

A*STAR RESEARCH



Issue 53 | May – June 2026

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biomanufacturing innovation from A*STAR

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A*STAR RESEARCH

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

*A*STAR Research* is published bimonthly, presenting research highlights and feature articles. All articles are first published online on the *A*STAR Research* website and available free to all readers. Register online to receive our monthly e-newsletter by email.

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*A*STAR Research* is published for A*STAR by the custom media publishing unit of Wildtype Media Group Pte Ltd.

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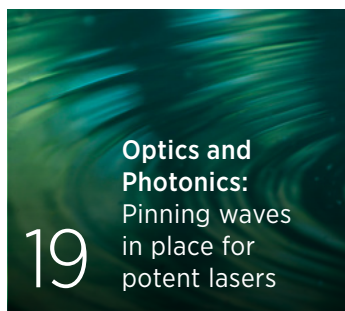
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EDITORIAL NOTES

More than a century after the first insulin trials to successfully treat diabetes, the hormone still stands as one of medicine's greatest success stories, transforming a once-debilitating disease into a manageable condition for millions worldwide. Beyond its discovery, a key breakthrough in the insulin story was when scientists managed to engineer simple microbes to produce insulin at industrial scale, replacing laborious extraction from animal sources and opening new horizons in mass production.

This issue explores echoes of insulin's journey through new developments in bioprocessing and biomanufacturing propelled by A*STAR and its ecosystem partners. Our cover story, 'Nurturing factories of the future (p. 08)', highlights research and innovation across the pipeline from drug discovery to manufacturing, and the collaborative efforts that are launching biotransformative marvels from benchtops to factory lines.

For a closer look at one innovation journey, we speak with Zach Pang, who balances the roles of researcher at the A*STAR Bioprocessing Technology Institute (A*STAR BTI) and entrepreneur

at A*STAR biotech spinoff AuctuCel. In 'Perfecting cell farms (p. 20)', Pang discusses how industry-wide challenges in optimising culture media motivated his mission to bring computational modelling to biomanufacturing.

Turning to foundational research at new frontiers, 'Tracking order in quantum chaos (p. 28)' follows A*STAR International Fellow Bo Xing as he investigates computational approaches for predicting the behaviours of quantum many-body systems. Xing reflects on his introduction to quantum physics, discusses how our understanding of quantum entanglement has evolved, and shares perspectives on the future of quantum computing.

Other articles in this issue highlight the latest A*STAR research developments ranging from new insights on tuberculosis's hidden risks to game-changing ways to upcycle single-use plastics. For more on these, turn to 'Microbial fortresses accelerate new infections (p. 04)' and 'Breaking barriers in polystyrene waste (p. 33)'.

To stay updated on the latest developments in A*STAR research, visit research.a-star.edu.sg. You can also follow us on LinkedIn at A*STAR Research and Telegram at A*STAR Research.



On the cover

A conveyor belt extended from a cell represents the essential upstream to downstream stages of a coordinated bioprocessing pipeline, turning cellular systems into living factories for useful biomolecules.



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INFECTIOUS DISEASES

Microbial fortresses accelerate new infections

A*STAR researchers uncover how bacterial hideouts created during tuberculosis infections can also protect and feed other opportunistic invaders.

Two armies at war can reach a stalemate, with both sides divided by sturdy fortress walls or a stretch of no man's land. Similarly, battles between our immune cells and invading tuberculosis (TB)-causing bacteria, such as *Mycobacterium tuberculosis*, often form tuberculous granulomas: long-lasting, capsule-like structures that isolate the bacteria within the body.

"Granulomas are like a walled city built by our immune system and TB-causing bacteria as a compromise, where the body lets TB do what it wants inside those walls," explained Stefan Oehlers,

a Principal Investigator at the A*STAR Infectious Diseases Labs (A*STAR IDL).

Though TB can be effectively treated by antibiotics, their granulomas can persist in the lungs and result in subclinical or asymptomatic TB. Notably, granulomas could also make patients more prone to infection by other invaders: non-tuberculous mycobacteria (NTM) such as *Mycobacterium abscessus*.

"Around 25 percent of patients with NTM infections in Singapore and the region have a recent TB diagnosis. Singapore's elderly are also a major demographic risk

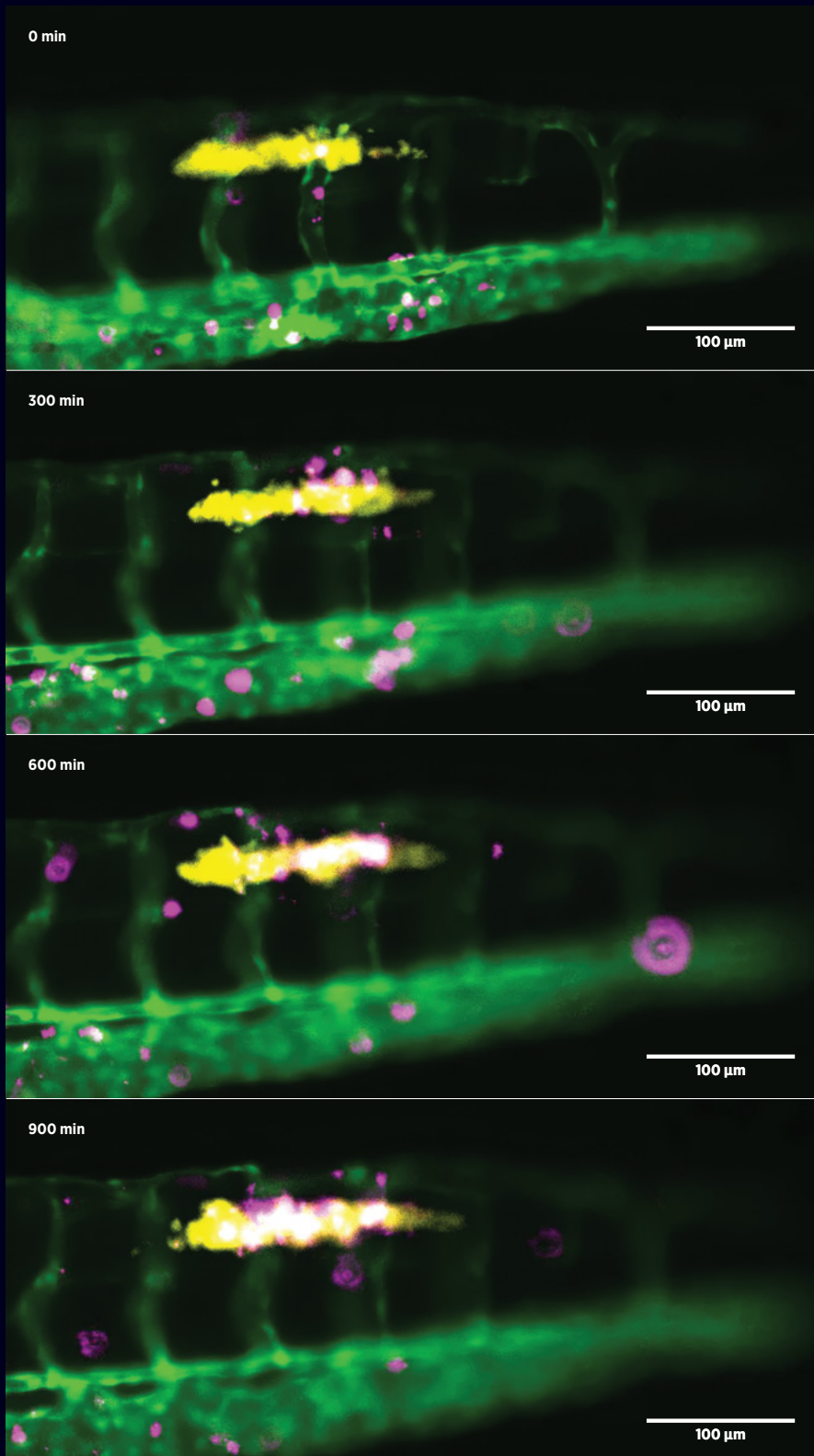
group for NTM infection, as they were endemically infected with TB decades ago," said Oehlers. "As antibiotics against TB usually don't work against NTM, we need to do everything we can to prevent infections by the latter."

While previous studies and clinical reports have observed NTM residing in granulomas, it's been unclear how exactly TB granulomas promote NTM infections. To shed more light on this relationship, an A*STAR IDL research team including Oehlers and Senior Principal Investigator Amit Singhal took a closer look at zebrafish infected with a fluorescent strain of *Mycobacterium marinum*—a human TB-like bacteria—which were then infected by similarly fluorescent *M. abscessus*.

"Our 'Eureka' moment came when we first performed timelapse imaging and recorded *M. abscessus* streaming into a tuberculous granuloma," said Oehlers.

