chem cam

Chemistry at Cambridge Newsletter

Autumn 2010

The dynamics of **protein folding**
Biotech and drug discovery

Biomimetic catalysts for solar fuel
Remembering **Dudley and Eric**

Nick Terrett went from a Cambridge chemistry PhD into the pharma industry, and then into the biotech world He tells Sarah Houlton why he thinks the biotech sector is so important

How did your Cambridge chemistry PhD take you into biotech?

I joined Pfizer in the early 1980s after I completed my PhD, working as a medicinal chemist in cardiovascular drug discovery, and then moved into what became the Viagra programme. That led to a role in the new opportunities research group, a rapid response team to pick up on new targets and other new ideas. This mutated into the chemistry team that supported the high-throughput screening operations in Sandwich, and we got into combinatorial chemistry – high speed chemistry and purification, parallel synthesis – which has a resonance with what I do now.

After the Warner-Lambert merger, I became involved with global integration of compound collections and databases, and although this was interesting it was more about logistics and policy than about science. I wanted to get closer to drug discovery again, and in 2003 I moved to Pfizer's site in Cambridge, Massachusetts to run the chemistry group there. I had a very exciting couple of years working with a talented group of people doing early stage hit-to-lead discovery, with our client groups spread across all the Pfizer research sites.

A couple of years later, the opportunity arose for me to move into biotech – like Cambridge in the UK, Cambridge MA is a real hub for biotech companies. I thought Ensemble sounded really interesting – it was a start-up based on a chemical technology doing drug discovery, which was exactly what I wanted to do. So I joined in early 2006 as chief scientific officer, and I'm still here. The idea behind the company came out of David Liu's work on DNA-programmed synthesis at Harvard, where DNA is used to drive the specificity of chemical synthesis. It has the potential to be used in many different ways, and we're focusing on making libraries of macrocycles to address tough targets in drug discovery.

Why is the biotech sector so important?

Where do I start? One answer is certainly to do things that pharma companies cannot do. Sometimes, they are established because someone, often an academic, has a really good idea and wants to try it out. But they need sufficient resources if they are going to take that gamble, and the best way can be to get the funding to set up a company to investigate the idea. It might be a specific drug discovery target, or perhaps a particular technology as with Ensemble, but either way it's important for the company to differentiate itself from every other company that is out there.

There are many things we could have done with the DNA programmed chemistry, but we focused in on making libraries of macrocycles as this was something few other people were doing. There was this great idea of a way to make a lot of compounds very quickly using DNA to drive the synthesis, and we now have more than a million compounds in our library.

I guess biotech is a way in which 'out there' ideas can be realised.

I think that's fair. Of course it doesn't mean that every idea is going to be resourced and prosecuted, but I think the biotech sector represents a group of people who can respond quickly to an idea or an initiative, and get funding that allows them to investigate the potential of the idea rapidly. There are different pressures and demands on big pharma, and that's why they are often reluctant to put resources into the sort of speculative approaches that biotech thrives on. Within the academic environment, the resources are unlikely to be there to fund the idea, and in a big pharma company it might get lost in the 'noise'. It can sometimes be difficult to get buy-in from a big organisation to do something that's a bit more speculative, but if you have a small group of people who are well funded by a venture capital company, they can be single-minded in their dedication to that idea, and demonstrate fairly rapidly whether it has legs or not.

There is, of course, the issue of getting that funding in the first place.

Yes, and that's why we have visionaries in the venture capital companies so they can see the potential! And their long term visions are fairly diverse. At one extreme, a company has an idea and pursues it, and there proves to be so much value in the idea that they quickly get bought up by a big pharma company, for example. Then there are also many biotechs that have been successful across a range of programmes, whether they're working on a target or a technology, and they will put a compound into development and become a self-sustaining drug company themselves. Some will go for a public share offering and others don't – it all depends on the financial environment.

But, in many cases, biotechs are driven by a couple of things – they are driven by the scientific creativity and the motivation of the scientists to be successful. And they are also being driven by the investors wanting a return on their investment. These two are not incompatible, and ideally they will go hand-in-hand, allowing both the scientists to get satisfaction from a successful delivery of the idea, while the investors who have put the money in and taken the risk get a return on their investment. My sense is that, after a bit of an economic dive a year or two ago, things are beginning to pick up and there is more funding out there again.

Of course the world full of biotechs that didn't work out, for whatever reason.

That's correct – drug discovery is a really tough business, and not all ideas are created equal! And things shift in the environment – an idea that looks great one year might not be so great five years later, because other things have come along and superseded it.

So are you optimistic about the future of the biotech sector in general?

Absolutely. I think there are a lot of ideas that could only be pursued through biotech. It comes back to where pharma puts its focus, and where biotech's is. There are things that only small companies will have the dedication to do and pursue. I'm not sure that it's as simple as pharma having a different agenda, or whether the way they think about risk is different, or even that the bureaucracy in a large organisation prevents them from being agile. But it's very clear that pharma is good at doing some things, biotech is good at doing another range of things, and I think we're increasingly seeing a move towards a model where pharma is becoming more and more reliant on small companies to feed their pipelines. I think the biotech sector is offering a really important resource to the pharma industry, and that will grow and even strengthen over the coming years.

Obviously the financial environment does affect the prospects for biotech companies, but pharma has clearly recognised their importance – just look a the number of biotech acquisitions that are being made by big pharma. And I believe biotech is a great place for a chemist starting out their career – there's the opportunity to become knowledgeable across a whole range of areas.

CV Nick Terrett

Born: Plumstead, London

Status: Married to Sheila, an academic publishing copy editor, and they have five children: Ben is 24 and maps oil pipelines for a living; Jack, 22, is studying chemistry in the US and plans to do a PhD; Fay is 20 and studying languages; and twins Alice and Rebecca, 16, are still at high school.

Education: Studied natural science here at Cambridge, with Part II in chemistry. After a couple of years working at Glaxo in Ware, he returned to Cambridge for a PhD with Ian Fleming on organosilicon chemistry.

Career: After his PhD, he returned to pharma and a job at Pfizer in Kent in 1984. He moved to Cambridge in the US with Pfizer in 2003, and then became CSO at Ensemble, also in Cambridge, MA, in 2005.

Interests: Photography and collecting Australian stamps from the 1930s. 'There's one particular penny stamp that I focus on, and I have hundreds of examples!' he says.

Did you know? Taking photos is more than just a hobby – he exhibits and sells his pictures. The last exhibition focused on photos of central France; he's now planning another for 2012 on wildlife. 'I sit in fields and photograph butterflies!'

Literary clarification

Dear Editor
I have been e-mailed by a number of readers (of obviously literary pretensions) of Chem@Cam for clarification of part of my letter published a couple of issues ago; namely, 'the contents sloshed across the bench, striking him in the same place that Hamlet stabbed Polonius... while, initially unbeknownst to him, a small personal tongue of fire was decorating his anatomy'.

Several correspondents maintain that Shakespeare was not anatomically specific as to the location of Polonius' wound. This is quite untrue, albeit only in the stage directions; Polonius was stabbed in the arras.

I trust that this will remove any confusion from the story.
Yours sincerely,
David Brewer
7204 Concession 1, RR2, Puslinch,
Ontario N0B 2J0, Canada

Alpha pressure

Dear Editor
I was interested in your article on the cleaning up of the southern basement. I remember a curious incident in 1949/50 when Alfie Maddock asked a research student to open up a sample of radium powder sealed by Rutherford many years earlier.

It refused to open in the fume hood, so the experienced scientist decided to crack it open in the open laboratory. Success! Immediately followed by disaster!! All the radium powder blew out of the quartz tube and contaminated the whole lab. The alpha-particles had become helium gas, and pressurised the tube so that, when it was cracked, the end fired straight across the lab and the contents were everywhere.

Today at Sellafield there is 100 tons of plutonium oxide powder in sealed containers. They will be pressurised by helium gas from the alpha-particles, and one day they will burst – but not in my lifetime!

Incidentally, the discovery that superfluid helium is solid helium was made at Sellafield in 1964 when making mixed oxide fuel for reactors – PuO_2 and UO_2 fuels of many different ratios.

This discovery also showed that there are, in fact, nine phases of matter – solid, liquid, gas and a total of six other distinct phases.

