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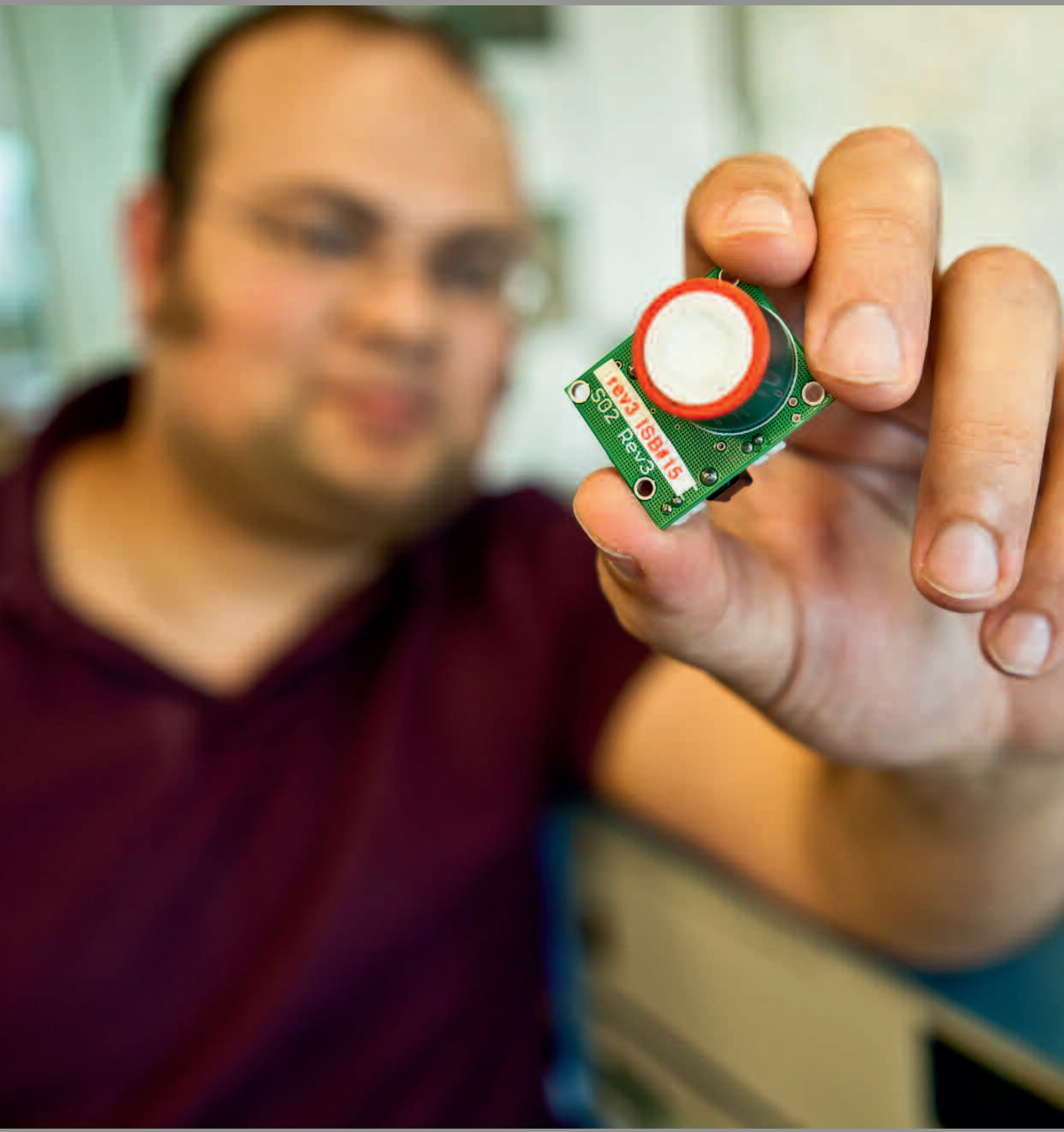
Chemistry at Cambridge Newsletter

Spring 2011



Studying **protein behaviour...**
...and the way they **form aggregates**

Physical chemistry in the 1950s
A chat with the new **Vice-Chancellor**

Sir Leszek Borysiewicz took over as vice-chancellor last October. He tells Sarah Houlton how his career brought him to this point and, on p12, his take on the university's future

Why did you want to be vice-chancellor of the University of Cambridge?

The answer is actually relatively straightforward – why would you not want to be vice-chancellor of the University of Cambridge? From my perspective, this is the best university in the world, and it's a chance to work with some of the best people whom I've got to know and admire, and try to help facilitate an environment where they can continue to deliver the very best that they can.

The university's reputation for education, for research, and for everything that it strives to do speaks of quality and excellence. One of the things you always want to do is work with the brightest and best to help make things happen for them.

How has your career led you up to this point?

I qualified in medicine at my home town university in Cardiff, at the Welsh National School of Medicine. During my time as an undergraduate I was already quite determined that research was going to be a big part of my career.

Having qualified, I moved to London to work at the Royal Postgraduate Medical School, and after completing my clinical training I moved on to do a PhD with Patrick Sissons, who's now Regius Professor of Physic here in Cambridge. After 10 years doing local medical rotations, but also moving on to a postdoc position as a Lister research fellow, I moved to Cambridge, where I became a university lecturer.

What was next?

The opportunity arose to become head of medicine in South Wales, and I moved back there. This brought me into direct contact with having to develop and deliver an undergraduate curriculum. This was for the whole of Wales – at that point there was one medical school, so some of the teaching was in Cardiff – and some in Bangor. It was a really interesting introduction to education, and also to more practical issues such as building research teams.

My research interest in human persistent viruses continued and developed there, with a particular focus on cervical cancer and human papilloma virus vaccines. After 10 years, I moved back to London to head the medical school at Imperial, and then became deputy rector to Richard Sykes there.

Having done seven years at IC, I thought it was time to move on to a different challenge – running the Medical Research Council, which I did for nearly three years before coming here.

How do the two compare?

There is something special about working in a university environment. Research councils give you a whole purview of strategy and direction, and it's enormously interesting to have the widespread debates on how you begin to formulate a direction going forwards that still allows us to encompass the bottom-up approach to science research.

But you don't have quite the same directness that you have within a university model, where you're working right alongside those people who are really engaged in the process of discovery. So it was absolutely great to have the opportunity to come back to this role at Cambridge. It's not just the science, though – it's the totality of what it's possible to do.

One thing that was very important during the time I was at Imperial was being charged with bringing together the various disciplines and being able to look at the interdisciplinary nature of research. Also, being next door to the Royal College of Art and the Royal College of Music, I was working with them to see how we could bring in disciplines that are quite different at first sight, but actually have a lot to offer each other. And therefore coming to Cambridge, one of the real attractions is the huge diversity of excellence there is within this one institution.

The breadth is incredibly exciting – we've got some fabulous people here working in the arts and humanities, and they engage and they're interested in what's going on in other parts of the university as well. I find it immensely challenging and rewarding.

So has it been a steep learning curve, an interesting challenge, or both?

It's certainly a learning curve, and I suspect that on the day I leave it will be a learning curve even then. There's an almost infinite array of activity going on in Cambridge, all of it very high level, and you learn every single day.

In a way, that makes the job very attractive, because you learn and meet people who are very special, both in their own fields, but also people who are trying to make connections and ensure that they can continue to grow their discipline, but also work with other disciplines to tackle challenges that we face globally.

There are not many universities in the UK that can actually claim they really work on the problems that are going to face the world in the future.

Turn to page 12 to find out his take on the funding problems facing universities, and why he thinks chemistry is important

Polymer thoughts

Dear Editor,
I very much enjoyed Brian Thrush's review of the early days of the department of physical chemistry. I can add some information on 1944-1948 and in particular on polymer chemistry.

