chem@cam

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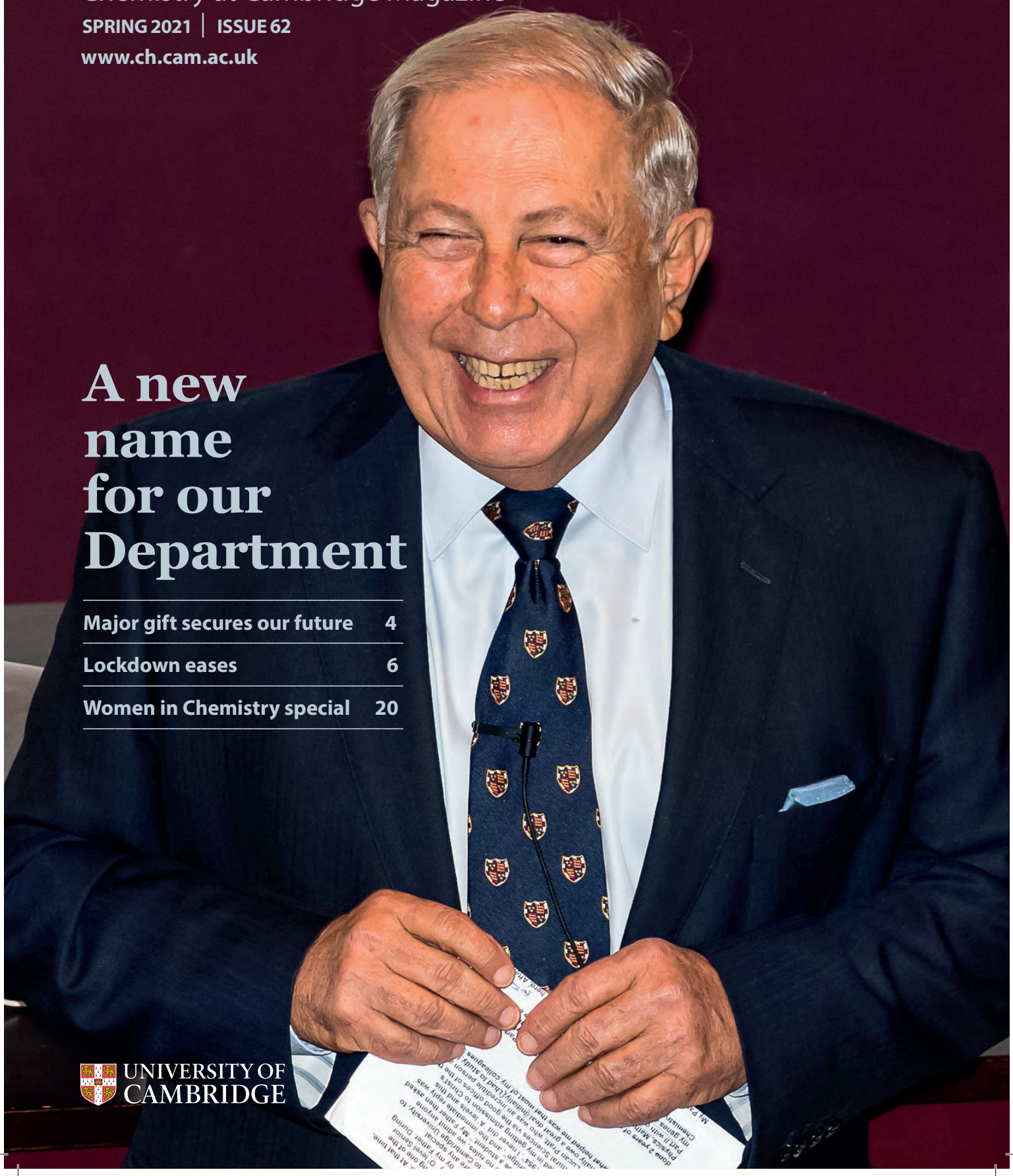

A new name for our Department

UNIVERSITY OF CAMBRIDGE

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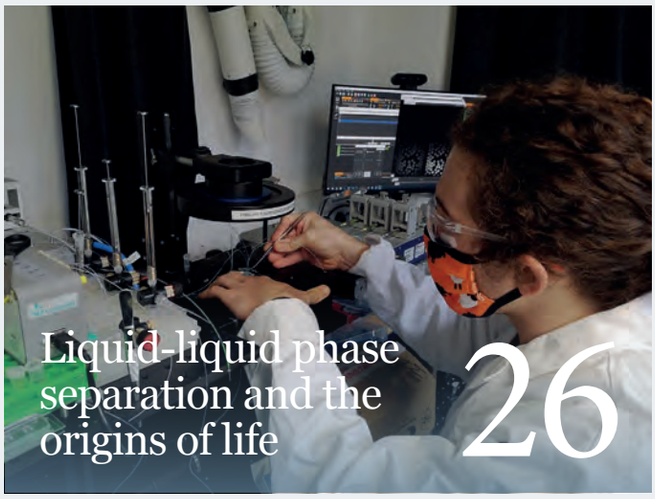

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Springing forward

As I write we are looking forward to the easing of restrictions as we move out of the third lockdown and this, combined with the lengthening days and the appearance of the spring blossoms, is making us all feel somewhat lighter and more optimistic. We have remained open for research throughout this lockdown, so it feels rather different to the first, but we will be glad to see the back of it all the same.

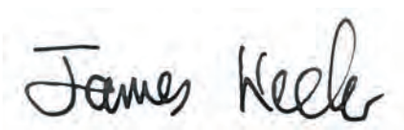
At the very end of 2020 we received the wonderful news that our distinguished alumnus and long-time supporter, Dr Yusuf Hamied, has made a major gift to the Department which will support research and teaching for generations to come. In recognition of this transformational gift we are now proudly called the Yusuf Hamied Department of Chemistry. You can read more about Dr Hamied's remarkable career and his long association with Cambridge in the lead article.

In the last issue of Chem@Cam we launched the appeal to fund a studentship in honour of Stuart Warren, and I'm pleased to say that the fund is growing rapidly towards its target. You can read more recollections of 'life with Stuart' in this issue, along with a fascinating interview of alumnus and entrepreneur Andy Richards.

To note the International Day of Women and Girls in Science on February 11, we have features on our colleague Professor Sophie Jackson and four members of the Reisner research group. Proving that chemists are multi-talented, I invite you to marvel at the beautiful and intricate artwork produced by PhD candidate Fahmida Khan.

As usual we highlight some of the cutting-edge work going on in the Department, this time with a focus on chemical biology, including the perhaps surprising role that computation has to play in this.

Here's looking forward to some glorious summer days and, of course, even more glorious chemistry!



James Keeler
Head of Department

Cover photo courtesy of Department of Chemistry

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Major gift secures the Department's future

A major gift from alumnus Dr Yusuf Hamied will support research and teaching for generations to come, and will secure the Department's leading position into the future.

Dr Hamied's generous gift will establish the Yusuf Hamied fund, which will help the Department to continue to attract and support the world's best and brightest academic talent at all levels. The gift will also establish the Hamied Scholars Programme, which will enable outstanding doctoral students from the UK and around the world to study here.

In recognition of the transformational nature of the gift, the Department has been renamed the Yusuf Hamied Department of Chemistry until 2050.

Dr Hamied said: "Cambridge gave me the foundation of an education in chemistry, taught me how to live and showed me how to contribute to society. As a scholarship student myself, I am delighted to be able to support future generations of students. I will always be indebted to this great institution and everything it stands for."

"Cambridge gave me the foundation of an education in chemistry, taught me how to live and showed me how to contribute to society."

Dr Yusuf Hamied

Dr Hamied is a leader in industry and philanthropy, focusing his attention on education and healthcare. As Chairman of Cipla in the early 2000s, Dr Hamied reduced the cost of treatment for HIV/AIDS in developing countries to under a dollar a day, saving countless lives. To help patients during the COVID-19 pandemic, Cipla is again providing medicines to healthcare organisations at affordable prices, making treatment more accessible.

The Vice-Chancellor, Professor Stephen J Toope said: "Yusuf Hamied has demonstrated an unequivocal commitment to changing and improving lives since his time at Cambridge. I am profoundly grateful for his remarkable gift to the Department of Chemistry, which will benefit generations of students and researchers."

Head of Department Dr James Keeler, said: "We are extremely thankful to Dr Hamied for his visionary support for Chemistry

Nathan Pitt

Yusuf opens the multi-use Todd-Hamied room, named after his mentor Lord Todd, in 2004.

at Cambridge which will allow us to respond flexibly to future opportunities. His gift will ensure we continue to attract outstanding scientists who will make the discoveries that help tackle some of the most pressing challenges in global society."

Dr Hamied is an alumnus and Honorary Fellow of Christ's College and completed his PhD in this Department in 1960 under the supervision of Nobel Laureate Lord Alexander Todd. He has retained close links with Cambridge over the past 66 years, and in 2018 he endowed one of the world's oldest academic Chairs in Chemistry, now known as the Yusuf Hamied 1702 Chair, which had been held by Lord Todd.

Among Dr Hamied's many honours are the Padma Bhushan, one of the highest Indian civilian awards in 2005; an honorary fellowship of the Royal Society of Chemistry in 2012; and an honorary Doctorate of Science from the University of Cambridge in 2014. In 2019 he was elected an Honorary Fellow of the Royal Society and a Fellow of the Indian National Science Academy. He received the Department's Alumni Medal for services to the community in 2016.

Nathan Pitt

Learning about glove boxes from Clare Grey in the Todd-Hamied Laboratory.

Nathan Pitt

Opening the Yusuf Hamied Laboratory for Chemical Synthesis & Catalysis Laboratory with Matt Gaunt.

Lockdown eases

As this issue goes to press, we are looking forward to an Easter term in which social distancing and other Covid-19 restrictions are gradually eased.

Labs will continue to operate with social distancing restrictions in place.

"We had been hoping that the majority of undergraduate students would be back in Cambridge for the Easter term – the place is just not the same without them," says Head of Department Dr James Keeler. "Unfortunately, the latest review of the government's road map leaves many of our students wondering when they may be able to return. I know Cambridge has at every opportunity been making a strong case to the government to move towards the easing of restrictions, but new guidance won't be given until at least 17 May."

