Chemistry Update

Newsletter 333, 30 June 2021

Inside this Issue

Calendar of Events

E&D Group Lunchtime Forum - 'Diverse Leadership'
Speaker: Chemistry E&D Group Discussion
Date: Wednesday 7 July
Time: 12pm—1pm
Location: Virtual

Come along and discuss some of the following:

- What are the benefits of having diverse leaders?
- Can we expect leadership from "diverse" individuals to be different?
- Will we expect more from diverse leaders?
- How can we encourage more diversity in leadership in HE and the Department?
- The discussion will be on Zoom, but if the weather is fine, there will be a chance to meet up in the quad and have lunch together after.

All in the Department are welcome.

Date of Next Issue:
30 July 2021

Step-closer to nasal spray drug delivery for Parkinson's disease

Scientists at the University of York have made significant progress in the development of a nasal spray treatment for patients with Parkinson's disease.

Researchers have developed a new gel that can adhere to tissue inside the nose alongside the drug levodopa, helping deliver treatment directly to the brain.

Levodopa is converted to dopamine in the brain, which makes-up for the deficit of dopamine-producing cells in Parkinson's patients, and helps treat the symptoms of the disease. Over extended periods of time, however, levodopa becomes less effective, and increased doses are needed.

Increased dosage

Professor David Smith, from the University of York's Department of Chemistry, said: "The current drug used for Parkinson's Disease is effective to a point, but after a long period of use the body starts to breakdown the drug before it gets to the brain where it is most needed.

"This means increased dosage is necessary, and in later stages, sometimes, instead of tablets, the drug has to be injected. Investigations into nasal sprays have long been of interest as a more effective delivery because of its direct route to the brain via the nerves that service the nose, but the challenge here is to find a way of making it adhere to the nasal tissue long enough to release a good dosage of the drug."

The researchers created a gel, loaded with levodopa, that could flow into the nose as a liquid and then rapidly change to a thin layer of gel inside the nose. The method was tested in animal models by a team at King's College London, where levodopa was successfully released from the gel into the blood and directly to the brain.

Better uptake

Professor Smith said: "The results indicated that the gel gave the drug better adhesion inside the nose, which allowed for better levels of uptake into both the blood and brain."

The team are now working to incorporate these materials in nasal spray devices to progress to clinical trials in humans. The approach may also be relevant to other neurodegenerative diseases such as Alzheimer's.

Khuloud Al-Jamal, Professor of Drug Delivery and Nanomedicine from King's College London, said: "Not only did the gel perform better than a simple solution, but the brain uptake was better than that achieved using intravenous injection of the drug. This suggests that nasal delivery of Parkinson's drugs using this type of gel may have clinical relevance."

International collaboration wins Royal Society of Chemistry Prize

An international research team, led by groups at The Crick (UK) and Stanford University (USA) and joined by Dr Jon Agirre (York Structural Biology Laboratory, Department of Chemistry), has been recognised with one of the inaugural Royal Society of Chemistry Horizon Prizes.

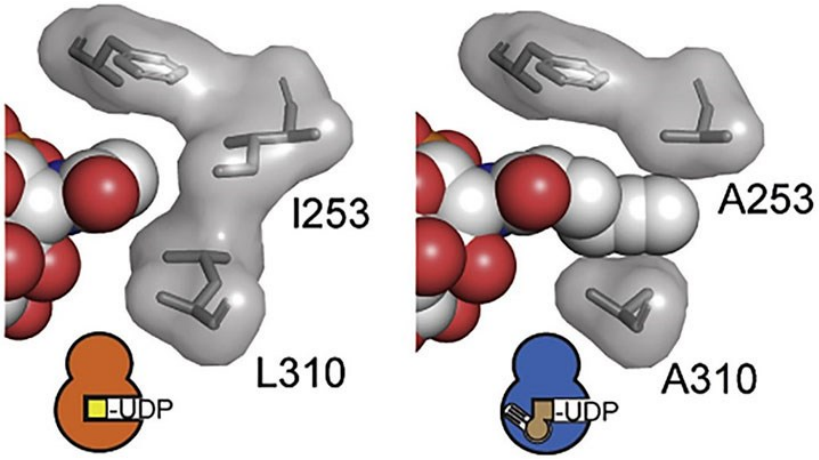


Image: original (left) and modified (right) complex with GalNAc-T (grey surface) and substrate (red and white spheres). The modified GalNAc-T has a hole that only the modified substrate can fill. Reproduced under Creative Commons licence from Schumann et al., 2020, Molecular Cell 78, 824–834.