R.G.W. Norrish's interest in polymerisation kinetics was apparent before the war. Copolymerisation studies with E.F. Brookman were particularly significant, and Norrish included a section on polymerisation and copolymerisation in his wartime Part II lectures.

In 1942 R.R.Smith's study of autoacceleration in methyl methacrylate polymerisation was published. From then until 1945, all research was of significance to the war effort.

John Bevington, a research fellow at Queens', studied cross-linking of poly(vinyl chloride) in metal pipelines and Tom Wright investigated the use of high boiling esters as plasticisers of PVC. The esters , synthesised by Donald Faulkner, were purified in a molecular still made by Fred Webber.

I joined John and Tom in 1944 and was given the third of a group of second floor labs overlooking the Mond. The Distillers Company, for whom Norrish was appropriately a consultant, provided me with a studentship to investigate the use of boron trifluoride in butyl rubber production.

I used a lot of dry ice and liquid air in these low temperature studies, all of which I had to pay for out of my studentship.

After the war, John Bevington turned to studies of aldehyde polymerisation and I made kinetic studies of isobutene polymerisation using a less active initiator. Ivor Bengough joined us to work on vinyl chloride polymerisation.

In Fred Dainton's lab, Ken Ivin, who began research in 1944 just as he turned 19, switched from titanium chloride smoke formation to studying heats and entropies of polymerisation. John, Ivor and Ken went on to make major contributions to the polymer research in British universities.

One Christmas there was no heat in the building and the water in my diffusion pump froze. Our technician, Fred Webber, quickly made the necessary repairs. My vacuum line was made of soft glass; the first pyrex line was, I think, put up by George Porter in 1946.

One day I heard a very loud crack in the basement. Doug Axford often shot off a gun in Morris Sugden's lab and I thought he was in some way involved. It was, however, a peroxide explosion. Fred Dainton was tickling acetyl peroxide from one container to another with a feather when it went off. Fred lost a finger but fortunately penicillin was available and he made a rapid recovery from his other injuries.

Christmas dances in the Perse Room were quite memorable.Tony Harding and George Porter were excellent organisers and they had the wholehearted support of their professor after a tour of the basement convinced him that the floorboards were taking the strain. One of George's poems for an elimination dance ended:

Or does fame still await ya,
I ask you now to leave this floor,
If you've written a letter to Nature

In the circumstances, we were extremely fortunate to have such an opportunity to begin our research careers. The building had its problems but we were much better off than the research students in Pembroke Street!

Ken Russell
Department of Chemistry,
Queen's University,
Kingston, Ontario

eChem@Cam

For the first time this issue, Chem@Cam is 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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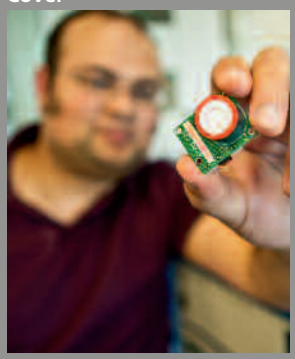

Iq Mead, a postdoc in Rod Jones' group, with one of the sensors they've developed to make field measurements of gases

Photograph:
Nathan Pit

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 visit from President Barroso

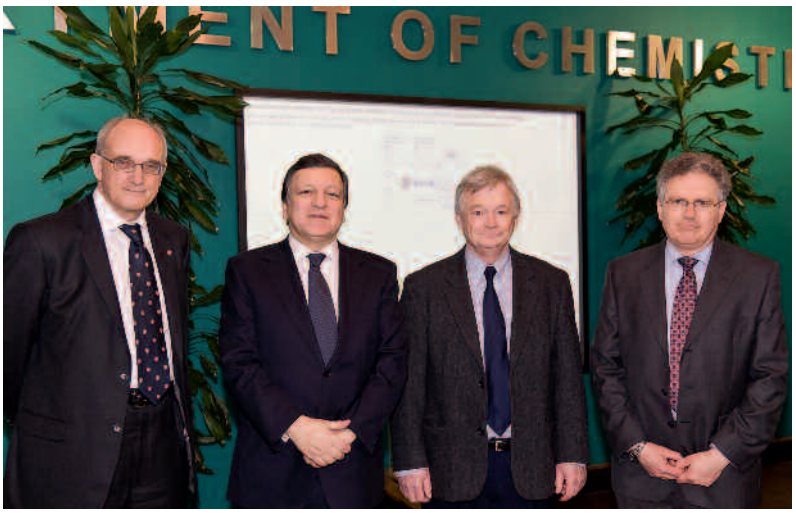


Photo: Nathan Pitt

President Barroso (second left) poses in the department foyer with Leszek Borysiewicz, Bill Jones and Jeremy Sanders

The department had a distinguished political visitor in February – José Manuel Barroso, president of the European Commission.

He was in Cambridge to give the annual Alcuin lecture, speaking about the relationship between the British nation and the European Institutions. Chemistry was asked to host him in the Bristol-Myers Squibb lecture theatre, as it's the university's largest.

'It was a very thought-provoking talk, and he had a great rapport with the audience,' says head of department Bill Jones. 'It was also good that plenty of time was left for questions, most of which were asked by students.'

Bill also reports that the president was fascinated to be in the chemistry department, and was particularly intrigued by the NMR machines in the basement – apparently his mother was a scientist!

Medicinal chemistry live

Photo: Nathan Pitt

The department once again hosted the annual RSC Biological Chemistry and Medicinal Chemistry postgraduate symposium in December. As well as presentations from nine PhD students and a range of poster presentations at lunchtime, lectures were given by guests Barry Potter from the University of Bath, Matt Tozer from Peakdale Molecular and Steve Lindell from Bayer CropSciences. The 2011 event has already been booked – it will be back here in the department on 9 December.

Tim's poster win

Brussels-born Tim Guilliams, a second year PhD student in Chris Dobson's group, had a very successful time at the recent Lorne conference on protein structure and function. His poster entitled 'Influence of nanobodies on the aggregation properties of α-synuclein' was judged the best student poster.

'The conference was amazingly interesting,' Tim says. 'The keynote speakers were wearing shorts and sandals which made them quite approachable, providing the ideal laid-back conditions for the start of fruitful collaborations.'

Lorne is a small town just along the coast from Melbourne in Australia. 'It was a real bonus to be able to get away from the English winter and see the sun!' he says.

He's pictured below with the diploma he received, which came along with a cheque for $100.

Peter's 15 minutes

There's been a lot of interest in geoengineering recently – the idea of solving global warming by finding some way to alter the climate artificially. Suggestions have included injecting sulfur dioxide into the atmosphere to form aerosols or installing space mirrors, both of which would dim the sun.

But what effect would this really have on the weather? Peter Braesicke and colleagues in atmospheric have been working on an atmospheric chemistry model, and thought it would be interesting to plug these effects into their model and see what happened.

Perhaps unsurprisingly, given the complexity of the earth's climate, they found that there might be unexpected consequences. 'The key element is the change in the distribution of the ozone in the stratosphere,' he says. 'By dimming the sun, it becomes cooler, but this also creates changes in the way low latitude weather affects high latitude weather – they are all interconnected.'

They published their results in *Atmospheric Science Letters*, and thanks to the journal sending out a press release, Peter got his 15 minutes of fame. 'Newsweek picked up on it, and ran a story quoting me and a couple of my colleagues,' he says. 'And I was a studio guest on the Naked Scientists radio programme – they ran a special edition focusing on geoengineering, which also featured Rod Jones talking about measurements made on flights, and some of our engineering collaborators.'

And his conclusion on the wisdom of geoengineering? 'I wouldn't really recommend it,' he says. 'But it's important that we do research like this into the potential impact in case someone in the future decides that it's a good idea.'

