chem@cam

Chemistry at Cambridge Magazine
WINTER 2021 | ISSUE 63
www.ch.cam.ac.uk

Focus on spin-outs

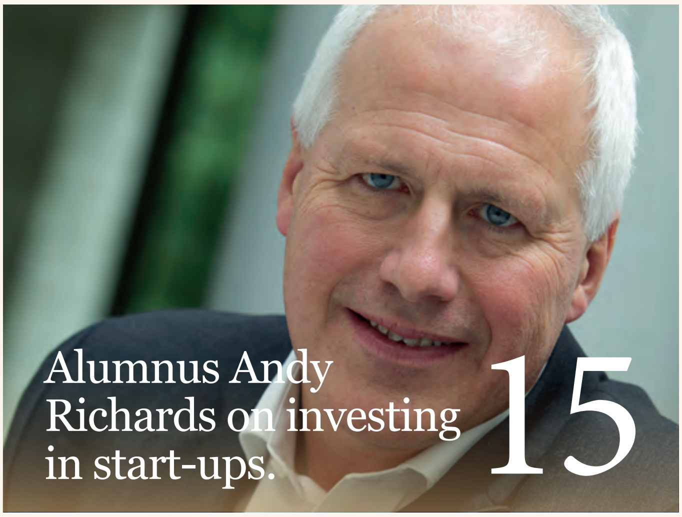
UNIVERSITY OF CAMBRIDGE

Contents

XAMPLA

NYOBOLT

AS I SEE IT



RESEARCH

Springing forward

The start of Michaelmas Term has really brought the Department back to life, and there is a welcome bustle about the place.

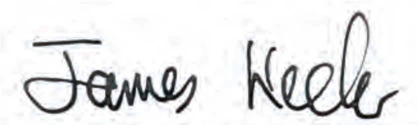
The undergraduates are back doing practicals and projects, lectures are being given in person, and supervision groups are dotted around the Department as the afternoons wear on. We have not thrown all caution to the winds though – we wear face coverings, keep to the left in corridors, and sit rather far apart in the Cybercafé. But all in all, things are pretty close to normal and it feels good.

This issue of Chem@Cam focuses on some of the many commercial ventures which have been 'spun out' by our researchers over recent years. The number and scale of these ventures is a testament to the energy and vision of our colleagues, and shows that our work is not only of the highest scientific and intellectual calibre but also that this excellence can be translated into real-world benefits.

I'm sure I won't be contradicted if I identify Solexa-Illumina Next Generation Sequencing as the most impactful and far-reaching spin-out from the Department so far. Co-inventors Shankar Balasubramanian and David Klenerman have been honoured with two major international prizes this year in recognition of the far-reaching impact that their invention continues to have (p. 5).

Elsewhere in this issue you can read about how our postgrads and postdocs are taking advantage of the Cambridge ecosystem to develop their own ideas, and Michele Vendruscolo reveals the innovative way in which a commercial partnership between the Centre for Misfolding Diseases and Wren Therapeutics benefits research in both directions (p.12).

There just isn't space in this one issue to cover all of the interesting spin-out activities which have originated in the Department, so we will continue to highlight more in future issues. And as always, there is much else to read about, including recent prizes and student and alumni activities. I hope you enjoy reading it all.



James Keeler
Head of Department

Cover photo Knowles group researcher Ayaka Kamada displays Xampla's revolutionary plastic substitute made from biodegradable vegetable waste products, courtesy Department of Chemistry.

Chem@Cam
Yusuf Hamied Department of Chemistry
University of Cambridge
Lensfield Road
Cambridge CB2 1EW

T 01223 761479
E news@ch.cam.ac.uk
W www.ch.cam.ac.uk
@ChemCambridge

Views expressed in this magazine are not necessarily those of the Editor, the Yusuf Hamied Department of Chemistry or the University of Cambridge.

Print: Orchard Press

2021
Yusuf Hamied Department of Chemistry
University of Cambridge
Chem@Cam is published twice a year, and is sent free to chemistry alumni, postdoctoral researchers, retired staff and friends of the Department.

CONTRIBUTORS

Diane Harris
Editor

Nathan Pitt
Head of Photography and Reprographics

Gabriella Bocchetti
Photographer

Contributors:
Sarah Collins

Focus on spin-outs

In this issue we are taking a behind-the-scenes look at what makes the Department so successful at "spinning out" our basic research into profitable companies that are also helping to provide solutions to some the world's most urgent problems from climate change to plastic pollution and chronic diseases.

Chemistry spin-out Pharmenable co-founders from right: Dr Hannah Sore (CEO, PharmEnable), Dr Natalia Mateu (Chief Scientific Officer, PharmEnable), Dr Andreas Bender and Professor David Spring.

Two rising stars to keep an eye on are Knowles Lab spin-out Xampla (p. 6), who are producing a biodegradable material as strong as engineering plastic that could replace plastics in many areas, and Grey group spin-out Nyobolt (p. 8), which is developing fast-charging, high powered batteries using more environmentally friendly materials to help power the carbon-neutral future.

We wanted to know what it takes to develop an initial idea into a business, so we've asked members of the Reisner group to talk about their first steps towards commercialisation, and we explore how the Centre for Misfolding Diseases has created a mutually beneficial two-way flow of research and ideas with spin-out Wren, based in the innovative Chemistry of Health incubator.

The Financial Times has said "Cambridge is having a moment" with money pouring into the newly dubbed "Silicon Fen", so we've talked to Cambridge Enterprise to find out how they are helping researchers to harness this support. And chemistry alumnus Andy Richards explains what he is looking for as an investor.

We don't have space to write about all our spin-outs, like PharmEnable, which uses advanced medicinal chemistry and artificial intelligence to design potential drug therapies (a 'hot theme' according to Andy Richards), Cambridge Photon Technology, which is developing new materials to improve solar panel efficiency, and Healx, which is re-purposing existing drugs to fight rare diseases, but you can read about them and other Chemistry success stories on our Collaboration and Impact pages (www.ch.cam.ac.uk/collaboration-and-impact).

More kudos for DNA sequencing revolution

In September Professors Sir Shankar Balasubramanian and Sir David Klenerman were awarded the 2022 Breakthrough Prize in Life Sciences for their development of Next Generation DNA sequencing.

Millennium Technology Prize

Shankar and David, who share the prize with Pascal Mayer from the French company Alphanosos, co-invented Solexa-Illumina Next Generation DNA Sequencing (NGS), technology that has enhanced our basic understanding of life, converting biosciences into 'big science' by enabling fast, accurate, low- cost and large-scale genome sequencing – the process of determining the complete DNA sequence of an organism's make-up.

The benefits to society of rapid genome sequencing are huge. The almost immediate identification and characterisation of the virus which causes COVID-19, rapid development of vaccines, and real-time monitoring of new genetic variants would have been impossible without the technique they developed.

The technology has had – and continues to have – a transformative impact in the fields of genomics, medicine and biology. One measure of the scale of change is that it has allowed a million-fold improvement in speed and cost when compared to the first sequencing of the human genome. In 2000, sequencing of one human genome took over 10 years and cost more than a billion dollars: today, the human genome can be sequenced in a single day at a cost of less than $1,000. More than a million human genomes are sequenced at scale each year, thanks to the technology, meaning we can understand diseases much better and much more quickly.

Earlier this year, Shankar and David were also awarded the Millennium Technology Prize. Together they co-founded the company Solexa to make the technology available to the world. What could be a better example of turning research into a real-world application that can improve lives?

A sustainable alternative to single-use plastics

Spin-out Xampla is developing a plant-based, sustainable material that could replace single-use plastics in many consumer products.

Researchers in the Knowles group have created a sustainable, scalable material that is as strong as the most common plastics in use today.

To do this, they developed a new approach for assembling plant proteins into materials which mimic silk on a molecular level. The energy-efficient method, which uses sustainable ingredients, results in a plastic-like free-standing film, which can be produced at industrial scale.

The new material is home compostable and will degrade naturally in a marine environment and in fresh water. Non-fading 'structural' colour can be added, and it can also be used to make water-resistant coatings.

The new product will be commercialised by Xampla, a Knowles group spin-out which develops replacements for single-use plastic and microplastics.

Professor Tuomas Knowles says: "One of the key breakthroughs is that we can now control the assembly of natural plant proteins into technologically useful structures. We can also now do this in a scalable way, which is critical to actually be able to start replacing plastics in real world applications."

From left: Researchers and product developers Marc Rodriguez Garcia (now Xampla's Head of Research), Ayaka Kamada and Tuomas Knowles.

Proteins behaving badly

For many years the Knowles group has been conducting basic research into the behaviour of proteins. Much of the research has been focused on what happens when proteins misfold or 'misbehave', and how this relates to health and human disease, primarily Alzheimer's disease.

"We normally investigate how functional protein interactions allow us to stay healthy and how irregular interactions are implicated in Alzheimer's disease," says Knowles. "It was a surprise to find our research could also address a big problem in sustainability: that of plastic pollution."

Strength out of weakness

As part of their protein research, Knowles and his group became interested in why materials like spider silk could be so strong when they had such weak molecular bonds. "You'd think to obtain strong materials you'd need strong interactions between building blocks, but the building blocks of spider's silk are based on weak, non-covalent interactions," explains Knowles.

"We found that one of the key features that makes spider silk strong is that the non-covalent hydrogen bonds are arranged regularly in space and at a very high density."

When Dr Marc Rodriquez Garcia joined the group as a postdoctoral researcher, he began looking at how to replicate this regular self-assembly in other proteins. Proteins have a propensity towards molecular self-organisation and self-assembly, and plant proteins in particular are abundant and can be sourced sustainably as by-products of the food industry.

Rodriguez Garcia was joined in the project by Ayaka Kamada, when she started her PhD in the group four years ago. "I was inspired by the potential of this idea," says Kamada. "Very little is known about the self-assembly of plant proteins, and it's exciting to know that by filling this knowledge gap we can find alternatives to single-use plastics."

Gousto

Xampla announced in October that meal subscription box retailer Gousto will trial an edible stock cube wrapper.

"We were inspired to ask: 'Can we generate silk-like structures from building blocks that were not related to silk at all?'" says Knowles. "In principle, this should be possible, but it was not clear if it was practical – that's the project that Ayaka and Marc took on and have now shown in spectacular fashion that this is possible."

A vegan spider?

The researchers can successfully replicate the structures found on spider silk, by using a protein with a completely different composition. "Because all proteins are made of polypeptide chains, under the right conditions we can cause plant proteins to self-assemble just like spider silk," says Knowles. "In the spider, the silk protein is dissolved in an aqueous solution, which then assembles into an immensely strong fibre through a spinning process which requires very little energy – those are all characteristics we keep. Even on a single-molecule level, the material looks like silk."

"Other researchers have been working directly on silk materials, but they remain an animal product with issues relating to sustainability. In a way we've come up with a 'vegan spider' – we've created the same material without having to have the spider."

The alchemy of protein assembly

The researchers initially chose soy protein isolate (SPI) as their test plant protein, since it is readily available as a by-product of soybean oil production. The new technique uses an environmentally friendly mixture of acetic acid and water, combined with ultrasonication and high temperatures, to improve the solubility of the SPI. Xampla now uses protein feedstocks from other plants such as pea and potato, and is identifying future protein sources from traditionally low-value plant by-products such as rapeseed cake, an agricultural waste.