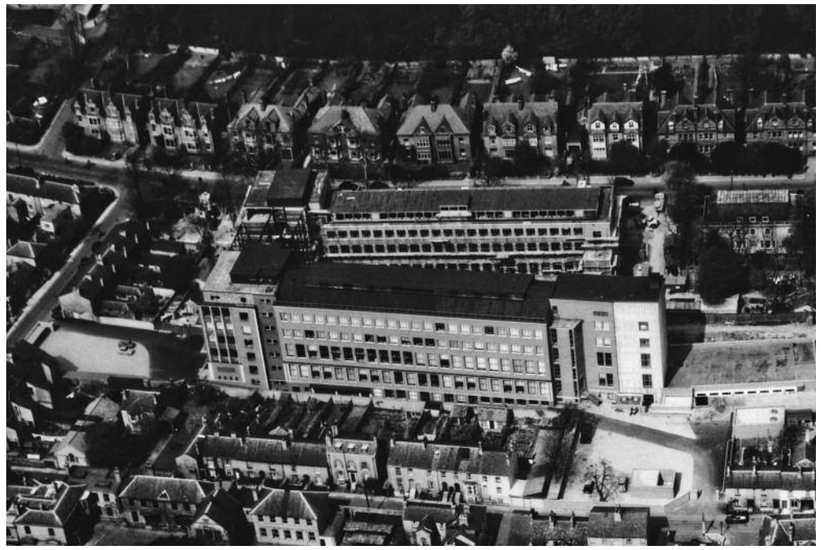
Superfluid helium is actually the simplest of all solids, and I told Alfie Maddock and John Barington about superfluid helium back in the 1970s.
Phil Holland (Queens', 1945)
8 Downfield Lane, Bigrigg, Egremont, Cumbria

eChem@Cam

Our speculative question in the last issue about whether any readers would be interested in receiving Chem@Cam electronically generated a good number of positive responses, so we've decided that we're going to offer readers the option of having their copy of the magazine emailed to them instead of posted.

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 Spring 2011 edition. To ensure you don't get missed, please send this email even if you already indicated you might be interested! And 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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Mark Miller inspects a molecular dynamics simulation of a gel network made from dipolar colloids near the percolation threshold

Photograph:
Nathan Pitt and 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.

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A heartwarming grant

The British Heart Foundation has given a £300k, three-year grant to Melinda Duer and her collaborators, electron microscopist Jeremy Skepper in the physiology department, and Cathy Shanahan, professor of cellular signalling at Kings College London, to study vascular mineralisation.

This process is still poorly understood, but it is clear that it relies on complex chemical interactions between the lipids, proteins and minerals that make up vascular plaques, as well as cellular processes.

'I'm really excited about the project,' Melinda says. 'My work has focused on bone minerals, but I got chatting to Cathy at a symposium in Cambridge, and she said that it seems that the same mineral that is in bone also appears in blood vessels.

'Previously, it was thought that the calcification of blood vessels resulted from a random crashing out of insoluble calcium phosphates, but in fact it's very controlled, like bone formation.'

The aim of the project, Melinda says, is to understand the detailed pathway by which vascular plaques form. 'We want to understand what influences their formation and use this to devise therapeutic strategies,' she says.

Chem online

The department's website has been redesigned and relaunched. The idea was to make it more user-friendly and easier to update, and the new version of the site went live in September.

The site now uses web content management technology. This allows information to be assembled and collated in real-time, based on options that users have selected.

A key feature of the technology is the ability to pull in data automatically from various sources, such as the department phone book, and the colloquia that are listed on the university's Talks@Cam page. This will make it much simpler to keep things up to date.

It also means that numerous staff around the department have direct access to web pages so they can update them, general information for staff and students can be kept current, and news stories can be added to the front page.

We've also made back issues of *Chem@Cam* available on the website, going back to when the magazine was redesigned in Spring 2006.

To check out the new site, go to www.ch.cam.ac.uk

Photo: Nathan Pitt

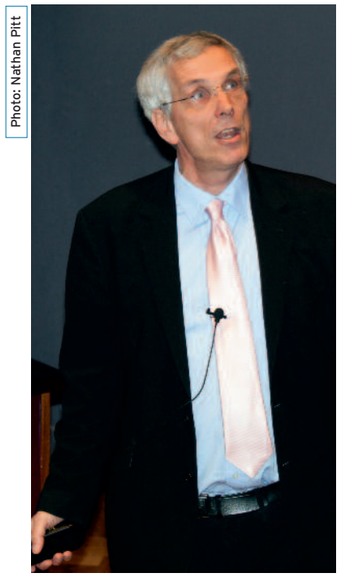

Photo: Caroline Hancox

We've had a couple more distinguished visiting lecturers in the past few months. Above, the 2010 BP Visiting Lecturer, Helmuth Möhwald of the Max Planck Institute of Colloids and Interfaces in Potsdam, who spoke about his work on multifunctional polymer films and coatings. We also hosted a Royal Society of Chemistry Liversidge lecture, with prizewinner David Clary of Oxford (left) speaking about the quantum mechanics of chemical reactions

Sean wins BMCS poster prize for TB

Photo: Caroline Hancox

Sean poses with his prize cheque and his supervisor, Chris Abell

Sean Hudson, a second year PhD student in Chris Abell's group, won the best poster prize at the recent symposium on the medicinal chemistry of tropical diseases organised by the Royal Society of Chemistry's Biological and Medicinal Chemistry section, and held at the London School of Hygiene and Tropical Medicine in November.

'In my project, I'm trying to make new anti-tuberculosis drug candidates, using the fragment-based approach,' Sean says. This involves screening small molecules – smaller than those that would ultimately make a drug – to see if they bind to the target site.

This then gives a starting point for making a molecule that binds more strongly, and also has all the properties needed to make a successful drug.

Tuberculosis is a real global health threat, because of the emergence of strains of *Mycobacterium tuberculosis* – the bacterium that causes the disease – that are highly resistant to current drugs. So there is a huge need for new anti-TB drugs that are active against these strains, and these are likely to work in a completely different way to existing drugs. And, as the greatest need is in the developing world, these new drugs also need to be cheap.

Sean's poster described the work he's done in the first year of his PhD – he's already found fragments that bind to one of the enzymes that occur in the bacterium's genome. He is now looking at elaborating the fragments that bind into something that might make a drug.

'I was surprised and delighted to win the prize, which was a cheque for £100,' Sean says. 'I'm going home to Australia for Christmas, and I plan to spend it on Christmas presents for my family.'

Two more prizes for Steve

Steve Ley's medal collection has increased by two. Above, he's seen being presented with the Tetrahedron Prize at the American Chemical Society's meeting in Boston on August by Diddel Francissen, executive publisher at Elsevier Chemistry. And below, he's being presented with the Paracelsus Prize of the Swiss Chemical Society at their Fall meeting in Zurich by its president, Peter Kündig.

Sphere cash for spin-out

The latest Cambridge chemistry spin-out company, Sphere Fluidics, has gained funding from the Royal Society Enterprise Fund. This is in addition to the seed funding it received from the university's Discovery Fund. It has also signed a research collaboration with a major pharmaceutical company

The company was set up in March and focuses on the picodroplet technology developed by Chris Abell and Wilhelm Huck that allows researchers to carry out large numbers of simultaneous reactions contained within small aqueous droplets just a fraction of a millimetre in size.

When the droplets are merged with others containing, say, a specific chemical reagent, they act as miniature reaction chambers.

The technology has potential uses in many different fields, such as analysing and isolating cell types, biomarket discovery in small volumes, and even molecular labelling and separation using proprietary catalysts and conditions. We hope to bring you more about the company next time.

Jean-Pierre's home award

Cambridge emeritus professor Jean-Pierre Hansen was particularly proud to receive his latest award – it's from the Institut Grand-Ducal in his home country, Luxembourg.

He is the first recipient of the Grand Prix des Sciences, which will be awarded every year to a scientist with a Luxembourg connection – they will either, like Jean-Pierre, be Luxembourgers, or scientists of any nationality who are active within Luxembourg.

This year's prize was awarded for physics; in future years, the discipline will change, rotating through maths, earth sciences, life sciences and chemistry, before returning to physics in 2015.