The prize recognizes the work of a team of more than 50 scientists from many different backgrounds, highlighting the importance of collaboration and diversity in science. Their careful work developed precision chemical tools to identify substrates of a glycosyltransferase enzyme directly in living cells.

The multidisciplinary team, led by Dr Ben Schumann (The Crick, UK) and Professor Carolyn Bertozzi (Stanford University, USA), used the 'bump-and-hole approach' to work with a modified version of a biologically-important enzyme that plays a key role in adding sugars to proteins. The modified poly-peptide N-acetylgalactosaminyl transferase (GalNAc-T) was capable of accepting tagged substrates that can be tracked in living cells. With these new tools, the scientists managed to pinpoint the 'landing area' of the modified substrates with unprecedented accuracy, hence identifying which proteins can receive a sugar substrate from GalNAc-T.

The work includes, among many other techniques, a wealth of protein crystallography. Dr Jon Agirre (YSBL, Department of Chemistry), who currently holds the Royal Society Olga Kennard Research Fellowship – a special position created for a Royal Society Research Fellow working in crystallography, and supported by a generous donation from the Cambridge Crystallographic Data Centre – assisted the team with the refinement of the atomic structures of the complexes. Dr Agirre is an expert in the refinement of carbohydrate structures, and ensured that the resulting atomic structures made chemical sense.

Dr Agirre explained: "This is the first time a glycosyltransferase's activity has been probed with the 'bump-and-hole' tactic and the results could not be more exciting. My participation in this study has allowed me to put our computational procedures to the test with challenging data. I am incredibly grateful to Ben and Carolyn for letting me take part in this and delighted to see this international collaboration recognised with an RSC Award."

Team led by York Chemists wins Inaugural Royal Society of Chemistry Horizon Prize

Research to explore the mechanistic details of important catalytic reactions, led by two academics in York, has been recognized with one of the inaugural Royal Society of Chemistry Horizon Prizes.

The prize recognizes work carried out by a team including scientists from York, the Central Laser Facility STFC and Syngenta Crop Protection. Working together, they managed to gain important new insights into carbon-hydrogen bond activation and functionalization reactions.

Carbon-hydrogen bonds are ubiquitous in the molecular world in both natural and synthetic compounds yet were historically considered inert and difficult to chemically modify. In recent years, selective metal catalysts that interact with specific carbon-hydrogen bonds and enable their modification have been developed. Understanding in detail how the metal catalyst operates is of high value in increasing the efficiency of such processes, but has been difficult to study directly.

Success in the project depended critically on cross-disciplinary collaboration, a state-of-the-art Central Laser Facility, spectroscopists, physical organic/organometallic, catalytic and industrial process chemists, allowing us as a team to naturally connect fundamentals with real-world applications.

Led by Professor Ian Fairlamb and Dr Jason Lynam in York, the team made use of a variety of analytical methods, including infrared and nuclear magnetic resonance spectroscopy, to understand the interplay between the metal and chemical substrates. Ultra-fast lasers at the Central Laser Facility were used to trigger chemical reactions and gain direct insight into the structure and behaviour of reaction intermediates that are formed on incredibly short timescales.

Professor Fairlamb explained: “The award recognises research spanning the three pillars of Chemistry – inorganic, organic and physical chemistry – and aligns with end-user applications in agrochemical, materials and pharmaceutical industries.”

Dr Lynam added “An interdisciplinary team was vital to the success of this project. The interplay between synthetic and mechanistic chemistry in York, the state-of-the-art spectroscopic methods at the Central Laser Facility and working closely with process chemists ensured that the key steps in important catalytic reactions could be observed. This has provided a step change in how we can probe and understand such reactions.”