"As an institution, our University has shown immense resolve and resilience. As a community, we have shown solidarity and kindness."

Vice-Chancellor Stephen Toope

During the Lent term the building has continued to be open for experimental research under strict guidance. "Everyone in the Department has behaved so responsibly that the number of positive Covid cases over this entire period has been less than 10," James notes proudly. "When a case has been identified our own version of track and trace goes into action, and because of this we have largely avoided onward infection."

Continued vigilance has been essential to this success, and the Department will continue to apply restrictions as long as they are needed. "The current understanding is that aerosol transmission in social settings is one of the most significant routes of infection. So social distancing, effective ventilation and the use of face coverings remain the key ways in which we will continue to keep ourselves safe," James notes. "Luckily, the synthetic labs, which are the ones we most need to use, all have excellent forced ventilation – you could say with some justification that working at a fume cupboard is probably, from a Covid point of view, a pretty safe place."

The one-way system is keeping Department members fit.

James also credits the University's successful and rigorous testing programme for the small number of cases in the Department. "I think it's safe to say that the University's asymptomatic testing programme has been an unqualified success," he says, noting that it was expanded last term to cover postgraduates living out of college accommodation.

"The University has also provided lateral flow tests to staff members whose work requires them to come into the Department regularly, or who are at higher risk because of the need to use public transport or because they interact frequently with other people. All this testing gives us confidence that the risk of coming into the Department is as low as we can make it – it has been a real boost to our confidence."

James is the first to admit it has been a difficult year for the students. "In the Lent term all our lectures, supervisions and even practicals were held online, which of course is not ideal," he says. "I especially feel for final year students who were not able to complete experimental work on their research projects – which is such an important experience. Students whose projects were principally theoretical or data based were mostly able to complete their projects. But those who really needed to do experimental work have been asked to write up what they have done and then supplement this with a critical literature review."

"My thoughts today are with all those colleagues and students who have been personally afflicted by COVID-19, who have endured losses, or who have had to take on extra caring duties over the past year."

Vice-Chancellor Stephen Toope

Despite the continued uncertainties ahead, James remains optimistic, and is grateful to all those in the Department who continue to work together to get us through this challenging time. "Now, we just can't wait for the students to be allowed back," he says.

Career Support Fund

The University has created a Career Support Fund to help staff (at all levels) whose careers have been disrupted as a direct result of the pandemic, or due to a career break taken for caring responsibilities. It provides grants of up to £10k and will run in three rounds for the 2020 to 2021 academic year.

www.hr.admin.cam.ac.uk/career-support-fund

Postgrad voices heard

Vivien Lechner and David Izuogu became postgraduate representatives in 2019, so have both coped with last year's lockdown due to Covid followed by the gradual re-opening with strict safety measures. We caught up with Vivien and David to find how they and their fellow postgrads have been coping.

David Izuogu and Vivien Lechner in pre-Covid times.

What is your role as Postgraduate Student Representatives?

David: We represent the concerns of postgraduate students on the Postgraduate Education Committee – we do regular student surveys so we know what the most pressing issues are.

Vivien: Postgrads can also fill out a confidential form on the postgraduate web pages which we receive immediately by email. If there's no upcoming committee meeting, we take anything that's urgent straight to the Postgraduate Education Team.

Why did you become a rep?

Vivien: Postgraduate welfare is something that I feel is extremely important, and I felt I could contribute to postgrad voices in the Department.

David: It puts us in a position to listen to students and see the diversity of experiences that students really have and try to help improve where it's needed.

Your most recent survey asked how students have been affected by the pandemic – what were the most common concerns?

Vivien: It's changed slightly over time. In the first survey, which we did toward the end of lockdown last year, people who rely on lab work had just lost a significant chunk of their research time and a lot of the concerns were about funding and PhD extensions. Since the department re-opened, a relatively constant concern has been overall Covid safety.

David: 65% felt the Department's Covid-19 policies were adequate. Some students wanted stricter measures, and some thought they were too strict.

How has the committee responded to the students' concerns?

Vivien: They are always willing to listen and give feedback. Sometimes it might be something that is out of their hands because it's a university policy, but for safety issues they've come up with responses or proposed solutions very quickly. There are a lot of people in the Department, including the Postgraduate Education team, who are always happy to talk

to students, so sometimes we just need to remind them of the pathways already available to solve their issues.

David: In 2019 we started looking at this whole issue because we realised when students have problems they don't always come forward, and we wanted to know the reason – was it lack of confidence, or worry about their PI? When I was international officer of the Graduate Union we developed a conflict resolution flow chart, which we adapted to the department framework, so it's very clear now where to go when you have a particular worry. We presented the flow chart at our 'student reboot' in October, and we've just recirculated it.

So how does a student complain if, say, they feel the lab they are working in is unsafe?

David: The first point of contact is always the PI (ie, group leader), but if this is not satisfactory, then they can go directly to the Postgraduate Education Team, Deputy Head of Department or the Head of Department. If they don't feel comfortable raising the concern with the department, they can follow the college channel by going to the college tutor and from there to the Office for Students Conduct, Complaints and Appeals (ASCCA) within 28 days of the matter arising if they don't feel that the university procedure has effectively dealt with their concerns.

What has been done about extensions?

Vivien: We discussed this with the Committee, who suggested that students should wait until they are about six months from their completion date, when they have a much better idea of how much extra time they'll need. They then must apply both to their funder for additional funding, and to the University for an extension of time. The Department is committed to being very charitable about extensions, but other extensions remain an issue depending on the funding body, and talks are still going on at University level about this.

David: Most funders have agreed to extend funding for final years who need it to complete their work, but conversations are still ongoing about students not in their final year. Some funding bodies have signalled that extension requests will be considered on a case by case basis, but it would be great to have all the funding bodies do the same, especially for UKRI. [Editor's note: Postgraduates can also submit a Research Impact Statement with their thesis that details the impact of Covid-19 on their research.]

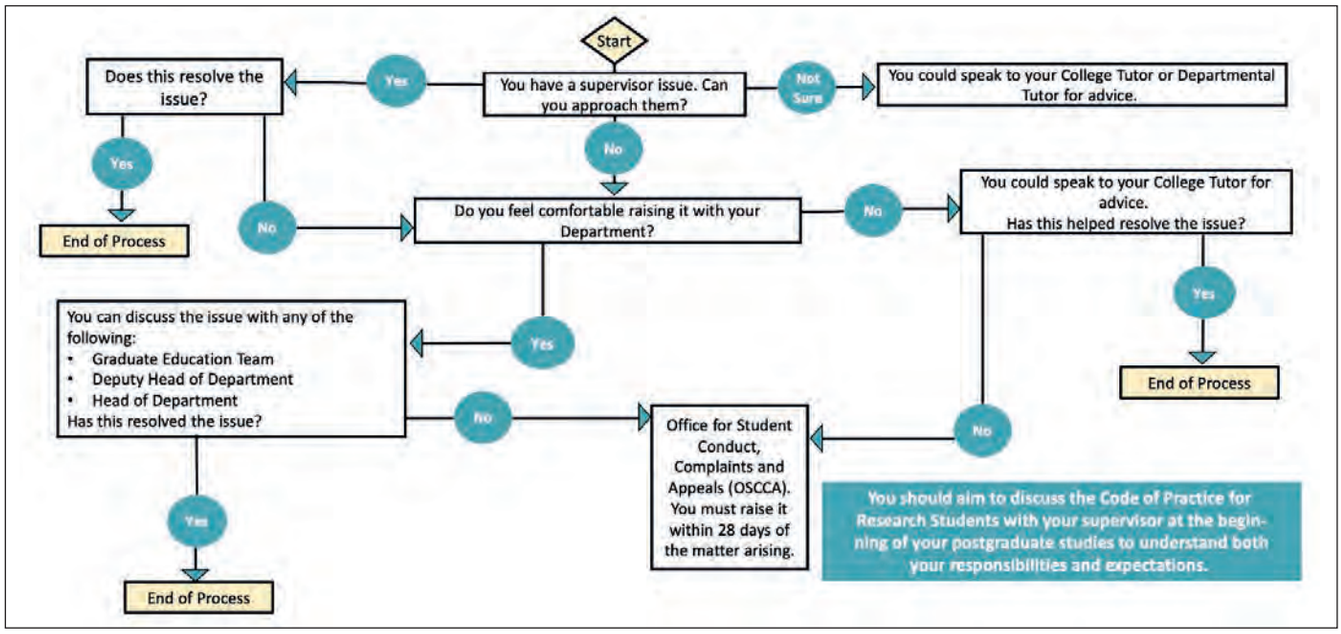
How have you been personally affected by the Covid restrictions?

David is in his fourth year at Wolfson. He is a theoretical chemist in the Thom group, funded by the Cambridge-Africa and Cambridge Trust.

To be fair, I'm not as affected as those in the experimental groups who need access to wet labs. In the beginning I had to leave my college, because fourth years are supposed to live out. There was no chair or desk in my new accommodation, and it was very uncomfortable, but I was eventually provided with an office desk and a wide screen. I was also supposed to travel to Japan in April 2020 to get some experimental data to show my programme was working, which of course didn't happen, so now I'm looking to see if there's someone I can collaborate with there who can provide the data I need.

Vivien is in her third year and does synthetic chemistry in the Gaunt group. She is funded by AstraZeneca.

The three-month lockdown did affect me quite a bit, as my project requires lab work to progress. There was a period where we were limited to working in shifts, and then in the summer we got extra capacity so we're back to normal. The only other thing that I was sad about is that I should have had a two-month placement at AstraZeneca in October, but now that's been postponed indefinitely.



David developed this flow chart that shows students where to go if they have a conflict in the Department.

Alumni correspondence

We continue to receive tributes and reminiscences about Stuart Warren, who died in 2020. You can find them all on our alumni pages at www.ch.cam.ac.uk/alumni.