From that one short movie, the team made two striking observations: the pre-existing granuloma fed the NTM, which rapidly grew in real time. The granuloma also sheltered the NTM from the immune system—by the end of the recording, most NTM that failed to reach the granuloma had been destroyed by immune cells.

Photo credit: Denise Wee / A*STAR IDL



Timelapse images of *Mycobacterium abscessus* bacteria (purple) migrating from an adult zebrafish's vasculature (green) into a *M. marinum* granuloma (yellow), where they proliferate. (Photo/video credit: Stefan Oehlers and Denise Wee / A*STAR IDL)

The team then compared the gene expression patterns of *M. abscessus* grown in the zebrafish infection model with *M. abscessus* grown in culture media. They observed that bacteria from the model had more upregulated lipid metabolism, which suggested NTMs fuel their growth by feeding on caseum: the lipid-rich cell debris at the core of TB granulomas, which are 'leftovers' of TB-causing bacteria. The scientists confirmed this when they saw *M. abscessus* grow rapidly in media with caseum.

Oehlers highlighted that these findings have implications for patients initially diagnosed with TB and NTM, but primarily treated for TB. "We need to think about monitoring and adaptably treating co-infection with antibiotics effective against both types of bugs," said Oehlers.

The team plans to validate their findings by studying the links between unhealed granulomas—as indicated by exit X-rays of patients who completed TB treatment—with subsequent secondary NTM infections. "While this won't immediately help at-risk patients, we think exit X-rays could be used to flag the patients at the most risk of secondary infections early, when the infections will be the most curable," Oehlers added. ★



Researchers

Stefan Oehlers and Amit Singhal,
A*STAR IDL

IN BRIEF

Zebrafish models reveal how primary tuberculosis infection creates lingering granulomas that shield non-tuberculous mycobacteria from the immune system and promote their proliferation, boosting the risk of secondary infection.

1. Wee, D., Pandey, M., Chen, Y., Lorenzini, P.A., Chow, E.W.L., *et al.* Primary tuberculous mycobacterial granulomas provide a niche for superinfecting *Mycobacterium abscessus*. *Nature Communications* **16**, 10760 (2025).

CANCER

Screening signatures of dodgy tumours

A new cellular model of colorectal cancer helps identify high-risk subtypes likely to resist standard treatments and proliferate in response.

Treating cancer with chemotherapy can be like spraying weedkiller on a crop field. By blanketing the landscape, both treatments aim to destroy every trace of their targets. However, just as a few tough weeds might survive the blast, some cancer cells can escape, becoming not only treatment-resistant but also more aggressive in spreading (metastasising).

That's an issue faced today with oxaliplatin, a long-time standard chemotherapy for colorectal cancer (CRC). While the drug has benefited many patients, some benefit much less than others for reasons that remain unclear, noted Mohua Das, a Scientist at the A*STAR Genome Institute of Singapore (A*STAR GIS).

"We need reliable models of metastasis driven by chemotherapy resistance, which can simulate what happens in patients whose tumours don't respond to oxaliplatin—or chemotherapy in general—and eventually spread," said Das, who is also a Senior Postdoctoral Fellow at the laboratory of Ramanuj DasGupta, A*STAR GIS Senior Principal Scientist. "These would help us uncover the biological 'control switches' linking drug resistance with metastasis, which

could in turn help us identify patients likely to benefit from existing therapies, and develop new therapies."

To this end, Das and Stephen Wong, a former graduate student at the DasGupta laboratory, recently co-led the development and transcriptomic analysis of a laboratory model for acquired oxaliplatin resistance in CRC. The team included A*STAR GIS colleagues such as Jiamin Loo, and research partners such as Iain Tan and colleagues from the National Cancer Centre Singapore; Experimental Drug Development Centre, Singapore; University of Geneva, Switzerland; and Katholieke Universiteit Leuven, Belgium.

The team first treated CRC cells with repeated cycles of oxaliplatin over time, closely mimicking the treatment regimes received by patients with CRC. Using bulk and single-cell technologies to analyse changes in gene activity, the team then examined how the surviving cancer cells adapted.

"We found that CRC cells progressively switch on specific gene programmes as they become resistant," said DasGupta. "Through computational analyses and experimental validation, we identified the gene *SERPINE1* as the most prominent and

targetable factor within these programmes, driving both chemotherapy resistance and metastatic behaviour."

Based on their discovery, the team performed drug screens to identify novel *SERPINE1*-inhibiting treatments, which validated their ability to stall metastasis in mouse models. They also developed a composite multi-gene signature, RESIST-M, and evaluated its ability to stratify independent CRC patient cohorts.

"RESIST-M consistently predicted poorer overall and recurrence-free survival, and was enriched in aggressive, fibrotic tumour subtypes, supporting its potential utility for patient stratification," said Das. "Identifying high-risk patients earlier based on RESIST-M status could help clinicians make more informed therapy selections, ultimately improving treatment outcomes and life expectancy."

In collaboration with the Chinese University of Hong Kong, the team is investigating anti-PD-L1 resistance in liver cancer, with results so far consistent with their oxaliplatin resistance models. "This suggests *SERPINE1* may mediate a broader, therapy-agnostic mechanism of cellular resistance across both chemotherapeutic and immunotherapeutic contexts," DasGupta added. ★



Researchers

Mohua Das and Ramanuj DasGupta,
A*STAR GIS

IN BRIEF

Models of acquired oxaliplatin resistance in colorectal cancer reveal that the *SERPINE1* signalling axis drives treatment-induced resistance and metastasis, and that RESIST-M, a *SERPINE1*-based multi-gene signature, can successfully stratify high-risk subtypes.

1. Wong, S.Q.R., Das, M., Tenzin, K., Shirgaonkar, N., Chua, H., *et al.* Modeling oxaliplatin resistance in colorectal cancer reveals a *SERPINE1*-based gene signature (RESIST-M) and therapeutic strategies for pro-metastatic CMS4 subtype. *Cell Death & Disease* **16**, 529 (2025).

BIOMEDICAL ENGINEERING

Linking up enzymes for wound healing

A nanogel-based tri-enzyme delivery platform restores biochemical balance and promotes healing in skin wounds.

Nothing gets a difficult job done better than great teamwork. In the human body, enzymes work together to facilitate tightly coordinated chain reactions, operating like catalytic tag teams. Molecular products are passed from one enzyme to the next in these cascades, resulting in complex biochemical processes that are essential for cell and organ function.

New therapeutic strategies inspired by these enzymatic cascades aim to restore biochemical balance in metabolically stressed environments, such as post-surgical wounds. After pancreatic surgery, for instance, skin wounds are often burdened by damaging reactive oxygen species (ROS), limited oxygen supply and high glucose levels that can nourish infection-causing bacteria.

Researchers such as Xiaotong Fan, a Scientist at the A*STAR Institute of Sustainability for Chemicals, Energy and Environment (A*STAR ISCE²), are hoping multi-enzyme therapies can help accelerate wound healing and tissue repair. “Earlier multi-enzyme delivery platforms have often suffered from enzyme leakage, limited stability and low reaction efficiency,” said Fan.

To address these design gaps, Fan, along with Chaobin He, a Senior Principal Scientist at the A*STAR Institute of Materials Research and Engineering (A*STAR IMRE), and Zibiao Li, Director of A*STAR IMRE’s Resource Circularity Division and an A*STAR ISCE² Senior

Principal Scientist, collaborated with researchers from National University of Singapore; and Fuzhou University and Fujian Provincial Hospital in China.

Together, they assembled a three-enzyme rescue team: glucose oxidase (GOX), superoxide dismutase (SOD) and catalase (CAT). Each enzyme was first encased in a thin polymer network to protect against harsh environments that could compromise reactivity. Acting as molecular glue, zinc ions then clustered the enzymes together, forming a zinc-coordinated tri-enzyme nanogel system (Zn@nGSC).

“This design not only prevents enzyme leakage but also ensures spatial confinement of the enzymes, thereby significantly enhancing cascade reaction efficiency,” explained He.

The team tested their system in a mouse model with skin wounds following partial pancreatic surgery. In Zn@nGSC’s choreographed reaction sequence, GOX consumes excess glucose and further sets off processes to prevent infection. SOD and CAT work together to neutralise ROS to drive down inflammation and to oxygenate tissues, accelerating skin repair.

Zn@nGSC-treated animals showed faster wound closure, reduced bacterial infections, and improved blood vessel formation. Crucially, the tri-enzyme system remained stable under physiological conditions and outperformed platforms carrying only one or two enzymes.

“Our results show that biological complexity cannot be effectively addressed by isolated enzymatic functions,” said Fan. “Instead, multi-enzyme systems like Zn@nGSC can reprogramme disease microenvironments in a more integrated and holistic way.”

To improve their tri-enzyme strategy, the team plans to adapt the system to other metabolically compromised environments beyond skin wounds. They also hope to improve the system’s responsiveness to dynamically meet the evolving demands of diseased tissues.