The combination of techniques enabled the team to observe chemical events which occur on timescales ranging from a trillionth of second through to hours. Understanding these important chemical reactions across all timescales is important, particularly when optimising syntheses for commercial-scale manufacture – for example in the agrochemical industry.

Commenting further on potential applications of the research, Dr Alan Robinson from Syngenta said

"From an industrial perspective, the advancements and breakthroughs in this project have the potential to offer us new and alternative catalytic systems, for key transformations that are difficult to access or currently require expensive and/or scarce metals. This can enable the implementation of cost-effective, value-adding and sustainable synthetic processes."

The Horizon Prizes were created in 2020 following an independent review of the Royal Society of Chemistry's recognition programmes. These prizes highlight the most exciting, contemporary chemical science at the cutting edge of research and innovation. In particular, the Horizon Prizes recognise teams or collaborations who are opening up new directions and possibilities in their field, through ground-breaking scientific developments.

Creating Disability Inclusive Science Careers

Online workshop • Wednesday 4 August • 10.00-15.30

Message from Dr Julia Sarju: Disability Inclusive Science Careers (DISC) is running an online workshop inviting scientists to hear from and talk to decision-makers across funders, senior managers in universities and Scottish Government representatives, alongside other academic workplace stakeholders such as the University and Colleges Union, and the National Association of Disabled Staff Networks.

The workshop will explore the changes necessary to make academic science careers more inclusive and accessible.

The morning session (10.00 -12.30) will focus on university decision-making and wider obstacles to career advancement and progression for disabled scientists. The afternoon session (13.00-15.30) will focus on organisations that can or should provide support and guidance to colleagues and employees and negotiate on our behalf.

The workshop will be informed by the evidence base created by DISC on the barriers and facilitators to disability inclusive careers in the sciences. An output of DISC has been the development of training for employers to improve inclusivity and accessibility in their workplaces. The workshop has been designed for scientists who are disabled, neurodivergent, D/deaf and those experiencing long term health conditions or symptoms. It will provide you with the opportunity to share your workplace experiences and needs, as well as ask questions of those in positions of decision-making about employment conditions and support in HE.

If you would like to attend, please complete this form to register.