The new method produces protein structures with enhanced inter-molecular interactions guided by the hydrogen bond formation. In a second step the solvent is removed, which results in a water-insoluble film.

"It's almost like alchemy – you start with a very uninteresting-looking brown powder that is not even soluble in water. First you must disassemble it and re-assemble it in a completely different way. It's not a straightforward process and If you don't get self-assembly, it just crumbles," says Knowles. "But with the technique developed by Marc and Ayaka, you end up with an incredibly high-performance material, equivalent to high performance engineering plastics such as low density polyethylene. And the self-assembly occurs not just on a molecular scale, but also on a metre scale and more."

"This is the culmination of something we've been working on for over ten years, which is understanding how nature generates materials from proteins. We didn't set out to solve a sustainability challenge – we were motivated by curiosity as to how to create strong materials from weak interactions."

Next steps

Xampla already produces biodegradable microcapsules, and will be introducing a range of single-use sachets and capsules later this year, which can replace the plastic used in everyday products like dishwasher tablets and laundry detergent. "We are developing new products all the time," says Rodriguez Garcia, who is now Xampla's Head of Research.

"The key breakthrough here is being able to control self-assembly, so we can now create high performance materials. There's always a gap from discovering something in the lab to making a product, but there's a lot of excitement about taking this type of technology that Ayaka has pioneered and industrialising it.

"It's amazing to realise that a discovery you make in a lab can have a big impact on solving a global problem. That's essentially why we are doing this – we really love the science, but we also wanted to do something meaningful about solving the overwhelming problem of plastic waste."

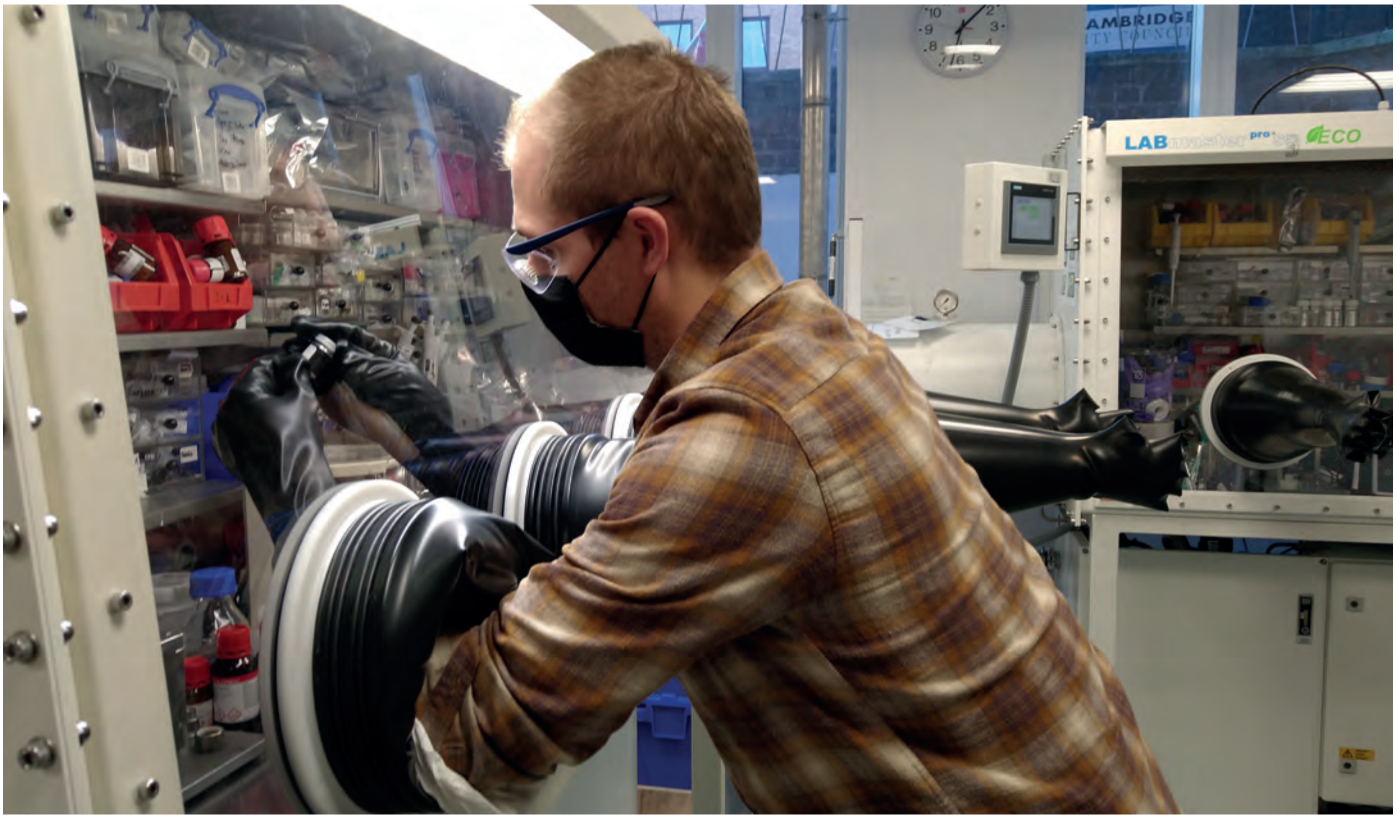
With grateful thanks to Sarah Collins for her contributions to this article.

Research

Controlled self-assembly of plant proteins into high-performance multifunctional nanostructured films, A. Kamada, M. Rodriguez-Garcia, F. Simone Ruggeri, Y. Shen, A. Levin and T.P.J. Knowles, Nat Commun, (2021), **12**, 3529.

Nyobolt: Supercharging the electric revolution

Imagine a future where it takes minutes instead of hours to charge any electronic device. Nyobolt aims to make this a reality with a new range of high-power lithium-ion batteries which use niobium oxides as anode materials.



Evan Keyzer, who completed his PhD in the Grey group, is now Principal Scientist at Nyobolt.

"Our world is very dictated now by the time it takes to charge our portables and how near to a socket we are – if we can rethink that, then it's game changing," says Nyobolt's Chief Scientist Professor Clare Grey, who co-founded the company with Dr Kent Griffith and Dr Sai Shivareddy in 2018 (originally as CB2Tech).

In February Nyobolt secured $10M in Series A funding, which has enabled it to expand its engineering and operational teams, and in addition to its Cambridge base it now has offices in Boston and Asia.

Electric vehicle goal

Nyobolt's ultimate goal is fast charging in the automotive sector. "Asking whether a car will go from Land's End to John o'Groats is the wrong question," says Grey, an internationally recognised battery expert who has won numerous awards for her research (see p. 27). "What we really need is a car that will be charged much more rapidly – that's what we are working towards."

"Asking whether a car will go from Land's End to John o'Groats is the wrong question"

And in a recent partnership deal, Nyobolt will be working with Williams Advanced Engineering, who are well known for their connection to F1 racing, to develop the next generation of battery-powered automotive drivetrains. "We are working with Williams to develop new high powered battery systems using our quick-charging technology, with possible applications in all shapes and sizes from mining trucks to cars," explains Dr Anna Wise, Nyobolt's Head of Strategic Programmes.

The company is also developing applications for small items like power tools and other consumer products for more immediate marketing. "There are myriads of applications where fast charging is important, and as a company we will start small while we work out the challenges," says Grey.

Niobium oxide revelation

Currently the best lithium-ion (Li-ion) batteries typically use either graphite or lithium titanate as anodes, but both have drawbacks. Batteries with graphite anodes are subject to dendrite formation, in which lithium-metal fibres begin to form, hindering performance and even causing batteries to catch fire. Lithium titanium oxide (LTO) batteries are considered much safer because they avoid dendrite formation, but this comes at a cost of lower lithium capacity and full-cell voltage and thus energy density.

Instead, Nyobolt is building on the discovery of niobium tungsten oxides as anode materials, to create super-fast charging batteries. Co-founder Dr Kent Griffith, now a postdoctoral researcher at Northwestern University in Illinois, first began researching the fast-charging behaviour of niobium oxides as a PhD student in the Grey group. "Clare and I initially were purely scientifically interested in these materials and their electrochemical performances for several years. We were excited to try to understand through fundamental research how lithium can move rapidly through materials, which was one of the things that set us off through this journey," he says.

Griffith's research showed that despite being larger than the typical nanometre-sized particles of LTO batteries, niobium oxides have structural motifs which speed up the diffusion or intercalation of lithium-ions, which in turn could provide a quicker charge and ultimately more power.[1] "The lithium transport in niobium tungsten oxide was completely unprecedented and we were really amazed by their ability to give a high-rate battery performance," he says.

Nyobolt prototype batteries.

This led to research published in *Nature* in 2018[2] in which Griffith and colleagues in the Grey group reported that niobium tungsten oxides were surpassing performance of what were considered state-of-the-art LTO batteries.

"Not just incrementally, but substantially. Their ion conduction was orders of magnitude larger than anything we had known," says Griffith.

The larger, micrometre-sized niobium tungsten oxides are not subject to the dendrite issues of other Li-ion batteries. And because the particles are larger and more dense, the electrodes can have higher energy density than LTOs, while at the same time avoiding the complexity and cost of nanoparticles.

"Unlike the nanostructured materials, which have chemical precursors that make it difficult to produce large quantities, we recognised how direct and waste-free the production of these materials was," says Griffith. "They are not rare earth materials, they are non-toxic, and they don't have the associated mining issues of other materials, like cobalt, although cobalt can be present in the cathode material to optimise the configuration of the battery for particular applications."

The future is fast charging

"In addition to super-fast charging, the new batteries can go through many, many charging cycles," says Wise. "It completely changes the way you think about how big a battery must be; enabling smaller, longer-lasting systems which has positive environmental implications, and it means we can look at designing new systems to make the most of this ability. It's a very exciting place to be."

CEO and co-founder Dr Sai Shivareddy says: "We are excited to be building on the discovery of these materials in the Grey group to commercialise a fast-charging battery system. Nyobolt batteries remove the limitations presented by conventional lithium-ion batteries, and provide a solution for applications that require high power and ultra-fast charge. Our strong partnership with the Department of Chemistry and the world-leading research facilities of the University are helping us to take this technology to market in record time."