“Our next goal is to enable precise activation of enzymes only when and where they are needed, so that local biochemical balance can be restored in a controlled and efficient manner,” said Li. ★



Researchers

Zibiao Li, A*STAR ISCE² and A*STAR IMRE, Xiaotong Fan, A*STAR ISCE², and Chaobin He, A*STAR IMRE

IN BRIEF

Zn@nGSC, a zinc-coordinated tri-enzyme nanogel system, links glucose oxidase, superoxide dismutase and catalase into a coordinated catalytic cascade that corrects multiple metabolic disruptions in post-surgical wounds, accelerating tissue repair.

1. Ma, Y., Xie, C., Liao, C., Huang, B., Liu, S., *et al.* Zinc-coordinated trienzyme nanogel cascade therapy for accelerated post-pancreatectomy cutaneous wound healing. *Advanced Materials* **37** (50), e08538 (2025).

NURTURING FACTORIES OF THE FUTURE

Whether for novel medicines or high-value chemicals, A*STAR teams are at the forefront of new developments across the pipeline and scaling up scientific breakthroughs for Singapore's growing bioeconomy.

Over several decades, Singapore has solidified its leading position in both the biomedical sciences and advanced manufacturing. The nation-state now stands as a global biomanufacturing powerhouse, housing over 60 plants dedicated to bio-based products and attracting more than S\$4 billion in investments in 2025.

To support this growing bioeconomy, dedicated infrastructure has laid the necessary foundations. Across the Biopolis campus in Singapore's one-north precinct, strong links between public and private research institutes have created an assembly line from basic life science research to practical biotech innovations. At the island's western end, the Tuas Biomedical Park offers purpose-built facilities that have drawn global biopharmaceutical firms to establish themselves on local shores.

The silent engine powering this booming industry is bioprocessing, which harnesses the power of living systems to synthesise bio-based products. Since 1990, research hubs such as the A*STAR Bioprocessing Technology Institute (A*STAR BTI) have been not only been pushing the frontiers of bioprocessing itself, but of the scalable end-to-end technologies in data analytics, automation and commercial-scale process design that successfully move such innovations from labs to factories.

"Biomanufacturing has come a long way, with advances in molecular and digital technologies enabling the production of complex biological products at larger scales and with improved consistency," said Boon Tong Koh, A*STAR BTI Executive Director. "Our research capabilities have grown alongside the industry's needs."

Today, interdisciplinary teams at A*STAR and associated partners are at the heart of bioprocessing and biomanufacturing value chains that are scaling research breakthroughs into transformative real-world products. In tandem with strategic investments in tech and talent development, these have made Singapore a globally recognised biomanufacturing launchpad, leading to tangible gains in healthcare solutions, industrial innovation and economic resilience.



BIOLOGICS: FROM SCIENCE TO SUPPLY

Some of today's most desirable biomanufacturing products are biologics: complex therapeutics derived from or generated within living cells. From antibody proteins to message-carrying nucleic acids, biologics can be potent alternatives to conventional chemically synthesised drugs and vaccines in fighting new and complex diseases.

A biologic's journey to the clinic usually begins with finding a promising treatment target—such as a critical protein a virus depends on—and developing a biomolecule aimed at that target. Then, cells or microbes are engineered into biological 'factories' that can produce that molecule at scale in specially designed bioreactors. Their outputs are then purified over several stages before being formulated into biologics.

To ensure biologics are as safe and clinically effective as possible, yet produced efficiently enough for mass distribution, every stage of biologics bioprocessing and biomanufacturing requires significant optimisation. In this area, A*STAR's research ecosystem spans the entire innovation pipeline, from discovery and process development to manufacturing and scale-up.

1. MAKING FOUNDATIONAL FINDINGS

A biologic's first step is discovery: a famously difficult task that can involve screening up to thousands of molecules for one that hits the mark. Of these, only 1 to 2 percent will obtain regulatory approval as medicines, even after long, complex and costly drug development processes.

Beating those odds, EBC-129, Singapore's first-ever antibody-drug conjugate (ADC), successfully cleared the drug development pipeline in a major multi-institutional effort between A*STAR BTI, the National Cancer Centre Singapore (NCCS) and Experimental Drug Development Centre (EDDC). Designed to attack cancer cells while sparing healthy tissue, an ADC is a powerful link-up between a highly selective antibody that latches onto and enters cancer cells, and a toxic drug payload that destroys those cells from within.

"They're like a magic bullet," said Andre Choo, A*STAR BTI Deputy Executive Director. "Their combination of specificity and potent cell-killing ability makes them more precise and less harmful than typical cancer treatments."

A*STAR BTI and NCCS researchers first discovered the antibody GR6A04, which binds to the CEACAM5/6 proteins abundantly found on cancer cell surfaces. Unlike other CEACAM-targeting drugs in development, GR6A04 targets specific sugar-binding sites on CEACAM5/6 that are exclusively present on cancer cells. Leveraging A*STAR BTI's bioprocessing value chain and antibody development capabilities, the team was able to scale up manufacturing of the antibody for further characterisation.

Next, through an A*STAR BTI-EDDC co-development programme, the team carried EBC-129 through preclinical and Chemistry, Manufacturing and Controls (CMC) development—including Good Manufacturing Practice (GMP) and toxicology studies—before advancing to clinical trials, for which EDDC led initiation and regulatory submissions.

In 2023, EBC-129 was approved by the United States Food and Drug Administration (US FDA) and Health Sciences Authority Singapore to initiate clinical trials. This was followed by its Fast Track Designation as a pancreatic ductal cancer therapeutic from the US FDA in 2025.

"EBC-129's success exemplifies how drug discovery is a team sport, uniting experts across the continuum for a common and larger purpose," remarked Choo. "Through this journey, we've also built a cadre of people with the experience to support future drug development programmes."

2. REFINING PRODUCTION

Biologics production also requires ‘cell factories’ that offer high yields, stability and quality of valuable biomolecules at large scales. However, living cells are less predictable than machines. Just as a class of bakers given the same recipe may produce cakes of different qualities at different speeds, a batch of cells transfected with the same plasmid vectors—genetic vehicles which ‘deliver’ recipes for a desired product into cells—can vary in output.

Typically, cell line development (CLD) selects the best candidate cells for biomanufacturing by painstakingly sifting through hundreds of thousands of clones. To streamline the process, A*STAR BTI Cell Line Development Group Leader Yuan Sheng Yang and colleagues have developed a multicistronic second-generation CLD platform which not only improves how genetic ‘recipes’ are delivered to cells, but also helps embed these instructions more effectively into each cell’s genetic blueprint, allowing them to be followed more reliably to create a larger pool of competent ‘baker’ cells to choose from.

“Through an optimised plasmid vector and targeted integration system, our platform generates stably transfected pools where most cells express antibodies at high titres for a long term,” said Yang. “This means optimal cell lines can be efficiently identified by screening relatively less clones; fewer than 100 in some cases.”

Designed for Chinese hamster ovary (CHO) cells—a widely used cell line—the platform’s multicistronic nature also enables more complex, multi-specific biologics. Transfected with a single DNA strand carrying multiple genetic instructions, a customised CHO cell line can synthesise multiple antibody chain types in specific ratios, or express multiple enzymes for tailoring ADC structures.

3. CONDUCTING THE DOWNSTREAM

Once produced in bioreactors at scale, desired biomolecules need to be purified from production cells before they can be formulated into medicines. From filtration to chromatography, a series of downstream processing operations must be synchronised like an orchestra even as each step calls for different reagents, conditions and equipment settings. As this stage can take a substantial fraction of biomanufacturing costs and time, optimisation through process intensification is key.

“However, intensification doesn’t simply mean running the whole process faster,” explained Wei Zhang, Group Leader of Downstream Processing at A*STAR BTI. “It’s about holistically reviewing and deliberately redesigning the process to maximise production efficiency while achieving high productivity, quality and purity.”

As an example, Zhang pointed to chromatography, a technique that separates biomolecules based on their physicochemical properties. Unlike conventional batch chromatography, continuous chromatography uses multiple columns in succession to enable uninterrupted purification and improve product consistency.

“Continuous processing also depends on reliable and robust Process Analytical Technology (PAT) to monitor critical process parameters (CPPs) and a product’s critical quality attributes (CQAs), enabling real-time feedback and rapid decision-making,” said Zhang. “Since deviations in one stage can affect the entire workflow, it must be sufficiently flexible and resilient, equipped with risk mitigation and process control strategies.”

With innovations in real-time monitoring as the goal, Zhang’s team and their A*STAR BTI colleagues are developing and assessing PATs for various unit operations, including in-line and at-line analytics that evaluate CPPs and CQAs as products move along the workflow.

“[Intensification is] about holistically reviewing and deliberately redesigning the process to maximise production efficiency while achieving high productivity, quality and purity.”

