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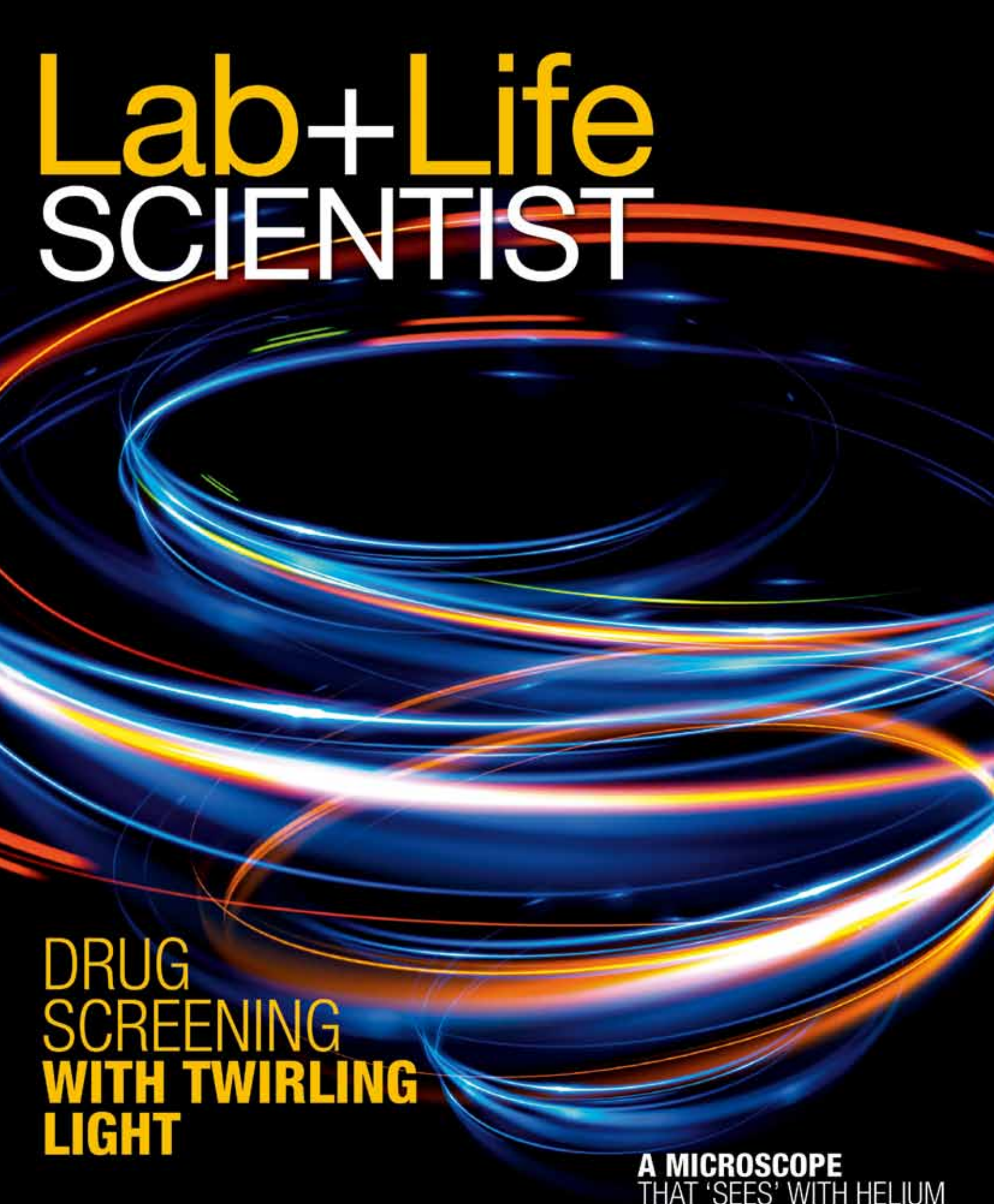

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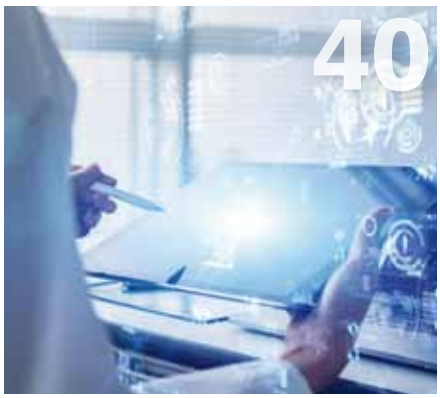

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Don't rain on my parade

In the weeks leading up to this issue going into production, I imagined that this editor's comment would be quite heavily focused on Japanese encephalitis virus (JEV) — the mosquito-borne viral disease that has been slowly but surely spreading throughout Australia's piggeries (infecting several humans along the way), aided by weather conditions which have led to particularly high mosquito numbers. Since then, the seemingly constant wet weather on Australia's east coast has become far more of a threat than the virus itself, leading to a number of flooding events, deaths and rising concern that climate change may cause such extreme weather to become something of a regular occurrence.

Indeed, the Intergovernmental Panel on Climate Change (IPCC) has released two separate reports since our last issue went to print, both of which paint a dire picture of the future unless significant changes are made. 'Climate Change 2022: Mitigation of Climate Change' states that limiting warming to around 1.5°C is possible but requires global greenhouse gas emissions to peak before 2025 at the latest, and be reduced by 43% by 2030, with immediate and deep emissions reductions necessary across all sectors. 'Climate Change 2022: Impacts, Adaptation and Vulnerability' meanwhile indicates that even this 'best-case scenario' will see the world face unavoidable climate hazards over the next two decades, with increased heatwaves, droughts and floods already exceeding plants' and animals' tolerance thresholds.

The world's scientists are of course doing their best to come up with novel solutions to save the planet, one of these being the capture and storage of carbon dioxide (CO_2) emissions in the form of hydrates under ocean floor sediments. Researchers from the National University of Singapore recently showed that CO_2 hydrates can remain stable in oceanic sediments for a period of up to 30 days, but they hope to eventually develop models that can predict the stability of CO_2 hydrates thousands of years into the future. Meanwhile, researchers at the RIKEN Center for Sustainable Resource Science have found a way to improve crop quality via a spray that introduces bioactive molecules into plant cells through their leaves, which could be used to help crops resist pests or become more resistant to drought. Mention must also be made of our own Australian Botanic Garden in Mount Annan, which carries out a significant amount of plant conservation work via its onsite nursery, the Australian PlantBank and the National Herbarium of New South Wales, the latter having officially relocated to the garden as of April this year — see our article on page 12 for more information.

Of course planning for the future should also take place at the laboratory level, and this issue we have multiple stories that showcase the importance of upgrading your technology. The article on page 15 highlights how digital pathology services have been critical during the pandemic, or flip to page 40 to learn the importance of connectivity in leveraging new technologies. You can also read on page 22 about a new type of microscope making use of a technique that is over 2000 years old, proving that sometimes the best new idea is an old one. That said, when it comes to solving climate change, I think we need as many ideas as we can get.

Regards,
Lauren Davis
LLS@wfmedia.com.au

Lauren Davis

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Peter Davis

Creating a genetic medicine manufacturing ecosystem

Part 3

Close to a year ago, when I wrote in the first article of this series, we were waiting for the federal government to deliver funding and a plan forward for a genetic medicine ecosystem, and to understand their commitment to the Modern Manufacturing Initiative.

Last article, I summarised the plan put forward by the Australian Academy of Science, the Delta variant was raging, Victoria and NSW were leading the nation in supporting this concept and we were rushing to get our second vaccination. The federal government were rocketing towards a conclusion to the much-anticipated approach to market (ATM)[1]. A great deal has happened since that time, including a disturbing trend that ultimately will compound and extend this pandemic. We need to talk about the elephant in the room: vax equity.

The PM speaks

The federal government announced Moderna as the successful ATM responder on 21 December 2021, when Prime Minister Scott Morrison said, "A new sovereign vaccine manufacturing facility will be built in Australia to produce respiratory mRNA vaccines for potential future pandemics and seasonal health issues as part of a new in-principle agreement between the Australian Government, Victorian Government and global mRNA company Moderna"[2]. This initiative should be applauded, but it comes with reservations as we are yet to be convinced this will back Australian research to the extent proposed by the Australian Academy of Science statement 'National RNA Science and Technology priorities[3]'. Perhaps we should find solace given Minister Simon Birmingham stated, "Moderna will become a vital part of Australia's mRNA research and development landscape, bringing investment and opportunities for the entire research sector"[2].

I was informed that "beyond Moderna specifically, the government will also invest up to $25 million in grants from 2022–23 towards mRNA Clinical Trials Enabling Infrastructure. That should support Australian medical research and medical innovation projects, including with equipment and infrastructure." I was told "the government is also looking at other opportunities to support an mRNA and RNA ecosystem, and for instance the recent Cooperative Research Centres Project (CRC-P) round that was open in October 2021 specifically identified mRNA projects as being of interest. Additionally, the government is also trying to make sure that there is a well-thought-out approach to supporting the mRNA/RNA community, given the

different investments by states, and the different opportunities and areas of potential of RNA, and so that's ongoing, but I think there will be further progress on that early in the new year."

And we wait

These initiatives and investments into science are extraordinary. Science is finally getting its turn in the sun, and even mainstream media is acknowledging it — *The Sydney Morning Herald* lauded the Australian RNA Production Consortium (ARPC) members in its article 'Who Mattered 2021'[4]. Discussions with some of the research community have however flagged that there seem to be no announcements around the $1.5 billion Modern Manufacturing Strategy touted by Minister Angus Taylor[2], and many are very anxious about the CRC-P funding. The relatively slow rollout of the funding announcements has ramifications as global pressures force prices up on much of the unique technologies creating a quandary where grant application amounts may fall short of requirements, heightening the adage 'time is money'.

In an ASX announcement in December 2021, IDT CEO Dr David Sparling said, "The company has successfully delivered on the Monash Institute of Pharmaceutical Sciences (MIPS) COVID-19 mRNA receptor binding domain vaccine candidate project, being Australia's first locally manufactured cGMP mRNA finished product and clearly showcases IDT's manufacturing capabilities in this regard." The announcement noted the company is also waiting to receive feedback on its submission to the Australian Government's $800m Modern Manufacturing Initiative (MMI) Manufacturing Collaboration Stream Grant Opportunity. At the time of writing, the company is still awaiting notification.

Around the grounds

I have mentioned the commitment and importantly the action of the Victorian and NSW Governments towards massive funding boosts into this sector; I have since learned of the entry of the Australian Capital Territory. Professor Thomas Preiss, an ARPC foundation member, is involved in ANU's Shine-Dalgarno Centre for RNA Innovation, bringing together experts from across the ACT to focus their collective efforts and expertise to maximise the power of RNA biology, while simultaneously addressing some of the pressing global healthcare issues. I feel this will be a formidable team with over 250 years of collective experience. For the uninitiated the name has immense providence, and I encourage you to check out the scientific rock stars behind this. Recently I also attended the inaugural symposium of the Australian Institute for Infectious Diseases in Melbourne — a collaboration of the University of Melbourne with the Doherty and Burnet Institutes, a $400 million investment by the Victorian Government, and I understand there are an array of commercial collaborators as well.

This brings me to consider other states and their investment into Australia's sovereign capacity. I recently attended a webinar supported by Life Sciences Queensland (LSQ) titled 'Medicines of the future: making them here' — with the descriptor "hear about our vision to develop sovereign capability here in Queensland". It was encouraging to note Queensland Chief Scientist Professor Hugh Possingham plus a raft of eminent scientists give their vision of the BioManufacturing Alliance (BMA)[5] established in late 2021. I imagine they are on the road to creating a world-class ecosystem in Brisbane or at least solving a puzzle piece for the whole ecosystem (think RNA production) — that is, if they can convince the Palaszczuk government to invest!

Sounds of silence

Anecdotally, the scientific industry perceives Western Australia as the poor cousin, where the researchers seem to punch well beyond their funding weight with exceptional work — oh what a difference a little investment would make. WA has a strong history of pioneering breakthroughs with genetic medicines: one of the world's first RNA therapies — the first FDA-approved treatment for muscular dystrophy — was developed in WA. Professor Steve Wilton and Professor Sue Fletcher developed this therapy whilst at UWA, in collaboration with Sarepta Therapeutics in the USA[6].

Scanning the media statements on the Government of Western Australia website, I could find little to no new funding into this sector specific to a genetic medicine ecosystem. I have contacted Minister Roger Cook to determine if I have missed an investment announcement, but to date I am yet to receive a reply. If this is the case, I concede I am astonished given the substantial contributions to build a national response made by NSW (UNSW RNA Institute) and Victoria (Australian Institute for Infectious Diseases — AIID), plus the establishment of the Shine-Dalgarno Centre for RNA Innovation in Canberra. Adding to this,

I noticed *news.com.au* reported on 6 October 2021, "Mr McGowan claimed his state's booming economy was propping up the Commonwealth government's financial Covid-19 relief to other states that had been hard hit by the virus." I believe this was around the time he handed down a $5.6 billion budget surplus, yet zero support for the national project to enable West Australian scientists to join in the local manufacture of genetic medicines. Understand that WA is one of the wealthiest places on Earth, with a GDP per capita of $100,367. This is a very poor report card, and it amplifies the divide — not something WA would like to have given they just 'opened the border'. I leave this to you to draw your own conclusions.

Vax equity

It has been described by Professor Brendan Crabb, Director and CEO of the Burnet Institute, that the inequity in vaccine supply to the planet is an own goal — if there are a bunch of unvaccinated communities and the virus is being transmitted, each time it replicates there is a potential to result in another variant, thus prolonging this pandemic. Prof Crabb made this point during the AIID symposium 'Lessons learnt from COVID: guiding pandemic preparedness and response'[7]; Nobel Laureate Françoise Barré-Sinoussi, Emeritus Professor at the Institut Pasteur and Emeritus Director of Research at the Inserm, echoed the tremendous error in the COVID-19 response with respect to vaccine equity, appearing to lament that we had not learnt from the HIV experience. Barré-Sinoussi stated during the symposium "the inequities is really a critical issue where we did not work enough; we already knew from HIV and still today from COVID we see how much inequities is critical in the response, access to treatment, access to prevention, access to diagnosis. We cannot continue to work like that; we must improve what's going on in terms of inequity in this world."[7]

Perhaps Professor Sharon Lewin, the inaugural Director of the Doherty Institute, summed up an interesting alternative to how the rich countries of the world quibbled over the few vaccines, securing so many for themselves, compounding the inequity. She mentioned that at the beginning of the pandemic, the Wellcome Trust were advocating they should just buy 7 billion vaccines upfront and have them for the world; apparently the logistics were there, just no one thought of it! Perhaps this is something to consider not just for future pandemics (not if, but when); perhaps we should be doing this now!