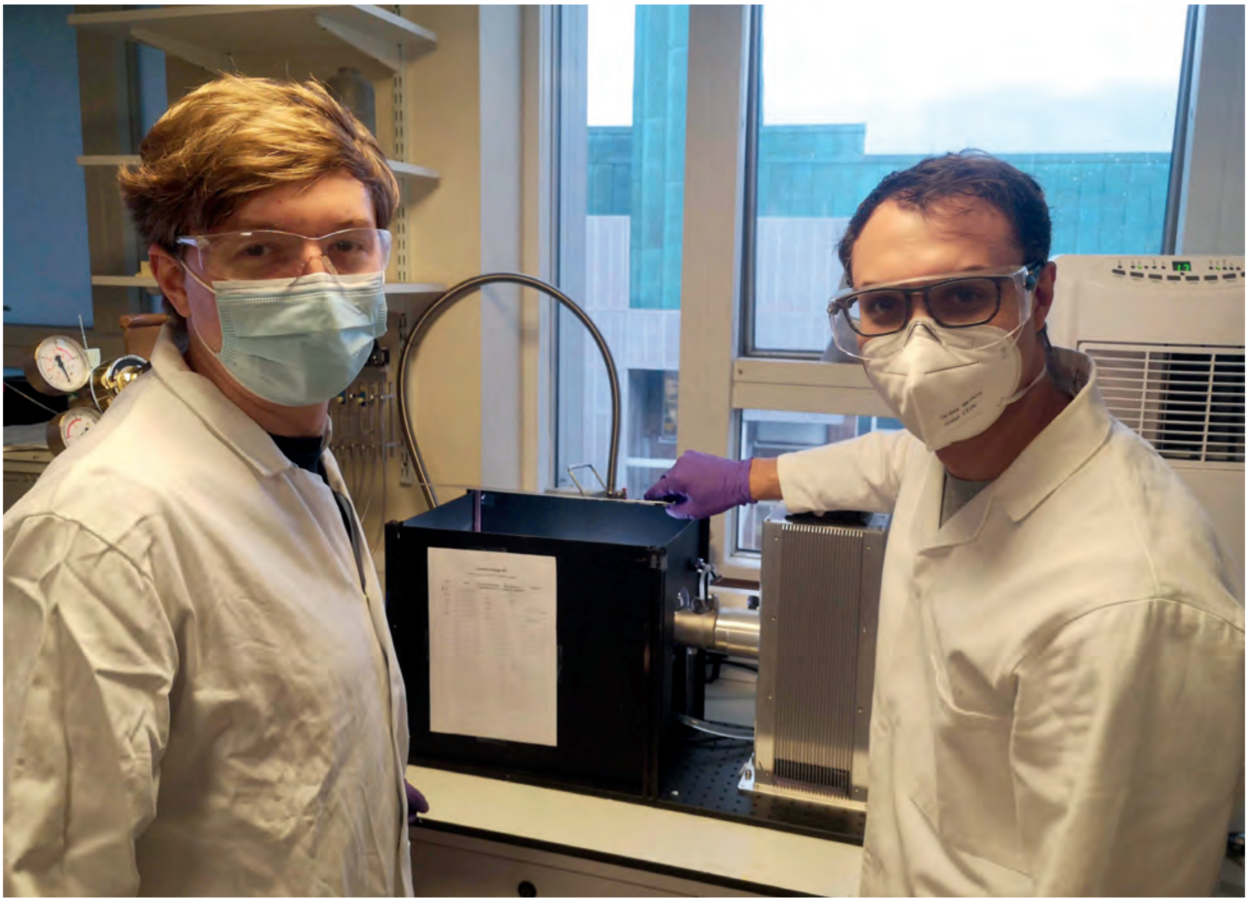
The prospects are exciting: "Our research has implications for high-power applications, fast-charging devices and all-solid-state energy storage systems, electrode design and material discovery. This is a step change in the state of the art of fast charging," says Griffith.

"If you can imagine a battery that can be charged safely, as fast as you have current to put into it, it opens up a completely different paradigm and the world looks very different," says Grey.

Research
[1] *High-Rate Intercalation without Nanostructuring in Metastable Nb_2O_5* Bronze Phases, K. J. Griffith, A. C. Forse, J. M. Griffin & C. P. Grey, J. Am. Chem. Soc., (2016), **138**, 8888.
[2] *Niobium tungsten oxides for high-rate lithium-ion energy storage*, K. J. Griffith, K. M. Wiaderek, G. Cibin, L. E. Marbella & C. P. Grey, Nature, (2018), **559**, 556.

First steps

The long road from brilliant research to a marketable product is dotted with metaphorical potholes. So, what is it like to take the first steps along this path?



The solar light simulator creates realistic operating conditions for testing the catalysts.

Dr Michael Stanton and Dr Stuart Linley are in the early stages of commercialising a photoreforming process developed in the Reisner Lab, which produces hydrogen fuel from plastic waste. They share their experiences here:

Stuart

This comes out of our colleague Taylor Uekert's work on photoreforming, which uses sunlight, water, and low-cost non-precious metal catalyst materials to 'reform' organic waste into hydrogen. Currently 95% of hydrogen production is via steam reforming, which uses methane--a fossil fuel and greenhouse gas. Our goal is to offer a green alternative that is price competitive with other methods.

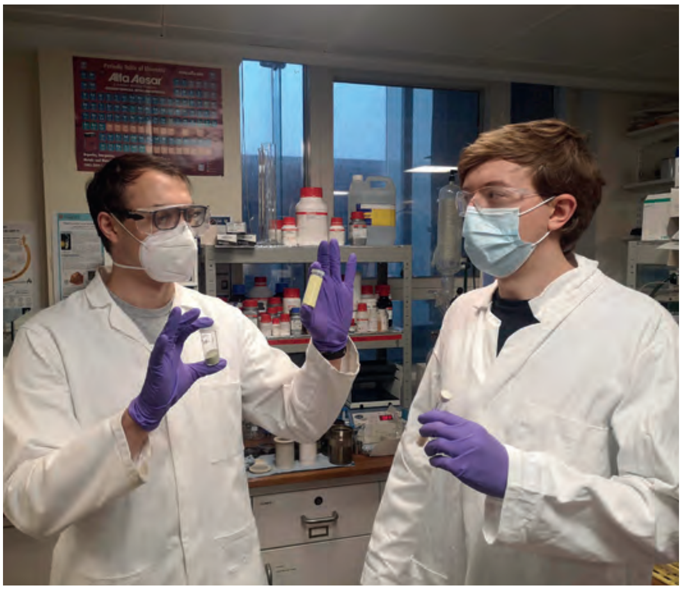
Michael

One of the big challenges is scalability. At the moment the process can only make a small amount - the biggest reactor Taylor used in her research was five by five centimetres. Stuart is developing a circular reactor with a 20cm diameter, but by the end of next year our aim is to produce a reactor which is one metre squared.

Stuart

And it must be economically viable. Towards the end of her project, Taylor was looking at immobilising catalysts on glass panels, so they can be retained and recycled when the waste solution is flushed away, which helps reduce costs. I am experimenting with panels, glass tubes and even floating photocatalysts such as micron-sized styrofoam or glass bubbles.

We can also make the catalysts more effective by using a larger portion of the solar spectrum. Taylor used carbon nitride and a nickel phosphide co-catalyst because carbon nitride is active under visible light



Michael Stanton (R) and Stuart Linley with tubes containing the catalyst materials.

unlike other catalysts, which only absorb in the ultraviolet region. Only about five percent of the solar spectrum is UV light, where 45 percent is visible light.

Michael

My focus is the commercial application of the research. We have a grant from the EPSRC Impact Acceleration Account follow-on fund, which specifically supports the early-stage development of technology to make an idea more attractive for commercial investment -- this will help fund the reactors and catalysts that Stuart is working on. We've also been awarded an ERC Proof of Concept grant, which covers activities at the very early stage of turning research into a commercial proposition. These grants have allowed me to meet companies and potential partners to survey their views on photoreforming and assess the market.

Stuart

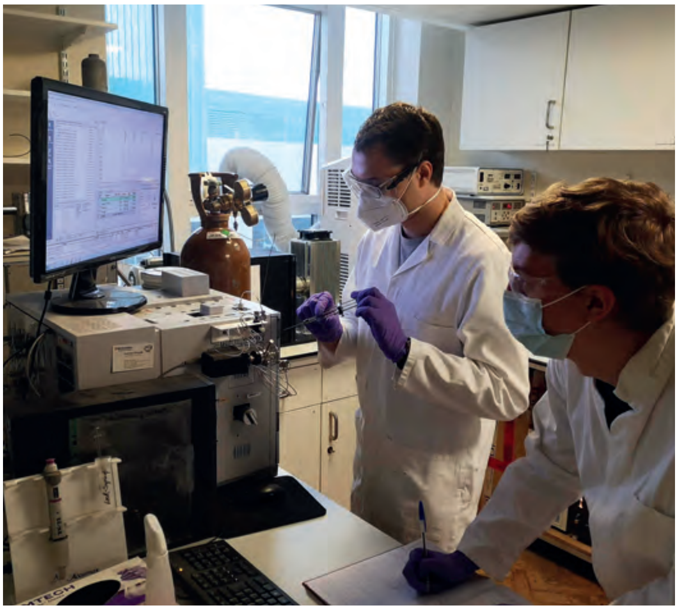
My undergrad and postgraduate degrees were in Nanotechnology and Engineering at the University of Waterloo in Canada. During my summers and holidays I worked with a Professor developing recyclable nanomaterials for water treatment. We eventually incorporated a company called H2nanO, which uses photocatalysis to treat oil sands wastewater. The process uses the sun and recyclable catalyst materials to treat contaminated wastewater. So my background made me a good match for this project. [Editor's note: Extracting petroleum from oil sands requires large amounts of water, which must then be treated.]

Michael

I did my PhD in the NanoDTC here, which exposed me early on to a great ecosystem of impact and entrepreneurship. We had courses on the basics of writing a business plan, pitching an idea and analysing a market. I enrolled in the E-tech programme at the Judge Institute (now called EnterpriseTECH), which provided in-depth training on raising investment, understanding a market and other aspects of start-ups.

I became interested in photoreforming after meeting Professor Reisner, who is one of the co-directors of the NanoDTC, and Taylor, who was one year behind me in the course. I was awarded the NanoDTC Translational Prize for the photoreforming topic, which gave me a one-year fellowship. This also funded me to attend the Impulse programme at the Maxwell Centre, where I had small-group mentoring and access to a network of successful entrepreneurs, angel investors and patent lawyers. I'm still in touch with many of the contacts I made through that programme, and regularly talk to my mentor.

The entire Cambridge ecosystem has been very supportive of translational research. The grants have allowed the funding and time to look into all of the issues we have mentioned, and time is very clearly what is needed.



Using a gas chromatograph to measure hydrogen output.

Editor's notes: Taylor Uekert was awarded her PhD and is now a postdoctoral researcher in the resources and sustainability group at the National Renewable Energy Lab in Colorado.

Photoreforming has been chosen as one of six finalists in the Chris Abell Postdoc Business Plan Competition run by Cambridge Enterprise. The contenders will pitch their business ideas in front of an audience of experts in spin-out investment at The Grand Finale on 11/11/21. Three prizes of £20k, 10k and 5k in funding will be awarded, and the first place winner will also have the opportunity to pitch at a Cambridge Enterprise Venture Partners dinner, an investor forum of venture capitalists and business angels.

A new way of working

Chemistry of Health hosts one of the only incubators to be completely integrated into a UK chemistry department. Professor Michele Vendruscolo, Director of Chemistry of Health, explains why this unique set-up works.

Nathan Pitt, ©University of Cambridge

CMD co-director Michele Vendruscolo.

What is the Chemistry of Health building?

About 15 years ago, with our colleague [the late] Professor Chris Dobson and our industrial partners at the time, we saw that a unique mix of interdisciplinary research and industrial resources would be needed to tackle the growing threat of protein misfolding disorders, such as Alzheimer's and Parkinson's diseases. The Chemistry of Health building was the result of his vision.

Who occupies the Chemistry of Health?

The Chemistry of Health incubator is on the ground floor and the Centre for Misfolding Diseases is on the second and third floors. The Molecular Production and Characterisation Centre, which offers biophysical instrumentation, fermentation, microscopy and tissue culture labs, is in the basement.

What does the CMD's research involve?

