A*STAR RESEARCH

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Tackling a new wave of digital safety risks

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A*STAR RESEARCH

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EDITORIAL

Agency for Science, Technology and Research

1 Fusionopolis Way, Connexis North Tower, #20-10
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BMRC: Biomedical Research Council
R&TD: Research and Talent Development
SERC: Science and Engineering Research Council
I&E: Innovation and Enterprise
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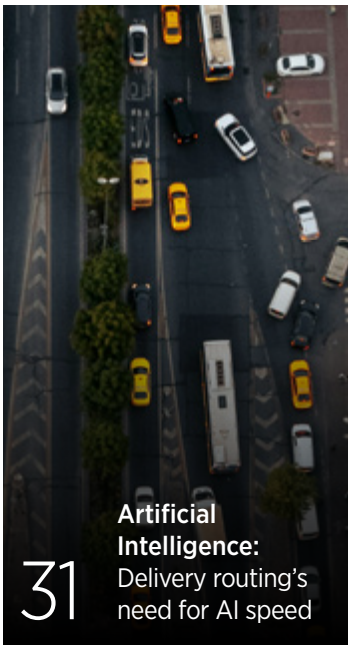

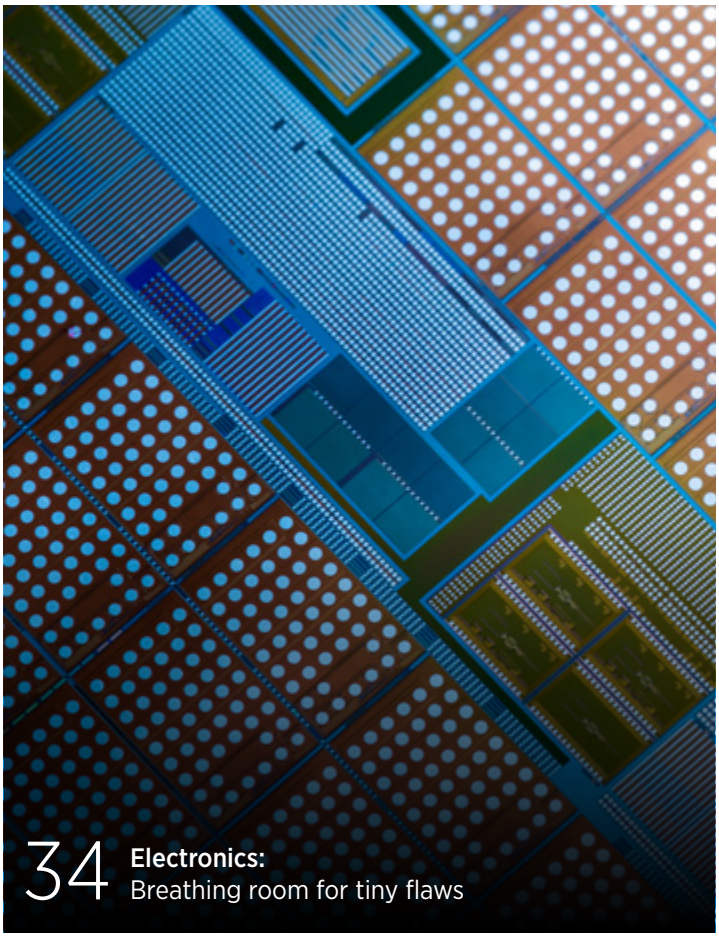

EDITORIAL NOTES

The internet today connects over two-thirds of the world's people to a sea of data and discourse. However, the same tools and platforms behind our modern connectivity are also open to exploitation for a growing tide of increasingly convincing misinformation and complex cybersecurity risks.

Our cover story this issue, 'Hidden hazards (p. 08)', reviews a range of A*STAR-supported R&D initiatives and projects in digital safety. We bring the spotlight to the Online Trust and Safety Research Programme, a recently-initiated funding initiative from Singapore's Ministry of Digital Development and Information to combat online harms with cutting-edge digital solutions.

Looking beyond to other fields, a special feature this issue highlights future innovations in infectious diseases, drug discovery and light-speed computing through three A*STAR researchers recently selected for the National Research Foundation (NRF) Fellowships. In 'Powering the changemakers (p. 20)', we speak to Yi-Hao Chan, Shuang Liu and Bowei Dong about their respective fields and how the fellowship will advance their aspirations in science.

Other articles this issue cover A*STAR research developments ranging from trials of non-invasive methods for skin disease monitoring, to new molecular insights for building better semiconductors. For more on these, take a look at 'Keeping tabs on psoriasis flare-ups (p. 04)' and 'Breathing room for tiny flaws (p. 34)'.

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 X/Twitter at **@astar_research**, LinkedIn at **A*STAR Research** and Telegram at **A*STAR Research**.

On the cover
A spotlight reveals otherwise-hidden digital risks in a range of network-linked devices.

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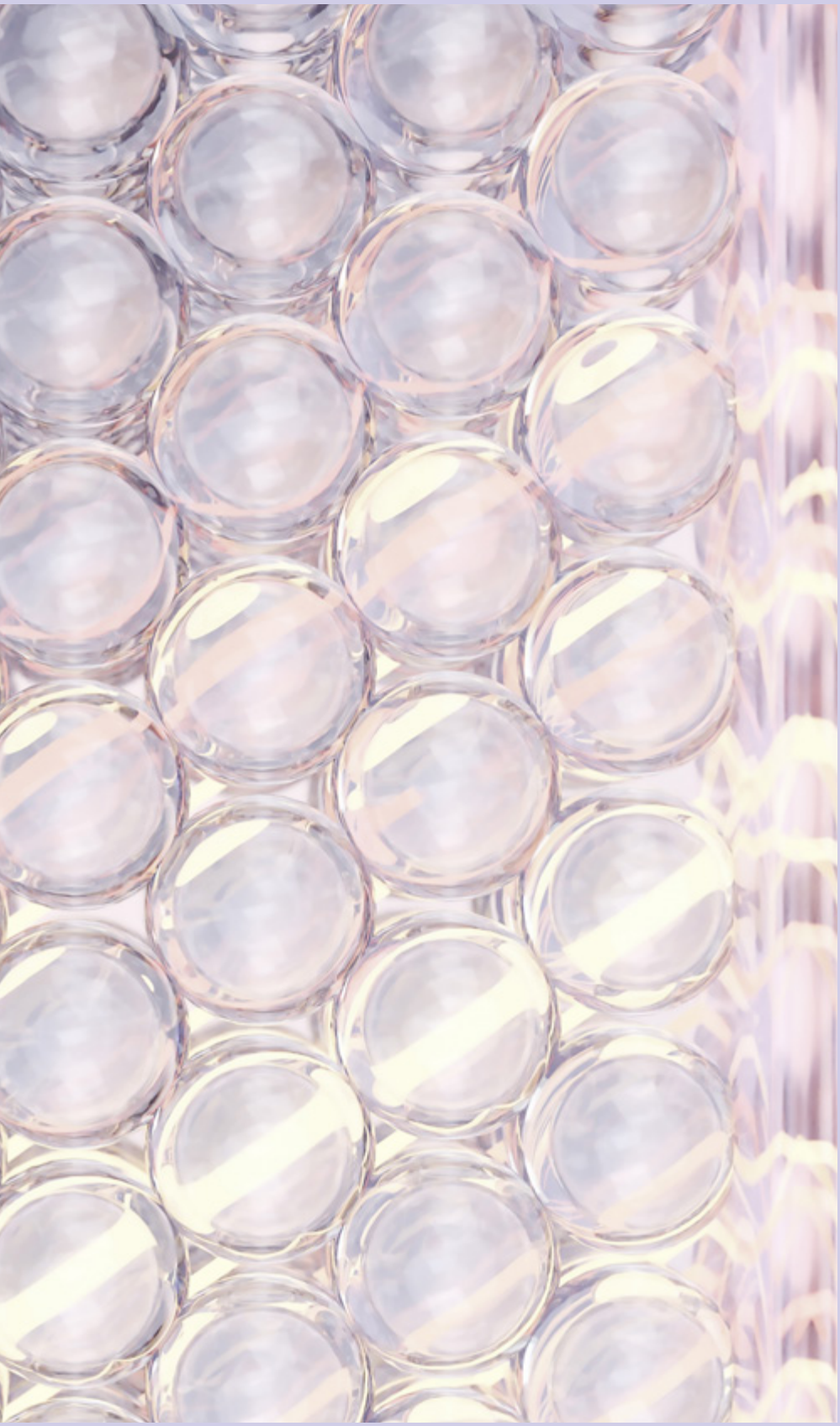


DERMATOLOGY

Keeping tabs on psoriasis flare-ups

A non-invasive imaging technique tracks psoriasis severity and treatment response with detailed 3D skin images, offering safer, more accurate monitoring.

Could diagnosing chronic skin conditions one day be as simple as scanning a bar code? Researchers at A*STAR and Singapore's National Skin Centre (NSC) are exploring this possibility using multispectral Raster-Scanning Optoacoustic Mesoscopy (ms-RSOM), an imaging technology that uses laser light and sound waves to create detailed 3D images of the skin. These images reveal features such as blood vessel thickness, oxygen levels and skin layer thickness, providing a gentle, biopsy-free method of monitoring chronic skin conditions.

Psoriasis, an inflammatory scaly skin condition, is currently assessed using clinical subjective scoring systems such as the Psoriasis Area and Severity Index (PASI), which rely solely on visual inspection. However, PASI can miss subtle changes happening beneath the skin's surface.

"Psoriasis presents with a variety of lesion types and severities, which can complicate the standardisation of imaging parameters and biomarker thresholds for

Photo credit: Alioui Ma / Shutterstock

accurate quantification," said U.S. Dinish, a Principal Investigator at the A*STAR Skin Research Labs (A*STAR SRL)'s Translational Biophotonics Laboratory.

Researchers led by Dinish and Malini Olivo, A*STAR SRL Distinguished Principal Scientist, collaborated with NSC to investigate ms-RSOM's potential to diagnose and monitor psoriasis. In their study, eight patients with varying severities of psoriasis underwent imaging sessions. By capturing 3D images of the skin before and after treatment, ms-RSOM identified increased blood oxygenation, total blood volume and epidermal thickening in affected areas, all correlating with disease severity.

"Structural details, such as epidermal thickness and vascular density, allow for precise assessment of inflammation and tissue remodelling, which are key indicators of disease severity," said Olivo.

The researchers also demonstrated ms-ROM's utility in monitoring treatment efficacy by detecting reductions in psoriasis biomarkers that matched improvements in the patients' PASI scores.

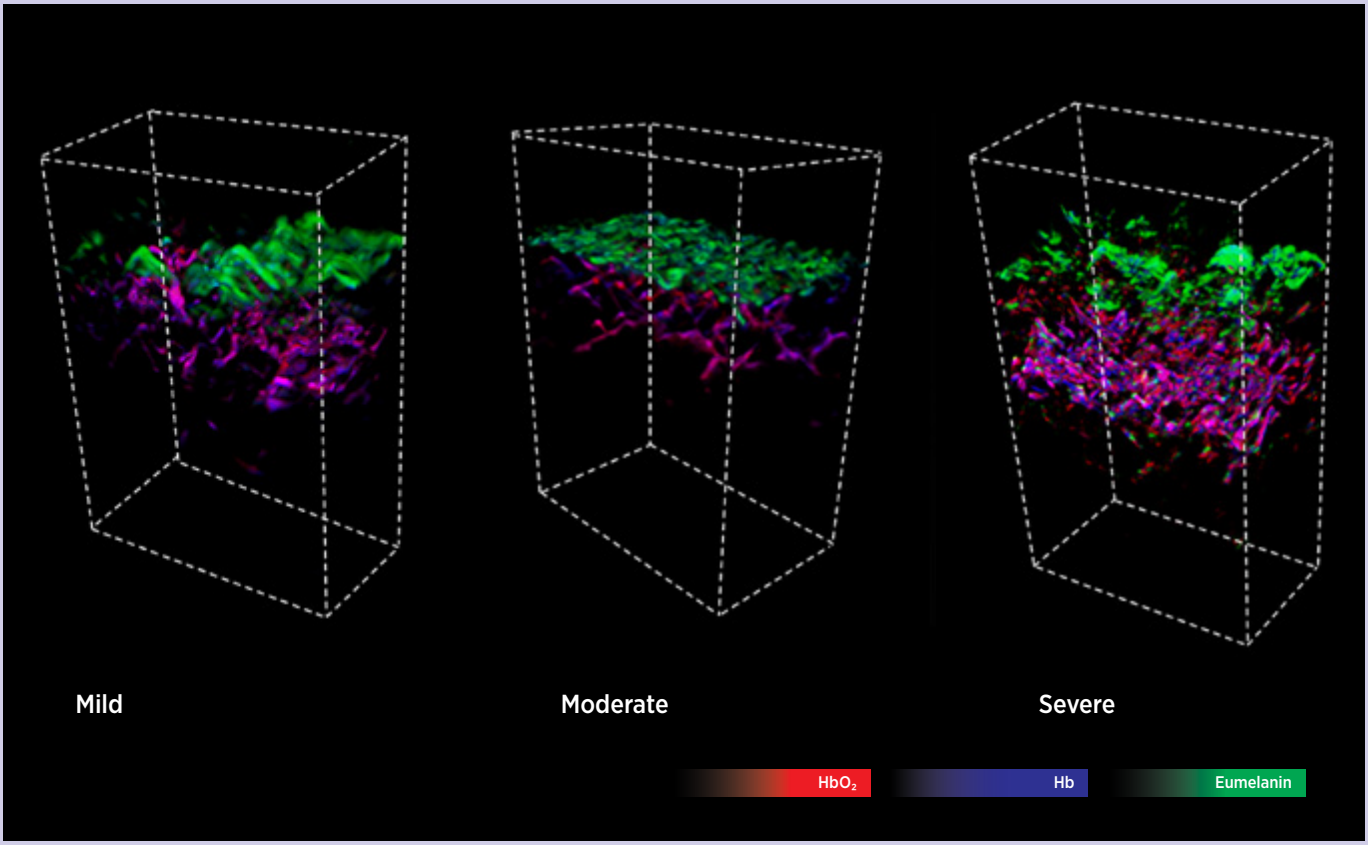
"The ms-RSOM tool can be repeatedly used for monitoring disease progression and response to treatment in a non-invasive manner, without causing discomfort or harm to patients," said Dinish, adding that its real-time imaging capabilities enable clinicians to adjust treatments more efficiently and accurately.

However, challenges remain before the technique can be implemented clinically. Limited depth penetration in darker skin tones and the need for portable, user-friendly devices are obstacles the team plans on addressing. Their future efforts will include expanding clinical studies to larger, more diverse populations and developing robust algorithms to accelerate data analysis. ★

Researchers
Malini Olivo and U.S. Dinish,
A*STAR SRL

IN BRIEF
A*STAR researchers use ms-RSOM, a non-invasive imaging tool, to measure psoriasis digital biomarkers such as blood oxygenation and skin thickness, demonstrating its potential for precise monitoring of inflammation and treatment effectiveness in clinical settings.

1. Li, X., Yew, Y.W., Ram, K.V., Oon, H.H., Thng, S.T.G., *et al.* Structural and functional imaging of psoriasis for severity assessment and quantitative monitoring of treatment response using high-resolution optoacoustic imaging. *Photoacoustics* **38**, 100611 (2024).



3D spatial maps of skin biomarkers derived from ms-RSOM, including melanin (green), oxyhaemoglobin (red) and deoxyhaemoglobin (blue) in patients with mild, moderate and severe lesional psoriasis.

FOOD SCIENCE

Bite-sized protein screening

A new miniaturised protein testing method reduces the sample volumes needed to evaluate plant-based food alternatives, accelerating their development.