Tremendous endeavours

In my wildest dreams I would never have thought the voice of a few would grow to such a chorus of the cognisant (to borrow a phrase from Professor Damian Purcell). Future Australian researchers may well look back on this pandemic as the critical point where genetic medicine went into warp speed in Australia; it certainly looks that way and a year on from the first of these articles[8], the outlook could not be rosier. We must not forget our friends in New Zealand — the Malaghan Institute of Medical Research, an independent biomedical research institute based in Wellington, has made a critical investment into its country's response securing the capacity to create mRNA vaccines when it took delivery of the NanoAssemblr Blaze from Precision Nanosystems9 in Vancouver. This critical step may help secure vaccine equity not just for NZ but surrounding island nations into the future. The efforts of the Vaccine Alliance Aotearoa New Zealand (VAANZ)[10], tirelessly working to collaborate with the ARPC to ultimately form the ANZRPC, are the foundations for a robust commercialisation of NZ research, making Wellington the epicentre for genetic medicines in New Zealand.

The pandemic is not over

I can conclude this article by saying this pandemic is far from over. Vaccines are amazing but are not perfect; variants will continue to emerge so long as the virus is replicating in the community. Get vaxxed and wear a mask indoors or where you cannot socially distance. Raina MacIntyre, Professor of Global Biosecurity within the Kirby Institute, was interviewed by the ABC Sydney local radio recently as mask mandates were being relaxed; her frustration was palpable. This is the single most effective non-medical intervention we can do. I concur with Raina; wear a mask if not to protect yourself, but to protect your family. Raina also suggested the Omicron variant caused more COVID deaths in Australia during January and February 2022 than all of 2020 and 2021 combined. Sobering information given that Shenzhen in China has been locked down[11].

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'Bionic' pacemaker reinstates heart rate variability

Researchers from The University of Auckland have designed a pacemaker that re-establishes the heart's naturally irregular beat, unlike other pacemakers that pace the heart metronomically. This puts it closer to the typical heart rate of a healthy individual, which is constantly on the move.

"If you analyse the frequencies within your heart rate, you find the heart rate is coupled to your breathing," said Professor Julian Paton, Director of the Manaaki Manawa Centre for Heart Research at The University of Auckland. "It goes up on inspiration, and it goes down on expiration, and that is a natural phenomenon in all animals and humans. And we're talking about very ancient animals that were on the planet 430 million years ago."

Prof Paton was part of a group of scientists who decided to investigate the function of this variability. They made a mathematical model that predicted it saved energy — which made them question why a metronomic heartbeat was used in heart-failure patients who lacked energy.

"All cardiovascular disease patients lose their heart rate variability, which is an early sign that something is going wrong. Prof Paton explained, "People with high blood pressure, people with heart failure, their heart rate is not being modulated by their breathing. It may be a little bit, but it's very, very depressed, very suppressed.

"We decided that we would put the heart rate variability back into animals with heart failure and see if it did anything good."

Following positive signals in rats, the latest research was on a large animal model of heart failure, published in the journal *Basic Research in Cardiology*. According to research co-leader Dr Rohit Ramchandra, the study showed that introducing a natural variation in the heartbeat improves the heart's ability to pump blood through the body.

"The other big news is that we get a 20% improvement in cardiac output, which is effectively the ability of the heart to pump blood through the body," he said.

"The pacemaker is almost like a bionic device," Prof Paton said. "It understands the signals from the body that tell the device when we're breathing in and when we're breathing out. And then the device has to communicate back to the body and pace the heart up during breathing in and down during breathing out."

Plans are now in place to recruit human patients into a trial planned for later this year in New Zealand.

CSIRO warns against spraying face masks with sanitiser

With face masks remaining a regular feature for most Australians, there may be a temptation to extend a mask's life by spraying it with sanitiser between uses. However, new research by CSIRO has now shown that increased exposure to alcohol-based sanitisers actually reduces a mask's effectiveness.

The CSIRO study is believed to be the first of its kind in the world to investigate the impact of vapours from alcohol-based hand sanitisers and cleaning solutions on the performance of (K)N95 and P2 face masks. The results were published in the *International Journal of Environmental Research and Public Health*.

"Single-use face masks will continue to be part of many of our lives as they provide us with a defence against COVID-19, its variants and any future pathogens, but we had been hearing stories about people trying to prolong the life of these masks by cleaning them," said Dr Jurg Schutz, lead researcher on the study.

"We started thinking about the kinds of products people have been using more during the pandemic, like alcohol-based hand sanitiser and cleaning solutions, and realised these could impact the electrostatic properties of face masks.

"These masks rely on having an electrostatic charge that attracts particles and traps them like a sticky spider web, but we also know this charge can be destroyed by highly concentrated alcoholic vapours."

The researchers found masks stood up well in three common scenarios used to prevent the spread of COVID-19: using hand sanitisers while wearing a mask; cleaning tables while wearing a mask; and spraying a mask with sanitiser or alcohol-based cologne once.

Disposable respirator masks were able to retain their effectiveness after either four hours of continuous exposure to alcoholic sanitiser vapours or one direct spray of sanitiser. More than one spray of sanitiser could seriously compromise the mask to the point of no longer protecting the wearer, and extended exposure to highly concentrated vapours by sealing it in a container with alcohol-based sanitising solution — for example, to 'clean' a single-use mask before a second use — will actually destroy it.

Dr Schutz said the study's findings will help inform people on how best to care for their single-use face masks. The team also expects the findings could help inform the development of future, pandemic-improved filtration products around the world.

A look inside the stomachs of carnivorous plants

Researchers from Curtin University, the Botanical and Zoological Natural History Collections in Munich and the Ludwig Maximilian University of Munich have found a way to take a sophisticated look inside the stomachs of carnivorous plants, overcoming a hurdle that had previously stumped entomologists. Their work has been described in the journal *Scientific Reports*.

Lead author Thilo Krueger, a PhD student at Curtin, explained that many carnivorous plant species are critically endangered, threatened by habitat destruction, environmental pollution and climate change. It is critical to their survival for scientists to understand exactly how many and what kind of insects carnivorous plants eat.

"Quite often, several carnivorous plant species are found in one habitat, and the question arises if different species may rely upon different food sources," he said. "To develop conservation plans that protect their future, it is essential to understand their biology, which includes what they eat — their natural prey spectra.

"Studying the prey spectra of carnivorous plants has previously been hampered by the fact that digested insect prey is often hard to identify, even by trained entomologists. Soft-bodied insects such as midges often turn into unidentifiable crumbs during digestion on the leaves."

Co-author Dr Adam Cross, also from Curtin, said the new method combines macro photography of the captured insects with DNA metabarcoding, a cutting-edge insect identification tool. He explained, "Any insect that is captured by a carnivorous plant will contain traces of its genetic material or DNA, even after digestion by the plant. This DNA can be detected and compared with DNA libraries of known insects, thus identifying the prey.

"Because DNA metabarcoding is prone to contaminations and does not allow us to estimate the quantity of prey, we carefully controlled our data using macro photographs of the prey items to achieve an unprecedented completeness of prey spectra data."

Senior author Dr Andreas Fleischmann, from the Botanical Natural History Collection and the University of Munich, said the new method of DNA metabarcoding was so sensitive that it even detected tiny amounts of insect DNA that were not obvious to researchers from field examination and macro photographs.

"Hence, our study of carnivorous prey spectra using genetic DNA fingerprints from the captured insects resembled reconstructing a crime scene — except our crime scene investigation was about finding out what a set of carnivorous plants had for lunch," Dr Fleischmann said.

Lauren Davis

New digs for the National Herbarium of NSW

Home to over 1 million residents and counting...

The National Herbarium of New South Wales has officially relocated from its long-time home in the Royal Botanic Garden (RBG) Sydney to the Australian Botanic Garden in Mount Annan, marking a new chapter in its 169-year history.

Established in 1853, the herbarium has grown from an initial collection of around 1800 native plant specimens to over 1 million today. With more than 8000 new specimens being added to the collection every year, the Sydney facility was running low on space and also experiencing problems with mould and insects. Thus, the momentous decision was made to move the entire collection to a brand new facility in Mount Annan, located around 60 km south-west of the Sydney CBD.

The Australian Botanic Garden was in many ways an obvious fit for the herbarium's new home. As one of three gardens owned by the Royal Botanic Gardens and Domain Trust estate (the others being RBG Sydney and the Blue Mountains Botanic Garden in Mount Tomah), it meant the collection would stay on the estate's land. The garden also sits on a massive 416 ha site, providing ample space for the purpose-built facility — appropriately inspired by a waratah seed pod — to store the collection now and as it expands in future. Furthermore, the garden is already home to the Australian PlantBank, which has since 2013 served as the largest native plant conservation seed bank in the country and played a key part in helping to restore certain species to the wild following the devastating Black Summer bushfires.

The relocation of the herbarium's collection has been no mean feat. As noted by Dr Brett Summerell, Chief Botanist and Director of Research at the Australian Institute of Botanical Science, "You can imagine moving 1 million specimens — and knowing at every point in the transportation process exactly where each particular specimen is, because we can't afford to get them mixed up." This resulted in the decision to digitise the whole collection, photographing each specimen at very high resolution — "almost as good as looking down the microscope", according to Dr Summerell.

Furthermore, these images will be publicly accessible to researchers all around the world, meaning the specimens in many cases will not need to be shipped to other institutions as they have been in the past — minimising the potential for damage en route and saving researchers from waiting months or even years for the specimens to come to them. And with a collection that includes both rare and historic specimens, that's a big advantage.

"The oldest specimen in the collection is from 1769 — we have a few specimens collected from Banks and Solander in Botany Bay," Dr Summerell said. "And then specimens collected by Leichhardt, by Cunningham, by Robert Brown on Matthew Flinders' voyage — all of the great exploratory trips in the early days of the colony usually included a naturalist/botanist. And 88–89% of the flora is endemic to the country and not seen anywhere else."

In instances where new specimens are added to the collection, these go through a strict quarantine process to make sure they don't bring any pests with them — a process which incorporates both

drying and freezing to kill adult pests as well as any potential eggs. In the very unlikely event that any pests make it through the seven-day quarantine period unscathed, the collection is housed across six separate vaults, so any infestations will be contained.

So what exactly do you do with over 1 million specimens? Dr Summerell explained that the facility's team of nearly 100 scientists, acting on behalf of the Australian Institute of Botanical Science, carries out a lot of work in terms of molecular understanding of plant groups and how various processes happen.

"It all comes down to DNA analysis — extraction of DNA from plant samples, looking at using DNA to be able to understand relationships between different species, how they might be related, whether they're unique, and also looking at that to understand the processes that have happened from the fossil record through to the future in terms of understanding how plants may have adapted or changed as a result of historical and prehistoric changes in climate, and maybe being able to use that to predict what might happen in the future given current trends," he said.

"So as well as looking at the historical facts, it's very much forward looking, using all the latest cutting-edge tools. In fact, a lot of the molecular work that happens in groups like plants or fungi are ways in which we can test different technologies and techniques so that we can actually start to look at them in mammals and in humans."

The herbarium also has a Botanical Identification Service that enables people to send in their own specimens to have them identified, or even to come in themselves to use the facilities. Dr Summerell said, "We get specimens sent in from a whole variety of different sources, whether it's for environmental assessments; weed identifications; where livestock get poisoned and they want to know the particular plant causing problems; even forensic botany, where there might be a piece of plant material or flower or whatever associated with a corpse."

Furthermore, it is not unusual for the herbarium to identify a species that is new to science, with Marco Duretto, Manager of Plant Diversity, saying, "We're one of those megadiverse countries where we have 26,000 different species of flowering plant, and we're describing a couple of hundred a year at least. And our institution does a good whack of that."

Indeed, back in 1994 the herbarium was the institute that identified the Wollemi pine, previously only known through fossil records. Now endangered, Wollemi specimens are being grown in the Australian Botanic Garden Mount Annan's nursery — which was recently relocated within the garden in order to make room for the herbarium — with the aim of finding ways to futureproof those that still exist in the wild.

The Wollemi is not the only species the nursery is helping to conserve, with some of its other specimens including the pink flannel flower from the Blue Mountains, which germinates under very specific post-bushfire conditions; *Polystichum moorei*, an endangered fern that can only be found in the wild on Lord Howe Island; and *Lenwebbia*, which is currently under threat due to myrtle rust — a fungal disease that has wiped out a range of Australian *Myrtaceae* species since it was first detected in 2010. Saving species from myrtle rust is a key initiative of the nursery as well as the Australian PlantBank, with the latter conserving affected specimens via novels methods including tissue culture and cryo preservation.

The herbarium thus appears to be in good company, surrounded in its new home by other facilities that are doing their bit to preserve Australia's precious biodiversity. With their powers combined, the future of our plant life looks to be in safe hands.

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Chemiluminescent western blotting takes advantage of the enzymatic reaction between horseradish peroxidase (HRP)-labelled secondary antibodies and an enhanced chemiluminescence (ECL) substrate to produce photons of light. The signal enhancement of the enzymatic reaction is useful for detecting small amounts of protein. The Sapphire is designed to deliver chemiluminescent detection with the same sensitivity as film, but with a broader dynamic range. The same three-detector technology that makes the Sapphire suitable for imaging western blots is also flexible enough to image a wide range of gels, whether they are ethidium bromide (EtBr)-stained DNA agarose gels, coomassie-stained protein gels or even 32P-labelled DNA acrylamide gels and more.

Other key features include image resolution down to 10 μm for high-quality image analysis and ultra-wide dynamic range for imaging and quantifying low and high abundance samples simultaneously. The system fully integrates with Sapphire Capture and AzureSpot software programs for quality imaging and analysis.

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Cell strainers

Biologix Cell Strainers are available in three sizes, which are colour coded for easy identification: 40 μm (purple), 70 μm (orange) and 100 μm (green). Individually wrapped in packs of 100, the sterile cell strainers are suitable for the filtration of various cells in biology and tissue culture laboratories.

The strainers feature a strong, high-performance nylon mesh, designed to be compatible with all brands of 50 mL tube, as well as a polypropylene frame with a moulded tab for easy handling. They are non-pyrogenic and gamma radiation sterilised.

Pacific Laboratory Products
www.pacificlab.com.au

Kees Wesdorp

The future of digital pathology

As we continue to battle the COVID-19 pandemic, cancer doesn't stop, and any delay in the diagnosis and treatment in oncology care can pose a high risk to patients.