— Wei Zhang, Group Leader (Downstream Processing) at the A*STAR Bioprocessing Technology Institute (A*STAR BTI)



4. EXPANDING NOVEL MODALITIES TO THERAPIES

In this space, the Nucleic Acid Therapeutics Initiative (NATi) brings together scientists and industry veterans with experience from the science behind medicines, to how they are developed, manufactured, protected by patents, approved by regulators and brought to market. Combining expertise in mRNA vaccines and immune-modulating therapies, NATi aims to advance next-generation RNA medicines beyond infectious diseases as well as innovative oligonucleotide drugs.

NATi is funding research across Singapore to develop stable, broadly applicable mRNA medicines. Its mRNA therapeutics are not limited to pandemic vaccines, but also cover a wider range of conditions, such as improving how lipid nanoparticles carrying mRNA medicines interact with the immune system to unlock more precise applications.

Beyond mRNA, NATi is also developing synthetic oligonucleotides, which complement mRNA's ability to influence biological signals. Together, these technologies provide more precise control over disease processes and support developing more flexible, targeted treatments.

Through its Accelerator programme, NATi also supports high-risk, high-reward biomedical research. "NATi operates like a biotech company with a venture arm. We develop competitive technologies and grow new businesses in peacetime, while remaining ready to redirect resources towards national health priorities during emergencies," said Mohamed ElSayed, NATi Executive Director.

Hilleman Laboratories, a vaccine research organisation established through a joint venture between US pharmaceutical company MSD and UK charity foundation Wellcome Trust, is among the organisations that engage with Singapore's biomanufacturing and innovation ecosystem, which includes initiatives such as NATi.

Guided by a mission to translate strong science into products with a line of sight to affordable manufacturing and equitable access—particularly for low- and middle-income countries—Hilleman works with a range of partners across the ecosystem, including A*STAR BTL, to help advance the translation of scientific innovation into scalable manufacturing solutions for global health.

Raman Rao, Hilleman's Chief Executive Officer, commented that as Singapore's ecosystem consistently prioritises quality, talent and trusted regulatory

standards, its infrastructure, connectivity and pro-innovation policies can help speed up ideas into public health-ready products.

"That matters because preparedness is not something switched on in a crisis, but built and tested continuously," Rao added. "Vaccines don't save lives simply when they exist, but when they can be produced reliably, transported through existing supply systems, and administered quickly at points of need. As such, we need resilient systems that can keep learning, improving and delivering across multiple diseases over time."

"Vaccines don't save lives simply when they exist, but when they can be produced reliably, transported through existing supply systems, and administered quickly at points of need."

— Raman Rao, Chief Executive Officer of Hilleman Laboratories





BEYOND MEDICINES: SCALING TOWARDS SUSTAINABLE INDUSTRY

Biomanufacturing routes can also lead to specialty chemicals and valuable ingredients for industries beyond healthcare. These include terpenes: plant chemicals essential to consumer care products from vitamin supplements to fragrances.

As with biologics, a promising alternative lies in metabolically engineering microbes to produce the same molecules directly. In this space, Xixian Chen, a Junior Group Leader at the A*STAR Singapore Institute of Food and Biotechnology Innovation (A*STAR SIFBI)'s Biotransformation and Engineering Department, made a breakthrough with her colleagues by developing a new production method for *cis*- α -irone, a terpene fragrance component of orris root oil with a market price above US\$15,000/kg.

Typical *cis*- α -irone production involves vast tracts of land paired with years of plant cultivation and processing, while attempts at metabolic engineering have been stymied by knowledge gaps about the biosynthetic pathways involved. To bypass this, the team engineered a pathway in *Escherichia coli* bacteria that starts with simple feedstocks to derive a known precursor and transform that to *cis*- α -irone—akin to detouring off a blocked road and returning to it at a later point.



“Our process was over 4,000 times more efficient than the traditional extraction route, successfully producing pure *cis*- α -irone in a bioreactor,” said Chen.

The team’s scalable terpene platform is being commercialised through A*STAR pre-spinoff AlterING, co-founded by Chen and A*STAR SIFBI Principal Scientist Simon Congqiang Zhang.

“AlterING seeks to harness biology to transform how chemicals are produced, enabling more sustainable manufacturing while supplying ingredients that are gentle on people and kind to our planet,” Chen added.

Besides reducing the need for petrochemicals, biomanufacturing can further shrink the chemical industry’s carbon footprint by making use of waste streams and untapped low-cost materials. As such, researchers led by Yee Hwee Lim, Director for Specialty Chemicals and Bio-Technologies at the A*STAR Institute of Sustainability for Chemicals, Energy and Environment (A*STAR ISCE²), aim to expand the range of chemical reactions that biological systems can perform.

The team’s Platform for Reversible Omics of Genes and Molecules (PROGeM) uses a combined protein and chemical language model to simulate how the molecular instructions encoded in a microorganism’s genome contribute to feasible biochemical processes and products, and vice versa.

“We can rapidly scan diverse kingdoms of life, from bacteria to plants, to find the enzymes or microbial strains best suited to produce a specific chemical,” said Lim.

This data-driven search feeds into an iterative workflow where generative artificial intelligence (AI) and computational modelling approaches help optimise stable and highly efficient enzymes. These then undergo functional tests by high-throughput platforms, which directly feed experimental results back into the model to improve enzyme design.

By engineering an established industrial bacterial species, the team have also developed a two-stage biotransformation platform that uses resting cells to avoid typical trade-offs between cellular growth and chemical production. Their pipeline converts ethylene glycol, a broken-down component of plastic bottles, into glycolic acid, an industrially relevant compound for cosmetics and textiles.



“Our approach delivers glycolic acid titre levels of nearly 100 g/L—among the leading results reported globally for this transformation—making it economically competitive with conventional chemical synthesis,” Lim said.

Ethylene glycol, alongside methanol, is also being used as a low-cost feedstock by the Sustainable Biomanufacturing Technology Platform (SBTP), a collaboration between A*STAR SIFBI, A*STAR ISCE², the A*STAR Singapore Institute of Manufacturing Technology (A*STAR SIMTech), biomanufacturing company MojiaBio and the National University of Singapore. SBTP leverages computationally powered enzyme engineering for scalable, bio-based green chemical production.

“As our platform works independently from a host cell’s metabolism, more carbon and energy can be directed towards target molecules, improving efficiency and creating cost profiles that can compete with petrochemical production routes,” said Min Hao Wong, A*STAR SIFBI Deputy Executive Director.

SBTP’s flagship product is 1,3-propanediol, widely used in high-performance textile fibres, protective coatings, biodegradable plastics and even skincare formulations. The platform’s use cases are being extended to other polyols, bio-based solvents and specialty monomer compounds, as well as downstream applications.

“SBTP functions as an innovation springboard for a burgeoning green chemicals market projected to reach US\$80 billion by 2035, while aligning with Singapore’s bioeconomy agenda and net-zero goals,” Wong added.

PARTNERSHIPS BRIDGING PIPELINES

The accelerated translation of bio-based products from today’s benchtops to tomorrow’s factory lines depends on building shared capabilities across public and private sectors. Reflecting the strength of such partnerships, biomanufacturing consortia for both healthcare and industrial applications are steadily thriving in Singapore, nurturing a prolific and resilient bioeconomy amidst an increasingly volatile global supply chain.

Upstream of the value chain, advances in synthetic biology are enabling the precise design of living systems to produce complex, highly specific molecular configurations with greater efficiency. As with many industries, AI-driven approaches are enhancing the bioprocessing engine, advancing novel biologics and green chemicals more seamlessly from lab to market.

“AI integration is shortening the design-build-test-learn cycle, enabling more predictive and scalable biological engineering,” said Matthew Chang, Director of the Singapore Consortium for Synthetic Biology (SINERGY).

Today, SINERGY engages academic, industry and government stakeholders locally and globally to consolidate their expertise into a single network. Their consortium model identifies potential synergies between academic groups with industry stakeholders, bridging them to catalyse the real-world deployment of bio-based products. This has led to platforms such as SBTP and the Wilmar-NUS Corporate Laboratory, which focuses on high-value oleocompounds.

“These outcomes demonstrate how targeted matchmaking between academic capabilities and industry needs can contribute to a more integrated and innovation-driven ecosystem,” Chang added. “SINERGY strengthens Singapore’s position as a global bioeconomy hub while supporting technological and talent developments, including in AI-biology integration.”

“As our platform works independently from a host cell’s metabolism, more carbon and energy can be directed towards target molecules, improving efficiency and creating cost profiles that can compete with petrochemical production routes.”

— Min Hao Wong, Deputy Executive Director at the A*STAR Singapore Institute of Food and Biotechnology Innovation (A*STAR SIFBI)



For Liang Hong Koh, Site Head of Sanofi Modulus at Tuas Biomedical Park, these public-private partnerships are a structural economic necessity, as no single organisation can drive the future of biomanufacturing.