We have several ongoing research programmes into Alzheimer's and Parkinson's diseases, and other misfolding diseases. The approach that we have taken is to prevent the formation of misfolded protein oligomers, which are particularly toxic small aggregates that play a major role in the build-up of the protein deposits associated with these diseases.

The approval of aducanumab by the FDA in June, which is the first disease-modifying drug for Alzheimer's, is a crucial validation of our approach, because it works with a similar mechanism of action as the drugs we that are developing here, by reducing the number of oligomers produced during the aggregation process. Many other different therapeutic strategies are still being investigated for this disease, but none of them has led to an approved drug so far – so it has been crucial to see that the route that we have taken has been validated.

Nathan Pitt, ©University of Cambridge

"A synergistic relationship that creates benefits for everyone involved."

How does the incubator fit in?

We develop the basic concept and methods in the CMD, but because the resources needed for a full-fledged drug discovery programme are much larger than those that can be typically supplied by academia, we turn it over to the Chemistry of Health incubator, which currently hosts Wren Therapeutics, the company we founded for Alzheimer's and Parkinson's diseases. While core technology and several Wren researchers are from the CMD, Wren also has many key people with an industrial background who can lead a drug discovery programme and scale it up to industrial size. We currently have two drug candidates for Alzheimer's and we are going through all the work that is needed to start clinical trials, planned for next year.

How is this different from traditional research?

In other translational programmes the interaction is usually in one direction – from academia to industry. This creates a gap, which often is responsible for failure in the translation process. In our case, to close the gap, we implemented a close feedback from industry to academia. The industry is funding fundamental research in directions that have translational potential, so the two-way interaction can happen more easily. And because of our physical locations, the communication is greatly facilitated. It's a synergistic relationship that creates benefits for everyone involved.

How do you mean the industry funds fundamental research?

Wren contributes to the running costs of Chemistry of Health, and funds research and PhD students through the Nidus programme, who don't typically work on Wren projects [see accompanying article]. If the projects become interesting from a translational point of view, Wren has first right of refusal.

Are there other advantages to this arrangement?

It provides a career path for students, who might do research in the Department as undergrads, but who can then start their careers in the spin-out companies in the incubator, if they are interested. Many times students approach me because they want to do academic research but they are also interested in industry, so I explain that it's not necessarily a binary choice.

Why did you set up the Chemistry of Health this way?

We want to overcome the traditional divide between academia and industry. The incubator on site is key to the vision behind the Chemistry of Health – we will see in time if it works or not, but judging from the start I am highly optimistic that the experiment has begun well.

A synergistic energy

Rob Horne explains why he chose to work at Wren Therapeutics before starting his PhD in the CMD.

I did my Part III project in the CMD, which involved identifying antibodies that bound to alpha-synuclein, the key culprit in Parkinson's disease. The project won the prize for best biological project that year which was a great start to my time in the CMD. I was considering a long-term career in science at that point but I knew I didn't want to do a PhD immediately, so I joined Wren.

Access to expertise

A lot of the people in the CMD tend to work for Wren at some point, which as a student gives you two spheres of expertise you can consult. Group members who are finishing off their PhDs or postdocs and might have headed off elsewhere also often stay and work for Wren for a couple of years, and so continue to share their knowledge.
At Wren I was given the opportunity to lead the alpha-synuclein project with the incredible support and mentorship of Xiaoting Yang, one of Wren's principal scientists, and Head of Research Johnny Habchi. It took a little over a year to get our first big partnership deal, at which point I realised I wanted to stay in science, but knew I needed a PhD.

Wren funds PhD projects in the CMD through a programme called Nidus. A panel with two members from Wren and two from the Chemistry Department selects which projects to fund. I was lucky enough to have my project selected, so now I am in the second year of my PhD in the CMD, but I also work (part-time) as a consultant for Wren, which gives me a lot of variety in what I do, plus some extra income!

My research involves developing machine learning and statistical learning methods to more efficiently identify and optimise molecules that could act as inhibitors of alpha-synuclein oligomer formations, which are implicated as pathological agents in Parkinson's disease. Part of the cool thing about this project is that I was able to combine computational methods with experimental work. Since machine learning is drastically changing everything, I was very keen to see if I could apply it, and since I had all the expertise necessary to test my model predictions I had the rare opportunity to both employ and experimentally validate my machine learning models. It's been a steep learning curve, but it's looking very successful so far.

Synergistic

I think we have a rather special synergistic situation here, where the CMD is doing important exploratory research, and if a project is of translational interest Wren can take it on and scale it up. I think that feeds into what most scientists want, which is to see their work applied in a practical way to benefit people. With Wren, you feel like someone will be using what you're doing.

My point of view is that it's probably wiser to try scientific work in biotech before doing a PhD, because it prepares you better than going straight from an undergrad and gives you a taste of whether scientific work is right for you. After my PhD I'll probably head back to Wren, at least for a while.

Nathan Pitt, ©University of Cambridge

In the CMD Rob Horne can experimentally validate his machine learning models.

As I see it

Andy Richards (Jesus 1978) has been involved in some 30 companies as founder, adviser, mentor, investor, board member or chair, and was an early-stage investor in Chemistry spin-out PharmEnable. Andy's current projects range across healthcare, therapeutics, digital health, data, genomics AI and mental health.

It's all about themes, teams and timing.

The theme I am particularly interested in at the moment is big data and where that meets what I would describe as 'artisanal science' – by which I mean a mixture of deep knowledge and creativity.

A good team is essential. It should have not only the right skill set, but also the right chemistry – including chemistry between the people! Ideas without people just won't succeed.

Timing is something I've come to learn over the years. If you get the timing right, there's a better impact, which in my experience aligns with financial and business success. There are lots of things I've been involved with where we were too early. That can be intellectually satisfying (thinking 'we were right all along!') but otherwise somebody else gets all the glory later on.

PharmEnable is a good example – its development of an artificial Intelligence and machine learning platform for drug discovery is a hot theme. The concept of adding AI approaches also satisfies the move toward much better validation of drug discovery targets. The team had experience working in real companies and covered a good mix of real chemistry and 'people' chemistry. I knew the timing was right because people started talking to me about it and asking questions – there was a real buzz.

Cambridge is a good environment for commercialising research. Cambridge Enterprise and the Judge Business School run many courses and workshops for anybody, from students to academics. Schemes like the business plan competition offer training on how to write a business plan, and winners get access to accelerators, experts and even funding. The CE team offer an abundance of resources and support, and interact well with the Angel network.

Accelerators are a good place to help develop an initial idea. There are accelerators for all stages – one of the Babraham accelerators (Startup@Babraham) supports concepts before they even become companies, and the Wellcome Genome Campus has a great start-up community for ideas in the genome space. KQ Labs, where I met the Pharmenable team, is an accelerator programme based at the Crick Institute in London and is specifically for ideas at the interface of data and life sciences.

It's never too early to start thinking about commercialising a good idea. It's good to get yourself orientated and thinking about what you want to do.

I like to invest early – I suspect that is not economically the best time – but it is the most interesting.

Profits in these sorts of science and R & D areas are usually a very long way down the track. If you engage with accelerators, mentors and other schemes, you'll get a sense of whether your idea is hitting home or not. But at some stage you need to know when to say 'this isn't really working' or understand what you need to do to make it happen.

Students get involved

PhD students June Park and Amy Rochford won first prize in the Wolfson Enterprise Competition in May for their start-up Lecta, which is developing bio-fabricated regenerative flexible electronics for neural interfaces.

Wolfson Enterprise Competition winners Amy Rochford (left) and June Park first started thinking about Lecta over dinner at King's College (background).

June, a Gates Cambridge Scholar and NanoDTC Associate, is in the third year of her PhD in the Scherman group and received her BSc in Chemical and Biological Engineering from MIT. Her work involves designing viscoelastic supramolecular hydrogels for stem cells, specifically for cell therapy. Amy, who is in the third year of her EPSRC DTP PhD in the Department of Engineering, studied Biomedical Science as an undergraduate and holds a Master's in Regenerative Medicine and Nanotechnology. Her research involves bio-hybrid technologies, which combine living cells with flexible electronics.

June and Amy, who are both at King's, explain how they got the idea for Lecta over a college dinner: "We were discussing a day in the lab plagued by slippery bioelectronic device surfaces," says Amy. "I was having a problem with my research and I needed the assistance of a chemist to help me with sticking hydrogels to flexible electronics."

"And we realised that with my background in chemical engineering and now hydrogels, and Amy's in flexible bioelectronics, we could work together to come up with a solution," says June.

Their solution combines surface chemistry, chemistry-based biomaterials, and stem cells with flexible electrodes to generate bioelectronic devices. June explains: "It's like trying to combine jello with cling film – there's no way to do it without some sort of chemical interface."

The pair realised that with this new chemistry, they could design implantable devices, which because of their bio-mimetic coating, are less likely to trigger the body's natural immune-response. "The problem is the human body fights off implants with an immune-response known as 'foreign body response'," explains June. "This results in fibrotic capsules being created around implanted devices, so they can't work effectively."

Some months after their initial collaboration, the researchers saw an ad for a business competition, "and that's how we began."

"We believed in what we were doing so it was just a big leap – and perseverance. The idea of starting a business is scary, but we just went for it. We had nothing to lose and wanted to give it a shot," says Amy. They applied to one previous business competition. "That was a process we learned from and going through that as a team we helped each other grow. And that helped us realise we had a really strong team working relationship, as well as friendship. So go out and have lots of dinners with your friends!"

The new biomaterials may not only ameliorate some of the fibrotic side effects of the implants, but excitingly they also appear to support stem cell growth. "Stem cells are finicky and difficult to grow even on tissue cultures, but our chemistry provides the environment that allows the stem cells to grow. So now our aim is to shift the devices from purely treatment of symptoms, to disease-modifying and even regenerative," says June. "Curative regenerative technology is very exciting right now." Their ten-year goal is to have the new devices in clinical trials, if not already reaching patients. "Working with materials that are already clinically approved is a realistic goal," says Amy.

Both researchers have family backgrounds that introduced them to entrepreneurship from an early age. "My Dad is an inventor – he's a bit of a crazy scientist, and we used to sit together and get parts from a junkyard and build things," says June. At age 12 she took her first entrepreneurial step when she sold a filtration system they created to a neighbour. Amy says: "My Dad is an engineer and entrepreneur. He's inspired my five sisters and I to go into business one day." June's experience working in healthcare consulting, and Amy's with a UCL spin-out have also prepared them well.

"The competition has also been really useful for us," says Amy. "The first exercise of doing a business canvas made us really think about what was important about taking our business forward. And the pitch was useful too – it gave us ideas on how to communicate our idea." June adds: "We were able to engage with non-scientists who asked good questions that challenged us and helped us think about our plans, and we met some great mentors."

The wider Cambridge environment also helps. "We hear a lot about the Cambridge ecosystem, and it's during competitions like these that you realise how much it exists, and how so many of us share the same excitement for entrepreneurship," says June. Amy adds: "Cambridge is good because it gives you opportunities to have a drink or a meal and discuss your work with each other--because we're in two different departments, I don't know how we would have met otherwise."

Additionally, Cambridge Enterprise put the team into contact with resident experts and advisors in the health care field, and helped them assess their patent strategy. CE sponsored part of the WES competition and will continue to support the winners.

The new company is called Lecta because: "It's a feminine form of the Latin word for excellence, and we are two female scientist pursuing excellence," says June.

