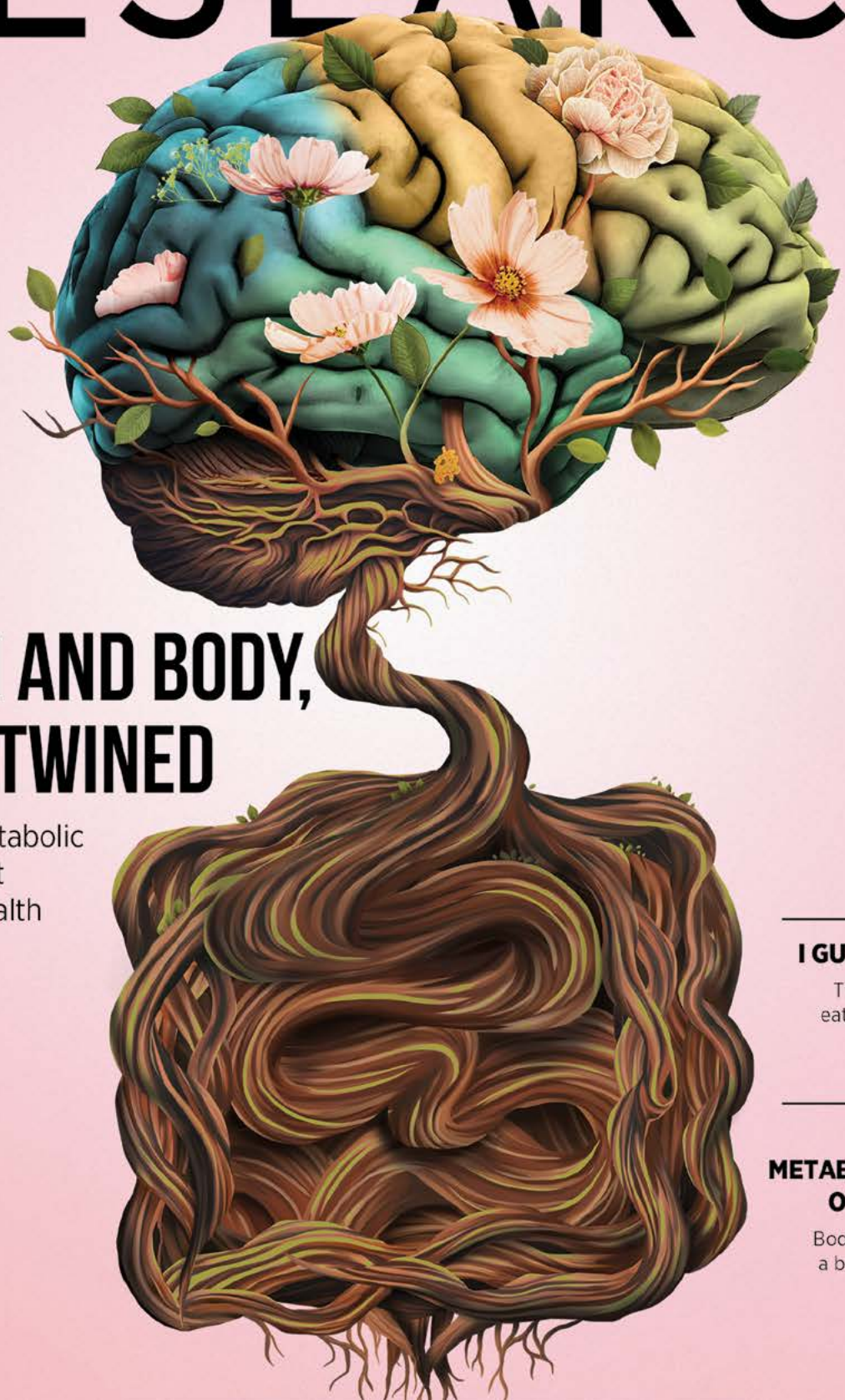
A*STAR RESEARCH

Issue 37 | September – October 2023



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*A*STAR Research* is a publication of the Agency for Science, Technology and Research (A*STAR) — Singapore's lead government agency for fostering world-class scientific research.

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A*STAR actively nurtures public-sector research and development in biomedical sciences, physical sciences and engineering, and spurs growth in Singapore's key economic clusters by providing human, intellectual and industrial capital to our partners in industry and the healthcare sector.

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A*STAR Skin Research Labs (A*SRL)
Advanced Remanufacturing and Technology Centre (ARTC)
Bioinformatics Institute (BII)
Bioprocessing Technology Institute (BTI)
Experimental Drug Development Centre (EDDC)
Genome Institute of Singapore (GIS)
Horizontal Technology Coordinating Offices (HTCO):
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- Artificial Intelligence, Analytics and Informatics (AI^3)
- Epidemic Preparedness (EP)
- Robotics
- Social Sciences and Technology (SST)
- Urban and Green Technology (UGT)

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Institute of High Performance Computing (IHPC)
Institute for Infocomm Research (I^2R)
Institute of Molecular and Cell Biology (IMCB)
Institute of Microelectronics (IME)
Institute of Materials Research and Engineering (IMRE)
National Metrology Centre (NMC)
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Singapore Institute for Clinical Sciences (SICS)
Singapore Institute of Manufacturing Technology (SIMTech)
Singapore Institute of Food and Biotechnology Innovation (SIFBI)

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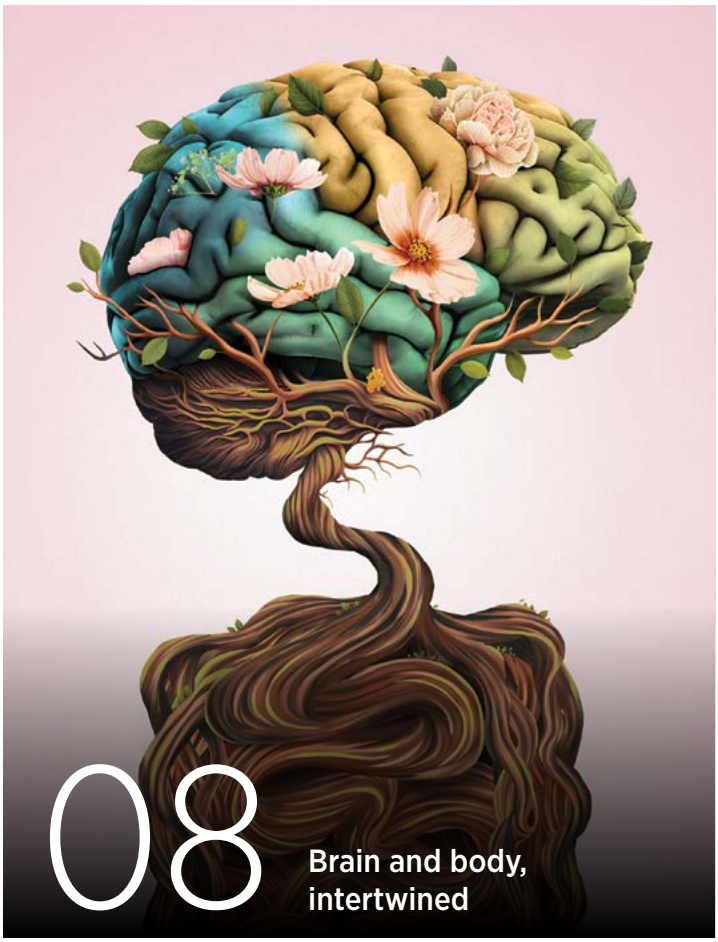

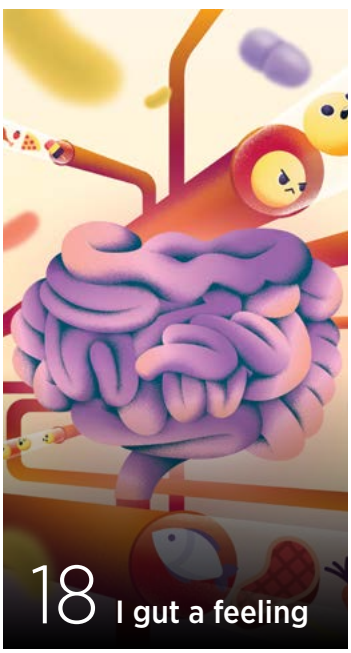

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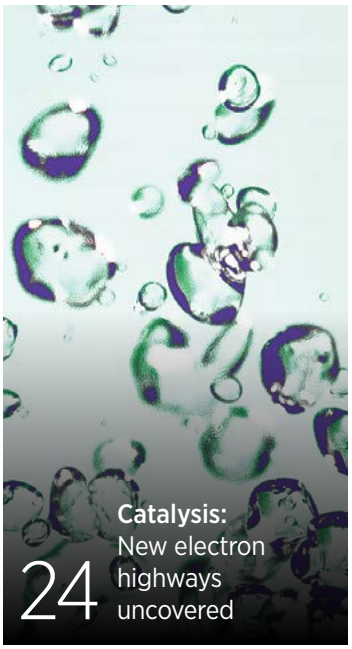
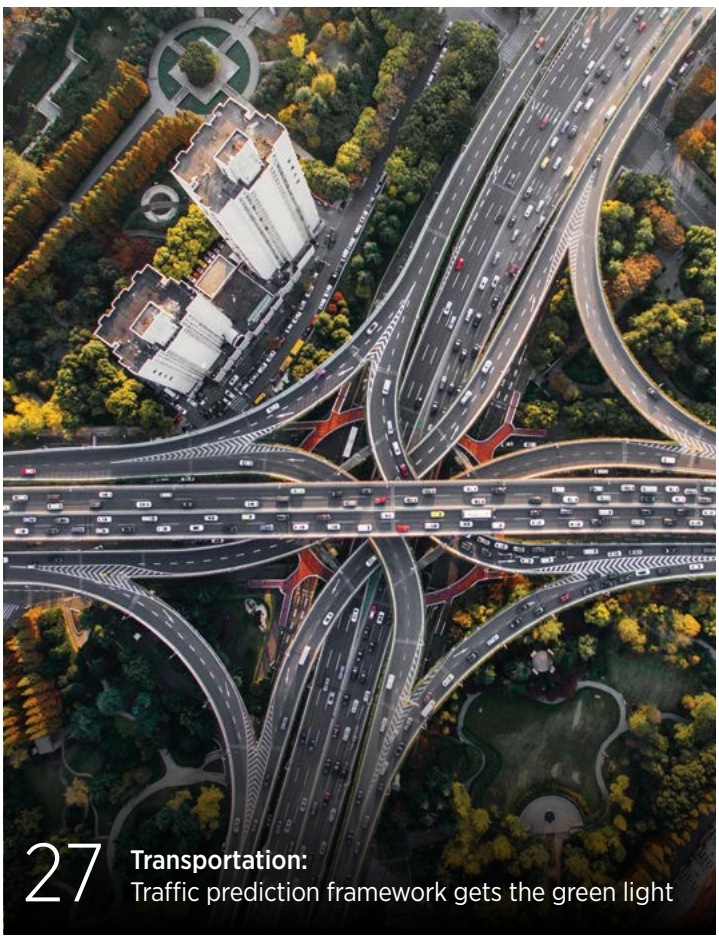




EDITORIAL NOTES

We might think of the brain as the body's command centre—a place which sends orders to a network of organs and muscles, controlling how and when they behave. Yet a growing body of evidence shows that this relationship goes two ways; the biochemical processes in our body likewise affects how our brain develops and functions.

To uncover a deeper understanding of these brain-body interactions and their impact on human health, A*STAR has formed diverse multidisciplinary teams from across its institutes under strategic research initiatives. In this issue's cover story, 'Brain and body, intertwined (p. 08)', we dive into these partnerships in neurometabolic research that weave together insights from the lab with expertise from the clinic.

"We are what we eat" is a saying often interpreted as "our diet shapes our physical form". However, more research into the gut-brain axis shows that what we eat also influences our moods and behaviour. In our first feature, 'I gut a feeling (p. 18)', Junior Investigator Hwei Ee Tan shares his insights from his work in this area at A*STAR's Institute of Molecular and Cell Biology (IMCB).

The human microbiome is also a key partner in the dialogue between our brain and our body. Specific species can help or hinder our body's efforts to maintain a healthy biochemical balance. In our second feature, 'Making metabolic sense of microbes (p. 28)', National Science Scholar Phyllis Phuah at IMCB talks about her research goals and motivations as she explores these interactions with our microscopic neighbours.

Across A*STAR's research institutes, work continues in critical areas with societal impact, ranging from improving cancer immunotherapy protocols to reducing industrial greenhouse gases. For more on these, turn to 'Tenacious T cells triumph over tumours (p. 16)' and 'Clean chemical plants create a buzz (p. 22)'.

For more of the latest developments from A*STAR researchers, visit our website at **research.a-star.edu.sg**. You can also stay up-to-date by following us on Twitter/X at **@astar_research**, LinkedIn at **A*STAR Research** and Telegram at **A*STAR Research**.

On the cover
A 'tree of life' represents the two-way relationship between the brain and body in human physiology.

For the latest on A*STAR's COVID-19 research, please scan the QR code or visit: https://research.a-star.edu.sg/tag/covid-19/

INFECTIOUS DISEASES

Red flags in wastewater

Wastewater surveillance in epidemiological studies can help researchers better understand and control COVID-19 outbreaks.

Keeping pace with an infectious disease outbreak is like solving a complex puzzle in a race against time. The good news is that there could be vital clues lying right beneath our feet—sewage systems could provide early warnings by providing critical epidemiological information to help keep communities safe.

Xian Jun Loh, Executive Director at A*STAR's Institute of Materials Research and Engineering (IMRE), listed some advantages of using wastewater-based epidemiology, or WBE: "Firstly, it provides a holistic view of infection rates within a community, including asymptomatic cases."

"Secondly, it is cost-effective and can detect outbreaks early. Moreover, it complements clinical testing by monitoring a larger population," added Loh.

