest in me as a person.

"I chose to spend the summer as a volunteer research assistant in colloid science rather than take a very dull organic analysis course"

He agreed to take me on as a dogsbody, which meant that I would try out for him the feasibility of an idea which he had hatched. This was a new experimental method for determining the isoelectric point of proteins by means of the Siedentopf-Szigmondy ultramicroscope. This project appealed to me enormously because there was a bit of mathematical theory to develop, and some apparatus to construct from the proverbial 'drawing on the back of an envelope'.

When I had developed the theory, which was just within the scope of the physics and chemistry that I'd done, but needed some ingenuity, I came to doing a model calculation. The result, however often I checked it, differed from the expected result by a factor of 300. This showed that my error was not in powers of 10 (although the square root of 100,000 was a possibility), and I eventually took the problem to Schulman. 'Ah, those confounded electrical units,' he said. 'We had better discuss it over tea.' So he took me to the Blue Boar and there explained a very difficult point relating to the units to be used in calculations involving electrical quantities.

I took the opportunity to present to him a theory which I had developed concerning the effect that milk has in taking the astringency from tea. 'The tannin is removed by dissolving in the fat globules of the milk,' I said: we had just had a lecture on emulsions, of which milk is a convenient example. 'Wrong,' he said. 'Tannin is insoluble in fats; it is removed by combining with the proteins in the milk, as in the tanning of hides. Next time you produce a theory, make sure first that you have the facts right,' – advice which I have cherished ever since. 'But keep on trying,' he added.

As far as he was concerned, he was content to have found the right kind of self-propelled and resourceful chap to tackle a new project, and as far as I was concerned I was deliriously happy at being accepted into the most exciting laboratory in Cambridge, with a small, window-less storeroom as my very own lab, and a really challenging problem. In addition, I had an excuse, very respectable in my father's eyes, for not going home to my parents' flat in dull London, but could continue to ride when it pleased me, spend evenings on the river, and make the most of the foreign language students (mostly female) who swarmed at that time of year.

The academic year of 1938–39, my third year, was in many ways the high point of my life for many years to come. Because of my wide acquaintance and social versatility, I became the social/society/gossip correspondent of the undergraduate weekly Varsity, and received free tickets to all the major balls. This, of course, was neither good for my standing with my academic superiors, nor conducive to academic progress.

There were many lessons to be learnt. For example, I was pulled up sharply to realise that my impersonation of an English upper class twit was far from perfect when the editor, with a pungent remark, corrected 'scarlet' to 'pink' in my account of the men's attire at a hunt ball. Although I had taken on the role of a champagne Charlie and socialite, I never actually neglected my work, and in particular I never failed to attend the laboratory classes: I was far too interested in chemistry to do that.

Maybe as a result of this genuine and unconcealed interest, at the end of that year in the summer of 1939 something wonderful and quite unexpected happened. I should have taken an end-of-year examination and, provided that I got even a minimum mark, I would have been awarded my BA because the main requirement was that one should have been in residence for nine terms, have kept out of serious trouble and not been rusticated, and the minimum required academic performance was meagre. However, having been much occupied with extracurricular interests, my performance in any exam would have been unremarkable at best. To my immense

surprise and astonishment my tutor, Patrick Duff, told me that if I applied for it in the correct manner he would recommend that I be awarded a certificate of diligent study, which would excuse me from all examinations and yet permit me to take my BA that summer. This really was the cherry on the cake.

Of course I wondered whence this happy event had originated, and concluded that there might be a simple explanation. The tutors were very experienced, and could recognise when a student was genuinely interested in his subject. This I had shown by my researching as a volunteer during the summer of 1938, and applying to do the same again in 1939.

Further, in the various practical classes, where one was directly under the eye of members of staff, I had made up for a below-average manual dexterity by an above-average degree of ingenuity. But what I guessed might have weighed most heavily in my favour was a radical innovation which I had introduced at the end of my third year.