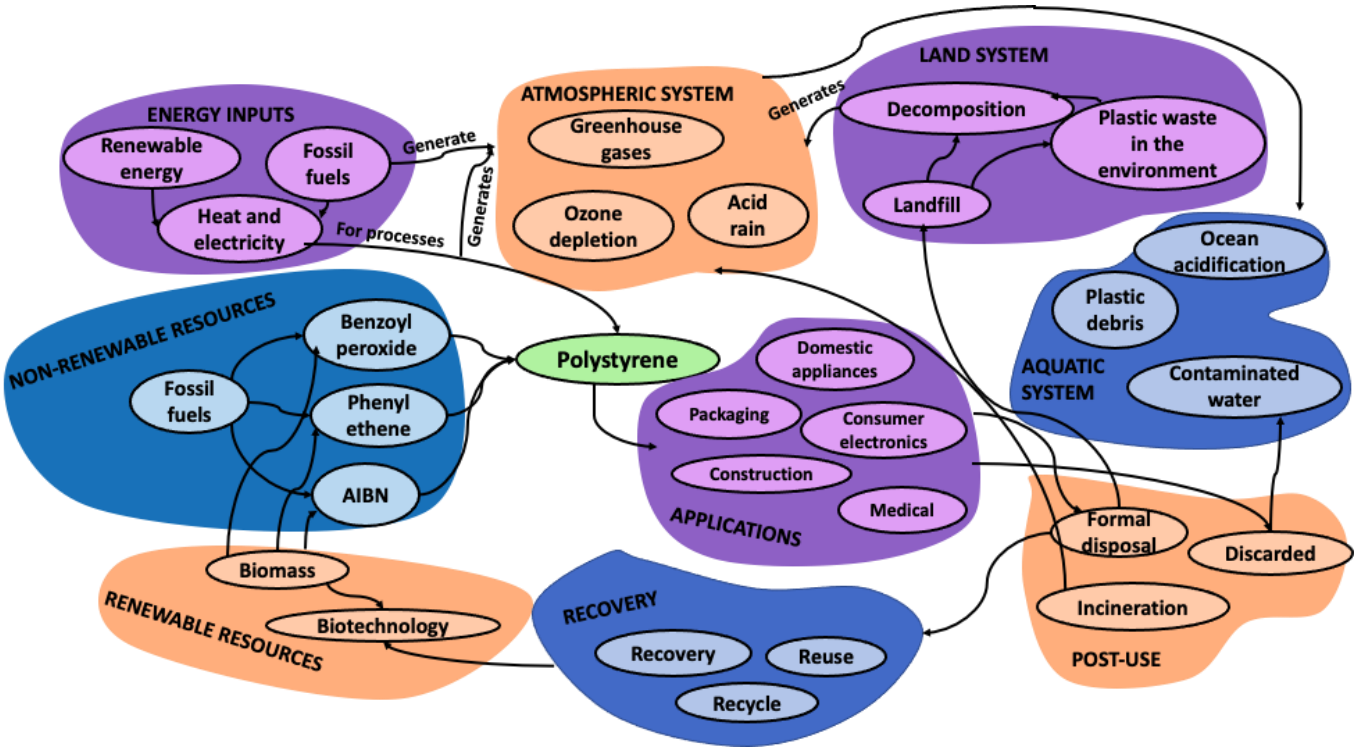
Online Department suggestion box

The online Equality and Diversity suggestion box has been extended to be a suggestion box for the whole Department. You can submit your thoughts/suggestions/ideas for general Departmental matters as well as matters relating to Equality and Diversity. You can find the Google form at this link.

Integrating systems thinking into chemistry education

Undergraduate student research investigating staff perceptions of a 'systems thinking' approach in chemistry education indicates it is viewed positively. In particular, the systems thinking approach has potential advantages in providing benefits to student learning, facilitating interdisciplinary teaching/ learning, enhancing student employability – ultimately leading to societal benefits.

A 'systems thinking' theoretical framework for learning chemistry has the potential to assist students in transitioning from a surface-level, reductionist understanding of subject knowledge to a more integrated approach to learning. Systems thinking aims to encourage students to explore complex inter-relationships between different aspects to gain a deeper understanding of the fundamental chemistry (see Figure for an example).



Systems Oriented Concept Map Extension (SOCME) for polystyrene showing how the production and use of this material integrates into a variety of different systems

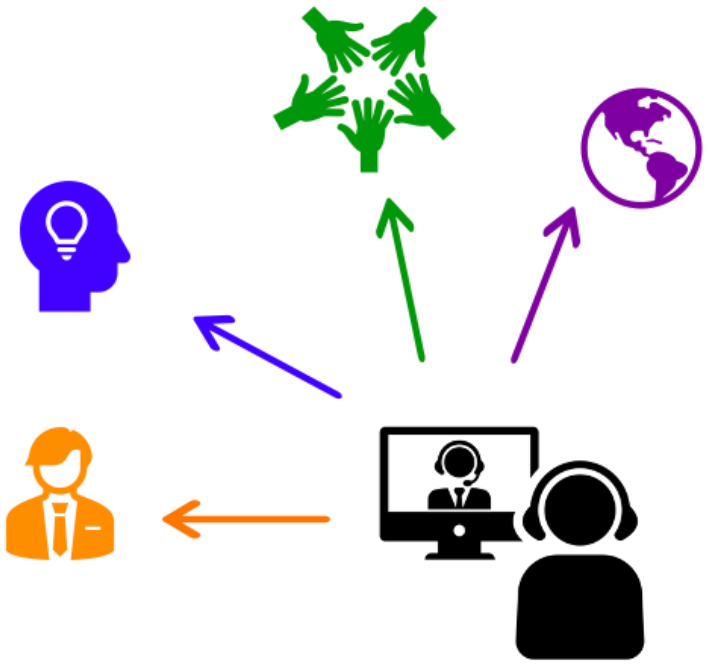
Systems thinking has the potential to act as a powerful method in preparing the next generation of scientists, engineers and policymakers to tackle global challenges such as the United Nations Sustainable Development Goals (UN SDGs), which require interdisciplinary and multi-faceted approaches to problem solving.