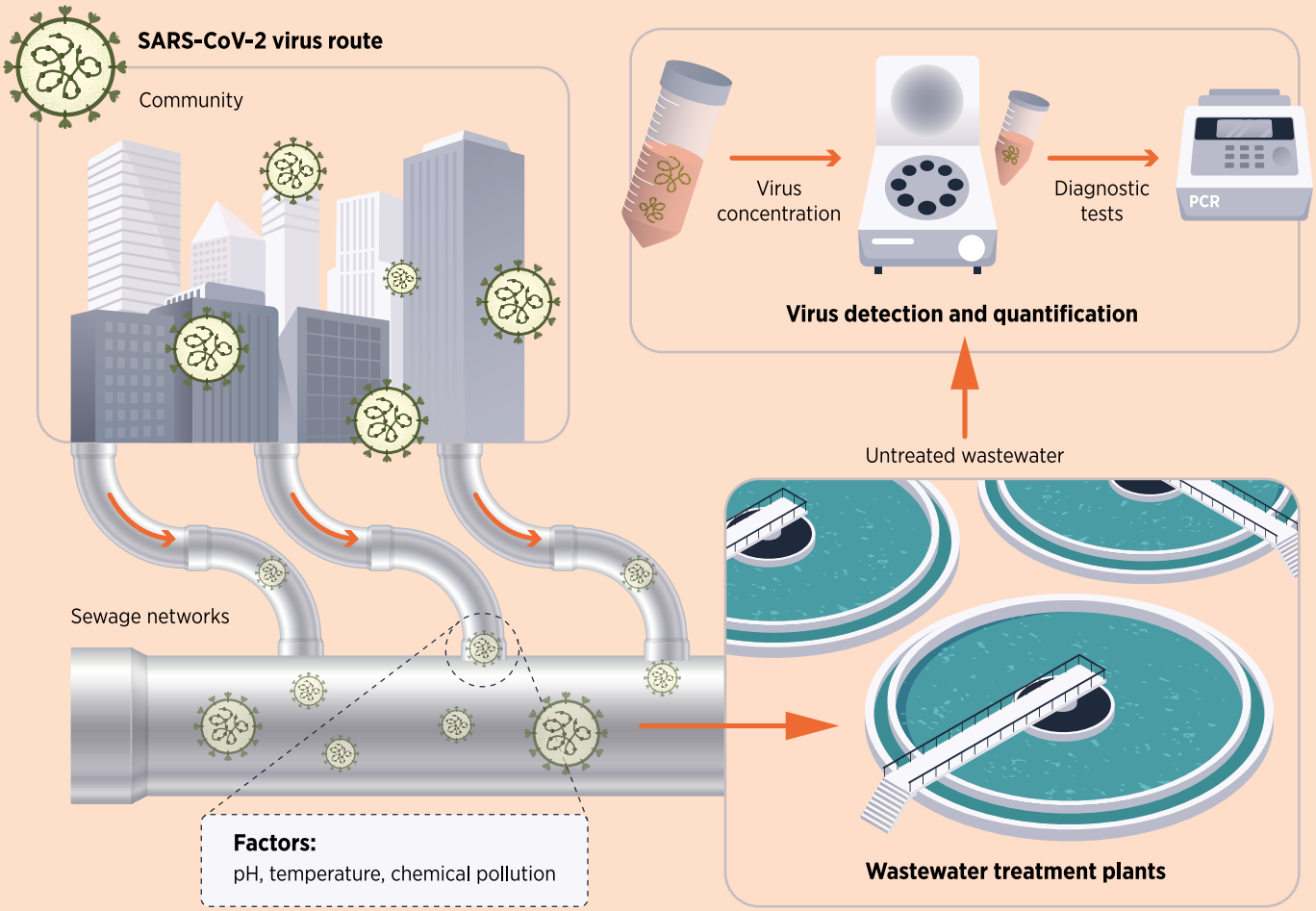
Together, Loh explained, those two aspects of WBE can be used to prompt swift public health actions, like focused testing, contact tracing and isolation protocols. This proactive strategy could effectively reduce a virus' spread and avert large-scale community outbreaks.

Using the COVID-19 pandemic as a framework, Loh teamed up with Ady Suwardi and other IMRE colleagues to provide insights on the latest knowledge about detecting and measuring SARS-CoV-2 in wastewater.

SARS-CoV-2 is shed by both symptomatic and asymptomatic COVID-19 patients.

"[Wastewater-based epidemiology] provides a holistic view of infection rates within a community, including asymptomatic cases."

Photo credit: Ivan Bandura / Unsplash



SARS-CoV-2 detection and quantification from wastewater sources as an infectious disease surveillance system for communities.

In certain instances, the virus was still found in faecal samples for up to 10 weeks after it was no longer detectable in throat swabs or urine samples.

They reported that despite its potential, community-level surveillance using WBE can be challenging—factors like temperature, pH levels, initial virus concentration and chemical pollutants in wastewater can affect the accuracy of readings.

"Statistical analysis and normalisation techniques were applied to account for these variables, ensuring consistency in the findings," explained Loh.

Also, because wastewater environments are in a state of constant flux, viral loads in wastewater samples tended to vary significantly, said Loh. "Different researchers addressed them by using multiple detection methods, spiking control samples and cross-referencing results with clinical data to validate their findings."

In their review, the team also provided the field with guidance for using wastewater surveillance in epidemiological studies to better understand and control COVID-19 outbreaks. They proposed establishing standardised procedures and guidelines for data reporting.

"Collaboration among research communities and regulatory bodies can facilitate harmonisation, enabling effective use of this tool in the fight against COVID-19," commented Loh. ★

Researchers
Xian Jun Loh and Ady Suwardi,
IMRE

IN BRIEF
A review of wastewater-based epidemiology for monitoring SARS-CoV-2 reveals how this technique can aid public health decision-making but also warns how various factors can impact the reliability and comparability of data.

1. Zhang, D., Duran, S.S.F., Lim, W.Y.S., Tan, C.K.I., Cheong, W.C.D., *et al.* SARS-CoV-2 in wastewater: From detection to evaluation. *Materials Today Advances* **13**, 100211 (2022).

IMMUNOLOGY

Mighty mice mirror maladies

A new genetically-modified mouse model offers a powerful and reliable platform to study human immune responses to complex infections.

The human immune system has been evolving for millions of years, adapting to various environmental pressures and the ever-changing landscape of infectious diseases. Now, researchers have developed a way of holding the complexity of the immune system in the palm of their hand.

Stem cell-based lab animals called humanised mice were developed to carry human immune cells including T-cells, B-cells and immune proteins and receptors as a means of modelling infections or testing experimental drugs.

However, as Qingfeng Chen, a Senior Principal Investigator at A*STAR's Institute of Molecular and Cell Biology (IMCB) explains, not all humanised mice models are equally useful for studying complex infectious diseases such as COVID-19.

"As humans have unique immune cells, non-human animal models used to evaluate disease pathogenesis and therapeutics may have variable outcomes," said Chen.

Together with groups from the Duke-NUS Medical School, Singapore, and the University of Melbourne, Australia, Chen's team embarked on a project to develop and characterise a specialised mouse model for studying COVID-19.

The researchers used an adenovirus vector to introduce human angiotensin-converting enzyme-2 (hACE2), a receptor the SARS-CoV-2 virus uses to enter and infect cells, into humanised 'NIKO' mice. They also transplanted human $CD34^+$ hematopoietic stem cells into the animals to generate a human immune system.

"Humanised mice can be a powerful tool to rapidly establish animal models for the study of human immune responses and the pathogenesis of new pathogens."

They then exposed the hACE2 NIKO mice to a suite of SARS-CoV-2 variants alongside the original isolate and discovered that the animals showed signs of an acute immune system response, inflammation in the lungs, lung damage and the release of pro-inflammatory chemicals.

Because these effects mirror those observed in COVID-19 patients, the researchers propose that this approach allows for the swift creation of animal models to investigate both human immune responses and the development of diseases caused by emerging pathogens. For example, the animals can easily be genetically tailored to express receptors like dipeptidyl-peptidase 4 to study MERS-CoV instead.

"Humanised mice can be a powerful tool to rapidly establish animal models for the study of human immune responses and the pathogenesis of new pathogens." explained Chen. "With such a simple and accessible model, we can design, test and improve therapeutics safely." ★

Researcher
Qingfeng Chen, IMCB

IN BRIEF
Researchers engineered a humanised mouse platform which mimics infection responses, induces inflammation and manifests disease-related changes associated with COVID-19.

1. Yong, K.S.M., Anderson, D.E., Zheng, A.K.E., Liu, M., Tan, S.Y., *et al.* Comparison of infection and human immune responses of two SARS-CoV-2 strains in a humanized hACE2 NIKO mouse model. *Scientific Reports* **13**, 12484 (2023).

Photo credit: Kim Green / Unsplash

STRUCTURAL BIOLOGY

Fine-grained anatomy of a viral enemy

Investigations into an under-explored region of SARS-CoV-2's spike protein reveals detailed structural insights that can represent valuable drug targets.

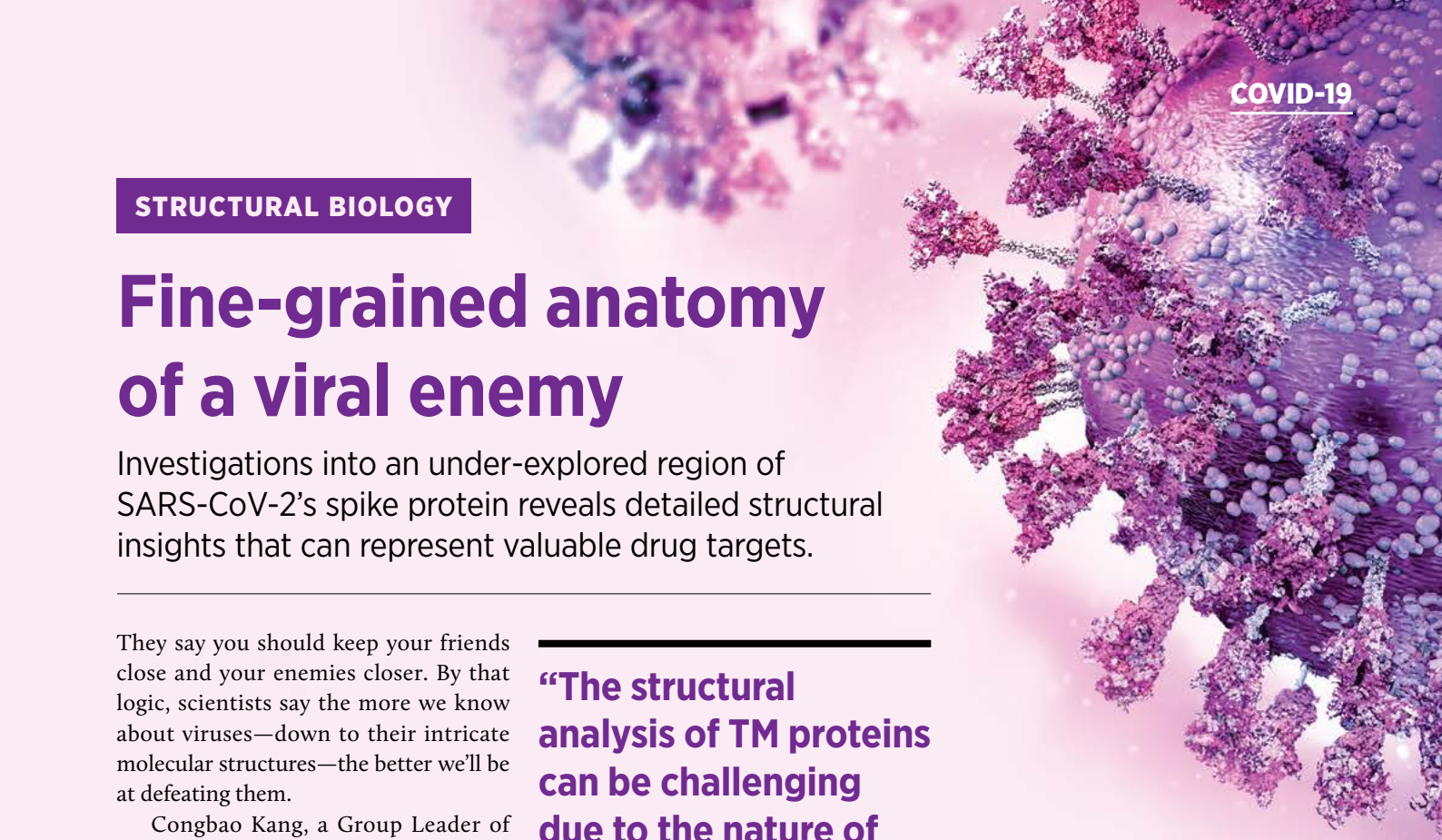


Photo credit: Naeblys / Shutterstock

They say you should keep your friends close and your enemies closer. By that logic, scientists say the more we know about viruses—down to their intricate molecular structures—the better we'll be at defeating them.

Congbao Kang, a Group Leader of the Structural Biology team at A*STAR's Experimental Drug Development Centre (EDDC), explained that until now, most drug discovery efforts to combat SARS-CoV-2 have focused on the N-terminal region of the virus' spike protein, for its role in gaining entry into host cells.

However, because the spike protein is particularly prone to mutations, these treatments can eventually be rendered ineffective.

Kang's team took a divergent approach, zeroing in on a specific part of the spike protein called the transmembrane domain (TM) instead. Thought to provide both flexibility and stability to the spike protein, the TM domain's dynamics during COVID-19 infections have remained elusive.

"The structural analysis of TM proteins can be challenging due to the nature of the transmembrane regions," said Kang. "To effectively study these proteins, it is necessary to use membrane-mimicking systems that replicate their native environment."

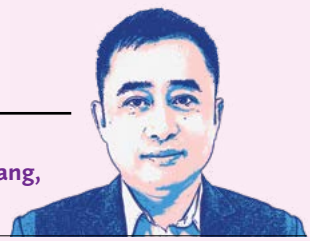
"The structural analysis of TM proteins can be challenging due to the nature of the transmembrane regions."

In their study, Kang and colleagues collaborated with a researcher from the Guangdong Academy of Sciences, China, to analyse the TM structure at high resolution with the help of microscopic 'bubbles' called micelles. These contain both water-loving and water-repellent environments that mimic the lipid bilayers of human cell membranes and help stabilise the TM proteins.

After visualising the TM-containing micelles using nuclear magnetic resonance spectroscopy, Kang's team observed that the viral protein formed a characteristic helical structure. They also identified a linker that acted like a flexible bridge between the TM helix and HR2 region in the spike protein.

In addition to these never-before-seen glimpses of the TM domain's architecture, the team also identified particular regions of the protein that can bind to small molecules—a feature which can be crucial for developing antiviral therapies.

The team is currently deploying alternative membrane systems to examine the delicate complexity of TM structures. Kang's team is also interrogating mechanisms in which small molecule inhibitors can bind to the TM domain to inhibit the infectivity of the SARS-CoV-2 spike protein. ★



Researcher
Congbao Kang, EDDC

IN BRIEF
The transmembrane domain of the SARS-CoV-2 spike protein, a crucial component for viral infectivity, forms a helical structure in detergent micelles as seen using nuclear magnetic resonance spectroscopy.

1. Li, Q., Huang, Q. and Kang, C. Secondary structures of the transmembrane domain of SARS-CoV-2 spike protein in detergent micelles. *International Journal of Molecular Sciences* **23** (3), 1040 (2022).

BRAIN AND BODY, INTERTWINED

Through close collaborations across scientific disciplines, A*STAR drives new discoveries in neurometabolism and its potential therapeutic applications.

What does it mean to be hungry? It might seem obvious: when your stomach feels empty. But how much of that 'feeling' comes directly from an empty stomach, and how much from the brain's electrical signals?

"The way we feed is controlled at multiple levels," said Weiping Han, Director of the Neurometabolism in Health and Diseases scientific programme at A*STAR's Institute of Molecular and Cell Biology (IMCB). "There's homeostatic eating: when our bodies need energy, they signal our brains to seek food. But we're also motivated by pleasure eating: despite a full stomach, we might still feel like having a slice of chocolate cake, as the brain's reward centres might crave the boost."

The complex chemical interplay between our bodies and brains—what's known as our neurometabolism—is a subject of increasing interest in biomedical research, as evidence mounts that imbalances therein drive many significant health disorders such as diabetes and obesity.

Understanding that interplay could also help treat those disorders. In 2012, a newly launched drug, semaglutide, would tap into the brain-body connection to treat patients with type 2 diabetes (T2D). By mimicking a naturally occurring hormone, glucagon-like peptide-1 (GLP-1), semaglutide activates receptors in the pancreas and brain that prompt the body to produce more insulin—lowering blood sugar levels, as well as suppressing appetite and triggering a feeling of 'fullness'.

Semaglutide rose to both commercial success and related controversy as a 'miracle weight-loss drug', with popular demand leading to supply shortages. However, despite the unintended buzz, for Han and others in the neurometabolic research community, the drug's scientific basis represents a step towards a whole-body approach to health and disease.

"There's a lot more to uncover about both sides of neurometabolism: how our brains' neural circuits affect the health of our bodies, and how our bodies' metabolic states affect our brain functions," said Han.

Across A*STAR, researchers from IMCB and various institutes are collaborating with external partners to untangle these mysteries, hoping to identify new potential targets and brain-body relationships that could be harnessed to tackle the century's evolving health challenges.

LINKING BRAIN AND BODY EXPERTISE

IMCB's neurometabolism programme was established to build a holistic, two-way understanding of brain-body interactions by bringing together physiologists like Han, neuroscientists, geneticists and other experts.

