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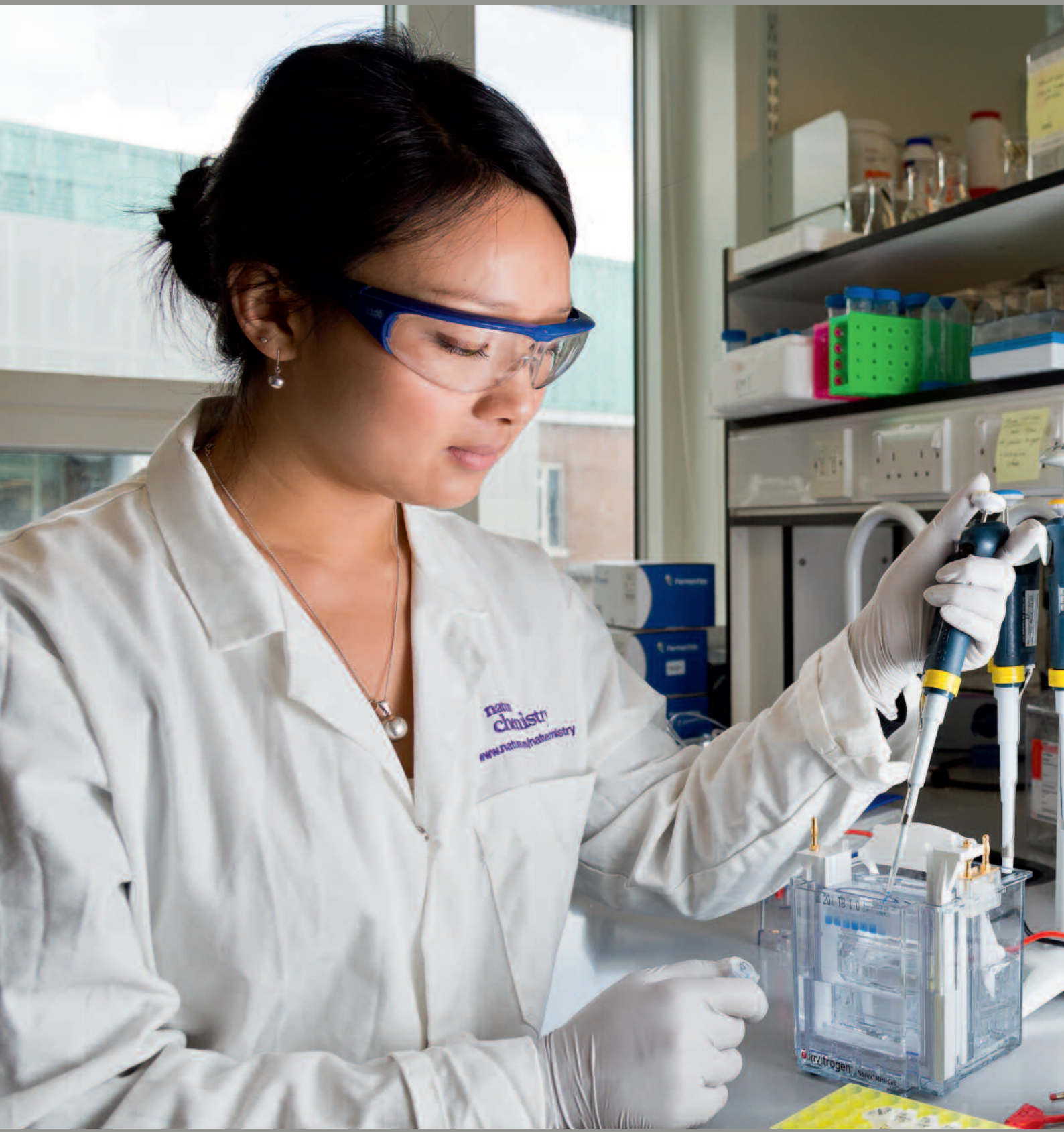
Chemistry at Cambridge Newsletter

Summer 2012



Investigating **tandem repeat proteins**

Commercialising chemistry via spin-outs

Dynamic hydrogels and drug delivery

Enthusing kids at the **chemistry open day**

Spin-out company Sphere Fluidics was set up to exploit science carried out here in the department. Sarah Houlton talks to chief executive Frank Craig about how it's going

How did Sphere Fluidics come about?

It has its roots in science from Chris Abell and Wilhelm Huck's groups in the department. I first became involved when I was asked by Cambridge Enterprise – the university's technology transfer group – to carry out technical and commercial due diligence. I thought the technology was really interesting, and had great commercial potential as there were many applications – in fact, one of the biggest challenges was that there were perhaps too many things it could be used for! Part of my job was to filter it down, and we focused in on biologics discovery and single cell analysis, rather than doing chemistry in droplets and other more chemistry-type applications. I became the company's chief executive officer and, with initial backing from Cambridge Enterprise, we were later awarded seed funding from the Royal Society Enterprise Fund.

How did you get involved?

I have an entrepreneurial background – I was a founder and vice-president of Aurora Biosciences, a drug discovery technology company, and I had worked with Cambridge Enterprise on a previous spin-out, Smart Holograms. They approached me as someone who had skills in working out the potential utility of science, and introduced me to Chris and Wilhelm. There has to be some chemistry between the founders and the entrepreneurs, and I found them very smart and articulate, with good ideas, and was sure I could work with them. Another factor that attracted me to work with the chemistry department was its track record of founding and helping successful companies in the past, and Cambridge Enterprise are also excellent. They know how to give support, handle IP licences, and make the entrepreneur's life very easy.

What is the company's technology – how does it work?

It's based on a mixture of microfluidics and emulsion chemistry. To make an emulsion, water and oil are mixed, and the water can be stabilised with surfactants to stop it separating. There's a lot of know-how in surfactant chemistry within the department, and thanks to novel surfactants and leading-edge microfluidics we can now carry out about a million separate tests on a single chip, about the size of a postage stamp.

The chip typically has three inlets. In one, there is a biological library of cells, another might contain assay components, and in the third could be an agonist or something to stimulate the cells. When the water in the inlets combines with an oil layer pumped laterally across the combined inlets, little aqueous droplets are pinched off by the oil because of the differences in intermolecular polarity. These droplets contain all the required assay components, and within about two minutes a library of about a million different cells has been made. All this can be done inside the volume of about a microlitre.

So where is the company at now?

We currently have three scientists working within the chemistry department – former postdocs from Chris and Wilhelm's groups who have built up expertise in the technology. Since gaining that Royal Society Enterprise Fund finance, we've also signed several commercial partnerships, one with a leading pharmaceutical company, and another with a biotech firm. We're now discussing larger repeat projects with them, so they're clearly very happy that we have innovative science results – resulting in both patents and papers. It's good for both sides – they are getting technology and know-how from us, and it's helping us to start to industrialise the science, and take it through to useful applications.

We decided to focus on the cell-based aspects as not only is it exciting scientifically, importantly, there has been a lot of commercial interest from companies who are looking at the involvement of single cells in causing cancers and antibiotic-resistance, and also as a new way of developing novel diagnostics. This is all backed up by a strong portfolio of patents.

What are the next steps?

After a six-fold increase in income in our second year, we are now planning to hire more people. We're currently in a venture capital round, which we hope will raise £2-3 million. This will enable us to spin fully out of the department into premises on one of the science parks near Cambridge, and increase to about 10 employees by the end of the year. However, right now we are still in the chemistry department, and Chris and Wilhelm help out as technical advisors. Once we're in our own space it will feel more like an independent entity.

We've already launched about 25 products, and are starting to look at mass manufacturing of the chips via an external manufacturer. Companies are able to do things that academic groups don't do in terms of making products, manufacturing and getting involved in a lot of commercial activity. We now have all the experience and skill sets, and a lot of innovations have been turned into products and are being sold. We've learnt a lot in our time here, but it's now time to go outside, where we will have more scope for industrial-scale activities and significant growth.

Is this the main reason why the best route to commercialise a novel technology within a university may be to spin out a company?

I think it's a natural thing. It's good to have very close relationships for the first year or two – as we have had – or hire their people so you capture the know-how. Often, in the early days, the technology isn't fully ready to be used in anger in industry, and a little inside help to resolve some of the remaining technical challenges is invaluable. Once you start setting up outside collaborations and making products, you're probably ready to move on – and that's the stage we're at now.