By the end of my second year, I had realised that despite the system of supervisors and directors of study, many students, like myself, had found the college system of supervisors unsatisfactory in that they could not readily get from within their college all the help that was needed. Therefore, when I became joint vice president of the student chemical society, my fellow vice president, Bernhard Jandorf, and I arranged that on certain afternoons during the summer term before the final examinations, some senior research students, research fellows and young members of the chemistry staff who saw merit in my scheme would make themselves available in the chemistry library to answer questions, to explain, to help with all sorts of chemical problems. This scheme, an original attempt at self-help, was as startling to the senior members of staff as it was welcome to my fellow students.

The summer of 1939 I spent researching in the colloid science department. I had become a familiar figure there, was classed among the research students and, of course, I then understood far more of what was being discussed over tea than during my first spell there. I had been told to have a look at some new aspects of Langmuir films, as usual with minimum instructions, being left to work things out for myself and to find apparatus where I could. The Langmuir films on which I was working are monomolecular films formed on clean water surfaces by compounds that will not dissolve in water, but which will anchor themselves on a water surface. They were discovered by an American of great ingenuity and versatility, Irving Langmuir, and we had a lecture course about them. In most other universities, they were not even mentioned in the standard courses. In recent years they have become of very great interest, and the equipment now used for their study is far removed from the Pyrex pie-dish, Meccano bits and – literally – wax and wire from which I built my instruments.

Despite Rideal's involvement with war-related committees and consulting, whenever he was in Cambridge he maintained his practice of making the round of the lab at least once a day. He knew exactly what was going on, asked well-aimed questions, and threw out volleys of ideas. I liked that style, and applied what I had learnt from him when I myself eventually came to direct a research group.

Peter Plesch is emeritus professor of physical chemistry at Keele University

continued from page 2

the whole treatment of HIV. Before then, very few people in Africa could afford the treatment. Now, according to the World Health Organization, there are 7 million patients on HIV medications, and 99% of these were made in India. It gives me tremendous satisfaction that 1.5 million of those are on Cipla medication.

Today, as well as AIDS drugs we are the leading supplier of antimalarial drugs in Africa, also at very low and affordable prices, and I take a personal interested in many other neglected diseases like schistosomiasis and leishmaniasis, and supply drugs for these also.

Success does not make a company great – what really matters is its contribution towards making life better for everyone. I've held by this all my life. I do not break laws – I live by the laws of the land, whatever the multinationals may say – we've never been litigated against in this sort of way. In Africa, I abide by African laws; in the US by American laws; in India by Indian laws. Why should I apply American laws to India? I don't see this as rational.

The whole scenario has now changed in India – it is a leading exporter of medicines, and 55% of Cipla's turnover is now exported, including to developed markets like Europe and the US, as well as Africa. But with all the changes the country has undergone since 1960, India is today a major force to be reckoned with, particularly in the low-cost generic markets of the world.

You have been very generous to Cambridge and the chemistry department – why do you think it's important to remember those who shaped you?

My entire career I owe to my education, and to two people in particular – Lord Todd, and Lucan Pratt, who was the senior tutor at Christ's when I joined in 1954, and took me under his wing. He was a loveable and likeable character.

My future career was moulded by my association with Christ's college, and in particular with Lord Todd. God has been good to me, and I thought I have to give back to the people and to the place that helped me when I was nobody – I have to repay the kindness and generosity that were shown to me during my education.

My father passed away in 1972, and I always used Lord Todd as a mentor – we used to meet as often as possible, and as a friend even when he had given up work. I am a great believer that I want to do things in my lifetime, not leave a legacy after I'm dead and gone – not that I won't do that! So it was important to give back to both Christ's and the chemistry department, where there is the Todd-Hamied seminar room, and now the Todd-Hamied laboratory which houses Clare Grey's group.

The other thing that I have done is set up a Cambridge Hamied fellowship. This is more of a partnership than a fellowship, and the idea is that three Cambridge professors come to India every year to give talks at various institutions, and three Indian academics visit India to update their knowledge. This has been going on for a couple of years now and has been very successful – it's like a Cambridge–India exchange programme. I want to extend it, and make it on a permanent basis if possible.