"There's been a lot of work on how neurones regulate our systematic metabolism; how the brain controls appetite, feeding and energy expenditure. But that's one half of the story," said Han. "The other half—how metabolic changes impact our neurones, brains and cognition—is less studied but deserves equal emphasis."

In 2021, not long after the IMCB programme's initiation, A*STAR launched the Brain-Body Initiative (BBI): a cross-council, multidisciplinary strategic research programme that harnesses the agency's ecosystem to support highly collaborative projects that focus on improving population health.

"To that end, BBI integrates A*STAR's diverse capabilities in neuroscience, metabolism, social sciences, data science and advances in technology," said Sze Wee Tan, Assistant Chief Executive of A*STAR's Biomedical Research Council. "As populations age, we want to explore how the interconnectedness of brain and body could support not just longer, but healthier lives overall."

Co-led by Han and Michael Meaney, Director of the Translational Neurosciences programme at A*STAR's Singapore Institute of Clinical Sciences (SICS), BBI works with multiple institutes of higher learning and public sector agencies such as the National University of Singapore (NUS), Republic Polytechnic, the Institute of Mental Health and the Early Child Development Agency to translate key findings to real-world applications.

A keystone project behind much of BBI's work is the Growing Up in Singapore Towards healthy Outcomes (GUSTO) project: a robust long-term birth cohort study with 1,200 mothers and their children that began in 2009 and continues today. Based at SICS, GUSTO represents a pool of data from the most deeply studied individuals in the world, shedding light on neurometabolic development from prenatal to adolescent phases of life, said Meaney.

"The data include extensive analyses of metabolic and brain functions, including magnetic resonance imaging (MRI)," Meaney added. "No other programme in the world offers a comparable ability to study how our brain-body interactions change over time."

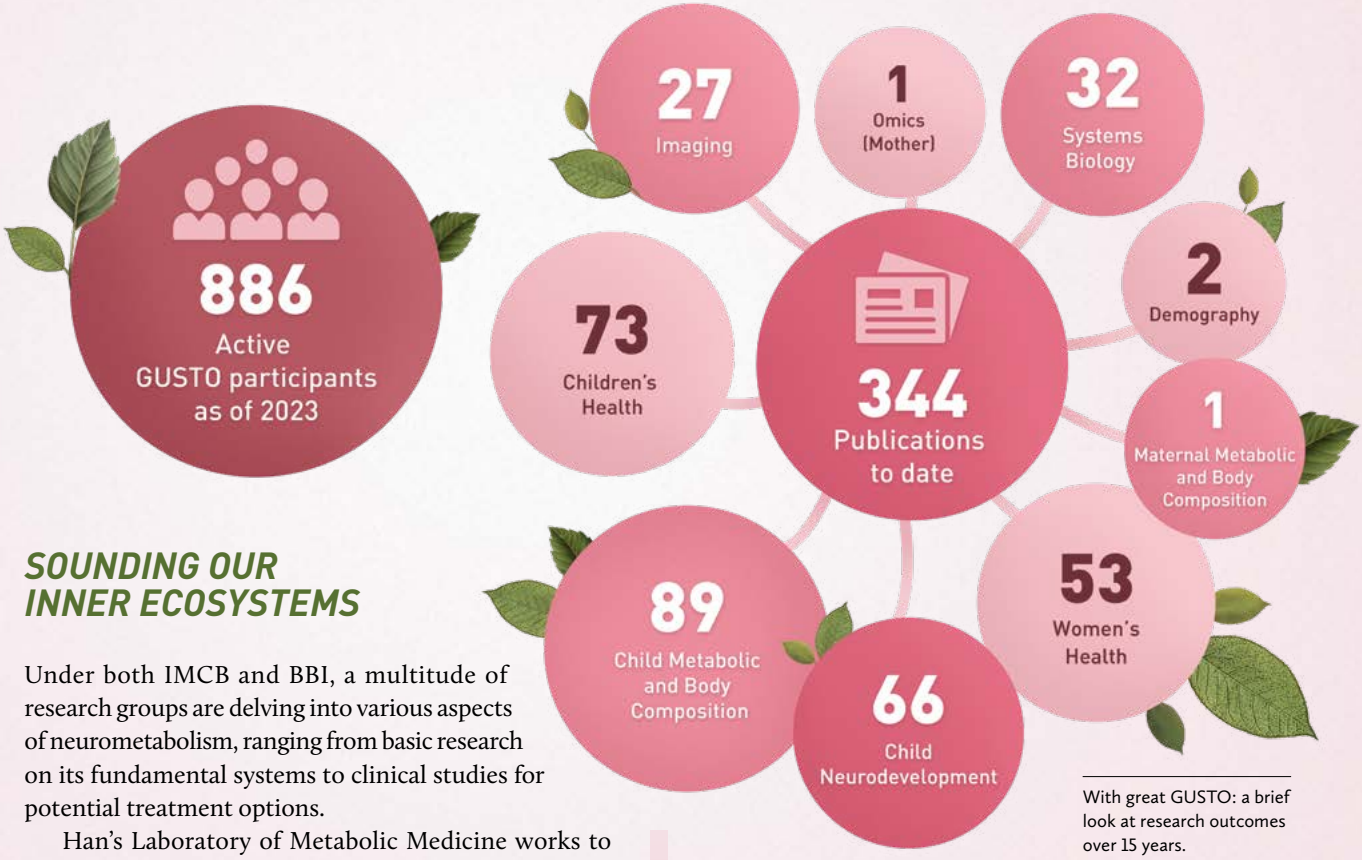
GUSTO's comprehensive 15-year data are publicly available to researchers and used extensively in many BBI studies. To manage such large amounts of data, BBI works with A*STAR's Bioinformatics Institute (BII) and the Institute for High Performance Computing (IHPC) to develop the necessary data infrastructure. IHPC and the Institute for Infocomm Research (I^2R) also aid BBI in developing new biosensors and monitoring methods for improved data collection.

BBI partnerships also extend beyond Singapore's shores. "BBI has served as a point of contact for international collaborations with the University of California at Los Angeles, Stanford, Cornell, McGill and Harvard among others," said Meaney. "For these researchers, BBI offers a combination of unique datasets and the exceptionally broad domain expertise required to understand brain-body interactions."

"We have resources we can rapidly mobilise: when we find an important question, we can leap to answer it with partners across A*STAR councils," Han added.

"There's been a lot of work on how neurones regulate our systematic metabolism; how the brain controls appetite, feeding and energy expenditure. But that's one half of the story."

— Weiping Han, Director of the Neurometabolism in Health and Diseases scientific programme at A*STAR's Institute of Molecular and Cell Biology (IMCB)



With great GUSTO: a brief look at research outcomes over 15 years.

SOUNDING OUR INNER ECOSYSTEMS

Under both IMCB and BBI, a multitude of research groups are delving into various aspects of neurometabolism, ranging from basic research on its fundamental systems to clinical studies for potential treatment options.

Han's Laboratory of Metabolic Medicine works to define how specific regulators and metabolic states affect the brain and nervous system; for example, the metabolic pathways that cancer cells hijack to promote their own growth, or the chemical imbalances that stress our cells and accelerate their decline.

"Many cells are specialists that function best under certain internal and external conditions," said Han. "For example, neurones evolved to mediate brain-body interactions by secreting neurotransmitters. But if the environment around them is out of balance—say it has an abnormal amount of sugar, as in diabetes—they're compelled into another task that they're less well-built for: in this case, to convert that excess for storage."

Distracted neurones can struggle to fulfil their original roles to release neurotransmitters when prompted. If forced to keep up the multitasking over a long term, their suboptimal functioning could be fixed in stone, leading to permanent issues like the early development of dementia, Han added.

Similar discoveries have been made by teams under IMCB Principal Investigators Sarah Luo and Caroline Wee. Using a multi-model approach with rodents and zebrafish, they aim to examine how nutrients and the gut microbiome can modulate brain health and function, and how the brain in turn regulates metabolism and dietary choices.

"We've found recent evidence of neurodegeneration in the peripheral nervous system and in certain organs, like the liver, under conditions of metabolic stress, maternal metabolic stress and potentially ageing," said Luo. "Through our work, we envision a future where we can exert enough neuromodulatory control to restore some of these neuronal signals, so we can maintain better long-term organ function despite the onset of old age."

Together with colleagues from SICS, the Singapore Institute of Food and Biotechnology Innovation (SIFBI), Singapore immunology Network (SIgN) and the Genome Institute of Singapore (GIS), the team also uses a reverse translational approach to analyse multi-omics data, including neuroimaging, to identify factors associated with metabolic and brain health in children from the GUSTO cohort.

"The neuroimaging analyses build on work led by SICS' Ai Peng Tan, showing that the size of the brain's nucleus accumbens—critical for appetite regulation—and peripheral fat mass are highly correlated, even at birth," commented Meaney.

Currently, the team is validating potential target factors in their respective preclinical models before reconfirming them in humans. "If we can establish a causative link between certain metabolites and neurodegeneration or brain function, then we can promote better brain health by modulating diet and nutrition," said Wee.

THE NEURAL CONNECTION

While much work at A*STAR delves into the body's influence on the brain, it retains strong research interests in the classic brain-to-body direction. Teams like those under IMCB Senior Principal Investigator, Yu Fu, aim to uncover new insights on the neural mechanisms behind metabolic regulation.

Fu's group focuses on excessive feeding—particularly the overconsumption of high-sugar and high-fat foods. In a recent publication, they identified a population of neurones in the hypothalamic area of a mouse's brain that appears to control appetite. While naturally activated by palatable food, this group of neurones can also be stimulated to drive mice to eat despite being satiated.

Currently, the team is working on a follow-up project focused on compulsive eating disorders. Using a custom-built, whole-brain neural circuit and active neurone mapping pipeline, they revealed connections between a cortical region of the brain—involved in memory, thinking, reasoning and sensory function—and a hypothalamic area. These connections are activated in response to a high-fat diet and may contribute to compulsive eating behaviour.

To move these insights from bench to bedside, the team works with SICS colleagues to analyse functional MRI (fMRI) data from GUSTO and examine if neural circuits in mice are also relevant for human food overconsumption. Early studies on the brain regions and neural connections behind anorexia nervosa are also underway, in partnership with human MRI researchers in France.

"We're actively collaborating with clinicians to translate our animal work into human clinical studies," shared Fu. "Conversely, findings from human studies may also help us form new ideas and hypotheses."

Similarly, Principal Investigator Crystal Yeo and her team at IMCB's Translational Neuromuscular Medicine Laboratory explore the biological mechanisms behind the heterogeneity of clinical phenotypes; how neurometabolic insights can be brought to patients; and how patient needs can direct research.

"Our work cycles between bench and bedside, focusing on evolving areas of medical need," Yeo explained. "To develop targeted biomarkers and therapies, we perform careful phenotyping of patient data, multi-omics analyses of large patient databases, clinical studies and research on patient-derived induced pluripotent stem cell (iPSC) models of neurological disease."

In collaboration with Harvard University, Yeo's team is studying the links between liver cells and motor neurones in spinal muscular atrophy (SMA), a disease driven by whole-body motor neurone degeneration. SMA was the leading genetic cause of infant death until recent genetic therapies were available. However, even with patients living longer, their motor functions are still abnormal, with reported cases of acute liver failure and death in young children despite treatment.

"Motor neurone loss in SMA causes skeletal muscle denervation, with systemic metabolic disturbances that could lead to fatty liver," said Yeo. "We've observed SMA-related fatty liver in animal models, but it was unclear whether humans were similarly affected. It's a poorly-studied area as patients previously rarely survived beyond infancy."

In their study, Yeo's team found evidence that fatty liver in both human models and human patients could be directly caused by SMA-specific genetic defects in liver cells that were not secondary to motor neurone loss.

"If so, patients may need genetic therapies which target the whole body, not just the motor neurones," said Yeo. "There's a need for systematic clinical surveillance and targeted treatments to ensure they have a better quality of life."

FROM THE BRAIN-BODY INITIATIVE

REPLENISH: Research on Probiotic, Lifestyle and Nutritional Interventions to Support Brain Healthspan

*IMCB, SIFBI, SICS, GIS, SigN, A*SRL[1], with NUS and NNI[2]*

Asian communities have unique neurometabolic phenotypes, gut microbiomes, diets and lifestyles, but are under-characterised in the global literature. REPLENISH will examine the gut-brain axis and its links to age-related cognitive and mental decline in Singapore's Asian population.

Drawing over 20 collaborators across eight institutes, the programme has three aims: to show how nutrition and lifestyle factors modulate brain health over ageing; to identify the gut microbiota and immune-metabolic pathways that mediate those factors; and to identify nutrient, microbiome and immune-metabolic pathways that promote healthy lifestyle behaviours. REPLENISH is currently in planning and grant application stages.

1. A*SRL: A*STAR Skin Research Labs
2. NNI: National Neuroscience Institute, Singapore

Circulation factors in primates on high-fat diets and their role in prediabetic states

IMCB, SICS with Duke-NUS

T2D occurs naturally in cynomolgus macaques, with early metabolic symptoms similar to humans. In this study, the team used a high-fat diet to induce prediabetes in a non-human primate model and a matching mouse model. By comparing transcriptomics, translatomics and proteomics analyses, the team aims to identify primate-specific metabolic factors involved in T2D and characterise their mode of action, hoping to develop effective therapies to prevent or reverse T2D progression.

"Motor neurone loss in spinal muscular atrophy causes skeletal muscle denervation, with systemic metabolic disturbances that could lead to fatty liver."

— Crystal Yeo, Principal Investigator
Translational Neuromuscular Medicine Laboratory
at A*STAR's Institute of Molecular and Cell Biology (IMCB)

Mechanisms of stress and resilience in nursing students entering the workforce

IHPC, IMCB with NUS

This project focuses on the impact of mental wellness challenges on healthy individuals moving from schooling to working environments, with a focus on stress, burnout and resilience. The team recruited students from the NUS School of Nursing for psychological and fMRI assessments, as well as activity tracking and biomarker collection, as they enter the stresses of full-time nursing work. The team hopes to identify risk factors and coping strategies that could help Singapore's nursing programmes and other demanding professions better support workforce resilience and long-term mental health.

BLOOMING INTO HEALTH

For researchers like Michael Meaney, the integrative approach taken by BBI embodies the necessary expertise to examine health and wellbeing as a big picture. "Many research programmes today are organised around specific organs or diseases," said Meaney. "But health emerges from interactions across all our organs, and it's increasingly clear the effect is bi-directional; our brains and bodies impact each other."

Sze Wee Tan adds that collaborations with external partners are pivotal in developing a research ecosystem around the field, as they bring added diverse expertise, amplify resources, accelerate innovation and ensure broader public impact.

"A*STAR plans to advance research efforts in neurometabolism and drive scientific innovations that benefit not only the region, but also the global community," said Tan. "We will do this by nurturing talents, fostering strategic partnerships, promoting knowledge exchange and collaborating closely with government agencies and industry partners to translate research findings into practical interventions and applications." ★

FOOD SCIENCE

A sweet end to food fraud

A new analytical technique to combat food fraud accurately profiles and differentiates meat samples based on their unique glycan profiles.

You can't always trust what's on your plate. According to some estimates, up to 20 percent of food consumed around the world has been subjected to food fraud, an increasingly pervasive issue that costs the global food industry tens of billions of dollars annually.

Now, researchers from A*STAR have developed an innovative quantitative method to accurately characterise and profile meat samples to ensure the authenticity of food products. Researcher Zach Pang leads a team that's pioneering the use of glycomics in food science, an approach that examines the structure, composition and function of sugar molecules called glycans attached to proteins in meat.

According to Pang, the idea started out as an exploratory experiment to characterise meat sources through methods such as mass spectrometry. "It was not funded by grants at the time. I was exploring this using equipment on core funding, and buying meat samples out of my own pocket," Pang remarked.

