Medical imaging techniques, like MRI, PET and CT, now give us very sophisticated information about the structure of organs, tissues, and even cells. But many of the most pressing questions in medical research today are actually on a much smaller scale, and are questions of chemistry rather than biological structure: how chemical (e.g. enzyme) reactions take place; where drug molecules interact with the cell; and how pH changes in health and disease. Traditional structural imaging techniques are no longer sufficient – we now need chemical information to diagnose and understand disease. This requires the use of chemical sensors, often called molecular imaging agents.

There are a number of molecular imaging agents that have already found widespread use. For example, PET scans almost exclusively use $^{18}$F-fludeoxyglucose (FDG), a glucose analogue that can therefore report on areas of the body that have highest glucose uptake. However, there remains an abundance of unanswered chemical questions of medical significance, and the development of new molecular imaging agents is an active and exciting research field.

We often think of the cell as a bag, containing mostly water and the odd organelle, DNA molecule, or protein, but this is far from the case. Molecular depictions, like the one of the mycoplasma bacterium shown in Figure 1, illustrate the cluttered environment.

**Figure 1:** Depiction of a mycoplasma (1000 times smaller than a human cell), showing how tightly packed it is with proteins and other macromolecules. Illustration by David S. Goodsell, the Scripps Research Institute.
of the cell. Molecular imaging tools therefore need to find the chemical of interest, and “light up” in some way so that this chemical can be seen over all others. In my research group, we make molecular imaging tools (commonly called sensors or probes) that give out information in the form of fluorescent light (for use in microscopy) or magnetic resonance contrast (for use in MRI).

One of the main chemical questions we are interested in studying involves oxidative changes in the body. Oxygen is so crucial to our survival, but in high concentrations it can also be highly damaging – it is itself an oxidant, and can produce reactive oxygen species (ROS), many of which are free radicals, which cause damage to DNA, proteins and lipids in the cell. In healthy cells, ROS are balanced by antioxidants to maintain healthy redox homeostasis, with short-lived ROS bursts playing important roles in cellular signalling and immune response. Prolonged elevated levels of ROS are termed “oxidative stress”, which is known to be associated with diseases of ageing, such as cancer, neurodegeneration and cardiovascular disease, but the exact relationships between oxidative stress and disease are not understood. At the other end of the spectrum, lack of essential oxygen, termed “hypoxia”, can also have damaging effects. Hypoxia arises in heart attack and stroke, where there is an insufficient supply of oxygenated blood to the heart and brain, and large cancerous tumours can also be hypoxic. We are therefore developing molecular imaging agents that are capable of detecting hypoxia and oxidative stress.

For studying hypoxia, we are developing magnetic resonance contrast agents. MRI contrast agents are used for over a third of all MRI scans. Contrast agents are typically metal complexes, which improve the overall contrast between bright and dark regions of an MR image. Recently, researchers have tried to make responsive contrast agents, which can report on a particular aspect of the body’s chemistry. We are working with Dr Paul Bonnitcha, an alumnus of the School and now a medical doctor, to develop MR contrast agents that only light up in the presence of hypoxia. Our agents are cobalt complexes, which are less toxic than the commonly-used gadolinium-based MRI contrast agents.

For studying oxidative stress, we have made fluorescent sensors. For example, we have made a sensor, FCR1, which changes from emitting blue light to emitting green light in oxidising environments [Figure 2]. When we look at cells treated with our sensor using a confocal microscope, we can use the ratio of green to blue fluorescence to identify regions that are oxidatively stressed. FCR1 and another one of our sensors are now sold by Stressmarq, a Canadian bioreagents company. We have also sent our sensors to more than twenty research groups around the world, who are using them to answer their own questions about oxidative stress.

With collaborators at the Florey Institute in Melbourne, we have used our sensors to image C. elegans, microscopic worms (often called nematodes) [Figure 3].

More recently, we have been developing sensors that localise only to specific parts of the cell, enabling us to specifically understand the chemistry within sub-cellular organelles [Figure 4].