A uniquely gifted tutor

Dr David Morris

I studied natural sciences at Churchill College (graduating 1978) and subsequently gained a PhD under the direction of Dr Dudley Williams (1981). As an undergraduate I found Stuart's lectures inspirational. I can remember arriving at the Lensfield Road lecture theatre on a Saturday morning with hands so cold from the cycle ride in that I could barely grip my pen – it didn't matter. Stuart's lectures were superbly organised and hugely informative as he developed his theme and revealed to us the secrets of organic chemistry. Stuart took you from where your knowledge base stood and by the end of the lecture you had a clear sense of advancement not to say a sense of being royally entertained.

As a Churchill College tutor he was uniquely gifted. Alert and responsive to an individual's needs he encouraged us to ask questions and then challenged us with his own questions. Supervisions were also focused on the learner's agenda and he had the ability to see with great clarity the perspective of his tutees. Stuart was such a great teacher.

I have taught chemistry and medicine in a variety of situations and have always tried to engage the teaching principles and approach that Stuart so clearly demonstrated.

Dr David Morris

The challenge of Godfrey's lemon buns

Alan Davidson in lab 287 with Les Hughes (in white coat) in 1975. "As a result of lockdown my hair now is almost the same length!"

I would like to contribute my own comments as I was one of Stuart's early PhD students (1973–76). I was greatly influenced by him and very grateful for all his help.

I was extremely fortunate to be taught by Stuart as an undergraduate and also to have him as my PhD supervisor. All supervisions were challenging, slightly nerve racking, but actually quite enjoyable. The same could be said for the research group meetings; I am not sure my teeth have ever fully recovered from the Godfrey's lemon buns. Not only did I learn a great deal of organic chemistry from Stuart but I also learnt how to run a research group – to get the best out of a PhD student and for the student to get the best out of a Ph.D. I hope some of my PhD students benefited from this training!

Alan Davidson

Coffee brewed in the fume cupboard

I was saddened to see the references in Issue 61 to Stuart Warren's death, but reading Philip Evan's memories nevertheless brought back a smile as I recall working in his small research group at that time (1970–1973).

Philip's recollections were correct: Stuart's first lecture course to undergraduates was to second year students in 1968/69 and his approach to teaching was such a breath of fresh air that I was very happy to accept the chance to subsequently work in his group and for 2 years I was actually the entire group! His approach to teaching was based on just a few teaching principles which subsequently have become accepted as best practice. Firstly he worked on the basis that it was not possible for students having up to 3 lectures in a morning to concentrate intensely for 60 unremitting minutes and so he would turn up 2 or 3 minutes late, would finish 2 or 3 minutes early and would have a couple of minutes break in the middle to amuse us with an anecdote. Secondly he appreciated that lectures were meant for passing information to students rather than them being a test of how a student could listen and write quickly and accurately at the same time. To ensure that concepts were absorbed in the lectures themselves and with students listening and focussing, he had prepared an A4 booklet which essentially contained the lecture notes. This seems so obvious now but at that time it was quite exceptional.

His analytical approach to all aspects of his life extended also to his practice as a Research Supervisor. Rather than coming round to my bench in Lab 287 "to not help me twice a day", he stressed throughout that it was my PhD and our contact was usually restricted to lunch on Fridays – indeed with coffee brewed in the fume cupboard. As we munched through sandwiches – his invariably beef with horseradish from the Panton Arms – we would laugh about his passion for off-spin bowling, the Goons, his occasionally-irreverent impersonations of the more senior members of the teaching fraternity, and life and everything. And then as lunch was finishing he would ask what I had been doing that week and we would then discuss where it was leading and he would make suggestions of possible avenues that I may care to explore. It was never dictatorial, he was always there to help if I asked for assistance and his man-management skills made me feel that I was part of a partnership even though, in truth, he was at the helm. They were really fun times in a colourful era in a colourful Department which had some lively young individuals – Stuart, Tony Kirby, Ian Fleming, Dudley Williams and others. I shall never forget those times, especially the humour, and will be eternally grateful for Stuart's analytical brilliance as a thinker, communicator and educator and how his example influenced my subsequent career. He was an exceptional person.

David Howells

Stuart Warren Studentship Fund

Thank you to everyone who has contributed to the Stuart Warren Studentship fund, which has raised an amazing £50,000 so far. With matching funds from the Cambridge Trust, another £35,000 raised will allow an outstanding student from sub-Saharan Africa to complete a four-year PhD in chemistry in this Department while living at Churchill College.

If you would like to support the fund, please contact our Head of Department, Dr James Keeler.

Tempus Fugit

When he was growing up, alumnus Andy Richards' mother often repeated these famous lines from Kipling to him: "If you can fill the unforgiving minute with sixty seconds' worth of distance run…" And with his remarkable accomplishments and activities, Andy has clearly taken this exhortation to heart.

Time is a theme that runs through Andy Richards' life. "My family will tell you I'm sort of obsessed with time," he says via Zoom from the office he has built in his back garden.

But this is because there is still so much Andy wants to do – not that he hasn't already managed to fit a lot in since he was an undergraduate here from 1978 to 1981. Andy applied to read the Natural Sciences Tripos after being inspired by the science teachers at his grammar school-turned-comprehensive in Cornwall, which had no track record of sending people to Cambridge. Andy was accepted at Jesus College, where his Director of Studies was Peter Edwards, an inorganic chemist who is now Head of Inorganic Chemistry at Oxford, and for Part II Andy specialised in inorganic chemistry with Jack Lewis and Brian Johnson.

This leads to the second running theme in Andy's life, which is people. "I had no plan and I had no real idea what I wanted to do," he confesses, "but I find people inspiring, attractive, interesting, stimulating, whatever you want to call it. So in a sense I was as much inspired to do inorganic my final year by the likes of Peter Edwards, Brian Johnson and Jack Lewis," he explains. "I've always been attracted to the 'who' and much as to the 'what.'"

A Chiroscience discovery which led to Romosozumab (Evenity) is used to treat osteoporosis.

Andy says the best parts about his time at Cambridge were "friends, stimulation, just the ability to think and see no limits." The worst part was, naturally, "there was just not enough time – it was all too short."

After Cambridge Andy completed his PhD in bio-inorganic chemistry with Professor Andrew Thompson at the University of East Anglia, researching the behaviour of metal clusters in proteins. "I had always been interested in biology as well, so to look at metal clusters in biological systems seemed to scratch two itches."

Dipping his toes

After UEA Andy was recruited to join ICI (now AstraZeneca). "I still never had a plan," he admits, smiling. "I have huge admiration for people who have their careers mapped out, but I also find it strange because the world changes and shifts and then there's serendipity."

ICI had set up a couple of early biotech units, which interested Andy. He says it was a great place to learn and develop, although even in these early stages of biotech he was worried about time and timing: "I was terrified that I had missed the boat and all the important and fun stuff had been done!"

Steep learning curve

When Andy's future wife returned to Cambridge for a research fellowship, Andy left ICI and joined Cambridge-based consultancy firm PA Technology. As a consultant Andy further honed many skills that later proved invaluable. He learned to give persuasive pitches, to sell and do last-minute research for presentations to clients who ranged from governments, large and small companies, investors "and basically all comers," he says. "It was great – we were permanently on the edge, I was constantly going up learning curves – it was exhilarating, scary and educational. I learned a huge amount from that."

It was during this time that Andy began to perceive his calling, which brought together the threads of 'people' and 'time' already running through his life: "I absolutely knew I had to be involved in start-ups," he says. "What I really loved was that spirit of being a sort of "band of brothers – and sisters. With early ventures all the energy is outwards, bright folks trying to do something difficult together – you're a team and there's that great feeling of camaraderie." Together with the people, there was also the feeling of being on the cutting edge of science, of riding the crest of the wave at just the right time – "timing is everything".

Curriculum Vitae:
Andy Richards

Born:
Cornwall

Education:
Undergraduate Jesus College 1978–1981
PhD University of East Anglia 1981–1985

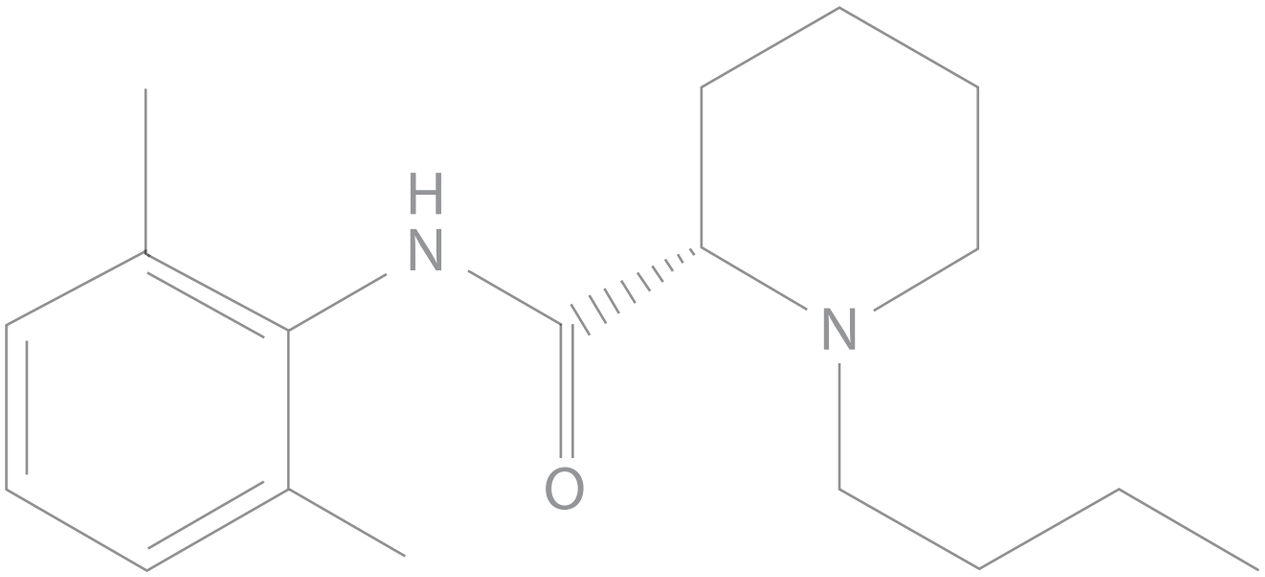
Start-ups:
Too numerous to mention

Honours:
CBE for services to life-science investment

First start-ups

So after one initial unsuccessful start-up attempt, Andy joined Enzymatix, a Cambridge-based biotech, to spin out a new company. The people and the timing were right. "We pulled technologies out and created a new company first called Chiros, which then became Chiroscience," he says. "The impact of chirality on pharmacology and medicine were being realised and there were lots of specific opportunities for optimising stereochemistry in pharmaceuticals. And the technology, patents and regulations had all come together at the same time to make it possible."