Chris and Wilhelm have been very good and we've had a lot of help from them, hiring some of their best people, and the department has been very generous in giving us some space. But if we want to have a dozen people – or even 70 in a couple of years – of course there is not the space for us! It's also a bit of an imposition – I've been inviting in a lot of external people such as venture capitalists, and that's a disruption to people who are wanting to concentrate on their research.

So do you have somewhere lined up to move to?

Not yet – we've looked at five different spaces, and once we've raised the capital we'll revisit our top three. We've scoped out space, location, cost and facilities – this is important as you cannot do chemistry in all facilities. We need a mixed space, with chemistry and biology labs, plus offices. Cambridge is the obvious place to be. There's a huge science and technology cluster, it's close to the university research, and there are about a dozen science parks nearby.

Are you optimistic for the future?

Yes, I am. Of course we're in a recession, and people may say we shouldn't be setting up in this climate, but I think entrepreneurs are generally more optimistic than the average person! But I also did a lot of diligence on the science, the people and the market, and I was sure there was a lot of promise.

We're already generating revenue and it's now growing rapidly so I think that faith has been proven. We did, initially, have the challenge of working out where the science fitted best, but the commercial potential is now coming through. Two years on, if the company had no partnerships, no products and did not have venture capitalists knocking on the door, you'd probably be thinking you'd got it wrong. But that's not the case here – we have all three. We are entrepreneurial optimists!

A flash possibility

Dear Editor
A friend from my former Cambridge years, having read my piece on physical chemistry at Cambridge published in *Chem@Cam* last summer, wondered to me about the technician who was said to have suggested to George Porter that he put the 'flash' in 'flash photolysis'.

On further reflection, I recall that that anecdote originated from Tom Fletcher, head technician in physical chemistry and my assistant in experiments involving recording of infrared spectra of samples at 4.2K. Despite intensive efforts at recollection of further details, no specific name comes to mind of the technician who prompted Porter.

Two possibilities are, however, Tom Fletcher himself who, from modesty, deigned not to disclose that fact, or, perhaps more likely, another technician who was succeeded by Donald Oliver in charge of the instrument store.

I never met this technician, but he was highly regarded by the other technical assistants, and he was reported to have left that employment in the department of physical chemistry to become a successful doctoral student (without an undergraduate degree) elsewhere in experimental astronomy.

Perhaps Brian Thrush or another survivor from the decade after 1945 might be able to shed some light on this mystery? The single occasion on which Tom Fletcher related, during incidental conversation, that anecdote to me preceded the award of a Nobel prize to Norrish and Porter by a few years, so there was no particular impetus to have invented history at that time.

The other sharer of that Nobel award was Manfred Eigen, whose contribution to rapid reactions was based on spectra involving nuclear magnetic resonance of aqueous solutions, in Gottingen; Professor Eigen subsequently recorded some piano concerti of Mozart. During his period as student and Research Fellow of Emmanuel College, George Porter participated in college concerts in singing arias by Gilbert and Sullivan.

As far as I am aware, Norrish had no particular musical interest, but with sufficient inducement by means of spiritous beverage he could wax somewhat eloquent about an alleged Fourth Law of Thermodynamics.

Yours sincerely, John Ogilvie
Department of Mathematics,
Simon Fraser University,
Burnaby, British Columbia, Canada

Fun with fluorine

Dear Editor,
I was interested to read Howard Clark's experience with the fluorine generator in his room at Pembroke Street in 1955-57. About the same time, I was working as a technical assistant in the fluorine group of the National Smelting Company at Avonmouth, having gone down in June 1954. The extract below is from 'An Early Career in the Heavy Chemical and Metallurgical Industry' which I wrote (from memory) in retirement in 2005. Howard (and others) may be interested to read of my experience!

Regards
Paul Stickland (Trinity 1951)
Newbury, Berkshire

Before my time, there had been a fluorine plant that bottled the product, using a cryogenic (liquid air) method of filling cylinders, as no mechanical compressor could then be found to cope reliably with fluorine. The filling plant still existed, but was disused. But the Ministry of Supply had a laboratory near the Fluorine Group that from time to time required a piped supply of elemental fluorine, and we had a commitment to supply them on demand. This was quite a nuisance for the Fluorine Group TA who ended up running the fluorine cells.

These were warm-water jacketed rectangular cells about 3m long and some 30cm wide (inside the jackets) with steel cathodes and graphite anodes; the anode and cathode compartments being separated by a skirt dipping into the potassium bifluoride KHF_2 electrolyte. The graphite anodes were supported in beryllium-copper mounts that connected them to the external DC supply. When trying to fit new anodes, I soon discovered that beryllium-copper is 'hot short' and you have to work it as cold as possible. The cements used to make the system leak tight to fluorine were very unusual. One was magnetic iron oxide Fe_3O_4 direct from the blacksmith's shop mixed with strong phosphoric acid; the other graphite mixed with Tate and Lyle's Golden Syrup. We had a gallon can of the last on the plant!

The plant rectifier gave a low voltage current of hundreds of amperes, and was turned on on demand from the MoS laboratory, where the fluorine may have been used for experiments on uranium hexafluoride. As the electrolyte was reduced, it needed topping up with HF while the plant was not in use. This fell to me on one Friday, and I was badly misled by Ted on how long it took to expel a certain quantity of anhydrous HF from a 100kg cylinder into the cell. The result was that the cell overfilled and the electrolyte rose up into the gas offtake pipes where it promptly froze.

As MoS had called for supply on the Monday morning, I spent the whole weekend on my own dismantling the gas pipes and using a gas torch to melt out the frozen electrolyte that had of course an excess of HF in it. This was an extremely unpleasant, not to mention dangerous, job, and my face was red raw by Sunday evening. I did get the occasional visit from the area shift foremen, but no physical help.

We had a stock of exotic metal fluorides that could only be made from elemental fluorine, including those of cobalt and molybdenum, and I filled various orders for these. There was also a small gasholder containing sulphur hexafluoride SF_6 made by burning sulphur in elemental fluorine. It is an almost inert gas with very good dielectric properties, but we did not make or sell any of it in my time.

For no very good reason, the area was also used to produce ammonium bifluoride ($NH_4.HF_2$) solution for use at another MoS laboratory near the Cadmium Plant where experimental work was done on beryllium extraction. The solution was taken down in a 100 l tank on a trolley. All the site staff were amazed that the MoS people had a fresh white coat every day — our brown lab coats were only changed when they fell apart.

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Chemistry at Cambridge Newsletter

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Amy Zhang from Shankar Balasubramanian's group, at work in the new Herchel Smith lab

Photograph: Nathan Pitt

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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Official opening for Herchel Smith lab

Photos: Caroline Hancox

Sydney Brenner gives the lecture (left) and unveils the plaque with Herchel Smith's son Marcus, watched by Shankar (below)

The inaugural Herchel Smith lecture was given by Sydney Brenner at the beginning of July. The lecture, entitled 'Reading the Human Genome', was delivered to a packed audience in the Wolfson Theatre at the beginning of July. Brenner won the Nobel Prize in 2002 for his pioneering work on the roundworm, a model organism now widely used to study genetics.

The lecture coincided with the official opening of the Herchel Smith laboratory, which now houses Shankar's research within the chemistry department – as Herchel Smith professor of medicinal chemistry, part of his group is also based at Cancer Research UK's Cambridge Research Institute near Addenbrookes.

Fellowship joy

The announcement of the new Fellows of the Royal Society brought great news for the department this year – both Shankar Balasubramanian and David Klenerman have been elected FRS.

Shankar's research on chemistry and its application to the biological and medical sciences gained him the honour, and David was elected for his work on the development and application of new general biophysical methods based on fluorescence and scanning probe microscopy to study a range of biological processes.

They were also the principal inventors of the DNA sequencing methodology that led to the successful spin-out company Solexa.

■ Jane Clarke and Shankar Balasubramanian were among a list of 55 scientists from around the world who were elected members of the European Molecular Biological Organisation in May.

Meanwhile, a prestigious fellowship has also gone Chris Abell's way – he has been elected a Fellow of the Academy of Medical Sciences.

Congratulations all!.