Hypoxia and oxidative stress are just some of the conditions that we are trying to understand better in my research group. We particularly love interacting with medical researchers to learn about what chemical problems they would like to study, and tackling challenges that we know will change our understanding of the human body in health and disease.

STUDENTS MAKE $750 DRUG CHEAPLY WITH OPEN SOURCE MALARIA TEAM

BY MS VIVIENNE REINNER

Synthesis of essential medicine challenges price-hike loophole.

Sydney Grammar students under University guidance have shown how simple it is to make a version of the life-saving medicine Daraprim, whose price was the subject of controversy last year when it jumped more than 5000 percent.

Daraprim - originally used as an antimalarial after its synthesis by Nobel Prize winner Gertrude Elion - is now more widely used as an anti-parasitic treatment for toxoplasmosis, which can be a dangerous disease for pregnant women and people with compromised immune systems, such as those living with HIV or AIDS.

Daraprim is listed by the World Health Organisation as an essential medicine. In September 2015, Turing Pharmaceuticals acquired the market rights to Daraprim and raised the price of a dose more than 5000 percent overnight. CEO at the time, Martin Shkreli, stuck by the price, despite criticism including from US Secretary of State Hillary Clinton.

To highlight the inequity of the monopoly, high school students in Sydney have been working with the Open Source Malaria consortium to make Daraprim in the laboratory using inexpensive starting materials, as part of the Breaking good – Open Source Malaria Schools and Undergraduate Program.

Scientists anywhere in the world were able to view all the data generated and mentor the students to accelerate the science under the coordination from The University of Sydney’s Dr Alice Williamson and Associate Professor Matthew Todd.

Dr Williamson from the School of Chemistry said the scientific community could provide advice and guidance to the students online in real time.

“Daraprim may be quickly and simply made, bringing into question the need for such a high price for this important medicine,” Associate Professor Todd said.

The findings were presented at the 2016 Royal Australian Chemical Institute Organic One Day Symposium today. The Sydney Morning Herald reports: Sydney schoolboys take down the most hated man in the world.

Open Source Malaria is supported by the Medicines for Malaria Venture and the Australian Government.
Professor Michael Kassiou is one of 8 Chief Investigators in receiving a $17M NHMRC program grant over the next 5 years to study frontotemporal degeneration of the brain which is a leading cause of morbidity due to a pathologically heterogeneous, rapidly-progressive group of disorders including behavioural, language and motor deficits. http://bit.ly/2kmEn3

Associate Professor Lenka Munoz and Professor Michael Kassiou have received $1.2M in funding from Lin BioScience for a new cancer fighting molecule. http://bit.ly/2nsGe3w

Associate Professor Deanna D’Alessandro has been awarded the 2017 Le Fèvre Memorial Prize by the Australian Academy of Science. Deanna’s research is delivering insights into an exciting area in nanoporous molecular materials, namely, their electronic and conducting properties. These fundamental advances have enormous potential as the basis of new devices for applications including electrocatalysis, sensing and solar energy conversion.

PhD candidate, Mr Liam Scarratt, has been awarded the "Postgraduate Research Prize for Outstanding Academic Achievement" for a paper published in 2016 entitled “Durable superhydrophobic surfaces via spontaneous wrinkling of Teflon AF”. http://bit.ly/2mqi1ez Third year PhD candidate, Ms Katrina Zenere has been awarded the Murray Student Talk Prize (named in honour of Emeritus Professor Keith Murray from Monash University) for the best student research seminar at the 2017 SANZ-O-MAG2 workshop. http://bit.ly/2iKMSA

PhD candidates, Ms Haihui (Joy) Jiang and Mr Andrew Giltrap have been invited to attend the 67th Lindau Nobel Laureate Meeting in Germany in June. This is a unique opportunity to interact with over 30 Nobel Laureates and 400 most qualified early career researchers around the world. http://bit.ly/2nlvGxL