Pang was surprised to discover that glycomics turned out to be a viable method of distinguishing between meat samples from different species. "We found very profound differences between species," he said, adding that in their study, the team described distinct glycan profiles in samples of beef, pork and chicken.

Pang and colleagues found that glycan molecules called N-glycolylneuraminic acid (Neu5Gc) and alpha-galactose (α-gal) are key to unlocking the origins of a meat sample. As detailed in the study, beef and pork contain unique Neu5Gc α-gal profiles, but they are completely absent in chicken, making them valuable markers for verifying food authenticity.

"The beautiful thing about a glycomics approach is that we can actually measure the magnitude of [glycan] expression, which isn't possible with other methods," said Pang. For example, advanced analytical techniques such as ultra-performance liquid chromatography-fluorescence-mass spectrometry (UPLC-FLR-MS) can help researchers detect minute amounts of a particular glycan present in a meat sample to measure its purity.

"The beautiful thing about a glycomics approach is that we can actually measure the magnitude of [glycan] expression."

Pang warns that though glycomics may not yet verify food identity with perfect accuracy, it has great potential for combating food fraud and ensuring product authenticity in the meat industry. The use of glycomics can also be extended to other high-value biotechnology industries such as lab-grown meats to provide a powerful quality control tool.

The team is currently working on scaling up the technology for commercial applications by developing a cost-effective, paper-based diagnostic chip for food screening. ★

Researcher
Zach Pang,
BTI

Photo credit: Nicolas Postiglioni / Pexel

IN BRIEF
Distinct glycan profiles identified in chicken, pork and beef samples can be leveraged to accurately determine the origin of meat samples for product authentication in the food and biotechnology industries.

1. Chia, S., Teo, G., Tay, S.J., Loo, L.S.W., Wan, C., *et al.* An integrative glycomic approach for quantitative meat species profiling. *Foods* **11** (13), 1952 (2022).

CANCER

Decrypting the breast cancer code

Researchers extract insights from large databases of genetic and clinical information in a bid to develop more robust, data-driven breast cancer screening frameworks.

If our genomes are instruction manuals for the human body, then exomes are the important chapters that describe how proteins are made. According to experts, a technology called whole exome sequencing (WES) can help reveal previously hidden genetic changes or mutations linked to a heightened risk of disease.

"Exome sequencing provides a comprehensive view of a genome's protein-coding regions, which are responsible for many disease-causing mutations," said Jingmei Li, a Principal Scientist II at A*STAR's Genome Institute of Singapore (GIS). "It can be particularly valuable when a disease's underlying genetic cause is unknown, or when there are multiple potential candidate genes."

Li said that this approach holds promise for breast cancer screening; WES can detect the array of gene changes that converge to trigger tumour growth. For example, mutations in the *BRCA* genes are associated with an increased risk of breast cancer due to the genes' role in repairing damaged DNA.

However, these more common gene mutations don't occur in isolation and are often coupled with rare coding variants in genes that have yet to be identified. This prompted Li and colleagues from the Breast Cancer Association Consortium (BCAC)—an international multidisciplinary consortium composed of over 100 research teams—to uncover these elusive breast cancer gene modifications.

The researchers tapped into multiple large databases containing exome sequencing data from over 26,000 breast cancer patients and over 200,000 healthy women. They focused their search on rare alterations called protein-truncating variants—in which the genetic code is erroneously shortened—and rare missense variants that produce faulty proteins.

Speaking to the rationale behind this two-pronged approach, Li explained, "Rare variants are often prioritised in genetic studies because they are more likely to be disease-specific and have larger effect sizes compared to common variants. Also, analysing protein-truncating variants and rare missense variants can be more tractable than studying all possible genetic variations in a large dataset."

The team's analysis revealed that protein-truncating variants likely account for around 10 percent of the familial risk of developing breast cancer. The majority of this contribution was mediated through mutations in six breast cancer susceptibility genes, including *BRCA1, BRCA2, ATM, CHEK2* and *PALB2*. Conversely, subtle changes in genes such as *LZTR1, ATR* and *BARD1* were found to have weaker associations with breast cancer risk.

The authors say that these findings are a step towards building personalised breast cancer screening and prevention strategies.

"Identifying specific genetic variants associated with breast cancer can enhance our ability to raise red flags for women at high risk of developing the disease in the future," Li added.

Researchers from the BCAC have since embarked on the Confluence project, which aims to build a repository housing genetic data from over 600,000 clinical cases and healthy volunteers across diverse ethnicities. On the back end, Li and collaborators are working on translating insights from the data into next-generation clinical tools for breast cancer screening. ★

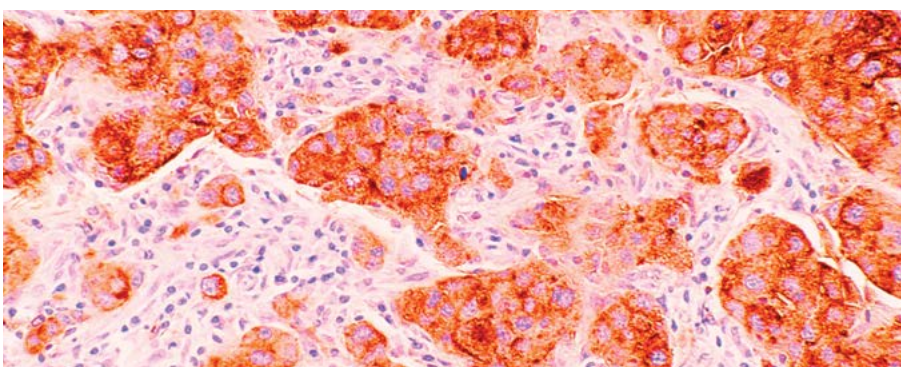


Photo credit: National Cancer Institute / Unsplash

Researcher
Jingmei Li, GIS

IN BRIEF
An in-depth analysis of whole exome sequencing data from breast cancer patients and healthy volunteers revealed rare missense and protein truncating gene variants associated with increased breast cancer risk.

1. Wilcox, N., Dumont, M., González-Neira, A., Carvalho, S., Beauparlant, C.J., *et al.* Exome sequencing identifies breast cancer susceptibility genes and defines the contribution of coding variants to breast cancer risk. *Nature Genetics* **55**, 1435–1439 (2023).

CANCER

Tenacious T cells triumph over tumours

Researchers develop a protocol to boost the effectiveness of and reduce the risk of potential side effects for T cell cancer therapies.

There's a mighty force coursing through our veins, capable of defeating even the most formidable opponents such as cancer. In recent years, scientists have discovered the key to unleashing this force. T cell therapies involve rewiring patient immune cells to recognise and target tumours, activating the body's inbuilt cancer-killing mechanisms.

One branch of T cell therapy employs infusions of T cells engineered to transiently express tumour-targeting receptors. Known as adoptive cell transfer (ACT), this approach is a safer option than those that use permanently-modified T cells, as it has no risk of introducing genetic mutations with potential long-term side effects.

However, ACT requires multiple rounds of treatment to achieve optimal results due to the harsh, immunosuppressive tumour microenvironment. Multi-dose T cell infusions are uncomfortable for patients, can trigger unintended side effects, and increase the overall cost of treatment.

To look for ways to enhance ACT's effectiveness and safety profile, Andrea Pavesi, a Young Investigator at A*STAR's Institute of Molecular and Cell Biology (IMCB), teamed up with colleagues from IMCB, the Bioinformatics Institute (BII) and Singapore Immunology Network (SIgN), as well as collaborators from Duke-NUS Medical School, Singapore and the Tisch Cancer Institute, United States.

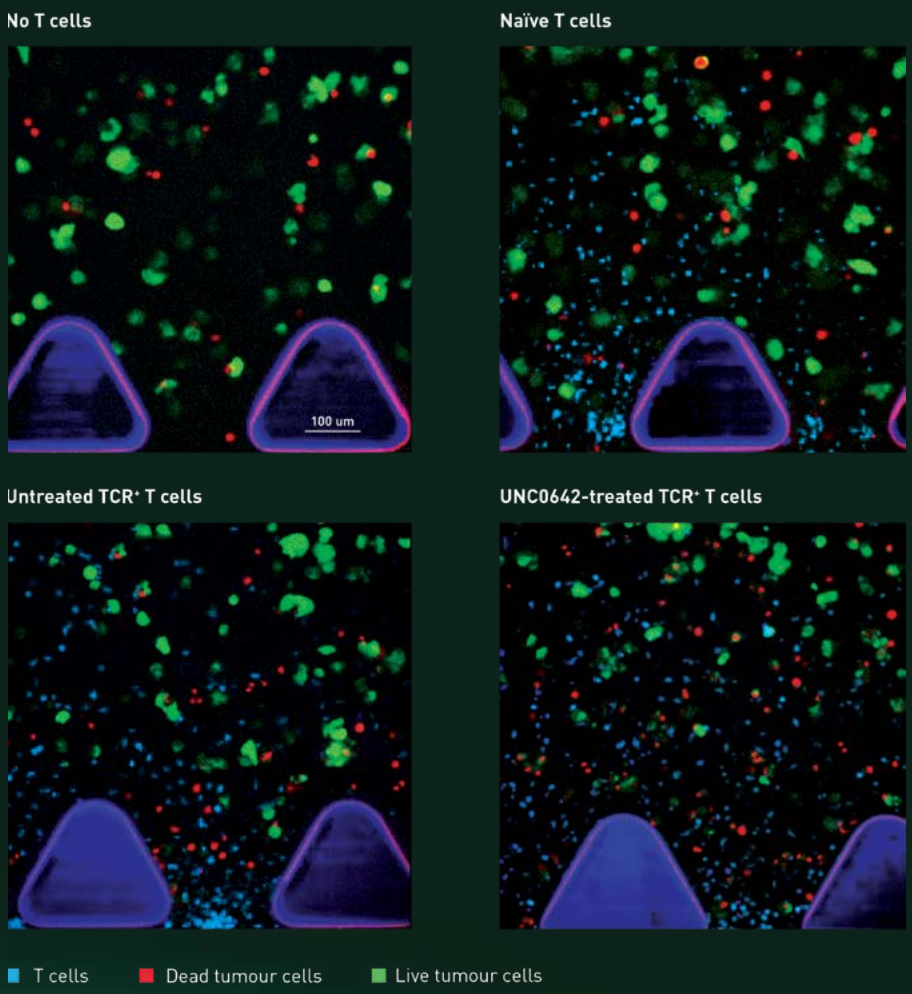
Together, they identified epigenetic inhibitors—substances that modify the chemical tags on DNA, tweaking gene expression without altering the underlying genetic code—as a means of creating next-generation T cell therapies.

"We focused on epigenetic inhibitors to induce a durable effect on the engineered T cells even after the therapy is removed," Pavesi explained. "To screen for potential inhibitors, we used 3D cell culture systems that mimic the complex cellular interactions and tumour microenvironment found in the human body."

The researchers found that inhibiting molecules called G9a and GLP enhanced the production of granzyme proteins which boosted cytotoxic cells' tumour-killing capabilities. Pavesi and colleagues also discovered the sweet spot for engineering—introducing G9a/GLP inhibitors when T cells are grown and activated in the lab, before reintroduction into the patient.

"By adding the epigenetic inhibitor solely during this *ex vivo* expansion stage, we sought to maximally enhance the T cells' efficacy against cancer cells, while minimising potential off-target impacts."

Photo credit: MattL_Images / Shutterstock

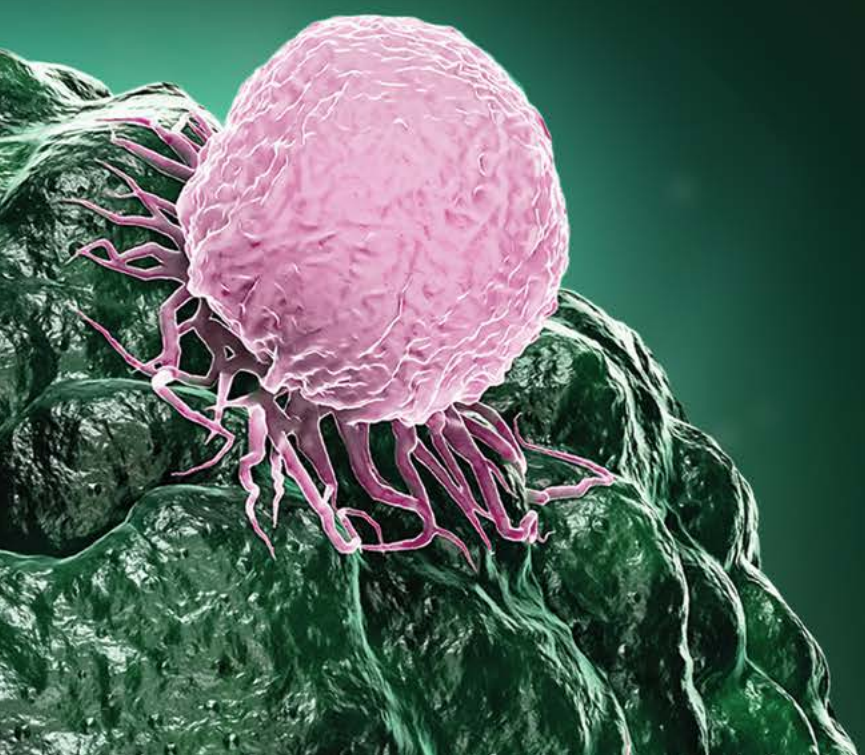


A look at live (green) and dead (red) tumour cells in culture when exposed to different T cell types. Using 3D cytotoxicity assays, the team analysed the degrees of tumour cell death in cultures with (from top left): no T cells; naïve T cells; T cells with activated tumour-targeting receptors (TCR⁺); and TCR⁺ T cells treated with UNC0642, a G9a/GLP inhibitor.

"By adding the epigenetic inhibitor solely during this *ex vivo* expansion stage, we sought to maximally enhance the T cells' efficacy against cancer cells, while minimising potential off-target impacts," said Pavesi, adding that a wash step in the workflow removes excess inhibitor from the T cell preparation, thereby further reducing the risk of toxic side effects.

Tests in both 3D human tumour cell cultures and experimental mice models of liver cancer demonstrated the effectiveness of the G9a/GLP inhibition strategy. The team was excited to find that the approach was successful not only with T cells from healthy donors, but also with T cells with potentially compromised function from patients who had undergone intensive chemotherapy.