Do you remember Rosemary Murray?
She came to Cambridge in 1946 as college lecturer at Girton and demonstrator in the chemistry department, and continued to teach and demonstrate for some years after she moved to New Hall in 1954 as tutor in charge. Alison Wilson of Murray Edwards college is writing her biography, and if you have any anecdotes or reminiscences of her time in the department she would love to hear from you (and so would we!) Her email is amw18@cam.ac.uk

A very popular paper!

Chris Dobson passes on the interesting news that a 2005 paper from him and Michele Vendruscolo on mapping long-range interactions in α-synuclein using NMR and molecular dynamics simulations was the *Journal of the American Chemical Society*'s most accessed paper last year.

'This is one of many theory/experiment papers from interactions between Michele's group and mine,' Chris says. 'It's good to see it at the top of the list!'

A symposium in honour of Peter Murray-Rust – who's reached retirement age – was held in January. Entitled 'Visions of a semantic molecular future', the programme featured speakers from academia and industry. Fittingly, the presentations even included a 'video tribute' from Alex Wade of Microsoft Research, and a live presentation via Skype by John Wilbanks of Creative Commons. Introducing the day, Bobby Glen presented Peter with a T shirt bearing his photo and the legend 'Semantic revolutionary' (right), which Peter proceeded to wear for the rest of the day, including for his own lecture (left)

Andreas' award

Andreas Bender has won another prize for his chemistry, this time the 2011 Innovation Prize of the German Pharmaceutical and Chemical Societies.

It acknowledges 'outstanding scientific achievements in the areas of medicinal and pharmaceutical chemistry'.

Andreas was cited for his work in the chemogenics analysis of pharmaceutical screening data, which contributes to boht the prediction and the understanding of adverse drug reactions.

'I am very honoured to receive this prize in particular, as it shows how important the integration and analysis of chemical and biological data now are in the life sciences,' he says. 'I plan to stay involved in "real-world" drug discovery projects to show what impact our work can make in the future.'

A tour of guides

It's not unusual for groups of chemistry teachers to visit the department for a tour and to find out what's going on. But recently Brian Crysell showed a rather more unusal set of visitors around – a group of official Cambridge city tour guides.

As it's International Year of Chemistry, they thought it would be a good idea to find out a little more about some of the famous chemistry that's been done here and what we're doing now, so they could include it in their tours when they're talking about science.

Jane Clarke was on hand to give them a presentation in the Todd Hamied room about Cambridge chemistry past and present, including her own work on proteins.

'They were delighted with the tour,' Brian says. 'We gave them copies of department publications – and back issues of *Chem@Cam*, of course, so they could discover more about the science that goes on in the department.'

Photo: Nathan Pitt

What a transformation!

It's involved a huge amount of work – and an investment of more than £2 million from the university – but the refurbishment of the long-disused labs in the southern basement for Clare Grey is finally complete.

The labs had been the home of Alfie Maddock, where he carried out his research into the radioactive isotope protactinium-231. Although this work ended in 1965, the department was left with a legacy of radioactive contamination, a problem which was compounded by the presence of asbestos.

Before the labs could be refurbished, they had to be decontaminated, a complex process that was finished about a year ago.

The transformation could then begin, and what was once an abandoned and dangerous space is now fitted out as gleaming labs for Clare's group – who have now arrived from the US – to carry out their research into energy storage.

Before, during and after: how the labs have changed!

Photos: Caroline Hancox

Single molecule investigations

Dave Klenerman is using single molecule techniques to study the behaviour of proteins on the surfaces of cells

Single molecule fluorescence is a powerful tool for studying biological phenomena. Having already developed biophysical methods largely based on this technique, Dave Klenerman is now focusing on applying them to biological problems. 'The group is now exploiting our ability to watch single molecules to do biological experiments that have not been possible to date using conventional methods,' he says.

'We have a great collaboration with Chris Dobson using single molecule techniques to look at the molecular events that occur as a protein such as β-amyloid aggregates to form oligomers, and then go on to form fibrils. It turns out that it's a really powerful way of identifying the oligomers, and characterising their conformations. Because we've spent so long developing single molecule techniques to study the cell membrane, we are very well set to look at how these oligomers interact with important cells such as neurons, which are the major cells that give effects in Alzheimer's (where the aggregating protein is β-amyloid) and Parkinson's (where it's α-synuclein).'

The single molecule technique is really simple, and Dave says it turned out to be much more powerful than they'd originally imagined. 'Initially, we were interested simply in identifying molecules that were associated – linked – in some way,' he says. 'This proved really useful when looking at oligomers and proteins on the surface of a cell, where we want to know if they are monomers or dimers. The idea is that we have a red-labelled molecule and a blue-labelled molecule, and as they pass through the probe there is a burst of red or blue fluorescence, depending on the colour of the label. But if they are associated in some way, there is a coincident burst of fluorescence, with two colours at the same place at the same time. It's really very simple!'

It may be simple, but it's also very sensitive, as the coincident bursts only appear if the molecules are associated, giving an easy way of detecting them. 'If the oligomer contains, say, 10 monomers, then the fluorescence burst is more intense,' he says. 'So once we've identified the associated molecules, we can use the intensity of the burst to work out their size. Conceptually it's very simple – it's not so trivial actually doing it! But we have now developed four instruments that are based on this method.'

The group is working on T-cells and the idea is to gain an understanding of the initial molecular events that give rise to the T-cell triggering which leads to a complex biochemical cascade. 'In the presence of co-stimulatory molecules, a single T-cell receptor – a single protein molecule on the surface of the cell – can give rise to this triggering,' he says. 'It is inherently a single molecule process, and we want to find out how these protein molecules reorganise leading to the triggering.'

The basic idea is to watch the molecules as they reorganise, and work out how that causes the triggering. 'It's not a trivial experiment, because the triggering results from contact between the T-cell and another cell,' he says. 'We mimic this by taking a lipid bilayer with fluorescently labelled proteins, and also labelled proteins on the T-cell using antibodies. We watch the cell come down onto the bilayer, and we have found we are able to directly watch the molecules as they reorganise.'

He believes that if this can be done for T-cells, it should be possible to study all other kinds of signalling proteins in a similar way. 'This is now really starting to bear fruit, and we are beginning to look at other important cell surface systems such as G-protein coupled receptors and toll-like receptors.'

UNFOLDING STUDIES

Another project involves looking at protein folding and unfolding with Sophie Jackson and Chris Abell. To do this, the proteins are, for example, encapsulated in a microdroplet containing a denaturant that causes it to unfold. 'We then use single molecule fluorescence to follow unfolding. This time, however, we have two dyes on the same molecule, and the relative intensity of the fluorescent bursts depends on the distance between them, and this allows us to follow changes in protein structure as the protein unfolds.'

Dave is part of a large collaborative project with groups at Cambridge, Bristol and Hamburg, funded by the Wellcome Trust and the MRC, investigating neuron damage in Alzheimer's disease. 'We want to understand which of the different oligomers damage neurons, in which conformations, and how,' he says. 'What is the molecular basis of the damage – do they bind to receptors, do they form a pore in the cell membrane, or do they enter the cell and interact with the mitochondria? No-one really knows. But we can watch the oligomers interact with the cell membrane, and we know what size oligomers are interacting, and what conformation they are in. We want to use this information to understand how they damage neurons, and our tech-

CV

Dave Klenerman

Born: Wrexham in Wales, but grew up and went to school in the City of London

Education: He came to Cambridge as an undergraduate, and stayed on for a PhD with Ian Smith on infrared chemiluminescence emission produced by simple gas phase chemical reactions

Status: Married to Maggie, who works as a fund manager in the City. They have two daughters – nine-year-old Laura, and Anna, who's seven

Career: After a postdoc with Dick Zare at Stanford, he spent seven years working for BP at Sunbury, before returning to Cambridge as a lecturer in 1994

Interests: He enjoys running, on the rare occasions he has spare time between working and playing with his daughters, and skiing

Did you know: His brother Paul is a professor of immunology at Oxford, and Dave rather hopes one day they'll manage to collaborate and produce a Klenerman & Klenerman publication!