REUNION DINNER OF THE ORGANIC CHEMISTRY DEPARTMENT

BY DR JOE MOCK (BSC ‘70, PHD ‘74) AND MS ARLENE GOFERS (NEE SLEE), BSC (’70)

On a sweltering night on Tuesday 17 January 2017, former members of the Organic Chemistry Department met for a very pleasant evening of good food, even better company and many reminiscences which included after dinner speeches from Malcom Rasmussen and Robert Norris at a Thai restaurant in Cammeray. Those who attended the reunion dinner ranged from graduates who completed their doctorates in the early 1980’s right through to the 1980’s. Also present were those who had been professional officers in the department. Many had travelled as far away as Tasmania, Townsville, Canberra, the Southern Highlands, and the Central Coast to attend - such is the camaraderie in the Organic Chemistry Department!

It had been envisaged to be a much smaller group but as friends were contacted everyone felt that it was important to get in touch with as many people as possible - however the distance from Sydney prevented some from attending. A few colleagues sent in summaries of what they have been doing since leaving the department which were printed, passed around during the dinner and read with great interest. Sev Sternhell, former Professor of the department and Head of the School of Chemistry, was in hospital recuperating at the time but we signed cards wishing him a speedy recovery and organized a get well gift. There was diversity in careers represented after a common background in Organic Chemistry. Naturally, there were a good number of academics present: the former Vice Chancellor of Monash, the former Vice Chancellor of the Australian Catholic University, an Associate Professor of James Cook University, a former Senior Lecturer at ANU, a former Senior Lecturer in Science Education at UNSW, two former Senior Lecturers of the University of Western Sydney, a former Senior Lecturer at UTS, a present adjunct professor of Southern Cross University, the present Senior Deputy Vice Chancellor of UNSW and a present Associate Professor at Macquarie University. Some of these did extensive consultancy with industry. Several had held senior research positions with the CSIRO or in industry. Three had been involved in teaching Chemistry in the TAFE system, including the former Head of OTEN. Three have been (or are) involved in drug analysis or detection. Three have been medical specialists (O & G, paediatrics, radiology) while one was a GP. One is an author of children’s science books. One is a present gemologist. One is the present Principal of Shore School. After stints in chemistry, two became church ministers (Anglican, Presbyterian). The former Dean of Science could not attend but sent this from Germany as part of a message to those at the dinner:

“To me it (Organic Chemistry) is a science that delicately balances predictability with unpredictability - predictable in that we can rationally design experiments which should work but unpredictable in that organic chemistry turns up surprises which in turn keep us interested.”

We were all grateful for the foundation we received in the Organic Chemistry Department and look forward to a subsequent reunion.
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A team of chemical researchers from the University of Sydney has honed in on a new technology that could lead to the ability to capture water from moist air.

The technology is inspired by an example of natural engineering, the surface structure on the back of a beetle native to the Namib Desert in southern Africa.

The researchers, from the School of Chemistry and Australian Institute for Nanoscale Science and Technology (AINST), which launched last year, have taken inspiration from this natural structure to design a viable coating technology for atmospheric water capture, to be used in circumstances of drought, emergency or isolation from the main water grid.

The results were published recently in the American Chemical Society journal Applied Materials & Interfaces.

The Physosterna cribripes desert beetle has a microstructured elytra enabling it to collect atmospheric moisture: the surface of the beetle’s back is covered in a number of microscopic bumps that are water-loving, in a background that is waxy and water-repellent.

This particular structure and chemistry allows the beetle to nucleate water droplets condensing from the moist winds blowing at dawn from the desert, and then to get the droplet to slide to its mouth.

“\textit{In an emergency or drought situation, this could literally mean the difference between life and death.}”

Co-author and leader of the AINST domain in Molecular Nanoscience, Associate Professor Chiara Neto, said her team’s approach used the spontaneous formation of micropatterns in thin polymer films from nanoscale intermolecular forces that lead to the instability, and were therefore intrinsically low-cost and up-scaleable.