“Closing the translation gap requires shared risk, shared investment and shared infrastructure,” said Liang Hong Koh. “The consortium model allows best practices, data and methodologies to be developed collectively and then adopted industry-wide, raising the baseline capability of Singapore’s entire biomanufacturing sector.”

Sanofi Modulus is a founding member of the Biologics Pharma Innovation Programme Singapore (BioPIPS), where shared technology translation comes to life. Biopharmaceutical firms bring manufacturing challenges to BioPIPS, aligning industry objectives with research directions at A*STAR and other institutions. Ongoing projects include the development of novel sensors as PATs for measuring and monitoring cell health, supporting optimised yields and improved process controls.

“Such novel technologies require close engagements with technology partners, equipment suppliers,

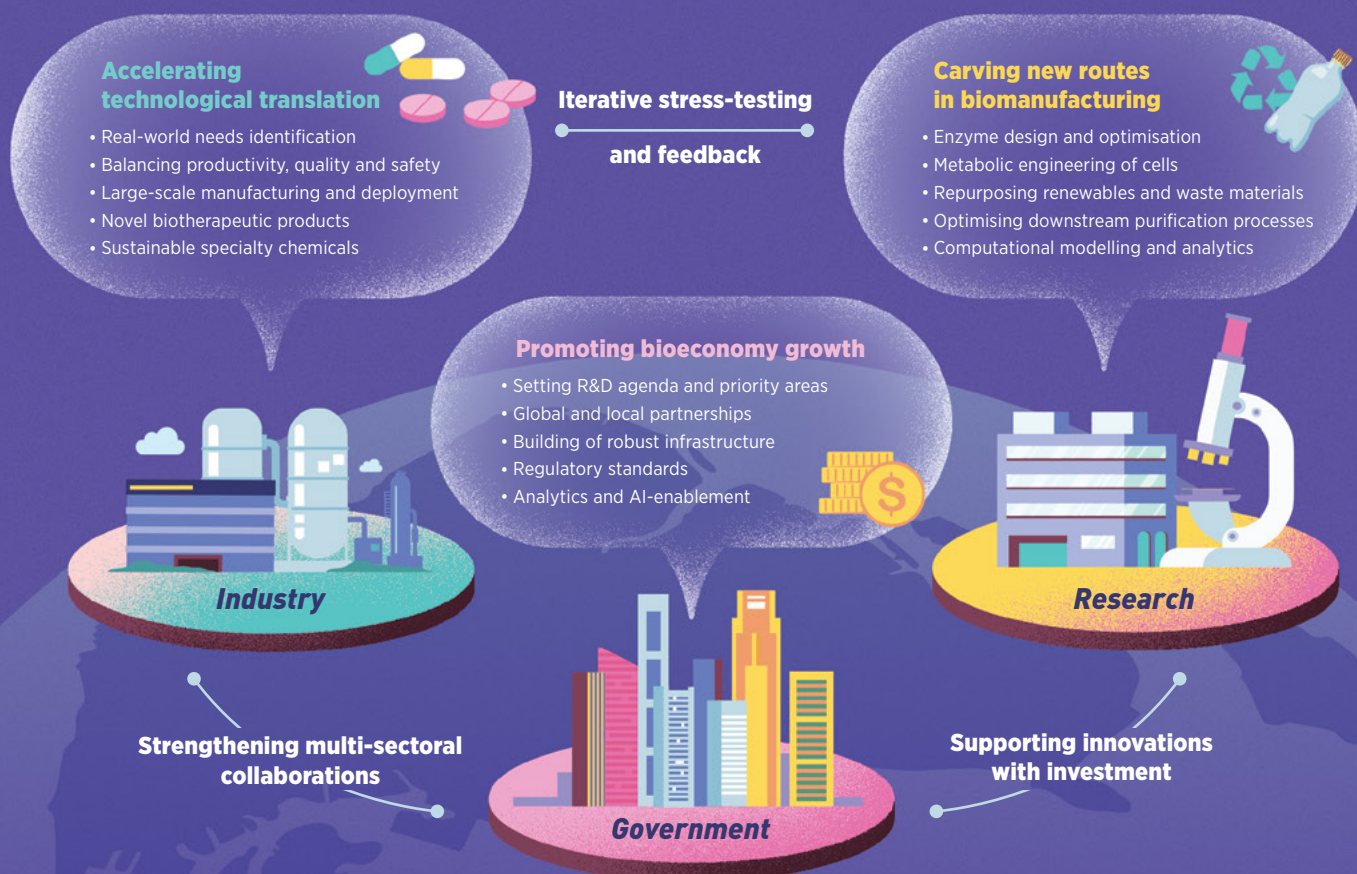
and regulatory and economic development agencies, including the Economic Development Board,” Liang Hong Koh added. “Technology translation in biomanufacturing isn’t a linear handoff from lab to factory; it’s an iterative, collaborative process that benefits enormously from structured consortia such as BioPIPS.”

The integration of adaptable technology platforms with real-time data analytics and smart process design, underpinned by regulatory rigour and trustworthy quality standards, are key enablers of reliable and scalable biomanufacturing in Singapore.

“Innovations will not only streamline manufacturing operations but also support rapid responses to emerging market demands and global health challenges,” said Boon Tong Koh.

Overall, strong and seamless linkages are as important within bioprocessing workflows as in the broader ecosystem, carving out collaborative spaces for translating scientific capabilities into dependable bio-based production lines.

“Bioprocessing is often invisible when it is done well; yet it is what enables society to benefit from scientific discovery,” said Raman Rao. ★



REMEMBERING DR YANG YINPING

It is with deep sadness that we share the passing of Dr Yang Yinping, Director of the Centre for Advanced Technologies in Online Safety (CATOS), Senior Principal Scientist at the A*STAR Institute of High Performance Computing (A*STAR IHPC), and member of A*STAR *Research* magazine's Editorial Board. Yinping was a well-respected and deeply kind-hearted researcher, colleague and leader who devoted herself to science at its best: advancing knowledge in service of people.

Yinping joined A*STAR in 2007, at a time when social media and digital technologies were beginning to reshape how people communicate. Even then, her passion lay at the intersection of computing, social science and human behaviour, grounded in the understanding that technology was closely tied to people and society.

Over the years, Yinping helped build A*STAR IHPC's research capabilities in affective computing, social technologies and artificial intelligence systems, developing new ways to understand how people think, feel and communicate. She cared deeply that research should make a difference beyond the lab and never lost sight of the people behind the data. Working closely with partners across the public and private sectors to translate technologies into practice, her innovations were successfully adopted by organisations and recognised as award-winning solutions with real-world impact. In commendation of her contributions, her work was featured among "A*STAR's 30 Innovations and Inventions" across three decades, and her authorship of numerous high-quality research publications had earned her many best paper awards.

When the COVID-19 pandemic struck, Yinping and her team recognised the psychological weight of the crisis and sought to better understand experiences that could not always be captured through conventional surveys. Using social listening technologies they developed,



the team examined public emotions and responses at a time when accurate information and clear communication were especially important. By analysing large-scale social media data across countries, they traced a marked shift in public sentiment from fear to anger as major events unfolded, providing timely insights into communities navigating an unprecedented global crisis, for which she received her first National Award (Public Administration Medal – Bronze) for COVID-19 in 2023.

What began as a small team of two at A*STAR IHPG researching computational social sciences would eventually lay the foundations for CATOS in 2023. As the digital landscape evolved, so did the focus of Jinping's team: from monitoring growing online risks to actively tackling them, cognizant that online safety is a developing human need. With support from the Singapore Government through the Online Trust and Safety Research Programme and under Jinping's leadership, CATOS was established as Singapore's national centre in this fast-emerging field, advancing technologies to detect, address and prevent harms in our digital world. Its mission is to develop whole-of-nation technological capabilities and an ecosystem to combat online harms. The Centre's growth is a testament to the firm foundations and broader ecosystem she cultivated, through bringing together people from different disciplines and organisations to foster open exchange and collaborations based on respect and genuine care she inspired in others. In recognition of her outstanding dedication, merit and competence in public service, she was honoured with a second National Award (Public Administration Medal – Bronze) in 2025.

We are also honoured to have had Jinping serve on the Editorial Board of *A*STAR Research* magazine in recent years, offering thoughtful guidance that helped the team present research with accuracy, context and relevance.

She also played a central role in shaping two issues of the magazine that reflected themes central to her life's work—“*Sensing Emotions in a Crisis*” and “*Hidden Hazards*”—helping readers understand both the human dimensions of technology and the responsibilities that come with it.

To her, science should inform, connect and serve, and people should understand not only what it achieves, but why it matters.