Measurements on the fly

Left: John Pyle, Michelle Cain and Nicola Warwick with the FAAM aircraft in Sweden

Not all chemistry practical work takes place in the lab – and chemists from the atmospheric chemistry group get to visit some rather unusual places in search of data. In July, John Pyle, Michelle Cain and Nicola Warwick headed off to the wilds of the Arctic as part of a project team measuring levels of the greenhouse gas methane there.

'The aim is to find out more about methane emissions in the Arctic, which are not very well known,' Michelle explains. 'Not only are the measurements in the Arctic quite sparse, as it's rather remote, but the emissions are also very variable.' One large source is wetlands, where bacteria produce methane – as the temperature rises, more methane is emitted. Thermokarst lakes are another source. These are frozen in winter and melt in the spring, releasing methane into the atmosphere.

The measurements were made using the Facility for Airborne Atmospheric Measurements, or FAAM, aircraft. It's a BAe 146 plane that has been kitted out to take airborne atmospheric readings of things like gases and aerosols, and is used by various different atmospheric science groups, including the team at Cambridge.

They also flew from their base in Kiruna in northern Sweden right up to Svalbard – the Arctic islands that are the most northerly part of Norway. Here, they were looking for bubbles of methane escaping from gas hydrates into the ocean. There is a line of these hydrates just off the west coast of Svalbard, and methane has been seen bubbling up from the underwater structures. The methane dissolves in the water while it rises to the surface, but can some of it also escape into the air?

'We didn't observe higher concentrations of methane in the air while we were there,' Michelle says. 'However, it's still possible that we, and our colleagues at Royal Holloway, Manchester and FAAM might be able to detect a signature when the final analysis is done in the lab.

'But even if we don't see emissions from the gas hydrates, it doesn't mean it never reaches the atmosphere. If the sea is warming gradually, we may reach a point where lots of methane starts to be released. We want to know if any of this can get into the atmosphere, where it would cause more localised warming.'

Academic promotions

This year's promotion round brought good news for four members of the chemistry department's academic staff. Jason Chin and Matthew Gaunt are being made professors, while Markus Kalberer and Oren Scherman are both promoted to reader.

Below: scientific experiments on board the plane

Christian Doppler Lab opens

Photo: Nathan Pitt

Erwin shows off the facilities in the new lab to the distinguished guests at the official opening

The department's new Christian Doppler laboratory for sustainable syngas chemistry had its official opening in April 2012.

Headed up by Erwin Reisner, the state-of-the-art lab is focused on research into using sunlight to power the sustainable conversion of carbon dioxide and water into syngas.

This high-energy gas mixture contains hydrogen and carbon monoxide, and can be used to create liquid hydrocarbon fuels. It is also an important feedstock in the petrochemical industry.

The lab is being funded for the next seven yearsj ointly by the Austrian Christian Doppler Research Association, the country's Federal Ministry of Economy, Family and Youth, the National Foundation for Research, Technology and Development, and OMV Group, the Austrian-headquartered international oil and gas company.

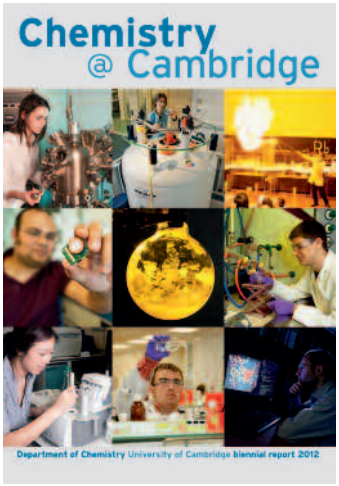
'The new laboratory aims to develop the basic principles to allow for a renewable production of syngas,' Erwin says. 'Our long-term vision is a transition from a fossil-based to a sustainable carbon-based economy.'

The main focus of the lab will be the development of molecular catalysts, which will then be integrated into nano-structured materials for syngas generation. Ultimately, the aim is that this will enable small-scale devices that make solar syngas to be assembled.

Photo: Nathan Pitt

The Melville Lecturer this year was Laura Kiessling, of the departments of chemistry and biochemistry at the University of Wisconsin, Madison in the US. Her talk was entitled 'Tailored polymers for controlling cell signalling'.

The department has recently published a biennial report, featuring information about our strategy and structure, and some of the scientific highlights from the past couple of years. You can download a pdf copy from the department's website, www.ch.cam.ac.uk



A shocking demonstration of explosive power

Above: the tubing is even safe to hold

The Bristol-Myers Squibb lecture theatre was a noisy place to be early July, when Chris Bishop of Microsoft Research here in Cambridge gave a spectacular family lecture, entitled Explosive Science. Unsurprisingly, given the title, there were plenty of loud bangs to be heard.

'During the final lecture, I wanted to talk about the idea of detonation, and how it's different from simply a fast burning,' Chris says. 'The idea was to take a commercial product called shock tubing, which transmits a detonation. It's a stiff yellow plastic tubing, with a diameter of 3mm, with the hole down the middle coated with the powerful high explosive HMX. If you were to set fire to it, it would just burn, but by using a device that produces a very high voltage electrical discharge, a mini lightning bolt produces the shock that initiates the detonation. But it's completely safe – I even had volunteers from the audience to hold it.'

The detonation travels at 2100m/s – nearly seven times the speed of sound. 'It's pretty nippy!' he says. 'I first tried it with a length of the tubing across the lecture theatre, but it only took 10 milliseconds to reach the end of the tube, and the human senses can't detect that a shock has travelled from one end of the other. You can see the bright flash with the lights down, but not that it is moving.'

To demonstrate the way the detonation moves took rather more tubing – about 800 metres of it, wound eight times around the lecture theatre by the technicians, and pinned to the walls a little above head height. 'I think this is a first – no-one I've spoken to in the explosives world knows of anyone doing this in a demonstration lecture before! he says. 'It was amazing – it took 0.4 seconds to go from the start to the finish, and we could actually see the eight individual flashes as it travelled around the lecture theatre. It was rather spectacular!'

Right: the lecture theatre lit up by the detonation. It's a shame you can't capture motion in a 2D photograph!

It's not always a false alarm…

Photos: Nathan Pitt

In late June, we had an unscheduled visit from the emergency services, thanks to a small fire in the Melville lab. But with Lensfield Road closed off completely for a couple of hours, the local press exaggerated the story from 'small fire in a safety cabinet that burnt itself out quickly' into 'firefighters battled the blaze for two hours'.

What actually happened was that a student spilt about 5ml of the strong oxidising agent chlorodiphenyl phosphine in a nitrogen dry glove box, cleaned it up correctly by diluting it using hexane/THF and mopping up with a paper towel. She then placed the towel in the solid waste bin within a fire safety cabinet – exactly as she should.

While the chemical is not pyrophoric, it does react violently with water, and (we assume) there must have been damp tissue already in the cabinet, as the towel spontaneously caught fire. Fortunately the student had the presence of mind to close the cabinet and raise the alarm rather than tackling the fire herself, which might have made it spread, and she immediately informed safety officer Margaret Glendenning that it wasn't a false alarm.

The result was seven fire engines from around Cambridgeshire showed up, along with two ambulance response units and several police cars. Two firefighters wearing breathing apparatus entered the now-evacuated building to check on the cabinet – a wise precaution as the cabinet also contained drums of chemical waste, so the exact contents were unknown. They used a thermal imaging camera to check the internal temperature of the cabinet, which automatically creates airtight seals if the temperature either inside or outside reaches 80°C and is fireproof for at least 90 minutes. They found that the internal temperature was below 40°C.

However, because the cabinet was vented – even though these vents automatically sealed at high temperature – they wanted to check the building's ventilation system by using a platform hoist to look on the roof, and they had also erected their inflatable emergency decontamination tent, which arrived on a large truck, complete with a fork-lift to unload it. Lensfield Road was closed to traffic while this was going on, and as it was late afternoon many people left their cars in the car park and found other ways to go home, as they couldn't return to the building to retrieve keys, and the way out was blocked by fire engines.

The department was cleared as safe at about 6pm, and the small fire had probably burnt itself out even before they had arrived. But it did provide a good opportunity for both the emergency services and the department's safety team to check that our evacuation procedures worked, and that the information the fire department have about the building was up-to-date.

'This time, it wasn't just an "unwanted fire signal" – it was a real fire,' Margaret says. 'Everyone – from the student to the fire safety team – did exactly what they should have done, preventing a small and controlled fire becoming a major incident. It serves as a great reminder of the importance of knowing exactly what to do if there is a fire in the lab, and always evacuating the building immediately if the fire alarm does go off.'