The creamy texture of mayonnaise, the light fluffiness of whipped cream and the satisfying bite of a plant-based protein burger all hinge on the essential role of proteins. Their techno-functional properties—such as emulsification, foaming and gelling—are crucial in determining how proteins behave in food systems, directly influencing texture, stability and overall product quality.

Scientists rely on these properties to evaluate how novel proteins perform during food processing to shape the final product's taste, appearance and consistency. However, conventional methods for testing these properties are often time-consuming and resource-heavy, hindering the rapid development of new plant-based proteins.

"Traditional testing methods use large amounts of protein and are not practical when testing many different samples at early evaluation stages," said Jordy Kim Ung Ling, a Scientist at the A*STAR Singapore Institute of Food and Biotechnology Innovation (A*STAR SIFBI).

"We have shown that our miniaturised assays work just as well as traditional tests."

Ling's research aimed to make protein testing faster and more efficient by developing smaller-scale assays that require less than 400 µl of protein solution—about the volume of a few drops from an eye dropper. This approach markedly reduces the time and resources needed for screening, making it easier to test a wider range of plant-based substitutes for animal-based ingredients in food.

Ling, alongside Senior Principal Scientist Siew Bee Ng and other A*STAR SIFBI colleagues, created miniaturised assays for three core techno-functional properties. The emulsification assay gauged the turbidity of protein-oil mixes by measuring their light absorbance, while the foaming assay measured the height of bubbles created by proteins in solution under mechanical force. Meanwhile, the gelling assay observed the effects of heat, cooling and inversion on protein samples in microtubes.

By incorporating automated liquid handling systems to boost speed and accuracy, the team retained the tests' core principles but reduced the sample volumes needed for high-throughput screening. They applied their miniaturised protocols to four different commercial proteins—egg white, soy, mung bean and pea protein isolates—and cross-checked the results with standard methods.

The miniaturised assays showed a strong correlation with traditional tests, while cutting down required sample volumes by 25 times for emulsification and gelling, and 100 times for foaming.

"We have shown that our miniaturised assays work just as well as traditional tests," Ling said.

The team is hopeful that their new screening methods will help small and medium-sized enterprises save time, resources and labour, accelerating innovation in the food industry. They are expanding their miniaturised platform to include more techno-functional properties and collaborating with A*STAR SIFBI scientists to create a comprehensive database of protein extract properties. ★

Researchers
Jordy Kim Ung Ling and Siew Bee Ng, A*STAR SIFBI

IN BRIEF
A*STAR researchers develop a high-throughput protein testing method that uses less than 400 µl of protein solution to efficiently assess emulsification, foaming and gelling properties, enabling faster screening and development of plant-based ingredients.

1. Ling, J.K.U., Gorelik, S., Subramanian, G.S., Sarwono, A.E.Y., Lee, D., *et al.* Development and validation of miniaturized assays to assess protein techno-functional properties. *Current Protocols* **4**, e1071 (2024).

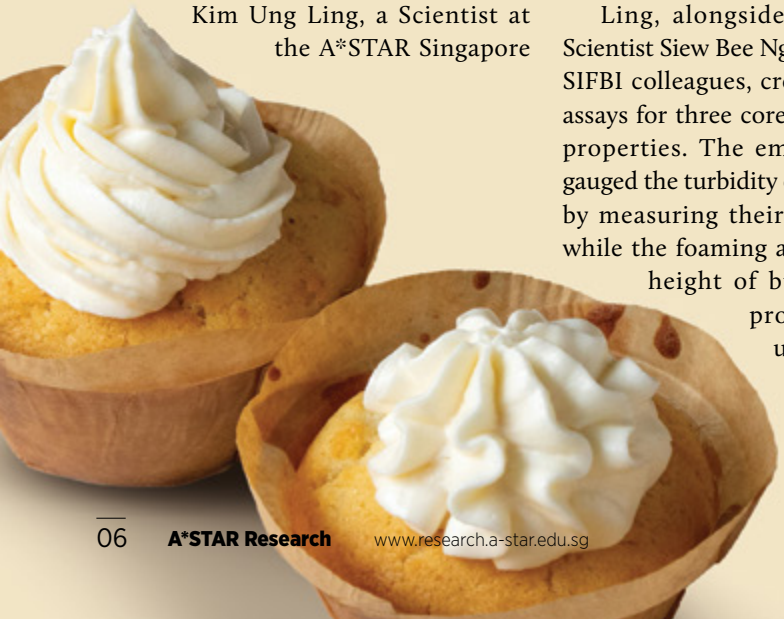


Photo credit: Chaman Raj / Unsplash

CELL BIOLOGY

Fatty liver poses silent risks to SMA survivors

In a multinational study, researchers discover that the genetic defect behind spinal muscular atrophy may also cause long-term liver issues for both patients and carriers.

Thanks to medical advances, spinal muscular atrophy (SMA) no longer casts a long shadow over young lives. Patients with this hereditary disease once faced an inevitable wasting of muscles and an early death. However, treatments that make up for the genetic defect behind SMA mean that even children with severe disease can now look forward to adulthood.

Yet these new prospects may also mean new health issues. "We've noticed a large proportion of children and adults with SMA have fatty liver (steatosis) on ultrasound scanning," said Crystal Yeo, Principal Investigator of the Translational Neuromuscular Medicine Laboratory at the A*STAR Institute of Molecular and Cell Biology (A*STAR IMCB), who directed this research. "As children with SMA live longer, the possibility of liver problems might become more apparent, as fatty liver may, in some cases, lead to inflammation, scarring and even liver failure."

Yeo, also a neurologist who specialises in neuromuscular diseases, explained that SMA is caused by a mutation in the gene *SMN1*, causing a lack of survival motor neuron (SMN) protein in muscle nerve cells. But SMN isn't found solely in such cells; it's present throughout the body and involved in RNA transcription.

To confirm if a lack of SMN could also be behind these liver issues, Yeo and her team worked with collaborators from A*STAR IMCB and the National University of Singapore; Harvard University and Boston Children's Hospital, US; and the University of Aberdeen, Scotland, in a multinational study of clinical data from patients with SMA and patient-derived stem cell models.

"We used stem cells from the patients to create liver-like cells (iHeps) in the lab to directly study how SMA affects liver function," said Yeo. "Compared to healthy cells, SMA iHeps showed fat buildup and impaired energy production, as well as issues with clotting blood, processing fats and sugars, and breaking down drugs."

Using CRISPR gene editing tools, the team then corrected the iHeps' *SMN1* defects, restoring normal SMN protein levels. This reversed the previous steatosis and metabolic issues, confirming that an SMN deficiency directly caused the liver problems. Further proteomics analyses also revealed proteins and molecular pathways affected in SMA liver, such as FMO3, a key enzyme in drug metabolism.

To the team's surprise, neither disease severity, treatment status nor age affected the presence of SMA fatty liver, suggesting a more widespread issue than anticipated. In addition, even iHeps that carried just one defective *SMN1* copy—reflecting people who carry only one defective SMA gene and live without symptoms (SMA carriers)—continued to have the same issues.

"Our study suggests that doctors should also monitor liver function in SMA patients, not just the nervous system," said Yeo. "As some SMA treatments rely on a healthy liver and can cause mild liver toxicity, this could help prevent serious complications."

Yeo added that further studies were needed to understand exactly how SMN loss causes fatty liver and affects other organs. "This is also important for other disorders with similar liver issues like amyotrophic lateral sclerosis (ALS), and for the estimated one in 50 people worldwide who carry one faulty *SMN1* gene," said Yeo. ★

Researcher
Crystal Yeo,
A*STAR IMCB

IN BRIEF
Using clinical research, patient-derived stem cells, proteomics, functional studies and CRISPR/Cas9 gene editing, researchers discover that defective *SMN1* genes are linked to issues in liver cells derived from patients with spinal muscular atrophy, correlating with clinical findings on liver ultrasound.

1. Leow, D.M.-K., Ng, Y.K., Wang, L.C., Koh, H.W.L., Zhao, T., *et al.* Hepatocyte-intrinsic SMN deficiency drives metabolic dysfunction and liver steatosis in spinal muscular atrophy. *The Journal of Clinical Investigation* **134** (12), e173702 (2024).

Photo credit: Steven HWG / Unsplash


HIDDEN
HAZARDS

As artificial intelligence and other digital innovations continue to reshape the internet landscape, A*STAR is accelerating efforts to combat a new wave of safety risks from harmful online content and cyberattacks.

False claims, scams, offensive comments, hacks and more: as our digital world evolves, so do the risks it presents. In recent years, high-profile incidents in digital Singapore have ranged from waves of fake news about the COVID-19 pandemic, to a highly realistic deepfake video of a national leader promoting a scam investment. A social media post that associated religious texts with toilet paper sparked public concern and prompted immediate action from local authorities over its offensive nature; elsewhere, massive cyberattacks have stolen reams of personal data and held corporate servers for ransom.

"These cases are non-exhaustive, but underscore the range, complexity and severity of digital harms," said Yinping Yang, a Senior Principal Scientist at the A*STAR Institute of High Performance Computing (A*STAR IHPC) and Director of the Centre for Advanced Technologies in Online Safety (CATOS).

The World Economic Forum has outlined a framework of six major categories of online harm, encompassing threats to personal and community safety, harm to health and well-being, hate and discrimination, violation of dignity, invasion of privacy, and deception and manipulation. The risks of those harms are compounded by the size of today's digital world; as of 2024, the International Telecommunication Union estimated that 68 percent of the global population had come online.

"We now have billions of different types of internet-connected devices—laptops, smartphones, industrial systems, wearables and even critical infrastructure—which expand the attack surface for potential threats," added Dinil Mon Divakaran, a Senior Principal Scientist at the A*STAR Institute for Infocomm Research (A*STAR I²R).

These challenges have made online trust and safety (OTS) and cybersecurity both significant areas of investment under Singapore's Research, Innovation and Enterprise 2025 (RIE 2025) programme. As the nation's lead public R&D agency, A*STAR is stepping up joint efforts with other research institutions, industry partners and public bodies to advance new solutions for a new generation of digital safety risks.

A CATALYST FOR DIGITAL SAFETY

Under RIE 2025, one new and ongoing funding initiative in digital safety R&D is the OTS Research Programme. Led by the Ministry of Digital Development and Information (MDDI) and administered by the National Research Foundation (NRF), the S$50 million initiative aims to improve digital safety at all levels of society by developing robust tech solutions for tackling online harms, and aligning translational efforts with high-impact OTS use cases.

The OTS Research Programme supports research under three themes: prevention, early detection, and mitigation and empowerment (*see sidebar*), with solutions aimed at various systems for the creation, distribution and reception of online content.

To host the programme, A*STAR established CATOS in March 2023 with support from MDDI, NRF and partner organisations. Intended as a hub for the combined research expertise of Singapore's OTS ecosystem, CATOS serves to drive the programme's key strategic pillars, including deep tech research, systems engineering and programme coordination.

"CATOS's vision is to be a technology leader with robust capabilities needed to counter online harms and create a safe online environment for all," said Yang, who is also Lead Principal Investigator of the OTS Research Programme. "In the longer run, CATOS will deliver a wide range of technologies to empower more effective policy enforcement and public education, and to connect people better and at scale, under a framework of 'tech for the public good'."

SIGNING ON TRUST

Content provenance tools are a critical area of digital safety R&D. These tools aim to build trust in digital media by making their histories—such as when and how they were created, modified and produced—verifiable by the public.

"Content provenance can be seen as a nutrition label on the media we consume," explained Therese Quieta, Head of CATOS Systems Engineering and an A*STAR IHPC Principal Research Engineer. "While it doesn't directly prevent the spread of inauthentic content, an understanding of media origins can support a more trusted media ecosystem."

As online distrust proliferates, global standards such as the Coalition for Content Provenance and Authenticity (C2PA) are being established to guide users, content creators and publishers. Through C2PA, a media file's origin metadata is identified, signed, and bound to the file through a manifest. Any file edits are tracked and added to the manifest, forming a chain of digital signatures that informs users of when, where and by whom edits were made. This allows content publishers interested in building trust to upload and sign their content with secure and traceable credentials.

OTS RESEARCH PROGRAMME

RESEARCH THEMES AND MAIN TECH PLATFORMS

PREVENTION

System : Content generation (government, C2PA and other organisations, mainstream media, websites, content platforms)

Goals : Establish authoritative sources of truthful information; preserve the integrity of publications and media propagation; build trustability by design

Platforms : PROVO

EARLY DETECTION

System : Information propagation (platforms, influencers, advertising)

Goals : Stem the spread of harmful content; nullify its effectiveness in collaboration with platforms and influencers

Platforms : SLEUTH, CrystalFeel Plus

MITIGATION AND EMPOWERMENT

System : Socio-cognitive (general public, organisations, influencers, community leaders)

Goals : Cultivate responsible information-sharing behaviour; foster digital- and information-savvy communities

Platforms : OTS Educational Hub

In 2024, CATOS signed a memorandum of understanding (MoU) with a software company and content authenticity leader, Adobe, to jointly implement content provenance technologies in Singapore. To bridge the gaps between C2PA and content publishers' needs, Quieta's team has developed the first version of PROVO, a seamless, user-friendly interface to facilitate digital signatures in news publications.

"You don't need to be tech-savvy to embed your credentials into a file with PROVO," said Quieta. "PROVO can also be integrated into existing publishing workflows and adapted to support site-building platforms."

DEEPFAKE DETECTIVES

As artificial intelligence (AI) technology advances, generative AI tools for text, video and audio content creation have grown not only more convincing, but also more accessible for actors with potentially malicious intent.

"Generative AI has led to increasingly sophisticated visual deepfakes that are harder to detect with the naked eye, as well as human-like text that may contain factual inaccuracies, whether intentional or accidental," said Soumik Mondal, a Principal Scientist and Principal Investigator of misinformation detection research projects at A*STAR I²R.

Mondal added that automated fact-checking (AFC) and deepfake detection tools have emerged as a crucial defence against misinformation. Like content creation tools, these digital detectives also leverage AI, but they use it to analyse visual media for subtle inconsistencies in facial movement, lighting, audio-visual synchronisation and physiological signals; identify and cross-reference text claims against trusted databases; or examine file metadata for signs of manipulation.

As part of CATOS's suite of OTS tools, Mondal's team developed SLEUTH, an integrated deepfake detector and AFC tool now being adapted for popular messaging platforms. "SLEUTH's dual detection framework combines AI-driven media forensics with a multimodal fact-checking engine to detect manipulated content across various media types—video, audio, images and text—and verify claims against reliable online sources," said Mondal.