I prefer this to just sponsoring undergraduates to come and study in Cambridge. They come here, study for three or four years, and then most of them don't want to go back to India. That doesn't suit my purpose – I want them to come back! And then with professors from Cambridge coming to India and lecturing to two or three thousand students, the awareness of Cambridge spreads. That's what I wanted.

Double trouble!

As regular readers will know, there are few things *Chem@Cam* likes better than a nice baby photo, unless it's two nice baby photos. So this issue, we're in luck! First up, we have Rosa Robert and her young son Ian. Rosa's a postdoc in Clare Grey's group, and Ian was born at the end of April, weighing in at 3.05kg (about 6lb 11oz in UK baby-units). He's the first child for Rosa, who's originally from Spain, and her German husband Jörg Tschierschke, a senior project manager at Credit Suisse. 'Ian's very smiley and chatty, and he says "dadada" all the time!' Rosa says. 'And he loves playing the drums at nursery.'

Baby number two has already featured in *Chem@Cam* – albeit in bump form. Paddy Rutterford, on the right, was born in August to Clare, who works in reception and is also Sophie Jackson's secretary, and her husband Simon. He was two weeks overdue, and weighed in at an impressive 8lb 11oz. He's named after Clare's dad – who's chuffed to bits with his first grandson!

No, it's not an escaped photo from the alumni pages – it's seven members of Shankar Balasubramanian's group, who grew moustaches for 'Movember', when otherwise face-fur-free men grow hairy adornments for charity. They celebrated raising £162 for cancer charities – and being able to use their razors again – by pretending to be chemists from the 1920s, when moustaches were all the rage, and their colleague Liang Wu committed it to sepia-tinted photographic posterity. From the left, Pierre Murat, And Lewis, Marco Di Antonio, Mike Booth, Gordon McInroy, Mike Gormally and Chris Lowe. When asked whether they'd go for a Mexican look next year, Chris said, 'If I grow another moustache, my family will disown me!' We'll take that as a yes, then...

Photo: Nathan Pitt

Anne Railton retired in September after a decade in the department, and took some persuading to let us hold a leaving lunch. But persuaded she was, and she was surrounded by gifts to wish her well

A mountain of coincidences...

Another sort of photo we love printing is department members in interesting places – and Alan Battersby's always good for a lovely shot in the mountains. But there's a little more of a story to this one! He was hiking from Mayrhofen at the head of the Zillertal valley in Austria, where several other valleys also join so it's surrounded by wonderful mountains in all directions, and this photo was taken on a climb up to one of the ridges.

'The ridge I am on here is at around 4000–5000ft.' Spookily, though, in the middle of the mountains Alan got a great reminder of what a small world it is. 'I go with a cooperative holiday programme and the group that assembles is random – I generally know nobody at the outset.

'But on the first day, a cheery female hiker said to me I had taught her chemistry in her second year at Cambridge. My surprise got even greater when on the second day, a man told me I'd taught him, too. The two students weren't connected at all, either – they were in different years. I was really bowled over thinking of the chances of the three of us randomly meeting like this!'

And finally, one that definitely falls into the 'rather them than me' category. Eagle-eyed photographer Nathan Pitt spotted workmen hanging precariously from a cradle on the outside of the building. One might have imagined they were cleaning the windows, but no – they were engaged in the vital task of fixing dodgy windowsills to prevent bits falling on unsuspecting folks down below!

Last issue's solutions

ChemDoku

Correct solutions came from Richard Brown, Godfrey Chinchen, Karl Railton-Woodcock, John Wilkins, Diana Sandford, Mark Alderton, Tim O'Donoghue, Morgan Morgan, Annette Quartly, Ian Fletcher, John Turnbull, Helen Stokes, Jim Dunn and A.J. Wilkinson.