The award is sponsored by engineering company Paul Wurth, and the ceremony took place at the Luxembourg headquarters of steel company Arcelor-Mittal. He also gave a lecture entitled 'The liquid state of matter: from disorder to complexity'.

He's pictured above receiving the award from Pierre Seck, president of the Institut Grand-Ducal's science section.

Photo: Vic Fischbach

European funding

Cambridge chemists have had some notable successes in recent months in attracting grants from the European Research Council.

John Pyle and David Wales have both received ERC Advanced Investigator grants in excess of €2 million. Another of these grants has been given to Alan Fersht. Although Alan has formally retired as Herchel Smith professor of organic chemistry, he is continuing his research at Addenbrooke's.

Matt Gaunt and Jonathan Nitschke have been awarded ERC Starting Investigator grants, in addition to the EPSRC leadership fellowships they received earlier in the year.

Matt's grant is for his work looking for a new blueprint for chemical synthesis via metal-catalysed C–H bond functionalisation, and Jonathan's to study directed evolution of function within chemical systems, looking at adaptive capsules and polymers.

We've got the power!

Photo: Nathan Pitt

Back in September, the department's mains electricity was switched off for two entire weekends to enable a new electrical transformer and transformer compound to be installed.

While we can live without lights and computers for a couple of days over the weekend – as long as people don't come in to work, of course – there's rather a lot of equipment that doesn't take too kindly to having its electricity turned off for very long, such as NMR machines and freezers.

A bank of generators was installed in the car park so the essentials could remain connected to a power supply. Of course, in a power-hungry environment like the department, the generators could only supply a fraction of the power that's normally needed to keep things running.

This meant that all large equipment such as the air handling units and the fume hoods were out of action both weekends, and for safety reasons the department was out of bounds to everyone other than the contractors, maintenance staff and security. And for an hour at either end of each weekend, there was no power at all to allow the generators to be connected.

The contractors worked overnight to get the job done. And the department now has sufficient electricity capacity to enable it to function successfully for the foreseeable future.

Chemical puzzles to tax the grey matter

A new competition aimed at Year 12 students is being organised by Peter Wothers and former members of the UK Olympiad committee.

The first part – a set of monthly online chemical puzzles – is open to anyone. The best Year 12 students will gain the opportunity to come for a residential chemistry camp here in Cambridge next August.

'There will be new puzzles on the website each month from January,' he says. 'The puzzles aren't exactly cryptic, but they are designed to make people think. They will have to use the internet but the answers can't be found by a simple Google search – each puzzle will require several steps, all of which need researching, to get to the correct answer.'

Five new puzzles will appear each month; answering the first of these will unlock the second puzzle and so on.

'When the fifth puzzle is answered correctly, entrants get to enter their name in the Hall of Fame,' Peter adds.

'Finally, in June, while the Year 12 students are still at school, we'll invite them to sit a 1.5 hour paper full of questions designed to make them think and use their chemistry knowledge. This will help us decide who would benefit most from the Cambridge experience.'

The January competition should be online by the time this issue of *Chem@Cam* hits the doormats – check it out at www.C3L6.org and see if you make the hall of fame!

We are very sad to report the deaths of Dudley Williams and Eric Walters. Dudley was on the academic staff here in the department from 1964 until his retirement in 2004, and carried out pioneering research using NMR and mass spec in chemistry and biology. Eric was an undergraduate here in the 1960s before a successful career in the city, and in recent years made a big impact on the department with his generosity. Both will be sorely missed. Full obituaries are on pp 10–11

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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.

Corporate Associate membership not only provides essential support for the department, but also provides numerous benefits to help members work with us and achieve their business objectives. Members enjoy many benefits through their enhanced partnership with the department, such as:

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Capturing the sun's energy as fuel

Solar panels turn sunlight into electricity, but they're not very efficient. Erwin Reisner is looking at an alternative idea – using sunlight to make fuel


Photo: Nathan Pitt

Photovoltaic solar panels harvest energy from sunlight as electricity, but unless it's going to be used immediately, perhaps to produce domestic hot water, it needs to be stored or transported. But this is very ineffective, and a more efficient solution would be to convert the sun's energy directly into some form of fuel. And this is what Erwin Reisner is trying to do.

'At the moment, we are looking at two possible strategies,' he says. 'One is simply to shine a light on water and try to extract hydrogen from it; the other is to fix carbon dioxide from the air, and reduce it to an energy carrier like carbon monoxide using sunlight. While photovoltaics are becoming more efficient, it will always be favourable to produce a fuel directly, without the intermediate production and storage of electricity.'

While we are now relatively good at harvesting sunlight, he says, what we really lack is the catalysts that are needed to produce the hydrogen or reduce carbon dioxide. 'Although these are simple processes on paper, they are fairly difficult to catalyse,' he says. 'We're looking to nature for inspiration, as enzymes have evolved as very efficient catalysts. However, they are expensive to isolate and purify, and stability is often a major problem. So we're studying the enzymes in detail, and using the information we gain to try and mimic their action by producing small molecules that are able to do comparable chemistry.'

Two catalysts are needed. A photocatalyst is first used to capture the energy from sunlight, and there are already a range of catalysts that can do this, for example based on ruthenium. The second catalyst is more of a challenge, and this is the focus of much of Erwin's work; it uses this energy to carry out the chemical reaction that creates the hydrogen or carbon monoxide fuel. Enzymes known as hydrogenases are a good starting point, as these are nature's catalysts for producing hydrogen from protons; he is also looking at dehydrogenases, which reduce the greenhouse gas CO_2 to a gaseous or liquid fuel.

ENZYME MIMICS

Enzymes are large proteins, and often incorporate at least one metal ion at the heart of the active site. 'We look carefully at these active sites, and try to create chemical catalysts that mimic their shape and activity,' he says. 'At first, people would just look at the amino acids closest to the metal in the first coordination sphere, but we are trying to incorporate more of the protein into our thinking as just looking at the first coordination sphere does not capture sufficient activity. 'We know proton and electron relays as well as substrate tunnels are very important for activity, particularly for our kind of chemistry,' he says. 'We want to incorporate as many of the protein's features as we can, while still creating relatively simple molecules.'

Currently, the strategy is to attach both catalysts to nanoparticles, but the plan is to construct photoelectrochemical fuel cells, where there is a photoanode and a cathode to carry out redox catalysis. He's already had some success, first using an enzyme as the catalyst, and now with a small and simple molecule attached to the nanoparticle instead.

'It works well even in neutral water and at room temperature, although the turnover numbers – the number of times the catalyst will catalyse a reaction before it becomes deactivated – are still fairly modest,' he says. 'But it's early days, and it shows that the principle does work – and the turnover numbers we can get with enzymes are impressive, so we hope to be able to mimic this using improved catalysts as the enzymes are far too delicate to be practical in the real world.

'Previously, almost all of the small molecule catalysts were reported to work only in organic solvents, and were often made of expensive metals like platinum. We solely focus on cheaper, abundant metals and desirable conditions for photocatalysis like pH neutral water. We do still need to extract an electron from somewhere, and eventually we hope it will be possible to get this from the water itself.'

The gases produced in this way also have huge potential as alternative feedstocks in the petrochemicals industry. 'Once you can make hydrogen and carbon monoxide efficiently and inexpensively, they can be used as the raw materials for all sorts of industrial organic chemistry by using existing industrial infrastructure,' he says. 'From a fuel perspective, renewable liquid fuels like methanol and hydrocarbon will become accessible.'

CV Erwin Reisner

Born: Upper Austria, in the foothills of the Alps between Salzburg and Vienna

Status: He met his wife Debora while he was working in Lisbon; she is a psychologist. They have a two-year-old son, Vasco.

Education: He studied chemistry at the University of Vienna, with an Erasmus project in Lisbon. His PhD with Bernhard Keppler on electron-transfer activation of azole-based ruthenium anticancer drugs in Vienna was partly carried out in Lisbon.

Career: After a two-year postdoc with Stephen Lippard at MIT on the biomimetic conversion of methane to methanol, he returned to Europe to work with Fraser Armstrong at Oxford on hydrogen production with enzyme-modified nanoparticles for 20 months, where he was also a college lecturer at St John's. His next move was to the University of Manchester as an EPSRC research fellow for a year, and this October he was appointed as a lecturer here in Cambridge.