Andy makes the subsequent history of Chiroscience sound rather like a game of caroms: "We roller coastered, pivoted, went on the stock market (becoming one of the first UK biotechnology IPOs in 1994), did science, did deals, bought a genomics company off Bill Gates in Seattle, travelled the world, morphed and shifted. All companies that succeed tend to go through these changes – the pace and chaos is part of what makes it a success."



Techelf

Chemical formula of ChiroScience discovery levobupivacaine (Chirocaine).

And success it was. Chiroscience developed a valuable and broad drug discovery pipeline and most importantly got treatments to patients. But by 1999, with a new product approved, and three in advanced stages of development, Andy recognised that the company was at a turning point. Chiroscience had always licensed its products to pharma companies to sell, but to grow further it needed a new model.

"We needed to move into a model where we could sell our own products, but for that I was I was the wrong guy. I did the deals and strategy and I had no experience in sales. If we kept doing the wrong thing I was the right person; if we were doing the right thing then I was the wrong person." The opportunity to merge with Celltech arrived at the right time, "and we created a great UK biotech company," he concludes. With the merger, Celltech Chiroscience became the UK's biggest biotechnology firm, subsequently bought by Belgium's UCB in 2004.

The deal left Andy financially able to pursue his own interests, but he had promised his wife he would take a year holiday. "We had just moved house, we had a young family and I was exhausted after the merger." But within four months Andy had founded four companies and was CEO to two of them. Again, it all came down to teams and timing. "It was about the people – people who I loved and rated arrived at the house with great ideas and energy and 'let's do this!' And I just couldn't resist. And that's what I've been doing ever since."

Innovator and Entrepreneur

In the 20 years since, Andy has been involved in some 30 companies as founder, adviser, mentor, investor, board member, chair – "whatever is needed." His current projects range across large swathes of healthcare, therapeutics, digital health, data, genomics, AI and mental health, and although he still "doesn't have a plan" he does say he hopes to continue doing the same thing "if the bright, young enthusiastic thinkers will tolerate me."

Andy is linked with other Cambridge-based entrepreneurs such as Hermann Hauser and David Cleevely in multiple ventures and the Cambridge Angels, who mentor and invest in innovative ideas. He is on the Commercial Board of CRUK, advises several investment funds, and was until recently a director of Cambridge University Hospitals NHS Foundation Trust. He has been heavily involved as Chair of the Babraham Research Campus community.

Andy is unsurprisingly a sought-after speaker on innovation and entrepreneurship, and in those talks he likes to weave together his threads of people and time with a third thread which he dubs "themes."

"I talk about themes, teams and timing," he explains. "So at any one time I have a set of themes. Themes are where a real 'now' problem can be matched with an innovation or technology that is a potential solution. Secondly, I cannot do any of this stuff alone – I build teams, I pull people together. And finally, timing is almost everything." When the theme, team and timing come together "that's when I can't resist getting involved," smiles Andy "And that's when impact results."

What advice would Andy give to entrepreneurs who are just starting out? "First, this really is a team sport – don't just pay lip service to that. The capability and resilience you gain from having a great and especially a diverse team is key. And second, enjoy the journey. I have, and I'm still enjoying it, but time is just too short - the unforgiving minute still hangs over me."

Alumni Postcard: Baby Smiles Club

Angela Wilson (Pembroke 1996)

Greetings from…
Denmark, where I moved nearly two years ago with my Danish partner, just after our son was born. The quality of life is really incredible, and the education system is great. We live right next to the sea, which is very uplifting.

I read…
Natural Sciences at Cambridge (Pembroke 1996) specialising in Chemistry, and then switched to a Postgraduate Diploma in Law, which to be honest I found a walk in the park after chemistry!

Studying chemistry…
at Cambridge taught me about intellectual rigour, to work hard, and about the value of science. We're seeing today how incredibly important science is in our lives, in dealing with climate change and the virus. I also had great fun working with friends in the day-long practicals! At my first law firm I learned the strength of working together and the importance of being ethical, honest and standing your ground.

I was inspired…
to start my new business, Baby Smiles Club, after seeing so many parents struggling with their baby's sleep. We've found that helping people understand about sleep cycles, hormones and the processes governing sleep (the circadian process and the homeostatic process) really helps them with their baby's sleep. As far as I'm aware, it's the most comprehensive ebook and program worldwide, underpinned by the most recent science of baby sleep.

Scientists…
like facts, theories and equations, while lawyers wield opinions and words. Being both helped me translate the science into easy-to-understand concepts and advice. I want my site to be a 'one stop' trustworthy and reliable source, so parents can spend time with their babies and not hours on the internet looking for answers.

Visit Baby Smiles Club website: www.babysmilesclub.com/

A. David Buckingham 1930–2021

Professor David Buckingham died in February at the age of 91, peacefully at home surrounded by members of his family.

Professor Buckingham was the first holder of the 1968 Chair of Theoretical Chemistry in our Department, having previously held academic appointments in Bristol and Oxford. He did his PhD here in Cambridge under the supervision of John Pople.

Throughout his long and very productive career Amyand David Buckingham, who preferred to go by David, made many important contributions in molecular physics, most especially in the area of intermolecular forces and in the understanding of the electric, magnetic and optical properties of molecules. His work was not only theoretical but also led to the development of experimental methods for measuring various quantities, notably the quadrupole moment of molecules and their hyperpolarizability. With Laurence Barron he pioneered the study of Raman optical activity. His also did pioneering work on the importance of long-range intermolecular forces in determining the structure and properties of clusters.

David received many honours: he was a Fellow of the Royal Society, a Fellow of the American Physical Society, a Foreign Associate of the United States National Academy of Sciences, a Foreign Member of the Royal Swedish Academy of Sciences, a Fellow of the Australian Academy of Science,. He received the first Ahmed Zewali prize, and was awarded a CBE. David also has the very special distinction of having a unit named after him: the Buckingham is the CGS unit of the electric quadrupole.

An Australian by birth, David was a skilled cricketer who played for the University and other first class teams in the late 1950s. His interest in the sport continued and he was for many years President of Cambridge University Cricket Club. Professor Buckingham was a courteous and gentlemanly scholar, but there was no doubt of his incisive scientific mind and the great depth of his knowledge and understanding. The Editor of *Molecular Physics*, a journal with which David had a long association, describes David as "a giant in the field of understanding intermolecular forces". Few would disagree.

I was greatly saddened by the news of David Buckingham's death. My time with him in Cambridge from 1969 to 1975 was a wonderful experience. We continued our collaboration long after I left Cambridge, our final paper together being published in 2010.

You mentioned our work on Raman optical activity (ROA). This constituted the first observation of vibrational optical activity in molecular vibrational transitions (as distinct from conventional ORD and CD which measures optical activity in electronic transitions). It is intriguing that an early unsuccessful attempt (via infrared ORD) at this long-sought extension of optical activity into the vibrational spectrum was made by C.P. Snow (The Two Cultures, etc.) as part of his Ph.D. work with T. Martin Lowry, a Cambridge Professor of Physical Chemistry (*Lowry and Snow*, Proc. Roy. Soc. A, 1930, vol. 127, 271)

Laurence D. Barron FRS, FRSE
Emeritus Gardiner Professor of Chemistry, University of Glasgow

Noticeboard

Dr Alex Forse has been awarded a Future Leaders Fellowship on electrochemical carbon dioxide capture to develop materials that can reduce greenhouse gas emissions and tackle the global climate crisis. He has also won this year's BRSG-NMRDG Prize, which is given to an early career research to for excellent contributions to magnetic resonance.

Nathan Pitt

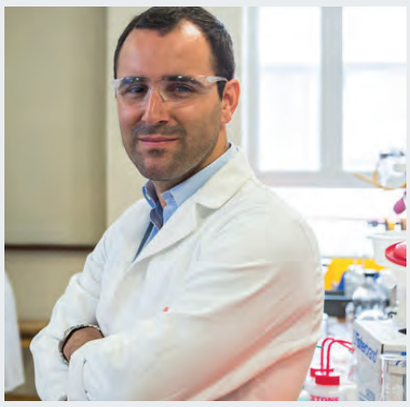
Professor Erwin Reisner has received a European Research Council Proof of Concept grant to support research into the scalability and eventual commercialisation of a process called photoreforming, which uses sunlight to transform biomass, food and plastic waste into hydrogen.

Caroline Hancox

Dr Jenny Zhang has been awarded the 2020 Royal Society of Chemistry Biotechnology Medal for her work in combining electrochemistry with natural photosynthesis to find sustainable ways to fuel the planet.

Gabriella Bocchetti

Dr Gonçalo Bernardes has been elected as a member of the Portuguese Diaspora Council (Conselho da Diáspora Portuguesa), which through the World Portuguese Network is strengthening the networks of talent and expertise in Portuguese communities across the world in economics, culture, science and citizenship.



Nathan Pitt

On February 14 **Professor Clare Grey** and her group celebrated their 10-year anniversary in the Todd-Hamied Laboratory, which opened in 2011. "It's a very special Valentine's Day today for the Grey Group," they tweeted. "Congratulations to Professor Clare Grey and to all group members former and current." Grateful thanks to Dr Yusuf Hamied for his contribution to this world class facility.

Race to the finish

Over 40 teams took part in this year's Chemistry Race on 6 February, a new competition for sixth form students organised by Adam Prada, a third-year PhD student in Stuart Althorpe's Theoretical Chemistry group.