Collaborative efforts

The wide range of collaborators Dave has worked with has been key in applying the techniques rooted in physical chemistry to biological problems. Some are in the department – Chris Dobson, Chris Abell, Sophie Jackson, Laura Itzhaki and, of course, Shankar Balasubramanian, with whom Dave founded the DNA sequencing company Solexa which was acquired by Illumina a couple of years ago. But the collaborations are much wider than that. He's working on toll-like receptors with Nick Gay in Cambridge biochemistry and Claire Bryant in the veterinary school, Yuri Korchev at Imperial on imaging cell topography, Simon Davis at Oxford on T cells, and Ernest Laue in Cambridge biochemistry and Tony Carr at Sussex on DNA replication and repair. 'Without this network of excellent people working on interesting areas of science, the work we're doing in biology would be impossible,' he says.

niques allow us to image live neurons and see what's going on. It's not quite a video, but it does give a sequence of real-time images – the fluorophores are quite delicate and photobleach fairly readily – and with the right frame rate you can watch what you're interested in. The idea is to use fluorescent labels that allow us to watch the key biological processes as they happen.'

Another idea with a great deal of potential is to use a nanopipette to deliver molecules to very precise locations on the cell surface and trigger a biochemical process. 'We've been working on this for a while with a group at Hammersmith Hospital,' he says. 'The pipette can be used to map out the topography of the cell surface at 20nm resolution, and we have shown that we can use the same pipette to we deliver molecules in a controlled fashion, in a few milliseconds, into regions less than $1\mu^2$. The aim is to start the biological process when we are ready to image it, rather than waiting for it to happen randomly.'

This project builds on earlier work drawing pictures in DNA, such as the Cambridge crest that got a lot of attention when it was first published. 'We now want to do this on a cell, and deliver molecule that triggers signalling by bringing the pipette close to the surface – 50nm away,' he says. 'We would then deliver the molecules, labelled with a fluorophore so we can image them, and follow how they move and reorganise once they have bound to the ligand.

Although his major focus is now on answering biological questions, work on improving the imaging techniques is still being done, for example so to enable imaging of live cells in real time.

Originally, the micropipette probe scanned across the surface, but if the side of the probe bumped into the cell or something on its surface, this caused problems. In the new method, the pipette hops up and down as it scans across the surface. The pipette stops its hop before it hits the surface, but not before it is able to sense what's going on.

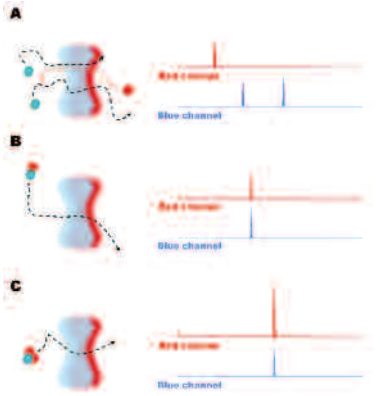
IMPROVED IMAGING

'This has really improved our imaging, and we've made some really detailed images of neurons,' Dave says. 'We've also combined it with single molecule fluorescence, and our collaborators at Hammersmith Hospital have even managed to create movies showing endocytosis – one process by which molecules enters cells. It clearly shows 100nm pits being formed on the cell surface.' The next technique development project is to build a super-resolution microscope that will enable them to create images down to 25nm resolution.

In the longer term, Dave believes the single molecule approach should be much more widely applicable to other biological questions, but various problems will need to be overcome. 'Every time we apply it to a new biological question, we need to do quite a lot of range-finding, with issues relating to labelling and the cells themselves having to be addressed,' he says. 'At the moment, we are pretty much limited to biological questions on the cell surface, although there are very many of those! But the next challenge is to do similar types of experiments within the cells.'

He's already starting to look at this, using a simple sausage-shaped yeast cell which makes it easier to work with to study DNA replication and repair in the cell nucleus. 'Our next challenge will be to do single molecule experiments in cells, but this will be far more complex than looking at the cell surface.

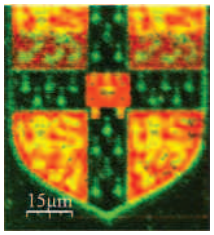
'We have invested a lot of time learning how to use the technique on cell surfaces, and we hope we will be able to translate it into looking at much more difficult problems like this. In the long run, we believe we will be able to use our methodology to study disease processes. As a physical scientist, it's fantastic to think that I might be able to contribute something important in this area.'



A red and blue laser are overlapped and focused to a diffraction limited spot. Non-associated molecules do not give rise to coincident events (A), apart from chance events that occur when two non-associated molecules enter the probe volume at the same time. In contrast associated molecules such as dimer (B) and trimers (C) give rise to coincident events

The Klenerman group posing under the cherry blossom in the Botanical Gardens. Back row, L-R: Steve Lee, Haitao Li, Shehu Ibrahim, Owen Richards, Dave Klenerman, Richard Clarke, Laura Weimann, James McColl, Anna Drews and Matthew Horrocks; front row: Shreyas Mukund, Nunilo Cremades, Jennie Flint, Sarah Shammas, Kristina Laura Tosatto. Priyanka Narayan is absent

Photos: Caroline Hancox



The Cambridge crest on the right is written in red and green fluorophore-labelled DNA, so it is yellow when both are present at the same point. 'We used a nanopipette to deliver the DNA by applying a voltage, and wrote it in 30 minutes – each pixel is a micron,' Dave says. 'This shows how well we can control delivery of biomolecules. We now want to do this on a cell and deliver a molecule that triggers signalling, and follow how the molecules on the cell surface, labelled with a fluorophore so we can image them, move and reorganise once they have bound the ligand.

Physics plus biology equals chemistry

Tuomas Knowles is using techniques from several different disciplines, from physics to engineering, to answer questions from biology

Tuomas Knowles' chemistry sits at the interface with both physics and biology. He uses methods rooted in physics to study biomolecular systems that lie at the heart of important biological events, including the self-assembly of proteins. 'The idea is to take complex systems and work out which are the elementary interacting units and microscopic processes that are important in determining macroscopic phenomena in biology, and how we can modify their behaviour,' he says.

LINEAR POLYMERISATION

The most basic form of protein self-assembly involves the growth of aggregates by polymerisation in a linear fashion. The most familiar of these are the actin and tubulin filaments in the cytoskeleton of cells, as well as amyloid aggregates. As Tuomas explains, these are a great place to start a quantitative study as they display the general features characteristic of protein assembly phenomena, including central role of self-organisation and thermal fluctuations, and they are, in many ways, prototypical examples of soft matter.

'We have been using both theoretical and experimental techniques,' he says. 'An interesting problem when studying protein self-assembly is that larger structures can become progressively less soluble, and it is difficult to study them using traditional biochemical techniques, as these generally work best for homogeneous samples and small complexes.' An additional challenge when studying a protein assembly is the difficulty of finding fluorescent labels that are specific to the structure. These are vital if a visual readout of what's going on is going to be possible.

'So we went about it another way, and asked ourselves, what is the simplest thing that changes when proteins filaments grow?' he says. 'And that, of course, is that the mass of the assembly will increase as more proteins molecules are incorporated. Even though the increases in mass are very small, we found it is possible to measure them directly using a quartz crystal microbalance. We could then follow the reaction without the need for any labels.'