Interests: He says his scarce spare time is used for travelling.

Did you know? You can tell Erwin is a child of the Alps – he won his first ski race at the age of 5!

Protein homeostasis: def ining our molecular age

As we age, our cells' quality control system becomes less able to get rid of insoluble proteins. Michele Vendruscolo is trying to find out more

Photos: Nathan Pitt

Proteins fold up to form beautiful structures, but when they fail to do so the result is often malfunction or disease. Michele Vendruscolo is looking at how misfolded proteins aggregate, and how this aggregation might be prevented. 'We have moved more towards understanding not just the folding and misfolding processes of proteins in terms of their structures, which is how we started out, but also the general behaviour of proteins in the cell,' he says. 'So we're now trying to study what they really do in living systems.'

This work is underpinned by an observation they made that the concentrations of proteins within cells are very close to their critical values. 'It's like living on the edge – our proteins are very much on the verge of becoming insoluble,' he says. 'Any stress at the cellular level can tip the balance and make proteins become insoluble and aggregate. This is something that concerns us all as ageing, at the molecular level, is associated with a gradual impairment of our cellular quality control systems that act to prevent aggregation.'

Because proteins are so close to becoming insoluble even under normal circumstances, they have a natural tendency to aggregate. The cell regulates this behaviour via a control system that helps maintain proteins in their soluble state, keeping the cell healthy. 'But as we get older', Michele says, 'we lose this ability as an ailing control system can become overwhelmed'.

Misfolded proteins are implicated in a wide variety of different conditions, including Alzheimer's and Parkinson's diseases, and diabetes. For example, people with Alzheimer's develop plaques of aggregated amyloid-beta peptide within their brains. While it remains unclear whether these plaques are just a symptom, rather than the direct cause, of the disease, it is evident that they are involved in the condition in some way.

'When the amyloid-beta peptide starts aggregating, it creates a stress on the cell, which begins to use a large portion of its resources for getting rid of aggregates,' Michele says. 'This means that it cannot keep up fully w ith its routine tasks, so other proteins escape and start aggregating. The result is an avalanche of effects, which gradually undermine protein homeostasis.'

Injuries to our quality control system are spread out over a lifetime, and as the balance between soluble and insoluble proteins is very robust, the organism is, by and large, capable of taking care of the aggregates. But in the long term – as we age – damage accumulates beyond safe levels. 'We stay close to the edge all our life and eventually, if something else doesn't kill us first, the insoluble proteins will stop our cells working properly and we will die,' he says. This is why the incidence of degenerative disorders such as Alzheimer's grows exponentially with age – close to one-in-five of those aged 75-84 have the condition, whereas over the age of 85, more than 40% are affected.

'Protein solubility is a chemical problem that underlies these medical conditions', Michele explains. 'So by studying the fundamental physico-chemical properties of protein molecules we can do a lot to address these types of disease. We are investigating how to use this concept for developing therapies for misfolding diseases.'

INCREASING SOLUBILITY

Michele is trying to develop drug treatments based on this idea – that by increasing the solubility of proteins it might be possible to delay the onset of misfolding diseases. 'It might become possible to use chemical methods to replace the biological mechanisms in the cell that can't keep up with the demands,' he adds. 'We are aiming to introduce small molecule drugs into the cell that help them maintain proteins in their soluble states.'

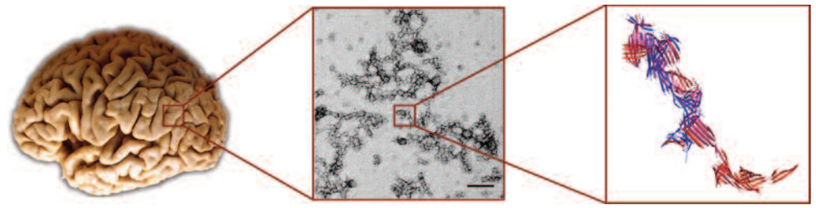
'If these ideas are correct, preventing amyloid-beta aggregation should delay the symptoms of Alzheimer's disease as it reduces the stress on the cell,' he says. 'It's a little like going to the gym – you remain healthy by keeping the cardiovascular system in good condition and reducing weight gain, so the diseases that result from an unfit heart or being overweight can be prevented. Misfolding diseases are clearly far more difficult to treat once our defence mechanisms have already become impaired than preventing them from occurring in the first place! So if it were possible to find some type of compound that can have a general effect on improving the solubility of many different proteins, this might be able to prevent a wide variety of neurodegenerative conditions developing in the first place.'

If it proves possible, then thinking about preventative treatments might be the answer to reducing the burden of such diseases on our society. If the first symptoms appear at 70 or 80, he says, then it might be a good idea to start treatment at the age of 60, or perhaps even earlier. 'We're trying to define the health of the system at the molecular level. The idea is to define a score, based on an analysis of our entire proteome. This score would look at the individual mutations that we have, and also at the general health of the "quality control" system, in order to quantify how close a person is to developing one of the diseases that result from protein aggregation. So if your score was poor, then you should start treatment, even in the absence of observable symptoms.'

This requires an interdisciplinary effort. 'We need to define which subset of our proteins are more at risk of aggregation, and then find large-scale rapid methods for measuring their concentrations and the effectiveness of our quality control systems to regulate them,' Michele says. ' It will involve technical developments in other fields of science, including physics, nanoscience and molecular biology. We are working in collaboration with many different groups on this project! My group is looking more at the theoretical side, in the sense of understanding how to analyse these data, and how to extract the relevant information, which in this case will be the overall score.'

SIMPLE BIOSENSOR

Ultimately, the ideal result would be to create some form of simple biosensor to enable a proteome-level analysis to be carried out, and determine when to start preventive drug treatment. The sensor might use microfluidics techniques, or perhaps based on mass spectrometry. 'There are methods available, but we don't yet know what the best way is going to be. We're trying to work that out now,' he says.



Above: an atomic model of the amyloid fibrils – insoluble aggregates – that are also shown by trasmission electron microscopy in the central panel, and are present in the brains of Alzheimer's patients

But what about drug treatments? Michele is using computational screening methods in his search. 'Computational methods are particularly important here, as many of the proteins that are involved in neurodegenerative diseases have highly dynamical structures – they don't fold into a well-defined conformation,' he says. 'Structural biology is in its early stages for these types of molecule. Essentially, we have to define – at high resolution – ensembles of conformations to represent the state of these proteins. We have been bringing together NMR spectroscopy and computational methods to achieve this goal. While these proteins are not folded, neither are they random – whether they aggregate or not depends on the details of their conformations and dynamics. We are looking at the way they move; sometimes they move in the "wrong" way, but the differences between the shapes are often only minor.'

The first stage is to define the ensembles of different structures, and once this has been done screening can be started. 'We then see where the potential drugs bind, and try to understand whether they affect the way the proteins move when they are soluble, or whether these compounds affect the conformational properties after they start aggregating,' he says.

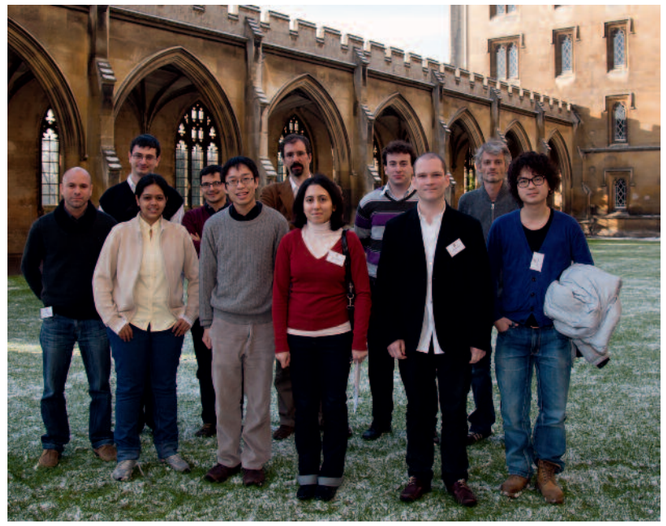
'We are following the aggregation process, as the proteins are structurally labile, to see what kind of structural features in the compounds perturb the aggregation process. These are not standard methods in structural biology – those methods that exist are well established for proteins that are in fairly rigid folded states, but we need to develop methods that allow us to look at natively unfolded states like these where the structures are highly dynamic.'