“We have been working in the area of biomimetic material for a few years now, and the idea of biomimetic water capture is particularly interesting for its potential to benefit the sustainable use of resources,” Associate Professor Neto said.

“In our most recent paper, we have refined our pattern formation approach using specific solvents for the polymer molecules in use, and made the approach even more amenable to large scale use.

“Importantly, we have identified the micropattern size and distribution that are most effective in nucleating and collecting water droplets without any energy input.

“Some of the patterns that we have designed are able to collect substantially more water (57% more in volume) than flat plastic sheets under harsh circumstances, for example under low humidity or with no active cooling of the surface. In practice, what this means is that exposing our micropatterned surfaces to the night sky will result in more dew events than on a flat plastic sheet.

“In an emergency or drought situation, this difference could literally mean the difference between life and death.”

Dr Omar Al-Khayat, who completed his PhD thesis on this topic late last year, said he had already applied and tested these patterns to large three-dimensional tubes.

“In the future, we can envisage applying these patterns to large sheets exposed to the night sky, to collect water from humid air, for irrigation or drinking,” Dr Al-Khayat said.
I am delighted to begin my first Head of School column by thanking Professor Kate Jolliffe for her leadership of the School of Chemistry over the last four years. I’ve seen first-hand over the last three months how hard Kate has worked on our behalf and I’m very pleased she will now be able to take a well-deserved sabbatical to focus on her research programme.

I’d also like to thank everyone in the School who have made me feel so welcome since I joined the University of Sydney in January. Having been a member of staff at my previous university for 17 years this move has been a big change for me but it has been made much easier by having such great colleagues in Sydney.

I’d like to welcome Drs Ivan Kassel, Shelley Wickham and Junming Ho to the School. Ivan is a theorist whose research concerns the simulation of energy and charge transport in disordered materials, including next-general solar cells and photosynthetic complexes. He is also interested in the interface between chemistry and quantum engineering, working on engineering quantum effects into molecular systems and developing algorithms for the simulation of chemical processes on quantum computers. Shelley is the Professor Harry Messel Research Fellow and Postdoctoral Research Fellow in the School of Chemistry and the School of Physics and has research interests in the self-assembly of matter on the nanoscale, and in particular in the design and assembly of programmable nanostructures out of DNA, with applications in cell biology, materials science and nanomedicine. Following the completion of her Professor Harry Messel Research Fellowship, Shelley will continue as a Lecturer in Physics and Chemistry beginning in 2019. Junming is a computational chemist with interests in molecular dynamics simulations, hybrid quantum mechanics/ molecular mechanics methods, solvent effects and physical organic chemistry. Junming joins us as a DECRA fellow.

I am excited to start my term as Head of School. The higher education landscape is evolving across the world. Significant funding is increasingly being directed to groups of researchers and consortia rather than individual academics. I’ve asked the research leaders in the School to look at our strategy to make sure that we are well placed to take advantage of future funding opportunities. This will involve a reorganisation of the research structure in the School and my aim is to have this process completed by the second half of this year. We will also begin to prepare for our next ERA submission and I have asked Prof Lou Rendina to take overall charge of this process as our ERA champion. Consequently, Lou will step down as Associate Head Research and I am pleased that A/Prof Deanna D’Alessandro has kindly agreed to continue as Associate Head Education and I am very pleased that A/Prof Peter Rutledge has agreed to take on the role of Deputy Head of School. The management team will be focusing on our revised curriculum, equity and diversity in Chemistry and improving our infrastructure over the coming year.

Professor Philip Gale
Head of School

Phil A. Gale received his BA (Hons) in 1992 and his MA and DPhil in 1995 from the University of Oxford before moving to the University of Texas at Austin where he spent two years as a Fulbright Scholar. In 1997, he was awarded a Royal Society University Research Fellowship and returned to the Department of Chemistry at Oxford. In 1999, he moved as a Lecturer to the University of Southampton and was promoted to Senior Lecturer in 2002, Reader in 2005 and to a Personal Chair in Supramolecular Chemistry in 2007. In 2014, he was awarded a Doctor of Science degree by the University of Oxford. In January 2017, he moved to the University of Sydney to take up the position of Professor of Chemistry and Head of the School of Chemistry.