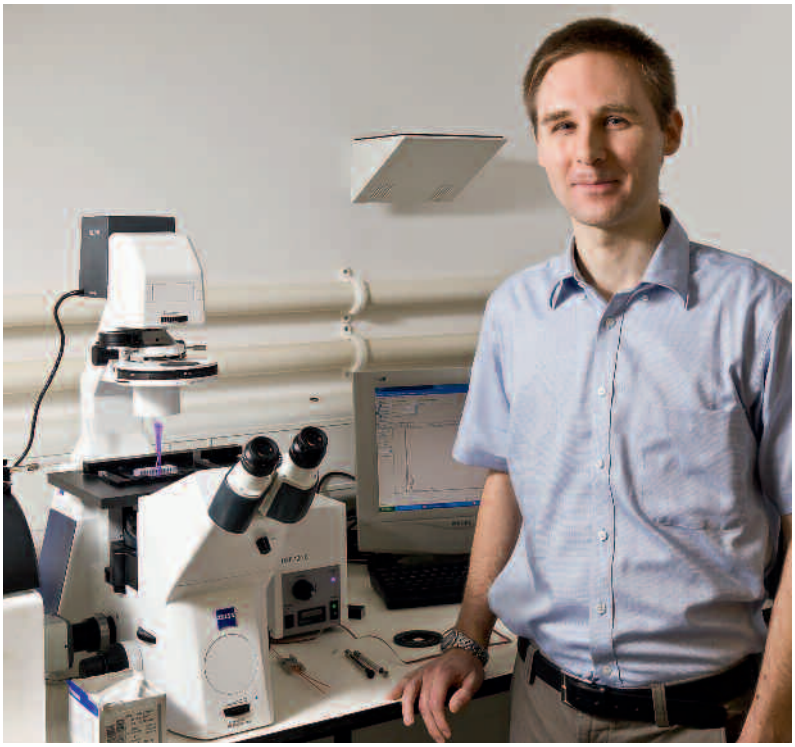


Photo: Nathan Pitt

Tuomas is particularly interested in what's going on right at the very start of protein aggregation, and what first triggers this process. 'Normally, most proteins are very happy in solution, but it has been shown that if their concentration increases too far they start to nucleate into insoluble aggregates,' he explains. 'Once this energy barrier has been overcome, it becomes much easier for further proteins to add on to the assembly, and uncontrolled aggregation can result. But this initial critical nucleus is transient, which makes it a difficult phenomenon to study.' Things are further complicated by the fact that several of these events are happening at the same time but the reactions aren't synchronised, so simply looking at an average across the whole system isn't very informative.

SYSTEM REDUCTION

'The critical step was to find a way to reduce the system,' he says. 'If it could be made so small that there would only be one nucleation event, it would be much easier and more meaningful to look at it over time, and this would allow us to watch the reaction propagating.' However, this gave a further problem – it's something of a back-of-an-envelope calculation to work out how big the reduced system should be. 'It's of the order of picolitres, and pipetting that amount is impossible!'

The answer lay in microfluidics, and creating a device that enabled tiny droplets containing the proteins to be manipulated and studied. 'We distributed the droplets into parallel arrays,

CV Tuomas Knowles

Born: Helsinki, Finland – his dad is English and his mum Finnish, and he's fluent in both languages

Education: Went to school in Geneva (becoming fluent in French), then studied Physics at ETH in Zurich (where the Swiss version of German largely eluded him), before moving to Cambridge for a PhD in the Cavendish. 'I've been in Cambridge on and off ever since!'

Career: After a postdoc in the engineering department, he was awarded a JRF from St Johns. 'I think I managed to confuse them – typically people are elected in a specific area, but I think they couldn't quite work out where I was, so I was elected in both biological physics and nanoscience!' He spent six months of his fellowship at Harvard working with Dave Weitz in the physics department, and was appointed as a lecturer here in chemistry last October.

Status: His wife Susanne is Swiss. She's a language teacher – including of Italian and Spanish, two languages Tuomas doesn't speak!

Interests: Outdoor pursuits, skiing.

Did you know? Tuomas has a microlight pilot's licence – and over 300 flight hours under his belt – although setting up a new group in the chemistry department has taken up his free time and his flying licence has recently lapsed.

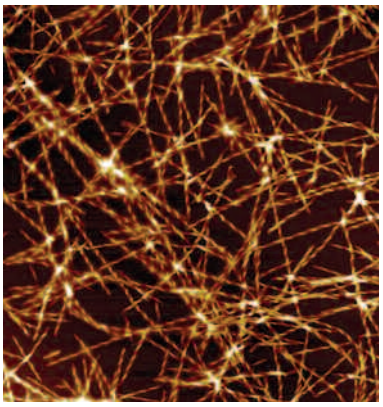
and were able to use a microscope to observe what was going on inside the droplets,' he says. 'It turns out you can indeed see individual nucleation events – you can see a primary nucleus forming, and we were surprised that we could also observe in real time the subsequent growth propagating from the nucleation sites.

As well as using methods from physics to look at complex biomolecular assemblies, there is a theoretical aspect to Tuomas's work. 'Even if it's possible to measure individual assembly steps such as filament elongation through physical properties such as changes in weight, it's still something of a challenge to see how the individual processes contribute to the overall phenomenon,' he says.

MICROSCOPIC PROCESSES

'One approach is to come up with phenomenological observables, such as the apparent lag-time prior to the onset of the aggregation reaction, but there are so many microscopic processes that contribute to these observables that it's difficult to get enough information to determine anything about the mechanism.' As a result, it's only really possible to observe phenomenological trends, rather than gain an insight into the complexities of the many processes that are happening simultaneously.

'What we want to do is turn the problem around,' he says. 'We know there are a number of microscopic processes. What we don't know is how they contribute to the macroscopic features of the overall reaction. While this problem can be formulated in terms of a system of differential equations, their non-linear nature has largely precluded the derivation of analytical solutions to this problem.



The image on the left shows an atomic force microscopy image of protein fibrils. The picture is 4 microns in size

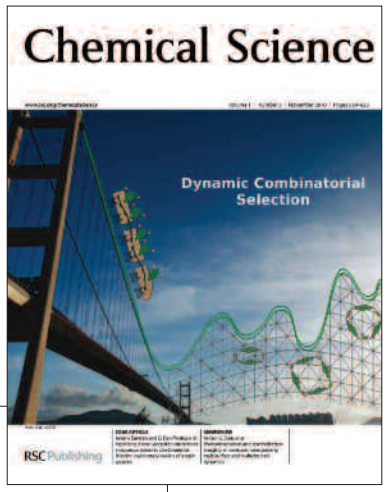
We have recently been able to make some progress in this direction and it has turned out that some surprisingly simple conclusions emerge, notably that while there are many different microscopic processes contributing to the overall picture, in most practical situations only a small number of very specific combinations of the rates of the microscopic processes really dominate the behaviour on the macroscale.

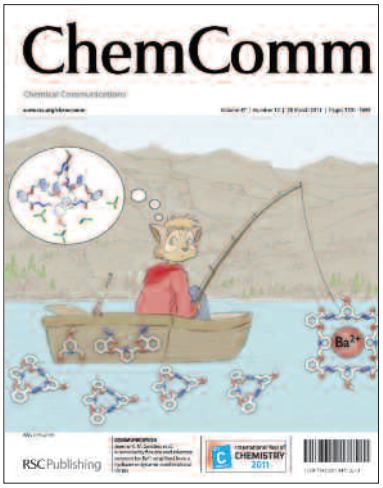
This enables them to interpolate between what they are doing in the lab, and what happens in a real living system. 'For example, this allows us to rationalise things like, say, how long it takes for prions to propagate to such an extent that they become a problem and hence predict the time of onset of disease under many conditions,' he says.