PROTEOME ANALYSIS

It is also important to develop efficient methods of analysing the proteome, and monitor the general state of the proteins in the cells to get an idea of what proportion of them are in immediate danger of aggregation. 'We try to predict these proteins on the basis of what can be readily measured – simple properties like the amino acid sequences of the proteins,' he says.

'We are making progress in understanding how to make predictions about disease that are based on these sequences. Additionally, if we can get access to quantitative measures of the abundance of these proteins, we might be able to understand whether the organism is faring well or not. We are developing bioinformatics methods for extracting predictions about the behaviour of cells on the basis of the physico-chemical properties of its components.'

Ultimately, he says, the goal is to improve our natural quality control mechanisms, and delay the onset of aggregation. 'We want to develop chemical analogues of the biological mechanisms that maintain our proteome's homeostasis,' he says. 'This could have a big impact on misfolding diseases. It would be impossible to eliminate them, because our proteins just appear to naturally prefer the aggregated state, but if we could prolong the transient state where our proteins remain functional, it could delay some of the problems that are directly caused by ageing.'



Left to right: Reynier Suardiaz, Aleksandr Sahakyan, Aditi Borkar, Carlo Camilloni, Alvin Leung, Michele, Farah el Turk, Luke Goodsell, Alfonso de Simone, Andrea Cavalli and Yanching Chu

CV Michele Vendruscolo

Born: Udine, Italy

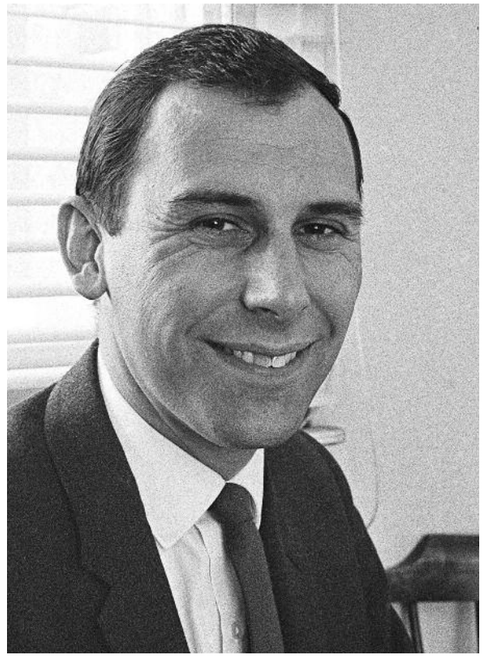
Status: He met wife Laura at university in Italy, and she has a PhD in ecology from Oxford. They have two children: Luca is 6, and Caterina is 2.

Education: Studied condensed matter physics at SISSA in Trieste, Italy, and stayed on for a PhD.

Career: After two years at the Weizman Institute in Israel and three years at Oxford, he came to Cambridge in 2001 as a Royal Society Research Fellow. He was made a lecturer WHEN, PROMOTIONS, and was made a professor in October 2010.

Interests: He loves playing with his children. 'My former hobbies have been put aside until they've grown up!' he says.

Dudley Williams



Photographed by Ian Fleming in 1970; and (below) in less formal mode, Christmas 2006

I first met Dudley early in 1969. I was 20 years old, an undergraduate at Imperial College in London. He was 31, and already established in Cambridge. I had read some of his pioneering research in NMR for my third year dissertation, and wanted to come to Cambridge to do my PhD work with him.

By the time that Dudley retired, I was head of the University Chemistry Department and was – in a purely formal sense – his boss. The 35 year period in between was a wonderful journey of discovery, both scientific and personal.

To go back a little: after a PhD in Leeds, working on Vitamin D chemistry, Dudley moved to Stanford in California to work with Carl Djerassi. In three stunningly productive years he showed how mass spectrometry and NMR spectroscopy could transform the way that organic chemists worked.

His textbooks – including, of course, 'Williams and Fleming Spectroscopic Methods' – and papers simply revolutionised organic chemistry over the following 10 years.

In 1964, he was appointed by Lord Todd to a junior position in Chemistry at Cambridge where he remained until his retirement in 2004. He made it a condition of his appointment that the department purchased a Varian 100MHz NMR spectrometer and an AEI MS9 mass spectrometer to bring it into line with its US competitors.

Throughout his career, he continued his flow of influential papers across a huge range of topics in chemistry and biology. He was one of the most cited chemists in the UK, and was elected a Fellow of the Royal Society in 1983.

Dudley was always keen that his expertise be used for practical benefit. In the early 70s, with Howard Morris, he showed how the inactive form of vitamin D that we eat is metabolised in the liver and then in the kidney to the active form, and that led to life-saving therapies for patients with kidney failure.

In late 1969, he was very excited about a new problem: a powerful antibiotic of unknown structure. He told us that using mass spec we would be able to solve this structure in six months. Those six months turned into almost four decades of science: difficult and frustrating for several years – with some very thin PhD theses – but ultimately successful.

NMR, mass spectrometry, thermodynamics, synthesis and molecular biology were all brought to bear by the group on the problem of understanding not only the structures of these molecules, but also the intermolecular interactions leading to molecular recognition and their antibiotic activity.

His contribution was enormous: vancomycin and its analogues have become key weapons in the fight against MRSA 'superbugs', with sales in 2007 of around $1 billion, and have saved tens of thousands of lives.

But throughout that time he also used vancomycin antibiotics and other systems as a test-bed for fundamental thinking about molecular shape and flexibility, or about the thermodynamics of solvation, binding and cooperativity. These are profound questions we still can't fully answer.

Dudley was never afraid to challenge conventional wisdom and to think the unthinkable. Some of his potential achievements were thwarted by others: he submitted to SERC many years ago a proposal on what we would now call combinatorial chemistry, but it proved to be years ahead of its time and was not funded.

He was a compulsive scholar: no conversation with him, whether in a research group meeting, the Panton Arms or a dull departmental committee, would be complete without him taking a philosophical diversion into Boltzmann distributions, entropy, or perhaps the evolutionary origins of the behaviour of colleagues. That severely reduced his value on a practical committee – conveniently optimising the time he had for research – but as a colleague and mentor he was wonderful.

When I was head of department I could always turn to Dudley for wise and unselfish advice, and for his deep insights into our colleagues' characters.

SCIENTIFIC FREEDOM

Of course, most of Dudley's results were actually obtained by other people: his many students and postdocs. The relationship between supervisor and research group is perhaps one of the greatest pleasures of academic life: we are privileged to have an academic family as well as a biological family. The influence, teaching and learning flow in both directions in a way that is infinitely enriching and rewarding.

Dudley gave his students scientific freedom, while also ensuring that everything we did was worth doing. He encouraged us to think laterally and imaginatively, to challenge orthodox thinking and to have the courage to work in new areas. He insisted that having provocative and testable ideas that might turn out to be wrong was more important than pursuing boring details. He demanded writing of absolute clarity, and eloquent simple diagrams. He was hugely proud of his students and postdocs, and he took great pleasure in our successful careers.

Throughout his career he had been a competitive squash player, but had to give up in his 60s when his hips became too painful. He had both hip joints replaced, but never fully regained his mobility or energy. On retiring at the age of 67, he largely withdrew from the scientific world. Music was a lifelong passion, and he was an excellent pianist. At various times in his life he played jazz, but latterly he concentrated more on Schubert.

He began to feel unwell in the summer of 2010, and was diagnosed with an aggressive carcinoma of the liver early in October. He faced his fate with his characteristic unflinching honesty, as ever analysing his own situation and the psychology of those around him.

More than 200 people came to his funeral: members of his family, ex-members of his group, friends, colleagues and neighbours, all enriched for having known him.

The flood of messages from Dudley's academic family has been sad and shocked, but they also have also celebrated Dudley's vital role in inspiring so many of us to become research scientists in his image. His legacy lives on, not only in his science, but also in his students and postdocs, and then through their students and postdocs, and so on.

Jeremy Sanders

Carol Robinson adds:

Dudley had two families – his biological family, which was always his priority, and his extensive and loyal academic family; one that expanded across the four decades of his career. He had a huge influence not just on the scientific careers of his academic family, but on our lives as a whole.