Left: one small fire, successfully contained; below: the safety cabinet that did its job; above: some of the fire engines that descended on the department, including the platform hoist used to check the ventilation system on the roof

Four prizes from the RSC

Four members of the department featured in this year's list of Royal Society of Chemistry prize winners.

Dominic Wright won the Main Group Chemistry award, which recognises outstanding research by a mid-career scientist in any aspect of the s and p block elements.

The Marlow award was given to Robert Best. This prize is awarded in recognition of the most meritorious contributions to physical chemistry or chemical physics by a chemist.less than 10 years after finishing their PhD.

Tuomas Knowles won one of this year's three Harrison-Meldola memorial prizes. These prestigious awards are for the most meritorious and promising original investigations in chemistry by chemists under the age of 33, regardless of speciality.

Finally, Daan Frenkel receives the Spiers Memorial Award. This prize is presented in recognition of an individual who has made an outstanding contribution to the field of a Faraday Discussion. These are international discussions held six times a year that focus on rapidly developing areas of physical chemistry.

■ Corporate Associates Junior Faculty Teaching Awards have been made to Ian Baxendale and Sally Boss, in recognition of their outstanding contributions to the undergraduate teaching programme within the department.

eChem@Cam

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

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

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

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

Mix-and-match proteins

What do tandem repeat proteins do, and how do they fold? Laura Itzhaki is trying to find out

Laura Itzhaki's current research focus has its roots in the chance finding of an interesting paper in PNAS following the one she was actually reading. 'It was about a phenomenon known as 3D domain swapping,' she says. 'This is a folding-related problem, in which two identical protein chains swap a part of their structures to form an intertwined dimer or higher-order oligomer.'

Very little was known about the mechanistic aspects of domain swapping, so she started to look into it using a protein engineering approach. 'We provided the first residue-specific insights into domain swapping and delineated the sequence specificity of the process,' she says. 'We also revealed that domain swapping can drive protein misfolding and aggregation, and can regulate protein function. It was through the protein in that paper – a cell cycle activator – that we became interested in cell cycle regulation, and from there, a class of proteins known as tandem repeat proteins.'

REPEAT PROTEINS

Accounting for about one-fifth of all the proteins encoded by the human genome, these contain small structural motifs of about 20–40 amino acids that are repeated multiple times in tandem. Many of them are transcriptional and cell cycle regulators, and they are frequently deregulated in cancer. They have also been identified as potential drug targets for the treatment of cardiovascular and respiratory diseases, for example, and for pain relief via ion channels involved in pain sensing.

'These motifs pack in a linear fashion to produce very elongated structures,' Laura explains. 'This makes them very different from the globular proteins that are more commonly studied, whose structures are stabilised by interactions between amino acid residues that are very distant in the sequence. In repeat proteins, all the interactions are between residues that are very close in the sequence, making them much simpler structures. The simplified architecture makes it easy to rationally engineer their properties. We can make them more stable, larger or smaller, and give them new functions – all of which cannot be done to globular proteins with anything like as much ease.'

Photo: Nathan Pitt

She believes there is a great deal of potential for targeting them with new chemical approaches, but before this can happen, they will need to be understood much better. She's looking at very basic properties like how they fold and how folding (or, rather, unfolding) controls their function.

One fundamental aspect that is particularly interesting, she says, is that their extended, superhelical structures make them behave a little like Slinky spring toys. 'It is likely that repeat proteins utilise elastic modes of action' she says. 'Examples include stretching and unfolding motions to facilitate molecular recognition or to regulate the activity of a repeat protein-bound enzyme towards its substrate; reversible repeat protein nanosprings to operate ion channels; and repeat proteins that wrap around their cargoes to transport them into and out of the cell nucleus.'

To study them, Laura uses a combination of conventional biophysical tools, such as fluorescence, circular dichroism and stopped-flow for kinetics, but because they have such symmetrical structures they can populate many different states of similar stabilities, so a new set of tools is needed.

'Single-molecule methods are essential as they allow us to directly detect heterogeneity in a way that simply cannot be done with conventional ensemble methods,' she says. 'We're working on this with Dave Klenerman's group. We also use atomic force microscopy, which is important for understanding their mechanical and elastic properties.'

Because the properties of these proteins are so easy to manipulate in a rational way, she is using them to try to understand mechanisms of biologically assisted protein folding and unfolding. 'We still don't really understand how proteins achieve and maintain their functional states in living cells. We believe repeat proteins will be particularly useful in this regard, because we can play around with their biophysical properties in vitro and see how that translates into altered behaviour in the cell. We are hoping to resolve how proteins are helped by cellular machinery, specifically folding on the ribosome and unfolding by the proteasome.'

Another collaboration is with David Spring's group, supported by MRC Technology, which provides funding to help bridge the gap between academic research and commercial development.

'We're trying to modulate the behaviour of cancer-associated repeat proteins for therapeutic purposes, and that's going very well,' she says. 'We've already found several molecules that are good starting points for drug development.'

The use of repeat proteins in the development of new nanomaterials also has tremendous potential, she says. 'A lot of work has been done on self-assembly with DNA building blocks, and also with peptides, but far less with proteins,' she says. 'Tandem repeat proteins are potentially excellent building blocks as they are so easy to redesign. Moreover, their natural functions are as scaffolds that bind to other proteins, and so there is an inherent functionality in them that has been lacking in the peptides that have been used to date. We're just starting to see if this is possible.'

Laura Itzhaki

CV

Born: Manchester, where she also went to school

Status: Husband Shafiur is a documentary film-maker. They have two sons – Pavel, 13, and Zain, 3.

Education: Studied chemistry at Oxford, with a final year project with Chris Dobson (before he moved to Cambridge!). This led to a protein folding PhD with Phil Evans in the biochemistry department here.

Career: After a postdoc and a Beit Memorial Fellowship in Alan Fersht's group, she started her independent research career in 1998 at the MRC Centre for Protein Engineering. In 2003, she moved to the MRC Cancer Cell Unit, before returning to chemistry last April with a fellowship from the Medical Research Foundation.

Interests: Most of her hobbies went by the wayside after having children, but she still loves travelling, only now with her family!

Did you know? Laura and her husband went to South America on honeymoon, but the guidebooks had convinced them they'd be robbed so they left their shiny new gold wedding rings behind. 'Once we were there, we realised the guide books were talking complete nonsense, so we went to a local market and bought some replacement (not gold!) rings to wear,' she says. 'So there we were in Quito, Ecuador, exchanging rings once more.'

Dynamic delivery design

Oren Scherman's high water content hydrogels have real potential in a variety of biomedical applications, from drug delivery to microcapsule formation

Hydrogels are used in many biomedical applications, whether as delivery agents, or structural material, as the chances of eliciting a cytotoxic response are reduced as most of the material mass they contain is water. Generally, if the amount of water within a hydrogel exceeds 80%, it's considered high water content. As part of a research programme to create dynamic supermolecular assemblies through molecular recognition processes, Oren Scherman's group is now able to make dynamic hydrogels that are 99.75% water.

These dynamic hydrogels are based on cucurbit[8]uril (CB[8]) host molecules. These barrel-shaped molecules act a little like molecular handcuffs, by containing two different things within them at the same time. 'If the two are attached to polymer chains, it is possible to bring the polymers together to form a hydrogel,' Oren explains. 'We simply add functional groups to a wide variety of polymer backbones, which enables us to bring large quantities of material together through the CB hosts, and start structuring it as a network material.'

The key to creating the network of material is the addition of those cucurbituril barrels, he says. 'Once we sprinkle in the magic dust of the cucurbituril, it brings the polymeric materials together and acts as a network former,' he says. 'We can then control the properties of the material, based on the ratios of the cucurbiturils to the functional polymers we put in.'

At first, the polymers they used to make the hydrogels were fairly simple, but now they have expanded the substrate range to include renewable materials such as celluloses, lignin and even hyaluronic acid – precisely the types of materials that are compatible with biomedical applications and devices. 'We're starting to take our chemistry and make it much more generic, so it can be applied to whatever type of polymeric backbone or cheap materials are necessary for the final product,' he says.