"Lecta is an outcome of what we were working on for our PhDs, and has now evolved into a project in itself," says Amy. "That's why it feels so dear to our hearts, it combines our expertise, our excitement, and our hopes for the future of medicines. It is both growing out of our PhD and is a personal growth.

"Having founded the Wolfson Entrepreneurs Society and initiated the Enterprise Competition myself, it was great to see a member of the Chemistry Department win the maiden edition!"

PhD student David Izuogu, a theoretical chemist in the Thom group.

It's never too early…

Dr Marcio Siqueira took up his post as Head of the Physical Sciences Technology Transfer team at Cambridge Enterprise (CE) during lockdown, while Commercialisation Director Dr Margaret Wilkinson has worked for CE and its precursor for 20 years. They both agree it's never too early to approach CE with an idea.

You may have noticed that most of the activities we've been discussing in this issue have one thing in common: they've been supported at some stage in their development by Cambridge Enterprise (CE).

First, a little history: The Wolfson Cambridge Industrial Unit was founded in 1971 by the University to help foster technology transfer. It was originally located in the Department of Engineering, but gradually acquired separate offices, new resources and different names, until 2006, when the University established CE as a wholly owned subsidiary.

The goal of CE is to help academics, researchers, staff and students commercialise their expertise and ideas. "We would like to be able to help the researchers fulfil their potential in terms of impact," says Siqueira. "We are here to help them, and we are prepared to do a lot of the guiding, facilitation and assistance that they need in order to do that."

From idea to opportunity

CE can help develop an idea into a successful licence agreement or spin-out in many different ways. "Typically a researcher would talk to me or another team member about their technology and their commercial aspirations," says Wilkinson. "We can help researchers evaluate the commercial potential of their idea, and work to transform their idea into a commercial opportunity that is attractive to organisations that can bring them to market. If the researchers are keen to form a spin-out and it looks appropriate, we introduce them to our seed funds team, whom we work in parallel with. We can help form the business team to take the idea forward, from finding mentors to a CEO, and we offer advice and regular follow-up."

"Some 'serial entrepreneurs' are very experienced," adds Siqueira, "so they need very little hand holding. And some are just starting out. We try to give the appropriate level of support."

It all starts with a chat. "In the good old (pre-Covid) days when we saw people in person, you might just have a chat to start off," says Wilkinson. And although Covid has decreased the serendipity of bumping into people in hallways, it's still possible to contact CE by email or through the website. "If you know somebody in CE, it's best to talk to them first, because they'll know your background. But you can also email us in confidence, and Marcio will decide who in the team is best to deal with your query," says Wilkinson.

Dr Marcio Siqueira

Dr Margaret Wilkinson

CE supported Cambridge Epigenetix (Balasubramanian), which has now raised $146m to date, and Sphere Fluidics (Abell), which recently closed a £30m investment round.

cambridge epigenetix

Sphere Fluidics

Never too early

This is where they both emphasise the importance of starting early. "Talk to us first," says Siqueira. "Don't talk to other people, because that counts as a disclosure and that could erode potential protection of the invention." Wilkinson adds: "It's never too early to come because it's often useful to be able to give a bit of a steer on thinking about which way to go and what to develop. And we can advise you on how you can maintain protection of your technology but still get feedback. We can also signpost people on how to make the most of the Cambridge ecosystem."

"There are so many people here who have done this before and want to help"

That Cambridge ecosystem again – is it really that important? "The ecosystem makes our life so much easier," says Siqueira. "There are so many people here who have done this before and who have useful ideas and pointers and want to share them. There's so much going on – colleagues, clubs, societies, friends, small businesses, the Cambridge network, Cambridge angels (takes a breath) -- it's probably one of the top three richest entrepreneurship ecosystems in the world."

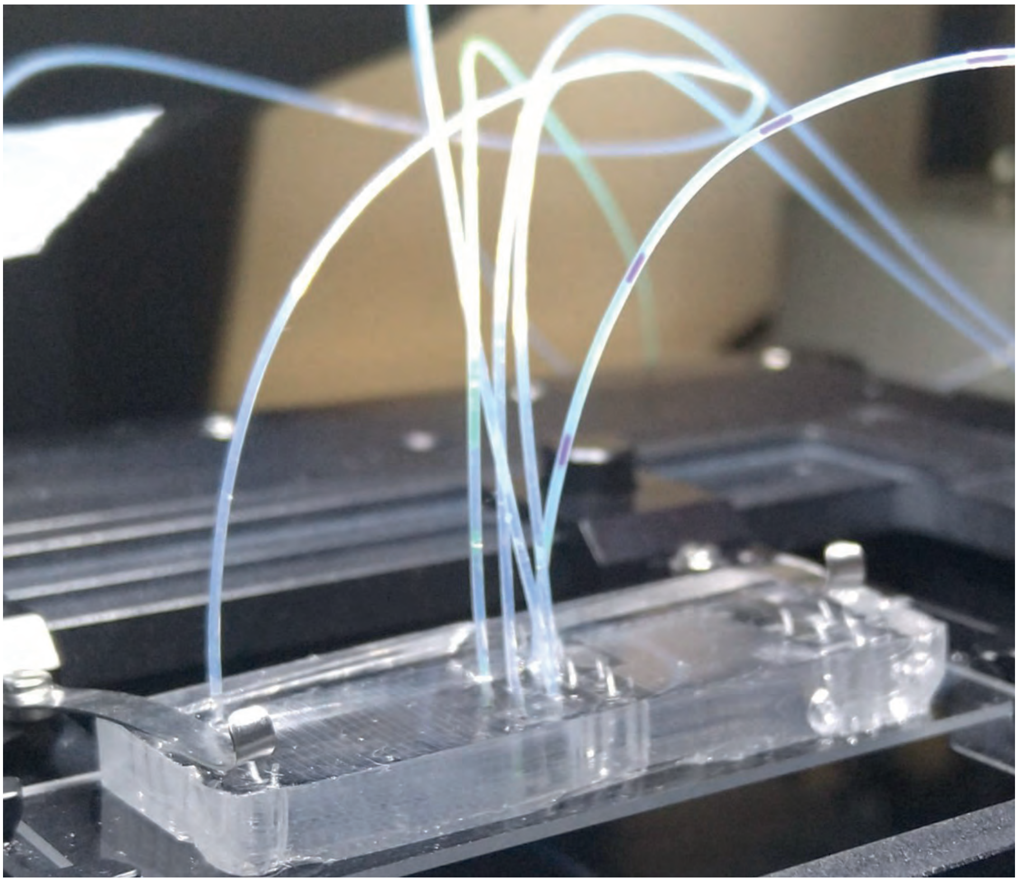
"There's a whole ecosystem for students as well as staff," adds Wilkinson. So much so that a whole website devoted to the University Enterprise Network provides ideas for students and staff on how to get involved in enterprise and innovation, including links to the numerous student societies and workshops, courses and webinars run by CE and the Cambridge Judge Business School. "It can be confusing, but if the first thing you find doesn't suit you, then you'll probably find another ten things that suit you better," says Wilkinson.

Be open to change

According to Wilkinson, one of the main pitfalls that researchers hit when developing a product is not talking to potential customers early enough. "Of course that has to be balanced with not giving away technical secrets," she says. "But it's really important to talk to potential users and to be open to changing your mind about how your tech will be used. Somebody may have a fantastic technology, but it may fall down if they haven't talked to the people who will use it and who may have different needs."

Siqueira adds: "Changing the world is hard – it takes a lot of concerted effort, and needs different kinds of research that our academics aren't necessarily used to. You must understand the market need and how you will address it. At first people think everything's going to happen at the drop of a hat, then reality starts to sink in. If they have something that strong, a compelling proposition, then we'll find a way to make it happen with them, but they must remain engaged."

The journey from idea to ultimate product can be long, and Wilkinson says research done a few years ago revealed it often take 8 years or more from first discussion of an idea to the first product on the market. The team have created a page on the CE website called *The journey of a University idea* to help researchers understand the difficult but potentially rewarding path they have chosen. Siqueira concludes: "It can be a very long and arduous process which requires a lot of engagement from the researcher, but it's very fulfilling when things come together – you get a real buzz and sense of achievement. Come talk to us and let's make the world better!"



CE contributed to the seed investment and filing of patents for Transition Bio (Knowles) to protect its new drug discovery engine based on droplet microfluidics and machine learning.

New centre delivers digital revolution

The multi-million pound Innovation Centre in Digital Molecular Technologies (iDMT) was officially opened in the Department on Friday the 26th of November.

Professors Alexei Lapkin (left) and Matthew Gaunt in the new centre's High Throughput Chemical Synthesis Laboratory.

The new centre's goal is to create a digital transformation in the chemical industry by helping companies make the transition to automated discovery processes and machine learning.

Using AI to make molecules

"Despite tremendous advances in chemistry, we still cannot always make all of the molecules we need on demand – to do this, we need to change the way chemical synthesis is approached. One way this could be achieved is by automating largely routine procedures that could be enabled by adopting artificial intelligence methods, so that the chemists' creative minds are freed to invent solutions to new problems," says iDMT co-Director Matthew Gaunt, who holds the 1702 Hamied Chair in Chemistry here.

"Up to now, one of the barriers to digitalisation has been the absence of a central location with the instrumentation and multi-disciplinary team that can help companies develop the right solutions for their particular services," says iDMT Director Alexei Lapkin, who is based in the Department of Chemical Engineering and Biotechnology. "The iDMT fills this gap."

Making molecules more economically

The iDMT helps small to medium enterprises (SMEs) learn about and adopt new digital tools and processes, which will enable them to make molecules more quickly and economically, and with fewer negative effects on the environment.

iDMT Project Manager Dr Celeste van den Bosch.

Access to iDMT facilities is provided to eligible SMEs based in England – this includes expert advice, an agreed consumables budget, instrumentation time and/or computational resources. SMEs only need to provide staff to benefit from this opportunity. "They simply need to work with our team to identify and agree a challenge that we can help them with, often leading to a new product, service or working methodology for the SME." says Dr Celeste van den Bosch, iDMT Project Manager.

"This transition to digitalisation is happening everywhere around the world"

Dr van den Bosch notes that the centre has attracted international interest. "Our funding at the moment is only for companies based within England, but this transition to digitalisation is happening everywhere around the world, and that's why a centre like this is so important. We want the processes to be open source, with everyone using similar standards – that's why iDMT researchers are championing data standardisation."

Cross disciplinary

The centre hosts researchers from global industrial partners Shionogi and AstraZeneca, as well as a number of postdoctoral researchers and PhD students. The centre has a close relationship with the SynTech CDT, directed by Professor Gaunt, and its core academic team combines expertise from the Departments of Chemistry, Physics, Engineering, and Chemical Engineering and Biotechnology. "Combining cross-disciplinary expertise from multiple departments at the University, with state-of-the-art facilities and support from two of the leading companies in this area has the potential to enable the development of many new solutions for the nascent industry of digital molecular technology," says Professor Lapkin.

"There is much to accomplish in this field, but it can be a challenge for companies to keep up to date and implement changes," says Dr van den Bosch. "Being able to access cutting-edge knowledge, equipment and collaborations is what is needed, so this project is very timely."

"Digitalisation will result in a radical increase in the throughput of chemical discovery, guiding synthetic chemists towards successful solutions more efficiently, and freeing up their time to develop new ideas," concludes Professor Gaunt.