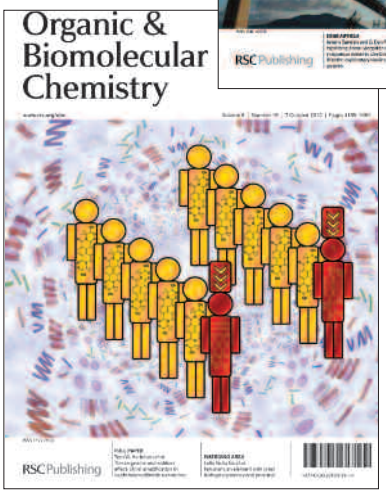
Tuomas believes that this approach will be key to understanding the majority of these assembly processes for which currently there is little quantitative data. 'I'm very interested in exploring the power of microfluidics to look at more complex biomolecular systems, different forms of assembly phenomena, and using this power of combining things at the micron scale to be able to study particular events in quantitative detail,' he says.

NEW MATERIALS

'The ultimate goal is to design, or rationally bias, a system to assemble in a certain way rather than another. It has applications for guaranteeing solubility of proteins in living systems, but also for generating new materials. If you can bias molecular self-assembly to generate certain types of structures rather than others, you gain enormous control of the fine structure of materials at a scale which is key for generating functionality.'







Covered up!

This issue's batch of journal covers from members of the department is somewhat biased towards Jeremy Sanders – he's somehow managed to score three covers in as many months.

The one on the above left shows a schematic potential energy surface turned into a fairground ride, which Jeremy says represents a 'molecular journey up hill and down dale to find the most stable molecules in a dynamic combinatorial chemistry library'.

On the left, there's a sergeant and his soldiers, showing how a 'sergeant' chiral building block can order achiral 'soldier' building blocks to form a helical structure. The third represents another DCC library, where barium ions are used to fish out successful molecules from a pool of unsuccessful ones. One of his group found the fishing boat image on the internet – it's from a commercial artist and, much to their delight, he was happy for them to use the picture in exchange for a 'thank you' inside the journal.

Steve Jenkins has also been getting in on the cover act again. This time, it was illustrating a review article on theoretical calculations concerning the properties of gold atoms and clusters at the surface of CeO_2.

Dear Editor,
I have recently come across your interesting newsletters and wonder if you (or perhaps one or more of your readers) might be able to assist in the identification of any of the individuals appearing in the attached photograph of research students in the newly established Colloid Lab. in 1931/32.

My father (P.S.H. Henry, who at the time was conducting research into the specific heat of gases) is sitting in the middle row second from left; next but one to him with pipe in hand is Professor E.K. Rideal.

Some time ago, I came across the following notes by C.P. Snow describing this particular era and his close friendship with Philip Bowden:

The Laboratory of Physical Chemistry where Bowden and I were working was specially eccentric. The Professor was Martin Lowry, a very clever man who had never been accepted in Cambridge (he was a bit of an injustice collector) and who had, with a curious kind of obstinacy, got stuck with researches on optical rotation that didn't attract many pupils.

Whereas E.K.. (now Sir Eric) Rideal, who was the Humphrey Owen Jones Lecturer, was willing to accommodate research on any topic from pure physics to biology, and his sub-department accordingly became a kind of hold-all for anyone who thought he had a decent problem. Bowden was busy with electrode potentials: Henry was following an idea of Blackett's on specific heat; I wanted to go on with molecular spectroscopy; and so on. The result was that we formed a fairly tight-knit community. We hadn't many undergraduate friends: we were rather too old for that, and we were leading a different kind of life. We worked pretty intensely, longish hours and, of course, most weeks of the year.

We talked a lot of science, played poker on Sunday nights, had supper together at the Bath when our college kitchens were closed. It was in that way that Bowden and I formed a friendship that lasted until his death. I think I realized very early that this was a character one wasn't going to meet twice in a lifetime.

Any help would be much appreciated and will, I hope, be put to good use in the form of a private biography of my father and his times.

Frank Henry
Southsea, Hants
frank.henry123@btinternet.com

Can any readers help? If so, Frank would love to hear from you — and so would Chem@Cam!

The Colloid Lab in 1931/2 – does anyone have any names for us?

The Corporate Associates Scheme

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Cambridge Display Technology
Cambridge Medical Innovations
CambridgeSoft
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Cornelius Specialties
Dr Reddy's Custom Pharmaceutical Services

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:

- Visibility within the department;
- A dedicated meeting room and office for members to use while visiting the department;
- Invitations to recognition days and networking events at the department;
- Access to emerging Cambridge research via conferences, special briefings and various publications;
- Access to the department library and photocopying/printing facilities;
- Regular communications about upcoming events and colloquia;
- Subscriptions to department publications, including *Chem@Cam*;
- Priority notification of and free access to departmental research lectures;
- Ability to hold 'Welcome Stalls' in the department entrance hall;
- Preferential conference rates;
- Free access to the teaching lectures held within the department;
- The full services of the Corporate Relations team to facilitate interaction with students, staff, and other parts of the University of Cambridge to help achieve your corporate objectives.

If your organisation would be interested in joining the Corporate Associates Scheme, then please email Sian Bunnage at cas-admin@ch.cam.ac.uk, or call 01223 336339.

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Royal Society of Chemistry
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More physical reminiscences

Dear Editor

I was interested to read the article about the 1958 photo of the department of physical chemistry, and I am writing with my own reminiscences, which may be of some interest.

I would myself be interested in any news of the student at the far right end of the back row (name Osborne?)

Yes, I do recognise myself. I am second from the right in the row behind the front row. In a recent *Chem@Cam* article based on the 1960 photograph outside the new chemical laboratories in Lensfield Road, I was upbraided (but not identified) by the author because I was not wearing a tie and jacket for the photograph. By contrast, for this 1958 photograph I was more formally dressed, wearing my Selwyn tie and blazer.

I was one of Prof Norrish's students, and I well remember the basement room in which I was working. It had no windows but two doors. The floor, ceiling and walls were indeed all painted black. Luckily, I am not claustrophobic and perhaps it was as well that the move to Lensfield Road was only a year away otherwise I might have needed dark glasses to protect my eyes from daylight!

I do recognise several other faces, but rather fewer names come to mind.

One particular incident at Free School Lane also comes to mind. Tony Callear, I believe, was doing work involving hydrogen telluride. The phial containing this accidentally broke, releasing its contents. This resulted in a mass exodus of everyone in the lab into Free School Lane. My wife, who was coming along Downing Street to meet me, became aware that something was amiss before she got to Free School Lane because the noxious smell had by then diffused into Downing Street.

I do not remember anything about the effort involved in dismantling the vacuum line at Free School Lane and rebuilding it at Lensfield Road. However, I do have a memory of when Princess Margaret came for the official opening of the new labs. The begowned research students (plus a guest) were all ranged around the back of the entrance lobby. The welcoming professors in their more magnificent gowns were waiting near the entrance.

The memory I have is of the anxious look on the face of the princess as she came in because she obviously had no idea in which direction she was expected to turn in order to be greeted.

I was working on the flash photolysis of hydrogen peroxide (in very concentrated form) to try and identify the spectrum of the HO_2 radical, thought to be an important intermediate in some combustion reactions. I tend to think that hydrogen peroxide was too involatile and too weakly absorbing to be a good source of HO_2.

Whatever, when installed in Lensfield Road, I tried to pep things up by using mixtures including both hydrogen peroxide and ozone. The ozoniser was mounted beneath my bench and suitably protected with Perspex screens. Liquid ozone is a very attractive deep blue colour but it is, of course, temperamental. I did have one or two explosions which involved rebuilding parts of my vacuum line. On one occasion, I was relieved that a short, fractured length of glass tubing from my vacuum line did not quite reach a surprised visitor on the far side of my lab.

Another memento of those days is a still-visible inch-long scar on my right forefinger, inflicted by a piece of glass tubing.