My memories on hearing the sad news went back to the time I first met Dudley as a young student excited by mass spectrometry. I was invited for an interview, and was in awe of this academic with a vast reputation. He quickly put me at ease – we discussed various projects and he invited me back to his house for lunch. This was my first meeting with Pat, and I also remember that Dudley had something important to do that day – choose a bike for his son Simon's birthday!

But he was also prepared to accept those from non-traditional backgrounds, and give them a chance – that day he offered to take me on for a PhD, despite my limited funding and false start. I remember being profoundly influenced by both these aspects of his character. Here was an academic who, in my mind, had his values exactly right: his family would always come first, and he would accept, with an open-mind, students and researchers from all walks of life.

When I look back on my time in his research group, it was actually very short – just two years. My memories are of Thursday evenings in the Panton Arms after group meetings, putting the world to rights or, less frequently, discussing the evening's seminar. Of garden parties in Fulbourn with hard-fought badminton and cricket tournaments on the lawn, of skiing trips, dinner parties and formal dinners at Churchill College. And, of course, the science!

Academically, Dudley's persistent questions remain in my head: 'Is that an interesting problem? Why should I care about the outcome of that research?' Those two very important years in his group were to shape the way I try to organise my family priorities, to run my own research group, and to recognise the talents of others.

More recently, during my return to Cambridge, Dudley acted as a mentor and also a friend as I got to know him personally. He and Pat were frequent visitors to my house, and we often dined together at Churchill. I also had the pleasure of organising, together with Jeremy, his retirement symposium and dinner at Churchill. My outstanding memory of that occasion was that Dudley paid a very moving public tribute to his wife and family. Dudley touched many lives, in diverse and meaningful ways. He also had a profound influence on the direction of my own.

Eric Walters

Eric Walters, a generous donor and advisor to Cambridge Chemistry and to Selwyn College, has died following a fall while hiking in Oman. Born in Warwickshire in 1944, Eric was a Natural Scientist at Selwyn, graduating in 1965. He met his Swiss-born wife Katharina in Cambridge; their joint 60th birthday party was a spectacular black tie event at the Science Museum in South Kensington.

After a couple of years' working for BP he moved upwards through a variety of major companies, finally leaving private equity firm Alchemy Partners to pursue what he called 'semi-retirement': he became a non-executive director of several companies, and Chairman of Capita, hiked across Greenland, explored jungles and supported a range of educational causes in the UK and Switzerland through his family's Walters-Kundert Trust.

I vividly remember the first day that Eric came to see me in late-2001: he briefly summarised his career and how Cambridge had made it possible, told me that it was time for him to give something back, and asked me what help the chemistry department needed. After a little thought I offered him a menu of possibilities, including support of Carol Robinson's research. She had just moved to Cambridge from Oxford, and I was looking for some help in setting up her research group.

Fortunately, Carol and Eric instantly bonded, and the Walters-Kundert Trust generously offered to support her. Together with Deborah Easlick we conceived the idea of the Next Generation Fellowship (NGF) scheme, and Carol was the first beneficiary.

A couple of years later, I asked Eric to support a Professorship for Carol and again the response was warm and generous. Soon afterwards, Carol was awarded a prestigious Royal Society Professorship, and Eric graciously allowed us to transform the donation into NGFs for two new lecturers, Oren Scherman and then Jonathan Nitschke.

These unrestricted grants to Carol, Oren and Jonathan gave them precious freedom and transformed their research capabilities. Thanks to this tremendous boost, all are now outstandingly successful, with major grants, big research groups and exciting research programmes. The investment in their NGFs has been rewarded many times over; it seems to be a successful model that is being emulated elsewhere in Cambridge, and a great legacy.

In addition, the Walters-Kundert Trust has generously funded theDepartment's Science Festival activities for some years. Eric's pleasure, and mine, in seeing thousands of small children excited by wearing lab coats and safety specs, and doing real experiments in a real lab, will always remain with me. Bringing the excitement of science to generations of children – and their parents and grandparents – is another wonderful legacy of Eric's generosity.

Eric was always warm, kind, informal, direct, and full of constructive, thoughtful questions about the future of the department and our science.

He was a true friend of Cambridge chemistry, and he made a huge contribution to our success over the past decade. I am proud to have had the privilege of knowing and working with him.

Jeremy Sanders

Canadian reunion

Ian Fleming sent along this photo taken in Canada this summer. It's of the Cambridge contingent at a meeting in Victoria, British Columbia, celebrating the retirement of Reg Mitchell, who did his PhD here with Franz Sondheimer in the 1960s.

From the left in the picture are Richard Williams, who did his PhD with Ian in the 1970s followed by a postdoc with Reg; Ian; Reg with the bottle of beer that, apparently, is *de rigeur* in photos of him; Klaus Grohman, who was also in the Sondheimer group; and Wes Borden, who spent a year in Cambridge with Christopher Longuet-Higgins in the 1960s.

A look back to 1954

Following on from the Pembroke Street group photo we published in the last issue, Bal Joshi has sent us several more photos from his days in Cambridge.

He came to Cambridge in 1953 on a scholarship from Bombay University to work with Lord Todd on the structural determination of aphid pigments. But before they could do the chemistry, they had to collect aphids from local farms when their pea plants and willow trees were infested with the insects.

Do any readers recognise themselves in the photos? We'd love to hear from you!

Clockwise, from above: S. Vandarajan, Bal Joshi and Jack Cannon drinking billy-can tea outside the chemistry building; Eddy Haslam and R.I.T. Cromartie collecting aphids; Jeff Watkins and Bal Joshi dipping the aphids in boiling water; lab assistants ? Woodcock and Cyril Smith; and S. Varadarajan, Lord Todd and Basil Chase Gilson at Jack Cannon's wedding reception

Physical chemistry: the early days

Brian Thrush describes the department of physical chemistry's time in Free School Lane, and some of the science that was done there

The arch over the entrance in Free School Lane still shows where the department was established in 1922 in buildings vacated by the department of engineering and, before that, the Perse School. Martin Lowry was the first professor in the subject. He was succeeded in 1937 by Ronald Norrish, who was born in Panton Street adjoining the present department.

When I became a research student in 1949, the department centred around its library in the Perse Room, which was the original school hall. Afternoon tea was served there with the injunction not to get jam on copies of *Nature*.

The building was a maze of awkward rooms, which were largely dependent on an overloaded and unreliable 220 and 110 volt DC electricity supply. The latter could reverse suddenly with alarming consequences if one were preparing H_2 or O_2 by electrolysis. Floods were common, and on one occasion mercury dripped through the ceiling of a room below.

The department relied on a loyal technical staff. The glassblowers were in constant demand. Eric Wilson made and repaired the fragile glass bourdon gauges, and kept the lab clock 20 minutes fast to justify his idiosyncratic time-keeping. Fred Webber worked marvels in quartz, despite his extreme short-sightedness.

Bill Symonds ran a precision workshop on Stalinist lines. Tom Rackham, whose passion was astronomy and who left to work at Jodrell Bank, supervised the student workshop where research students could undertake simple metal work and make their own furnaces, incorporating asbestos paper and asbestos string – health and safety, please note! In the dark room, Eric Smith needed much skill to produce convincing prints and slides from photographic plates of spectra.

Fred Dainton, who was primarily a polymer chemist, left for the chair at Leeds in 1950. Charles Kemball, who was a demonstrator in the department between his time at Princeton and accepting the chair in Belfast, used mass spectrometry to study exchange processes on metal surfaces.

Liquid phase processes were studied by two long-term staff members, the electrochemist John Agar and E.A. Moelwyn-Hughes, whose interest in reactions in solution, particularly of amines, led a barber to ask him if he was in the fish trade.

The gas phase studies largely reflected Norrish's interest in photochemistry, combustion and kinetics. Sandy Ashmore and Tony Harding worked on combustion and ignition processes downstairs, while upstairs Howard Purnell and John Knox pioneered product analysis by gas chromatography. Morris Sugden, who had worked on suppressing gun flash during the war (dripping toluene down artillery gun barrels proved effective but impractical) had moved onto ionisation processes in flames, a problem related to the control of guided missiles, and then onto microwave spectroscopy.

I worked for one year with Sugden using microwaves to measure ionisation in luminous flames. A change of research grants caused my move to build the first flash photolysis apparatus to use electronic timing between the light pulses.