Spurred by the success of their study, the team is currently investigating the molecular mechanisms underpinning G9a/GLP inhibition with the hopes of translating their work to a clinical setting in the future. ★



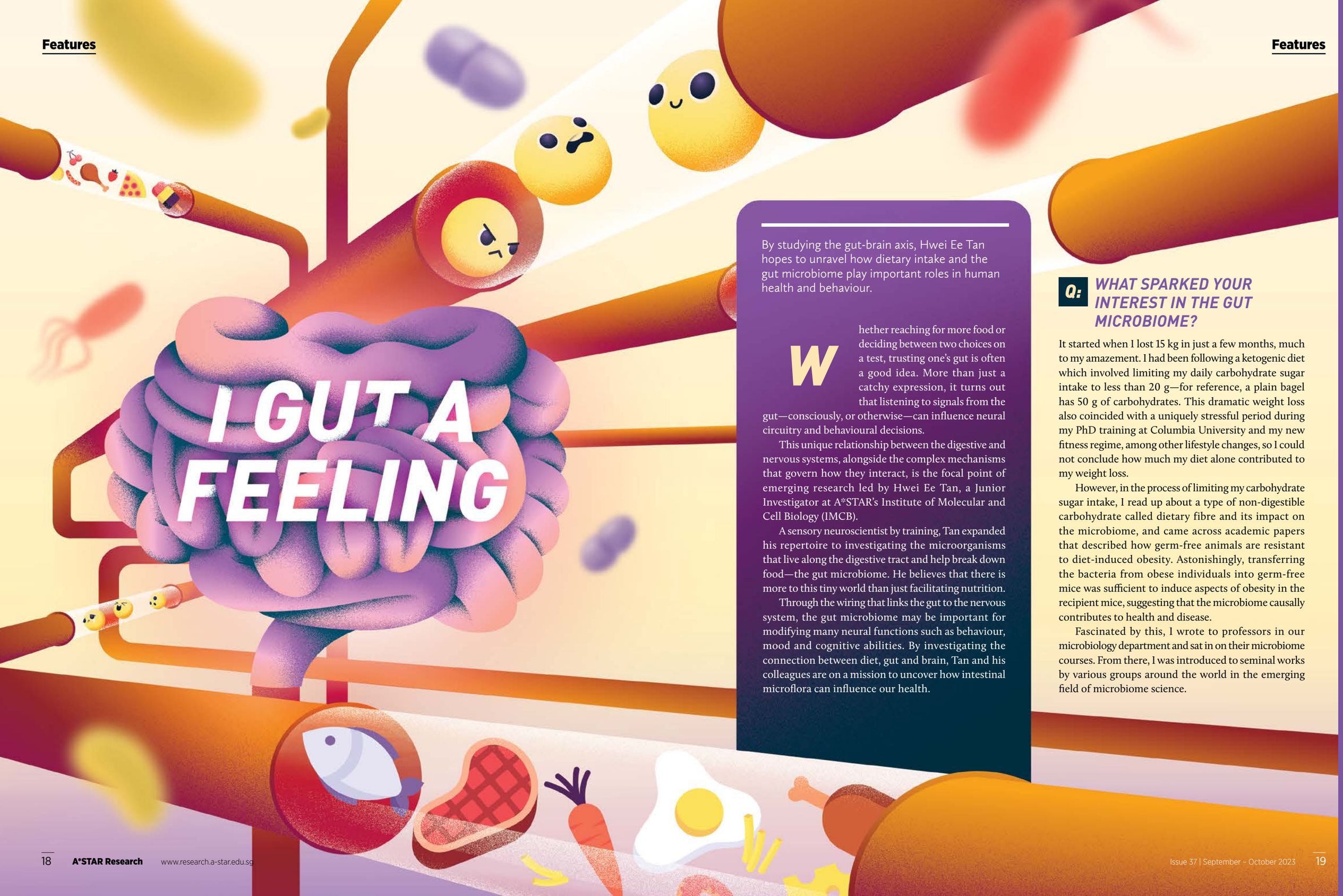
Researcher
Andrea Pavesi, IMCB

IN BRIEF

Epigenetic inhibitors against G9a and GLP administered during the expansion stage of T cell engineering have been shown to improve T cell cytotoxic activity in both cell cultures and mouse models of liver cancer.

1. Lam, M.S.Y., Reales-Calderon, J.A., Ow, J.R., Aw, J.J.Y., Tan, D., *et al.* G9a/GLP inhibition during *ex vivo* lymphocyte expansion increases in vivo cytotoxicity of engineered T cells against hepatocellular carcinoma. *Nature Communications* **14**, 563 (2023).

Features



By studying the gut-brain axis, Hwei Ee Tan hopes to unravel how dietary intake and the gut microbiome play important roles in human health and behaviour.

Whether reaching for more food or deciding between two choices on a test, trusting one's gut is often a good idea. More than just a catchy expression, it turns out that listening to signals from the gut—consciously, or otherwise—can influence neural circuitry and behavioural decisions.

This unique relationship between the digestive and nervous systems, alongside the complex mechanisms that govern how they interact, is the focal point of emerging research led by Hwei Ee Tan, a Junior Investigator at A*STAR's Institute of Molecular and Cell Biology (IMCB).

A sensory neuroscientist by training, Tan expanded his repertoire to investigating the microorganisms that live along the digestive tract and help break down food—the gut microbiome. He believes that there is more to this tiny world than just facilitating nutrition.

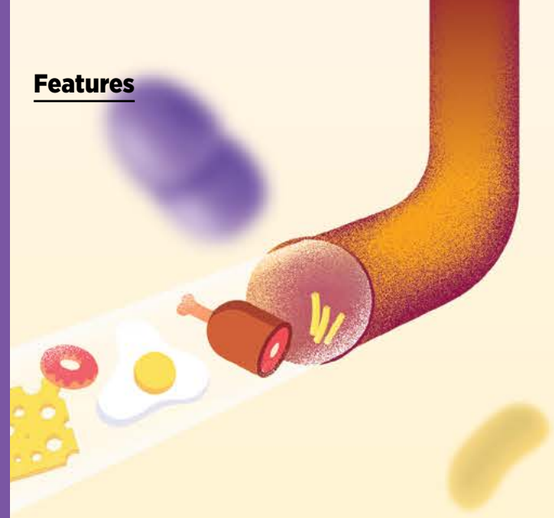
Through the wiring that links the gut to the nervous system, the gut microbiome may be important for modifying many neural functions such as behaviour, mood and cognitive abilities. By investigating the connection between diet, gut and brain, Tan and his colleagues are on a mission to uncover how intestinal microflora can influence our health.

Q: *WHAT SPARKED YOUR INTEREST IN THE GUT MICROBIOME?*

It started when I lost 15 kg in just a few months, much to my amazement. I had been following a ketogenic diet which involved limiting my daily carbohydrate sugar intake to less than 20 g—for reference, a plain bagel has 50 g of carbohydrates. This dramatic weight loss also coincided with a uniquely stressful period during my PhD training at Columbia University and my new fitness regime, among other lifestyle changes, so I could not conclude how much my diet alone contributed to my weight loss.

However, in the process of limiting my carbohydrate sugar intake, I read up about a type of non-digestible carbohydrate called dietary fibre and its impact on the microbiome, and came across academic papers that described how germ-free animals are resistant to diet-induced obesity. Astonishingly, transferring the bacteria from obese individuals into germ-free mice was sufficient to induce aspects of obesity in the recipient mice, suggesting that the microbiome causally contributes to health and disease.

Fascinated by this, I wrote to professors in our microbiology department and sat in on their microbiome courses. From there, I was introduced to seminal works by various groups around the world in the emerging field of microbiome science.



Q: TELL US ABOUT YOUR RESEARCH JOURNEY TO DATE.

My research journey started in molecular and developmental biology. As an undergraduate intern at the University of California, Berkeley, I studied the biological development of structural colouration in the wing scales of butterflies and moths. From iridescent blues to vibrant purples, some wing colours come from nanostructures that bend light.

In the following year, I studied the other side of this phenomenon: how do we see light and its component colours? Through an exchange programme at Osaka University, my research focused on rhodopsin, the molecule that converts light into biochemical signals in our cells.

However, sensing is not the same as perceiving, which happens higher up in the brain. As such, in graduate school I decided to study how sensory stimuli are perceived in our brains. At Columbia University, we studied the perception of taste. To mice and humans, sweet compounds are universally attractive and bitter compounds are innately aversive. We dissected how taste stimuli activate consistent brain circuits that lead to these reactions. Serendipitously, we found taste is dispensable for sugar preference, and subsequently uncovered novel gut-to-brain circuits that mediate sugar and fat preferences.

Upon returning to Singapore, I joined IMCB to conduct independent, postdoctoral research on the microbiome and gut-brain axis. I also secured additional research support from the Young Individual Research Grant by the National Medical Research Council; and the LKCMedicine-Imperial College London postdoctoral fellowship under Nanyang Technological University.

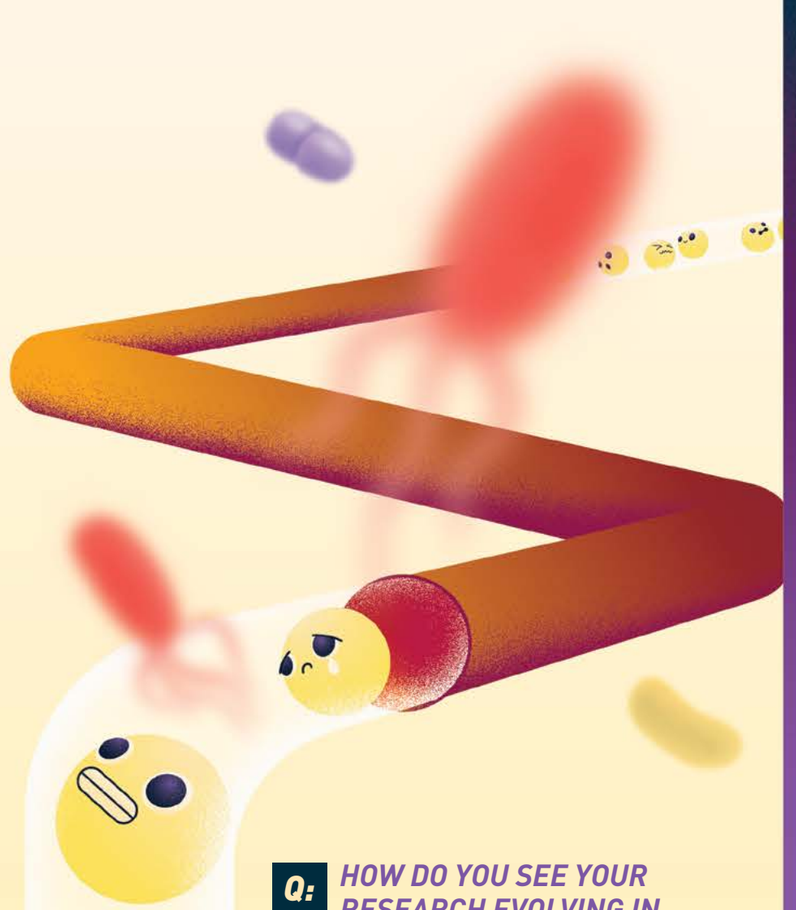
Q: CAN YOU TELL US MORE ABOUT YOUR ONGOING RESEARCH?

Phrases such as 'gut feelings' and 'butterflies in my stomach' suggest that elements in our gut shape our emotions and behaviours. In fact, the gut microbiome is associated with many aspects of health and behaviour—from metabolic health and eating disorders to cognition and depression.

This realisation aligns with the research I have been working on. Over the past years, my colleagues and I have discovered how nutrients in our food activate a neural circuit from the intestines to the brain. I wondered whether this circuit, commonly referred to as the gut-brain axis, could also explain how diet and microbiome interactions influence our health and behaviours. More recently, our research has demonstrated exciting evidence that substrates in our gut engage specific neural circuits in the brain to influence internal states and behaviours.

Hwei Ee Tan

Junior Investigator
Institute of Molecular and Cell Biology (IMCB), A*STAR



Q: HOW DO YOU SEE YOUR RESEARCH EVOLVING IN THE NEXT FEW YEARS?

The Human Genome Project has already dramatically transformed society, health and medicine. Now, another genomic revolution marked by the Human Microbiome Project is catalysing rapid advances in our understanding of the microbiome. Collectively, the bacteria living in our body encode over 46 million genes, whereas the human genome encodes less than a thousandth of that. Its sheer diversity and size make studying the microbiome far more challenging, but also represent the immense potential of such research endeavours.

Elucidating the biological mechanisms of the gut-brain axis, especially including the contribution of the complex gut microbiome, will require continued investment in basic research and will rely on multidisciplinary, collaborative teams. By working together with the various neuroscience and microbiome research groups in Singapore, as well as international collaborators, I hope our research can unveil important insights on the microbiome-gut-brain axis in the years to come.

Features

"Phrases such as 'gut feelings' and 'butterflies in my stomach' suggest that elements in our gut shape our emotions and behaviours. In fact, the gut microbiome is associated with many aspects of health and behaviour—from metabolic health and eating disorders to cognition and depression."

— Hwei Ee Tan, Junior Investigator at A*STAR's Institute of Molecular and Cell Biology (IMCB)

Q: WHAT ADVICE CAN YOU SHARE WITH STUDENTS HOPING TO PURSUE A CAREER IN RESEARCH?

I consider a career in research more of a lifestyle choice than a job. I find joy in testing ideas, troubleshooting problems and making discoveries, so a research career is an excellent fit for me.

The research process involves a lot of trial-and-error and navigating obstacles that come our way, so resilience and problem-solving skills are important. We are also more likely to stay motivated and driven if we find the science that captivates and excites us. To find their passion, I encourage students to experience a variety of research areas by taking advantage of the wealth of science opportunities in Singapore and abroad. ★

CHEMICAL ENGINEERING

Clean chemical plants create a buzz

Researchers identify a high-efficiency approach that can cut greenhouse gas emissions from plastics and fertiliser manufacturing.

The simplest everyday acts—like carrying groceries home in plastic bags—can leave a trail of carbon footprints with potentially devastating impacts on our planet. Within the chemical industry, over half of all greenhouse gas (GHG) emissions come from the basic processes to make just two groups of products: ammonia-based fertilisers for farming, and oxygen-containing chemicals (oxygenates) for plastics.

"We make large volumes of ammonia and oxygenates due to how pervasive they are in modern life," said Wan Ru Leow, a Scientist at A*STAR's Institute of Sustainability for Chemicals, Energy and Environment (ISCE²). "Unfortunately, both products use manufacturing processes with high carbon footprints, leading to a global release of 0.9 billion tonnes of carbon dioxide (CO_2) each year."

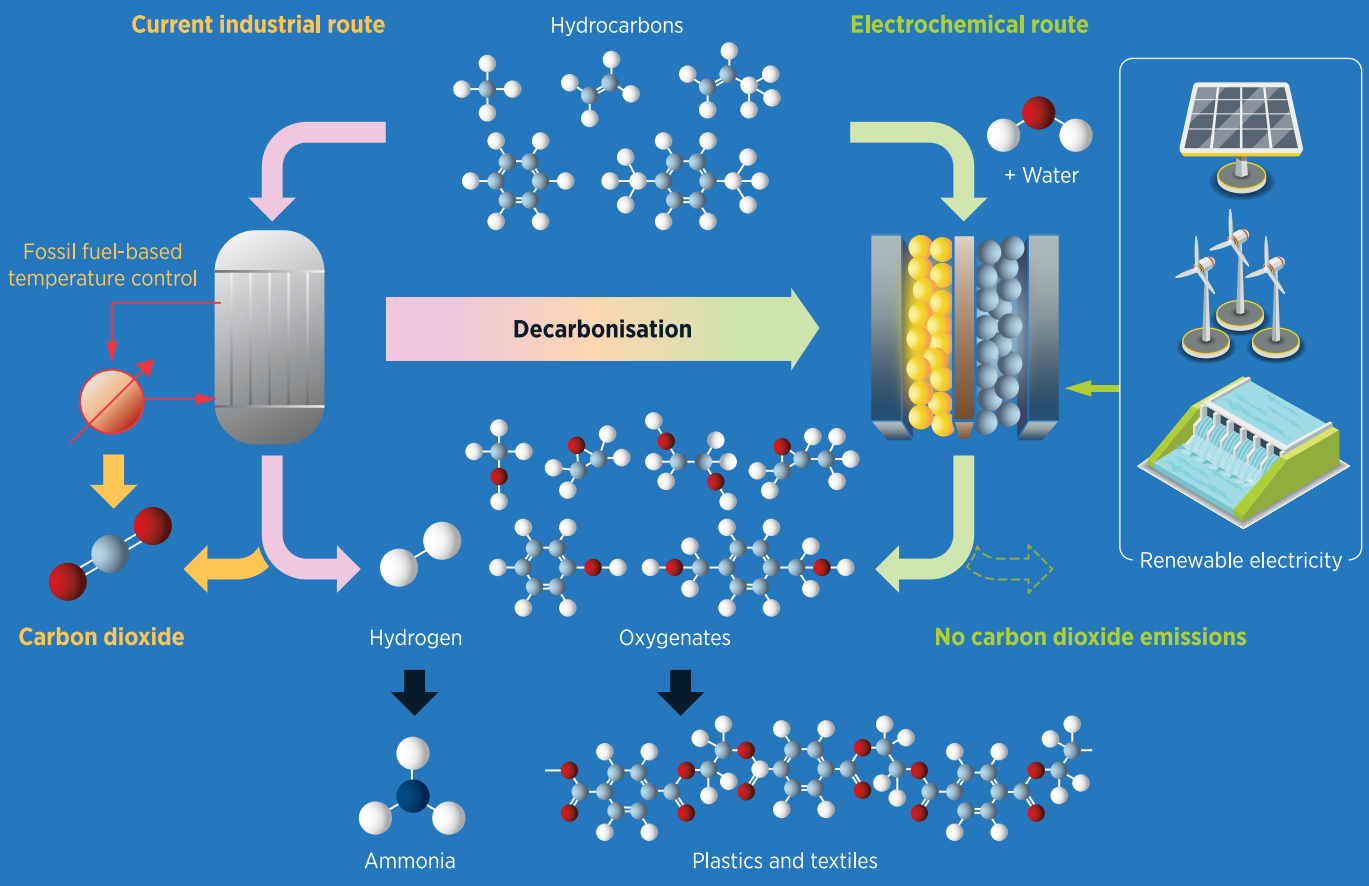
Leow explained that hydrogen gas, a key ingredient in ammonia, is currently extracted from methane using high-temperature reactions that directly create CO_2 and are often powered by fossil fuels. Likewise, to turn hydrocarbons into oxygenates calls not only for energy-intensive heating and cooling, but inefficient reactions where up to 20 percent of a hydrocarbon feedstock may be lost as waste CO_2.