From 2010 to 2016 Phil was the Head of Chemistry at the University of Southampton. During this period, he successfully led the department through a period of change and growth, working with colleagues to restore Southampton Chemistry to its place amongst the best chemistry departments in the UK.

Phil is the author or co-author of over 250 publications including an Oxford Chemistry Primer on Supramolecular Chemistry (1999) and an RSC Monograph in Supramolecular Chemistry entitled Anion Receptor Chemistry (2006). He is the Editor-in-Chief of Coordination Chemistry Reviews and Supramolecular Chemistry and also serves on the Editorial Board of Chem from Cell Press. He is a member of the Advisory Board of the RSC flagship journal Chemical Science.

HEADLINE NEWS

Ivan Kassel

Ivan Kassel is a theorist working on the simulation of energy and charge transport in disordered materials, including next-general solar cells and photosynthetic complexes. He is also interested in the interface between chemistry and quantum engineering, working on engineering quantum effects into molecular systems and developing algorithms for the simulation of chemical processes on quantum computers. He is the Professor Harry Messel Research Fellow and Postdoctoral Research Fellow in the School of Chemistry and the School of Physics, and has research interests in the self-assembly of matter on the nanoscale, and in particular in the design and assembly of programmable nanostructures out of DNA, with applications in cell biology, materials science and nanomedicine. He will continue as a Lecturer in Physics and Chemistry at the University of Sydney beginning in 2019.

BIOGRAPHY

Phil Gale

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Professor Payne talks about his work and passion for finding a cure for highly infectious diseases such as tuberculosis.

Believed by many to be a relic of past centuries, tuberculosis (TB) causes more deaths than any other infectious disease including HIV/AIDS. In 2015 there were an estimated 10.4 million new cases of TB and 1.4 million deaths from the disease.

The bacterium causing TB (Mycobacterium tuberculosis) is becoming increasingly resistant to current therapies, meaning there is an urgent need to develop new TB drugs. In 2015 an estimated 480,000 cases were unresponsive to the two major drugs used to treat TB. It is estimated more than 250,000 TB deaths were from drug-resistant infections.

An international collaboration led by University Professors Richard Payne, from the School of Chemistry, and Warwick Britton, from the Sydney Medical School and the Centenary Institute, has discovered a new compound which could translate into a new drug lead for TB.

The findings were recently published in *Nature Communications*.

The group was drawn to soil bacteria compounds known to effectively prevent other bacteria growing around them. Using synthetic chemistry the researchers were able to recreate these compounds with structural variations, turning them into more potent compounds called analogues.

When tested in a containment laboratory these analogues proved to be effective killers of *Mycobacterium tuberculosis*.

“These analogues inhibit the action of a key protein needed to build a protective cell wall around the bacterium,” said Professor Payne. “Without a cell wall, the bacterium dies. This wall-building protein is not targeted by currently available drugs.

“The analogues also effectively killed TB-causing bacteria inside macrophages, the cells in which the bacteria live in human lungs.”

Professor Payne said the findings are the starting point for a new TB drug. Planning for further testing and safety studies is underway.

The research was done in collaboration with Colorado State University in the USA, Simon Fraser University in Canada, Warwick University in the UK, Monash University and the University of Queensland. It was funded by Australia’s National Health and Medical Research Council (NHMRC).

Professors Payne and Britton also belong to the University’s Marie Bashir Institute for Infectious Diseases and Biosecurity. Professor Payne won the Malcolm McIntosh Prize for Physical Scientist of the Year at the 2016 Prime Minister’s Prizes for Science. [http://bit.ly/2mjQOcT]