At the end of my three years as a PhD student, I had a postdoctoral post at Liverpool University to combine kinetic spectroscopy techniques with shock-tube methods. The tube itself was a wave guide of rectangular cross-section but we ran into problems because the tube bowed inwards when evacuated – not good when the shock wave was intended to be of uniform rectangular cross-section.

After two years at Liverpool, I returned to Cambridge to take up a post at the Local Examinations Syndicate, thinking that I might be more at home with a pen rather than a screwdriver, a soldering iron or a blow torch. This brought me into renewed by indirect contact with the department.

The department of physical chemistry in 1958 – do any other readers recognise themselves? We'd love to hear from you!

An early task at UCLES was for me to draft a revised A-level chemistry syllabus. Two others joined me in polishing my ideas, namely Miss B Longbottom (a senior chemistry teacher at the Perse School for Girls) and Sandy Ashmore. The new syllabus was radically different form its predecessor, and was initially issued in 1963 as an alternative to the then-current syllabus to allow schools more time to accommodate the changes.

The syllabus has, of course, been revised several times since then. Nevertheless, some features of that 1963 revision are still evident in the present syllabus. Indeed, I can still recognise words that I originally penned before I retired some 17 years ago – this I know because I continue to draft multiple choice questions for A-level chemistry, as well as GCSE.

I recognise that the latter part of these reminiscences do not relate directly to the department, but my days there – as well as the teaching I had for my BA degree – were formative with respect to my career, and I trust that my work at UCLES has had a beneficial influence on 18+ chemistry education both in the UK and overseas.

Bob Tuffnell
Long Bennington, Newark

The funding environment is looking increasingly difficult for universities. What is Cambridge doing to meet these challenges?

The first challenge the university faces is that, like any other institution, we have to be able to fund the work that we do appropriately. At the moment, undergraduate education costs a lot more than we can actually bring in to cover it. The current cost of educating an undergraduate student in this institution is £17.1k a year, and that's an average across all subjects – some are rather more expensivet than that.

But even on average we are bringing in somewhere in the order of £8.5k from government sources annually per student. We're investing more than 50% more than the government is putting in per student. We must try to continue to do that because undergraduate education is very special and we must be able to sustain it. But we have to find that resource from somewhere, and if we're taking it from another area it's money that was intended for something else.

At the same time, we have to remain globally competitive on the research side, as well as the many other academic activities that we undertake. It's essential that we are able to reduce the dependence on internal resources as much as possible. Council debated this issue, and of course, in line with all previous statements, we deplore all reductions by government in higher education funding, but we're now in a position that we will have to be taking decisions on what the fee level should be in order to deliver the highest possible quality education that we are able to.

But we also have to satisfy the Office for Fair Access (OFFA). We must show that we are responsive, but also that we will not compromise on what we fundamentally believe – that we have an extremely strong collegiate structure which delivers an education that's second to none for the very brightest and best students that we attract. We must deliver the best education we conceivably can. There will be tensions around that area, and these discussions we are now having are key. But the idea that we would not be seeking to charge an appropriately high fee would not be very sensible.

There has been talk about only being able to charge the maximum fee if you show you are attracting students from all backgrounds.

Well, the wording, as I understand it, is that we will only be able to charge £9k as an 'exceptional' institution. But if Cambridge isn't an exceptional institution, who is? And that is important. There are balances in terms of where students come from, the opportunities we make available to students who can achieve our academic standards – that's the key thing to remember.

Vice-chancellor Sir Leszek Borysiewicz: chemistry is fundamental to scientific study

We will make it possible for them, I believe, through fee waivers and bursaries, and make them feel that Cambridge is no more expensive than any other major university in the UK. That's vital, as we do want to continue to attract the brightest and the best, whatever their background, in a completely needs-blind way of admission. That is a challenge for us, but one that we will need to rise to, because it's the right thing to do – and not necessarily because OFFA tells us it is.

Chemistry, of course, is at the more expensive end of the scale. Is it going to have an impact on the number of students who are going to be able to study chemistry?

I don't think so. My own view is that the important thing about chemistry, and some of the other more technically demanding disciplines that require specific facilities, will continue to attract a premium from HEFCE, so I don't think that should affect it.

In particular, I believe that those who receive a training in chemistry at Cambridge will be very well placed to go either into the jobs market or the academic research market in the future. So I would hope that chemistry in Cambridge will not be adversely affected at all.

I also believe that chemistry is a hugely important discipline for the country in the future, and this should not be adversely affected because I think it's going to be seen to be an extremely attractive option for people to seek degrees in subjects such as chemistry.

The reputation of chemistry as an 'employable' subject has taken a few knocks recently, with job cuts and site closures, particularly in pharma. Do you think chemistry will get a double hit, with students thinking university is expensive, and worrying that studying chemistry won't lead to a job?

Well, I think the real issue here is about the discipline itself. The problem is that you can raise perceptions such as these – but I think they really are perceptions rather than realities.

Chemistry is so fundamental to so much scientific study. From my own perspective in the life sciences, the bottom line is that if you want to know how two molecules interact, you ask a chemist as they understand the problem. And that's a key problem we're going to face across the whole of pharmacology, physiology, biochemistry and elsewhere. So, in many ways, it would be a discipline I'd advise students to look at as it's got so much to offer for the future.

The key thing for me is that the recently announced job losses in the pharma industry and other sectors in the UK are not allowed to detract from that. This country is going to need highly qualified, brilliant chemists if it's going to be able to continue to be the powerhouse that it should be, and I think it's a great discipline for people to get into, and one that I would certainly be encouraging students to consider.

And, of course, here in Cambridge the course is second to none, and the achievements of the department speak for themselves – I don't need to add any further plugs to that!

Another factor, I guess, is the way the course is structured as natural sciences, and with science in general and chemistry in particular becoming so interdisciplinary, this makes the subject even more relevant?

I think that is fair. I think the other thing is that, in other fields of research, as you get older you suddenly realise how much more you wish you'd paid attention to chemistry!

Because it's a very fundamental discipline to our understanding of science. If, for example, you want to get into the real details of understanding the molecular mechanisms of proteins in biochemistry or pharmacology, say, you run into basic chemistry, as well as physics and mathematics.

I think these are core disciplines, and it's absolutely essential that they are maintained at the highest possible standards in Cambridge. I genuinely believe that it is vitally important for the UK that these disciplines are maintained.

Comings & goings

Leavers
Peter Johnson
Jonathan Todd

Retired
Jane Snaith

New staff
Shirley Allen

A partial eclipse in the Cybercafé

The first day back after the Christmas holidays coincided with a partial solar eclipse, and when photographer Nathan Pitt arrived in the department a little bird told him that there was a rather fine view of it from the Cybercafe's terrace.

This was too good a photo opportunity to miss, so he dusted off the solar eclipse safety filters that had been acquired ahead of the total eclipse back in August 1999, grabbed his camera, and headed for the terrace.

'I held the filter in front of the lens, fiddled around with the exposure a bit, and ended up with some rather nice pictures of the moon taking a bite out of the sun,' he says.

The filters are now sitting accumulating dust again – the next partial eclipse visible in Cambridge won't happen until June 2021. And if you're hoping to see a total eclipse in the near future, you'll have to go travelling – there won't be another in the UK until 2090!

Running rings around town

Back in the autumn, several members of Dave Spring's group entered the Chariots of Fire race here in Cambridge. The charity relay race involves teams of six people, with every participant having to run 1.7 miles in a course through the city centre and some of the colleges.

The Spring team comprised – in the order they ran – Jamie Stokes, Warren Galloway, Kieron O'Connell, Henning Beckmann and Albert Isidro-Llobet. 'Our main aim was to have fun, but we also had an athletic target – completing the course in less than one hour and five minutes,' says Albert. 'But to do that we knew we'd need the support of our lab mates – and also some training!'