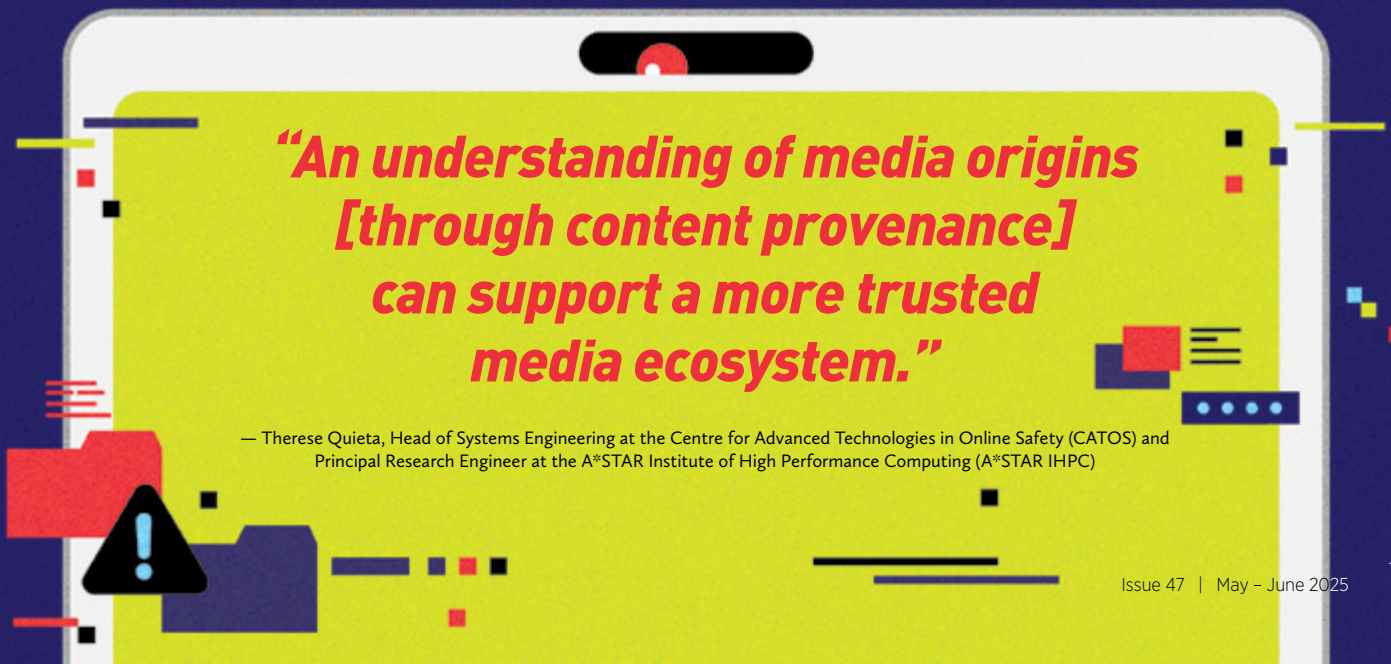
SPOTTING SMOKE BEFORE FIRE

Digital safety also involves tackling toxicity in the form of harassment and bullying, and hate. "As toxicity is a subjective concept, its definitions can vary, and cultural contexts can alter how different people perceive the same content," said CATOS and A*STAR IHPC Senior Scientist Yunlong Wang.

Within CATOS, researchers such as Wang, CATOS and A*STAR IHPC Research Scientist Hui Si Oh and Principal Scientist Raj Kumar Gupta are focusing on hateful or socially divisive social media content directed at racial or religious groups.

"A 2024 MDDI survey reported 42 percent of internet users in Singapore encountered content inciting racial or religious tensions—up from 13 percent in 2023," said Oh. "Given Singapore's multicultural society, the stakes of such content are especially high; it can fuel frictions and hostilities between racial and religious groups and contribute to social polarisation online."

To address the issue, Gupta, Wang, Oh and the CATOS team have built a suite of tools, collectively known as CrystalFeel Plus, which comprise an AI-powered analysis engine that can score, predict and identify intense emotions in text, as well as a new beta function that flags the presence of hateful content.



Curated with local knowledge bases and data, CrystalFeel Plus's engines draw on a list of commonly used expressions in Singapore's unique blend of English and local dialects. "This 'Singlish emotion lexicon' helps our engine achieve accurate and robust emotion sensing across standard English and colloquial or informal language use," said Gupta.

The original CrystalFeel is currently licensed for use by multinational organisations and public agencies; it has been scientifically validated for its accuracy in describing global-scale emotional behaviours online during the COVID-19 pandemic, as well as predicting news virality and mental health needs. CrystalFeel Plus is an enhanced version in development that aims to incorporate engines for detecting hateful content, sarcasm (Crystalace) and emotion-related expressions in videos (Digital Emotions).

"Emotions are at the heart of human communication," said Gupta. "They reveal our preferences, opinions and even mental well-being. CrystalFeel's potential applications span a wide range—from market research and social listening to healthcare and education."

SECURING BACKEND NETWORKS

Beyond efforts under CATOS to address harmful online content, A*STAR researchers are also working to secure networks and systems in general. The rise of the Internet of Things (IoT), cloud computing and AI have introduced new vulnerabilities and complexities to the cybersecurity landscape.

"We're in an era where attackers are starting to exploit AI for automated, sophisticated cyberattacks," said Dinil Mon Divakaran. "Yet the growing number and variety of devices connected can make it difficult for users to keep security measures up to date."

Divakaran added that IoT devices often lack robust security, making them vulnerable to exploitation for access to larger networks. Meanwhile, today's increased network traffic volume can make threats such as botnet communications over encrypted channels harder and costlier to locate.

Working with industry partners and public agencies, Divakaran's team is developing automated cybersecurity solutions using AI-based models. For instance, by detecting anomalies and threats based on changes in user, device and application behaviour, these solutions could be invaluable for securing enterprises and 5G network infrastructure.

"We also recently developed an agentic-AI approach to automatically detect code vulnerabilities in software repositories," said Divakaran. "Our proposal uses Reasoning and Acting (ReAct) AI Agents to distinguish vulnerable code from benign code, using AI-based thought-action-observation and inter-procedural context."

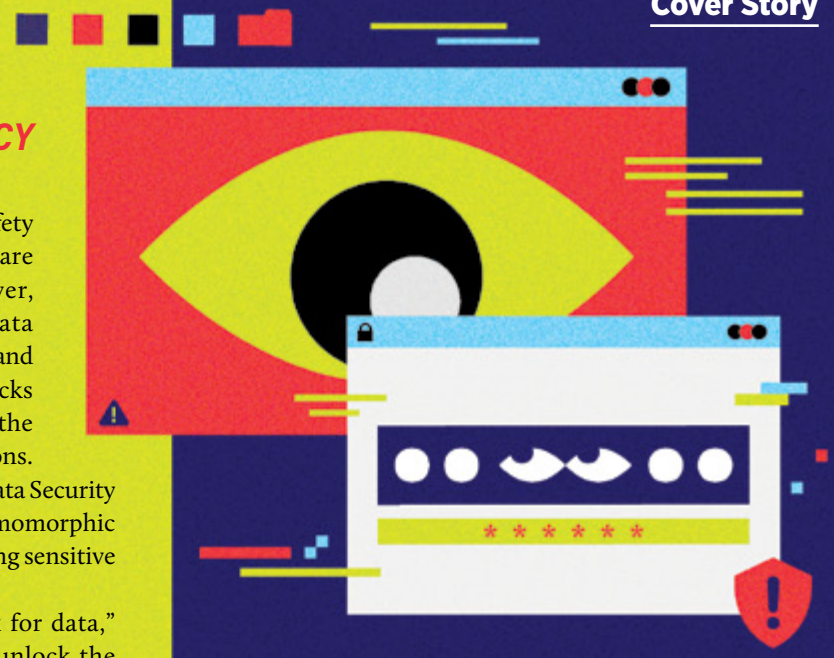
The team has also been building their expertise in tackling online phishing and scams, most recently developing a large language model (LLM)-based pipeline that detects these activities. Going further, Divakaran and Soumik Mondal developed an engine comprised of in-house models, multimodal LLMs and heuristics that can detect phishing and scam content in messages, websites and other online platforms. The tool also explains its reasoning when flagging content as a potential threat, helping users understand and trust its decisions.

These security solutions are also moving to real-world use through A*STAR I²R's close engagement with ecosystem partners. Divakaran highlighted the recent establishment of the Telecom Cybersecurity Innovation Centre (TCIC) at A*STAR I²R in collaboration with ST Engineering, which focuses on enhancing Singapore's digital and cyber resilience for 5G networks and beyond.

Besides developing AI-based solutions, Divakaran regularly evaluates the robustness of new network protocols from a security and privacy perspective. A recent joint work with A*STAR I²R Senior Scientist Levente Csikor and the National University of Singapore seeks to understand how cyberattackers may learn sensitive information about internet users by leveraging AI models, even when data is transmitted in encrypted payloads.

"Network attacks such as website fingerprinting can potentially infer the websites a user visits even when they use the latest protocols that support encrypted communications," said Divakaran.

ADVANCING HEALTH DATA PRIVACY



The biomedical sector poses some unique digital safety challenges. Data privacy is paramount, as healthcare records contain highly personal details; however, cutting-edge clinical research often requires data sharing between multiple institutions to study larger and more diverse patient groups. Large-scale cyberattacks such as the 2018 SingHealth data breach illustrate the need for stronger healthcare data protection solutions.

For A*STAR I²R Senior Principal Scientist and Data Security Group Leader Khin Mi Mi Aung and colleagues, homomorphic encryption (HE) offers a powerful solution for sharing sensitive healthcare data while preserving patient privacy.

"Imagine traditional encryption as a lockbox for data," said Aung. "To analyse that data, you'd need to unlock the box, which exposes it. In contrast, HE lets you analyse its contents while staying locked. Only your final analytical outputs are accessible to authorised parties, and only those with the right key."

During the COVID-19 pandemic, Aung and colleagues developed CoVnita, a HE-based end-to-end privacy-preserving framework for SARS-CoV-2 viral genome classification. Built on an international award-winning HE-based solution developed by the team in 2021, CoVnita aimed to enable organisations to jointly train a secure model that would quickly and accurately classify SARS-CoV-2 strains for improved patient triage.

Building on these efforts, in February 2024, A*STAR I²R and the A*STAR Bioinformatics Institute (A*STAR BII) signed an MoU with the Singapore Translational Cancer Consortium; the University of Nottingham, UK; and Nottingham University Hospital NHS Trust, UK, to create a secure international framework for healthcare and biomedical research data sharing.

Aung also highlighted the recent formation of a joint lab between A*STAR and health data analytics provider BC Platforms as an important milestone in the same area.

"The joint lab will enable secure connections with clinical cohorts and health data for cross-entity, cross-border collaborations, leveraging A*STAR's privacy-preserving tech and expertise in bioinformatics, clinical sciences and precision medicine," said Aung.

AN EVOLVING SPHERE

Yinping Yang noted that digital safety remains a highly dynamic field that encompasses more than a technological arena; through platforms such as the OTS Education Hub, CATOS also supports other organisations in public education efforts. These include a community roadshow with the National Library Board's "Source, Understand, Research, Evaluate" (SURE) initiative, which aims to empower Singaporean communities with AI literacy and awareness of deepfakes.

"In developing OTS tools, we must ensure our research is informed by the latest developments, and evaluated and tested based on real-world needs," said Yang. "As these research capabilities and technologies advance towards their applied stages, their uses and use cases must also be carefully handled."

Both Yang and Dinil Mon Divakaran noted that researchers working on OTS and cybersecurity are mindful that these spaces are tremendously important, yet may have far more problems than solutions.

"The same tools that enhance security, such as encryption, can also be used to threaten it," said Divakaran. "The use of AI, especially agentic AI, can inadvertently create new attack vectors, necessitating careful design and thorough evaluations of their access policies, deployment and potential risks."

However, Yang is cautiously optimistic that A*STAR's work will make a significant impact to uplift digital safety through the range and quality of its technological solutions and translational efforts.

"In the coming year, we will release more robust tech features for the prevention, early detection and mitigation of online harms, contributing to a safe and thriving online space for all," said Yang. ★

DRUG DISCOVERY

A twist in the tale of stapled peptides

A new molecular dynamics study reveals how some stapled peptides shapeshift to slip through cellular barriers and target key disease-related proteins within cells.

Designing a new drug often begins with finding the right molecules to hit the right protein targets and disable important mechanisms in disease-causing cells. However, when the ideal target sits inside a cell rather than on its surface, many prospective drugs run into a Goldilocks-like conundrum of being too small or too big for their chosen beds.

"Most biological pathways are mediated by protein-protein interactions (PPIs) inside cells," explained Chandra Verma, a Senior Principal Investigator at the A*STAR Bioinformatics Institute (A*STAR BII). "These PPIs have been undruggable by today's two main drug modalities: small molecules, which have trouble targeting the large, flat binding surfaces on most PPIs; and antibodies, which are too large to enter cells at all."

Stapled peptides may be a 'just right' solution. This emerging class of therapeutic molecules consists of short, linear chains of amino acids—the building blocks of protein—braced by chemical 'staples' that hold them in a specific shape.

"Being proteins themselves, stapled peptides can mimic the surfaces of target proteins, boosting their specificity," said Verma. "Stapling also reorganises peptides into the most efficient shapes to bind target proteins; protects them against degrading enzymes; and helps them permeate membranes."

To understand the molecular mechanics behind how staples enable peptides to slip into cells, Verma and joint first author, Jianguo Li, worked with pharmaceutical company Merck & Co, US and MSD, Singapore, to explore the trans-membrane journey of ATSP-7041M, a modified version of a stapled peptide known to inhibit tumour growth. Using solid state nuclear magnetic resonance (ssNMR) imaging, the team measured the peptide's shapes and interactions with cell membranes, then used their resulting data to guide molecular dynamics simulations of its entry into cells.

The team found that when ATSP-7041M came in contact with cell membranes, it coiled into a corkscrew-shaped α-helix structure, turning its hydrogen bonds inward. The peptide's affinity for a cell membrane was enhanced by a special interaction called cation-p between the peptide's phenylalanine side chain and positively-charged atoms on the membrane's surface. This enabled ATSP-7041M to enter the membrane's hydrophobic interior, which further enhanced the peptide's shapeshifting.

"Peptide chains are normally polar, which cause the lipid (fat)-based membranes of cells to repel them," said Verma. "However, we found that ATSP-7041M's helical conformation basically buries its polar groups inside the peptide, allowing it to more easily pass through membranes."

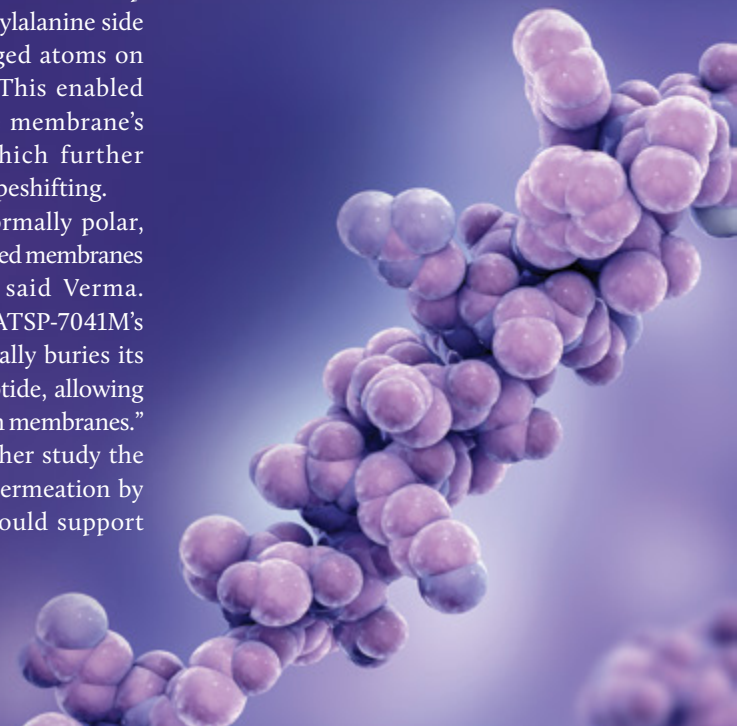
The team plans to further study the mechanics of membrane permeation by stapled peptides, which could support the design of future therapeutics aided by artificial intelligence platforms.