Previous studies have shown that electrolysers—devices that use electricity, rather than heat, to facilitate chemical reactions—can reduce GHG emissions from chemical manufacturing processes, sparking a greener future for the industry. Leow joined forces with international collaborators to explore the potential of electrolysers that coupled two processes: electrified hydrocarbon-to-oxygenate conversion, and water-to-hydrogen evolution reactions.

Via a thorough life-cycle assessment, Leow and colleagues aimed to weigh up the approach's efficiency and measure their GHG emissions versus traditional manufacturing methods. They found that by carefully tuning manufacturing conditions for optimal hydrocarbon-to-oxygenate conversion, they could cut the GHG emissions involved in making ammonia and oxygenates by up to 88 percent.

To their surprise, the team also found that the coupled systems could substantially slash GHG emissions even without using clean energy sources such as wind or solar power. Emissions were reduced by up to

Photo credit: Andreas Felske / Unsplash



A conceptual diagram for how electrolyser systems can cut carbon emissions in ammonia and plastics manufacturing. Apart from replacing fossil fuel-based inputs with renewable energy, electrolysers that couple two chemical processes (e.g., hydrocarbon-to-oxygenate conversion and hydrogen evolution from water) can make more efficient use of both energy and industrial feedstocks.

"We make large volumes of ammonia and oxygenates due to how pervasive they are in modern life."

39 percent even with power grids using primarily fossil fuel-based electricity, such as those found in China and the United States.

"This is important as low-carbon electricity is still limited in most industrialised countries today," said Leow, adding that as around 20 percent of global chemical sites manufacture both ammonia and oxygenates on-site, these facilities represent prime targets for implementing electrolyser technologies.

The study provides much-needed insights and opportunities that Leow hopes will spur positive change in tomorrow's chemical manufacturing industries and encourage the scientific community to further develop such 'carbon-lite' manufacturing processes.

Moving forward, the team is positioning themselves to tackle other areas for improvement in the chemical industry, such as the development of greener hydrocarbon building blocks to pave the way for a carbon-neutral future. ★

Researcher
Wan Ru Leow, ISCE²

IN BRIEF
Electrolyser systems that couple hydrocarbon-to-oxygenate conversion with hydrogen evolution reactions can reduce carbon dioxide emissions from chemicals manufacturing by up to 88 percent on green electricity and up to 39 percent on fossil fuel-dependent grids.

1. Leow, W.R., Völker, S., Meys, R., Huang, J.E., Jaffer, S.A., *et al.* Electrified hydrocarbon-to-oxygenates coupled to hydrogen evolution for efficient greenhouse gas mitigation. *Nature Communications* **14**, 1954 (2023).

CATALYSIS

New electron highways uncovered

Subtle molecular differences in nickel-based electrocatalysts can open the path to more efficient water-splitting chemical reactions for clean energy generation.

Since the Industrial Revolution, we've leaned heavily on burning fossil fuels to power our homes, factories and offices. Through combustion reactions, we break down hydrocarbon molecules in oil, coal and natural gas to release not just energy but carbon dioxide, a major contributor to climate change.

Thankfully, greener alternative fuels are close at hand. These include hydrogen, which can be cleanly produced by splitting water using renewable electricity in a process called water electrolysis. Consisting of two half reactions—the oxygen evolution reaction (OER) and the hydrogen evolution reaction (HER)—water electrolysis produces hydrogen, which can then be burned in fuel cells that convert it back to water.

However, a bump in the road is that today's water-splitting technologies still need efficiency boosts before they can be rolled out into green energy infrastructure. To that end, researchers like Shibo Xi, a Senior Scientist at A*STAR's Institute of Sustainability for Chemicals, Energy and Environment (ISCE^2), are examining how chemical electrocatalysts such as nickel oxide hydroxides (NiOOH) can enhance OERs.

Previous work led by Xi found that seemingly identical-looking NiOOH variants derived from different starting materials turned out to exhibit varying OER activities, suggesting that the catalysts' structures might hold clues to unlocking their optimal performance.

"However, there have been challenges in determining these variations due to our past reliance on partially-reconstructed models," explained Xi. "These models aren't entirely accurate in representing the structures of electrocatalysts, which prevented us from fully understanding how they affect OER efficiency."

To bridge this gap, Xi and colleagues from A*STAR's Institute of High Performance Computing (IHPC) and the National University of Singapore used an advanced, high-resolution approach to investigate how using one of three different possible starting materials to create NiOOHs—NiS_2, $NiSe_2$ and $Ni5P_4$—exerted an effect on the resulting compound's OER-catalysing ability.

"A broader highway allows more electrons to move more freely, which translates to enhanced catalytic performance."

Using a technique called X-ray absorption fine structure spectroscopy, they focused on probing the local structures around nickel and oxygen atoms. Through their analyses, they established never-before-seen connections between the distortion of the NiO_6 octahedron within the NiOOH, a broadening of the compound's density of states (e_g*), and an enhanced ability to catalyse OERs.

"Think of the e_g* band as a highway for electrons," said Xi. "A broader highway allows more electrons to move more freely, which translates to enhanced catalytic performance."

The researchers also tested this concept in a different binary nickel-iron oxyhydroxide catalyst with similar results, suggesting that molecular design strategies to broaden e_g* bands could lead to a new generation of high-efficiency OER electrocatalysts—and another step towards a clean energy future.

Xi said that the group is currently exploring how variations in catalyst boosters called dopants could further enhance NiOOHs' catalytic capacities. "By understanding this relationship, we can further optimise the efficiency of materials used for water-splitting reactions," concluded Xi. ★

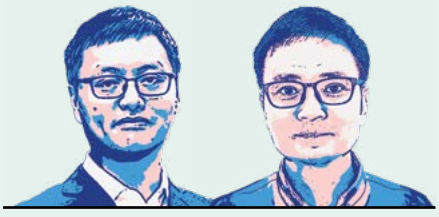


Photo credit: Sebastian Sørensen / Pexel

Researchers
Shibo Xi, ISCE^2 and Zhigen Yu, IHPC

IN BRIEF
Nickel oxyhydroxide electrocatalysts derived from different starting compounds show varying distortions in electronic band structure, which influence their electron transfer abilities and catalytic performance in oxygen evolution reactions.

1. Zhong, H., Wang, X., Sun, G., Tang, Y., Tan, S., *et al.* Optimization of oxygen evolution activity by tuning e_g* band broadening in nickel oxyhydroxide. *Energy & Environmental Science* **16** (2), 641–652 (2023).

MATERIALS

Crack-resistant alloys take off

A new ultra-strong, ductile aluminium alloy overcomes the long-standing problem of cracking, opening up new possibilities for 3D printing high-strength aluminium aerospace components.

There's a careful balancing act involved in building aircraft components—they need to be strong and safe, while staying light to maximise fuel efficiency. At around one-third the weight of steel, aluminium alloys have become the go-to choice for this tough ask thanks to their remarkable strength and lightweight resilience.

Another advantage of aluminium alloys is that they can be manufactured using selective laser melting (SLM), a method akin to 3D printing. SLM allows manufacturers to fabricate intricate metallic components with complex geometries.

However, SLM can stumble when working with specific alloys such as Al7000, a blend of aluminium, zinc and magnesium commonly used in aeroplane manufacturing.

"When the Al7000 series undergoes the SLM process, it often shows signs of cracking, attributed to its inherent microstructure of columnar grains," said Sharon Nai, a Senior Principal Scientist and R&D Director at A*STAR's Singapore Institute of Manufacturing Technology (SIMTech). "Such vulnerabilities can compromise the alloy's strength and durability, which are vital for aerospace use."

Together with researchers from the Southern University of Science and Technology, China and the Max-Planck-Institut für Eisenforschung, Germany, Nai led a team set on taking Al7000 to new heights by developing an alloy variant that can be produced using SLM. They first formulated a new alloy composition by incorporating elements like scandium and zirconium into Al7000. These additions were designed to boost the alloy's microstructure, minimising its cracking risk and bolstering its mechanical strength.

"Producing stronger, more resilient components using SLM can revolutionise how we design and manufacture crucial components—potentially leading to lighter, more fuel-efficient aircraft and vehicles."

The team then faced a complex optimisation phase: they had to find the perfect balance of microstructural features, including grain size and the presence of specific phases, to achieve the highest yield strength while maintaining reasonable ductility.

After a comprehensive series of mechanical tests, Nai and colleagues reported a high yield strength of 647 MPa with a reasonable ductility of 11.6 percent.

Speaking on the impact of their work on the aerospace engineering and manufacturing sectors, Nai said, "Producing stronger, more resilient components using SLM can revolutionise how we design and manufacture crucial components—potentially leading to lighter, more fuel-efficient aircraft and vehicles."

With new horizons for their enhanced Al7000 alloy in sight, A*STAR's researchers are working closely with their industry partner, Proterial, to commercialise this technology while exploring whether a similar approach can be used to tackle similar alloys that have challenged SLM. ★

Researcher
Sharon Nai, SIMTech

IN BRIEF
By adding scandium and zirconium to the Al7000 alloy series during selective laser melting, researchers optimised the material formulation to produce alloys with high yield strength and ductility.

1. Zhu, Z., Ng, F.L., Seet, H.L., Lu, W., Liebscher, C.H., *et al.* Superior mechanical properties of a selective-laser-melted AlZnMgCuScZr alloy enabled by a tunable hierarchical microstructure and dual-nanoprecipitation. *Materials Today* **52**, 90-101 (2022).

Photo credit: Max Zhdanov / Unsplash

ARTIFICIAL INTELLIGENCE

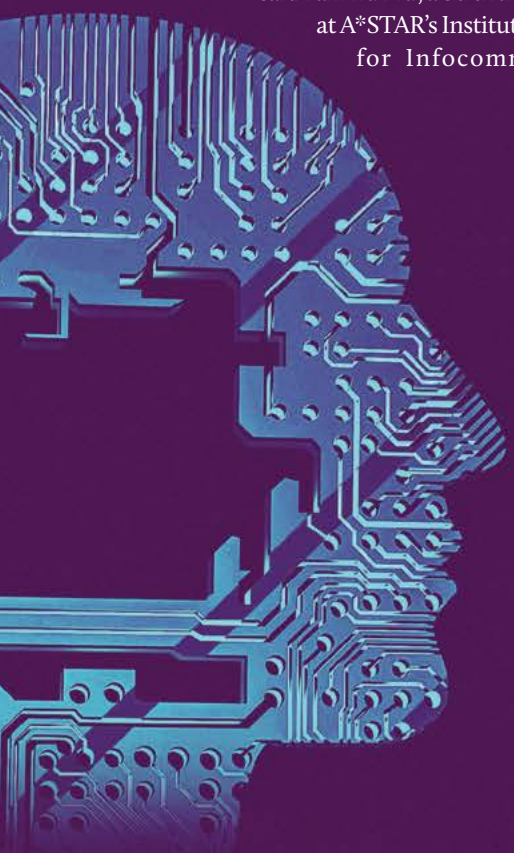
Making machines wonder

Researchers teach artificial intelligence systems how to process information by mimicking human introspection.

What if you had accepted that job offer? Or if you had invested in that stock years ago? The ability to ponder on the infinite spectrum of hypothetical scenarios—a process known as counterfactual reasoning—is a natural part of the human experience.

In the world of artificial intelligence (AI), scientists are working on instilling a similar sense of inquisitiveness into machines. Until now, they've focused mostly on training AI to understand cause-and-effect type of relationships, but it's much tougher to nudge AI to wonder, "What if?"

"Without a 'mental' framework and logical structure, it's hard for AI to truly grasp counterfactual reasoning," said Yanzhu Liu, a Scientist at A*STAR's Institute for Infocomm Research (I²R) and Centre for Frontier AI Research (CFAR).



Liu led a research team to build a new framework based on structural causal models (SCM), which enables AI to predict how things would have evolved differently in a system if certain conditions or events differed from what actually occurred. Termed 'counterfactual dynamics forecasting', this technique lets AI study real events and then, drawing from them, forecast the progression of hypothetical situations over time.

"This new formulation not only quantifies relevance and dissimilarity in counterfactual reasoning, but also lays the groundwork for integrating such reasoning into deep neural networks," said Liu, adding that SCM uses both middle-level abstraction and low-level quantitation computation.

"This new formulation not only quantifies relevance and dissimilarity in counterfactual reasoning, but also lays the groundwork for integrating such reasoning into deep neural networks."

Liu and colleagues tested their SCM framework on two dynamical AI systems and found it to be effective. Their results suggest that in future, rather than just being a tool for repetitive tasks, AI can take more of an active role in supporting many different industries.

Consider health monitoring systems that collect data on vital signs and pre-emptively issue warnings based on potential health concerns. Likewise, in the sports arena, AI-based tools may evaluate an athlete's potential performance by simulating actions they have yet to make—all rooted in real-time data.

With these exciting possibilities in view, the researchers have outlined future steps to amplify their study's impact. While their current work relies on simulated data, they intend to gather more large-scale, practical data from real-world scenarios to put the framework through more stringent tests. They are also addressing bottlenecks in AI training protocols.

"Currently, manually pairing up instances for training is a time-consuming task," added Liu. "To streamline this, we are exploring ways in which the AI system can autonomously pinpoint and pair pertinent data segments, a process which can significantly enhance the speed and depth at which the system learns and evolves." ★

Researchers
Yanzhu Liu, Ying Sun and Joo-Hwee Lim, I²R and CFAR

IN BRIEF
Counterfactual dynamics forecasting allows AI to predict hypothetical outcomes from real-time data, a feature which could revolutionise fields like video technology and healthcare.

1. Liu, Y., Sun, Y. and Lim, J.-H. Counterfactual dynamics forecasting—a new setting of quantitative reasoning. *The Thirty-Seventh AAAI Conference on Artificial Intelligence* **37** (2), 1764-1771 (2023).

Photo credit: Steve Johnson / Unsplash

TRANSPORTATION

Traffic prediction framework gets the green light

A new machine learning platform offers more accurate traffic predictions for safer, less-congested roads.

It's hard to escape bumper-to-bumper traffic during peak hours, but high-powered computational platforms can help us get our cities moving smoothly again. Traffic prediction analyses large amounts of data from traffic sensors and is an important aspect of managing traffic flow.