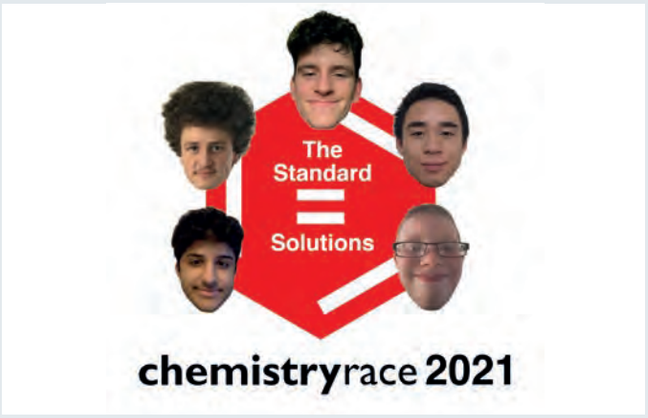
In the competition, teams 'race' against the clock and each other to solve unusual chemistry problems suitable for sixth-form chemistry students.

Each participating five-member team is given six questions at any one time, so team members can work in parallel and submit answers as soon as they are finished. Points are scored for correct questions, although the number of points decreases with the number of submission attempts.

"If a team is struggling we can also ask them what the problem is and give hints, which is a good educational experience for both the organisers and the participants," says Adam. The team with the most points at the end of the two-hour period wins.

Of course, Covid has changed the nature of the competition this year. The advantage of moving the competition online meant that more teams were able to participate, up from 24 last year. The teams also came from a much wider region, with the farthest being *DJ Chemistry* from Durham Johnston Comprehensive School in Durham. And although the organisers couldn't completely recreate the social interactions between teams, which is part of the fun, they were still able to give hints and encourage questions using video chats, and even had a 'live' closing ceremony on the interactive site Gather Town.

Chemistry Race was founded at the University of Pardubice in Czechia (formally known as the Czech Republic) in 2015. "I was involved in the Czech competition for a few years while I was already at Cambridge, because it was founded by my friend Jan Hrubeš," explains Adam, who came to Cambridge from Czechia in 2014. "And two years ago, I thought 'why not bring it to Cambridge?" His offer was "met with enthusiastic support" by Head of Department James Keeler, and the first competition was held last year.



Competition winners *The Standard Solutions*.

This year's winning team was *The Standard Solutions* from King Edward VI Camphill School for Boys, a state-funded selective school in Birmingham. Radley College's team *Cerious* came in second. After an initial three-way tie, third place was awarded to Westbourne School, who edged out *DJ Chemistry* and *Chem Taj* (Queen Elizabeth's School) on points scored for the highest question solved.

In addition to other prizes, all three top teams were awarded the ever-popular drinks mugs shaped like beakers: "Because it's a chemistry competition, we wanted to have a prize related to chemistry," says Adam. Fittingly, the beaker mugs are made in Chechia, where the competition started.

Photo competition winners *The Curly Arrow Appreciation Society*, The Skinners' School, Tunbridge Wells, who will each receive a Chemistry Race t-shirt printed with their winning photo.

Diversity in Chemistry webinar

Racial injustice and Covid 19

"Everyone is not experiencing Covid in the same way," said Dr Karen Salt, Deputy Chair of the UKRI External Advisory Group for Equality, Diversity and Inclusion. "Covid has highlighted what is already unfair."

Salt was speaking on the topic of "Racial Injustice and Covid 19"at the first of our Diversity in Chemistry Webinars held in February, joined by successful businesswoman and entrepreneur Dr Maggie Semple, the two speakers led a thought-provoking session on systemic racial injustice. Semple pointed out that people who are categorised as BAME (Black, Asian and minority ethnic groups) "are not categorised of their own choosing." She asked: "How can the BAME community trust systems that have systemically worked against them?"

The webinar was followed by a wide-ranging question and answer session, fielded by Professor Melinda Duer, which many viewers said they wished could have been longer.

Unseen disabilities

The second webinar featured Professor Hisham Ziauddeen, a Clinical Senior Research Associate in the Department of Psychiatry and Kenneth Ewing, Specific Learning Difficulty advisor at the University's Disability Resource Centre, and was on "Unseen Disabilities", which can range from neurodiversity, sensory impairment, chronic physical, neurological and mental illness.

"People with an unseen disability are just telling you about the tip of the iceberg – they have gone through all this numerous times and most have already received a diagnosis," pointed out Ziauddeen, who is also a University Wellbeing and Disability Champion. "You don't need to question them about their disability or determine whether their needs are genuine – the most important thing to do is ask them what they need and listen."

Ewing explained the concept of Universal Design, in which workplaces are set up in an inclusive manner, so adaptations are seen as being 'add-ons' and people with an unseen disability don't stand out. The webinar was again followed by a stimulating question and answer session.

Redressing racial injustice

- Find someone with a completely different view and convince them otherwise – don't be silent.
- Note the culture you are in and make efforts to change it.
- Small actions make a huge difference.
- Be kind.

Unseen disabilities

- Be less judgmental/more empathetic.
- The 'cost of functioning normally' may be exhausting.
- The problem is real and they have already tried other options.
- Listen.

Karen Salt

Maggie Semple

Hisham Ziauddeen

Kenneth Ewing

The Department received very positive feedback from the webinars, and will be discussing our own action plan for dealing with some of the issues raised. We intend to continue these annual Diversity events, and our grateful thanks go to the University Diversity Fund for their financial support.

Both webinars were recorded and are available to view on the Department YouTube channel: www.ch.cam.ac.uk/watch-us-action

Celebrating Women in Chemistry

Many of our research groups drew attention to the work of their women scientists to mark the International Day of Women and Girls in Science in February. The Grey Group highlighted papers published in the last year which had their women colleagues as first authors, and the Reisner Lab interviewed their women researchers, four of whom you can read about below. In the following pages we also feature one of our senior Professors, and interview a postgraduate in the Clarke group who has shared her remarkable drawing talent with her colleagues during lockdown. As the Grey Group noted: "Let's all (especially those in positions of privilege) work to make science – and the world – a more equal place for all women."

Ava Lage, third year PhD

My research focusses on using carbon-based materials for solar-driven CO_2-reduction or H_2-evolution. In other words, I am trying to store the sun's energy as fuel. Achieving this would help us create a more dependable supply of renewable energy and with CO_2-reduction, even let us continue to use conventional fuels in a sustainable way by closing the carbon cycle. In my free time I enjoy spending time outside, especially rowing on the Cam. If the weather isn't cooperating, you can find me curled up with a good book or playing the piano.

Melanie Miller, final Year PhD

Solving the world's energy challenge and increasing CO_2 levels requires sustainable and scalable solutions. My work on the application of enzymes in semi-artificial systems for solar-driven CO_2 conversion to valuable fuels is now focusing on the critical shift from enzyme to microorganism-based systems, where the fragile enzymes are protected within a whole cell.

In my free time, I enjoy participating in long-distance running events across Europe. Whether it is the arts or innovative products, I enjoy discovering new ideas and finding inspiration in unexpected places. I love traveling and learning about different cultures.

Carolina Pulignani, first year PhD

I am studying carbon-based photo-electrocatalysts as part of the @SOLAR2CHEM European project. We are looking for a greener alternative approach to common industrial processes, in which we can minimise waste, pollutants and energy consumption.

I am Italian, from the amazing capital Rome! Being the daughter of two flight attendants, I have a passion for travelling running through my veins and I have spent most of my life travelling around the world. I used to be a professional runner, and I love walking, running or simply moving around.

Taylor Uekert, postdoctoral researcher

I use sunlight and photocatalysts to convert plastic and mixed waste intro hydrogen fuel through the process called photoreforming. I am also interested in the wider role of science and technology in a carbon-zero future and circular economy. My hobbies include hiking, dancing, baking, and reading and writing fantasy.

Constant learner

Professor Sophie Jackson never envisaged herself as an academic, and still feels surprised and lucky to keep learning about the work she loves.

At her comprehensive school in Cheshire, Sophie chose to study double maths, physics and chemistry at A level because she thought they might be more 'useful' than art subjects. "I thought I didn't like biology so I didn't even consider it," she recalls. And although she excelled at Maths and Physics, she gradually realised that she loved chemistry best, eventually becoming only the second student from her school to be accepted to an Oxbridge college.

Like many students, Sophie suffered from imposter syndrome, and was constantly comparing herself to her classmates. She says it came as a surprise to be awarded a first-class degree at the end of her studies. "It was a big shock to me – and to my friends, because I'd convinced them I was going to fail. I realised retrospectively that the chemists in my college were a brilliant cohort who included the top chemist the University had seen for ten years, and I'd been comparing myself to them!"

Sophie discovered biological science during her final-year project, which was on electron transfer in metalloproteins. She was fascinated by both the biological and chemical aspects of the research, and became intrigued by proteins and protein folding. "I learned to love biological science, and realised I wanted to learn more," she says.

Sophie wanted to go to London, so she applied for a PhD with Professor Alan Fersht at Imperial College, who was at that time noted for his work on enzymology and was just getting into the field of protein folding. Shortly after she started, Professor Fersht informed the whole group they were moving to Cambridge. "So that's how I ended up in Cambridge!" she laughs. Sophie again had a slow start. "My first two years went horrendously badly," she recalls ruefully. Her experiments produced no results and her project was further disrupted by the move to Cambridge. In her third year Sophie felt fortunate to obtain additional funding to pursue a new project she had designed, to develop a simple system for studying protein folding, using a barley protein known as CI2. The project was a success, and her first paper on the results became a classic in the field, which has been cited over 800 times.[1]

After being awarded her PhD in 1991, Sophie won a research fellowship at Peterhouse, and published numerous papers during her continuing time as a postdoc in the Fersht group. In 1993 she went to Harvard as an International Human Frontiers Postdoctoral Fellow, but this proved to be a fallow two-year period which produced no publications. Sophie is philosophic about this: "These are terrible experiences at the time, but they teach you a lot which stands you in good stead." In 1995 Sophie returned to Cambridge and Peterhouse, starting her own research group as a Royal Society University Research Fellow.