The rapid adoption of digital pathology services has been critical in ensuring the continuation of clinical services during the pandemic, with pathologists able to conduct primary diagnoses from home while also protecting themselves and those around them.

Throughout the pandemic, the pathology department experienced a significant transformation at a scale not seen before in the field. In fact, digital pathology — the acquisition, management, sharing and interpretation of pathology information in a digital environment — has 'come of age' over the last two years, with research from Signify indicating the market saw 40.9% growth year over year in 2020.

Health providers and CMIOs are increasingly focusing on pathology within their wider digitalisation strategies, enabling a fully digital care solution to speed up the processing of viewing slides to help enhance decision-making. While challenges lie ahead, the power of virtualisation and the ability to connect with other teams, coupled with advances in AI, mean digital pathology is key to a new paradigm of diagnostic precision.

The power of virtualisation and care orchestration

One of the main challenges pathology departments face is an increasing shortage of pathologists. In addition, pathologists are spread across multiple locations while trying to be subspecialised to provide the right expertise for difficult cases. This creates a complex workflow, where slides must be distributed optimally to the pathologists across the system, balancing workloads, but also targeting the right cases to the right experts. Complicating matters, once acquired digitally, pathology data is growing exponentially, housed in disparate systems and scattered across various departments. This lack of a fully integrated, interoperable and secure set of harmonised systems keeps data, clinicians and workflows siloed and inefficient.

Enterprise-wide digital pathology solutions are able to tackle this issue head on with technology designed to accommodate current histopathology needs for routine use in high-volume labs and integrated pathology networks. Through virtualisation and better care orchestration, cases can be routed anywhere within the network to be read, scaling access to specialists, optimising workloads and decreasing the rate of interpretation errors conducted by non-subspecialised pathologists.

Virtual networks also enable pathology departments to moderate the impact of increased caseloads as a result of the pandemic by enabling efficient diagnoses and facilitating the speedier transfer of complex cases for second opinions. Connections to other teams also provide the opportunity for pathologists to collaborate with multiple professionals, helping to improve knowledge transfer and learning opportunities.

Enabling AI in pathology for deeper insights

Digital pathology also opens the door for artificial intelligence (AI) and automated tools for reading slides to help empower clinicians to deliver clear care pathways with predictable outcomes for every patient.

AI-powered workflows have the potential to provide a continuous pathway, where critical patient data is made visible to both pathologists and oncologists more rapidly, helping improve the clinician experience and enhance patient care. This will be particularly important in the years ahead, as the industry balances workforce shortages with the need to meet the increasing demand for pathology services and the ongoing impact of COVID-19.

The key to a new model of diagnostic precision is bringing together multiple diagnostic insights within the healthcare continuum — like radiology, pathology and genomics — at critical states along a patient's journey. By providing pathologists with the interoperability and connectivity to share high-quality images, utilise new technologies enabled by digitisation (such as AI) and expand diagnostic insights across networks, they will become key stakeholders in the data-driven healthcare systems of the future.

Kees Wesdorp is the Chief Business Leader of Precision Diagnosis at Philips. Reposted with permission from HealthCare Business News.

Philips Healthcare
www.philips.com.au/healthcare

Imaging platform

Leica Microsystems has launched Mica — a type of wholly integrated imaging solution that leverages machine learning software, automation tools and fluorescence unmixing techniques to automate the imaging workflow for researchers, regardless of their microscopy experience levels. The product has been built for those who wish to utilise complex imaging in their research, while focusing more on their biology than the specialism of microscopy.

All researchers, regardless of expertise, can now work in a single digital imaging platform, moving from set-up to beautifully visualised results. The product intelligently automates sample-finding, parameter-setting and focus constancy, replacing manual set-up with just one push of a button. It is designed to eliminate over 85% of the tedious set-up steps in the conventional imaging workflow.

Users can visualise four labels simultaneously in widefield using Leica's FluoSync technology, claimed to offer four times more data with 100% correlation compared to traditional fluorescence imaging methods. They can then switch seamlessly to confocal without moving the sample, to explore unexpected paths with no constraints.

The platform also fully integrates everything a researcher needs for radically simplified workflows, using automation and AI to enable deep understanding and a fast track to publication. For example, to perform a complex experiment such as a fluorescence multi-well plate assay, the current workflow can be simplified from 24 steps using a conventional microscope to just eight steps.

Leica Microsystems Pty Ltd
www.leica-microsystems.com

Anti-daratumumab antibodies

Bio-Rad Laboratories has launched a range of anti-daratumumab antibodies that are specific for daratumumab (Darzalex) and inhibit the binding of the drug to its target, CD38. The highly specific and high-affinity recombinant antibodies are suitable for bioanalysis and drug monitoring of daratumumab and its biosimilars.

Daratumumab is an anticancer drug that binds to the CD38 protein overexpressed in multiple myeloma cells, leading to immune-mediated apoptosis of the tumour cell. The range of anti-daratumumab antibodies comprises three fully human IgG1 inhibitory antibodies with varying levels of affinity. The antibodies are suitable for use as surrogate positive controls in anti-drug antibody assays, and for the development of pharmacokinetic bridging ELISAs to measure free drug.

Bio-Rad offers a portfolio of recombinant, monoclonal, nonanimal-derived anti-idiotypic antibodies and drug–target complex binders for the development of highly selective and sensitive assays. These critical reagents enable researchers to develop robust methods in a short timescale and produce translatable and reproducible results. The antibodies are generated using the Human Combinatorial Antibody Libraries (HuCAL) and CysDisplay, a proprietary method of phage display, along with guided selection methods to obtain highly targeted reagents.

The company's recombinant production methods result in batch-to-batch consistency, so the anti-daratumumab antibodies should deliver reproducible results over the life cycle of the user's bioanalytical assays. The antibodies are approved for in vitro research purposes and for commercial applications providing in vitro testing services to support preclinical and clinical drug development.

Bio-Rad Laboratories Pty Ltd
www.bio-rad.com

Chiral spectroscopy:
quality control for twisted molecules

It's not easy to be sure that drugs and supplements with twisted (chiral) structures are turning in the correct direction. Now researchers in the US and Brazil have shown that twirling infrared light can probe both the structures of molecular crystals and their twists, confirming that they are safe and effective.

Walking along the supplement aisle, you might notice that some have an L or D in front of the names. This denotes the direction in which the molecule twists, ie, clockwise (D) or anticlockwise (L) — the human body typically only uses one version. Molecules with the wrong twist can be nuisance fillers or cause side effects that can be unpleasant or dangerous. But quality control for twisted molecules is tough, and monitoring the chiral structures of drugs and supplements kept in storage isn't usually done.

"The methods most commonly used at pharmaceutical companies are very sensitive to impurities, but measuring chirality is expensive," said Wonjin Choi, a research fellow at the University of Michigan (U-M) and first author on the study. The method developed by Choi and colleagues can quickly recognise wrong twists and wrong chemical structures in packaged drugs using terahertz radiation, a portion of the infrared part of the spectrum. It has been described in the journal *Nature Photonics*.

"Biomolecules support twisting, long-range vibrations also known as chiral phonons," explained U-M Professor Nicholas Kotov, co-corresponding author on the study. "These vibrations are very sensitive to the structure of molecules and their nanoscale assemblies, creating the fingerprint of a particular chiral structure."

The team was able to measure these phonons in the spectra of twisted terahertz light that passed through tested materials. One of these, L-carnosine, is currently used as a nutritional supplement.

"If the twist of the molecule is wrong, if the twist in the way the molecules pack together is not right, or if different materials were mixed in, all of that could be inferred from the spectra," Prof Kotov said.

Study co-author Professor John Kruger, from Michigan State University, provided bladder stones from dogs, and the team discovered their chiral signature. The researchers thus hope their method could enable rapid diagnostics for pets and perhaps later humans, diagnosing harmful accumulations of twisted molecules in the body including bladder stones, insulin fibrils and amyloid aggregations such as the plaques that appear in Alzheimer's disease.

In addition, the researchers studied insulin as it grew into nanofibres that make it inactive. If the terahertz light technology can be adapted for home health care, it could verify the quality of insulin.

The team also explored how light can influence structures, rather than just measure them. Calculations carried out by co-corresponding author Professor André Farias de Moura, from the Federal University of São Carlos, show that multiple biomolecules vigorously twist and vibrate when terahertz light generates chiral phonons.

"We foresee new roads ahead — for instance, using terahertz waves with tailored polarisation to manipulate large molecular assemblies," Prof de Moura said. "It might replace microwaves in many synthesis applications in which the handedness of the molecules matters."

Based on Prof de Moura's calculations, Prof Kotov and Choi believe that the twisting vibrations of chiral phonons caused by terahertz light may make disease-causing nanofibres more vulnerable to medical interventions. Future work will explore whether that interaction can be used to break them up.

Control software for autosamplers

Scientists who are performing analytical assays, or need to process a lot of samples, are likely to require the use of an autosampler. Cytiva has now announced the launch of its SampLink ver 1.0 control software for the company's ALIAS autosamplers. The software is designed to provide a more user-friendly solution when using ALIAS autosamplers together with ÄKTA lab-scale systems.

Cytiva has added the functionality to enable two-way communication between the ALIAS autosampler and UNICORN software. This should make it easier to synchronise the SampLink and UNICORN methods and avoid sample loss due to the autosampler and ÄKTA flow paths not being aligned during critical parts of the run.

There are two different versions of ALIAS autosamplers. The ALIAS Bio is intended for microscale and analytical applications. ALIAS Bio prep for larger sample volumes is used in preparative protein purification like antibody development and screening.

Global Life Sciences solutions Pty Ltd trading as Cytiva
www.cytivalifesciences.com/en/au

Chromatography and mass spectrometry consumables

Thermo Fisher Scientific has released a collection of caps, vials, inserts, kits, well plates and mats designed to improve analytical performance and sample security for chromatography and mass spectrometry users in routine and research laboratories, across a diverse range of sectors such as pharma, biopharma, clinical, food, environmental and academia.

The Thermo Scientific SureSTART consumables portfolio is compatible with all add-on and chromatography autosamplers, allowing analysts to use the portfolio regardless of the instrument vendor. The collection provides sample security and low compound adsorption, even for challenging, low-level analytes. This should provide laboratories with confidence in their results every time, and reduce the time needed for reviewing background peaks or identifying analytes that have shifted retention times. The range is also said to provide precise and consistent measurements between different vials and different lots.

The consumables are built from high-quality materials in order to meet users' performance requirements. Additionally, the collection is fully compatible with GC, GC-MS, LC and LC-MS analytical instruments and includes three performance levels to help laboratories choose the right product for their experimental needs.

Thermo Fisher Scientific
thermofisher.com

Ultrafast handheld spectrophotometer

The Tip Biosystems Photopette device is an ultrafast, precise handheld fixed wavelength spectrophotometer universally used in the life sciences, environmental surveillance, food and beverage and chemical industries to measure concentrations in liquid samples.

Available exclusively from Banksia Scientific Company, the Photopette personal spectrophotometer is designed to offer the convenience, performance and seamless integration with cloud, web and mobile computing expected from contemporary devices and applications, saving users precious samples and time, whilst still producing precise results.

Other benefits include: direct measurements (no sample transfer); recalibration and maintenance free; small footprint; Bluetooth connectivity; intuitive software; no warm-up time; results within 2 s; and battery powered.

German engineered and easy to use, the device enables users to improve workflow and increase productivity through speed and portability.

Banksia Scientific
www.banksiascientific.com.au

The S-Monovette® is the revolution in blood collection.

The S-Monovette is an innovative enclosed blood collection system that allows the user to draw blood from the patient using the syringe or vacuum method, uniting the advantages of both techniques in a single product.

When used as a syringe, the phlebotomist has full control over the speed at which the blood is drawn into the tube. This is particularly useful for patients with fragile veins, such as the very young or elderly, where the use of the aspiration technique prevents even the most fragile veins from collapsing. When the tube has been filled, the plunger is simply snapped off to leave a primary sample tube which can be centrifuged and is compatible with all major analysers.

The S-Monovette can also be used as an evacuated tube by drawing the plunger fully down and snapping it off immediately prior to blood collection. This creates a fresh vacuum and ensures a precise filling volume, ensuring a correct dilution ratio.

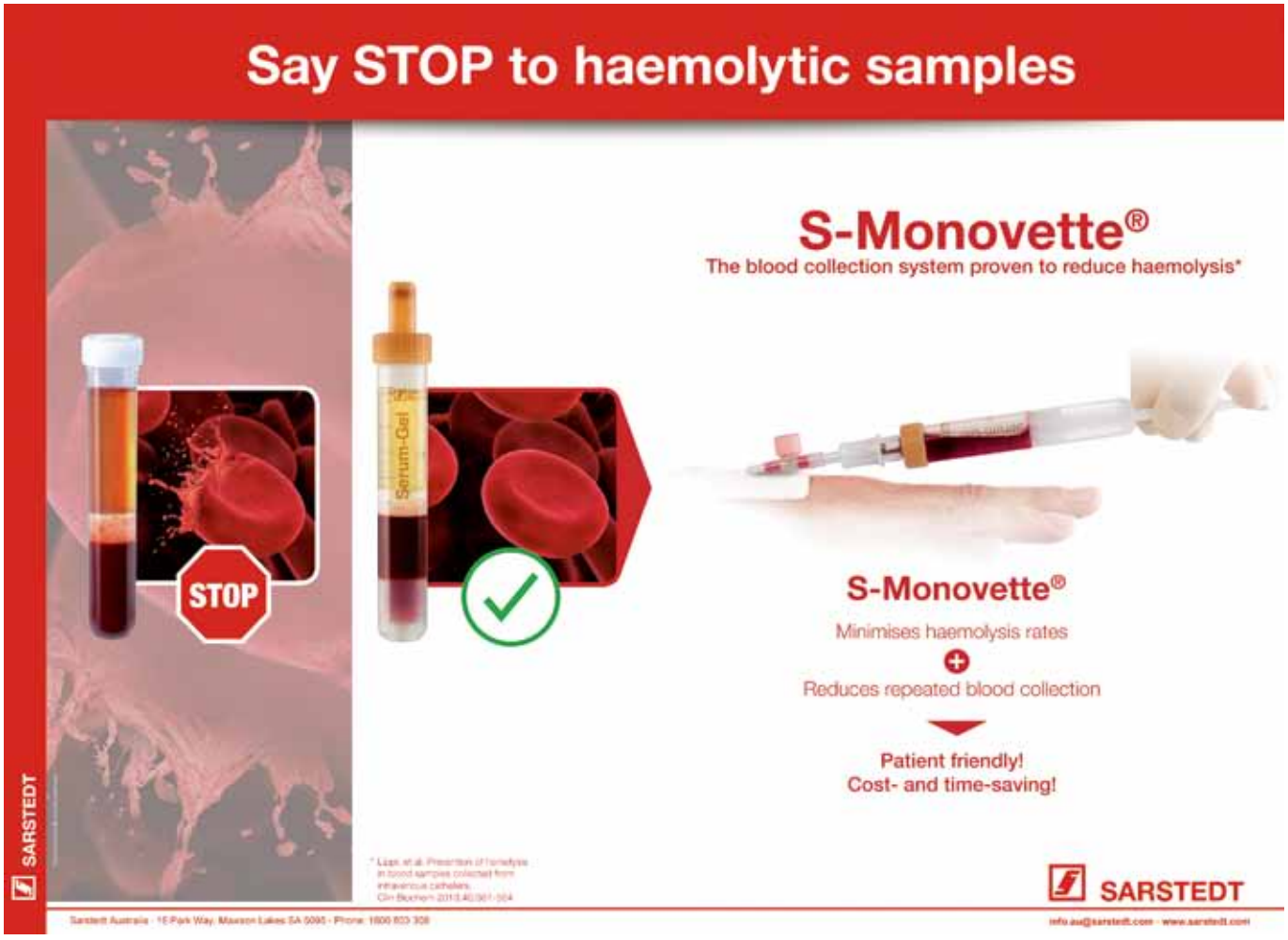
The reduced vacuum pressure in the S-Monovette drastically reduces the rate of haemolysis and vein collapse, meaning increased sample quality and reduced costs associated with repeat collections. Furthermore, unlike pre-evacuated tubes, the S-Monovette does not have to hold a vacuum for many months after manufacture, which allows the membrane stopper to be thinner and more easily penetrated by the needle sheath. This minimises the movement of the needle in the vein when attaching the tube, ensuring optimum patient comfort.