No-one came up with the correct answer to the 'what's the link?' question. However, Diana Sandford suggested that No MEN means a name, and none of the symbols are named after places or people, and even mercury, whose symbol Hg comes from the Greek 'hydrargyrum' meaning 'silver water' which they used as it described the way mercury behaved. Frankly, that's a much better suggestion than the real answer, which was simply that none of the elements – Ni, Zn, Co, As, S, Au, P, Ag and Hg, end in the letters M, E or N. There are surprisingly few of these!

Chem@Cam's shiny new non-Cambridge office is in an eyrie with railings opening onto the living room below, which gave her a novel technique for determining the winner – write all the names on pieces of paper, drop them over the side, and see which landed first. Air currents won out over Galileo and they didn't all land together (fortunately!) – and the first to land was the entry from Morgan Morgan.

Elementary cubes

This one proved nice and tricky. Puzzle setter Graham Quartly says 'Haddock' in the question was a subtle clue that three of the hidden words related to oceanography!

His answer is that the top die should have O, Re and At, giving BOAtS, BReAtH and SHORe, and the lower P, Ra and W giving PRaISe, WISP and WRaSSe.

Correct answers came from Karl Railton-Woodcock, Richard Brown, Godfrey Chinchen (with the alternative lower die InCISe, RaISIn and CRaSeS – the plural of crasis), Annette Quartly (with the alternative upper die of BHArAl, BOArS and SHOAl – disagreement in the Quartly camp!), and Ian Fletcher who got both of the two upper die possibilities, plus RaISIn, SeRaCS and InCISe for the lower – the same as Godfrey but with a spot of anagram going on.

John Wilkins suggested P, N and O for the lower die to give POSSe, NOISe and SNIP (or PINS), but that doesn't quite work as SNIP/PINS can't be read consecutively around the die. Or at least *Chem@Cam*'s addled brain can't make it work...

Well done to all valiant solvers, and the first scrap of paper to land came from Karl Railton-Woodcock, so the prize is Australia-bound. We're so international here at *Chem@Cam*!

This issue's puzzles

Literary chemistry

Here's another chemistry-to-arts puzzle from David Wilson. Authors of classic works can be linked to chemistry in that the initial(s) of one of their works are also the symbols of a chemical element. For example, a halogen is linked to Charles Dickens by the symbol Br, being the initials of the title of one of his works, namely, Barnaby Rudge. Can you link the following, providing both symbol and title?

A halogen to Evelyn Waugh
A different halogen to Mary Shelley
Yet another halogen to Sir Walter Scott
An alkali metal to Jane Austen
A different alkali metal to Robert Louis Stevenson
A radioactive element to Percy Bysshe Shelley
A semiconductor to Charles Dickens
A precious metal to Anne Bronte
A transition metal to Charlotte Bronte
A rare earth to George Eliot

ChemDoku

		Se				Xe		
	Ge		Xe		He		Ne	
He				Te				Fe
	Xe				Te		Se	
		Ne		Be		Te		
	Fe		Ge				Be	
Te				Fe				He
	Se		Te		Ne		Ge	
		Be				Ne		

£20 prizes are on offer for each puzzle. Send entries by email to jsh49@cam.ac.uk or by snail mail to Chem@Cam, Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge, CB2 1EW

Eee bah gum, it's ChemDoku… Nowt complex this time – simply the nine non-rare-earth elements whose symbols have 'E' as the second letter. Only 8 appear in the diagram so you need to work out what's missing!

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Thanks to the generosity of the department's Corporate Associates, we have been able to benefit the education and environment for students and staff. For example, the Associates make significant contributions to the library for journal subscriptions. Moreover, they provide exam prizes, faculty teaching awards and summer studentships, and have recently funded the refurbishment of a state-of-the-art meeting room with teleconferencing and display facilities.