The centre was officially opened by Professor Andy Neely, the Pro-Vice-Chancellor for Enterprise and Business Relations, with lab tours and presentations from supported SMEs, industrial partners AstraZeneca and Shionogi and University of Cambridge academics.

The iDMT is part-funded by the European Regional Development fund.

iDMT Administrator Kerstin Enright.

Alumni support Chemistry@Cambridge Opportunity Fund

Alumni have kickstarted the launch of our new Opportunity Fund with two generous gifts.

Inaugural gift

A gift of £10k from Dr Eddie Powell (Churchill 1967) was used by the Department to inaugurate the fund. Eddie completed his PhD in inorganic chemistry here under Martin Mays, and after an eventful career in finance and start-ups, he has become a well-known entrepreneur and business angel in the Cambridge bio-tech hub.

These days Eddie has reduced his business commitments to his collaboration with fellow alumnus Shamus Husheer in Heartfelt Technologies, a start-up which was featured in Chem@Cam Issue 60. Heartfelt has developed a device which uses photo technology combined with artificial intelligence to detect when the feet of an individual who has suffered heart failure are swelling, which could indicate a potential recurrence.

Since he (mostly) retired ten years ago, Eddie says he and his wife have been fortunate to travel to many countries, and for him one of the most frustrating side effects of the Covid epidemic was the restriction on travel. Now that things have opened up, they plan to re-start their voyages, but they will also try to avoid flying wherever possible – not only because they've grown to dislike airports over the years, but also as a nod to climate change and reducing their carbon footprint. "We love travelling by train – that's where you'll find us," he says.

Eddie in 1985.

"I'm delighted that my gift is going to be used for the new fund," says Eddie, who is also a generous supporter of Churchill College. "It seems like a good thing to do for a Department which is one of the most prestigious in Cambridge and the UK, and I'm glad the fund will be there for people to benefit from."

Eddie says he has no specific hopes for how his gift will be used. "To be quite honest, I think the Department is much better placed than I am to decide how to direct the funds, so I'm happy with that," he says.

Building the fund

A second gift of £20k, left as a charitable bequest by Mrs Pamela Goldhill, has been directed to the fund by her son and executor Dr Jonathan Goldhill (Darwin 1976). Jon completed his PhD in organic chemistry under Professor Ian Fleming.

Eddie now with his prize possession.

When Jon made the gift from his mother's estate, he wasn't aware that it would qualify for the Harding Challenge, which means that the donation has been matched, pound for pound, by a contribution to a University fund for undergraduate financial support. So Jon has not only helped our Department, but he has also doubled his impact by helping undergraduates in the greatest need across Cambridge.

Jon as a PhD student in Ian Fleming's group,1977.

"All my gifts from my mother's estate went to educational establishments of one sort or another," says Jon, who is also a regular giver to his college. "My aim was to help people less fortunate than myself. We came from a relatively privileged age, when university education was free."

Jon's hope for the gift is "only that someone benefits from it". He says: "I hope that somebody can do something that they otherwise wouldn't be able to. I'm not going to direct it – I'll leave that to someone who knows what they're doing."

After completing an undergraduate degree in Chemistry at the University of Edinburgh, Jon joined Ian Fleming's group for his postgraduate research "because of the type of research that was taking place", he says. "It was not absolutely conventional organic chemistry and it was very interesting research." Just down the bench from Jon was Ian Paterson, who is now a Professor Emeritus in this Department.

Quenching their thirst

Professor Paterson recalls: "Jon and I worked and played hard together in Ian Fleming's group. At the end of a long day in the lab, we often frequented the Panton Arms to discuss the latest results while quenching our thirsts, then heading back to check our reactions. I remember Jon's sense of humour and they were fun and happy times, as well as producing a good number of highly cited publications. It's fantastic that he has remembered the Chemistry Department by making this generous gift."

After being awarded his PhD in 1979, Jon decided not to stay in academia. "In some ways I would have liked to, but in other ways I could see that there were people who were better than me, and also I didn't think it really matched what I wanted to do", he says. So after a few years in industry, Jon completed an MBA at London Business School, and began

Jon recently in the Dolomites.

working in a large innovation group. "That's when I realised I should never be working for a big firm", he says, concluding that he preferred to be in charge of things and make his own decisions.

From that time on Jon has worked for himself, becoming co-founder of two telecommunications firms. After selling those, Jon and his business partner developed a search engine for data – graphs and tables on the internet. "We didn't really know about software, but our ignorance was a big help or we wouldn't have done it!" he says now.

Jon and his business partner then founded one of the few businesses in the world which employs image recognition software to extract data from unstructured documents. The technology is useful, for example, to get numbers from tables in financial statements or industry reports. Jon also acts occasionally as an angel investor if a new technological start-up sounds interesting. His advice to young entrepreneurs is: "Don't expect it's going to be easy".

Supporting our researchers

The Chemistry@Cambridge Opportunity Fund was set up to enable the Department to provide a range of support to postgrads and postdoctoral researchers, for example, by funding their participation in important workshops and conferences, and most recently to mitigate against interruptions or difficulties with funding due to Covid or other unforeseen circumstances.

Head of Department Dr James Keeler says: "We are so grateful to Eddie and Jon for being the first to contribute to our new fund. We hope others will follow their example, so the fund can continue to grow and help department members for many years to come. I would be happy to meet or speak with anybody who would like to find out more."

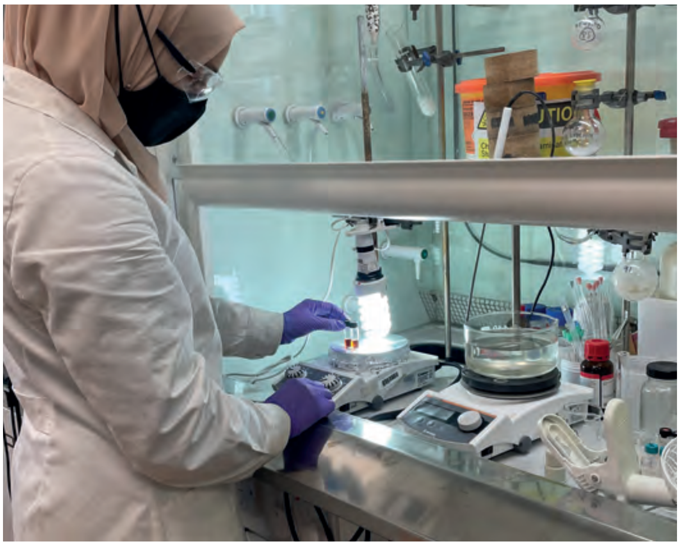
Research bites

Single-step catalysis platform speeds drug discovery

Gaunt Group

Researchers in the Gaunt group have developed a single-step method to synthesise a structure found in beta-arylethylamine molecules which is important in drug discovery. This will dramatically speed the search for new drug therapies for pain, neurological disorders and opioid addiction.

"This structure, or motif, is very important in medicine, because it can target a series of diseases," says first author, Dr Ala Bunescu, who was a postdoctoral researcher in the Gaunt group and is now a Junior Professor at the University of Bonn. "Our new methodology enables researchers to access potentially useful compounds with this structure in a much quicker way. Previous methods needed four or five steps, but this is a one-step method which allows researchers to quickly create and test a series of compounds, and also to build up a library of 'target' molecules."



Yusra Abdelhamid

Co-author Yusra Abdelhamid, who is starting her second year as a PhD student in the group, says she will now be working on developing the chiral form of this reaction, which could lead to another important class of compounds. Abdelhamid already has some promising results. "It's more challenging than it initially seemed, but as I've gained a deeper knowledge of the project and worked on this paper, it's helped me to develop the work I'm doing now."

Multicomponent alkene azido-arylation by anion-mediated dual catalysis, A. Bunescu, Y. Abdelhamid, M. J. Gaunt, *Nature*, (2021).

Nano 'camera' made of molecular glue

Scherman Group

A team of researchers led by Professor Oren Scherman has made a tiny camera held together with 'molecular glue,' that allows them to observe chemical reactions in real time. The device combines tiny semiconductor nanocrystals called quantum dots and gold nanoparticles using molecular glue called cucurbituril (CB). When added to water with the molecule to be studied, the components self-assemble in seconds into a stable, powerful tool that allows the real-time monitoring of chemical reactions.

The platform could be used to study a wide range of molecules for a variety of potential applications, such as the improvement of photocatalysis and photovoltaics for renewable energy.

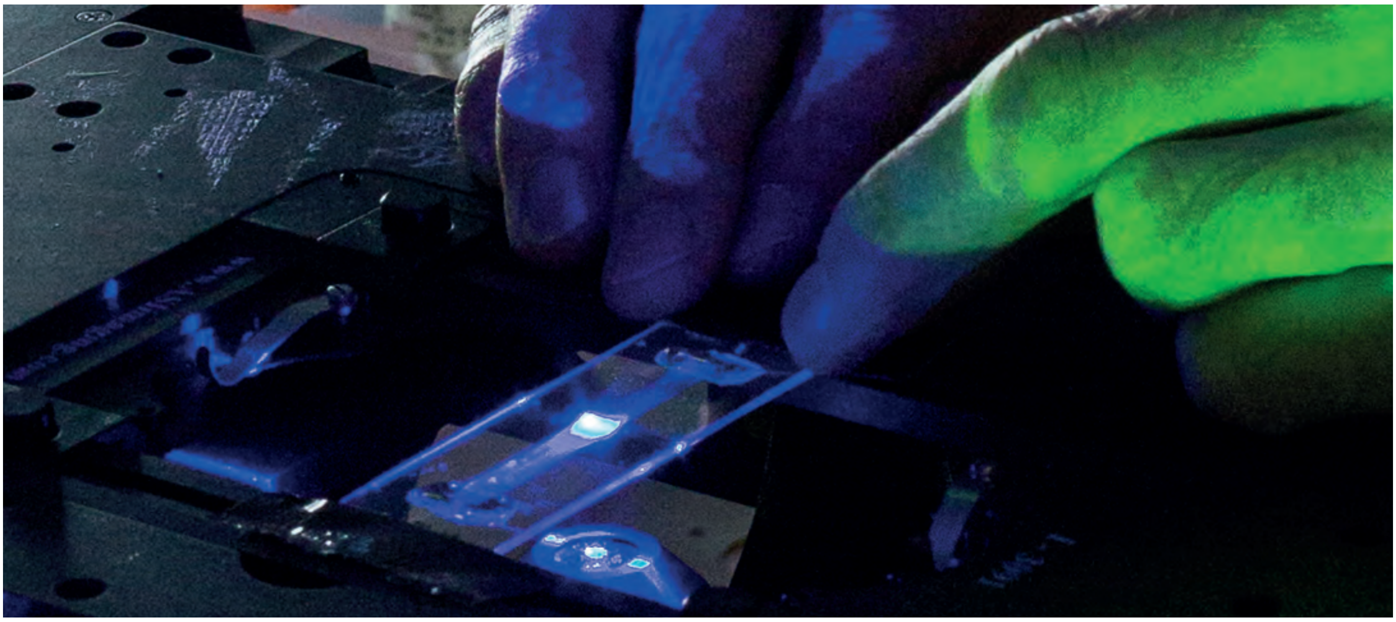
"We were surprised how powerful this new tool is, considering how straightforward it is to assemble," said first author Dr Kamil Sokołowski, a postdoctoral researcher in the Scherman Group.