The S-Monovette needle is ready to use so that there is no need for assembly to a holder. The needle is of a compact, low profile design, which reduces the chance of haematoma by allowing for a reduced angle of puncture and eliminates the possibility of needle stick injury caused by assembly of the needle and holder. The compact design also results in approximately one sixth of the sharps volume caused by using a pre-evacuated system, giving significant cost savings.

If you would like a visit from one of our Sales Representatives to demonstrate this system, please contact us on **toll free 1800 803 308**.

SARSTEDT

Sarstedt Australia
www.sarstedt.com



Collaboration between Bürkert and Bovogen improves BSA yield

Established in 2001 in Melbourne, Bovogen Biologicals commenced manufacturing bovine serum albumin (BSA) on a commercial scale in 2003. In addition to manufacturing high-quality BSA and other novel proteins, Bovogen has grown to become a major supplier of sterile filtered specialty animal serums.

An acquisition by ANZCO Foods (New Zealand) in 2016 created new opportunities for Bovogen. It enabled the company access to large volumes and consistent supply of high-quality controlled and tested raw materials (serum and plasma), coupled with vertically integrated real-time traceability of materials.

BSA is the major protein species found in bovine blood plasma and has applications in life science disciplines such as cell culture, in vitro diagnostics, human and veterinary pharmaceutical manufacture, vaccine development, viral transfer medium, molecular biology, serology and general research. The largest-selling protein manufactured by Bovogen is its premium BSA, Bovostar, which is used worldwide for these areas of science.

Centrifuges a central part of BSA extraction

Central to the production of BSA is the separation of the blood plasma using centrifuges. Centrifugation is a process used to separate the particles or the concentrated material, such as the cell, subcellular organelle, viruses and large molecules (including proteins and nucleic acids), to obtain pure samples of the entire particle or material. Bovogen uses two centrifuges to separate the plasma, with one fraction then processed further to purify the protein.

In 2018, Bürkert supplied and commissioned a control system with PID loop control to manage the inlet flow to the centrifuges. The application included a standalone PLC/HMI control system for two centrifuges, including hygienic modulating Bürkert 2380 bellow control valves with ELEMENT 8693 process controllers in conjunction with 8056 sanitary magnetic flowmeters for closed-loop process control.

The 2/2-way 2380 bellow control valve is a pneumatically operated process valve with a single-acting diaphragm actuator. A PTFE bellow ensures the separation between medium and actuator, and the design of the media space allows the valve to be used under hygienic or aggressive conditions. The compact, lightweight and CIP/SIP-capable valve is useful for demanding control tasks with low-flow rates, for which diaphragm valves are not suitable.

This initial control system was built to improve the monitoring and control over process flow rates and speed of production in support of Bovogen seeking improvements in yield.

"There has been an ever-increasing demand for high-quality proteins to support the sciences they are used for," said Matthew Bartlett, General Manager at Bovogen. "Bürkert's support and devices were key to improving the Bovogen centrifuge application process — with the right equipment and smart automation controls — enabling ongoing production while ensuring a consistently high quality of product."

Avoiding product loss by preventing leakage

At the output of the centrifuges, a needle valve was being used to match the output flow rate to the input flow rate, to manage any backpressure that may occur. Fluctuations in the inlet flow rate can lead to changes in backpressure resulting in unwanted bubbles, and sometimes leakage from the centrifuge.

In order to limit the likelihood of backpressure leaks, Bovogen operators had to continually monitor the pressure and adjust the outlet valve. Leakage has been known to cause product loss of around 6–8%.

In 2021, Bürkert was engaged to provide automation of the outlet flow rate, so that the manual intervention of operators would not be necessary to prevent product leakage. Adding control of the outlet pressure and flow, synchronised with inlet flow variations, allows the overall pressure of the system to be regulated, eliminating leaks.

The backpressure system provided by Bürkert again utilised closed-loop process control with the 2380 hygienic bellow valves with ELEMENT 8693 process controllers in conjunction with 8325 sanitary pressure sensors. The application of automated control over both inlet and outlet flow rate successfully achieved Bovogen's objective of reducing protein loss and increasing batch yield of BSA.

"The backpressure system is working flawlessly and my team is very pleased with the result," said Rowan Whittaker, Production Manager. As a result of the new closed-loop centrifuge flow control, Bovogen is now successfully reducing waste, while improving production efficiency and yield.

Burkert Fluid Control Systems
www.burkert.com.au

IP66/IP69K stainless steel panel PCs

Aplex's ViTAM-9B series stainless steel panel PCs are designed for a wide variety of industrial applications where sanitation is of serious concern, including food and beverage manufacturing. The series offers a highly protective panel solution, beyond the basic standard, by achieving IP66- and IP69K-certified protection with M12 connectors.

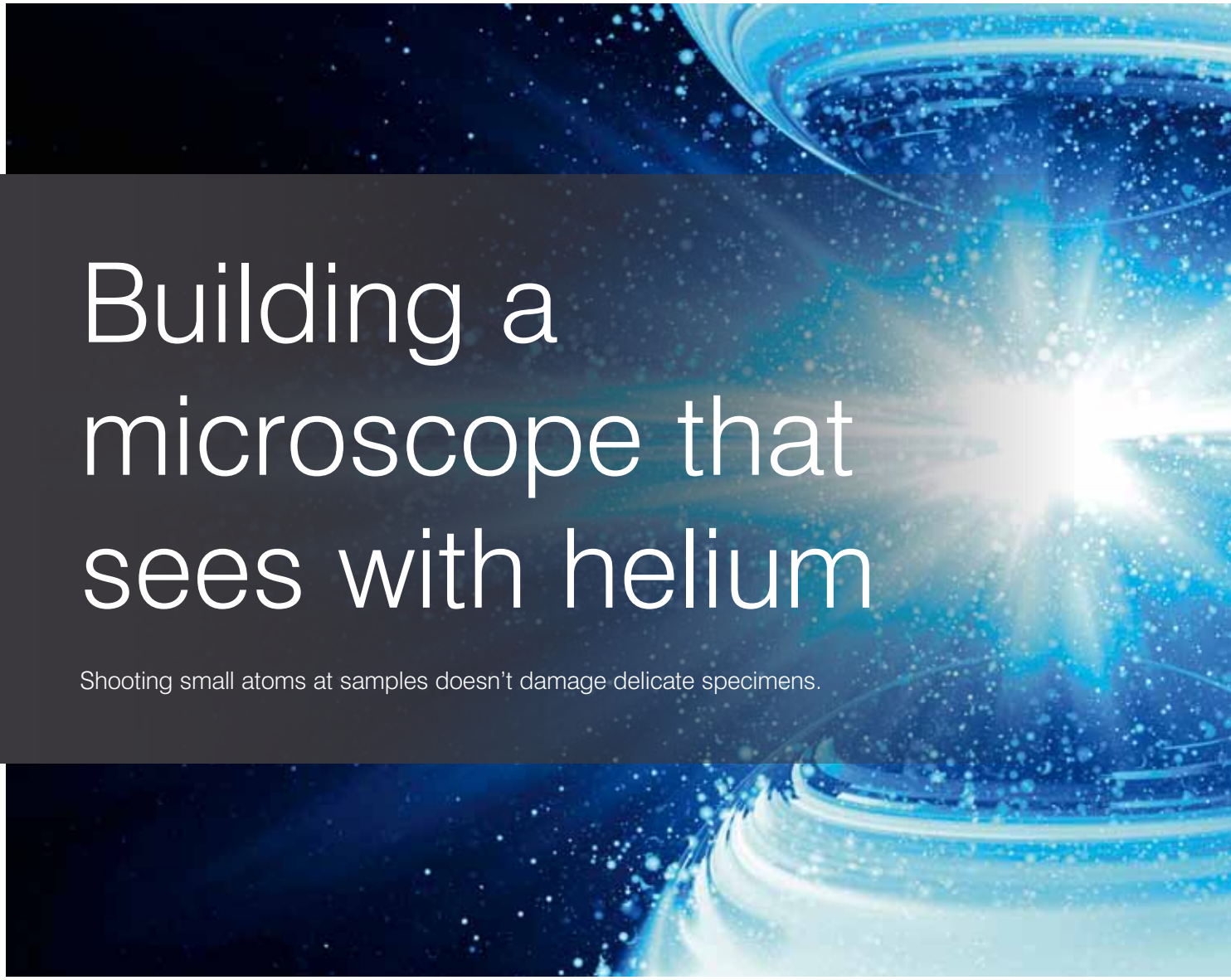
The 304 (or optional 316) stainless steel chassis of the series makes it suitable for the food and beverage manufacturing industry due to its slim design, high corrosion resistance and germ resistance, helping to prevent bacterial contamination. Stainless steel should also make the chassis easy to clean (capable of withstanding high-pressure cleaning), increase the life cycle of the chassis due to its rugged nature and help to lower the cost of maintenance.

To assist with cleaning of the display, the series includes a touch on/off button that allows the touch screen to be temporarily disabled during the cleaning process. This allows the display to be hygienically wiped down without having to shut down any process control applications.

The fanless design of the series makes it easy to maintain the equipment and further helps to prevent the accumulation of dust. The optional PCT multi-touch screen with 7H anti-scratch surface helps to improve usability, while also providing the screen with tough protection. Optional high-brightness features help to make the screen visible in increased sunlight areas.

The series offers a range of versatile mounting solutions — including floor stands, swing arms, Yoke mounts and VESA mounts — making it suitable for most applications. Other features include DC 9–36 V wide range power input; 15–24″ screen sizes available; 8th Gen Intel Core i3/i5 processor; up to 64 GB DDR4 RAM; and a wide temperature range of 0 to 50°C or -20 to +60°C (optional upgrade).

Interworld Electronics and Computer Industries
www.ieci.com.au



Building a microscope that sees with helium

Shooting small atoms at samples doesn't damage delicate specimens.

Sometimes, the 'light' we need to look at something can damage it. That's the inspiration for a new class of microscope being developed at the University of Cambridge, England, and the University of Newcastle, in Australia.

Scientists already have a plethora of imaging methods. Optical microscopes, which focus light through lenses, can resolve features down to about 0.3 µm. Scanning electron microscopes use an electron beam to reach a resolution of about 1 nm or better. The highest-resolution microscopes are scanning tunnelling microscopes, in which a sharp tip passes just above the surface of a sample and electrons use quantum mechanics to 'tunnel' from the tip to the sample, generating current and a computer image. These microscopes can see individual atoms, a fraction of a nanometre across.

But all of these methods have drawbacks — most important, light and electrons can damage a sample. Certain materials, such as ice and wax, can melt. Biological samples, such as skin specimens, can suffer structural damage. Electrons pummel bacteria biofilms and also organic electronics like photovoltaics and transistors.

That's why the labs of Andrew Jardine, a professor of experimental physics at Cambridge, and Paul Dastoor, a professor of physics at Newcastle, are developing a scanning helium microscope, or SHeM. Along with their colleagues from the two universities and several international collaborators, including those from Professor Bodil Holst's group in Bergin, Norway, they have invented a new microscope that takes images using neutral helium atoms instead of light or electrons.

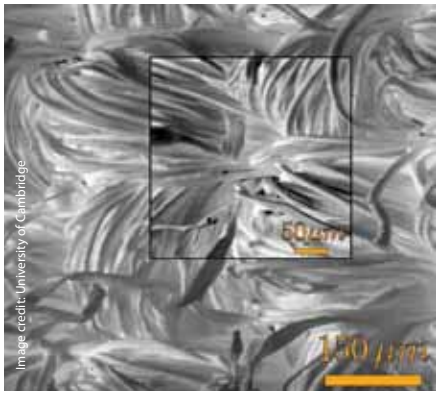
Electron microscopes also require insulating samples with a conductive layer such as gold, which can obscure the material underneath. The photons used in light microscopes can penetrate beneath the surface of a sample before reflecting, clouding the image of the surface structure. Helium avoids these challenges. The teams have already used the SHeM to image sensitive biological samples like bio-films and insulators such as PPE fabric.

Helium atoms carry much less energy than photons or electrons. They are also electrically neutral and chemically inert, so in addition to not battering samples with energy, they won't interact with them electrically or chemically.

Unique instrumentation

This new microscope is making use of a very old technology: the pinhole. More than 2000 years ago, scholars including Aristotle understood what's called the camera obscura, in which tiny holes act as focusing devices. Researchers are now using 'pinholes' much smaller than tips of pins to narrow rays of atoms, creating images of objects much too small to see with the naked eye.

As well as using pinholes, the Cambridge lab has applied broad beams of neutral helium to study the fundamental structure of and dynamics on surfaces for many years. They aim a wide beam of helium atoms, a few millimetres across, at a sample. The angular distribution and speed changes of the scattered atoms enable them to decipher the positions and movement of the surface atoms. But for decades, researchers had hoped to directly image fine surface structures with helium atoms, including for a major European project.