Once again Sophie had a tough start. The only other female academic in the Department was Melinda Duer, although Jane Clarke (now Master of Wolfson College) joined soon after. "In all my time I had never felt any experience of sexism, then when I came back to run my own research group I got numerous sexist remarks – and most of the men were not even aware what they were saying was sexist." Despite these obstacles, Sophie's research began to flourish. She was appointed University Lecturer in 2000 and moved up the ranks to become a Professor in 2017. As one of only four female Professors in the Department, Sophie would still like to see more female role models. "I had no female lecturers as an undergraduate, and when I doubted myself as a young researcher, there were no people like me to emulate. Of course, it has got much better, but there's still some way to go."

About five years ago, Sophie became severely affected by Chronic Fatigue Syndrome, and her research group wound down while she took care of her physical health. Now she is much better, although she knows she has to be careful. "I can do a normal working day, but not what I used to do," she admits. She is thrilled to be re-building her group which

currently has five postgraduates. She is aiming for six to eight members, which she feels would achieve a 'critical mass'.

Fortunately, after the initial lockdown in March 2020, her group members have been able to access the Cambridge lab to continue their experiments. Sophie meets with each of them frequently online to discuss their progress and where to go next.

"We look at protein folding/unfolding and we also look at peptide aggregation, which is when peptides (chains of amino acids typically shorter than proteins) self-assemble into fibrillar structures and other states," she explains. "Some of our research is very 'pure' in that we're doing it without an application in mind – for example, we were the first group in the world to study how knotted proteins fold.[2] Peptide self-assembly, on the other hand, is much more applied and is particularly relevant in drug formulation and potentially drug delivery."

When looking at peptides, Sophie explains that sometimes it is desirable to suppress aggregation. This is something the group has been investigating for GLP1 (Glucagon-like peptide), which is used in the treatment of diabetes. At other times peptide self-assembly is advantageous, for example in a drug called Teverelix, which is used in the treatment of prostate cancer. "Teverelix forms a highly unusual colloidal microcrystalline suspension, and there are many advantages to giving it to patients in that form," explains Sophie, "So we are working on understanding how and why it self-assembles into this microcrystalline state. Ultimately if we understand this, we might be able to induce a similar self-assembly in other peptides for other drug delivery."

A third research area involves the capping of antibodies. "All therapeutic antibodies have some off-target activity, and that results in side effects and limits the doses at which they can be given," Sophie explains. "We are trying to develop a new method which involves capping the antibody so that it's in an inactive state when it's given to the patient, and only activates when it gets to the target site, which could be a tumour for example."

One of the things Sophie enjoys most about her work is watching the next generation of scientists develop. "I love watching PhD students develop over the course of three or four years. It's really rewarding to watch them grow in many different ways, particularly scientifically, and to become confident and extremely competent scientists." She is also clearly still excited by her research and the new paths it is taking. "I like the fact that we're constantly learning, we're learning new things all the time," she says.

Sophie working at her desk pre-Covid.

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[1]*Folding of Chymotrypsin Inhibitor 2: 1. Evidence for a two-state transition*, Jackson, S.E. & Fersht, A.R., *Biochemistry*, (1991), **30**, 10428 -10435.

[2]*How to fold intricately: using theory and experiments to unravel the properties of knotted proteins*, Jackson, S.E., Suma, A. & Micheletti, C., *Curr. Opin. Struct. Biol.* (2017). **42**, 6-14.

Renaissance woman

Fourth-year PhD student Fahmida Khan loves the Renaissance, that period of European history when philosophy, literature, and the natural sciences blossomed, and art was transformed through the application of new scientific knowledge.

"I love the way artists started using scientific principles, including the newly discovered ways to depict light, to develop their art," she explains enthusiastically. Fahmida is particularly interested in Leonardo da Vinci, whose experiments in optics and human vision led him to favour 'sfumato,' in which fine shading creates a soft transition between colours and tones to achieve a more believable image. "I liked how Leonardo and others mixed art and science," she says.

Fahmida herself has always been fascinated by both art and science from an early age. "This goes a long way back," she smiles. "When I was a child I was introduced to one of the laboratories in Cambridge, and ever since then I was interested in labs and the ways scientists work, so I made up my mind I wanted to do a PhD." But Fahmida also loved art, and at high school in Luton she combined chemistry, physics, maths and art, continuing these subjects through A levels.

"That was when I started looking into the Renaissance and realising that a lot of the artists were polymaths – Leonardo was one of my models, because he was interested in so many different things. A lot of his art books look like diagrams you see in a thesis," she explains. "I liked how people in the Renaissance era had that common theme."

The golden ratio

While still at school Fahmida also did a project on the golden ratio and how it applies to both art and science. For example, Penrose tiles, discovered by Roger Penrose in the 1970s, use shapes based on the golden ratio (designated as Phi or 1.618) to cover a two-dimensional area in five-fold symmetry, and Dan Shechtman's Nobel Prize winning discovery of quasi-crystals have a three-dimensional five-fold symmetry defined by the golden ratio. "But Leonardo also used the golden ratio in his drawings and paintings, and that kept me interested in art," she says.

Fahmida went to University College London for her undergraduate degree, where she combined physics with surface chemistry, while also working in a research group at Imperial College. Following her life-long dream, she then applied for a PhD at Cambridge. Her degree in Chemical Physics turned out to be a good fit with Stuart Clarke's materials research group.

Research

In the Clarke group Fahmida has been researching passivation, and in particular finding effective ways to prevent steel structures from corroding. Like many other researchers, Fahmida's experiments were interrupted by Covid, but she believes she will have sufficient results to finish up by her autumn deadline, and she is trying to stay hopeful.

Although Fahmida didn't have much time for art at Imperial, she started drawing again when she came to Cambridge. "I needed an outlet," she explains. "It first started when I was taking notes and I'd doodle images on the side of the paper. Then I started bringing in my sketches and during breaks I would work on them." Fahmida found art was an effective way to take her mind away from her research and start to relax. "With drawing I could concentrate and refocus myself."

Inspiration

Fahmida found a new focus for her drawings in 2018 when the Hindi-language film *Padmaavat* was released. She became entranced by the artistry of the period saga, and started creating complex pen and ink depictions of the film frame by frame, which she shares on her Instagram account using the name Fahmida Liza K.

Padmaavat is based on an epic poem which follows the story of a Rajput queen. The film attracted controversy on its release because it depicts the Hindu practice of Jauhar, which is the self-immolation by women to avoid enslavement or rape by foreign invaders. Fahmida has

One of Fahmida's drawings – Fahmida loves the combination of art and science.

watched the film over and over, and often has it playing in the background when she is working.

The film is directed by Sanjay Leela Bhansali Bhansali, who is known for his artistic vision. "Watching his films is more like watching art," Fahmida says, " he is like the Renaissance person of film. I started drawing from it because I appreciated the cinematography." Fahmida's painstaking and beautiful recreations attracted the attention of the Indian press, and were featured in a recent Times of India article celebrating the film's third anniversary.

Padmaavat perhaps particularly strikes a chord with Fahmida, because although she was born and raised in Luton, her family is from Bengal. Her ancestry has led to another of her many interests, the *Bishad Shindhu*. Known in English as *Ocean of Sorrow*, this epic novel is regarded as a central work of Bengali literature, and is one of the first works produced during the Bengali Renaissance, which occurred in the 19th and early 20th century.

The book tells the metaphorical account of Muharram, in which Shia Muslims remember the death of the prophet Muhammad's grandson in the *Battle of Karbala*. "If I were ever going to create my own original pictures, I would like to do ten drawings to illustrate the ten days of mourning," she says.

Fahmida says anyone can pick up pencil or pen and start drawing. As proof of this, she was asked to give informal drawing classes to her fellow researchers at the start of lockdown. These went very well. "One of the points I make

Fahmida started drawing images from the film *Padmaavat*.

is art is not expensive – you don't have to buy anything, you don't have to be amazing, you can use a normal biro, which is what I do. If you make mistakes, you cover it up with the pen."

Future plans

For the future, Fahmida plans to go into industry, at least to start. "Four years has been quite a long time in academia so I'd like to try something different for a bit and let's see what I can do. When we were in high school we were told to write a letter to ourselves to say what we saw ourselves doing in ten years' time. I said I want to be in Cambridge doing research, and that's what I'm doing." And by combining her science with her artistic passion, Fahmida has become her own Renaissance woman.

Liquid-liquid phase separation

New research from the Knowles and Collepardo labs has implications for therapies against cancer and other diseases, and could even contribute to theories about the origin of life.

In a paper published in *Nature Communications*, a multi-disciplinary team with lead co-authors Dr Georg Krainer, Timothy Welsh and Dr Jerelle Joseph, has shown for the first time that liquid-like protein compartments, known as condensates, can re-enter a phase-separated regime in response to different salt concentrations. This discovery may help develop future therapies for cancer and neurodegenerative diseases, and may even have implications for the origin of life on earth.

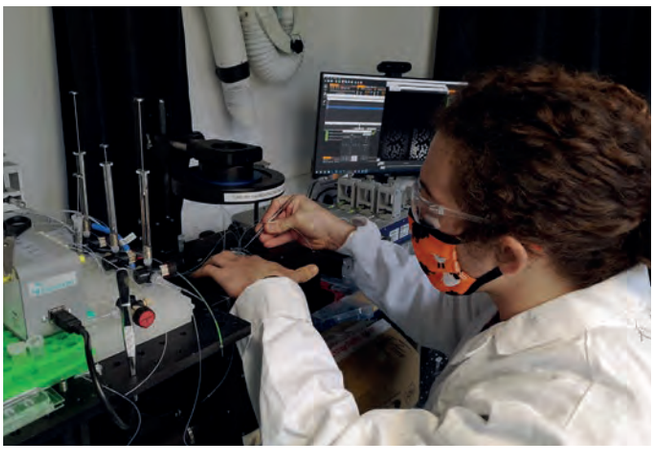
Understanding aberrant condensates in cells

Cell interiors contain a myriad of proteins and other biomolecules which must be carefully organised in space for the cell to function correctly. To do this, the nucleus and other well-known cellular compartments enclose groups of proteins with membranes, but membrane-less compartments known as biomolecular condensates are also common.

Condensates are protein-rich liquid drops that remain segregated through the physics of liquid–liquid phase separation, which is analogous to the separation of oil and water into distinct liquid phases. The advantage of these phase separated compartments or condensates over their membrane-bound counterparts, is that the cell can dynamically trigger their formation and dissolution simply by changing its environment.