Nanoparticle surfactants for kinetically arrested photoactive assemblies to track light-induced electron transfer, K. Sokolowski, J. Huang, T. Foldes, J. A. McCune, D. D. Xu, B. de Nijs, R. Chikkaraddy, S. M. Collins, E. Rosta, J. J. Baumberg and O. A. Scherman, *Nat. Nanotechnol.*, (2021), **16**, 1121.

Oren Scherman

New approach could lead to improved therapeutic antibodies

Knowles and Bernardes Groups



Gabriella Bocchetti, ©University of Cambridge

Using microfluidic devices to understand how internal forces affect biomolecules.

A new approach to measuring how internal forces affect biomolecules has increased understanding of, and perhaps even the ability to influence, the behaviour of therapeutic antibodies.

In a new 'bio-mimetic' approach, members of the Knowles and Bernardes groups used tiny microfluidic devices developed in the Sir Rodney Sweetnam Microfluidics Laboratory to replicate the shear forces exerted by capillary walls in the bloodstream. "In chemistry, biomimetic approaches have often focused on copying nature's chemical toolkit, but we decided to complement this by emulating nature's physical architectures, which as a tool to control chemical reactions have remained largely unexplored," says Professor Tuomas Knowles.

The team used the tiny microfluidic reactors to replicate the smallest dimensions and shear stresses found in human capillaries. Shear stress occurs when forces acting on a single body, such as a cell or a protein, pull it in different directions at the same time.

They then conducted microfluidics experiments at various shear stresses while observing amino acids susceptible to post-translational modifications, which are modifications to amino-acid side chains that occur naturally after a cell produces a protein. The team observed how the chemical reaction rates changed in the selected amino acids by tagging them with fluorescence-generating reporter molecules. They found that biologically plausible shear stresses could double some chemical reaction rates.

Using this approach, it could theoretically be possible to select therapeutic antibodies less likely to dissociate in the circulation. The results also suggest that bio-physically mimetic chemistry is a link between biophysics and biochemistry in which the variety of forces utilized by nature to alter biomolecular behaviour can be exploited for human purposes.

Accelerating reaction rates of biomolecules by using shear stress in artificial capillary systems, T.A. Hakala, E.V. Yates, P.K. Challa, Z. Toprakcioglu, K. Nadendla, D. Matak-Vinkovic, C.M. Dobson, R. Martinez, F. Corzana, T.P.J. Knowles and G.J.L. Bernardes, *J. Am. Chem. Soc.*, (2021), **143**, 16401.

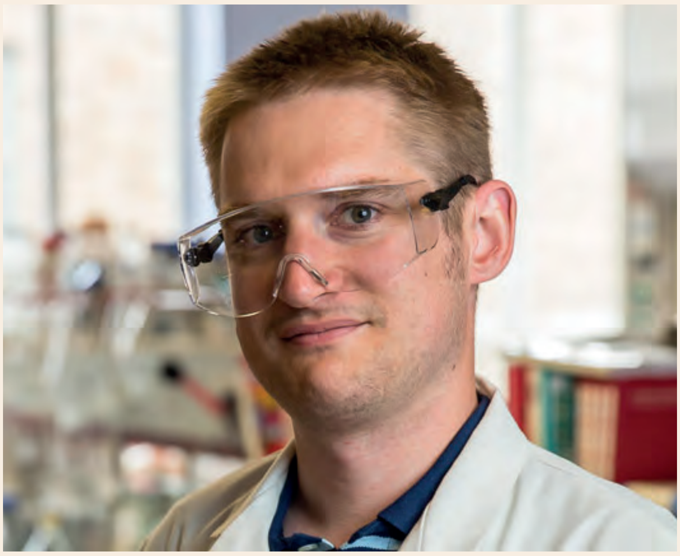
Joint first authors Emma Yates (left) and Tuuli Hakala.

Noticeboard

Awards and recognition

Dr Robert Phipps has been appointed to the position of University Lecturer. Phipps and his synthetic research group are perhaps best known for their work using weaker, non-covalent interactions to control selectivity, rather than more traditional approaches based on steric repulsion. "We are not the only ones who are investigating this strategy, but we are trying to push the limits in terms where these interactions can be applied, in areas that have not been looked at before," he says.

Rob emphasises that the real goal of his group is to solve problems. "Broadly, we are trying to solve problems in synthetic chemistry – whatever work we are doing, it always comes from a problem we are trying to solve." The tenured position will give Rob the stability to continue with his long-term research goals.



Nathan Pitt, ©University of Cambridge

Dr Stephen Cox has been awarded a prestigious Royal Society University Research Fellowship. Cox's research centres on understanding and controlling the structure of materials at the atomic scale. He says: "I am working on solving a very basic science question, which is 'In a given solution environment, what are the stable surface structures of a material?' Not only is this a question of fundamental scientific interest, but it is also relevant to the discovery of new materials relevant to pharmaceuticals, energy and catalysis." The fellowship will allow Stephen to recruit students and postdoctoral researchers and expand his current research.

Dr Anja Schmidt has been awarded the American Geophysical Union 2021 James B. Macelwane Medal for significant contributions to the geophysical sciences by an outstanding early career scientist. The medal is awarded annually to five or fewer early career scientists in recognition of their significant contributions to the Earth and space sciences community. Anja's selection was based on the depth and breadth of her research, and its impact and creativity. Other criteria included service, outreach, and diversity.

Anja is an Interdisciplinary Lecturer in Climate Modelling jointly affiliated with Chemistry and Geography. She combines expertise in atmospheric science, climate modelling, and volcanology to advance the current understanding of volcanic impacts and hazards.

Leading researcher awarded Körber Prize

Professor Clare Grey, one of the UK's leading battery researchers, has been awarded the Körber European Science Prize 2021.

The prize is awarded for excellent and innovative research approaches with high application potential. The prize has been awarded to Grey for her pioneering use of NMR spectroscopy to investigate batteries. Her work has been instrumental in the development of next-generation batteries and cost-effective, durable storage systems for renewable energy, and has helped to significantly increase the performance of lithium-ion batteries, which power mobile phones, laptops and electric cars.

Koerber-Stiftun/David Ausserhofer

Prof Grey with Körber Chairman Dr Lothar Dittmer (left) and Prof Dr Martin Stratmann, Chairman of the Körber Prize Trustee Committee and President of the Max Planck Society.

"There have been significant advances in lithium-ion batteries since they were commercialised in the 1990s," says Grey. "Their energy density has tripled and prices have fallen by 90 percent." Grey's research has made key contributions to these developments, and is an important contribution to achieving net-zero emissions by 2050.

In addition to her work improving lithium-ion batteries, Grey is developing a range of different next-generation batteries, including lithium-air batteries (which use oxidation of lithium and reduction of oxygen to induce a current), sodium batteries, magnesium batteries and redox flow batteries.

Grey was one of the first in her field to use NMR to follow the processes at work inside batteries in real time, and help determine the reactions that cause batteries to degrade. She is working on further optimising the NMR method

Alice Whitby

Battery being assembled.

to design even more powerful, faster-charging and more environmentally friendly batteries.

Grey co-founded Nyobolt (see p. 8), which is developing ultra-fast charging batteries using a new class of materials and technology based on research in the Grey group. Another company supplies the NMR measurement technology she designed to laboratories around the world.

To achieve climate goals and transition away from fossil fuels, Grey believes it is vital that "basic research into new battery technologies is already in full swing today – tomorrow is too late."

Since 1985, the Körber Foundation has honoured a breakthrough in the physical or life sciences in Europe with the Körber European Science Prize. The prize was presented in September in the Great Festival Hall of Hamburg City Hall.

Koerber-Stiftun/David Ausserhofer

Prof Grey gives her prize talk.

Edible hydrogels could replace some plastics

Researchers in the Vignolini lab have found a way to make a sustainable, edible cellulose gel that changes colour when you press it.

In a paper published in *Advanced Materials*, the researchers demonstrate how hydroxypropyl cellulose (HPC) can be mixed with gelatine and water in a scalable fashion to create a material that changes colour in response to certain stimuli, making it ideal as a sensor, especially where biocompatibility and/or cost are key considerations.

HPC is a highly viscous, biodegradable cellulose derivative used widely in the medical and other industries, for example as an eye treatment and as a thickener and stabiliser in various foods. Interestingly, HPC can form structural colour, which is colour achieved through its inherent structure rather than through any external pigments or dyes. This is termed photonic HPC.

Although extensive studies have been conducted on photonic HPC, the development of cellulose applications has been slow, most likely due to the prevalence of plastic alternatives. However, as environmental concerns become more widespread the search for more eco-friendly materials has become increasingly urgent, with potential applications for bio-compatible cellulose derivatives again receiving attention.

"My goal is to take HPC and find applications for it that can easily be scaled up," explains Charlie Barty-King, a PhD student here and the paper's first author. "Chemistry is good at finding amazing new materials but they often cost too much or are difficult to handle -- we're focused on the opposite of that – we want to find economic and scalable materials that can begin to compete with plastics."

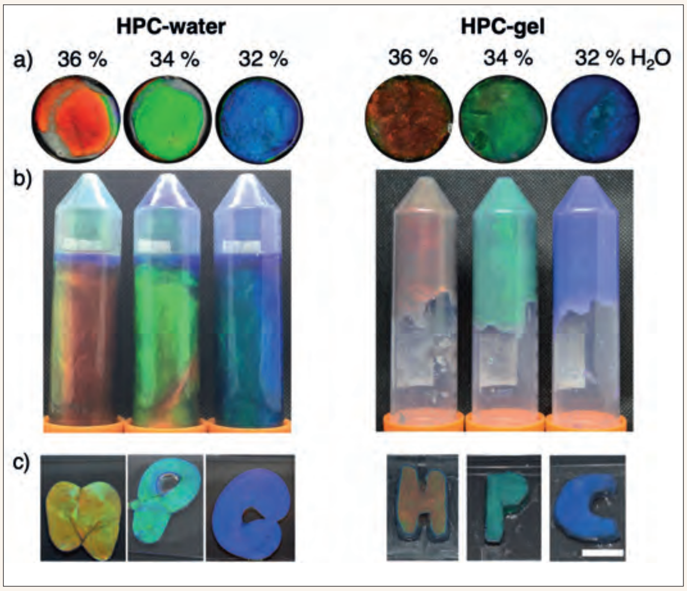
To do this, Charlie and colleagues in the Vignolini Bio-inspired Photonics group and the Institute for Manufacturing (IfM) mixed HPC with gelatine and water, all of which are widely available, to create a gelled material that is mouldable as a continuous, unsupported solid. "Before, if people wanted to capture the photonic HPC state, which is a liquid, they needed an external architecture," he explains, "but here we've actually added an internal architecture, so it's a solid gelatine network with pockets of HPC within it which can still flow, providing a dynamic colouration yet solid material."


Nathan Pitt, ©University of Cambridge

Professor Silvia Vignolini led the research

One advantage of the gel is that it maintains the liquid HPC's vibrant colouration as well as its ability to change colour in response to pressure, known as mechanochromism. "Other researchers have devised ways of capturing the photonic HPC state into a solid, but without retaining its ability to change colour," says Charlie.