The cucurbiturils themselves are synthetic macrocycles, and Oren's group can now make them at a significant scale. 'We've managed to find ways to manufacture, separate and purify the larger cucurbituril homologues CB[7] and CB[8] at a multikilo scale,' he says. 'This was very challenging in the past, as the separation technology was based on classical precipitations and re-crystallisations. Instead, we exploited supramolecular host-guest chemistry in our separation strategy. A number of companies have said they are interested in licensing the technology, as there are a variety of potential commercial applications ranging from viscosity modifiers in oil-field uses, for long-term drug-delivery formulations, and in the construction of self-assembled microcapsules.'

Photo: Nathan Pitt

Perhaps the most important potential applications are in drug delivery, and they have recently found it is possible to deliver both small and large proteins over very long time periods – not just a couple of weeks or months, but six to eight months. As the hydrogels are dynamic, with the crosslinks constantly forming and falling apart, the matrix that holds the proteins or other cargo enables a much slower delivery, while keeping the biomolecules folded and in their active form. This has enormous potential – protein drugs generally have to be given by injection or infusion, and if a single depot injection or an implant of hydrogel could be given which then releases slowly over time, this would dramatically reduce the number of injections a patient needs to receive for long-term treatment.

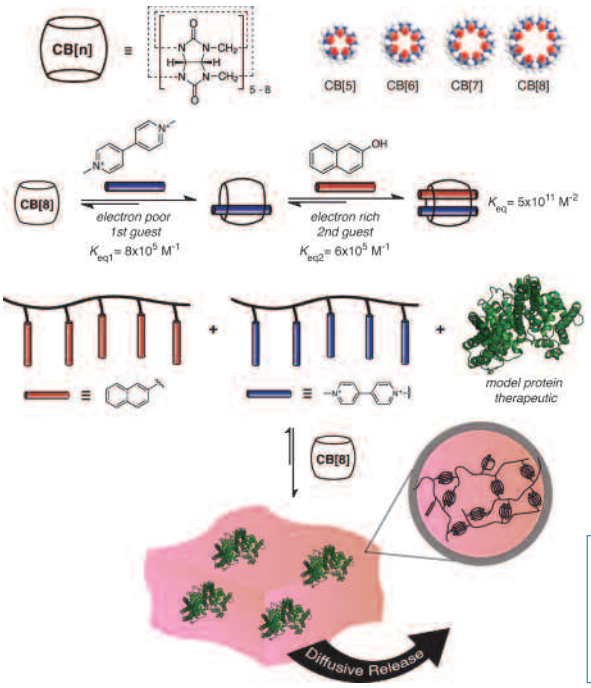
'Essentially, we can tune the delivery of proteins and other materials from micrograms to milligrams a day,' he says. 'For example, people with type II diabetes might be able to have insulin administered just twice a year, with the insulin slowly released into the bloodstream. We are now working on systems with active feedback such that the release rate can be tuned or controlled by environmental factors.'

Because of the structure that the hydrogels provide, it might also be possible to use them in the treatment of brain cancer. 'We're working on this with Colin Watts in the Cambridge Centre for Brain Repair,' he says. 'As a neurosurgeon, he carries out open brain surgery to remove cancerous tumours, but this leaves behind a void within the brain which must be filled, and we're really excited about the potential of our hydrogels here. Because we can tune their mechanical properties to make anything from a really hard structure to a squashy jelly material, they could provide the necessary structure to match the mechanical properties of the surrounding brain tissue.'

But that's not all – it might be possible to use the implanted hydrogel to release anticancer drugs slowly to the site of the removed tumour to kill any remaining cancer cells. So it wouldn't just be a space filler – by delivering drugs it enables a two-pronged approach to cancer treatment.

Another feature of these hydrogels is that the high water content and their dynamic nature causes them to shear-thin. This means that when you apply a shear force to them they become more liquid, before recovering their viscosity – a little like non-drip paint.

'You can put them into a syringe, apply a shear force by pressing the plunger, and the mixture becomes liq-



Below: structure of the curcubiturils and the formation of a hydrogel, enabling the slow release of medications

Image: Eric Appel

uid allowing for delivery through a very small needle, before reassembling into a gel,' Oren says. 'These materials are some of the fastest recovering materials we know of, and they recover their gel structure within three to four seconds after injection. So as well as having great potential in biomedical applications, they could even be used to make self-healing materials and coatings.'

Another exciting area of research is a collaboration with Chris Abell's group that uses the fast self-assembly capabilities of functional materials with CB[8] to create hollow microcapsules templated from perfectly monodisperse microdroplets formed at the rate of several hundred to several thousand per second within microfluidic devices. 'What's unique about these microcapsules is that the functional polymeric materials can "find" each other at the water-oil interface of the microdroplet in an amazingly short amount of time – often in less than one one-thousandth of a second,' he says. 'That's how the hydrogels themselves dynamically assemble.' This work was published in the journal *Science* earlier this year.

At first, they thought they would create many different types of jelly beads, by controlling the amount of each of the two functional materials and the cucurbit[8]uril that went into each microdroplet within the microfluidic device. This, they believed, would allow them to tune the properties of the beads all the way from really soft jelly-like materials to extremely strong hard glass beads. To their surprise, that's not what happened – instead they ended up with hollow capsules.

'All the materials that have the ability to interact with each other make their way to the water/oil interface of the microdroplet,' Oren explains. 'A microfluidic device puts a flow of water perpendicular to a flow of oil, causing droplets of water to form that are all identical in size and volume, and they continue to flow in a field of oil. Prior to the oil phase meeting the water phase, several streams of water can combine into one, so all the functionalised materials are added in separate water streams, and then meet up just before the 90° junction with the oil phase. This causes aqueous droplets to form with all of the necessary components in the water phase within the droplet, and each droplet is surrounded by oil. So the water/oil interface exists for each and every droplet and all of the assembly components then do their magic, forming hollow capsules.

'They do this so fast because of the interactions of the guests. These are the specific chemical functional groups that act as guests for the CB[8] host molecules we put on the different materials. The barrel-shaped cucurbit[8]uril molecules pull them together, and because it is so fast the microcapsules they form are perfectly hollow.'

In the past, making hollow microcapsules like this was an elaborate process, akin to making papier mâché – taking a form, covering it with layer upon layer upon layer of material, then pulling out the original form, leaving behind a hollow structure. 'This way, we can make tens of thousands of these hollow capsules in a very short amount of time,' Oren says. 'We can control the size, and if we put an additional inlet into the microfluidic device that carries a cargo which does not interact with either of the functional or the CB molecules, it becomes encapsulated inside the hollow interior of the microcapsule.

'It's a great way to make a "shrink wrap" around pretty much anything you like as a cargo. We're really excited about its potential, and are now in the process of setting up a spin-out company to take the technology further. There are so many possibilities – we could encapsulate anything from cells to viruses to RNA or DNA.'

Another collaboration Oren's group has recently entered into is with Jeremy Baumberg in the Cavendish, whose speciality is nanophotonics. They've found that, because the cucurbitrils are rigid and hollow, they can act as passivating agents. 'It allows hard spheres or metal nanoparticles to come within 0.9 nm of each other – the height of the curcurbiturul molecules,' he says. 'It gives extremely high optical field intensities for sensing small molecules, and especially apolar polyaromatic hydrocarbons in water such as contaminants in water reserviors, but it also allows us to start doing chemistry in between the voids between the metal nanoparticles . It's a really new area, and we've filed several patents on the work.'

There has been a tremendous amount of commercial interest, he says, because there is potential to detect small molecules including important structures such as neurotransmitters and hormones right down to the parts-per-trillion level.

'We're now looking at trying to use this to look directly at blood, plasma or urine samples for analysis, where it has the potential to be several orders of magnitude more sensitive than existing techniques,' he says. 'For example, samples being tested for performance enhancing drugs first have to be prepared before the test is carried out, adding a manual step to the process. Here, it should be possible simply to take the unprepared sample, and subject it directly to the test , making the whole process cheaper, quicker and easier.'