Those who worked with Jinping remember not only her intellect and scientific acumen, but also the warmth and kindness she brought to every interaction, often accompanied by a gentle smile that reflected her generosity of spirit. A highly accomplished professional, she was also a loving, devoted and responsible mother, wife and daughter. She was known to make time for people—whether friends, colleagues, collaborators or strangers—and was deeply loved for the care she brought to her work and relationships. Many shared that conversations with her often left them feeling heard and encouraged, with younger researchers motivated to contribute. She believed that strong science depended not only on asking better questions and seeking practical solutions, but also on supporting people to do their best work while remaining mindful of those her research was meant to serve. This philosophy shaped her leadership, from strengthening strategic planning and team alignment for CATOS through support from an A*STAR Fellowship Grant, to her active involvement in the A*STAR Diversity and Inclusion Workgroup in her advocacy for trust, inclusivity and a shared sense of purpose. Having personally participated in the CATOS off-site retreat that Jinping organised in September 2025, I witnessed these leadership qualities firsthand—passion, dynamism and positivity, while remaining deeply people-oriented and driven to achieve meaningful outcomes.

We pay tribute to her research achievements, leadership and mentorship, as well as her contributions to science communication and the broader mission of demonstrating research impact. Her passing is a significant loss to A*STAR and the research community; her greatest legacy lies not only in the research programmes and technologies she developed, but also in the people she uplifted and inspired. Her influence will continue to be felt through the people she mentored, the teams she built, the communities she served and the foundations she helped establish.

On behalf of A*STAR, I extend my deepest condolences to Jinping's family, loved ones, colleagues and all who had the privilege of knowing and working with her. ★

Prof Andy Hor

Editor-in-Chief, A*STAR Research Publication
Deputy Chief Executive (Research), A*STAR

TRANSPORTATION

When close shaves save ships

Near-misses and close encounters between vessels reveal the hidden dangers of busy waterways, according to a new maritime risk assessment tool.

When two ships collide at sea, the incident often goes on record. An unusual number of accident reports from a certain waterway draws the attention of authorities and maritime operators. Such numerical data is an essential part of maritime risk studies that boost operational safety for all at sea.

However, that data can be too sparse to be useful. “The problem is that traditional maritime risk studies rely on records of actual collisions, but these are relatively rare events, especially in well-regulated waterways,” said Liangbin Zhao and Jiaxiang Cai, Senior Scientists at the A*STAR Institute of High Performance Computing (A*STAR IHPC). “This means there are often too few cases on which to perform detailed statistical analyses.”

To address the issue, Zhao, Cai and A*STAR IHPC colleagues recently tested a novel statistical framework for maritime risk assessment: the Binomial test for Risk Analysis Involving Near misses (BRAIN). Developed with the support of the Singapore Maritime Institute under its Artificial Intelligence Research Project, BRAIN draws on a wider pool of maritime incident data: near-misses and close encounters between vessels.

“Close encounters—where two vessels pass each other within a predefined safety threshold—are often identified automatically from automatic identification system (AIS) data,” explained Zhao. “Near-misses are a serious subset of close encounters where collisions were narrowly avoided, as indicated by late evasive manoeuvres, abnormal turning behaviour, communication difficulties, misunderstandings between vessels or other signs.”

BRAIN works by identifying close encounters from AIS traffic data, then using expert review and data analysis methods to highlight genuine near-miss events. It then calculates how frequently close encounters turned into near-misses under different conditions, such as vessel features, time of day and spatial distribution. These groups are then statistically compared against an overall average.

In collaboration with local maritime authorities, the researchers validated the BRAIN framework on a real-world historical dataset from a busy narrow section of the Singapore Strait, documenting

40,653 close encounters and 84 near-miss incidents over two years.

“We made several interesting findings. Bulk carriers showed significantly above-average risk; close encounters involving them were around 1.5 times more likely to become near-misses,” said Cai. “Nighttime operations were also noticeably more dangerous than daytime—especially during the period between midnight and 4 am. This likely reflects the reduced visibility and higher crew fatigue of overnight operations.”

Certain traffic convergence zones also emerged as clear risk hotspots: areas where vessels from multiple directions came together in relatively disordered traffic patterns showed much higher near-miss risks than more structured traffic areas.

The team aims to extend BRAIN toward real-time operational use, potentially supporting live traffic monitoring. They also aim to incorporate weather conditions, traffic management interventions, human factors, vessel communication patterns and other contextual factors into the framework.

“We’re also interested in integrating BRAIN with intelligent maritime systems and decision-support tools so that near-miss analysis can support proactive safety management, rather than retrospective investigation,” said Zhao. ★



Researchers

Liangbin Zhao and Jiaxiang Cai,
A*STAR IHPC

IN BRIEF

The BRAIN statistical framework quantifies maritime collision risk through AIS data analysis and expert review of near-miss and close encounter incidents, supporting evidence-based decision-making for safer operations in high-traffic waterways.

1. Cai, J., Zhao, L., Sun, S. and Fu, X. Novel collision risk assessment in busy waterways via near-miss-based statistical analysis: The BRAIN approach. *Reliability Engineering and System Safety* **269**, 112030 (2026).

Photo credit: Vidar Nordli-Mathisen / Unsplash

OPTICS AND PHOTONICS

Pinning waves in place for potent lasers

A new approach to trapping light waves inside tiny flat structures could enable more energy-efficient lasers in next-generation photonic devices.

Drop a rock in a still pond, and it creates ripples that gradually flatten as they travel outward. But what if those waves—and the energy they carry—could be held in place? Researchers such as Son Tung Ha and Thu Ha Do, respectively a Principal Investigator and a Senior Scientist at the A*STAR Institute of Materials Research and Engineering (A*STAR IMRE), are exploring how to achieve this with light.

“Many optical systems, such as lasers or sensors, rely on confining light in one place, as the longer it stays, the more effectively it can be used,” said Ha.

These systems rely on optical cavities: components designed to trap, amplify and release light in a controlled manner. A key challenge in designing such optical cavities lies in balancing a high quality (Q) factor—a strong ability to trap light—with the ability to release light efficiently under practical operating conditions.

Now, a multidisciplinary research team has designed a new optical cavity for nanoscale lasers that effectively ‘holds’ light waves in place within engineered nanostructures by leveraging an optical effect known as bound states in the continuum (BIC).

The work was the product of a close international collaboration between the research group led by Ha at A*STAR IMRE; the National Semiconductor Translation and Innovation Centre, Singapore; Nanyang Technological University (NTU),

“The trapping effect [through our approach] is far less sensitive to small changes in ambient conditions.”

Singapore; the Université de Lyon and École Centrale de Lyon, France; and joint French-Singaporean research laboratory CINTRA at NTU.

“A BIC is a special situation where light remains trapped, even though it exists in a setting where it should be free to escape,” explained Do. “It’s like a ripple on water that can’t spread because different wave components cancel any outward motion.”

Many existing BIC-based optical cavities only achieve extremely high Q-factors under very precise conditions, which limits their practical applications. To make BIC a more practicable approach, the team engineered a system that ‘flattens’ a BIC’s band, preserving its light mode over a wider range of operating conditions.

The team’s device consisted of a carefully designed array of titanium dioxide nanopillars with a slight stretch introduced to its periodic pattern. This brought together different light modes in the structure—which would otherwise spread in various directions—causing them

to cancel out each other’s behaviour and form a flatband BIC state that effectively traps light in all directions.

“This approach balances two opposing tendencies so that overall, light waves in the cavity have no strong preference to move or spread,” said Do. “As a result, the trapping effect is far less sensitive to small changes in ambient conditions. It also increases the number of available optical states, enabling stronger interactions between light and device materials.”

Experiments confirmed that the device successfully produced laser emissions from the flatband BIC mode with a Q-factor of around 9,100 at room temperature conditions. The team also found that the device required four times less energy to initiate lasing compared to conventional BIC-based devices.