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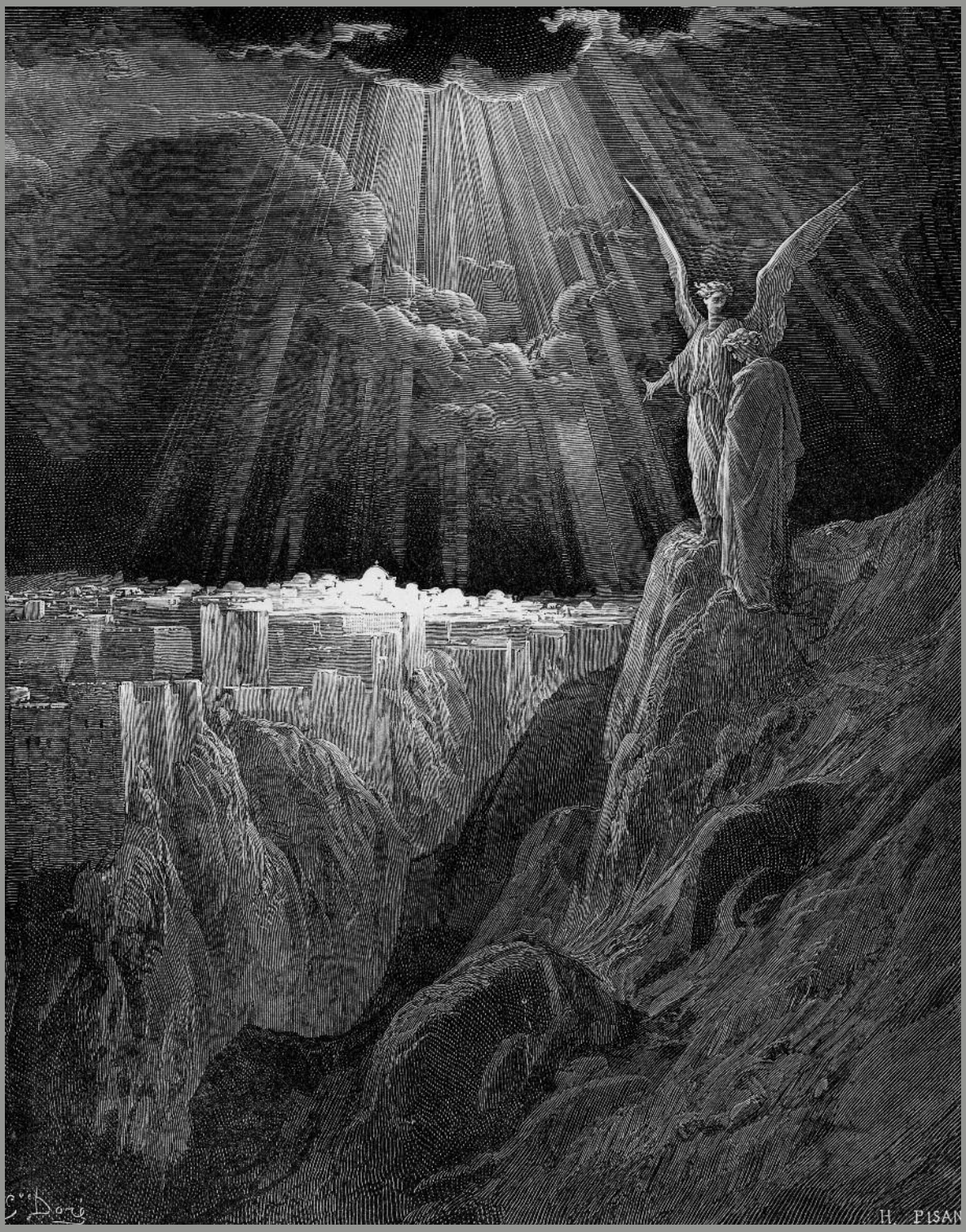

And lo! After many years of decontamination and refurbishment, we've finally reached the promised land: the new Todd-Hamied laboratory!

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Chem@Cam is written, edited and produced by Sarah Houlton

Printed by Callimedia, Colchester