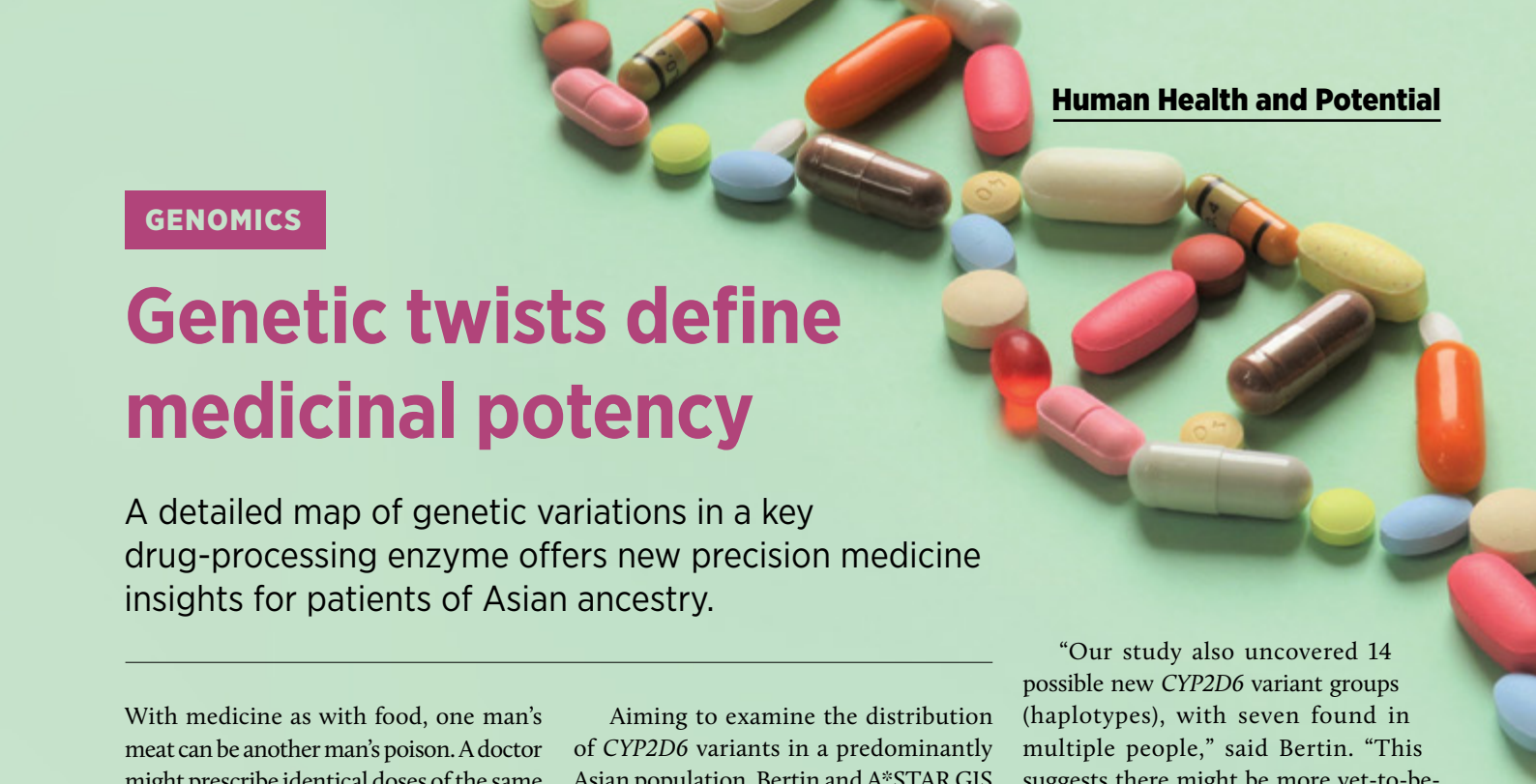
"The ATSP-7041M story signifies the importance of understanding detailed molecular mechanisms for drug discovery," Verma added. "We'd like to also acknowledge the research groups of David Lane and Christopher Brown of the A*STAR Institute of Molecular and Cell Biology (A*STAR IMCB); and Charles Johannes of the A*STAR Institute of Sustainability for Chemicals, Energy and Environment (A*STAR ISCE²) for their contributions to this work." ★

Researchers
Chandra Verma and Jianguo Li, A*STAR BII

IN BRIEF
Researchers show that the modified anti-tumour stapled peptide ATSP-7041M undergoes structural changes on membrane binding that reduce its polarity, improving its ability to penetrate lipid membranes.

1. Li, M., Li, J., Lu, X., Schroder, R., Chandramohan, A., *et al.* Molecular mechanism of P53 peptide permeation through lipid membranes from solid-state NMR spectroscopy and molecular dynamics simulations. *Journal of the American Chemical Society* **146**, 23075–23091 (2024).





GENOMICS

Genetic twists define medicinal potency

A detailed map of genetic variations in a key drug-processing enzyme offers new precision medicine insights for patients of Asian ancestry.

With medicine as with food, one man's meat can be another man's poison. A doctor might prescribe identical doses of the same drug to treat two patients for the same disease, only to find what works for one patient may be ineffective—or toxic—for the other. This is partly because a drug's efficacy isn't just based on what it's made of, but on how well our bodies process it.

"A single liver enzyme, CYP2D6, critically influences how we metabolise nearly one in five clinically-prescribed medications, from painkillers and heart-rate regulators to anti-cancer drugs and antidepressants," said Nicolas Bertin, Group Leader at the A*STAR Genome Institute of Singapore (A*STAR GIS). "Yet as many as 170 different versions of the *CYP2D6* gene have been identified in the global population, each affecting medication safety and efficacy to varying degrees in different people."

Although *CYP2D6* stands among the top 20 genes known to have strong gene-drug interactions, the prevalence of its variants remains relatively under-characterised, especially among people of non-European ancestries. Bertin, who leads A*STAR GIS's Genome Research Informatics and Data Science (GRIDS) Platform, explained that *CYP2D6*'s complex variation patterns pose challenges when trying to accurately determine—via short-read whole-genome sequencing-based methods—the specific versions of *CYP2D6* carried by an individual.

Aiming to examine the distribution of *CYP2D6* variants in a predominantly Asian population, Bertin and A*STAR GIS colleagues teamed up with the University of the Witwatersrand, South Africa, and the A*STAR GIS-seeded startup Nalagenetics. They drew on a cohort of 1,850 Singaporean residents of Chinese, Malay and Indian ancestries whose genomes had been sequenced as part of the SG10K_Health dataset. SG10K_Health was assembled in Phase 1 of Singapore's National Precision Medicine programme, for which GRIDS is responsible for developing the genome data analytics infrastructure.

To enhance the accuracy of variant identification, the team developed a dedicated bioinformatics workflow that used three different tools to comb through short-read sequencing data, as well as a novel consensus algorithm—developed in-house—to confirm variants when two of the three tools concurred.

The results showcased the unique genetic makeup of East, South and Southeast Asian populations. Normal *CYP2D6* metabolisers were the most common, yet made up a smaller proportion of the cohort compared to global studies (53.9 versus 64–68 percent). Poor metabolisers were found in all three ethnic groups, although at a much lower frequency than in Caucasian populations, while the prevalence of ultra-high metabolisers was double that of poor metabolisers.

"Our study also uncovered 14 possible new *CYP2D6* variant groups (haplotypes), with seven found in multiple people," said Bertin. "This suggests there might be more yet-to-be-characterised versions of *CYP2D6* prevalent in people of Asian ancestries."

Critically, the team pinpointed actionable *CYP2D6* variants—those with direct implications for treatment selection and drug dosing strategies—in over 80 percent of the cohort when focusing on the 10 most common *CYP2D6* haplotypes.

"This research represents the most comprehensive cataloguing of the variation landscape of *CYP2D6* in East, South and Southeast Asian populations thus far," noted Bertin, adding that their findings could help refine diagnostic testing and improve prescription guidelines for patients based on genomic profiles. ★

Researcher
Nicolas Bertin,
A*STAR GIS

IN BRIEF

A specialised bioinformatics workflow highlights population-specific *CYP2D6* genetic polymorphism trends in a multi-ethnic Singaporean cohort, and helps characterise 14 previously-unknown variant groups, paving the way for improved, individual ancestry-tailored treatment strategies.

1. Maulana, Y., Toro Jimenez, R., Twesigomwe, D., Sani, L., Irwanto, A., *et al.* The variation landscape of *CYP2D6* in a multi-ethnic Asian population. *Scientific Reports* **14**, 16725 (2024).

Photo credit: Katy Pack / Shutterstock

FUTURE FOODS

Fashioning faba-lously familiar fats

A*STAR researchers explore the potential of faba beans and olive oil in creating a healthier plant-based chicken fat substitute.

When taking a bite of a juicy wagyu steak, we can savour a distinct flavour, creaminess and richness thanks to thanks to its tasty, unique mix of fats. Yet though delicious, too much animal-based fats in one's diet can cause health complications due to their high saturated fat content. As such, consumers are looking to plant-based fat substitutes—not only for health reasons, but also for ethical and environmental ones, as intensive livestock farming has been linked to climate change and animal welfare issues.

However, it isn't easy to make these substitutes as delicious or nutritious as their originals. "Early fat substitutes—mainly mixtures of fatty acids, or structured or modified lipids—had potential drawbacks. They had detrimental gastrointestinal effects, or could inhibit the absorption of fat-soluble vitamins and minerals," explained Shaun Sim, Group Lead of Food Materials Science at the A*STAR Singapore Institute of Food and Biotechnology Innovation (A*STAR SIFBI).

Though new techniques have led to new substitutes that retain natural lipids, such as emulsions and gels, Sim added that their production often involves high temperatures and pH changes. These conditions make it challenging to infuse these substitutes with delicate flavour and bioactive molecules that could improve their nutritional value, sensory properties and overall consumer appeal.

Sim, A*STAR SIFBI Research Officer Yan Kang and colleagues teamed up with the A*STAR Skin Research Labs (A*STAR SRL) to develop a protein emulsion gel (PEG) that could closely mimic chicken fat in look, feel and taste, while containing less saturated fats.

"Our PEG is formed by high-pressure processing (HPP), which uses pressure instead of heat to structurally modify food while retaining its nutrients and sensory properties," said Sim.

Photo credit: jemylk / Freepik

"Our protein emulsion gel is formed by high-pressure processing, which uses pressure instead of heat to structurally modify food while retaining its nutrients and sensory properties."

To create their PEG, the team combined olive oil and water with faba bean protein concentrate. Olive oil was chosen as it contains mostly unsaturated fat, while faba bean was chosen as a promising but underexplored high-protein crop that can be sustainably grown.

After producing PEGs with different concentrations of oil (40–60 percent) and protein (7–10 percent), the team compared them to chicken fat in various parameters such as appearance, colour, texture, oil-holding capacity and freeze-thaw stability.

They found that faba bean PEGs with lower protein concentrations—especially PEGs composed of 7 percent protein and 40 percent oil—most closely resembled chicken fat in texture and gel strength. On the other hand, gels with more protein were closer to the colour of chicken fat and had better oil-holding capacity.

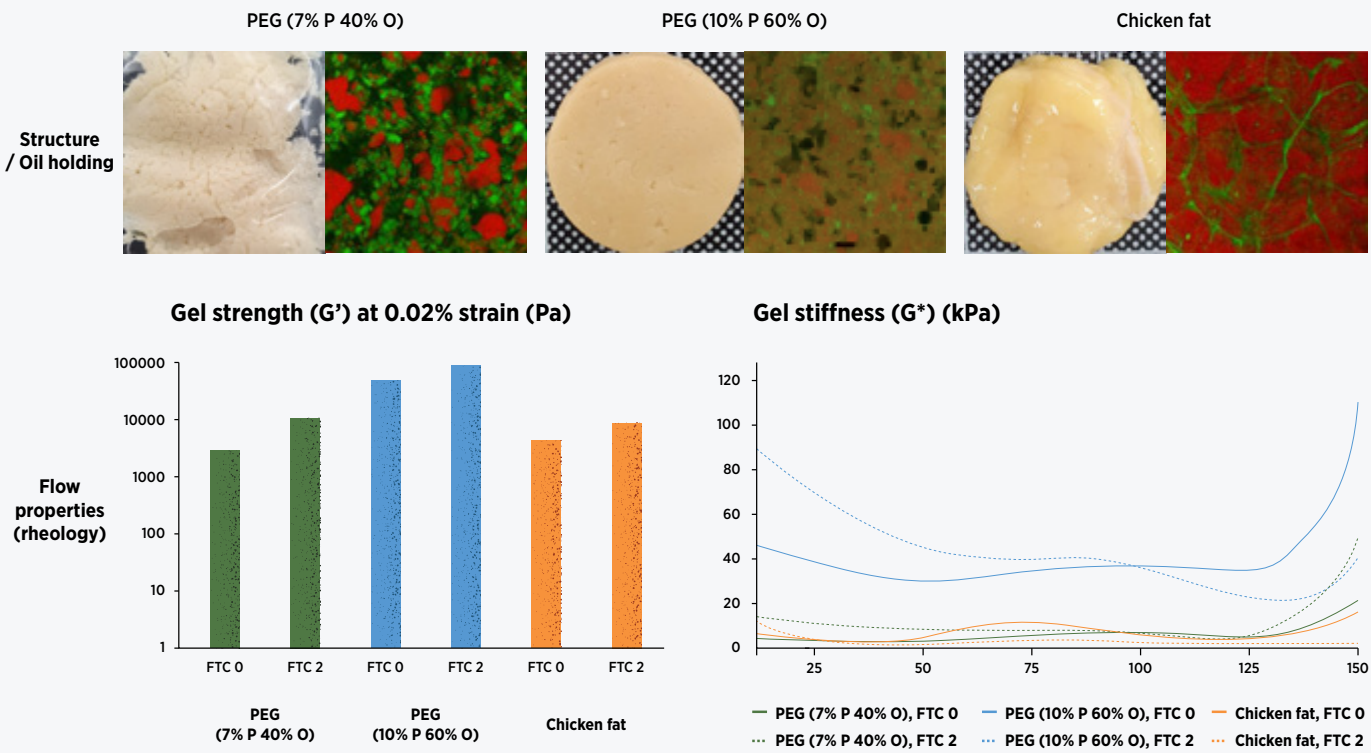
Sim noted that their findings showed how PEG protein and oil concentrations can be tweaked to suit different uses. "For instance, we can increase a PEG's protein concentration to better mimic pork lard, which is generally harder and denser than the fats found under chicken skin," said Sim.

The team is currently improving their PEG's freeze-thawing stability for cold storage and transport. "We will also work on modifying the PEG's taste, texture and effectiveness in retaining specific flavours and nutrients," Sim added. ★

Researchers
Yan Kang and Shaun Sim,
A*STAR SIFBI

IN BRIEF
Using high-pressure processing, protein and oil concentrations of faba bean-based protein emulsion gels can be varied to mimic the various physical properties of chicken fat.

1. Kang, Y., Ng, S.M., Aruchunan, U., Ma, X. and Sim, S.Y.J. Development of non-animal chicken fat using faba bean protein-based emulsion gels. *LWT* **214**, 117124 (2024).



A comparison of the appearance, oil-holding microstructure and flow properties (rheology) of chicken fat versus two PEGs with different protein (P) and oil (O) concentrations. In the micrographs, fats appear as red components while proteins appear as green. Flow properties were measured at baseline and after a second freeze-thaw cycle (FTC).

ENERGY

Catching on to magnesium's potential

Through a unique molecular clamping effect, a novel organic-inorganic composite material provides a new foundation for next-generation batteries.

Crack open your phone case and you'll likely find a familiar label on the battery: 'Li-ion', or lithium-ion. Thanks to its excellent energy density and discharging abilities, lithium makes up the bulk of battery electrolytes used everywhere from personal electronics to electric vehicles.

Yet the world's lithium supplies are struggling to keep up with demand, especially as economies transition to renewables. In search of lithium alternatives, researchers such as Zhigen Yu, a Senior Principal Scientist at the A*STAR Institute of High Performance Computing (A*STAR IHPC), are turning to metals such as magnesium.

"Magnesium is earth-abundant, non-toxic and cheap, enabling scalable and sustainable battery products," said Yu. Magnesium ions (Mg^{2+}) can also theoretically carry twice the electrical charge of lithium ones, offering further boosts to battery storage and charging speeds.