Alice Jackson (MChem 2021) carried out her undergraduate research project working with Dr Glenn Hurst and the results have been published in the prestigious international journal, *Chemistry Education Research and Practice*.

Alice conducted semi-structured interviews with a range of academic staff from the Department of Chemistry and evaluated responses qualitatively (via the Framework method) and quantitatively (via

Likert-style question). Instructors expressed positive opinions of systems thinking and believed it should be implemented into the undergraduate chemistry curriculum to some extent, offering a range of possible benefits.

Curriculum reform is only successful with support from both instructors and students and while such positive opinions of systems thinking from participants with expertise from a variety of areas within chemistry show great promise for future implementation, the student perspective is of critical importance for widespread integration – this will be examined going forwards.



Reflecting on the work, Dr Hurst said: "We have done a lot of work in recent years using systems thinking as a framework to teach green and sustainable chemistry – it is particularly exciting to learn that there is significant potential for systems thinking to be a valuable tool to teach chemistry more broadly."

Alice and Glenn are currently collating and reporting results of the work at the Science Faculty level. Early results indicate that positive opinions of the systems thinking as an education tool are held throughout the sciences. If systems thinking was incorporated more broadly throughout the sciences, this may facilitate more interdisciplinary teaching and learning, including associated research projects. This would enable grand challenges, such as those outlined by the UN SDGs, to be addressed.

Alice comments: "Although completing my masters project during the pandemic brought additional challenges, this project was extremely rewarding and I am very grateful that the participants were willing to take the time out of their busy and stressful schedules to take part."

Alice will present her research at the institutional Annual Learning and Teaching Conference and it is published in *Chemistry Education Research and Practice*.

New starters

Lyndsey Stoner, Aerosol Society Administrator
Room: C/G119; Ext: 1219; Email: lindsey.stoner@york.ac.uk

Dr Estelia Borquez-Sanchez, Research Associate in Science Education
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One of the largest ever land mammals evolved into a dwarf elephant, study finds

An extinct species of dwarf elephant experienced a weight and height reduction of 8,000kg and almost two metres after evolving from one of the largest land mammals that ever lived, a new study has confirmed.

Remains of the dwarf elephant *Palaeoloxodon mnaidriensis* uncovered in Sicily's Puntali Cave. Credit: Gemmellaro Geological Museum

The research team, which included academics from University of York, found that the island-dwelling Sicilian dwarf elephant – thought to have become extinct about 19,000 years ago – was just 15% of its original body mass by the time its dwarfing process was complete.

The team found that the less than 2m tall dwarf elephant reduced in weight and height by a maximum 200kg and 4cm per generation.

By combining DNA and fossil evidence, the researchers were able to determine that this specific Sicilian elephant's maternal lineage diverged from the straight tusked elephant *Palaeoloxodon antiquus*, which stood at almost 4m tall with a weight of ten tonnes.

Evolution

Because of their insular and isolated environments, evolution on islands is a process which can lead to a variety of extreme changes in a short timeframe, including dwarfism and gigantism and is often referred to as 'evolution in action'. To put the extent of the size reduction of the dwarf elephant into context, it would be comparable to modern humans dwarfing to approximately the size of a Rhesus monkey.

For the project, the team successfully recovered ancient DNA from dwarf elephant remains from Sicily's Puntali Cave, which had an estimated age of between 175,000 and 50,000 years.

Palaeoloxodon antiquus lived on the European mainland between 800,000 and 40,000 years ago and the team believes it will have colonised Sicily some time between 70,000 and 200,000 years ago. Colonisation probably occurred during periods of cold climate when sea levels were lower, exposing land bridges that the elephants could have utilised to colonise the islands.

It is thought that the dwarfing process at the earliest began once the Puntali elephant diverged from its mainland relative.

Using the estimated age of the Puntali elephant fossil, the size and mass of the straight-tusked elephant, and the estimated start of the dwarfing process, the team was able to calculate size and body mass reduction rate per year and per generation.