Photo: Caroline Hancox

Left: Oren's group. Top row, from the left: Tim King, Xian Jun Loh, Maggie Tsai, Nan Zhao, Paul Williams, Louisa Quegan, Yang Lan, Emma-Rose Coad, Setu Kasera, Chi Hu; bottom row: Zarah Walsh, Anna Andreou, Feng Tian, Vincenzo Spalluto, Dezhi Jiao, Fiona Christie, Frank Biedermann, Silvia Sonzini, Chris Toprakcioglu, Jesus del Barrio, Urs Rauwald and Eric Appel

Oren Scherman

CV

Born: Norman, Oklahoma, US

Status: Oren and his partner, architect Sandra Leythaeuser, have two children – Julius, who's nearly 3, and 18-month-old Benjamin

Education: He studied chemistry at Cornell University in the US, including stints abroad at Bayer in Leverkusen, Germany and at the Technion Institute in Haifa, Israel. His PhD was with Bob Grubbs at Caltech, working on catalyst design and functional polymer synthesis using ring-opening metathesis polymerisation.

Career: He spent two years as a postdoc with Bert Meijer in Eindhoven, and came to Cambridge as a lecturer in in October 2006, being promoted to reader this year. Since 2010, he has been the acting director of the Melville Laboratory for Polymer Synthesis.

Interests: He claims he used to have an exciting life, but then he had kids! Much of his precious spare time recently has been taken up by renovating the house he and Sandra have just bought in Cambridge. 'It's incredible how much time interacting with the contractors takes up!' he says.

Did you know? Oren received his 'indefinite leave to remain' in the UK status in August last year, after passing the Life in the UK test. While he has become a true convert and even takes his tea with milk, he says the authorities insist on a better accent and manners before UK citizenship (and passport) will be granted!

Chemistry for kids...

The department open day is a chance to show kids how much fun chemistry can be. Nathan Pitt and Gaby Bocchetti took the pictures that prove it!

Our annual open day, part of the university-wide Science Festival in March, was once again a roaring success, with hundreds of children and their parents flocking to the department to find out how exciting chemistry is.

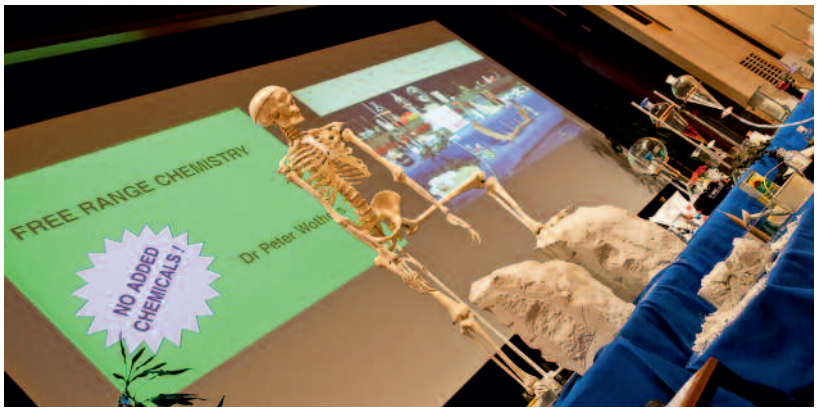
This year, Peter Wothers' demonstration lecture was entitled 'Free range chemistry – no added chemicals'. Many people associate the word 'chemical' with evil, man-made substances. The action packed lecture featured flashes and bangs made only from the chemicals that can be found in nature, illustrating the fact that our whole world is made of chemicals. How can copper be extracted from a semiprecious stone? What acid can be made from fools gold? And how can the scrapings from the walls of a cowshed cause an explosion? Amid loud bangs and explosions, those lucky enough to have tickets to the talks found the answers to these questions – and plenty of others.

As well as multiple performances of Peter's lecture, visitors could experience chemistry in action via hands-on experiments and demonstrations.

Cornflour Slime showed just how amazing cornflour can be when it's mixed with the right ingredients – run on it and it's solid as a rock, but keep still and you'll sink like one! The kids could also test out Cryocream, where demonstrators showed how to make instant ice-cream with liquid nitrogen. Other highlights included the opportunity to make blue goo, investigate colourful chromatography, make DNA models and grow crystals.

A display by Atmospheric Science, British Antarctic Survey, and the Facility for Airborne Atmospheric Measurements gave an insight into how scientists in Antarctica can help scientists in Cambridge understand the Earth's climate and how it has changed. Visitors could learn about volcanoes and local pollution, understand the atmosphere and climate, experiment with state-of-the-art atmospheric sensors, and find out about life in Antarctica.

Our grateful thanks go to the Walters Kundert Charitable Trust for their generous support of the day once again, and also to all the volunteers who made it possible.

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Cambridge life in the early 1960s

Dear Editor:
I graduated with a PhD in Organic Chemistry from Cambridge (St. Cath's) in 1964. I was quite obscure, so may not be remembered. I am writing to inform anyone who is interested of my foray into literature.

I have written and self-published an autobiographical novel, 'Amanuensis', that covers not only my growing up in the East End of London and experiences with antisemitism, but the cultural trauma I experienced in going to Cambridge.

In my novel I mention the chemistry department on Lensfield Road, as well as some of the colorful characters I met there. The book is available from Amazon and a description can be found at jackcohenart.com/Bookart.html

Jack Cohen
Formerly Professor of Pharmacology at Georgetown Medical School, Washington DC, US

A few extracts from the chapter on Cambridge follow…

In the beginning, alone... I walked the endless corridors. Finding the laboratory, I entered, with trepidation. Serried ranks of bottle-bedecked benches. The light shattered by the glistering glass. Reflection, aesthetic of science. A group occupied the foreground with their noise. A loud, friendly voice intoned a greeting.

The laboratory covered an entire wing of the chemistry block. To the right the Victorian girth of Cambridge, which even in the bright sunshine affected a grey, sombre air. To the left directly below, stood the Scott Institute, dedicated to that chap who did the right British thing. Lensfield Road ran beyond it, and at the corner with the High Road was the large Catholic church. Mercifully, this was almost obscured, except for the spire, by a huge tree. It reminded me of the view from my bedroom window in Bethnal Green. I neither knew, nor cared, what was the species of the tree. Behind the houses across Lensfield Road a glimpse of Downing College was visible.

It was several years since I had come to Cambridge to take the scholarship examinations at Downing. The first bright hope of an earnest new headmaster I had been sent to impale myself upon the sharp spires. It had been an irreversible experience. I had become friendly with two other hopefuls, one from Blackburn, the other from Llandindrod Wells. We were all overawed, but acted cocky.

I had stayed in the room of a scholar who had left books of poetry scattered around. What was a 'metaphysical poet', I wondered. The other two had been in the rooms across the landing. We each had such different accents it was almost impossible to carry on a mutually comprehensible conversation. They had taken me to a pub. It was the first time I had ordered and tried to drink a pint of bitter. When I told them, they couldn't believe it and laughed heartily.

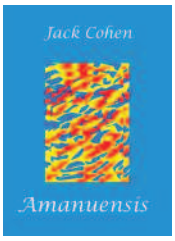
In our shared living room endless discussions ensued, profound and silly, personal and political, literary and scientific, with Cambridge stories about climbing into College after curfew, '

'There was the story, its true mind you, of the chap who had to climb into Christ's very late one night, and I don't suppose you know this, but a very easy way, especially if you're a bit smashed, is up a tree through the window of the Master's Study, across it, and out the window the other side into the quad.

'Well, this chap found the window unlocked so he climbed in, and as he was crossing the room he heard someone at the door, so he dived behind a sofa, and the light went on, and he heard someone moving around, and then sit down and light a pipe and turn some pages and write a bit, and the chap was going bonkers behind the sofa trying not to make a sound. Then eventually the person, presumably it was the Master, got up and walked over to the door, and as he went out he said, "I don't know about you but I think its about time to turn in," and then he switched the light off and went out.'

I arranged for my parents to visit Cambridge. They came up on a Sunday, when the labs were usually empty. That way there was less likelihood of them embarrassing me. As I took them around the chemistry department, showing them the labs and the equipment, they were suitably impressed.

I introduced them to fellow students who were working that day, but I hoped they would not engage in long conversations, 'Hullo,' 'Pleased to meet you,' 'Goodbye,' that was enough. I didn't want my mother gushing about her clever son, or my father showing his lack of education and his cockney accent. Did they realise my apprehension? Was I being openly rude to them? I wanted them to be proud and to enjoy the visit, for they had certainly contributed enormously to the fact that I was there. Yet I was ambivalent. They clearly had no conception of what it was that I actually did, even when I tried hard to explain things. 'Now tell me, does this have anything to do with curing cancer?' my mother asked for the umpteenth time. How could they understand. I could not communicate



with them any more, if I had ever really done so. I now inhabited another world, from which they were excluded.