However, research on aqueous (water-based) Mg^{2+} energy storage is still in its early stages, Yu noted. Major hurdles include strong interactions between Mg^{2+} and host materials that limit usable capacity; a poor understanding of the Mg^{2+} storage mechanism; and the low conductivity of typical cathode materials when interacting with Mg^{2+}.

To enhance Mg^{2+} battery designs, Yu and A*STAR IHPC Distinguished Principal Scientist Yong-Wei Zhang, as well as colleagues from A*STAR IHPC; Liaoning University, China; and RMIT University, Australia, recently tested a performance-boosting strategy: the use of a novel organic-inorganic composite as a cathode. Using hydrothermal treatment, the team coated manganese (III) oxide (Mn_2O_3)—a mineral commonly used in magnets and electronics—with ethylenediamine (EDA), an organic base for many industrial chemicals.

"Mn_2O_3 offers a high theoretical energy capacity versus traditional cathode materials. Organic materials like EDA can also capture and store charged particles, adding to that capacity," Yu said. "The coupled structure helps speed up the movement of charged Mg^{2+} in and out of the cathode."

When the team tested their prototype cathode in an aqueous Mg^{2+} battery and studied it with X-ray diffraction tools, they found that the EDA coat reduced the otherwise strong electrostatic interaction between Mg^{2+} and the cathode, improving the flow of charged ions. As the battery discharged, EDA molecules also acted like 'clamps' that plucked Mg^{2+} from the electrolyte fluid, boosting the cathode's storage capacity and cycling stability.

The EDA-Mn_2O_3 cathode also produced an approximately 1.5 times higher discharge capacity than a pure Mn_2O_3 cathode of similar energy density, the team reported.

"Our study demonstrates that organic-inorganic coupling can unlock synergistic effects that significantly enhance energy storage and performance," said Yu. "It suggests that future energy storage systems can greatly benefit from the intelligent integration of organic functionalities into traditional inorganic materials."

The team aims to investigate more organic molecules to fine-tune ion capture and exchange for Mg^{2+} and other potential electrolytes. Using high-throughput computational simulations and machine learning, they will also screen new organic-inorganic combinations to speed up the discovery of electrode materials. ★

Researchers
Zhigen Yu and Yong-Wei Zhang, A*STAR IHPC

IN BRIEF
EDA-Mn_2O_3, an organic-inorganic composite material, demonstrates superior ion exchange and capture over inorganic materials when used as cathodes in magnesium-ion batteries, paving the way for more sustainable and efficient next-generation designs.

1. Li, M., Ding, Y., Zhang, S., Liu, M., Li, J., *et al.* Organic-inorganic coupling strategy: clamp effect to capture Mg^{2+} for aqueous magnesium ion capacitor. *Angewandte Chemie* **63** (52), e202412735 (2024).

Photo credit: Isaac Del Toro / Unsplash

DECARBONISATION

A molecular anchor for green fuel

A tough yet thin coating for functionalised copper catalysts offers a performance boost for carbon dioxide-to-ethanol conversion.

With rising carbon dioxide (CO_2) emissions being one of the biggest drivers of climate change, researchers are working to recapture CO_2 from the air in bulk. While some propose storing that carbon underground, others aim to turn it back into clean-burning fuels or other useful chemicals, such as ethanol, using green electricity to power the process.

"Converting CO_2 to ethanol is a powerful way to fight climate change and store renewable energy," said A*STAR Institute of High Performance Computing (A*STAR IHPC) Principal Scientist, Jia Zhang. "But it can be challenging to selectively produce ethanol from CO_2, as it requires fine control over reaction intermediates. Most systems produce other chemicals such as carbon monoxide (CO) and ethylene instead."

Catalytic electrodes are a key part of such systems as they propel CO_2's carbon atoms through reactions with many possible intermediate and final products. Tiny tweaks to an electrode's surface—such as a 'decorative' coating of small molecules—can help steer those reactions to favour ethanol production. However, these additive molecules can be easily leached away by intense voltages or liquid components of the system in operation.

Aiming to boost the viability of CO_2-to-ethanol conversion, Zhang and A*STAR IHPC colleagues joined researchers from the A*STAR Institute of Sustainability for Chemicals, Energy and Environment (A*STAR ISCE²) and the National University of Singapore (NUS) in testing a method to keep small molecular additives intact on catalytic electrodes.

The team applied a thin protective layer of polyvinylidene fluoride-co-hexafluoropropylene (PVDF-HFP), a stable water-repelling polymer, over the surface of a copper-based electrode. The electrode itself had been treated with 4-dimethylaminopyridine (DMAP), a small molecule additive with unique electronic properties.

Using detailed kinetic analysis, *in situ* spectroscopies and theoretical calculations, the team observed that DMAP—with the protection of PVDF-HFP—helped prevent CO and other carbon intermediates from prematurely escaping the catalyst. This boosted the catalyst's selectivity towards multi-carbon (C_{2+}) products, especially ethanol. The PVDF-HFP layer also seemed to enhance DMAP's effect by preventing its leaching from the catalyst.

"Optimising the PVDF-HFP layer was crucial: it needed to be thin enough to allow efficient ion transport, but thick enough to protect the DMAP additive," said Zhang.

Through careful adjustments, the NUS team found that a 4 µm-thick layer of PVDF-HFP was optimal for C_{2+} production. Compared to an uncoated copper catalyst, PVDF-HFP improved the catalyst's reaction selectivity by two- to threefold, yielding about 47 percent of ethanol as its final product.

"This system demonstrates how tailored surface chemistry through molecular additives, combined with a smart protective design, can significantly enhance ethanol production from CO_2," Zhang said.

The team aims to leverage CatPlat, A*STAR IHPC's inhouse computational catalysis platform, to potentially explore and screen for other organic molecules that could enhance the efficiency of CO_2 conversion to targeted chemicals. ★

Researcher
Jia Zhang, A*STAR IHPC

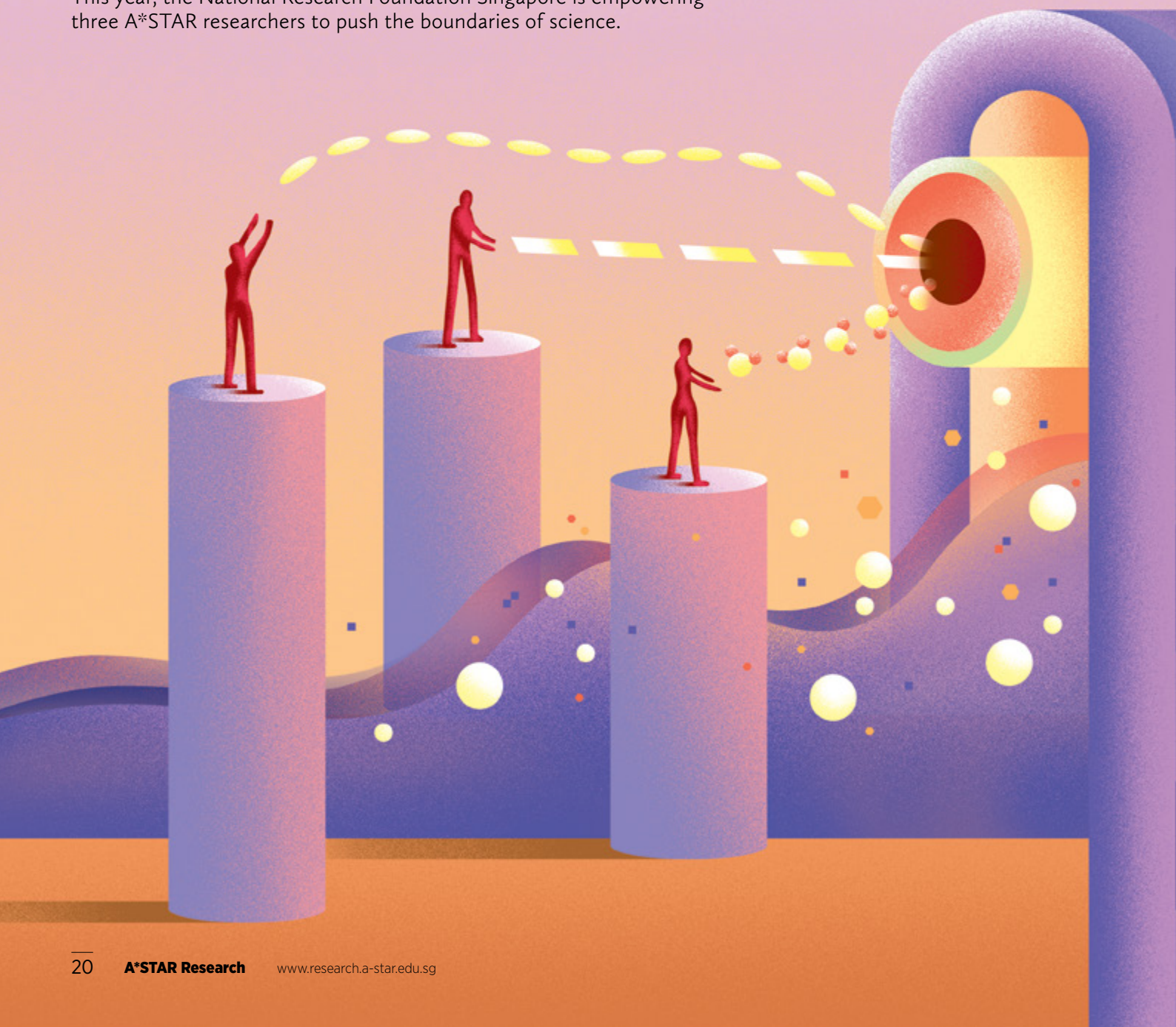
IN BRIEF
A protective layer of polyvinylidene fluoride-co-hexafluoropropylene helps retain small molecule additives on copper-based catalysts, enhancing their selectivity for CO_2 conversion to ethanol.

1. Fu, W., Li, Y., Chen, J., Chen, J., Xi, S., *et al.* Preserving molecular tuning for enhanced electrocatalytic CO_2-to-ethanol conversion. *Angewandte Chemie* **63** (47), e202407992 (2024).

Photo credit: Daniele Levis Pelusi / Unsplash

POWERING THE CHANGEMAKERS

This year, the National Research Foundation Singapore is empowering three A*STAR researchers to push the boundaries of science.



Why do some people breeze through viral infections which leave others fighting for their lives? Could we find special molecules that coax cellular proteins to work in our favour, disarming harmful proteins or helping protective ones to stick around? And in a world overflowing with data, could light-powered computers, modelled after the human brain, revolutionise how we process information?

These questions drive three unique research journeys led by rising scientists at A*STAR. This year, they were selected for the prestigious 2025 National Research Foundation (NRF) Fellowships, which recognise Singapore's most promising early-career researchers and their visionary, high-impact projects in science and engineering.

Open to scientists of all nationalities and disciplines, the NRF Fellowship (NRFF) provides a competitive, five-year research grant to chart bold directions in science and technology.

In this issue of *A*STAR Research*, we sit down with the 2025 cohort of NRF Fellows to uncover what inspires their curiosity, the big questions they are determined to answer, and how their discoveries might shape our world in the years to come.

YI-HAO CHAN

Principal Investigator
Genetics of Host Immunity Lab
*A*STAR Infectious Diseases Labs (A*STAR IDL)*

Q: TELL US ABOUT THE VIRAL DISEASES YOU'VE STUDIED.

I've had the opportunity to work on a range of viral diseases that are important both in Singapore and globally.

During my PhD degree, I studied the disease mechanics of several mosquito- or arthropod-borne viruses (arboviruses) such as chikungunya (CHIKV), Zika and O'nyong'nyong (ONNV). One of our key findings was that CD4+ T cells—immune cells that coordinate our response to infection—contribute to joint inflammation in patients with CHIKV or ONNV. This discovery opens new avenues for drug development.

When the COVID-19 pandemic hit, I seized the chance to contribute to Singapore's national health response by working closely with clinicians in Singapore's public hospitals. We found that T cell responses, in particular T Helper 2 responses, were important in controlling SARS-CoV-2's disease severity. This was evident when we compared patients who remained asymptomatic to those who developed COVID-19 pneumonia. These insights were especially valuable during the early days of the pandemic when much about COVID-19 was still unknown.

For my second round of postdoctoral training at the Rockefeller University, US, under Jean-Laurent Casanova's tutelage, I studied why certain individuals develop severe brain inflammation after infection by viruses like herpes simplex virus (HSV) and SARS-CoV-2. Though common, these viruses can cause devastating outcomes in rare cases. We found that these can be due to single-gene mutations that affect the body's antiviral defences. Identifying these genetic vulnerabilities not only reveals essential parts of our immune systems, but also uncovers potential targets for future treatments against infectious diseases.

Q: WHAT LINKS OUR GENES AND VIRAL DISEASE OUTCOMES?

While studying genetic factors in HSV infection, I identified its first human restriction factor in the brain: a transmembrane protein called TMEFF1. Restriction factors are natural proteins that block viruses from entering and replicating in cells, acting as part of the body's built-in antiviral defence.

In two unrelated cases of herpes simplex encephalitis (HSE)—a rare but serious brain infection—we discovered harmful mutations in the *TMEFF1* gene that either disabled the protein or misdirected it within the cell. This resulted in the virus gaining unrestricted entry into brain cells and ultimately triggering severe inflammation in the brain.

This discovery has important biological and medical implications, as there is currently no vaccine for HSV-1, and its standard treatment—acyclovir—only targets general viral replication. A TMEFF1-based therapy that blocks viral entry, whether as

"Identifying these genetic vulnerabilities not only reveals essential parts of our immune systems, but also uncovers potential targets for future treatments against infectious diseases."

— Yi-Hao Chan, Principal Investigator (Genetics of Host Immunity Lab) at the A*STAR Infectious Diseases Labs (A*STAR IDL)

a soluble protein or as an antibody-drug conjugate, would be a new and more targeted way to treat not just HSE, but also common conditions of mucosal and skin surfaces, such as cold sores. We are now working to translate this discovery into clinical use.

Q: WHAT WILL THE NRFF AWARD HELP YOU ACHIEVE?

The NRFF is a major boost to my goal of tackling the infection enigma around viral infections: that is, why the same virus can lead to vastly different clinical outcomes across infected individuals. Why do some patients experience severe illness while others don't? By easing our lab's mental bandwidth and resource constraints, the award lets us explore more ideas and make more discoveries in this area.

Our research is focused on uncovering the genetic and immunological factors behind life-threatening viral diseases. We are recruiting patients who developed severe illness alongside individuals who remain asymptomatic or have only mild symptoms despite exposure to the same virus. By genetically sequencing both groups, we aim to pinpoint key genetic variants that cause life-threatening disease outcomes. We also aim to identify unique, essential antiviral pathways that dampen disease, which would in turn deepen our understanding of human biology.

Q: WHAT'S NEXT FOR YOUR LAB?