Scanning helium microscope image of fabric for personal protective equipment (PPE).

According to quantum mechanics, matter behaves as a wave just like light does, and helium atoms have a shorter wavelength than optical photons do, so helium microscopes have a better theoretical resolution. "Everybody wanted to go straight for the full potential of the technique," said Sam Lambrick, a PhD student in Jardine's lab. "People were trying to build a complicated machine that gets you there immediately."

The problem is that you can't focus helium beams using optical lenses, because the atoms won't pass through, and you can't focus them using electric or magnetic fields, because the atoms aren't charged.

One option involves building an atom mirror, a curved mirror that precisely deflects atoms. But building one with sufficient smoothness on the atomic scale has turned out to be phenomenally hard, so Jardine's lab took an easier route. "In the end," Lambrick said, "we switched to this pinhole approach. We made that work."

The microscope starts with a high-pressure cylinder of helium attached to a nozzle. Atoms expand supersonically into a vacuum, where they approach a skimmer, a cone with a small hole. Only helium travelling in a straight beam from the nozzle makes it through the skimmer. The beam then passes through a pinhole a fraction of a micrometre across. After the pinhole, the atoms hit the sample, attached to a movable platform, at a 45° angle.

When the helium atoms hit the sample, they are repelled by electrons in the surface and scatter in a range of directions. Atoms that leave in a particular range of directions are collected and counted in the detector, which is used to give the brightness of an individual pixel. The sample is then moved, to scan the atom beam over the surface, which builds up the image pixel by pixel.

One of the trickiest bits of equipment to construct, Jardine said, was the detector. They needed a type of mass spectrometer. A mass spectrometer separates particles according to their mass, typically by bending their paths in a magnetic field and directing those with a certain mass — four atomic mass units, in the case of helium — to hit the counter.

But commercial devices would detect only one in a million helium atoms. The first stage in a mass spectrometer is to ionise the atoms, by 'knocking off' an electron using another, fast-moving, electron. However, helium is very difficult to ionise. The Cambridge detector is specially made for helium, so it removes the electrons much more efficiently. This device detects one in a hundred entering helium atoms instead of one in a million.

"It's home-built," Jardine said, "so it's a little bit temperamental, but we are working on a new and much more stable version at the moment."

Trace the atom

To control their custom kit, the Cambridge team wrote custom code in MATLAB; Lambrick noted, "Some of the equipment that we use has provided drivers that work well with MATLAB." The code tells the microscope to move the stage 5 µm to the left, or to record the stage position, or record the detector signal. The MATLAB language also provides lots of flexibility.

"When you're doing research," Jardine said, "you don't want to be restricted to the way that somebody else has designed a program to run the machine." He said MATLAB's software customisation offers a research approach.

"It's a different way of doing it," he said. "You don't get stuck in this loop where somebody 10 years ago thought you'd want to do only these experiments, and therefore you can do only these experiments." The flexibility allows the team to, say, combine multiple measurements, or use the same software environment for both debugging and normal operations.

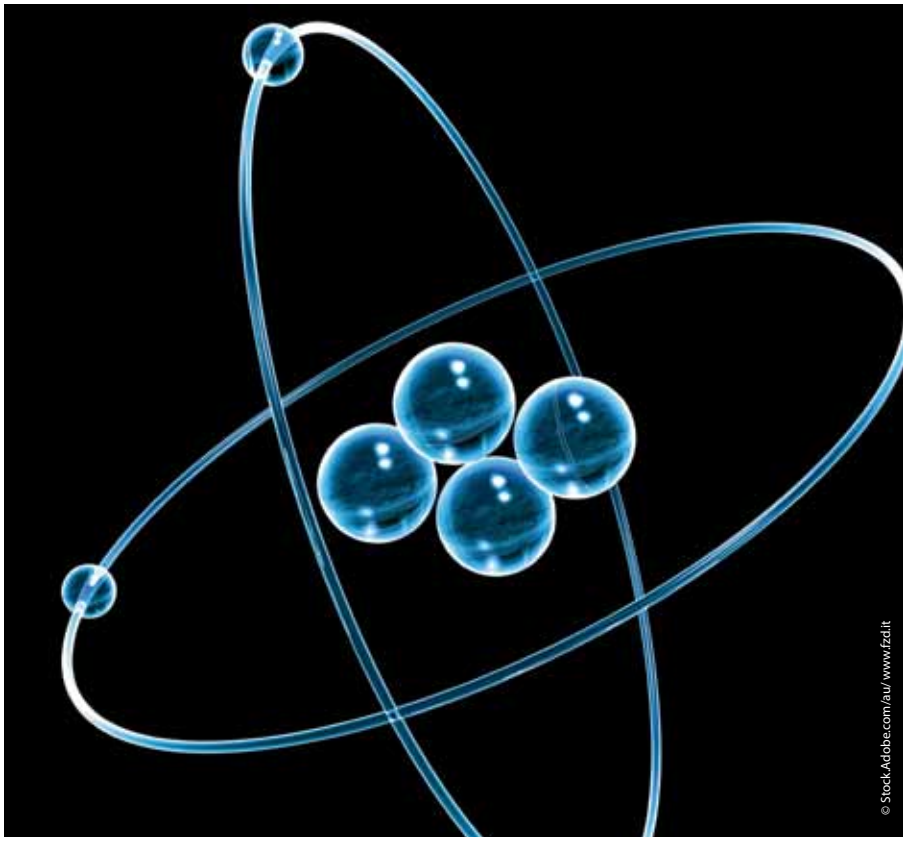
The flexibility also allows them to build up layers of commands into longer scripts: perform a series of actions for one pixel, then move the platform and perform those actions on the next pixel. Lambrick uses the App Designer in MATLAB to make the most popular scripts accessible to anyone in the lab through a user interface. He can create a window, then drag buttons and boxes into place and connect them to scripts.

The team also uses MATLAB to simulate the machine and better understand its design and operation. Lambrick created a ray-tracing framework, allowing them to send virtual atoms through the virtual microscope, then change the microscope or the sample and rerun the simulation. For computationally heavy aspects, he can write code in C and use MEX functions in MATLAB to call upon those bits of C code.

Ray-tracing has helped them interpret what they see with the real microscope. Lambrick noted, "Many structures can be really complicated and can have deep pores into them. We wanted to understand better how these deep features will affect the contrast."

In one experiment, they looked at a series of precisely machined trenches in a sample. As the trenches grew deeper, they fell into 'shadows' and looked darker — until they were deeper than they were wide and became light again. After that point, they all looked the same shade of light grey.

"When we first looked at the image, it didn't really make sense," Lambrick said. Then they ran a ray-tracing model. They found that in the deep trenches, helium atoms bounced around a lot, and eventually many of them escaped toward the detector, creating brightness. The team could then look at porous scaffolds that biomedical researchers use to grow tissue samples and know what they were looking at. What appeared to be bright spots were actually deep holes.



Lambrick created a ray-tracing framework, allowing them to send virtual atoms through the virtual microscope, then change the microscope or the sample and rerun the simulation.

The team also uses simulations to improve the microscope's design. They can draw parts in a CAD program, import the files into MATLAB, and test them. If all works as planned, they'll send the files to the workshop. Otherwise, they'll refine and repeat.

One upgrade they're currently exploring is the replacement of the pinhole with what's called a zone plate. Instead of a single hole, it's a series of concentric circular slits forming a bullseye pattern. The slits slightly diffract the atoms so they approach a focal point, which the researchers target right on the sample. Zone plates could improve resolution from 1 µm to maybe 10 nm, a 100-fold improvement. The team is also building a version of the SHeM with four detectors instead of one, enabling 3D imaging.

So far, they've completed three microscopes (two in Cambridge and one in Newcastle). Labs in Bergin, Norway; Hyderabad, India; and Portland, Oregon, have built similar machines. Jardine hopes to commercialise the device for wider use and some researchers are already using it to make discoveries. The Newcastle team looked at tiny structures on the surfaces of leaves and shark skin to inform taxonomies.

Jardine said more findings will come, but they still have much to learn about the tool they're building. "There's lots of interesting science and engineering that you can do with this," he said.

MathWorks Australia
au.mathworks.com

Bronkhorst flow metering for low flows

What do micro reactors, catalyst research and additive dosing have in common? They all require handling low-liquid flows.

In control and measurement, 'low' and 'high' flows are often arbitrary. At Bronkhorst, 'low flow' is our business.

For us, 'low flow' is less than 100 g/h and ultralow flows are below 5 g/h (100 g/h is equivalent to about 2000 water droplets/hour, while 100 drops is around 5 grams).

Where do we need accurate instruments for low liquid flows up to 100 g/h?

- Chemical catalysts: Low liquid flows of hydrocarbon compounds, at high pressure, are dosed at a stable flow.
- Biotechnology and pharmaceutical: Labs-on-a-chip and other microfluidic devices significantly reduce chemical use and experimental time.
- Odorising of gases: Injecting small but continuous amounts of liquid additive causes 'warning' odours.
- Where performance of an experiment is determined by measuring the correct amounts of liquid.

What is different about liquid flows of less than 100 g/h?

Laboratory-based low-flow applications involve phenomena not observed in, or not relevant to, larger flows. Due to the amount of liquid transferred, they are sensitive to even the tiniest disturbances in process or ambient conditions. Key is minimising the influence of external conditions on flow stability.

For example, a small leak of gases or liquids within the process can considerably influence the intended liquid flow; particles or contamination cause obstructions that can change the flow in an undesired way; and inconsistent pressures, excessive pump stroke pulsations and pressurised gases in a liquid all lead to instability.

Bronkhorst excel at optimising complex low-flow applications. An in-depth knowledge of fluid characteristics and system components in a wide range of circumstances ensures best practice.

Measurement options also help. Bronkhorst's portfolio includes thermal-based, ultrasonic and Coriolis flow meters and controllers. All are suitable for low- and ultralow-flow applications. To reflect, a flow meter consists of a sensor that measures the medium's flow rate; a controller combines that sensor with a control valve that controls the medium's flow rate.

Reiterating, optimal performance requires much more than just an excellent flow meter/controller. By eliminating leaks and dissolved gases, keeping tubing volumes small, the flow controllers can generate a stable flow.

The different working principles offers choice. With thermal-based mass flow devices, a constant temperature difference is created along the flow tube. The energy needed to maintain that temperature difference while liquid flows is proportional to the mass flow rate.

For Coriolis flow meters, flow is through a thin vibrating tube, causing it to twist. The change in deflection is a measure of the mass flow. Interestingly, the change in vibration frequency of the flow tube gives the density of the product/medium.

When to choose a Coriolis flow meter/controller?

Most applications! Specifically, where absolute accuracy and stability are essential; where thermal sensitivity issues exist; where the product density needs to be monitored. Coriolis meters are useful on liquids with unknown properties. That said, Coriolis meters might need installation measures to reduce shock and vibrations.

When to choose a thermal flow meter/controller?

The economical choice. Specifically, where the fluids are stable (constant liquid density, viscosity, thermal conductivity and heat capacity); reproducibility is excellent; they generally have small pressure drop, which can help where there might be dissolved gas, helping to keep the flow stable.

Tips 'n' tricks

The following can be expanded but might help in respect to low liquid flows:

- **Tip 1:** Choose a flow meter that suits the process and conditions.
- **Tip 2:** Ensure a stable (inlet) pressure.
- **Tip 3:** Minimise the containment or dissolution of gas in the medium.
- **Tip 4:** Use piezo control valves on low flows.
- **Tip 5:** Minimise volumes between the flow device and process.
- **Tip 6:** Purge well before operation.

AMS

AMS Instrumentation & Calibration Pty Ltd
www.ams-ic.com.au

Multifunctional mass flow meters/controllers

Bronkhorst's FLEXI-FLOW compact thermal mass flow meters/controllers, for flow ranges up to 20 ln/min, are designed to be 35% smaller than traditional instruments. Combining the advantages of a through-chip sensor with bypass technology, the instruments feature stable flow control but also fast control, with settling times smaller than 150 ms.

The instruments have integrated temperature and pressure sensors and an onboard gas database to enable high accuracy, even at varying process conditions. They are adaptable to many applications through their wide dynamic flow ranges (up to 1:1000). The temperature and pressure signals may provide the user with information about the actual process conditions. The product is therefore more than just a flow meter or controller — it is a multiparameter measurement/control device.

The unit is available in two preconfigured models, as a built-to-order version or as a customised, multichannel solution, each including free and easy software tools for configuration, diagnostics and predictive maintenance. For easy set-up and monitoring of the instruments and the user's process, Bronkhorst introduces a USB-C port, optional Bluetooth communication and NAMUR status indication by means of coloured LEDs and digital output parameters.

AMS Instrumentation & Calibration Pty Ltd
www.ams-ic.com.au

Ultracentrifuges

Eppendorf is going beyond the benchtop with its line of ultracentrifuges and micro-ultracentrifuges. The floor-standing CP-NX series provides a comprehensive rotor portfolio for vessels up to 230 mL, while the CS-NX series offers top speeds of 1,050,000 x g (150,000 rpm) in either a floor-standing or benchtop model. From nucleic acids to proteins to vesicles and viruses, the company's expanded portfolio now supports all sample separation needs.

With advanced features and innovative technology, the ultracentrifuges and micro-ultracentrifuges are designed to maximise performance and safety while providing simple, user-friendly operation. The Automatic Rotor Life Management System (RLM) digitally tracks rotor run times, eliminating the need for manual logs and extending rotor lifetime (CP-NX series). The self-locking rotor system meanwhile enables quick and easy rotor exchange in seconds.

High imbalance tolerance of up to 5 mm allows for visual balancing of samples by eye, so there is no scale required (except for rotors P21A2, S140AT, S110AT, S80AT3 and S50A). The intuitive touchscreen interface meanwhile features user management and documentation functions for enhanced security as well as support for GxP/GLP compliance.

To help maintain high performance and maximum safety of the user's instruments, Eppendorf is committed to providing sincere and reliable services and tools. This includes a comprehensive range of carefully designed service solutions performed by the company's dedicated Technical Service teams worldwide.

Eppendorf South Pacific Pty Ltd
www.eppendorf.com.au

Personal microplate reader

As technology advances, scientific instruments are evolving form bulky and complicated equipment to compact and simple devices. With this in mind, Enzo Life Sciences presents its revolutionised, personalised plate reader.