The team is currently scaling up and integrating their technology into existing semiconductor platforms. “We’re translating these flat optics concepts into manufacturable devices using industry-compatible fabrication methods,” shared Ha. “This will enable mass production of compact, high-performance optical components for on-chip lasers, optical communications, sensing, advanced displays and other applications.” ★



Researchers

Son Tung Ha and Thu Ha Do,
A*STAR IMRE

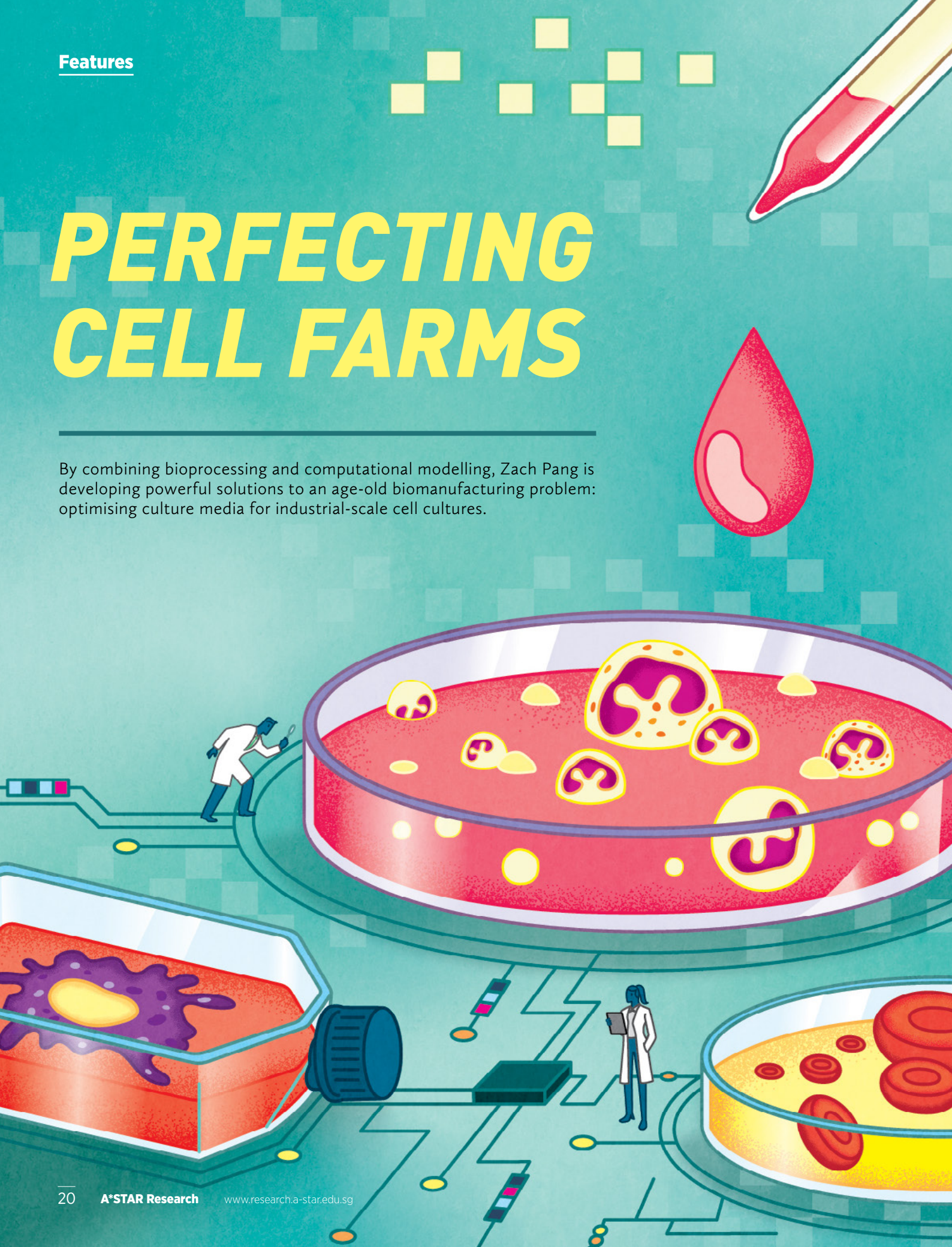
IN BRIEF

Slight geometric adjustments to a titanium dioxide nanopillar-based optical cavity produces flatband bound states in the continuum that keep light confined for longer durations, enabling energy-efficient room-temperature lasing for advanced photonics.

1. Do, T.T.H., Yuan, Z., Durmusoglu, E.G., Shamkhi, H.K., Valuckas, V., *et al.* Room-temperature lasing at flatband bound states in the continuum. *ACS Nano* **19** (20), 19287–19296 (2025).

PERFECTING CELL FARMS

By combining bioprocessing and computational modelling, Zach Pang is developing powerful solutions to an age-old biomanufacturing problem: optimising culture media for industrial-scale cell cultures.



Growing things at a large scale can be a finicky affair. Whether it's a field of sweet corn, or a vat of insulin-producing cells, the smallest differences in the conditions they both grow in can make the difference between a successful harvest or a meagre one. For corn, that environment is soil; for cells, it's culture media.

Fine-tuning culture media formulations can be especially challenging for scientists and biomanufacturers, as the cell types they're interested in normally function as part of a bigger living organism, making them reluctant to thrive on the benchtop or in factory lines. Too often, finding the perfect culture media 'recipe' for a particular cell type involves many time-consuming, costly and frustrating rounds of trial and error. Yet, this effort is often necessary to pave the way for advanced therapeutics, alternative foods and other biotechnology products that could revolutionise our lives.

Having personally experienced the persistent setbacks caused by suboptimal culture media, Zach Pang, a Group Leader at the A*STAR Bioprocessing Technology Institute (A*STAR BTI) and Senior Scientist at the A*STAR Bioinformatics Institute (A*STAR BII), has made it a lifelong mission to make culture media development faster, smarter and more accessible for scientists and biomanufacturers.

As co-founder and Chief Scientific Advisor of A*STAR spinoff company AuctuCel, Pang is part of a team of entrepreneurial researchers that are bringing artificial intelligence (AI), computational modelling and bioprocessing together in pursuit of that goal. AuctuCel's flagship technology, Fluxperior, combines mathematical modelling with AI to predict what cells need and optimise culture media formulations based on those needs, reducing development time and costs while supporting higher-yield and more scalable biomanufacturing.

In this A*STAR Research feature, Pang reflects on the origins of his mission to improve culture media development; the potential for models like Fluxperior to accelerate bioprocessing R&D across diverse industries; and the benefits and challenges of a career spanning both research and entrepreneurship roles.

Q: WHAT SPARKED YOUR INTEREST IN CHANGING THE CULTURE-MEDIA DEVELOPMENT PROCESS?

During my PhD degree, I worked with primary cultures of human endothelial cells; specifically, those isolated from donated umbilical cords and human aortas. These cells are notoriously difficult to grow, and they're very particular about what culture media they grow in. In my first year of research alone, it took months of trying out different brands of culture media to find one that ensured the best cell growth—which also turned out to be the most expensive.

The thing about many culture media products is that they might be off-the-shelf, but they're not one-size-fits-all. Different cell types from different sources cultured in different contexts will require different formulations. This presents a big problem for companies involved in the biomanufacturing and biotech industries, which is why they spend lots of money and time developing their own formulations, or engage third-party vendors to do it for them.

Q: WHAT WAS THE JOURNEY LIKE TO FLUXPERIOR'S DEVELOPMENT AND AUCTUCEL'S FOUNDING?

The Fluxperior platform started as a project by our former A*STAR BTI colleague, Meiyappan Lakshmanan, which we then applied to—and very successfully validated in—an industry project with a partner company. After that collaboration, we published an article about the work; our partner also launched their product in the market, crediting A*STAR in its development.

Later, in 2023, I was nominated by A*STAR BTI to attend the Gap Champion programme run by A*StartCentral (A*SC) and Singapore Biodesign. The programme arms scientists and business development officers with the business acumen to scope an industry-relevant grant proposal. While I was there, an A*STAR Innovation and Enterprise colleague asked me if I was interested in spinning off our technology into a company, considering it had already attracted

industry interest. I took up the challenge, joined A*SC's Essentials Bootcamp with my co-founders, and here we are.

We picked the name 'AuctuCel' by combining the Latin word 'auctus'—meaning growth, enhancement and prosperity—with 'cell'. Our goal is to help companies successfully grow their cells with minimal hurdles, allowing them to enhance productivity, which leads to prosperity.

Q: *HOW DOES FLUXPERIOR WORK? WHAT MAKES IT A NOVEL APPROACH?*

Fluxperior is a mathematical model coupled with advanced AI, allowing its users to design the best formulations for the culture media they need. By simulating intracellular metabolism, the model provides a glimpse of what happens in cells in culture, especially the metabolic bottlenecks present. Users can then simulate increasing or decreasing amounts of individual culture media ingredients to see what unlocks those bottlenecks, boosting cell growth and productivity.

Q: *WHAT ARE SOME REAL-WORLD APPLICATIONS OF FLUXPERIOR?*

Our tool can be applied to any field that relies on biological cells grown in culture media. In the past, we've helped Ajinomoto develop a culture media product for Chinese hamster ovary (CHO) cells, which are commonly used by the pharmaceutical industry for antibody production. We've also applied our tool to projects involving vaccines, cell therapy and cultivated meat.

Zach Pang

Group Leader
A*STAR Bioprocessing
Technology Institute
(A*STAR BTI)

Senior Scientist
A*STAR Bioinformatics
Institute (A*STAR BII)

Chief Scientific
Advisor and Co-founder
AuctuCel



“Fluxperior is a mathematical model coupled with advanced AI, allowing its users to design the best formulations for the culture media they need.”