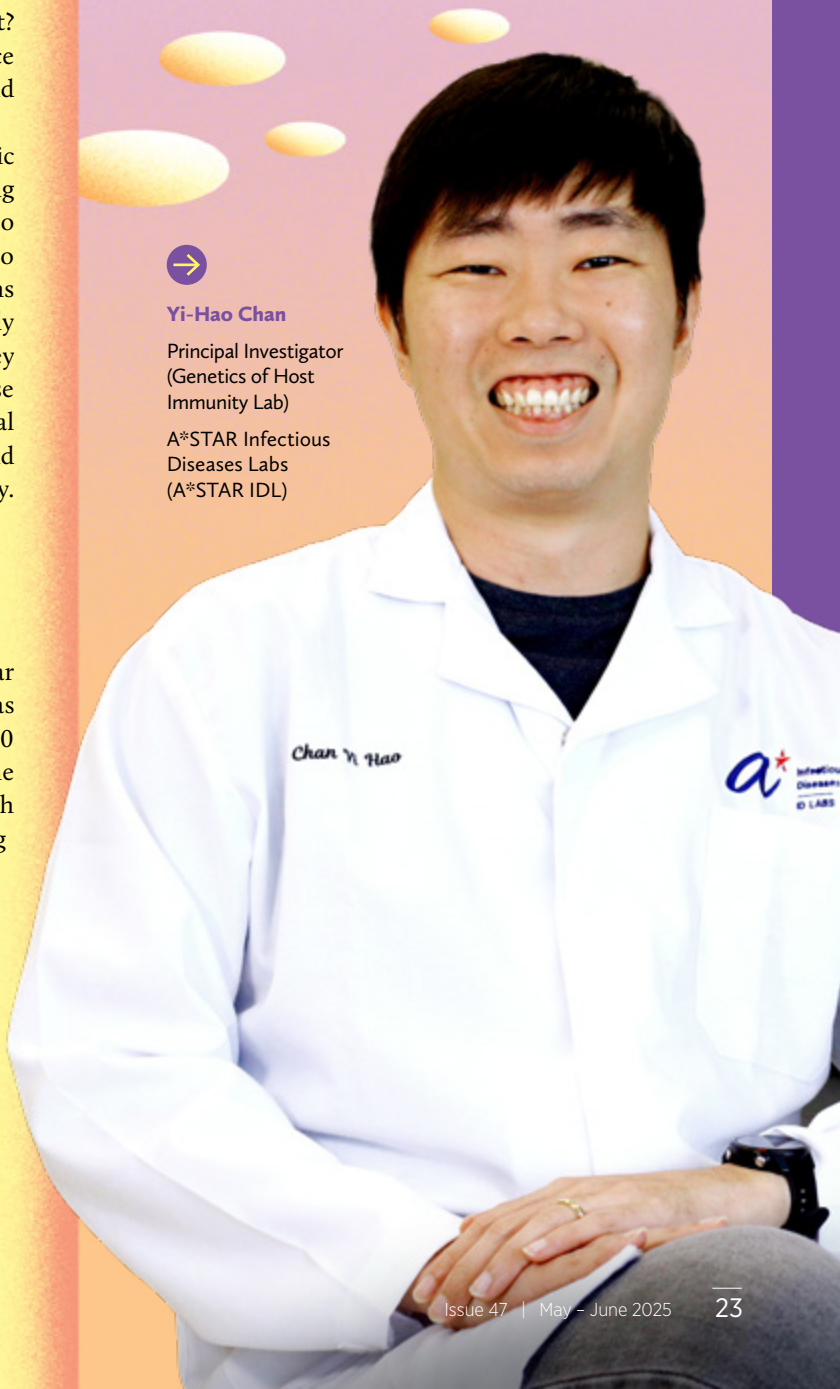
I plan to grow my research group over the next year and delve deeper into deadly arboviruses such as dengue. In 2024 alone, there were more than 13,000 reported cases of dengue in Singapore, and in some years—such as 2020—that number climbed as high as 35,000. Rising global temperatures are expanding mosquito populations, which are in turn driving arbovirus transmission and escalating the threat they pose to public health.

Since my work centres on human genetics, it needs access to cohorts of patients with infectious diseases. I'm actively seeking partnerships with infectious disease clinicians who are keen to unravel the infection enigma and to advance more personalised, mechanism-targeting treatments for affected patients.

Q: WHAT WOULD YOU SAY TO YOUNGER ASPIRING SCIENTISTS?

Persevere, even when the going gets tough. Keep pushing forward and surround yourself with people who uplift and challenge you. I highly encourage finding an experienced mentor who is willing to guide and support you. I've personally benefited from mentors who believed in me, especially during moments of doubt.

Don't give up!



Yi-Hao Chan

Principal Investigator (Genetics of Host Immunity Lab)

A*STAR Infectious Diseases Labs (A*STAR IDL)

SHUANG LIU

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

Q: TAKE US DOWN THE JOURNEY IN SCIENCE THAT LED YOU HERE.

My passion lies in transforming how we approach drug discovery, a field at the intersection of many scientific disciplines. I began my journey in medicinal chemistry as an undergraduate at Imperial College London, UK, where I was supported by A*STAR's National Science Scholarship and studied how small molecule drugs are designed and made.

At A*STAR's Experimental Therapeutic Centre (ETC), now the Experimental Drug Development Centre (EDDC), I had my first experience in fragment-based screening for promising drug candidates. For my PhD degree at the University of Oxford, UK, I investigated how drugs interact with proteins, with a focus on isocitrate dehydrogenase (IDH)—a key enzyme mutated in brain cancer.

As a postdoctoral fellow at the Broad Institute, US, I pioneered a targeted way to discover molecular glue-like compounds using DNA-encoded library (DEL) screening: a method that uses DNA barcode tags on millions to billions of small molecules to rapidly screen for protein binding. Molecular glues had traditionally been found by serendipity, but we were among the first to systematically identify them using a high-throughput platform.

Returning to A*STAR IMCB, I was honoured to receive the A*STAR Young Achiever Award, which supported the launch of my independent research in this area. Each phase of my training—from building molecules, to understanding how they work in cells, and to innovating methods to screen them—has shaped the integrated research approach that was recognised by the NRFF award. I've come to appreciate that meaningful breakthroughs often emerge not from complexity, but from the elegant combination of simple ideas across disciplines.

Q: HOW CAN MOLECULAR GLUES HELP TREAT CANCER AND OTHER DIFFICULT DISEASES?

Molecular glues are small molecules that work differently from most traditional drugs. Rather than targeting a single protein, they bring together two proteins that don't normally interact—typically a disease-related target and a 'presenter' that influences the target's fate.

This mechanism is powerful because it's versatile enough to modulate a wide range of cellular processes. For instance, if the presenter is an E3 ubiquitin ligase—a protein that tags others for destruction—molecular glues can drive the breakdown of harmful proteins, such as those linked to cancer and neurodegenerative diseases. Conversely, when paired with a presenter such as deubiquitinase, which removes those destruction tags, glues can also stabilise beneficial proteins like tumour suppressors.

What makes molecular glues especially exciting is their ability to target proteins previously considered 'undruggable', which make up over 80 percent of the human proteome—the full set of proteins our cells can make. This offers enormous potential for treating complex diseases.

Shuang Liu
Principal Investigator
A*STAR Institute of Molecular and Cell Biology (A*STAR IMCB)

"I've come to appreciate that meaningful breakthroughs often emerge not from complexity, but from the elegant combination of simple ideas across disciplines."

— Shuang Liu, Principal Investigator at the A*STAR Institute of Molecular and Cell Biology (A*STAR IMCB)

Q: WHAT DOES THE NRFF AWARD ENABLE YOU TO WORK ON NEXT?

The award gives me the resources and collaborative environment to build on the momentum of my work and take it to the next level. It allows me to assemble a team of talented, motivated scientists who share the same vision, and marks a pivotal step in my longer journey to push the boundaries of chemical biology and drug discovery.

At the heart of my project is the goal of accelerating the discovery of molecular glues using DEL screening. While DEL is already transforming drug discovery, it hasn't been widely applied to the search for new monovalent molecular glues. With the NRFF's support, I can develop a robust screening platform for that very purpose.

As a proof-of-concept, I will apply this platform in two biological systems—first, the induced breakdown, via molecular glues, of drug-resistant, cancer-causing protein mutants. The next would go beyond degradation: the disruption of harmful protein complexes, using molecular glues that can pull key proteins out of those complexes.

Insights from these systematic screens will also guide the design of entirely new families of molecular glues. Ultimately, this could transform how we tackle hard-to-treat diseases.

Q: WHAT DO YOU HOPE TO ACHIEVE IN THE COMING YEARS?

I aim to conduct a series of proof-of-concept studies showing how different presenter proteins can regulate specific cellular functions. While most research on molecular glues has focused on protein degradation, I'm particularly keen on exploring their other effects. These include disrupting protein-protein interactions, stabilising useful proteins, and modulating cell signalling pathways. These studies will not only advance fundamental science but also provide the blueprints for new therapeutic strategies.

On the translational side, I plan to develop promising molecules identified through DEL screening into preclinical candidates for cancer treatment, working closely with drug development experts at EDDC. The focus on oncology is just the start; the same approach could be extended to many other disease areas.

To bring this vision to life, I look to collaborate with academic groups, biotech firms and pharmaceutical companies interested in applying molecular glue strategies to their own targets of interest. I also warmly welcome young scientists eager to contribute to and grow with this emerging field.

Q: WHAT ADVICE WOULD YOU OFFER ASPIRING EARLY-CAREER RESEARCHERS?

Identify what makes your research and training unique. Carve out a niche where your skills and experiences give you an edge in tackling important scientific questions. Becoming a top expert in your field can set you apart. For me, a deep understanding of IDH's biochemical mechanisms ultimately informed DEL screening strategies that others might not have considered for different protein targets.

Don't shy away from ambitious goals. Sometimes, it is the seemingly modest pursuits that lead to the most transformative insights. Be patient and diligent in building your track record. The dots often only connect in hindsight, but the depth and integrity of your work will speak for itself.

Stay curious, stay committed, and the rest will follow.

BOWEI DONG

Principal Investigator
*A*STAR Institute of Microelectronics (A*STAR IME)*

Q: WHAT EXCITES YOU ABOUT YOUR RECENT WORK?

I study emerging high performance computing systems known as photonic neuromorphic computing (PNC), which process information using the dynamics of light and draw inspiration from the brain's architecture. These systems can be designed to handle the ultrafast data transfer and energy efficiency demands of modern artificial intelligence (AI) models. However, they typically need high-quality light sources to maintain stable optical signals—sources that are challenging to produce and operate.

In our recent work, we demonstrated something surprising: PNC can actually work better using lower-quality light sources, if you design a system right. These light sources are much easier to manufacture, cost less, consume less energy, and are simpler to control— yet they can boost the system's computing performance.

When we used this technology to identify patients with Parkinson's disease, we achieved an accuracy of 92 percent. This discovery pushes the boundaries of what was previously thought possible and opens new doors to more affordable, energy-efficient AI technologies. Our findings have been published in *Nature* and featured in the journal's "Seven Technologies to Watch in 2025" list.

Q: IN YOUR OPINION, HOW CLOSE IS PNC TO REAL-WORLD USE?

We can be very optimistic about PNC's adoption in ways that make real-world impact. In the international sphere, two leading startups have recently unveiled PNC prototypes.

There's Lightmatter, which reported developing a universal photonic AI processor that can run versatile advanced AI models and deep reinforcement learning algorithms, which rely on a lot of trial and error to optimise decisions. As their processor delivers near-electronic precision on many tasks, it's a notable entry for photonic computing to compete with established electronic AI accelerators.

The other startup, Lightelligence, has reported an integrated large-scale photonic accelerator with over 16,000 light-based components, achieving ultralow response times of just three nanoseconds. It can handle the same computational workload as a commercial high-performance A10 graphics processor—but using light instead of electricity as a data medium.

Beyond these design and prototype breakthroughs, we're also seeing momentum on the mass manufacturing side. Taiwan Semiconductor Manufacturing Company (TSMC)—the world's leading chipmaker that produces semiconductors for other companies—has begun investing in photonic computing. That's a strong sign that the industry sees it as the next near-term tech wave.

Some PNC systems are already at mid-to-high technology readiness levels. At this pace, it is reasonable to expect PNC architectures in real-world settings within the next two to five years.

> ***"We're aiming for a future where computers can run self-driving cars, real-time speech recognition and other complex AI applications in the blink of an eye, using less power than current technologies."***
>
> — Bowei Dong, Principal Investigator at the A*STAR Institute of Microelectronics (A*STAR IME)

Q: WHAT DOES THE NRFF AWARD MEAN TO YOU?

The award is a meaningful recognition of the potential of PNC and my work in this field. It reflects the confidence of the research community in PNC as they place their bets on its development. It also highlights NRF and A*STAR's commitment to investing in innovation and deep tech by supporting early-career researchers such as myself in tackling some of the world's most challenging but critical problems.

This prestigious award also affirms my dedication to research and strengthens my resolve to push the boundaries of PNC. It motivates me to climb R&D's steepest mountains with greater confidence.

With the NRF's generous support, I aim to develop the world's best PNC system: a light-based computer so powerful, it can handle massive amounts of data at unprecedented speeds with extreme energy efficiency.

Bowei Dong
Principal Investigator
A*STAR Institute of Microelectronics (A*STAR IME)

The key innovation involved is a photonic computing system that sees the big picture and functions as a unified whole, rather than a collection of smaller parts.

This goes beyond faster internet searches or smoother movie streaming; we're aiming for a future where computers can run self-driving cars, real-time speech recognition and other complex AI applications in the blink of an eye, using less power than current technologies.

Q: WHAT RESEARCH GOALS LIE AHEAD FOR YOU?

My long-term goal is to push for the market adoption of PNC technology and establish it as a core component of future computing systems—much like the CPU is today. Achieving this vision will require building a strong global ecosystem through close collaboration between industry, research and technology organisations (RTOs) and institutes of higher learning (IHLs).

In the near term, with the support of the NRFF award and A*STAR, I aspire to build up the PNC capabilities at A*STAR IME, which provides world-class photonics R&D facilities and the multidisciplinary expertise essential for developing practical PNC systems.

I also plan to collaborate with other RTOs and IHLs to address key PNC challenges—such as scalability—and nurture a new generation of R&D talent and leadership to propel the field forward. Furthermore, by working with public agencies, I hope to expand industry outreach efforts to anchor PNC R&D activities in Singapore.

These combined efforts will drive a vibrant PNC R&D ecosystem and bring us closer to taking this technology to market.

Q: WHAT IS YOUR ADVICE FOR YOUNGER RESEARCHERS?

Take action now—there's no better time than the present. And remember, failure isn't a setback, but a valuable learning experience. ★

BIOMEDICAL ENGINEERING

Stretching the limits of health monitoring

A new wearable sensor continuously detects key chemical biomarkers directly from the skin, circumventing more invasive clinical methods.

Smartwatches, fitness trackers and other wearables have brought us a new era of health literacy and empowerment with their ability to continuously collect real-time data. However, there's still room to improve on what they can tell us, according to Sherwin Tan, a Research Engineer at the A*STAR Institute of Materials Research and Engineering (A*STAR IMRE).

"Current devices primarily measure biophysical parameters, such as heart rate and oxygen saturation level (SpO_2)," said Tan. "Yet there's also a strong need for them to capture biochemical data, like cholesterol levels, to provide a more holistic picture of one's health and vital signs."