However, sometimes these normally useful cell components transition into malfunctioning or 'aberrant' condensates, which tend to display different chemical and physical properties than healthy ones. These 'bad' condensates have been implicated in different forms of cancer and neurodegenerative diseases such as Alzheimer's disease and Amyotrophic lateral sclerosis (ALS).

In order to understand the process of protein phase separation further, researchers from the Knowles and Collepardo labs here, working together with groups from the Technical University in Dresden, the Max Planck Institute of Molecular Cell Biology and Genetics, and the University of Toronto, investigated how the liquid phase separation of certain proteins is affected by different concentrations of ionic salts.



PhD student Timothy Welsh with the lab set-up.

The researchers discovered that some proteins form condensates under low-salt conditions, then turn into a well-mixed state under medium-salt concentrations, but transition once again into a condensate-forming regime at higher concentrations of salt.

Reentrant phase transition

This behaviour is known as 'reentrant phase transition' because the proteins have gone from a phase-separated state to a diluted, well-mixed solution and then re-entered the phase-separation state. "Reentrant phase separation for proteins has been reported before in multicomponent systems; for example, by changing the concentration of RNA. Our work shows that proteins can also re-enter the phase-separated regime simply by variations in salt concentration," says postdoctoral researcher Dr Jerelle Joseph. "We knew that the low salt phase separated regime existed, but it was not clear that the reentrant phase transition at high salt concentration occurred."

Postdoctoral researcher Dr Georg Krainer, explains further: "Other researchers have shown a transition from no condensate to a condensate and back. But now we showed that this reentrant phase separation can occur without the aid of additional molecules such as RNA. This means we have shown that the transition happens because of the intrinsic properties and interactions of the protein itself in response to its changing environment."

The team demonstrated that the molecular interactions which drove the phase transitions in the low and high salt regimes were fundamentally different. Krainer says: "In the low-salt regime, hydrophobic and electrostatic interactions are important, but in the high salt regime the condensates needed hydrophobic and non-ionic interactions to form."

This discovery has implications in creating drug therapies. "Understanding how the molecular interactions that stabilize condensates can be fine-tuned is important when designing drugs to inhibit phase-separation or to dissolve condensates before they can get to the aberrant stage. If there is a reentrant phase, you need to ensure that the drug does not invoke changes that move the proteins back into a phase-separated regime," explains Joseph. "We also found that some cancer-related proteins also display this transition behaviour, so our work could be relevant in developing cancer therapies," adds Krainer.

Collaborative methods

The researchers used a combination of experimental and computational techniques to conduct their investigation. Krainer and Welsh are in the Knowles research group, and conducted their experiments in the Sir Rodney Sweetnam Laboratory

"We used advanced fluorescence imaging using a fluorescence microscope with a high sensitivity camera to study the proteins," explains Welsh, who is a second-year postgraduate student. "Two of the proteins we studied, known as FUS and TDP-43, are thought to transition from liquid condensates to solid-like states, and this transition may be implicated in ALS. This shows how a single protein sequence can behave massively differently in terms of phase separation," he says.

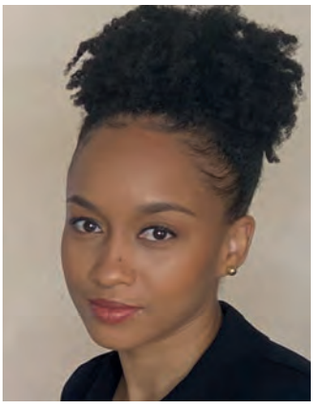
Joseph, working in the Collepardo research group based in Chemistry, Physics, and the Department of Genetics, carried out computer simulations to quantify the relative strength molecular interactions, using PMF (Potential of Main Force) calculations. All the simulations were conducted on the supercomputers of the Cambridge Service for Data-Driven Discovery.

Joseph says, "I've always worked on purely simulation-based papers, and it was wonderful to get the opportunity to work alongside the experimentalists and get a feel for how they work. Having multidisciplinary teams is what is going to help us answer these questions – being able to see the problem from many different viewpoints, using different types of thinking and different techniques that can complement each other very well."

Krainer agrees. "You can describe the phenomenon with experiments, but with computational tools you can really get answers on a molecular scale. I wouldn't put one above the other – they are on one continuum. As a scientist with a background in molecular biosciences, I am proud that this study really embodies this multi-disciplinary character – it's really fascinating to see how these areas complement each other."

Origin of life

And what about the origin of life? "That's another cool hypothesis stemming from our work," says Joseph enthusiastically. "In the origin of life, the higher concentrations of salt present in the oceans at the time could have facilitated formation of protocells via protein phase separation to keep selected biomolecules phase-separated." Krainer agrees: "The implications for evolution and the origin of life on earth in high salt bearing waters are fascinating."



Jerelle Joseph

Georg Krainer

Gabriella Bocchetti

Reference
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Click here to change RNA

Researchers in the Bernardes lab have created a new tool to modify RNA in living cells, which opens new possibilities for drug discovery and medical treatments.

Madoka Hazemi and Unnikrishnan Bindu

Fourth year PhD student Sigitas Mikutis.

RNA controls many processes in a cell, so that even minor modifications to the RNA can determine whether a cell stays healthy or becomes cancerous.

One way to modify a cell's RNA is to use CRISPR-Cas13, a technology often referred to as "genetic scissors," because it can be used with extremely high precision to alter RNA. Jennifer A. Doudna and Emmanuelle Charpentier were awarded the 2020 Nobel Prize in Chemistry for the development of the CRISPR method of gene modification.

But the CRISPR technique does have some drawbacks, explains Sigitas Mikutis, a fourth year PhD student in the Bernardes group, and first author on the group's recent paper *meCLICK-Seq, a Substrate-Hijacking and RNA Degradation Strategy for the Study of RNA Methylation*, published by the American Chemical Society.[1]

"Unlike CRISPR, we can use our system directly in living cells without genetically modifying them first," says Sigitas. CRISPR modification also requires complex biochemical machinery such as enzymes and nucleic acids, that often introduce biases. "Our technique uses only small molecules, so it is very simple and selective, and not subject to the same biases."

Hijacking methylation

RNA modification occurs naturally in living cells through several processes, of which the best understood is methylation, in which a methyl group (CH_3) is appended to RNA, thereby changing its properties such as protein translation efficiency.

The researchers have for the first time devised a system which 'hijacks' these processes to induce selective degradation of natively methylated RNA species, by using a degrader which acts as a minimalistic enzyme to break down RNA acids. "So like scissors it cuts the RNA around the place where you would normally have the methylation – this is the position we hijack," explains Sigitas. The group innovatively uses "click chemistry" to attach the degrader to targeted RNA.

Click chemistry

Click chemistry describes a way of rapidly and irreversibly assembling two synthetic molecules without any by-products. These click reactions can run inside living organisms because they are relatively non-toxic and can be done at room or body temperature.

"Click chemistry was defined for the first time in 2001, and chemical biologists took a while to catch up, but its use has been exploding, and just a few weeks ago the first click- chemistry based therapy has entered clinical trials," says Sigitas.

"To the best of my knowledge this is the first time that click chemistry has been applied to living cells with a measurable output that is not microscopy-based, and we can directly measure what is happening in the cells." The group synthesises the molecules used in the click reactions themselves. "We're trying to make the synthesis as simple as possible so they can be used across different labs."

Sigitas believes this system could be used to create precise and easy to carry out diagnostics: "In healthy cells, all the RNA is in equilibrium, and so you expect particular species to be in certain concentrations with identifiable methylation signatures," he says. "But in diseased cells, these methylation signatures go way off.

"With our system you can diagnose what's happening with a particular methylation for a specific RNA species, and from there determine whether a cell is healthy or cancerous, for example. My dream is that you can draw a sample of blood, apply our technique, and then provide a clear diagnosis."

One advantage of this new system is that it could easily be adapted to target different types of cellular systems. In addition to diagnostics, the group is now looking into more sophisticated biological applications. "We are looking at things like organ tissues, so we can compile a sort of methylation atlas across many different types of cells, and use different ways to apply our RNA degradation strategy."

Sigitas would also like to look at using the degrader in contexts different from methylation. "So for example, acetylation is another type of RNA modification which we're interested in. The role of acetylation is much less defined, so we'd like to establish this first."

A C&EN article praising the research notes that it "opens the door to novel nucleic acid editing technologies" and states: "Now we finally have a very specific and efficient technology to cleave RNA on demand."[2]

"Having a better tool to fragment RNA will help biochemists better understand the secrets of life," concludes Sigitas.