Both lab mates and training clearly worked out well. 'Several people from the group came to cheer us on very enthusiastically, and we managed to finish the run in one hour, four minutes and 15 seconds!' he says. 'We finished 21st out of 300 teams. But the most important thing for us wasn't our finishing position but the day out. The atmosphere was amazing, with everyone cheering everybody else on.'

Andy's baby delight

We love a nice baby photo here at Chem@Cam, and much to our delight, here's two for the price of one from Andy Wheatley and his wife, Wendy Cooper. Abigail Louise Wheatley was born on 26 November, weighing in at a healthy 6lb 1oz.

Abi made her appearance during the rather unseasonal snow we had back then, and the new father had to improvise and de-ice the car using a CD case when he left the hospital!

Wendy also reports that fatherhood had another bonus for Andy – Abi's arrival gave him a great excuse to keep up with England's magnificent performance in the Ashes while helping out with the night feeds – though if the photo below is anything to go by, he found it all a little tiring...

Jane's retirement

Jane Snaith, who was a secretary in the department for nearly 10 years, retired at the end of February. She has worked with various academics and their groups over the years, and also administered the Corporate Associates Scheme.

As well as the flowers she's receiving from Bill Jones in the photo below, she received a watch, an amber necklace, National Trust membership for a year and a SatNav system as farewell gifts.

Say it with flowers: it was a very happy 30th birthday for secretary Lucie Riches!

Sad news has reached us that Miss Cooper, who worked in the lecture theatres until she retired nearly 40 years ago, died at the beginning of March at the age of 98. Readers with long memories may remember she popped in to the department for a cuppa five years ago, and found her old tea cosy was still around! A service of thanksgiving was held in Histon Baptist Church, which former assistant staff Brian Crysell, Jim Watson and Tiger Coxon attended.

Christmas cheer!

Familar faces old and new popped in to the annual assistant staff party in December. Nathan Pitt was there with his camera

Clockwise from above right: Xiao Hua and Rosa Robert; Richard Preston, David Miller and Donato DiFranco; Isabelle de Wouters and Bill Jones; Jane Snaith and Bill; Liz Alan, Jane, Vicky Spring and Anne Railton; Dick Barton, Jim Staunton and Finian Leeper

Earlier in the day, an unusual sight greeted visitors to the Cybercafé – a group of ladies taking their tea in hats!

'We wanted to do something a bit unusual in the run up to Christmas, and raise money for the Breast Cancer Appeal at the same time,' explains Liz Alan. And they thought it might be fun to bring their best hats and fanciest fascinators in to work, and wear them at tea time.

Liz sent an email around the department giving a little advanced warning, and explaining that they would be accompanied by a collecting tin – and if they made people smile then they'd appreciate a donation.

A grand total of £160.57 was raised, and Liz wants to thank everyone for their good-humoured contributions to their charity collection.

Last issue's solutions

ChemDoku

One or two readers speculated that the ChemDokus are getting more difficult – and this might be borne out by the number of entries we received this time. Tom Banfield clearly did a good job with his puzzle-setting! But we're back to our regular setter this issue (me…) so maybe it will be normal service resumed. We shall see. Anyway, several intrepid readers solved it successfully – and may or may not have noticed the big clue that Tom put in the puzzle: the first letter of each element in the middle row spells out 'Cambridge'! They are:

Jim Dunn, Alison Griffin, Christian Hill, Diana Sandford (who reports that she studied chemistry from 1974-77, then became a chemistry teacher in Edinburgh and Bristol, head of science in Bristol, then a university senior lecturer in Bristol and Bath training science teachers, and now does hume tutoring in deepest Kent so she's still using her chemistry knowledge), Morgan Morgan, Richard Brown, Will Watkins, John Turnbull, Nick Broughton, A.J. Wilkinson (who wonders if it's his age – he's 82 – or are the ChemDokus becoming harder? He thinks they used to be rather easy, but says he despaired of solving this one at one stage, and muses that it would have helped if he had spotted the 'Cambridge' across the middle – but didn't until he'd completed the puzzle), R.N. Lewis , T.J. Wald, H. Stokes (who asks, after last issue's puzzle victory, whether she should open a Swiss bank account), Andrew Milner from maintenance here in the department, and Sarah Taylor.

And the lucky winner – randomly chosen by this issue's husband-shaped glamorous assistant – is Alison Griffin.

Life on a buckyball

Graham Quartly's puzzle which had spiders bravely traversing a buckyball proved something of a challenge, and only one reader – Richard Brown – came up with a solution, which was semi-correct.

As we rather liked this puzzle, we'll leave it open for another issue and see if any other readers can come up with an answer. Richard – feel free to re-enter with a semi-altered solution!

Here's the puzzle again... 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 from David Wilson proved a bit of a poser, but it did draw a couple of responses.

The 5.5.2 grouping, he says, was that there are five quartz minerals (jasper, chalcedony, sardonyx, chrysoprase and amethyst); five silicates (emerald, chrysolyte, beryl, topaz and jacinth) and two alumina (sapphire and amethyst). The fluorine-containing element is topaz; jacinth contains hafnium, chrysoprase contains nickel, there's titanium in sapphire, and emerald contains vanadium.

For reference, these are the compositions of the minerals. Trace elements are given in round brackets but square brackets denote variable composition of more significant components:

Jasper: SiO_2 (Fe)
Sapphire: Al_2O_3 (Fe, Ti)
Chalcedony: SiO_2
Emerald: $Be_3Al_2(SiO_3)_6$ (Cr, V)
Sardonyx: Mixture of onyx and chalcedony, both in turn forms of quartz SiO_2
Sardius: Al_2O_3 (Cr) – a variety of ruby
Chrysolyte: [Mg, Fe] SiO_3 – a variety of olivine, though some authorities however suggest that chrysolyte should be translated as a variety of beryl
Beryl: $Be_3Al_2(SiO_3)_6$ (Cr)
Topaz: Al_2SiO_4 [F, OH]
Chrysoprase: SiO_2 (Ni)
Jacinth: $ZrSiO_4$ [Hf, OH] – a variety of zircon
Amethyst: SiO_2 (Fe, Al) – earlier thought to have trace Mn

Responses were received from Richard Brown and Ian Potts. Both were close, so we've decided to award the prize anyway; the husband-shaped glamorous assistant flipped a coin and it came down tails, so the £20 is going to Ian Potts.

This issue's puzzles

Shakespearean elements

First, a literary-based quiz to help you brush up your Shakespeare, courtesy of David Wilson. I've a feeling this one might be a little more straightforward to solve than his last effort!

1. Who wished to be roasted in sulfur?
2. Whose tears scalded like molten lead?
3. Who chose the casket made of gold?
4. Who ate great meals of iron?
5. Whose oars were made of silver?
6. Who had the elements so mixed in him that nature might say 'This was a man'?

Anyone for Bletchley Park?

Keith Parsons returns with this short and sweet (and probably tricky!) offering…

The letter string below is a coded version of a process used by chemists, with any spaces between words eliminated. The code is best described as 'progressive', which makes it more difficult to solve because any letter that is repeated in the code does not necessarily represent the same letter in the uncoded version each time it appears.

FXYBVETHIUYHAUDPBCWFUI

ChemDoku

		Cr			Cm			Ce
	Co			Ca			Cs	
Cs			Cf			Cr		
					Cd			Co
	Cr			Cm			Ca	
Cf			Ce					
		Cf			Cu			Cs
	Cu			Cf			Cr	
Cm			Cs			Cu		

And finally… a small spot of ChemDoku. This time, we've come over all C, but not in an organic way – all the elements this time are metals beginning with C. Carefully constructed to confound and confuse.

£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

Blocking the sun's rays didn't have quite the effect they hoped for

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