I steered them around the tourist route, through the historic buildings, the ancient quads, pointing out where Newton had lived, where Blake had trod. I noticed how I now towered over them. I was nearly a head taller than my father. I imagined how ridiculous we must look together, the tall, bearded, gesticulating student and the short plump mother and father, dressed in their Sunday best. In my self-conscious embarrassment I had forgotten that my father's short stature and bowed legs resulted partly from early deprivation, and my own height resulted entirely from their careful nurturing.

When we reached the Backs behind St. John's, looking across towards the soaring King's Chapel, my father surveyed the scene, the elegant greensward, the immaculate gardens, the turreted buildings, the tessellated pavements, and he said, 'They could build plenty of worker's flats 'ere.' I was preparing to explode, when I noticed the gleam in my father's eyes, and we all burst out laughing.

In the lab, I learnt how to do research. It was a mysterious art. Serving new Gods. Synthesising substances that had never before existed. I raised up a flask and shouted, 'with this I could conquer the world!' But, in retrospect I was glad that I had chosen to work with molecules rather than men; molecules were more predictable.

I weighed out the fine white powder. Carefully I sprinkled the grains of the precious substance onto the non-absorbent paper. The balance pan oscillated as I released the counter-weight. It was well damped and equilibrated quickly. The luminous dial showed the weight to the fourth decimal place ...0.3671 ...0.3673 ...0.3675 ... 'Does the precise value matter, does it really mean anything,' I mused as I watched it slowly alter.

The sun was shining brilliantly through the large window, making the small weighing room very stuffy. I went to the window and stared dreamily across at the great tree waving in the wind and the white clouds skiffing behind it. Needing to feel the cool breeze upon my face I turned the latch and flung the window wide open. I leaned out and luxuriated in the combination of cool wind and warm sun.

Someone entered the weighing room. As the door opened there was a strong draught. The unattended balance klunked, and the fine, white powder flew from the pan into the air, an ephemeral sparkling cloud.

A brace of bouncing babies

Aileen, Graeme and Leela (left), and Eric, Nicki and Paxton (right). Aaaaaaaaaah!

It's a double dose of beautiful babies this issue. First up is Leela Ann Day, daughter of research fellow Graeme Day and his wife Aileen. She put in her appearance late in the evening on 4 April at the Rosie maternity unit at Addenbrooke's, weighing in at 7lb15oz.

'She's very cute,' says not-at-all-biased dad Graeme. 'She smiles a lot, and is already starting to talk – not that we understand what she's telling us!' And she's even now letting him get some sleep. The family will soon be leaving Cambridge as Graeme's been appointed a reader at Southampton. So it's congratulations all round!

Baby number two is Paxton Stanley Appel, son of Eric – a PhD student in Oren Scherman's group – and his wife Nicki. Born on 24 May, also at the Rosie, he weighed in at 3.03kg in Euro-babyunits (that's about 6lb9oz in UK-babyunits).

Dad Eric reports that the funniest thing about him is his hair – it always seems to be styled as a mohawk, whatever they try to do with it. 'He also grunts a lot in his sleep,' Eric says. 'This makes us wonder if he'll talk in his sleep when he's older!'

What a waste (store)!

Photos: Nathan Pitt

A new chemical waste store arrived earlier in the summer, giving Nathan Pitt a great excuse to take some photos of the crane-related palaver involved in getting it into place.

The new temporary structure replaces the old temporary structure, which was rotting away and not big enough. The new waste store is 50% larger, is plumbed in to the building's fume cupboard extraction system, and comes complete with automatic fire detection sensors.

It's due to be replaced with a permanent store in the new Chemistry for Health building, once that has been constructed.

A theatrical interlude

Photo: Nathan Pitt

From the left: director and author Carl Djerassi, Michael Fenner, Jack Klaff and Nicola Bryant

The Wolfson lecture theatre played host to something a little different from its usual chemistry talks in May – a reading of the play 'Insufficiency' by chemist Carl Djerassi.

Perhaps best known for his pioneering work on the contraceptive pill in the 1950s, Djerassi is emeritus professor of chemistry at Stanford University, and also a member of the Cambridge Chemistry Advisory Board – and also a playwright and author.

Described as a play of 'academic manners and fashion in science', Insufficiency deals with the science of 'bubbleology' as applied to champagne and beer bubbles, and whether an assistant professor can obtain tenure working on such a specialised topic.

The parts were read by actors Jack Klaff, Mark Oosterveen, Nicola Bryant (who will be familiar to Doctor Who fans as the Doctor's assistant Peri back in the mid-1980s), and Michael Fenner.

We have all experienced individuals whose personalities and behavour have influenced the way we live and work. In the first of this new series, Jeremy Sanders reflects on four of the very different people who have had a major impact on the way he works and thinks

As Pro-Vice-Chancellor, I am responsible for all of the University's 9000 staff. Sometimes, one can feel bogged down in bureaucracy, legislation, dispute and process, but in the end the job is about much more than that: my heroes and mentors showed me that supporting and inspiring people is just as satisfying as the thrill of discovering new science.

Dudley Williams was my PhD supervisor from 1969–72, and then colleague and friend for the rest of his life. The relationship between supervisor and research group is surely one of the greatest pleasures of academic life, and Dudley showed us that we are privileged to have an academic family as well as a biological family.

Dudley gave us scientific freedom, while also ensuring that everything we did was worth doing. He challenged our sloppy thinking and lazy responses. 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 taught by example how to write well, and showed us that good illustrations are the best way of communicating difficult ideas.

Unlike some other supervisors he treated his research group as friends, people and equals. He was hugely proud of his students and postdocs, and he took great pleasure in our successful careers.

Ralph Raphael was the head of department who appointed me in 1973. I first met him a year earlier when we were both newly-elected fellows of Christs: I had just finished my PhD and he was arriving in Cambridge as the new 1702 Professor.

I expected to be overawed and even intimidated by him, but he surprised me through his informality and his enthusiasm for my first publications. That freshness never left Ralph: just weeks before he died he noticed a new paper of mine in the library and then came to congratulate me.

He still delighted in my new molecules and particularly in our use of acetylenes – he would engage in my chemistry in a way that is supposed to happen between colleagues all the time, but rarely does.

Ralph would hate the word manager, but he taught me by example how to be simultaneously hard-headed and humane, and why it is at least as important to care about secretaries and technicians as it is to look after academic staff.

He seemed to know instinctively what one was good at, and to know how to channel that talent; by putting me on the Faculty Board in 1981 he set me on the path leading to my present role. Ralph defined his success not in selfish terms of his own scientific or monetary triumphs but the collective success of his department, and above all in the success of his young appointees.

Ruth Lynden-Bell taught me much about NMR spectroscopy, especially about spin-lattice relaxation, in the 1970s, enabling me to be one of the first organic chemists to make practical use of this "new" dimension of NMR to assign spectra and solve structures.

Ruth was – together with Anthony Stone – one of the few theoreticians willing to engage with the questions of ordinary practical chemists like me. More importantly, despite her frustration at not being appointed to the lectureship she so clearly deserved, she took a full part in the life of the department.

In particular, I was influenced by the way that she chaired examiners' meetings: brisk and to the point, but thorough and fair. I realised that one could chair even boring committees in such a way that everyone finished the meeting in a good mood, feeling that they had done something worthwhile.

Ruth moved to a physics chair in Belfast in 1995, but on her retirement she returned to chemistry in Cambridge: she is still active in research, still helping others, cycling regularly to and from Murray Edwards College where she is acting president.

Sidney Sanders is my dad, 90 years old and still an inspiration. Family circumstances forced him to leave school at 16 and get a job. By the age of 19 he was married to my mother, and working as a clerk in an office.

His potential was spotted when he had to join the RAF in 1942, and by the end of the Second World War he had been trained to repair radios, could touch type, was editor of his squadron magazine and had taught himself music.

By the time he retired in his 70s he was a much-loved company director who inspired loyalty and affection in all who worked with him. After my mother died in the 1980s he married Miriam, and he has now been happily married for a total of more than 70 years.

Today he uses the internet and email to organise University of the Third Age concert trips for up to 50 people, sings in his synagogue choir, runs financial spreadsheets, and helps others wherever and whenever he can. He also stills irons his own shirts...