Unnikrishnan Bindu

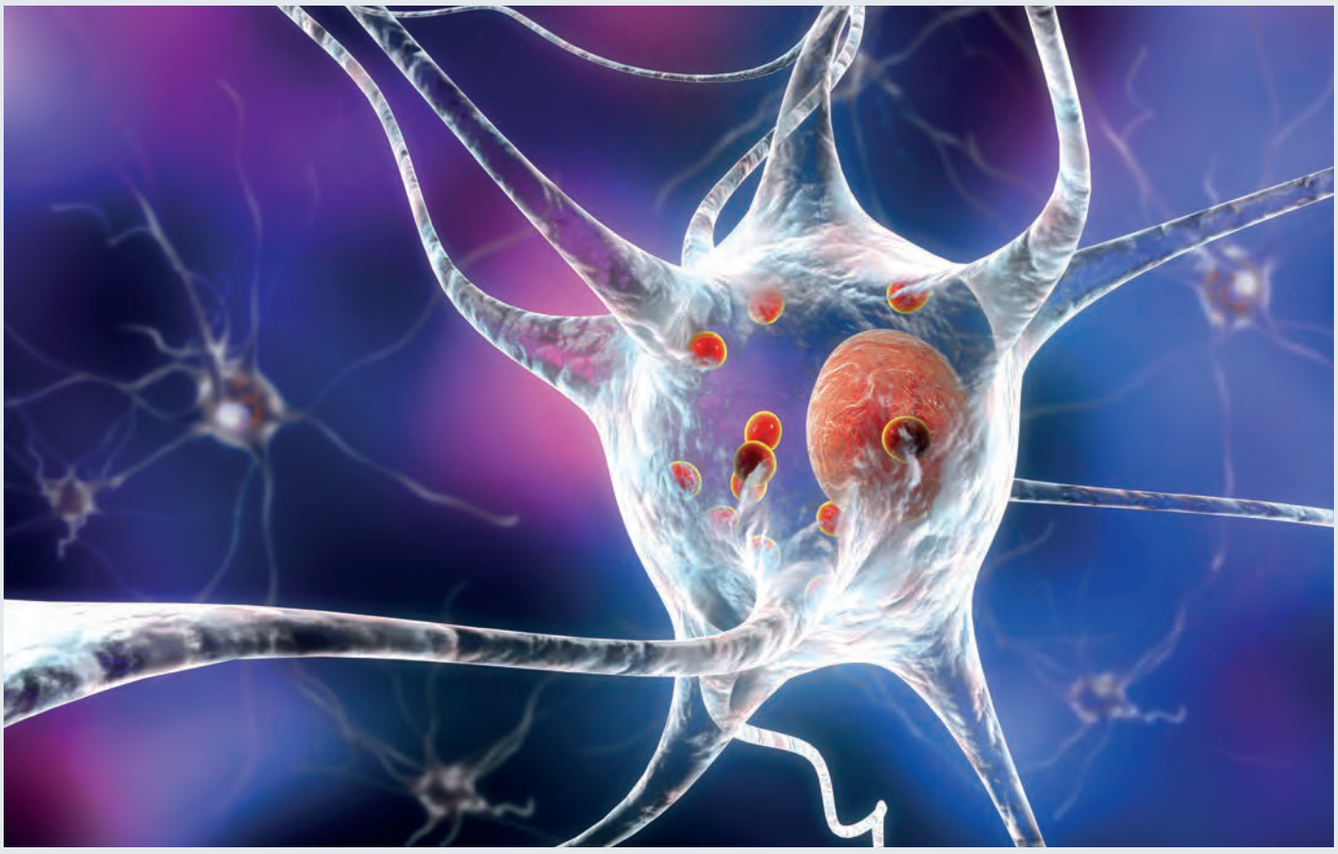
Sigitas (right) with colleagues Hannah Kiely-Collins (centre) and Madoka Hazemi.

References

[1]Mikutis, S., Gu, M., Sendinc, E., Hazemi, M.E., Kiely-Collins, H., Aspris, D., Vassilou, G.S., Shi, Y., Tzelepis, K., Bernardes, G.J.L., *ACS Cent. Sci.*, (2020), **6**, 2196-2208).
[2]*New system cuts RNA using only small molecules, C & EN* (2020).

Investigating the origins of Parkinson's Disease

Scientists in the Centre for Misfolding Diseases have identified the function of a 'mystery protein' that kills healthy brain cells of people with Parkinson's disease.



Kateryna Kon

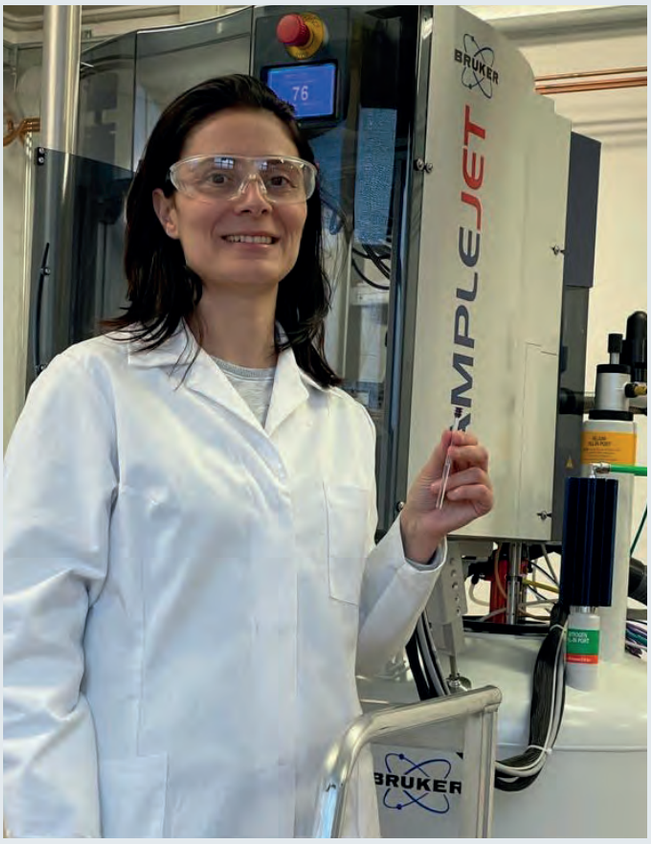
3D illustration showing neurons containing Lewy bodies.

The research presents compelling new evidence about what a key protein called alpha-synuclein actually does in neurons in the brain.

Dr Giuliana Fusco, a researcher in the Centre for Misfolding Diseases and lead author of the study, says: "If we want to cure Parkinson's, first we need to understand the function of alpha-synuclein, a protein present in everyone's brains. This research is a vital step towards that goal."

Parkinson's disease is a progressive neurological disorder that causes nerve cells in the brain to weaken or die. The disease has a variety of symptoms including tremors – particularly in the hands – gait and balance problems, slowness and extreme stiffness in the arms and legs. Parkinson's develops when cells in the brain stop working properly and can't produce enough dopamine, a chemical that controls movement in the body by a cting as a messenger between cells.

The disease mostly affects people over 60 and gets worse over a number of years, but early onset Parkinson's can affect people even younger.



Dr Giuliana Fusco

It is not yet known why people get Parkinson's, but researchers think it's a combination of age, genetic and environmental factors that cause the dopamine-producing nerve cells to die, affecting the body's ability to move.

"To cure Parkinson's we need to understand the function of a protein present in everyone's brains – this research is a vital step towards that goal."

Giuliana Fusco

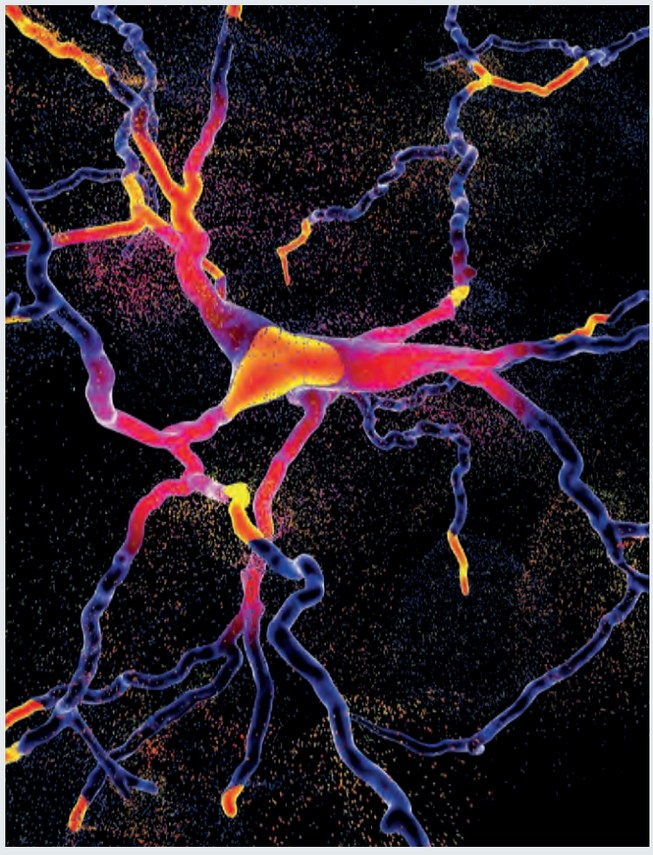
The new study looked at what was going on inside healthy conditions to help pinpoint what is going wrong in the cells of people with Parkinson's. All cells in the body have a plasma membrane that protects cells and usually transports nutrients in, and clears toxic substances out.

Fusco explains: "One of the top questions in Parkinson's research is: 'What is the function of alpha-synuclein, the protein that under pathological conditions forms clumps that affect motor and cognitive abilities?'

"Usually you discover a protein for its function and then you explore what is going wrong when disease strikes. In the case of alpha-synuclein the protein was identified for its pathological association but we didn't know what it did in the neuron. Our research suggests that the alpha-synuclein protein sticks like glue to the inner face of the plasma membrane of nerve cells but not to the outer– a crucial new piece of information."

The research was carried out by Dr Fusco and her colleagues in our Centre for Misfolding Diseases, in collaboration with researchers at the University of Naples "Federico II" and Imperial College, London.

There are treatments and drugs available to Parkinson's patients and the disease isn't fatal, but nothing is available to reverse the effects of the disease. "This study could unlock more information about this debilitating neurodegenerative disorder," says Fusco.



Kateryna Kon

Degeneration of dopaminergic neuron, a key stage of development of Parkinson's disease.

Reference

The docking of synaptic vesicles on the presynaptic membrane induced by α-synuclein is modulated by lipid composition, Man, W.K., Tahirbegi, B., Vrettas, M.D., Preet, S., Ying, L., Vendruscolo, M., De Simone, A., and Fusco, G, *Nat Commun*, (2021), **12**, 927.

How you can contribute

As we slowly ease out of lockdown, we are looking forward to an exciting future.

The Yusuf Hamied Fund

The Yusuf Hamied fund will help us continue to attract and support the world's best and brightest academic talent well into the 21st century and beyond, maintaining a tradition of excellence which began over 300 years ago. The Hamied Scholars Programme will enable outstanding doctoral students from the UK and around the world to study here. We are grateful to Dr Yusuf Hamied for establishing these initiatives.

Chemistry@Cambridge Opportunity Fund

We have also created a new Chemistry@Cambridge Opportunity Fund to support researchers at the start of their careers. This fund will help researchers to participate in workshops and conferences, and aid those affected by unforeseen funding difficulties, such as those caused by the recent Covid crisis. Your contribution to this fund will nurture the discoveries of the future.

Contact our Head of Department, Dr James Keeler, to find out how you can support Chemistry@Cambridge.