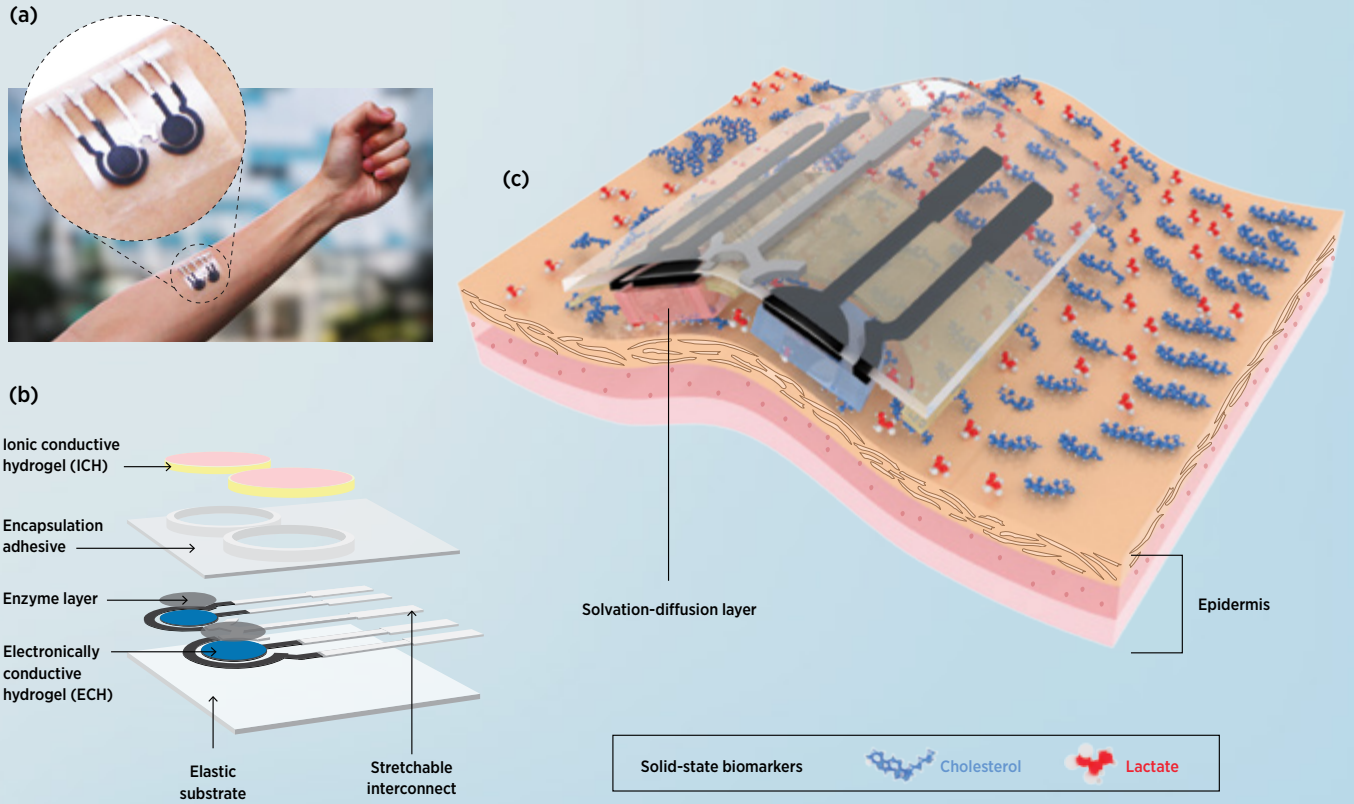
Typically, those biomarkers are assessed through bodily fluids like sweat, urine or blood. This can be problematic, particularly for those who are less active or unable to draw frequent blood samples.

A team co-led by Le Yang, Head of the Printed Organic Flexible Electronics and Sensors (PROFESS) Group at A*STAR IMRE, and Yuxin Liu from the Institute for Health Innovation and Technology, National University of Singapore (NUS), pioneered a new generation of continuous wearable sensors capable of detecting solid-state epidermal biomarkers (SEBs). Found on the skin's epidermal layer, SEBs—which include cholesterol, lactate and proteins—have shown potential to reveal various physiological states or diseases without the invasiveness of traditional methods.

In a recent innovative work, Tan, Yang, Liu and colleagues from A*STAR IMRE, the A*STAR Institute of High-Performance Computing (A*STAR IHPC) and A*STAR Institute of Molecular Cell and Biology (A*STAR IMCB); NUS and Nanyang Technological University, Singapore, proposed that a stretchable ionic–electronic bilayer hydrogel—one that adheres directly to the skin—could enhance SEB detection sensitivity and accuracy, while also reducing motion artifacts that often compromise the performance of current sensors.

"There's also a strong need for [health monitoring devices] to capture biochemical data, like cholesterol levels, to provide a more holistic picture of one's health and vital signs."

Photo credit: Luke Chesser / Unsplash



(a) Photograph of the team's SEB sensor placed on human skin. (b) Schematic of the SEB device structure. (c) Illustration of the SEB sensor on the skin, with SEBs such as cholesterol and lactate passing through the ICH solvation-diffusion layer.

Their sensor comprises two distinct layers: an ionic conductive hydrogel (ICH) and an electronically conductive hydrogel (ECH). "The ICH layer is in direct contact with the skin and dissolves SEBs, allowing them to diffuse rapidly toward the ECH layer, where enzymes trigger an electrochemical reaction," explained Yang. "This process generates an electrical signal that correlates to the targeted biomarker's concentration."

In tests, the hydrogel sensor achieved low detection limits for lactate and cholesterol which outperformed certain mass spectrometry techniques. Its design also reduced motion-related errors threefold versus conventional sensors, boosting its reliability during physical activities. During clinical trials, its stability and strong correlation with blood biomarkers highlighted its suitability for long-term health monitoring.

"Whether for watches, armbands or headbands, our sensor is designed to be seamlessly incorporated into daily items, offering a non-invasive, continuous view of important biochemical markers," said Yang.

With two patent applications underway for their hydrogel sensor technology, the team is also eager to advance their newly launched BLISS (Bettering Lives with In-situ Solid-state Sensorics) programme, which aims to improve SEB sensing, boost the durability of enzyme components and progress the development of flexible electronics. ★

Researchers
Le Yang and Sherwin Tan,
A*STAR IMRE

IN BRIEF
A bilayer hydrogel skin sensor non-invasively detects solid-state biomarkers such as cholesterol and lactate, offering precise health monitoring with minimal motion interference for integration into daily wearables.

1. Arwani, R.T., Tan, S.C.L., Sundarapandi, A., Goh, W.P., Liu, Y., *et al.* Stretchable ionic–electronic bilayer hydrogel electronics enable in situ detection of solid-state epidermal biomarkers. *Nature Materials* **23**, 1115-1122 (2024).

QUANTUM COMPUTING

Classical-quantum hybrid divides and conquers

Combining the best of both classical and quantum computing, a new mathematical approach promises faster solutions for complex modelling of real-world phenomena.

Scientists frequently turn to mathematics to explain and model everyday events. These often include processes that unfold over time, such as the fluctuations of financial markets or the spread of a disease. For complex phenomena where past events and long-term effects are major factors, fractional differential equations (FDEs) offer a way to capture every stage of the process in numbers.

"Solving an FDE is challenging because it requires keeping track of everything that has happened before—like remembering every step you've taken on a long hike. The longer the hike, the more memory you need," said Fong Yew Leong, a Principal Scientist at the A*STAR Institute of High Performance Computing (A*STAR IHPC).

These memory costs can be a nightmare for even the most powerful conventional computers we have today. As such, Leong and colleagues at A*STAR IHPC and the Singapore University of Technology and Design have turned to quantum computers, which have the potential to solve mathematical problems in new and faster ways over classical computers.

However, today's quantum computers are still limited in size and easily affected by hardware noise, which can muddy their solutions for FDEs. The team believes the answer lies in variational quantum algorithms (VQAs), a class of mathematical approaches which leverage the best of both quantum and conventional computing.

"VQAs work by setting up a guess-and-check system: a quantum computer guesses a possible solution, while a classical computer checks how good that guess is, then adjusts settings until the solution is found," Leong explained.

The team developed a VQA based on a divide-and-conquer strategy to solving FDEs, tapping into both the processing power of quantum computing and the precision of its classical counterpart. In their VQA, a quantum computer evaluates quantum state overlaps, then classical computers sum up the resulting values for numerical integration. Where conventional methods would rely on large solution vectors to store information, the team's approach uses shorter parametric vectors to reduce memory costs when tracking long-term history in FDEs.

> "Solving an FDE is challenging because it requires keeping track of everything that has happened before."

To test their classical-quantum hybrid approach under real-world conditions, Leong and colleagues implemented their algorithm on IBM quantum hardware. As they expected, the noise issues faced by current quantum hardware proved a formidable challenge and limited the size of the FDE that their VQA could solve.

Still, the researchers remain hopeful that as error-resilient quantum devices emerge, the performance of VQAs and other near-term quantum algorithms will also improve significantly. According to Leong, such hardware improvements are already on the horizon, as the next generation of fault-tolerant quantum computers could offer greater resistance to noise and errors.

The team now looks to further optimise their algorithms, extending their work to these fault-tolerant devices.

"This will allow us to move beyond the limitations of near-term quantum hardware and design algorithms that are more robust, scalable and practical for real-world applications," Leong said. ★

Researcher
Fong Yew Leong,
A*STAR IHPC

IN BRIEF
A new variational quantum algorithm proves capable of solving memory-intensive fractional differential equations, moving quantum computing a step towards practical and scalable applications.

1. Leong, F.Y., Koh, D.E., Kong, J.F., Goh, S.T., Khoo, J.Y., *et al.* Solving fractional differential equations on a quantum computer: A variational approach. *AVS Quantum Science* **6** (3), 033802 (2024).

Photo credit: Marek Piwnicki / Unsplash

ARTIFICIAL INTELLIGENCE

Delivery routing's need for AI speed

Computational models offer an AI boost to logistics planners by identifying the most efficient transport routes through cross-problem learning.

Photo credit: Colin Lloyd / Unsplash

From the shipping of online shopping goods to the delivery of postal mail, optimised transport routes save time and resources for companies and customers alike. Today, artificial intelligence (AI) models can help human coordinators plan delivery routes that cover multiple locations as efficiently as possible. However, such vehicle routing problems (VRPs)—which fall under a bigger umbrella of combinatorial optimisation problems (COPs)—are often time-consuming and computationally taxing to solve.

"COPs involve finding the best solution from a finite but extremely large set of possibilities," explained Zhuoyi Lin and J. Senthilnath, respectively a Scientist and Senior Scientist from the A*STAR Institute for Infocomm Research (A*STAR I²R). "These problems are crucial as they also occur in manufacturing and even biology; think of production schedules and protein folding."

In collaboration with a global team from Singapore Management University; Eindhoven University of Technology, the Netherlands; and Shandong University, China, Lin and Senthilnath investigated whether VRPs could be more speedily solved through a cross-problem learning approach based on neural heuristics.

"Heuristics are 'rules of thumb' that help to quickly find good solutions without searching every possibility," said Lin and Senthilnath. "Neural heuristics are specifically those learned by neural networks—a type of AI model—instead of being manually designed."

Inspired by how the human brain extracts patterns from data, neural networks can use training datasets to adapt and improve on their own rather than rely on hard and fixed rules encoded by developers. Much like how one might learn to solve a puzzle, the team wanted their model to not just identify the best VRP solutions, but—more importantly—to pick up on the logic behind efficient route planning, then apply these rules to solving other types of COPs.

The team first pre-trained a neural network on a basic routing problem, then explored different fine-tuning strategies for more complicated routing problems.

"We found that adapter-based fine-tuning achieved nearly the same performance as full training, but with far fewer parameters, making the model lighter and more efficient," said the researchers. "One unexpected but exciting result was achieving over 90 percent parameter efficiency, where fine-tuning the model on just a single task significantly improved performance across other complex routing problems. This dramatically reduces computational cost and training time, making the approach highly scalable and efficient."

Based on the proposed cross-problem learning approach, the team's model learnt how to navigate a theoretical delivery network and decide on the best routes, effectively generalising its heuristics across different VRPs.

"Knowledge learnt from solving one type of routing challenge can be reused for other problems," said Lin and Senthilnath. "Our approach reduces the need to manually build a new heuristic algorithm from scratch for each specific task. This can lead to faster, more adaptive logistics and transport solutions."

Looking ahead, the researchers aim to extend their approach to a broader spectrum of real-world optimisation challenges, such as job scheduling and bin packing. They also envision integrating the reasoning capabilities of large language models, which could enable real-time, adaptive decision-making in complex logistical environments. ★

Researchers
Zhuoyi Lin and J. Senthilnath, A*STAR I²R

IN BRIEF
Applying a pre-training then fine-tuning approach accelerated the development of neural networks for optimising vehicle delivery routes, and enabled the networks to generalise learned rules to other combinatorial optimisation solutions.

1. Lin, Z., Wu, Y., Zhou, B., Cao, Z., Song, W., *et al.* Cross-problem learning for solving vehicle routing problems. *Proceedings of the Thirty-Third International Joint Conference on Artificial Intelligence,* 6958-6966 (2024).

CHEMISTRY

Corralling ions for carbon conversion

A simple yet effective solid-state design for acidic electrolysers solves a dilemma in atmospheric carbon conversion for industrial use.

Picture yourself boarding a train at rush hour with a crowd that won't queue, and no railway staff in sight. Now imagine the chaos that can ensue as people rush for the doors, pushing and cutting ahead of others, sparking tempers and exhausting moods.

Engineers working on acidic electrolysers for carbon capture currently face a similar 'crowding at doors' problem, though with particles instead of people. These systems use catalysts to fuse carbon dioxide (CO_2) from the air with hydrogen ions (H^+) from a liquid, converting them into useful industrial products such as ethanol. However, a 'crowd' of H^+ beside a catalyst can change the chemical reactions it favours, producing unwanted hydrogen gas and bicarbonate/carbonate salts instead.

"As bicarbonate and carbonate salts are unreactive and cannot be converted further, they're essentially a waste of CO_2 feedstock," said Yanwei Lum, an Adjunct Scientist at the A*STAR Institute of Materials Research and Engineering (A*STAR IMRE). "What's more, the precipitation of these salts can degrade the entire system's durability and performance, greatly inhibiting CO_2 reduction."

To solve the issue, a group of researchers from A*STAR IMRE, the A*STAR Institute of Sustainability for Chemicals, Energy and Environment (A*STAR ISCE²) and the National University of Singapore (NUS) looked to solid-state batteries for inspiration. The team—which included Lum, A*STAR IMRE PhD student Bo Wu, A*STAR IMRE Scientist Zainal Aabdin and A*STAR ISCE² Senior Scientist Shibo Xi—designed a new solid-state electrolyte (SSE) system for electrochemical CO_2 reduction.

"In a conventional flow cell for this process, the catalyst's surface is in direct contact with an acidic liquid electrolyte, which concentrates H^+ around it," said Lum. "However, in our SSE system, the catalyst doesn't directly touch the electrolyte; an SSE layer between the catalyst and electrolyte keeps extra H^+ from reaching the catalyst's surface."

The SSE layer consisted of a proton conductor previously used by NUS partners to create concentrated carbon product streams. The team found that this layer could act as a filter, allowing just enough H^+ into the catalytic system to create an internal environment that favoured CO_2 reduction.

Through multiple tests with various electrolytic conditions, the team confirmed that their SSE system worked well with a wide range of catalysts, with one setup for carbon monoxide production achieving a Faradaic efficiency of 87 percent. The team also showed that the SSE system was stably operable for more than 110 hours, and could attain a high single-pass carbon efficiency of 82.8 percent.

"Our SSE system also achieved a high selectivity towards carbon products even with a very diluted CO_2 feedstock: 5 percent CO_2, 95 percent nitrogen gas," said Wu. "This opens up possibilities for the direct utilisation of flue gas, which typically has low CO_2 concentrations."

The team plans to further study the local environment between the catalyst and SSE layer to improve the system's efficiency, while further stabilising the system for industrial and practical use. ★

Researchers
Bo Wu and Yanwei Lum, A*STAR IMRE

IN BRIEF
By regulating hydrogen ion flow, a solid-state electrolyte layer between catalysts and acidic electrolytes enables more selective electrolytic CO_2 reduction, potentially boosting carbon conversion efficiency in many catalytic systems.

1. Wu, B., Wang, B., Cai, B., Wu, C., Tjiu, W.W., *et al.* A solid-state electrolyte facilitates acidic CO_2 electrolysis without alkali metal cations by regulating proton transport. *Journal of the American Chemical Society* **146**, 29801-29809 (2024).

Photo credit: Peter Werkman / Unsplash

METALS AND ALLOYS

Strengthened alloys hit a new stretch

Small tweaks in the microstructure of 3D-printed aluminium alloys add exceptional mechanical and thermal properties for semiconductor and aerospace applications.