Tooth samples

As part of the study, researchers from York's Department of Chemistry used a technique called intra-crystalline protein degradation (IcPD) dating. This technique assesses the breakdown of proteins and

amino acids found in the elephants' fossil tooth enamel, and uses this to estimate the age of the sample by comparing it to other elephant tooth samples from the region.

Dr Marc Dickinson, a postdoctoral researcher at the University of York, said "It was brilliant to be able to use IcPD analysis to help date these dramatic changes to elephant body size, and to contribute to such an exciting multidisciplinary study."

The study, involving Nottingham Trent University, the University of Potsdam in Germany, the Natural History Museum, the University of Iceland, the University of Palermo and the University of Cambridge is published in *Current Biology*.

Dr Victoria Herridge, an evolutionary biologist based at the Natural History Museum London, said: "It's such an achievement to successfully sequence an ancient mitochondrial genome from a Sicilian dwarf elephant, and to finally have DNA from a southern European straight-tusked elephant."

"It opens the door for more studies of this kind, and with it the chance to finally crack one of the big mysteries of evolutionary biology: why elephants evolve to be so small on islands."

Further information

The dating work undertaken at York by Dr Marc Dickinson and Professor Kirsty Penkman was funded by Natural Environment Research Council (NERC) and the Quaternary Research Association.

The dwarf elephant remains are kept in the Gemmellaro Museum (University of Palermo) where the specimens were sampled.

Sponsored Cycle for St John Ambulance

A small group of cyclists including David Pugh and Adrian Whitwood are cycling from Bridlington to York on 3 July, a distance of about 100 km, to raise money for St John Ambulance.

During the COVID emergency, St John Ambulance have lost a lot of income due to the cancelling of both events where we provide first aid cover and First Aid at Work training. Despite this, we stepped up to the cause and our volunteers provided:

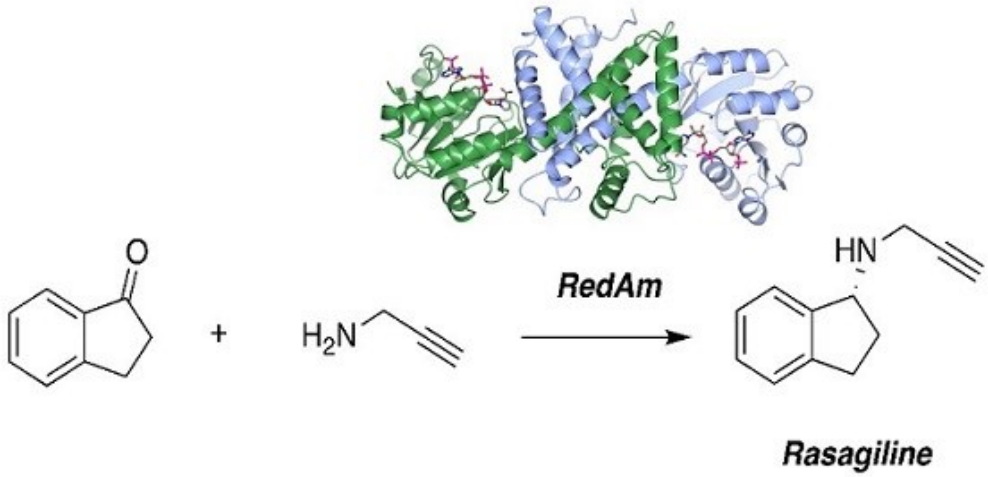
- support in NHS hospitals providing extra carers and logistics.
- ambulances and crew to supplement both emergency and non emergency NHS services
- training and support for over 30,000 vaccination volunteers - your vaccine may be (or have been) delivered by a SJA volunteer

If you'd like to sponsor the cycle, please visit the JustGiving page.