"Accurate traffic prediction empowers road users to make informed decisions and contributes to the alleviation of traffic congestion," explained Peisheng Qian and Ziyuan Zhao, Research Engineers at A*STAR's Institute for Infocomm Research (I^2R). They added that these systems can also enhance the efficiency of public transport systems and promote safety.

However, the root of the challenge lies in the dynamic, ever-changing nature of traffic. Moreover, road congestion is dependent not only on current road conditions, but also on events that may have already occurred.

One machine learning (ML) model, spatial-temporal graph neural networks (GNNs), is particularly suited for this problem with its ability to make deductions using historical information from any given node alongside neighbouring nodes. Nonetheless, GNNs face limitations when the target prediction is outside the primary region of interest in the data distribution, which is known to cause accuracy levels to plummet.

Qian and Zhao worked with colleagues from Sichuan University, China and the Nanyang Technological University, Singapore to fundamentally change how the ML model is optimised for the accuracy of traffic predictions.

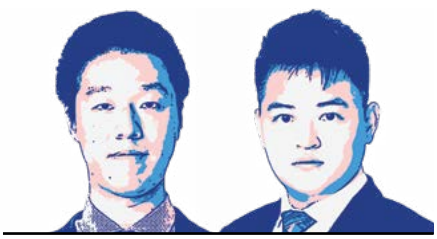
"Choosing an appropriate loss function prevents regression models from overfitting to outlier points, or classification models from overfitting to the majority class," noted the duo.

The team's new loss function, dubbed mean-residue loss, involves a two-step process: conditional distribution learning followed by speed regression. In the first step, traffic sensor data is analysed to understand the conditional probability distribution of speeds given certain conditions. Next, information from the learned conditional distribution is leveraged to predict actual speed values.

They tested their model against current state-of-the-art traffic prediction platforms using three widely used traffic datasets, with the results of experimental and theoretical demonstrations putting their model in the top spot.

"Our approach can be advantageous in other domains characterised by spatial-temporal correlations, including bioinformatics, climate science, video analysis and supply chain management," said Qian. The team is currently exploring their GNN mean-residue loss approach for other applications such as age estimation. ★

"Accurate traffic prediction empowers road users to make informed decisions and contributes to the alleviation of traffic congestion."



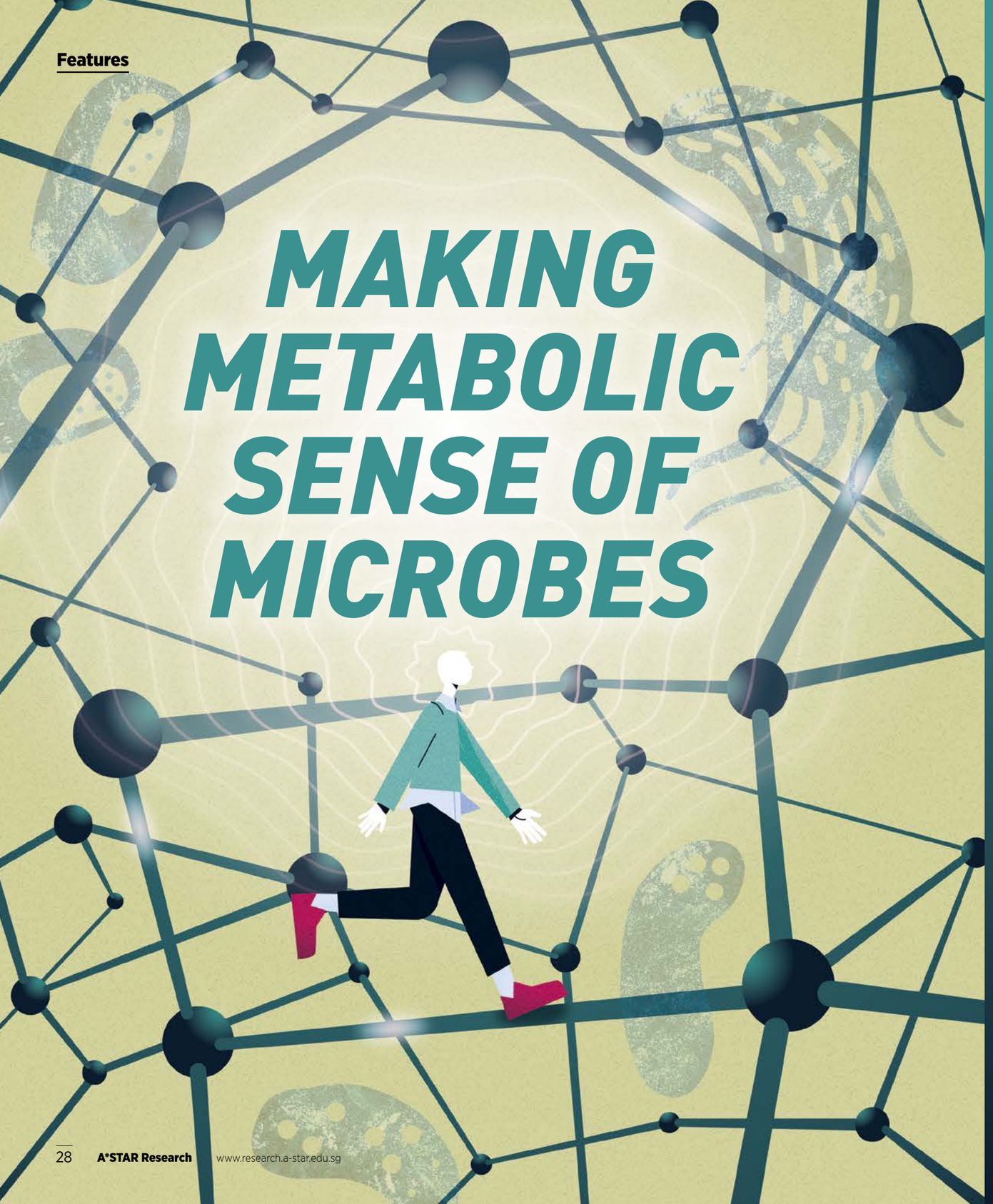
Researchers
Peisheng Qian and Ziyuan Zhao, I^2R

IN BRIEF
By refining the loss function, researchers demonstrate how mitigating inaccuracies in data overfitting can create more reliable machine learning platforms for traffic prediction and other applications.

1. Zeng, Z., Zhao, W., Qian, P., Zhou, Y., Zhao, Z., *et al.* Robust traffic prediction from spatial-temporal data based on conditional distribution learning. *IEEE Transactions on Cybernetics* **52** (12), 13458-13471 (2022).

Photo credit: Denys Nevozhai / Unsplash

MAKING METABOLIC SENSE OF MICROBES



A*STAR scholar Phyllis Phuah aims to develop better treatments for metabolic diseases by understanding how gut microbes help (or hinder) the connections between our body and brain.

To achieve peak performance, athletes follow strict diet plans mapped out by nutrition specialists. Bodybuilders alternate between scheduled 'cuts' and 'bulks' to attain the perfect physique. Frail patients in healthcare facilities are advised on planned meals and supplements to meet their nutritional needs.

For the rest of us, the question "what to eat, and when?" is often answered with what our body tells us. We feel that 'talk' as physical signals: lethargy, hunger pangs, a dry (or watering) mouth.

Behind those signals, however, are complex interactions between networks of cells, nerves and organs throughout our body. They monitor our internal environment and prompt our brain about our needs—more salt or sugar?—to keep it in a state of chemical and physical balance, or homeostasis.

What we eat adds another layer of complexity to those interactions. For example, the communities of bacteria that reside in our gut—our microbiome—produce their own metabolites, which can upset the healthy balance our body tries to maintain. Certain foods can promote or hinder the development of different bacterial species, altering the microbiome in ways that have knock-on effects on our bodies, for better or worse.

At A*STAR's Institute of Molecular and Cell Biology (IMCB), Phyllis Phuah works alongside others in the Brain-Body Initiative (BBI) to learn more of how the interactions between the body, diet and microbiome impact human health. Understanding these links could help us develop better treatments for metabolic diseases like type 2 diabetes (T2D) and obesity.

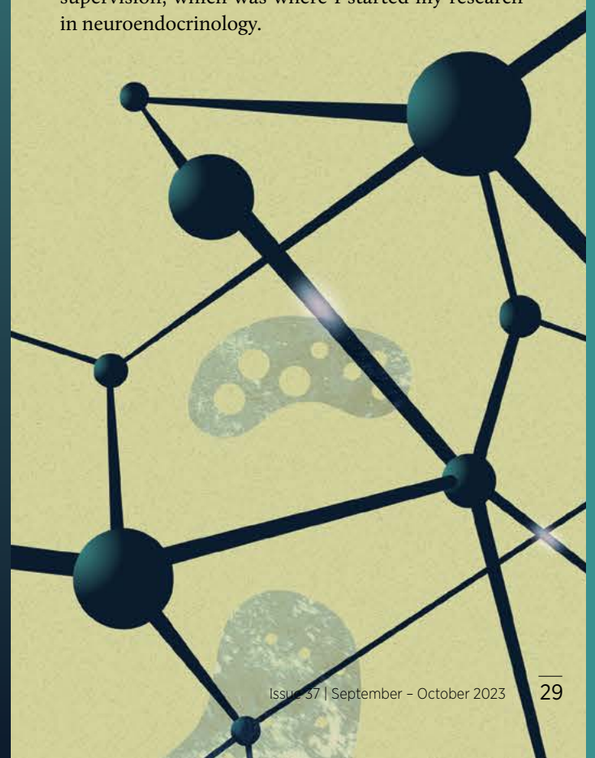
In this interview with *A*STAR Research*, the National Science Scholar shares how her love for biology and fitness led to her interest in obesity research, and her advice for researchers aspiring to study neurometabolism.

Q: WHAT SPARKED YOUR INTEREST IN NEUROMETABOLISM RESEARCH?

During my undergraduate studies at Imperial College London, one of most interesting lectures I attended was on anti-obesity drugs. This was when I first learnt that some of the most promising drug therapies in the obesity field involved manipulating the normal gut hormone system to induce satiety and reduce appetite.

I was deeply intrigued and wanted to better understand the science underpinning anti-obesity drugs. Furthermore, as a fitness enthusiast, I enjoy reading about exercise physiology, different diets like intermittent fasting, keto and 'performance-enhancing' nutrition. Studying obesity felt like a natural fit. Furthermore, with the rising numbers of individuals living with metabolic diseases globally, I thought that contributing to obesity research would be deeply meaningful and impactful.

I reached out to the lecturer, Kevin Murphy, and the rest is history. I undertook a PhD degree under his supervision, which was where I started my research in neuroendocrinology.



Q: TELL US ABOUT YOUR JOURNEY AS A YOUNG RESEARCHER.

I had always enjoyed biology lessons in school because I love learning about how the human body works. Applying for the National Science Scholarship felt like an obvious choice; it provided me with the opportunity to pursue a world-class education for both my undergraduate and PhD studies.

During this time, I grew both as a scientific thinker and as a person. I learnt so much about good science from the many brilliant scientists within my department and built professional networks at international conferences.

For my PhD degree, I studied indole (a gut microbial metabolite) and its effects on hormone secretion and glucose control. I also developed a keen appreciation for the gut-brain axis. I found it fascinating how the gut, which senses nutrients consumed during a meal, communicates with the brain to regulate body functions like energy homeostasis. Some questions I've always wondered about started to make sense—how do we know when to stop eating? Why do we feel 'hangry' when we haven't eaten?

I was intrigued to further pursue this area of research. I was quite fortunate that there was a cluster of neurometabolism labs at IMCB, and the BBI research programme was just starting up in A*STAR towards the end of my PhD studies. It all aligned perfectly with my research interests and created an exciting space for me to contribute to after I returned to Singapore.

"I believe that we're only at the tip of the iceberg of unravelling the complexities of brain-body circuits. We're only beginning to appreciate the role of inter-organ neural circuits in metabolic regulation. I think it is exciting that many research groups have started moving beyond the gut."

— Phyllis Phuah, National Science Scholar (BS-PhD) at A*STAR's Institute of Molecular and Cell Biology (IMCB)

Q: CAN YOU TELL US ABOUT YOUR CURRENT WORK AT A*STAR?

As a postdoctoral research fellow in Sarah Luo's lab, I've been part of the collaborative BBI to better understand host-diet-microbiome interactions—which has been very exciting!

Using data obtained from the Growing Up in Singapore Towards healthy Outcomes (GUSTO) birth cohort study, we've identified some microbe species that appear to correlate with signatures of metabolic health or disease. We are now validating these targets using a range of *in vivo* models and are hoping to identify specific microbes that can modulate human metabolic health. One method could be through prebiotic supplementation.

Another project I've been working on looks at teasing out liver-brain neural circuits. We're interested in identifying novel brain regions that are connected to the liver and understanding how these regions may regulate liver function in both health and disease.

Q: WHY ARE METABOLIC BRAIN-BODY CIRCUITS WORTH INVESTIGATING?

I strongly believe that a better understanding of normal human physiology—such as the neural circuits governing feeding and energy expenditure—provides important insights into disease states, like obesity, that can help us identify novel therapeutic targets.

Such research has never been more relevant given the global epidemic of obesity and T2D. One example that comes to mind is the new weight loss drug, tirzapetide, which was developed based on our understanding of how gut hormones normally work in the body to induce satiety and enhance insulin secretion.

In recent years, there have been many exciting new advances in neurobiology that have really shaped our understanding of how our body senses and integrates internal signals to regulate homeostasis. We also now know that in obesity, many of these neural circuits implicated in feeding and reward are dysregulated.

I believe that we're only at the tip of the iceberg of unravelling the complexities of brain-body circuits. We're only beginning to appreciate the role of inter-organ neural circuits in metabolic regulation. I think it is exciting that many research groups have started moving beyond the gut. They're looking at other densely innervated peripheral metabolic organs—like the liver, pancreas and fat—and how they communicate with the brain or with each other to influence organ function.

Q: WHAT DO YOU HOPE TO ACHIEVE AS A YOUNG RESEARCHER?

I hope that my contributions to the research field of neurometabolism will translate into real-world impact. Ultimately, I hope that my work will help to improve human health by identifying novel interventions for the prevention or treatment of chronic metabolic conditions, which will help people enjoy a better quality of life as they live longer.

I also hope that improving the visibility of young female scientists and participating in scientific outreach activities will inspire future generations, especially women, to pursue STEM as a career whether in research or beyond.

Q: WHAT ADVICE WOULD YOU OFFER YOUNG STEM TALENT?

A career in research is a marathon and not a sprint. The most important thing is to never give up. As scientists, we are constantly exposed to failure, and so we must remember not to take it personally and to keep trying again, no matter how daunting it may seem.

Also, treat every day like a school day. The research landscape in Singapore, and science itself, is ever changing. It is so important to keep relevant by staying open to new ideas and learning constantly.

Lastly, don't be afraid to advocate for yourself by seeking out good mentors who can guide and support you along the way. ★

Phyllis Phuah
National Science Scholar (BS-PhD), Institute of Molecular and Cell Biology (IMCB), A*STAR

ADVANCED MANUFACTURING

Solid approaches to fault finding

New equations and methodology enable the uncertainty of porosity measurements to be evaluated in additively manufactured metals for safer, high-quality components.

Sometimes, the empty spaces in a material are just as important as the material itself. Take the porous network inside human bones, for example. These pockets decrease the overall weight of bones while keeping them strong and resilient to impact.

Similarly, the porosity of metal parts made using additive manufacturing (AM) influences their overall physical properties. The AM process can sometimes introduce a level of unwanted defects such as tiny cavities hidden inside the metal, termed porosity.

"These imperfections can compromise the structural integrity of AM components, leading to failure," said Joseph John Lifton, Technical Lead in the Intelligent Product Verification Group at A*STAR's Advanced Remanufacturing and Technology Centre (ARTC).