Brian Thrush, back in the 1950s

FLASH PHOTOLYSIS

Methods for studying free radicals and their very rapid reactions were then very limited, but government surplus equipment and advances in electronics offered new approaches. Norrish acquired a searchlight, and George Porter initially used this to focus a powerful mercury arc on fast flowing gases in an unsuccessful attempt to detect free radicals downstream using the Paneth mirror technique.

Porter then built the first flash photolysis apparatus, where the discharge of a huge bank of condensers donated by the Royal Navy could provide large photochemical decompositions in a very short time. This was housed in one of a series of small windowless basement rooms painted black to eliminate reflected light, but the technique soon expanded into the neighbouring odoriferous photochemistry laboratory.

Initially, a rotating wheel timed the recording spectroscopic flash to delays as short as one millisecond but with electronic timing lifetimes of a few microseconds were accessible. ClO, BrO, N_3 and C_5H_5 were among the first free radicals to be detected along with strong absorption spectra of many radicals present in combustion as well as the triplet state of aromatic molecules in solution.

In 1955, Porter moved to the British Rayon Research Association, and then to the professorship of physical chemistry at Sheffield. He concentrated on processes in solution such as photosynthesis and the triplet state, which Maurice Windsor had studied in Cambridge.

The gas phase processes were studied in Cambridge where Francis Lipscomb, and subsequently Bill Magrath, showed that highly vibrationally excited oxygen molecules are formed in the secondary reaction of oxygen atoms in the photolysis of NO_2, ClO_2 and O_2. However, Norrish's main interest was in combustion reactions where Karl Erhard and Tony Callear used flash photolysis to elucidate the role of anti-knock agents such as lead tetraethyl to prevent deterioration in combustion.

After a partially successful attempt to observe far ultra-violet spectra of free radicals by flash photolysis, I took an early sabbatical in Washington in 1957-58 and the vacuum spectrograph passed to David Husain, for whom it provided yeoman service. Returning to the newly opened laboratory in Lensfield Road, I moved to studying rapid reactions by discharge-flow methods.

In this brief account I have emphasised the work on flash photolysis, a technique for which Norrish and Porter were awarded the Nobel Prize in Chemistry in 1967 - the year of and the actual week of Norrish's 70th birthday.

The department of physical chemistry in 1958. Do any readers recognise themselves? We'd love to hear your reminiscences of your days in the department!

Melinda's big bike ride

This summer, Melinda Duer set off on an expedition to cycle down the entire Pacific coast of the US in aid of UNICEF's Sport for Development fund. She'd set herself a real challenge – to pedal every one of the 1,685 miles between Vancouver and Los Angeles, without any support crew. 'Since my idea of bike maintenance is to take my bike into the shop and then go and have coffee, I thought the repairing bit might be as much of a challenge as the pedalling part!' she says.

All her clothes, tools and even her living quarters – a tent – were packed into four panniers, and to start with things went swimmingly, albeit hard going in windy and rainy conditions without the sun she'd been hoping for to work the solar panel battery chargers on her helmet! She also discovered that chipmunks may be cute but they're also a real nuisance – they played outside her tent all night, and as soon as she came out they snuck in behind her in search of food.

However, disaster struck half way through Oregon, and Melinda's horseriding history came back to haunt her. 'I've fallen off my horse so many times I have long-standing whiplash problems, and the cycling aggravated it so much my neck seized up and I could barely move,' she says.

Despite her best efforts finding physiotherapy, it was too badly inflamed and the only sensible course of action was to halt the attempt. 'So many of the locals were so very kind to me, and despite the problems I had it was a great experience. The plan is to finish the trip next summer, but next time I will take someone with me who can manipulate my neck to prevent the same thing happening again!'

Comings & goings

Leavers

Ian Castle
Joanne Castle
Trevor Groves
Alessandra Manzoni

Francisco and Zoe's happy day

This issue's *Hello* magazine moment goes to Francisco Newby, a PhD student in Chris Dobson's group, who married Zoe Pollington – another Cambridge chemistry graduate – in September.

The happy couple met through the Christian Union, and Zoe is currently working for Eden Baptist Church, where they are both members. The wedding took place at Ridley Hall Evangelical Church in Battersea, London, followed by a reception in the Italian Garden at Cannizaro Park in Wimbledon.

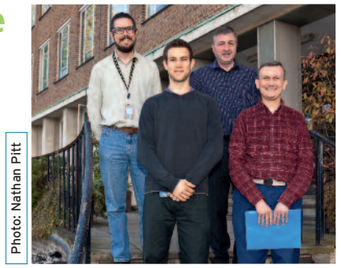
For their honeymoon, the pair spent a couple of weeks in Italy, first on the shores of Lake Garda, and then Venice.

'We were so blessed with a lovely day to share with friends and family, and a chance to talk about what God has done in our lives,' Fran says. 'Also, we had lovely sunshine, which was extremely fortunate given that we didn't really have much cover at the reception venue!'

All change for Ian & Joanne

Baby Maria (left) and Ian poses for an escape photo with his stores colleagues (right)

Photo: Nathan Pitt



Life has changed dramatically recently for Ian and Joanne Castle – they've become parents, left the department and have moved to the Isle of Wight. Fortunately for readers, they haven't forgotten us, and sent a photo of baby Maria Clare along so we can admire her.

Maria was born just after midday on 24 October, weighing in at 7lb 2oz. To start with there were quite a few sleepless nights thanks to colic, but Joanne reports that she's now feeling much more back to normal!

The pair had both worked in the department since 2004. Before they moved, Ian worked in stores, and Joanne was Shankar Balasubramanian's PA, having previously been a secretary in the organic sector. Joanne missed their joint leaving do as she was already on maternity leave, but Ian stood in for both of them

Photo: Caroline Hancox

Life begins at 60!

We've had two 60th birthdays to celebrate recently. On the left, theoretical sector secretary Sue Harding clutches birthday flowers and poses with Liz Alan, while on the right, corporate associate scheme administrator Jane Snaith sits at her decorated desk

Photo: Nathan Pitt

Photo: Nathan Pitt

And finally… a touch of festive cheer. Teaching technician Sara Collins poses with a clamp and cotton wool Christmas tree – complete with round bottomed flask baubles. Every lab should have one!

Last issue's winners

ChemDoku

Our alchemical ChemDoku provided a golden selection of replies – an impressive 31 correct solutions in total. Correct solutions came from:

Richard Brown, Grant Buchanan, Tim O'Donoghue, Matthew Brooker (who attempted to bribe the editor by putting 'Sheffield Wednesday are the finest football team in all of Yorkshire' as the subject of his email – what a shame *Chem@Cam* is unbribable!), Kim Whittaker, Paul Littlewood, Christian Hill, Morgan Morgan, Tom Banfield, Godfrey Chinchen, Stephen Quick, Neil McKelvie, John Carpenter, Annette Quartly, Will Watkins, Hazel Stedman, Karl Railton-Woodcock, Richard Chambers, Kit Bird (who says he suspects the puzzles must have been easier than usual as he solved them without the customary mental strain, and although no longer an active chemist he enjoys Chem@Cam and keeping up with the tremendous progress in the chemistry department), Pat Lamont Smith, Bill Collier, Nick Broughton, Peter Keefe, R.N. Lewis, A.J. Wilkinson, Keith Parsons, Jim Dunn, John Turnbull, Audrey Herbert, Robin Foster and Helen Stokes.

Chem@Cam is home alone at the moment (although at least she's not snowed in, like she was last week) and the cat, very sensibly, is having a nice nap, but a well-timed knock on the door provided a postman-shaped random number generator to select the winner. And the winner is… Matthew Brooker, despite his shameless attempt at bribery!