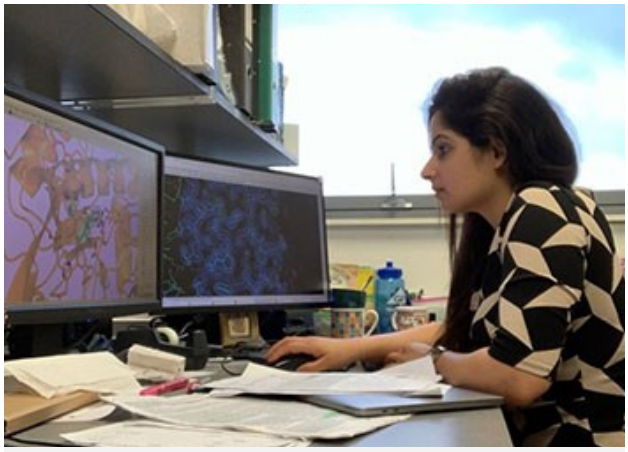
York Enzymologists part of team to win Horizon Prize

Researchers at York, in collaboration with colleagues at the University of Manchester, GSK and Prozomix Ltd, have been recognized with one of the inaugural Royal Society of Chemistry Horizon Prizes.

The prize recognizes the discovery, characterisation and application of enzymes – 'RedAms' - that catalyze a reductive amination reaction, an important reaction in chemical synthesis for the formation of amines, molecules that are important as pharmaceutical compounds and their precursors. Using enzymes to catalyze amine synthesis enables more selective, green and sustainable synthesis of molecules such as rasagiline, used in the treatment of Parkinson's disease.



Synthesis of Parkinson's disease drug Rasagiline using a RedAm enzyme



Postdoctoral researcher Dr Mahima Sharma analysing the structure of a RedAm enzyme

The interdisciplinary nature of the project was crucial to its success. York scientists were able to apply their expertise in molecular biology and protein structure, to help understand how the RedAms work, and suggest ways of improving their activity using protein engineering. The structural work at York was performed by Professor Gideon Grogan, postdoctoral researcher Dr Mahima Sharma and PhD student Henry Man. More work on the enzymology and chemistry was performed at the University of Manchester, led by Professor Nick Turner. Prozomix have discovered many new and different RedAms in nature, allowing their application in the formation of many different amines. Researchers at GSK worked on scaling up the enzymatic reactions for use in the synthesis of a medicine in its oncology portfolio. As a result of close cooperation between the partners the time from discovery to application was less than four years.

The Horizon Prizes were created in 2020 following an independent review of the Royal Society of Chemistry's recognition programmes. These prizes highlight the most exciting, contemporary chemical science at the cutting edge of research and innovation. In particular, the Horizon Prizes recognise teams or collaborations who are opening up new directions and possibilities in their field, through ground-breaking scientific developments.

Professor Eleanor Dodson Honoured by Australian Academy of Science

Professor Eleanor Dodson FRS, an Emeritus of the Department, has been elected as a Corresponding Member of the Australian Academy of Science.

The citation for her award reads:

'Professor Dodson's work has brought the ability to understand large molecule structures into the public realm, revolutionising science and medicine. Known as a great teacher and influencer in the field of protein crystallography, she has made major contributions to both theory and practice.'

Corresponding Membership of the Australian Academy of Science is a special category within the Fellowship, comprising eminent international scientists with strong ties to Australia who have made outstanding contributions to science.

Head of Department, Professor Duncan Bruce said: "There is no doubt whatsoever of Eleanor's outstanding contribution to science and of course to York Structural Biology Laboratory (YSBL) and the wider Department of Chemistry. It is wonderful to see her many achievements receiving well-deserved international recognition."