Since the first 3D printer prototype emerged in 1981, 3D printing methods have found many exciting applications that range from customised prosthetics to life-sized homes. These techniques adopt a layer-by-layer approach not unlike crafting traditional *kuih lapis* (layered rice cakes). The similarities don't stop there; just as an ideal *kuih* needs to be springy, yet rigid enough to stay in shape, an ideal 3D-printed material needs to carefully balance strength and ductility.

These two features are especially critical in metal alloys meant for heavy-duty use in aircraft and cars, but there's often a trade-off between them. "Making a material stronger usually makes it less flexible," said Sharon Nai, a Senior Principal Scientist at the A*STAR Singapore Institute of Manufacturing Technology (A*STAR SIMTech).

Together with collaborators from the A*STAR Institute of High Performance Computing (A*STAR IHPC) and Nanyang Technological University, Singapore, Nai and A*STAR SIMTech colleagues are exploring different processing methods to tune the microstructural features of a modified aluminium alloy based on Al6061, aiming for its optimal use in additive manufacturing (AM)—3D printing at an industrial scale. Al6xxx series aluminium alloys such as Al6061 are widely used in high-value industries such as semiconductors and aerospace, which are strategically important sectors in Singapore's advanced manufacturing landscape.

However, Al6061 parts built by AM tend to have cracks. One current solution is to add nucleation agents like scandium and zirconium, which form ultrafine grains within an alloy's microstructure during printing. Previous studies reported that the formation of such grains, instead of long columnar ones, can help prevent cracks and strengthen the material. Yet when stretched and bent, these mixed microstructures deform in an unstable pattern, forming localised stretch marks known as Lüders bands.

"Even though Lüders bands are sometimes helpful for strengthening materials, we've found they have a negative effect in AM-produced Al6xxx alloys," said Zhiheng Hu, an A*STAR SIMTech Senior Scientist.

In a recent study, Nai, Hu and colleagues tested a modified strategy: making the grains larger, which created both soft and hard regions within Al6061. They began by changing the alloy's composition so that nucleation agents would naturally form at the start of solidification, helping to eliminate cracks. The alloy was then subjected to a high-temperature T6 heat treatment to induce grain growth while retaining some ultrafine grains, which made the material deform more evenly and significantly reduced Lüders band formation.

"This process enables faster, more flexible and more efficient AM of complex, lightweight and high-performance parts that are difficult or impossible to make using traditional methods," said Nai.

The team has since patented their material and production process with Japan-based company Proterial. They are also amid plans to develop more robust and reliable AM processes, and to extend their work to other advanced alloys like Al7075.

"To accelerate this effort, we invite collaboration with industry end users through the A*STAR Additive Innovation Centre (AIC)," said Nai. "We're keen to co-develop applications, validate materials and qualify parts with industry partners to help bring next-generation materials from the lab to practical use." ★

Researchers
Sharon Nai and Zhiheng Hu, A*STAR SIMTech

IN BRIEF
By tailoring microstructures with both process and post-fabrication heat treatment, researchers improve the plastic stability of an additively-manufactured Al6xxx series aluminium alloy, outperforming similar products in the balance of strength and ductility.

1. Hu, Z., Gao, S., Mikula, J., Shen, X., Seet, H.L., *et al*. Enhanced plastic stability: achieving high performance in a Al6xxx alloy fabricated by additive manufacturing. *Advanced Materials* **36** (34), 2307825 (2024).

Photo credit: nj.ap / Shutterstock

ELECTRONICS

Breathing room for tiny flaws

A detailed look at a tungsten-based semiconductor reveals how the spacing of surface defects can improve the material's stability in atmospheric conditions.

Imagine a sheet of paper dotted with a hundred pinholes. At first glance, it might seem fragile—but the spacing between those holes makes all the difference. Cluster them together, and the paper weakens enough for a finger to push through. Spread the holes out evenly, however, and the sheet could hold up almost as well as a pristine one.

For tungsten disulphide (WS_2), the distribution of atom-sized 'holes' may have similar effects, as A*STAR researchers recently discovered. Within the semiconductor industry, two-dimensional (2D) sheets of WS_2 currently stand out as a promising new material for compact transistors and photodetectors—key parts of smartphones, televisions and other everyday electronics. The catch, however, is that existing methods of processing 2D WS_2 often leave S-vacancies—defective 'holes' from missing sulphur (S) atoms—on the material's surface.

"We've found in previous studies that such vacancies, even at a relatively low density, can dramatically reduce how well WS_2 and other 2D transition metal dichalcogenides (TMDs) transport electrical charges," said Kuan Eng Johnson Goh, Pillar Director and Senior Principal Scientist at the A*STAR Quantum Innovation Centre (A*STAR Q.InC) and the A*STAR Institute of Materials Research and Engineering (A*STAR IMRE). "These vacancies also trigger chemical reactions with air, oxidising TMDs faster and degrading their electronic performance."

However, that degradation isn't always even, as noted by A*STAR IMRE Senior Scientist Fabio Bussolotti and colleagues from A*STAR IMRE, A*STAR Q.InC and the A*STAR Institute of High Performance Computing (A*STAR IHPC). Existing literature has indicated that cracked or uneven TMD sections—which have more closely-packed defects—seemed to degrade faster in air than less-damaged sections.

"This led us to hypothesise a direct relationship between vacancy concentration and air degradation in TMDs," said Goh. "Previous studies have focused on 2D WS_2 flakes with uneven structures and a wide range of defect variations, obscuring a possible connection."

To investigate that link, the team cleaved high-quality WS_2 single crystals in ultra-high vacuum conditions, creating a surface with minimal defects. They fired high-energy argon ions at the surface to introduce S-vacancies in controlled amounts, then exposed the material to atmospheric conditions typical of factory cleanrooms.

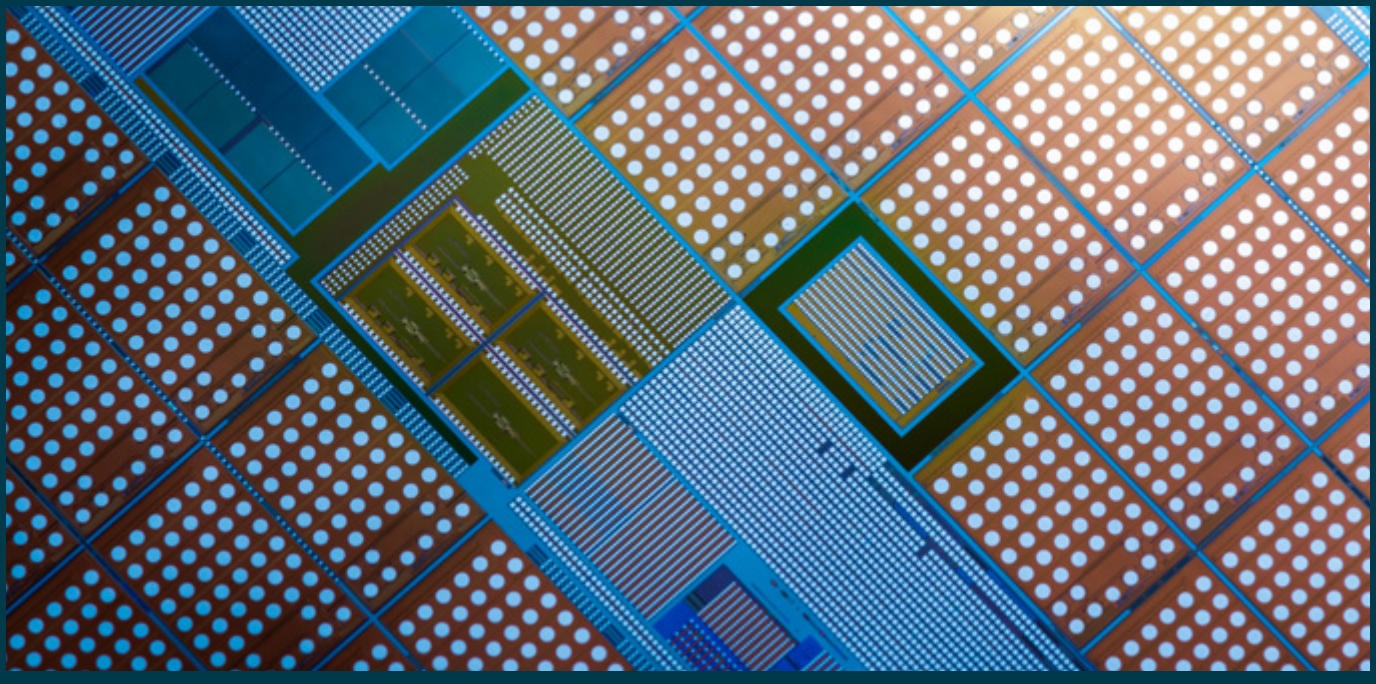
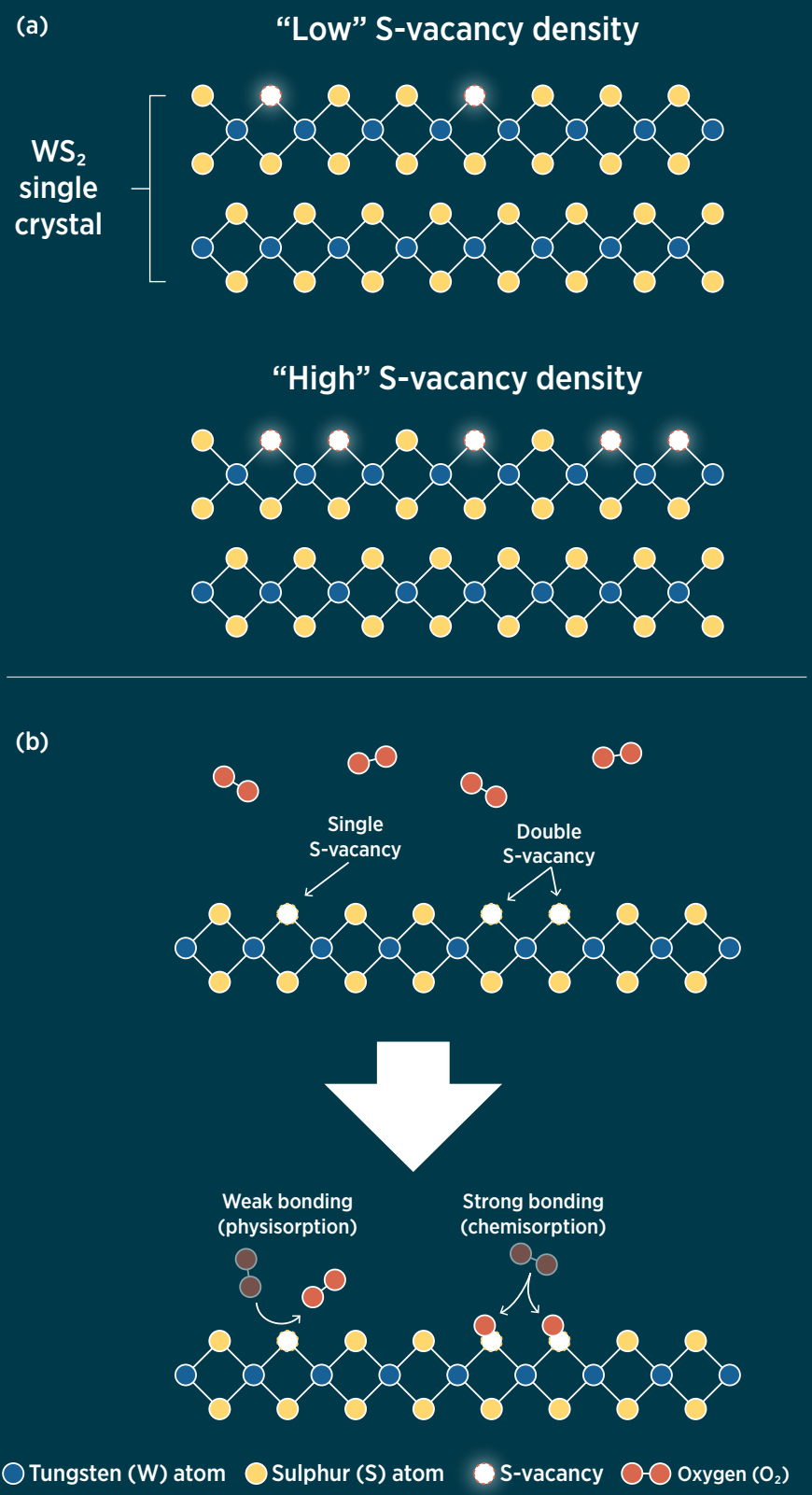


Photo credit: Shyachlo / Freepik



(a) Molecular schematic of low- versus high S-vacancy formations on the surface layer of WS_2 single crystals. (b) Molecular schematic of single versus double S-vacancies on WS_2 when exposed to atmospheric oxygen (O_2). Double S-vacancies tend to absorb O_2, causing WS_2 to degrade.

Through X-ray photoelectron spectroscopy and computer simulations, the researchers found that at S-vacancy concentrations over 10 percent, defects were more likely to cluster and lead to WS_2 oxidation. Surprisingly, this degradation did not occur when S-vacancies existed in isolated units at a concentration under 10 percent, even at ambient conditions.

"It's fascinating how WS_2's chemical reactivity can be so deeply affected by a defect site's physical configuration, a factor quite overlooked to date," said Bussolotti, the study's co-corresponding author. "As perfectly defect-free TMD growing methods don't exist, these findings are encouraging; they can help redefine fabrication strategies that avoid defect clustering, creating more air-stable TMD semiconductors."

The team recently published a follow-up theoretical paper (Kawai et al., 2025) that generalised their findings to the family of semiconducting TMDs. They have also filed three patents related to the work and are exploring techniques to selectively induce oxidation patterns on 2D TMDs for high-quality devices. ★

Researchers
Kuan Eng Johnson Goh and Fabio Bussolotti,
A*STAR IMRE

IN BRIEF
S-vacancy concentrations below 10 percent on tungsten disulphide are enough to minimise the material's degradation under air exposure, enabling its wider use as a semiconductor in next-generation electronics.

1. Bussolotti, F., Kawai, H., Maddumapatabandi, T.D., Fu, W., Khoo, K.H., *et al.* Role of S-vacancy concentration in air oxidation of WS_2 single crystals. *ACS Nano* **18**, 8706–8717 (2024).

2. Kawai, H., Bussolotti, F., Khoo, K.H. and Goh, K.E.J. Propensity of oxidation of transition metal dichalcogenide monolayers in relation to physical configuration of chalcogen vacancies. *Physical Review B* **111**, 094107 (2025).

Next Issue

SNEAK PEEK

A brief look at upcoming research highlights in the next issue of A*STAR Research

CANCER

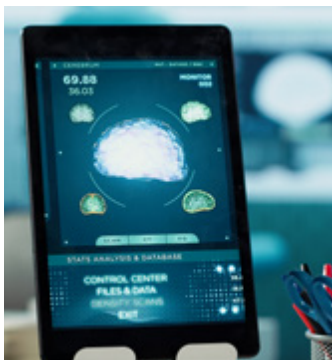
BETTER TIMES FOR LIVER CANCER PATIENTS

A new spatial genomic scoring system outdoes existing tools to identify patients at risk of recurring liver tumours.

MICROBIOLOGY

MICROBIAL NEIGHBOURS KEEP GOLDEN YEARS SHINING

An expansive genomic survey of gut microbiomes in elderly Singaporeans reveals how such communities shape healthy ageing.



ARTIFICIAL INTELLIGENCE

DOCTOR AI ON CALL

An AI-based framework adds a personal touch to medical dialogues, supporting diabetes patients with their health management plans.

MATERIALS SCIENCE

IONOGELS CHARGE ON TO GREENER WEARABLES

A new generation of flexible polymers offers a recyclability boost for wearable bioelectronics.

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