The Absorbance 96 Plate Reader is a personal, 96-well format microplate reader that can be used for a variety of applications including ELISAs, protein quantification assays, cell-based assays and more. Despite its small stature, it is designed to deliver precise and correct results. It features a USB connection for power supply and access to user-control software. Together with the Byonoy proprietary software, it is suitable for a variety of applications, extending from ELISA to protein and cell-based assays.

The Absorbance 96 Plate Reader is designed to run everyday assays with ease and speed. The four standard filters — 405, 450, 492 and 620 nm — allow for a wide variety of ELISAs such as PNPP, ABTS, OPD and TMB. Other filter combinations for protein (Bradford or BCA), cell-based (MTT, XTT) or cell density assays can also be provided.

The product contains 96 individual detection units. Without the need to scan across multiple wells, the Absorbance 96 has no moving parts. In combination with long-life LEDs, the solid-state design provides a maintenance-free user experience for high-quality results.

United Bioresearch Products Pty Ltd
www.unitedbioresearch.com.au

Transferring customised media for COVID diagnostic tests

A Brazilian specialist culture media manufacturer for microbiological diagnosis, bioBoaVista, has developed a viral transport medium (VTM) for more efficient nasal tests for the diagnosis of COVID-19. The novel medium stabilises samples for significantly longer — up to 48 hours at room temperature and up to five days between 2 and 8°C, compared to standard saline samples that last only 12 hours.

The VTM is prepared with a cell culture medium, supplemented with proteins for viral stabilisation and the addition of antibiotics and antifungals to inhibit the growth of other microorganisms present in the nasal mucosa and the throat. This exclusive formulation prevents any interference in the stability of the virus through competition and contamination by other existing pathogens. Samples are collected using flexible plastic swabs that break inside the tube of transport, avoiding splashes and potential contamination. This process is designed to protect the quality of the sample for a longer period than traditional means, enabling more efficient transport and processing.

bioBoaVista needed to efficiently fill its tubes up to the required 3 mL level, so the company chose the Flexicon PF7 benchtop filling machine from Watson-Marlow Fluid Technology Group (WMFTG) for its low-shear, gentle pumping action. This is designed to ensure the valuable viral transport medium is transferred undamaged with high accuracy and precision.

With current batch sizes of 2 million units, bioBoaVista plans to increase its production to four times this and as such has scaled out capacity with additional PF7 machines. By choosing Flexicon, the company also has the option to scale up further while retaining confidence in the technology. The FF30 is also available to semi-automate the filling and capping process.

Precise, aseptic filling

bioBoaVista required a compact, efficient filling mechanism to fill its specialist media to the required level into the diagnostic test tubes. With precision filling from as low as 0.2 mL and repeatable filling accuracies of better than 0.5%, the PF7 enables bioBoaVista to efficiently fill its tubes to the required level without costly overfilling.

Flexicon products are suitable for the biotechnology and diagnostic industries, providing the required aseptic guarantees necessary for contamination-free processes. The PF7 comes with a five-year warranty as well as IQ/OQ documentation available on request to assist with process validation. It is designed to work with single-use fluid paths and connects to a range of balances and printers for error-free calibration to help compliance with GMP and regulatory demands.

The PF7 is simple to operate, with a powerful user interface to reduce the risk of errors. Its clear and intuitive colour display and large keypad facilitate ease of use when gowned up in cleanroom environments. This enabled bioBoaVista to fill its tubes while maintaining sterility to meet regulatory requirements.

Scale-out to scale-up

The global challenge of the COVID-19 pandemic requires widespread testing to diagnose those with the virus and to limit the spread. The availability of reliable tests is therefore essential, and organisations worldwide have been developing tests and expanding their production to meet this need. bioBoaVista's test media maintains sample stability for significantly longer, allowing samples to be taken in isolated areas and shipped back to testing facilities without degradation or contamination.

In order to rapidly scale up the number of tests bioBoaVista produces, it has increased its PF7 filling capacity to seven machines that will run in parallel. This trend towards increasing capacity by scaling out identical production lines is becoming more common with the growth of single-use technologies, a valuable development that enables rapid scale-up when time is scarce.

The Flexicon PF7 has ensured that bioBoaVista can efficiently fill its viral transport media to precise volumes while maintaining sterility. Its ease of use has led the company to significantly expand its production capabilities with additional machines that will increase the number of testing kits produced by four times and facilitate essential widespread testing.

Watson-Marlow Fluid Technology Group
www.wmftg.com.au

In vivo imaging and DXA analysis of lab animals

The iNSiGHT is a fully shielded DXA (DEXA, dual energy X-ray absorptiometry) cabinet system, designed by OsteoSys specifically for use on preclinical small animal models such as mice and rats. The DXA technology provides quantification of body composition, such as bone mineral density (BMD), bone mineral content (BMC), bone/tissue area, fat % and fat(g), lean(g) at each ROI and total weight by fast scan.

The system provides high-resolution images (X-ray DR image, bone-enhanced image, body composition image) with multiple ROIs with a flat panel detector, said to enable accuracy and precision. It provides researchers with a state-of-the-art tool to study body composition non-invasively, with low-dose radiation, and is suitable for longitudinal studies on the same animals. Due to its fast scan time of 25 s, a simple treatment with anesthesia is all that is required with no sacrifice of animal.

iNSiGHT presents a DXA image with high resolution of 100 μm. DR image and colour mapping for lean and fat distribution is optimised for visual analysis and assessment. As a pivotal tool enabling a genuine longitudinal study, it is equipped with multiple ROI settings and history analysis.

A transparent window and wide imaging area of 16.5 x 25.5 cm provide a secure measuring environment and process for in vivo imaging and DXA analysis. A magnification shelf supports high-end imaging analysis up to 4x geometric magnification.

SciTech Pty Ltd
www.scitech.com.au

HEK cells vs CHO cells in recombinant antibody production

What's the better choice?

The demand for therapeutic proteins is constantly growing and gives further reason for continuing the development of high-quality protein production technologies. Mammalian cell lines are the preferred choice to create recombinant proteins, in particular Chinese hamster ovary (CHO) cells and human embryonic kidney (HEK or HEK293) cells.

However, with the higher demand also comes a higher confusion of which cell line to pick for one's own studies. HEK cells are known to be very popular due to their easy handling and use for protein production, while CHO cells are the most used mammalian production cell line within the biopharmaceutical industry. Due to the many possibilities as well as advantages and disadvantages, it can be quite troubling to decide which cells would serve specific research the best. This article is designed to help scientists make the right choice.

HEK: common host for transient expression in R&D labs

HEK cells are popular protein expression hosts among researchers due to their fast transfectability and protein production. Adding to that, HEK cells are easy to reproduce and to maintain and are suitable for various transfection methods. They are also known to be a reliable base for the translation and processing of proteins and can therefore be used for many experiments. As Dr Desmond Schofield, Director of Business Development at evitria, explained:

"HEK cells are a well-established and commonly used host for transient expression in R&D labs. They are easy to transiently transfect using a variety of different and low-cost methods, and produce fully human glycosylation patterns. Their transfectability is the main reason for their widespread use and popularity."

However, HEK cells are rarely used beyond research settings, due to several limitations. One of the biggest obstacles a researcher could face when using HEK cells is that they are difficult to grow in large-scale, serum-free cultures. They form clumps that hinder nutrient transfer and growth, and cause heterogeneity in the culture process. Furthermore, these clumps reduce the efficiency of downstream processing and purification.

CHO cells: the workhorse of the biopharma industry

CHO cells are the workhorse of the biopharma industry — over 70% of biopharmaceuticals, and almost all antibodies, are produced within this cell line. A review by Dumont et al found that only five FDA-approved biotherapeutics are produced within HEK, and 50 with CHO (as of 2016).

CHO cells are robust hosts that grow well in suspension culture, can easily be adapted to serum-free media, and can produce and secrete recombinant antibodies in the multi-gram scale. As they are hamster-derived cells, they are less susceptible to contamination by human viruses, but still perform human-compatible glycosylation. They do lack α[2-6] sialyltransferase α[1-3/4] fucosyltransferases, and they produce glycans that are not expressed in humans, namely α-gal and NGNA. However, the glycosylation modifications from these changes are rarely required for the function of a given product, and the additional glycans only occur

at very low (<2%) levels that can be screened out from the host in later stages.

"CHO cells are difficult to transiently transfect — there are few CROs that offer this service, fewer still with their own IP-free cell line, and none with the experience of evitria," Dr Schofield said.

CHO cells are the go-to cell line for clinical and commercial production of therapeutic antibodies and proteins. Their production processes are well established and embedded at all major biopharma and CDMO companies, and have been repeatedly approved by regulatory authorities. Therefore, using CHO for a therapeutic antibody or protein is more an inevitability than a choice.

However, due to the difficulties in using transient CHO, biopharma research teams often use in-house transient HEK production for screening and development purposes, then switch to CHO after lead candidates have been selected and a stable cell line is required. This introduces risk into the commercialisation process, as differences in the post translational and glycosylation machinery can change product activity. Developing a stable CHO cell line alone requires an investment of >€1 million, and this comes on top of the time and financial investment of early discovery and development work.

Conclusion: CHO is the way to go

The lesson is clear: using a transient CHO service provider to supply material for early-stage development work significantly de-risks the commercialisation process whilst minimising effort for any in-house scientists.

Diagnostic companies can also benefit by using transient CHO to generate recombinant antibodies for their assays. The improved scalability and robustness of CHO cells allows large-scale cultures to be grown and processed, delivering >10 g quantities for commercial, population-scale diagnostics. By using a transient process, this can be accomplished without a significant upfront investment and under short timelines, as no stable cell line is required.

"At evitria this only takes a few weeks for all scales," Dr Schofield said. "Our tightly controlled, transient process was built and optimised for therapeutic applications, where generating material with the same activity and quality, regardless of batch size or time between productions, is essential."

This robust process is then perfect for supporting the development and commercialisation of a diagnostic, where identical performance is needed at both the 1 mg and 10+ g scales.

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evitria
https://www.evitria.com/

Adjustable tip spacing pipette

How can scientists save precious time when pipetting samples from 1.5 mL microcentrifuge tubes to a 96-well plate or from a 96-well plate to a 384-well plate? Eppendorf's Research plus Move It 4.5 mm adjustable tip spacing pipette can do just that.

The adjustable tip spacing pipette has a piston cylinder (no tubing) system for fast and easy tip spacing adjustment. Tip distance between source and destination can be easily adjusted and locked with the format limiter, and once set allow users to quickly transfer samples between the two formats with a simple turn of the adjustment knob.

The tubeless design is unique to Eppendorf, the company states, and said to offer users the following advantages: fewer moving parts in the pipette require less maintenance; no cable tangling or leaks commonly associated with tube systems; fully autoclavable for user and sample safety; lack of heat transfer to the air cushion from motor or hand for high precision and reproducibility; and a fully rotatable (360°) pipette head to easily change the pipette orientation between labware formats and read settings.

The Research plus Move It 4.5 mm pipette is supported by the Eppendorf PhysioCare Concept and ergonomically designed to minimise physical tension for comfortable handling. It is available in eight and 12 channels, and a volume range of 1–20 and 5–100 μL.

Eppendorf South Pacific Pty Ltd
www.eppendorf.com.au

Screening of nanomedicine formulations

Nanomedicines are believed to represent the next era in drug innovation, with improved performance, reduced side effects and new treatment strategies for otherwise 'undruggable' targets like personalised medicine. Consisting of active pharmaceutical ingredients (API) such as small molecules or nucleic acids, nanomedicines are packaged into nano-sized carriers like lipids and polymers that are designed to protect the cargo, enhance solubility and control distribution and targeted release.

Screening active ingredients, excipients and formulation conditions are important in the discovery and early development stages. Traditional methods used to develop nanomedicines can present several challenges. Ingredients can be costly or in limited supply, while the final product can lack consistency, have low throughput, be a slow and laborious process and be difficult to scale. The NanoAssemblr series from Precision NanoSystems is enabling drug innovators to overcome these and many other challenges by making purpose-designed manufacturing technology to support all stages of nanomedicine development.

The NanoAssemblr Spark offers the ability to formulate small-scale uniform particles using microlitre volumes quickly and reproducibly, with near complete sample recovery. Requiring little or no training, users can simply add starting materials into wells, push a button and pipette completed formulations in less than 10 s, allowing hundreds of formulations to be made in hours. Electronic control minimises batch-to-batch and user variability. Plus, formulations can be made on demand in a sterile hood for immediate cell culture application, making the Spark suitable for screening formulations that use scarce or expensive APIs or excipients.

Precision NanoSystems' GenVoy-ILM T Cell Kit for mRNA accelerates T cell therapy from an idea to clinical applications.

ATA Scientific Pty Ltd
www.atascientific.com.au

SARS-CoV-2 panels

Meso Scale Discovery's electrochemiluminescence technology eliminates many difficulties associated with commonly used sandwich assay methods, with its high sensitivity and fast, simple workflows allowing for the detection of biomolecules of interest. The use of an electrochemiluminescent label, SULFO-TAG, conjugated to a detection molecule allows for custom-designed and curated panels for a wide variety of biomedical and pharmacologic research applications.

The combination of electrochemiluminescence and arrays brings speed and high density of information to biological assays. The technology is designed to enable precise quantitation of multiple analytes in a single sample requiring less time and effort than other assay platforms. Multi-SPOT plates measuring up to 10 different analytes per well is said to increase throughput and assay multiplexing in 96- and 384-well formats.

The immunoassay technology provides good analytical performance and customer value. The V-plex SARS-CoV-2 Panel 2 was selected by US-government funded initiative Operation Warp Speed as the basis of standard binding assays for immunogenicity assessments in all US-funded Phase III clinical trials of vaccines.

Currently the range of V-plex SARS-CoV-2 Panels includes over 20 different multiplex serology assays and ACE2 neutralisation assays for antibodies to spike, RBD and nucleocapsid antigens from variants of SARS-CoV-2. Panels for over 35 SARS-CoV-2 variants including Alpha, Beta, Gamma, Delta, Lambda, Mu and Omicron variants are available and all human V-plex serology panels for the range are provided as complete kits with reference standards and controls.

Bio-Strategy Pty Ltd
www.bio-strategy.com

Custom-made specimen bags

Harcor's specimen bags will be of interest to those who are looking for custom-made products. The bags can be compartmentalised to prevent contamination during transportation to the laboratory for testing.

The commonly ordered specimen bag style is a three-layered LOPE bag that is 45 μm thick, 155 mm wide, 250 mm high and features a press-top closure. Custom printing, sizing and colour options are available to suit each user's specific requirements.

As a bag specialist, Harcor offers a broad array of different styles, colours and sizes — from padded bags used to transport samples to biohazard bags and more. Interested customers are welcome to contact the company to discuss their specific requirements.