SAQN funds new research into air quality

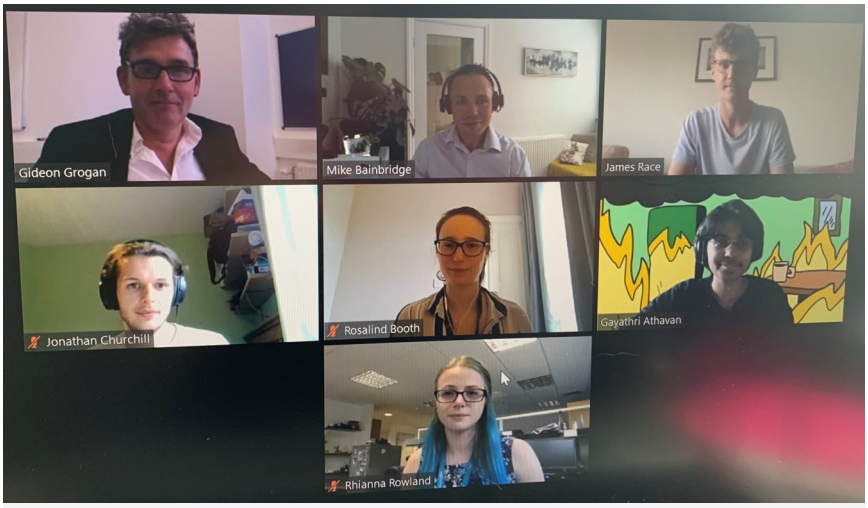
The STFC Air Quality Network (SAQN) has funded four new Scoping Studies through their innovative online Collaboration Building Workshop. The workshop was the second run by the network, and aimed to develop new interdisciplinary collaborations between air quality scientists and researchers at the Science and Technology Facilities Council (STFC). Participants came from a range of backgrounds, including particle physics, public health, social science, software engineering, modelling and many more.

The funded projects address the workshop question "How might we respond collaboratively to societal air quality challenges using STFC capabilities to explore the potential of new research ideas?". The projects focus on nanoparticles in the brain, Persistent Organic Particles (POPs), developing a next generation Delta sensor and biomass burning. Each project has been awarded £8,000. Further details of the Scoping Studies will be shared on the SAQN website, where blog posts and presentations from past Scoping Studies are currently available.

SAQN PI, Dr Sarah Moller said, "We are delighted to be funding these new studies. All of them are taking a first step towards tackling a major air quality research gap, and we look forward to seeing the outcomes. We are keen to support the Scoping Studies to develop their research idea and apply for future funding as a result of strong, productive collaborations."

Johnson Matthey Poster Competition: June 2021

On Wednesday 9 June, our annual Poster competition for PhD students took place, but with a slight difference. The event, kindly sponsored by Johnson Matthey, usually takes place in a busy room in the department, with lots of poster boards and a loud buzz of conversation. Having had to cancel the event in 2020, this year we moved the event online and used the power of Zoom and breakout rooms to allow participants to share their work, and for discussions to take place in a safe and Covid-secure manner.



Johnson Matthey Poster Competition 2021 winners

The competition requires participants to display a poster about their research, which is scored by a panel of judges who consider Poster Presentation, Scientific Content, and Student Discussion. This year's added challenge was that posters had to also be decipherable on a computer screen!

Overall the event went very well, with only minor technical hitches (what Zoom event would be complete without at least a couple!). We had 24 posters on display and both judges and members of the department were able to move between rooms to talk to participants and enjoy an opportunity to talk science and share work. After the viewing, we were delighted to welcome our guest speaker, Dr Mike Bainbridge from Johnson Matthey who talked about his career path, and current work at Johnson Matthey, particularly related to technologies for hydrogen production. The event ended with the announcing of our winning poster participants who each win £300 to spend on something related to their research:

Gayathri Athavan (IJSF/RNP)
Understanding the Role of Ag(I) Salts in the Pd–catalysed C–H Activation of Fluorinated Aromatics

Rosalind Booth (AKDK/KSW/GJG)
Optimising Artificial Enzymes by Altering the Nature of the Active Metal Complex

Jonathan Churchill (PAOB/VC/AP)
Synthesis of Sterically Hindered Tertiary Amines by Electrochemically Generated α-Amino Radicals

James Race (ASW)
Rhodium Complexes of Ortho-aryl substituted DPEphos ligands; Understanding Anagostic Interactions and Agostic Bonds

Rhianna Rowland (GJD)
Insect-Baculoviral Production of Human β-Glucocerebrosidase Enables Atomic Resolution Analysis

We would like to thank all participants, judges and attendees for making the event a success in this revised format, and of course a big thank you to Johnson Matthey for their support and sponsorship.