Au	Pb	Cu	Fe	Sb	Ag	As	Sn	Hg
Sb	Sn	Ag	As	Cu	Hg	Au	Fe	Pb
Hg	Fe	As	Au	Pb	Sn	Cu	Ag	Sb
As	Cu	Sb	Pb	Ag	Fe	Sn	Hg	Au
Pb	Au	Sn	Cu	Hg	Sb	Fe	As	Ag
Ag	Hg	Fe	Sn	Au	As	Sb	Pb	Cu
Fe	Ag	Hg	Sb	Sn	Cu	Pb	Au	As
Cu	As	Pb	Ag	Fe	Au	Hg	Sb	Sn
Sn	Sb	Au	Hg	As	Pb	Ag	Cu	Fe

Elementary recognition

Graham Quartly's latest chess move-based puzzle drew plenty of admiring comments from readers for its ingenuity, and a goodly stash of entries, most of which were correct. However, a couple of entrants managed to miss the end of the solution, and submitted just 'Watson and Crick found helical pattern', without the 'in DNA' required to complete it. But we had a large number of entries that were correct . These came from:

Robin Foster, Audrey Herbert, Keith Parsons (who again complimented Graham on his ingenious and superbly constructed puzzle), Ian Fletcher, A.J. Wilkinson, Nick Broughton, Bill Collier, Keith James, Pat Lamont Smith, Kit Bird, Richard Chambers, Karl Railton-Woodcock, Hazel Stedman (née Cooke), Annette Quartly, Ron Thompson, Neil McKelvie, Morgan Morgan, Godfrey Chinchen, Michael Goodyear, Martin Stentiford (who confesses to a little assistance from his better half, Claire, who spotted the solution in seconds – apparently she is something of an aficionado of the cryptic crossword and their anagrams), Tom Banfield, Alison Griffin, Judith Pederzolli, Autumn Wray, Christian Hill, Jeff Coleman, Paul Littlewood, Richard Moss, Kim Whittaker, John Wilkins, Gill Bergman, Matthew Brooker, Tim O'Donoghue, John Carpenter, Ian Potts and Richard Brown.

And this time the postie picked Keith James' number. Congratulations – the £20 will be on its way to you in sunny San Diego.

Life on a buckyball

Here's another creative puzzle to tax readers' brains from Graham Quartly.

A little while ago the technician at St. Anne's made a simple molecular model of C_{60} (buckminsterfullerene) with the familiar football-like pattern of regular pentagons and hexagons. Over the summer holiday, the model has been colonised by two tiny spiders, residing at diametrically opposite vertices.

Assuming the model is made of rods of unit length, with atoms of negligible size: (a) How far is it between the two spiders, walking along the rods, and how many different routes are there of that length? (b) One of the spiders chooses to do a 'circular walk', i.e. a path returning to his starting point, without travelling twice along the same rod. There are routes of 5 and 6, but no such routes for 7 or 8. What is the maximum length that can be done without traversing any rod twice?

Biblical chemistry

This puzzle was sent in by David Wilson, who suggests that the puzzles recently have been rather strongly biased in favour of maths and logic. 'Here's something (sort of) literary to redress the balance!' he says.

Although this can obviously be tackled using works of reference, he hopes readers will see how far they can get from knowledge and guesswork before resorting to books and search engines…

And the foundations of the city were adorned with all kinds of precious stones; the first foundation was jasper, the second sapphire, the third chalcedony, the fourth emerald, the fifth sardonyx, the sixth sardius, the seventh chrysolyte, the eighth beryl, the ninth topaz, the tenth chrysoprase, the eleventh jacinth and the twelfth amethyst. [Revelation of St John, ch. 21]

1. A chemist might well put these in groups of 5, 5 and 2. Which ones would fall in each group? In some tables of gematria '552' stands for 'Satan', and in others for 'Sex magick', not that I'd want chemists to be associated with either!

Which stone contains (in an amount which may be small or only trace):

2. Fluorine?
3. Hafnium?
4. Nickel?
5. Titanium?
6. Vanadium?

As a tiebreaker, David suggests that the reader who, in addition to a set of correct answers, supplies the most imaginative numerological interpretation for the regrouping, and supplying a website reference. The usual £20 prize will go to the winner.

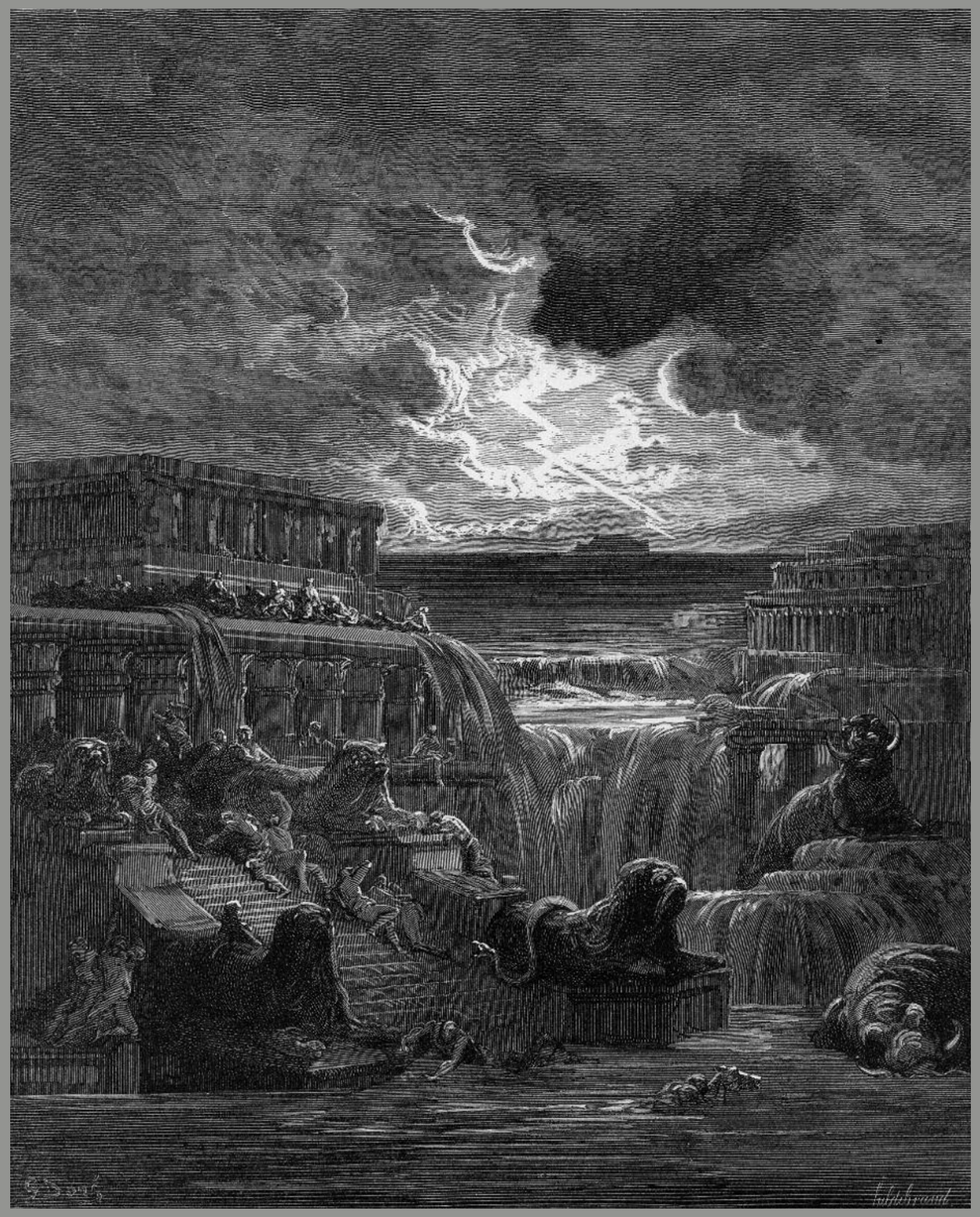
ChemDoKrostic

In	Gd							
		Er	Mn				Ac	
					Br	Gd		
			Co	Ac			In	Mn
		Mn				Dy		
Er	Br			Gd	Mn			
		Ac	Gd					
	Dy				Rb	In		
							Mn	Dy

This issue's ChemDoku was sent in by Tom Banfield, who professes himself increasingly amused by *Chem@Cam*'s strenuous attempts to choose nine elements with some chemical affinity between them.

'May I offer a puzzle which eschews any attempt at chemistry whatsoever?' he says. 'It simply includes nine elements whose initial letters spell out the word Cambridge. Would this be called a ChemDoKrostic?'

£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



The experiment to turn sunlight and water into fuel got a little out of hand

UNIVERSITY OF CAMBRIDGE

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