Harcor
www.harcor.com.au

Semi-automatic filling and capping system

The Flexicon FlexFeed 30 is a tabletop bottle handling and capping machine that is designed to provide consistent cap torque and reduce operator repetitive strain injuries. A useful alternative to fully automatic solutions for flexible, small-scale production, the product meets the demands of flexible small-batch production, while delivering a consistent production quality that is not possible with manual filling and capping.

A complete bottle and cap changeover can be completed in less than 5 min. The entire fluid path has been designed for single use, preventing cross-contamination. The machine's small footprint makes it easy to use at different locations within a production facility, including use within a laminar airflow cabinet.

On a standard FlexFeed 30, the filled and capped bottles will leave the machine on a tray. However, it can be customised so that all bottles will be pushed onto a conveyor belt going to labelling machine, to further improve productivity. The system can also be connected to a Flexicon PF7 or a 520Di peristaltic filler. This will add the benefits of a high flexibility in fill volumes, no overfilling, reduced foaming and no dripping between individual fills.

Other benefits include: handling screw caps, pipette caps or other screw caps with a special shape; filling and capping of up to 1200 bottles per hour, with diameters from 12 to 50 mm; and consistent cap torque to prevent the problem of leaking bottles.

Watson-Marlow Fluid Technology Group
www.wmftg.com.au

HEPA 14 air purifier

GAMA Healthcare Australia has announced the launch of the Rediair air purifier, which is suitable for healthcare and commercial settings such as hospitals, aged care, pharmacies, general practice centres, dental clinics, pathology centres, offices and schools. The product is claimed to be 10 times more effective than a HEPA 13 filter, providing clean air for high-traffic environments.

When used in conjunction with other safety measures, the HEPA 14 air purifier can reduce the transmission of harmful particles such as aerosols, bushfire smoke, pollen, dust, paint, bacteria and even SARS-CoV-2. It does this by incorporating two advanced composite HEPA 14 and carbon filters which trap particles down to 0.3 μm in diameter.

The innovative air purifier is designed to provide maximum efficiency at low noise levels, making it suitable for use in high-density environments such as schools, workplaces and medical settings where patient comfort is a priority. It has a clean air delivery rate (CADR) of 600 m^3/h and is said to trap 99.995% of particles.

GAMA Healthcare Australia Pty Ltd
www.gamahealthcare.com.au

CRISPR cancer therapy doesn't kill healthy cells

A new cancer therapy called CINDELA, developed by researchers from South Korea's Institute for Basic Science (IBS), employs CRISPR-Cas9 to kill cancer cells without affecting normal tissues. The breakthrough has been published in the journal ***PNAS***.

Radiation and chemotherapy destroy cancer cells by producing DNA double-strand breaks. Unfortunately, since both treatments target DNA in normal cells as well as cancer cells, indiscriminate killing of healthy cells and side effects are unavoidable when using these treatments. Scientists have long been searching for a method to selectively target only cancer cells without affecting normal cells; now, researchers at the IBS Center for Genomic Integrity (CGI) have combined the concepts of cancer genomics and CRISPR-Cas9 (commonly called genetic scissors) to propose a potential solution.

Cancer genomics projects have found that regardless of their origins, most cancer cells accumulate many mutations including small insertion/deletion (InDel) of several nucleotides, single nucleotide changes and large chromosomal aberrations. Meanwhile, CRISPR-Cas9 can be used to make DNA double-strand breaks in a sequence-specific manner. The CGI researchers proposed that by using CRISPR-Cas9 to produce DNA double-strand breaks at cancer-specific mutations that only exist in cancer cells, they could trigger cell death in cancer cells without affecting normal cells.

First, the researchers confirmed that enzyme-driven DNA double-strand breaks using CRISPR were able to induce cell deaths in cancer similar to physical or chemical breaks driven by radiation or chemotherapies, respectively. Then, they performed bioinformatics analysis to identify unique InDel mutations in several different cancer cell lines, including breast, colon, leukaemia and glioblastoma, which are not found in normal cells. Based on this information, they successfully made CRISPR-Cas9 reagents targeting those mutations.

The scientists named this new treatment CINDELA, which stands for 'cancer-specific InDel attacker', and confirmed that it was able to selectively kill cancer cells without affecting normal cells. It was discovered that CINDELA-driven cancer cell death was dependent on the number of DNA double-strand breaks created by CRISPR-Cas9; for example, a CINDELA reagent which induced 50 breaks in the DNA was much better at killing cancer cells than the reagent that induced only 10 breaks.

In addition to cancer cell line experiments, the researchers conducted further animal studies to verify CINDELA's efficacy in living organisms. To do so, tumour cells (colon and lung cancer) were derived from patients and were xenografted into mice. It was found that the CINDELA treatment can substantially suppress the growth of tumours in these mice. Notably, since CINDELA targets InDel mutations which are generated as by-products during tumorigenesis, CINDELA can be applied to treat most tumours.

"We believe CINDELA can become a novel therapeutic application for cancer treatments as personalised and precision medicine for all cancer patients without severe side effects," said CGI Director Kyungjae Myung. The researchers have already started applying this technology in tumours directly taken from patients, with research groups having expertise in the relevant technologies, such as gene delivery, companion diagnostic platform and cancer genomics.

One obstacle that the researchers had during all these experiments was the delivery of CINDELA reagents to tumours. Although the researchers could achieve significant tumour growth inhibition using a high titre of the virus to deliver the CRISPR in mice, as of yet this may not be enough to directly treat human patients. However, such an obstacle is one of the major issues in the current CRISPR-Cas9 field. Researchers believe that in the near future, the development of new delivery systems will eventually help establish the CINDELA cancer treatment technology in cancer patients.

Microplastics found in the human bloodstream

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Dutch researchers have demonstrated that minuscule pieces of plastic from our living environment are absorbed into the human bloodstream, publishing their results in the journal *Environment International*.

The researchers from VU Amsterdam, Deltares and Amsterdam UMC developed an analytic method for establishing the trace level of micro- and nanoplastic particles (MNPs) in human blood, which was applied to the blood of 22 anonymous donors. Nanoplastics are defined as being less than 0.001 mm in size, while microplastics, at 0.001–5 mm, are to some extent still visible to the naked eye.

Three-quarters of the test subjects appeared to have plastics in their blood, proving that plastic particles can end up in the human bloodstream. The overall concentration of plastic particles in the blood of the 22 donors amounted to an average of 1.6 µg/mL, which is comparable to a teaspoon of plastic in 1000 L of water (10 large bath tubs). Polyethylene terephthalate (PET), polyethylene and polymers of styrene were the most common types of plastic found in the blood samples, followed by poly(methyl methacrylate); polypropylene was also analysed but the concentrations were too low for an accurate measurement.

"This dataset is the first of its kind and must be expanded to gain insight into how widespread plastic pollution is in the bodies of humans, and how harmful that may be," said analytical chemist Marja Lamoree, from VU Amsterdam. "With this insight, we can determine whether exposure to plastic particles poses a threat to public health."

Separately to this, researchers from the Medical University of Vienna revealed that 5 g of MNPs on average enter the human gastrointestinal tract per person per week — roughly equivalent to the weight of a credit card. While the health risk of ingested MNPs is largely unknown to date, the researchers summarised the current state of scientific knowledge in a review article for the journal *Exposure and Health*.

MNPs enter the food chain from packaging waste, among other sources, and are trafficked into the body via food such as marine life and sea salt. Drinking also plays a part, with one study showing that anyone who drinks 1.5 to 2 L of water a day from plastic bottles ingests around 90,000 plastic particles per year in this way alone; those who choose tap water can, depending on their geographical location, reduce the amount ingested to 40,000 plastic particles. The researchers also demonstrated widespread contamination of mineral water with xenohormones leached from PET bottles, known to exhibit oestrogenic activity which can act carcinogenic in the body.

Experimental studies indicate that ingested MNPs passing through the gastrointestinal tract lead to changes in the composition of the gut microbiome; such changes are associated with the development of metabolic diseases such as diabetes, obesity or chronic liver disease. In addition to the effects on the gut microbiome, the scientists also described specific molecular mechanisms that facilitate the uptake of MNPs into gut tissue. Analysis showed that MNPs in the gastrointestinal tract could increasingly be taken up into tissue under certain physicochemical conditions and activate mechanisms involved in local inflammatory and immune responses. Nanoplastics in particular are associated with biochemical processes that are crucially involved in carcinogenesis.

According to study co-author Lukas Kenner, the potential adverse health effects of plastic particles could be particularly impactful for people with a chronic disease burden. "A healthy gut is more likely to ward off the health risk," he said. "But local changes in the gastrointestinal tract, such as those present in chronic disease or even negative stress, could make them susceptible to the harmful effects of MNPs."

Melbourne Convention and Exhibition Centre

South Wharf, MELBOURNE 27 - 30 September 2022

We extend a warm invitation to you to be part of ComBio2022 to be held at the Melbourne Convention and Exhibition Centre (MCEC). After a long pause in our plans, we anticipate that this will be a vibrant return to face-to-face scientific exchange with our colleagues.* ComBio2022 will be held in a spectacular arm of MCEC that is adjacent to the Yarra River and walking distance from numerous restaurants and cafes serving the widest imaginable variety of food. Melbourne is home to many sporting and cultural events and world class museums and galleries plus an aquarium are in the immediate vicinity. There is also an abundance of budget priced accommodation within walking distance of MCEC. ComBio in Melbourne in the Spring of 2022 should be a 'must' for all. (*Covid-safe protocols will be in place as advised closer to the date)

We are pleased to announce that the Opening Keynote Plenary Lecturer is Nobel Laureate Jennifer Doudna and the ASBMB Grimwade Keynote Plenary Lecturer is Cynthia Kenyon.

Jennifer Doudna is an internationally renowned Professor of Chemistry and Molecular and Cell Biology at U.C. Berkeley. She and her colleagues rocked the research world in 2012 by describing a simple way of editing the DNA of any organism using an RNA-guided protein found in bacteria. This technology, called CRISPR-Cas9, has opened the floodgates of possibility for human and non-human applications of gene editing and was the basis for her co-award of the Nobel Prize in 2020. Jennifer is a Howard Hughes Medical Investigator, a member of the National Academy of Sciences, the National Academy of Medicine, the National Academy of Inventors and the American Academy of Arts and Sciences.

Cynthia Kenyon is Vice President, Aging Research, at Calico and expert on the genetics of aging. In 1993, Cynthia's discovery that a single-gene mutation could double the lifespan of the roundworm *C. elegans* has led to a new understanding of the genetics of aging. She has received many honors and awards for her findings. Cynthia is a member of the US National Academy of Sciences, the American Academy of Arts and Sciences, and the Institute of Medicine and she is a past president of the Genetics Society of America.

Plenary Speakers:

- **Siobhan Brady,** *University of California, Davis, CA, USA*
- **Jamie Cate,** *University of California, Berkeley, CA, USA*
- **Jennifer Doudna,** *University of California, Berkeley, CA, USA*
- **Niko Geldner,** *Université de Lausanne, Switzerland*
- **Wolfgang Haak,** *Max Planck Institute, Germany*
- **Tony Hunter,** *Salk Institute, CA, USA*
- **Cynthia Kenyon,** *Calico LLC, South San Francisco, CA, USA*
- **Cristina Lo Celso,** *Imperial College London, London, UK*
- **Jodi Nunnari,** *University of California, Davis, USA*
- **Roy Parker,** *University of Colorado, Boulder, USA*
- **Daniel St Johnston,** *Gurdon Institute, Cambridge, UK*
- **Emma Teeling,** *University College Dublin, Ireland*
- **Lisette Waits,** *University of Idaho, USA*

ASBMB Education Plenary

- **Martin Westwell, Chief Executive** *SACE Board of South Australia*

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KEY DATES:

Earlybird Registration Deadline:
Friday, 24 June 2022

Abstract Submission Deadline:
Friday, 24 June 2022

Guaranteed Hotel Reservation Deadline:
Friday, 5 August 2022

ComBio2022 incorporates the annual meetings of:

- Australian Society for Biochemistry and Molecular Biology
- Australian Society of Plant Scientists
- Australia and New Zealand Society for Cell and Developmental Biology
- Genetics Society of AustralAsia
- New Zealand Society for Biochemistry and Molecular Biology

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- Biochemistry and Metabolism
- Cell Biology and Signalling
- Education

Photos courtesy of MCVB

Siglo Bar on Spring Street by Ben King

Software and analytical columns for analysis of biomolecules

The Waters Intact Mass app on waters_connect allows scientists using the BioAccord LC-MS System to confirm the mass of biomolecules and impurities made by synthetic or recombinant processes nearly twice as fast as other commercially available options, the company claims. The app is available for new BioAccord LC-MS Systems and as an upgrade to previously installed systems.

Intact mass analysis is routinely performed during all stages of the development of biological drugs including proteins, peptides, oligonucleotide therapies and conjugates. In early stages of drug discovery, biochemists must analyse hundreds or even thousands of different samples per week. To help speed up this process, the app provides a fast and automated solution to facilitate mass confirmation and purity determination of novel biotherapeutics. The application features intelligent automated deconvolution to process sample results within minutes of their capture, with minimal user input.

Complementing the app is a line of analytical columns for analysing intact biomolecules and their subunits. The ACQUITY Premier and XBridge Premier Protein BEH C4 300 Å columns for the BioAccord LC-MS System feature MaxPeak High Performance Surfaces (HPS) technology that prevents the loss of sample analytes due to adsorption of phosphorylated and carboxylated molecules between the sample and metal surfaces of both the LC system and column. This enables high sensitivity for low-level intact mass analysis and for intact mass analysis of phosphorylated proteins and low-level subunits of monoclonal antibodies.

Waters Australia Pty Ltd
www.waters.com

Total protein extraction kit for insects

Despite significant variation in body organisation, insects all have the same general body structure. They have segmented bodies divided into three regions: head, thorax and abdomen. The body segments are protected by a hard exoskeleton or cuticles.

From a protein extraction point of view, the unique structure of the exoskeleton makes it hard to homogenise. It is also difficult to lyse cells protected by cuticle for total protein extraction. The traditional solution-based protein extraction method such as RIPA is inefficient and protein yield is low; the profile of extracted protein using the traditional method is usually incomplete.

The Invent Biotechnologies Minute Total Protein Extraction Kit for Insects provides an efficient method for total protein extraction from insects by a combination of mechanical extraction and chemical lysis. The cell lysis buffers used are designed to be much stronger than RIPA buffer.