In fact, the new cellulose gel's mechanochromism is enhanced in two ways: First, because the gelatine gives elasticity to the material, the gel has a quicker mechanochromic relaxation time, which is the time the material takes to return to its original colour after the pressure is relaxed. Second, this same elastic quality means a greater pressure is needed to achieve a colour change. So a sensor made from this gel would be able to respond at



First author PhD student Charlie Barty-King.

greater frequencies and have a broader working range than a sensor which uses liquid HPC, with a final advantage that it can be moulded as a solid.

The new hydrogels have potential applications as short-term sensors in, for example, biodegradable "smart labels" for food packaging. "A sensor made with this material gives you a simple visual indicator and is easy to understand. All you need to know is if the sensor changes to a particular colour, then it's bad – you don't need a range of electric sensors and the training to understand them, and they can be made to work with any common colour camera technology, like smart phones." This, and the low cost of the hydrogels, makes them especially useful in underdeveloped parts of the world, as well as medical uses where quick and correct identification is imperative. Because they are also edible, the hydrogels could be used as additive-free novelty food colorants and decorations.

Charlie completed a Masters of Research in the Bio-inspired Photonics group of corresponding author Professor Silvia Vignolini as part of Cambridge's Ultra Precision Engineering CDT, before moving on to PhD research. He is now based in co-author Professor Michaël De Volder's Nanomanufacturing research group at the IfM, but is co-supervised by Professor Vignolini and has continued to collaborate with her group. His background in materials science, formulation chemistry, and the science of mixing and scaling has proved to be ideal for this research.

"Chemistry is often about finding novel chemicals, synthesis and materials – but sometimes less thought can be given to their practical application and how to do these things at scale," says Charlie. "My work with Professor De Volder is on nanomanufacturing with a focus on being feasibly scalable, so my PhD is on combining those two ideas of producing new, sustainable materials in an economic and scalable way."

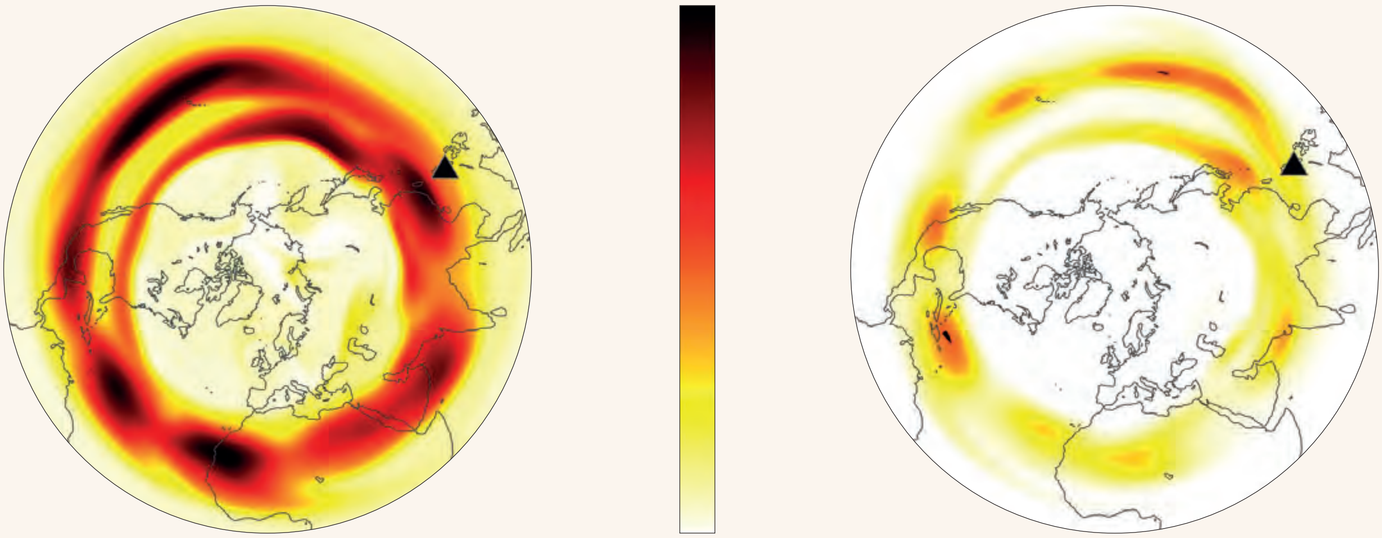
With scalability in mind, Charlie introduced the use of a Planetary Centrifugal Mixer, a type of industrial mixer which not only allows greater consistency of results but also greatly reduces preparation time. "We also went pretty much exclusively for gelatine because besides being edible it's so industrially well-known and scalable," he explains. Although this research used gelatine derived from pork, Charlie points out that vegan alternatives such as xanthan gum or carrageenan could also possibly be used.

Charlie is also keenly aware that cellulose is a sustainable, biodegradable material that won't pollute the environment. As a member of Wolfson College, he founded its Green Society and helped launch and drive the College's Sustainability and Conservation Interdisciplinary Research Hub. He holds an NUS Green Impact Challenge Student Leadership Award and was a recipient of the Vice-Chancellor's Social Impact Award 2021 for his activities. He says: "One of the main reasons I've focused on cellulose and HPC materials, is to show that they are a viable alternative to petrochemical plastics. The problem with plastics is that they are so useful – but there are a lot of applications where you do not really need plastic, and could use an alternative."

Research
Mechanochromic, Structurally Colored, and Edible Hydrogels Prepared from Hydroxypropyl Cellulose and Gelatin, C.H. Barty-King, C. L. C. Chan, R.M. Parker, M. M. Bay, R. Vadrucci, M. De Volder, S. Vignolini, *Adv Mater*, (2021), **33**.

Climate change may transform cooling effects of volcanic eruptions

Dr Anja Schmidt has participated in a study with colleagues in Cambridge and the Met Office which shows that human-caused climate change will have important consequences for how volcanic gases interact with the atmosphere.



Present-day climate | **Simulated volcanic sulfur gases concentration** | **Future upper-end warm climate**

“Climate change isn't something that's coming – it's already here, as clearly demonstrated by the most recent IPCC report,” says Anja, who is an Interdisciplinary Lecturer in Climate Modelling jointly affiliated with the Departments of Chemistry and Geography. “The effects of climate change and some of the feedback loops it can cause are becoming more obvious now. But the climate system is complex: getting a grasp of all these feedback loops is critical to understanding our planet and making accurate climate projections.”

The study shows that large-magnitude eruptions will have greater effects as the climate continues to warm. However, the cooling effects of small- and medium-sized eruptions (see figure above) could shrink by as much as 75%. Since these smaller eruptions are far more frequent, further research is needed to determine whether the net effect will be additional warming or cooling.

Where and when a volcano erupts is not something that we can control, but as the atmosphere warms due to climate change, the plumes of ash and gas emitted by large, but infrequent, volcanic eruptions will rise ever higher. Climate change will also accelerate the transport of volcanic material – in the form of small, shiny droplets called volcanic sulfate aerosols – from the tropics to higher latitudes.

For large eruptions, the combined effect of these phenomena will cause the haze created by volcanic aerosols to block more sunlight from reaching Earth's surface, ultimately amplifying the temporary cooling caused by volcanic eruptions.

When Mount Pinatubo in the Philippines erupted in 1991, the effects were felt worldwide. The plume from the eruption – the second largest of the 20th century – reached more than 30 kilometres into the sky, forming a layer of global haze. In 1992, this haze caused global temperatures to drop by as much as 0.5 degrees Celsius. In comparison, human activities have warmed global temperatures by over 1 degree Celsius since 1850. However, the effect of volcanic aerosols only persists for one or two years, while anthropogenic greenhouse gases will affect the climate for centuries.

Volcanic plumes rise like hot air balloons: they keep rising to a height where they're naturally buoyant. The Cambridge study looked at how high in the atmosphere these plumes can rise and be transported globally under different warming scenarios.

The researchers used global climate models combined with volcanic plume models to simulate how the aerosols emitted by volcanic eruptions might be affected by climate change.

They found that for large eruptions like Mount Pinatubo, which typically occur once or twice per century, climate change will cause the plumes to rise higher and the aerosols to spread faster over the globe, resulting in a cooling effect amplified by 15%. Changes in ocean temperatures are expected to further amplify the cooling, and the melting of ice sheets is also projected to increase volcanic eruptions frequency and size in places such as Iceland.

However, for moderate-sized eruptions such as the 2011 Nabro eruption in Eritrea, which typically occur on a yearly basis, the effect will be reduced by about 75% under a high-end warming scenario (see figure left). This is because the height of the tropopause – the boundary between the troposphere and the stratosphere above it – is predicted to increase, making it harder for volcanic plumes to reach the stratosphere. Aerosols from volcanic plumes confined to the troposphere are washed out by precipitation in a matter of weeks, making their climatic impacts relatively minor and much more localised.

"The new feedback loops between climate and volcanic eruptions that we highlight in this work are currently unaccounted for by the IPCC," says Dr Thomas Aubry, a Junior Research Fellow at Sidney Sussex College and first author on the paper. "It could shed new light on the evolution of future volcanic influences on climate. Even if volcanoes have a limited influence on climate compared to human greenhouse gas emissions, they are an important part of the system."

"Due to more frequent and more intense wildfires, as well as other extreme events, the composition of the upper atmosphere is changing in front of our eyes, and so is our understanding of the consequences of these changes," says Anja. "As we continue to emit greenhouse gases, the way that volcanic emissions interact with the atmosphere will continue to change and it is important to quantify these interactions in order to fully understand climate variability."

The researchers hope to bring together more volcanologists and climate scientists to understand not only the mechanics behind volcanic plume rise and aerosol lifecycle, but also how changes in eruption frequency and magnitude, driven by deglaciation and extreme precipitation, will shape the future climatic effects of volcanic eruptions.

The research was funded by the Royal Society, the European Union's Horizon 2020 research and innovation programme, and the UK Natural Environment Research Council.

Gabriella Bocchetti, ©University of Cambridge

Research
Climate change modulates the stratospheric volcanic sulfate aerosol lifecycle and radiative forcing from tropical eruption, T.J. Aubry, J. Staunton-Sykes, L.R. Marshall, J. Haywood, N.L. Abraham, A. Schmidt, *Nat Commun*, (2021), **12**, 4708.

How you can contribute


Shankar back then

Supporting the journey from student to world-class researcher

Shankar Balasubramanian is world-renowned for inventing Next Generation DNA sequencing with David Klenerman – this year alone the pair were awarded the prestigious Millennium Technology and Breakthrough Prizes (see article inside this issue). But Shankar came from relatively humble beginnings, arriving from India as a nine-month-old and attending a comprehensive school in the north of England. Shankar became the first member of his family to attend university in the UK; he was drawn to Cambridge by the Natural Sciences tripos, which allowed him to explore a wide range of scientific topics before settling on chemistry. Although he initially found the Cambridge environment "inspiring and overwhelming" at the same time, Shankar was supported and inspired by the mentors he had along the way: people like Brian Johnson, his Director of Studies at Fitzwilliam, and Stuart Warren and Tony Kirby, who gave supervisions. Shankar completed his PhD with the late, great Chris Abell, supported by a PhD studentship and a CASE award. He says now that "Chris Abell is the reason I was drawn into research."

By supporting our new Chemistry@Cambridge Opportunity Fund or exploring a joint studentship with your college, you could create the next opportunity for another young scientist to be inspired by our host of world-class researchers – and to change the world.