Yet, accurately gauging porosity in metals fabricated using AM remains a challenge in industry. A technique like optical microscopy, while providing high-resolution images, only offers limited information because test samples have to be ground and polished layer-by-layer, which can cause important defects to be missed entirely. Furthermore, because optical microscopy is destructive, the approach cannot be used for final product verification.

"X-ray computed tomography provides non-destructive, 3D insights into a metal component's porosity, but struggles with scanning large AM components made from dense metals," said Lifton, adding that with further R&D effort, the technique can become the new gold standard for ensuring that AM components are safe and defect-free.

Lifton and his team used the Archimedes' principle, a method widely used in industry to calculate a component's density by first weighing it in air and then in a liquid. Comparing these values to the density of the bulk material allows manufacturers to accurately detect the presence of any porosity.

The team developed equations to calculate the measurement uncertainty—i.e., the doubt associated with a measurement result—of porosity measurements. No measurement result is complete unless accompanied by a statement of uncertainty. The work enables AM researchers and manufacturers to understand the quality of their porosity measurements, and thus make informed engineering decisions on the safety and performance of AM components.

"X-ray computed tomography provides non-destructive, 3D insights into a metal component's porosity, but struggles with scanning large AM components made from dense metals."

Lifton and his team have been awarded funding by the National Additive Manufacturing Innovation Cluster to advance their work on standardising porosity measurement using X-ray computed tomography. "We are also developing methods to measure and characterise the internal surface roughness of AM samples, with a particular focus on internal channels and lattice structures," concluded Lifton. ★

Researcher
Joseph John Lifton, ARTC

IN BRIEF
Uncertainty analysis reveals the quality of porosity measurements for additively manufactured metal parts.

1. Lifton, J.J., Tan, Z.J., Goh, B. and Mutiargo, B. On the uncertainty of porosity measurements of additively manufactured metal parts. *Measurement* **188**, 110616 (2022).

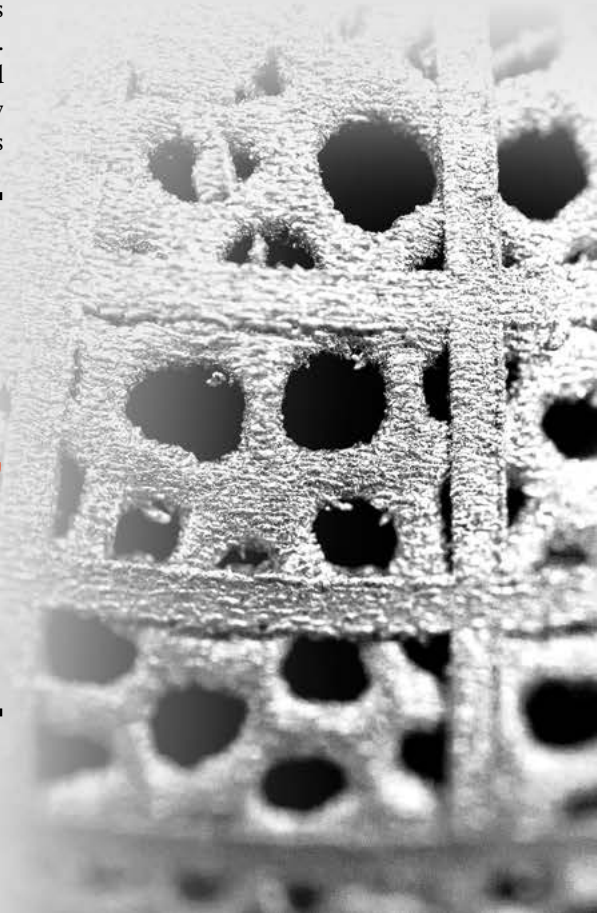


Photo credit: MarinaGrigorivna / Shutterstock

OPTICAL MATERIALS

Rise of the light-benders

With their unique optical properties, customisable ultrathin metasurfaces can enable the next wave of high-performance optoelectronics devices.

Picture the electronics of tomorrow: paper-thin TVs, holographic displays and augmented reality (AR) glasses. Such devices can be made possible by metasurfaces: ultrathin, lightweight materials that can manipulate how light behaves in precise and customisable ways.

For researchers like Ramón Paniagua-Domínguez, Deputy Head of the Advanced Optical Technologies Department at A*STAR's Institute of Materials Research and Engineering (IMRE), metasurfaces can replace traditional optical components for applications ranging from smartphone cameras to light detection and ranging (LiDAR). "They can be 1,000 times thinner than a human hair, making them far more compact than glass lenses," said Paniagua-Domínguez.

However, the first generation of all-dielectric metasurfaces—made from materials like silicon—typically have their light-bending properties set in stone once manufactured. Phase-change materials (PCMs) offer exciting new possibilities for a new generation of metasurface designs, because their optical properties can be modified by external stimuli like heat, light or electricity.

"In a camera, 'zooming' works by moving a bulky system of lenses back and forth, with each lens having fixed optical properties; they bend light in a certain way, and that's it," said Paniagua-Domínguez. "But what if you could dynamically tune a lens to change how it bends light? You could control a camera's zooming using the lens itself, meaning you'd need less electronic parts to achieve the same optical functions."

Still, materials scientists have found it challenging to develop transparent PCM-based metasurfaces that work well in the visible light range; well-known PCMs like germanium-antimony-tellurium (GST), widely used in DVDs, tend to reflect light rather than let it pass through.

In collaboration with Robert Simpson's group from the Singapore University of Technology and Design, Paniagua-Domínguez and the IMRE team investigated a new potential PCM for next-generation programmable metasurfaces: antimony trisulfide (Sb_2S_3). Transparent in the visible spectrum, Sb_2S_3's atoms can be fluidly rearranged between two states—amorphous and crystalline—when subjected to heating or laser light. This alters how they refract light, offering more optical flexibility over conventional silicon-based metasurfaces.

"What sets Sb_2S_3 apart is its swift phase-changing ability, clocking in at nanoseconds, all while being more energy-efficient than conventional devices," said Paniagua-Domínguez. "Plus, since its phase changes don't tamper with its overall structure, the material retains its mechanical robustness."

The researchers reported that their prototype Sb_2S_3 metasurfaces could change the phase of light by an impressive 2π while still allowing most light wavelengths to pass through. Such capabilities would make the material a prime candidate to enhance AR experiences, improve collision sensors in autonomous vehicles, and enable advanced spatial light modulators for holographic projection.

Still, Sb_2S_3 metasurfaces need inherent kinks to be ironed out before they can be considered for use in device prototypes. "Our next steps involve refining the material and ensuring its optical properties stand up to intense long-term use," said Paniagua-Domínguez. "We're also exploring electrical switching mechanisms, aiming for a seamless integration into next-gen electronics." ★

"We're also exploring electrical switching mechanisms, aiming for a seamless integration into next-gen electronics."

Researchers
Ramón Paniagua-Domínguez, Arseniy Kuznetsov and Parikshit Moitra, IMRE

IN BRIEF
Using antimony trisulfide, a novel phase-change material, the researchers developed dynamic, low-energy metasurfaces which can be rapidly tuned for flexible spatial light modulation.

1. Moitra, P., Wang, Y., Liang, X., Lu, L., Poh, A., *et al.* Programmable wavefront control in the visible spectrum using low-loss chalcogenide phase-change metasurfaces. *Advanced Materials* **35** (34), 2205367 (2022).

Photo credit: Arthur Mazi / Unsplash

MATERIALS SCIENCE

Peeling back the layers of emerging materials

Computer simulations uncover novel atomic configurations of layered materials used in electronics and energy storage.

Croissants get their signature flaky texture through a process called lamination, where alternating layers of dough and butter rise in the oven to create the perfect bite. Likewise, MXenes are special materials made up of ultrathin layers of transition metals and carbon atoms.

Their hallmark stratified structures make them remarkable heat and electricity conductors, while also giving them strength and durability—properties that make them highly prized in electronic, technology and energy industries.

However, much of how MXenes' atomic structures influence their properties have remained elusive. Until a few years ago, most MXenes were composed of just one or two metals. Now, experts say tremendous leaps in the field have enabled researchers to double the number of metallic building blocks, significantly expanding both the complexity and potential of these so-called high-entropy (HE) MXenes.

Photo credit: Ricardo Gomez Angel / Unsplash

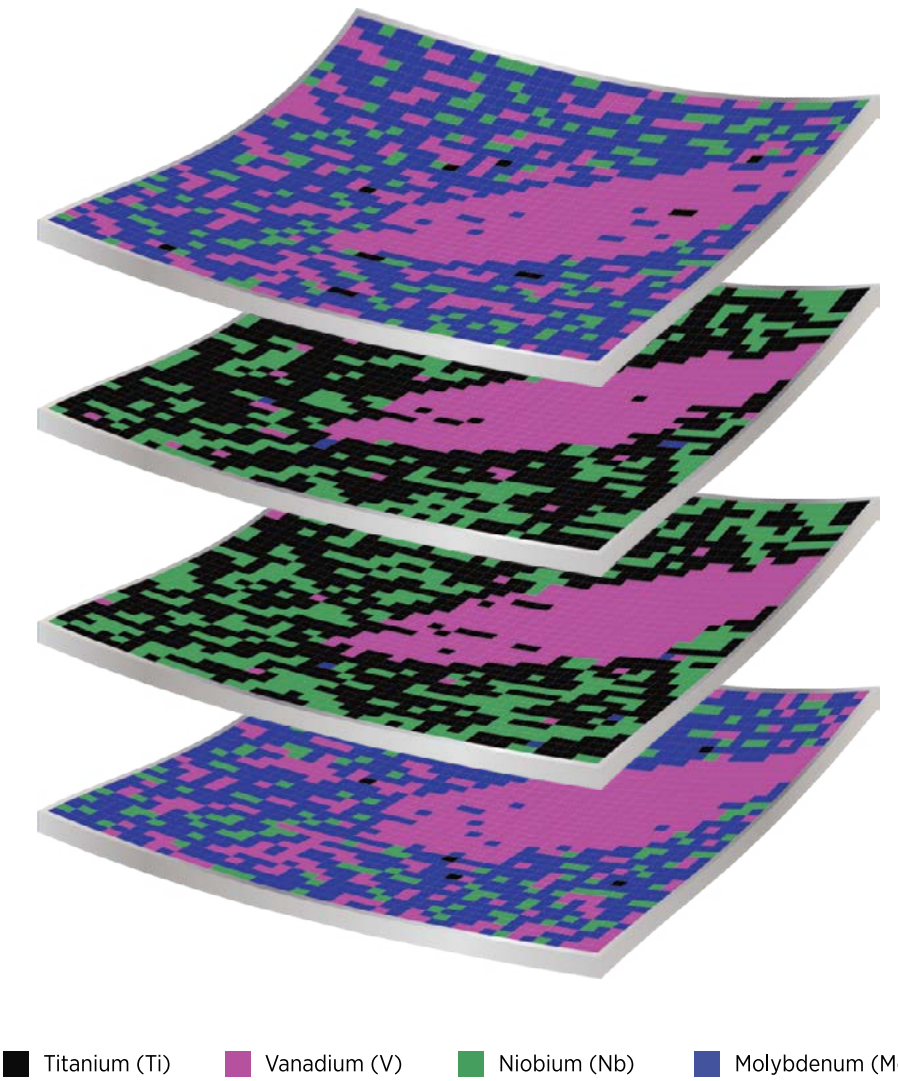
"Designing HE MXenes with certain properties is often a process of experimentation and intuition, especially with the complexity introduced by four metals, which makes navigating the design space challenging," said Teck Leong Tan, a Senior Scientist and the Director of the Materials Science & Chemistry Department at A*STAR's Institute of High Performance Computing (IHPC).

On a mission to unravel the intricacies of HE MXenes, Tan and his team from IHPC collaborated with researchers from Purdue University, using advanced computer simulations to help model how atoms are distributed over the layers. The researchers studied two new HE MXenes ($TiVNbMoC_3$ and $TiVCrMoC_3$) with surprising results.

Contrary to previous assumptions that the elements are randomly distributed, their simulations revealed a preference for Cr to position itself on the material's surface, followed in order by Mo, V, Nb and Ti. Even when the MXenes are heated to high temperatures, they retain this atomic arrangement.

"The precise arrangement of metals can vary based on their composition, allowing us to fine-tune these MXenes for targeted applications," said Tan, who added that these and future studies can help expand the future application landscape of MXenes.

Not stopping here, the research team has plans to collaborate with other materials scientists to validate their simulated predictions on HE MXenes' structure. They also aim to formulate reliable models to simulate and study more of HE MXenes' unique structures. ★



A simulation of the outer and inner atomic layers of the high-entropy MXene $TiVNbMoC_3$ at a relatively low temperature (464 K). Mo and Ti show strong preferences towards outer and inner layers respectively; V and Nb show similar preferences but to a lesser extent.

"The precise arrangement of metals can vary based on their composition, allowing us to fine-tune these MXenes for targeted applications."

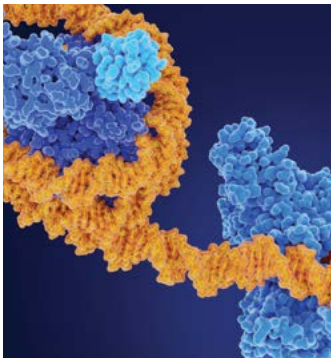
Researcher
Teck Leong Tan,
IHPC

IN BRIEF
For the first time, researchers identify the characteristic way that atoms arrange themselves in high-entropy MXenes to expand their application potential.

1. Leong, Z., Jin, H., Wong, Z.M., Nemani, K., Anasori, B., *et al.* Elucidating the chemical order and disorder in high-entropy MXenes: a high-throughput survey of the atomic configurations in $TiVNbMoC_3$ and $TiVCrMoC_3$. *Chemistry of Materials* **34**, 9062-9071 (2022).

NEXT ISSUE

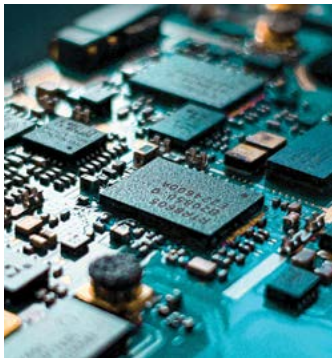
Here's a sneak peek of the material covered in the next issue of *A*STAR Research*



MOLECULAR BIOLOGY

CORRALLING PROTEINS CLAMP DOWN ON CANCER GENES

A newly discovered epigenetic pathway, when disabled, stops aggressive breast cancer cells from further growth.



ELECTRONICS

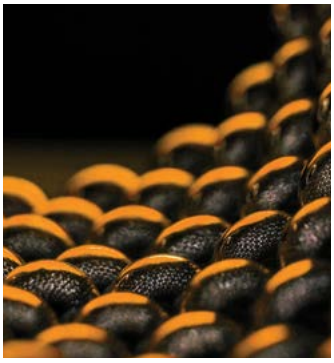
MICRO-NOSES SNIFF OUT GREENHOUSE GASES

New infrared gas sensors can enable compact devices that detect even tiny changes in ambient carbon dioxide and methane levels.

ARTIFICIAL INTELLIGENCE

GETTING AHEAD OF THE CROWD

A new machine learning method helps computer navigation systems predict how groups of pedestrians move in real-world traffic settings.



CATALYSIS

METAL NANOCRYSTALS SUPERCHARGE REACTIONS

Tunable nanoparticles made from multi-metal alloys can boost the efficiency of key chemical reactions in renewable energy systems.

Agency for Science, Technology and Research
SINGAPORE

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Dr Ang Qi Yan
*A*STAR National Science Scholarship (PhD) Recipient*

Senior Research Fellow,
Genome Institute of Singapore

"The brilliance of the stars would be invisible without the vast darkness of space behind them."

Dr Ramanpreet Singh Pahwa
*A*STAR National Science Scholarship (PhD) Recipient*

Scientist III,
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