The kit features a simple and rapid single tube protocol and optimised buffers for insect tissues. Researchers will have the option to choose either denaturing cell lysis buffer or native cell lysis buffer, which are specifically tailored for insects. The whole procedure takes less than 10 min to complete, and the protein yield is in the range of 1–3 mg/mL. The materials provided are sufficient for 50 extractions.

Sapphire Bioscience
www.sapphirebioscience.com

Accelerating Australia's RNA Capabilities

It is one thing to invest into pure research, but to invest in a future that has, at its core, collaboration and accelerated development is a giant leap.

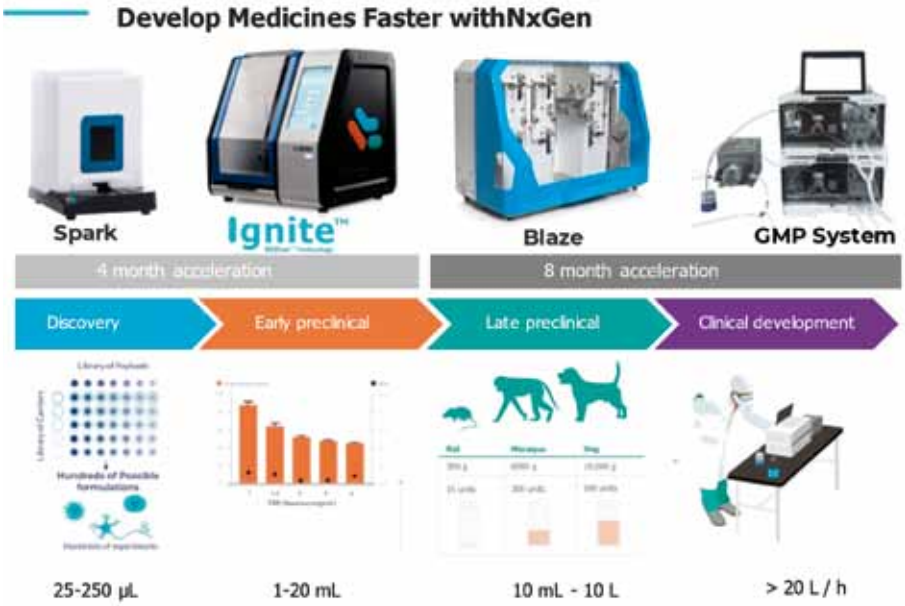
The UNSW RNA Institute (RNAI), Australia's leading RNA science, therapeutics, and translational facility, has officially opened[1]. Countless hours of planning and developing have transpired; now the Director of the Institute, Professor Pall Thordarson, says "the RNA revolution is just getting started"[1].

How to Scale — easily

Having a platform to scale up a drug candidate in country is a gamechanger and a catalyst for all research scientists in this field. Previously it was so daunting, with what can only be described as an underwhelming random pathway. Australian and New Zealand RNA scientists (ANZRPC[2]) have begun to build the core requirements to emulate the Precision Nanosystems NanoAssemblr Platform[3] that has proven to accelerate therapeutic drug development. In their recently published poster, 'Accelerated Development of Self-amplifying mRNA (saRNA) Vaccines using Microfluidics'[4], the collaboration between Precision NanoSystems and Imperial College London concluded:

- LNP-based Vaccine candidates manufactured using the PNI NanoAssemblr® platform showcased effective cellular and humoral immune response.
- SARS-CoV-2 self-amplifying RNA-LNP made with PNI proprietary ionizable lipid had similar Critical Quality Attributes (CQAs) such as size (~60 nm), polydispersity (<0.2) and encapsulation efficiency (>90%) across all scales tested with two different LNP compositions.
- Downstream processing time and particle stability during large scale TFF should be considered as a critical parameter during scale up.
- Vaccine candidates made with PNI proprietary ionizable lipid and NxGen™ microfluidic platform protected hamsters in a SARS-CoV-2 challenge study.

These findings are expanded on in their earlier poster 'Scale Up and Manufacturing of Self-amplifying RNA-LNPs for a COVID-19 Vaccine Using the NanoAssemblr GMP System'[5] showing just how they achieved a vaccine in 9 months from project funding. It is



astounding to see the theoretical scale concept come to fruition in such a way employing the NanoAssemblr Ignite, Blaze and GMP with NxGen microfluidics, confirming them as 'A Disruptive Technology Enabling Transformative Medicine'.

London is Calling

As was the case in the darkest periods of the second world war, the COVID pandemic brought out the best of British research. Robin Shattock's lab made strong advances with a Self-amplified RNA (saRNA) vaccine for SARS-CoV-2. This is exceptional research with incredible potential to transform vaccines. Dr Anna Blakney presented a webinar outlining how a saRNA differs from mRNA plus, importantly, how not all lipids are created equal[6]. We feel confident that in the future we will be announcing 'Australia Calling' now that we have the capacity to level the playing field for our scientists.

Investing in more than hope

Discussing the merits of RNA research with the Hon Gabrielle Upton MP, it was considered these investments into RNA facilities do more than translate medicine; they harvest possibility for our future crop of young scientists, illuminating a robust pathway for their discoveries. RNA is not just for vaccines; RNA will transform medicine as we know it. Strong investments will turbocharge Australia's presence in global genetic medicines, securing our sovereign capacity.

How can we help?

ATA Scientific are determined to help establish a network of scale-up platforms throughout Australia to service the growing research need to translate drug candidates through to the clinic. Contact ATA Scientific for more information about the NanoAssemblr range, request a demo or a meeting to discuss your project.

Call Peter Davis 0417 778 971 or email pdavis@atascientific.com.au.

References

1. Australia's RNA capability strengthens as UNSW RNA Institute opens https://bit.ly/3lKQs5y
2. Creating a Genetic Medicine Manufacturing Ecosystem Part 2 https://bit.ly/38yLUzo
3. NanoAssemblr Platform https://bit.ly/3wCpCKq
4. Accelerated Development of Self-amplifying mRNA (saRNA) Vaccines using Microfluidics https://bit.ly/3tDtI2V
5. Scale Up and Manufacturing of Self-amplifying RNA-LNPs for a COVID-19 Vaccine Using the NanoAssemblr® GMP System https://bit.ly/3tDtI2V
6. Effect of saRNA Formulation on Protein Expression and Vaccine Immunology. https://youtu.be/z6DH2MJ0Gbg

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Daniela Jansen, Director of Product Marketing, BIOVIA, Dassault Systèmes

The lab of the 21st century

For many years the laboratory informatics community has been talking about the 'lab of the future', 'Lab 4.0', the 'smart lab' or the 'lab of the 21st century'. We have been in the 21st century for quite a while now — but what has happened so far?

Labs have moved from paper to electronic (paper on glass) and some of them have moved to the digital lab by implementing digital workflows. But if the lab of the 21st century is supposed to be new and transformative, this isn't enough. Labs need to become truly digitalised (using digital technologies to change a business model).

The key to digital — and even more for digitalised lab operations — is connectivity to build the foundation for a new way of working.

Many companies have considered and even tested new technologies that have come up: cloud computing, data lakes, the Internet of Laboratory Things, AI and machine learning, virtual and augmented reality, voice control. Are these technologies relevant for the lab of the 21st century? Are they providing any value?

Only connectivity allows organisations to leverage these new advanced technologies and to make an impact on the experience of lab scientists, the productivity of the lab and the reuse of scientific data.

Connectivity

The most basic connectivity in the lab is between data generators like instruments or any application to capture/enter data and data consumers. These are the tools to create reports and documents, to generate analytics and dashboards, and to provide secure long-term storage of the large amount of valuable data generated in the lab.

However, laboratory operations encompass more than this, and connectivity must go much further. Systems to manage samples and chemicals, as well as equipment and personnel, are part of the lab environment. It also includes processes like the development of methods and their execution, the preparation of samples and experiments, and the analysis, reporting and decision-making. Moreover, it must be able to bi-directionally communicate with an organisation's business systems like the enterprise resource planning (ERP) system. It sounds complex to integrate all these elements but the benefits are significant.

Technology and standardisation

What is required to enable this connectivity? The basis will be an infrastructure that is platform-based to provide the required backbone, cloud-enabled to ensure an agile collaborative way of working with a low total cost of ownership (TCO) and that can leverage a data lake to ensure long-term storage of many different data types. However, technology is not enough. Standardisation is key — and different aspects of standardisation have to be considered.

An important aspect is the actual data format and a standardised framework. A standard data format must define the specifications for a vendor- and technique-agnostic format to store the data and contextual metadata so it allows for long-term and real-time access to the data. The standardisation of taxonomies and ontologies (vocabulary) allows for a controlled vocabulary and relationships for the contextual metadata about material, equipment, process, results and properties. The outcome of the work of pre-competitive consortia like Allotrope and the Pistoia Alliance can help.

In addition, labs should ensure their scientific data are FAIR (findable, accessible, interoperable, reusable). The FAIR data principles act as a guideline to support the implementation of technology. They make data more valuable as it is easier to find, combine and integrate thanks to the formal shared knowledge representation.

The value of connectivity

- Enables the liquidity of data and information flow between people and systems, vertically and horizontally.
- Helps to overcome data silos and departmental disconnect.
- Supports processes like materials characterisation, formulations, process development, stability studies or batch releases in one seamless experience.
- Increases lab productivity up to 40%.
- Ensures data integrity and improves data quality.
- Drives collaboration and data sharing on a global scale.
- Allows integration of new advanced technology and devices.
- Enables data- and knowledge-based decision-making — in real time.
- Creates a new transformative user experience.

One step further

What if we think a bit further? If we connect to experts in modelling and simulation, we can replace physical testing by virtual testing without having to build the in-house expertise. If we connect to other labs, in-house or externally, we can optimise the scheduling of lab work in unprecedented ways, removing the testing bottleneck throughout the organisation. This additional level of connectivity will elevate the productivity of the laboratories across departments, provide deeper insight into work throughout the value chain and drive successful innovation in a complex business environment.

How far are you on your journey into the lab of the 21st century? To explore this, watch this webinar about labs in the 21st century: shorturl.at/lqACG.

BIOVIA, Dassault Systèmes
https://www.3ds.com/biovia

Microplate reader

BMG LABTECH's VANTAstar microplate reader was conceived for ease of use and flexibility for a wide range of applications in basic research and life sciences. The compact, multimode microplate reader is equipped with three features to enable effortless detection set-up and improve data quality: enhanced dynamic range (EDR) technology, a rapid full-plate auto-focus and automatic luminescence cross-talk reduction.

The EDR technology grants a dynamic range spanning over eight concentration decades in a single measurement, which should simplify sensitivity settings and make gain adjustments superfluous. With EDR, every plate is automatically read with a setting that provides optimum sensitivity with no manual intervention.

The device incorporates a rapid, full plate auto-focus for both top and bottom reading in all plate formats up to 384 wells. Combined with EDR, this feature makes detection easy; every sample on the microplate is automatically detected with the optimal settings without any action prior to the start of measurement.

Data quality in luminescence assays is often negatively affected by signal cross-talk from neighbouring wells. The cross-talk reduction package automatically reduces non-specific signals reducing data variability, background noise and false positive signals, which should improve data quality.

For full flexibility, the product is equipped with BMG LABTECH's dual LVF Monochromator system for high wavelength flexibility and good performance in each assay, with filter detection and a UV/vis spectrometer for ultrafast full absorbance spectra. In addition, the reader can be equipped with the company's Atmospheric Control Unit for physiological cell-based assays and with a reagent dispenser module with up to two injectors, heater and magnetic stirrer plate.

BMG LABTECH Pty Ltd
www.bmglabtech.com

2022 RACI National Congress

July 3–8, Brisbane

As the national professional body for chemists in industry, academia and government, the Royal Australian Chemical Institute (RACI) promotes the critical role of chemistry in tackling global challenges. Every five years RACI brings together chemistry professionals to showcase the latest breakthroughs, explore new opportunities for collaboration, and network with preeminent members of the international chemistry community.

The theme for the 2022 National Congress is 'Chemistry: Catalysing solutions to global challenges'. The conference will engage members from all fields of chemistry in efforts to formulate genuine and sustainable solutions to our biggest global challenges, including alternative energy sources, climate change, food security and antibiotic resistance, through presentations and discussions.

https://www.raci2022.com/

Science on the Swan 2022
May 9–11, Perth
https://scienceontheswan.com.au/

ANZAN 2022 ASM
May 10–13, Melbourne and online
https://www.anzan2022.com/home.html

Cutting-edge Symposium on Integrated Systems Biology: Challenges and Future Perspectives
May 18–20, Brisbane and online
https://wp.csiro.au/sisb/

Threads + Opportunities: Science engineering sustainable fibres
May 23–26, online
https://events.csiro.au/Events/2022/February/8/Threads-and-Opportunities

AusMedtech 2022
May 24–26, Melbourne
https://www.ausmedtech.com.au/

Australasian Society of Diagnostic Genomics 2022 Interim Scientific Meeting
May 27–29, Sydney
https://aacb.eventsair.com/asdgconference2022/

ASID Annual Scientific Meeting
June 16–18, Perth and online
https://www.asid.net.au/meetings/asid-annual-scientific-meeting-2022

ASM 2022
July 11–14, Sydney and online
https://www.theasmmeeting.org.au/

AOGS2022 Virtual
August 1–5, online
https://www.asiaoceania.org/aogs2022/public.asp?page=home.asp

AMSA 2022
August 7–11, Cairns
https://www.amsa.asn.au/2022-cairns

National Science Week
August 13–21, Australia-wide
https://www.scienceweek.net.au/

Energy Oceania 2022
August 29–31, Melbourne
https://www.energyconferenceaustralia.com/

ASCIA 2022 Conference
August 31–September 2, Melbourne and online
https://ascia2022.com/

ComBio2022
September 27–30, Melbourne
https://www.combio.org.au/combio2022/

AACB 59th Annual Scientific Conference
October 18–20, Perth
https://aacb.eventsair.com/aacb-59th-annual-scientific-conference

AusBiotech 2022
October 26–28, Perth
https://www.ausbiotech.org/events/event/AusBiotech2022

Australasian Cytometry Society Conference
November 20–23, Melbourne
https://cytometryconference.org.au/

Human Genetics Society of Australasia Annual Scientific Meeting
November 24–27, Perth
https://aacb.eventsair.com/hgsa-45th-annual-scientific-meeting

32nd International Congress of Antimicrobial Chemotherapy
November 27–30, Perth
http://32icc.org/

Materials Oceania 2022
December 5–8, Gold Coast
https://www.materialsconferenceaustralia.com

Australian Institute of Physics (AIP) Congress
December 11–16, Adelaide
https://aip-congress.org.au/

Lorne Genome 2023
February 12–15, Lorne
https://www.lornegenome.org/

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