Last issue's solutions

Chemdoku

We had another bumper crop of entries from our keen Chemdokuists. Most spotted that the link between the elements was that the symbol derived from a non-English name – one or two suggested that the link was merely that they were metals, but that's a little too unsubtle for us here at *Chem@Cam*. Though maybe one day we'll surprise you!

Anyway. Correct entries came from: Ian Fletcher, Richard Chambers, Tom Banfield (who admits that, as he's directly done no chemistry whatsoever since finishing his PhD in 1968, he has no idea what the link is), Godfrey Chinchen, David Wilson, Norman Sansom (who asks if *Chem@Cam* has been watching the BBC quiz programme 'Pointless' as they had a very similar question about elements with a chemical symbol, the letters of which do not appear in the common English name. *Chem@Cam* loves Pointless and is delighted that their question setters are clearly Chemdoku fans), Dave Stone, Diana Sandford, Tim O'Donoghue, Neil Mckelvie (who reports that Chemdoku took a valuable half-hour out of his piano practice time – back in 1949 he had to choose between medicine at Cambridge or the Royal Academy of Music as a pianist; he didn't care for a life of piano practice and didn't fancy cutting up cadavers, so ended up in organic chemistry. Now he's an 81-year-old emeritus prof, it's back to the piano!), Paul Littlewood, Bill Collier (who wonders if this is why O-level Latin was required for entry to Cambridge 56 years ago), John Wilkins, Kim Whittaker, John Turnbull, Jim Dunn, A.J. Wilkinson, Keith Parsons, Helen Stokes, and Peter Keefe. *Chem@Cam*'s office pest (a cat called Ginola, who even has her own Facebook page, which she writes in lolcat, of course) picked out lucky £20 winner by sitting on it, and it came from Neil Mckelvie. As he's in the US we might even magic it into $30.

Missing element

Karl Railton-Woodcock's puzzle was clearly one of those some people got immediately, judging by the speed at which some of the entries arrive. The link between the elements is, of course, that they're all also two-letter abbreviations of US states. And the missing element was mendelevium, or Md, aka MD or Maryland. Correct answers came from: Paul Cheshire, Mike Forrest, Richard Moss (who adds that for non-states, we could also have had fermium/Fm for the Federated States of Micronesia, and curium/Cm for the Commonwealth of the Northern Mariana Islands), John Nixon, Kim Whittaker (who adds praseodymium/Pr for Puerto Rico and arsenic/As for American Samoa), John Wilkins, Paul Littlewood (who said that the puzzle wouldn't have worked had the discoverers of Md had their way, as they wanted it to be Mv!) and Richard Chambers. The feline winner-picker sat on Paul Littlewood's entry, so the £20 is his.

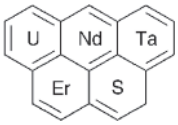
PVC labelling

Unsurprisingly, Graham Quartly's dodecahedron puzzle garnered fewer solutions – but three readers got their heads around it. In third place, Ian Fletcher came up with two 19-letter compounds that could be spelt around the dodecahedron – phosphorus pentoxide and phosphoric anhydride. In second place was Keith Parsons, who suggested the 25-letter chloroacetylglycylglycine. But the winner is David Wilson, who came up with vinylcyclopropylacetoacetate, with 27 letters. For good measure, he submitted an extract from an academic paper authored by himself and Professor Haddock entitled 'Goflyakiteanes: a new class of molecules subject to dodecahedral folding', in which they report an analogue with a chain of cyclopropanes, and a 105-letter name including 'cyclopropyl' a lot of times. We leave it to readers to construct the molecule and work out why the trivial name is goflyakiteane!

This issue's puzzles

Olympic Word Record

To celebrate the glorious year in which olympicene was first produced, here's a chemical puzzle from Graham Quartly very loosely based on its structure. The picture shows the five carbon rings each containing a single atom indicated by their symbol. Following a path between neighbouring cells, returning to some as needed, one finds the 11-letter word 'UNdErSTaNdS'. What is the longest word that can be traced through the rings by moving to adjoining cells?



£20 prizes are on offer for each puzzle. Send entries by email to jsh49@cam.ac.uk or by snail mail to Chem@Cam at the address on p3

ChemDoku – ahaaaaa!

				Ra			Ca	Ta
Na								
		Ba	Na			Pa		
			Ga			Ca	Na	
	La	Pa			Ma			
		La			Ba	Ga		
								La
Ca	Ra			Ta				

Finally, a spot of Chemdoku. Lots of As this time, with one archaic symbol. Which?

The Corporate Associates Scheme

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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:

- 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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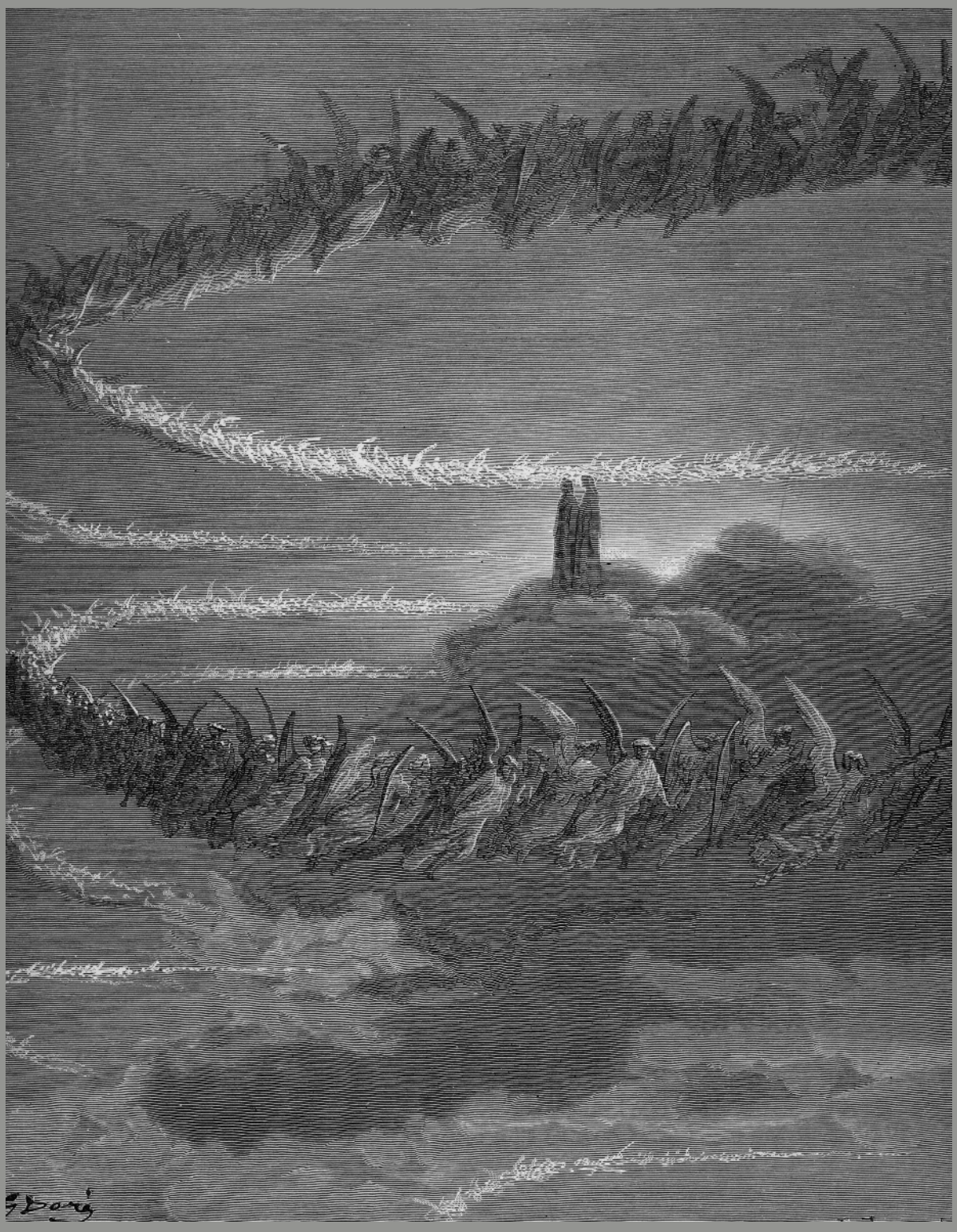

Aha! So **that's** what you mean by dynamic assembly!

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