— Zach Pang, Group Leader at the A*STAR Bioprocessing Technology Institute (A*STAR BTI), Senior Scientist at the A*STAR Bioinformatics Institute (A*STAR BII) and AuctuCel Chief Scientific Advisor and Co-founder

Q: WHAT IS IT LIKE BALANCING YOUR MULTIPLE ROLES IN RESEARCH AND ENTREPRENEURSHIP?

It's great and exciting to work on many things, but it can also be tough and mentally draining. While I'm not involved in AuctuCel's operations today, in its early stages I helped advise it and kickstart its operations. Recruitment, fundraising, logistics and manufacturing all take time and effort; most of my evenings and weekends are spent talking to my co-founders and discussing strategy. At the same time, I also juggle my main job at A*STAR and adjunct professor positions at the National University of Singapore and Nanyang Technological University, Singapore.

However, I have no regrets; I'm loving it. Being involved in both research and entrepreneurship gives me a wide lens to see how the whole landscape works, from basic science discovery, translational research and software development, all the way to industry application and business development. I get to see the challenges that lie in different stages, which really broadens my perspective on how to do science.

I'd like to advocate for more scientists to be cross-trained—I don't mean to move scientists away from the bench in favour of business relations, but to allow them to spend half their time engaged in business and commercial activities.

I can say it hits the brain differently; I've even had to learn how to do accounting.

Q: HOW IS AUCTUCEL KEEPING AHEAD OF THE CURVE IN AI AND BIOMANUFACTURING?

The field of AI is growing crazily fast, but we don't compete in the AI space itself. Since Fluxperior is a mathematical model, it has explainability; it lets us perform simulations and know the exact biological pathways that influence cell growth. AuctuCel has also pivoted into manufacturing and selling off-the-shelf culture media. To date, its product catalogue comprises over 200 products. The company aspires to be the next big biotech suppliers in Singapore and the region.

Q: WHAT ADVICE WOULD YOU GIVE YOUNGER SCIENTISTS WITH AN INTEREST IN AI-FORWARD BIOPROCESSING?

Stay grounded in your domain—whether biology or biotechnology—and expand your expertise in AI. We need more AI scientists who also speak the language of biotech and bioprocessing! ★



ADVANCED MANUFACTURING

Perfecting 3D printing for top-tier alloys

A close look at an additive manufacturing technique for titanium alloys reveals how tiny process variations can shape high-performance components.

Print the same photo on 10 different printers, and you'll often notice differences in their outputs. Colour hues and line sharpness might vary; there might be gaps or blots of ink. Without calibrating your printers' settings, you're unlikely to get prints of the same quality across the board.

Likewise, machine settings matter in additive manufacturing (AM), where high-performance titanium alloys such as Ti-6Al-4V can be 3D-printed into complex components. Despite the material's excellent strength and corrosion resistance, small process variations can determine whether a vital piece of an airplane, surgical implant or reactor holds up with use and time.

"It's critical to simultaneously achieve both high density and fine microstructure in advanced Ti-6Al-4V applications," said Pan Wang, a Senior Scientist at the A*STAR Singapore Institute of Manufacturing Technology (A*STAR SIMTech). "High density delays fatigue crack initiation and improves long-term durability under cyclic loading; a fine microstructure provides high strength, damage tolerance and wear resistance while maintaining enough ductility."

Electron beam powder bed fusion (PBF-EB) could help build Ti-6Al-4V parts with those ideal features. Using a near-instantly deflectable electron beam, this AM technique builds parts in a vacuum at elevated temperatures, which minimises contamination, reduces the need for post-processing heat treatments, enables fast scanning and efficiently produces large or bulk components with consistent quality.

"However, previous studies on optimising PBF-EB for Ti-6Al-4V have produced conflicting recommendations, due to multiple parameters being tuned simultaneously, over narrow ranges, and under machine-specific conditions," Wang noted.

To address the issue, Wang and A*STAR SIMTech colleagues collaborated with Nanyang Technological University, Singapore, in a comprehensive investigation of how PBF-EB parameters affected the morphology, porosity, microstructures and mechanical properties of Ti-6Al-4V parts.

After systematically isolating the individual effects of key process parameters—scan speed, line offset, focus offset and preheating temperature—the

team then varied each one independently over a wide processing window, producing over 100 distinct parameter sets.

"We showed that optimal Ti-6Al-4V fabrication requires a careful balance between sufficient fusion and microstructural refinement," said Wang. "Excessively high energy inputs ensure good bonding but lead to microstructural coarsening, surface distortion and—in extreme cases—large spherical pores. Conversely, excessively low energy inputs refine the microstructure, but introduce lack-of-fusion defects that severely degrade tensile performance."

The team consolidated their findings into a process map that identifies threshold boundaries governed by melt pool geometry and thermal behaviour, making them transferable across different PBF-EB machine systems.

"Based on our results, we recommend operating close to, but within, the good-fusion boundary identified in the process map," said Wang. "This means using relatively higher scan speeds combined with moderately reduced line offsets under normal preheating conditions."

The team is now evaluating how the optimised parameters perform under real-world industrial conditions. Their approach is also being extended to other performance-critical properties and PBF-EB alloy systems, with the aim of accelerating process qualification and reducing reliance on post-processing. ★

Researcher

Pan Wang,
A*STAR SIMTech



IN BRIEF

A detailed process map of Ti-6Al-4V electron beam powder bed fusion identifies the optimal parameters for high-density alloy products with fine microstructures, enabling advanced applications in aerospace, biomedical devices and other industries.

1. Ngiam, C.X., Hu, Z., Aw, B.L., Dong, Z., Zhou, K., et al. Electron beam powder bed fusion of Ti-6Al-4V: Augmenting mechanical properties with low porosity and fine microstructure. *Journal of Materials Science and Technology* **256**, 97–115 (2026).

ARTIFICIAL INTELLIGENCE

F(AI)rnness without the full picture

A new approach to training AI models can help improve their fairness in decision outcomes even for the most disadvantaged groups.

Every day, algorithms make quiet decisions that shape people's lives. It could be who gets called back for a job interview, who is approved for a loan, or who is deemed likely to become a repeat offender. The introduction of artificial intelligence (AI) into these processes has often resulted in a mirroring of existing societal prejudices rather than support for more effective and fair decision-making solutions.

"In job recruitment, for example, AI tools have been shown to systematically disadvantage women or ethnic minorities because the models involved learned from historically biased hiring patterns," said Jing Li, a Research Scientist at the A*STAR Centre for Frontier AI Research (A*STAR CFAR).

To check whether models are treating different groups fairly, one would need to compare decision outcomes against demographic information such as gender and race. However, such sensitive data is typically limited in real-world datasets due to critical privacy measures.

"You know bias might exist, but you can't directly measure or correct it because you don't know who belongs to which group," said Xiuju Fu, a Senior Principal Scientist at the A*STAR Institute of High Performance Computing (IHPC). "It is precisely because this demographic data is unavailable that we need a new model training approach that can protect vulnerable groups without ever identifying who they are."

Li, Fu, A*STAR CFAR Director Ivor Tsang, Research Scientist Yinghua Yao and Senior Research Scientist Yuangang Pan used a framework inspired by John Rawls, who proposed that when societal group memberships are unknown, the natural response is to design a system that prioritises the most disadvantaged.

Translated into machine learning, the question shifts to asking whether the worst-off group is adequately protected. Such an approach also only requires a statistical estimate of the size of the most vulnerable group, rather than needing individual-level demographic data.

The researchers implemented a method called intrinsic reweighting (IRW), which assigns each training sample a certain importance, or weight, based on their expected impact on the worst-performing group. "We compute the weight using gradient information, measuring how each sample's learning signal aligns with what the model needs to improve fairness. This gives a more accurate picture of each sample's contribution to how the model learns," explained Li.

When tested across four standard fairness benchmarks, the IRW framework consistently matched or outperformed existing fairness methods. The resulting models even showed comparable results to those that had access to demographic labels during training.

"Integrating this approach into standard AI development would make it much more accessible to those who are not fairness researchers themselves," said Tsang.

To advance the IRW framework towards adoption, the researchers are focusing on reducing its computational demands and improving scalability. They also hope to work more closely with policymakers to derive more accurate measures of worst-off cases within real-world contexts and privacy measures. ★



Researchers

Jing Li, A*STAR CFAR,
Xiuju Fu, A*STAR IHPC
and Ivor W. Tsang, A*STAR CFAR

IN BRIEF

An intrinsic reweighting approach to AI model training reduces algorithmic bias without requiring access to sensitive demographic data, outperforming existing fairness methods across multiple benchmark datasets.

1. Li, J., Yao, Y., Pan, Y., Wang, X., Tsang, I.W., et al. Alpha and prejudice: Improving α -sized worst case fairness via intrinsic reweighting. *IEEE Transactions on Neural Networks and Learning Systems* **36** (10), 18005-18019 (2025).

ARTIFICIAL INTELLIGENCE

Sharpening shears for AI pruning

Inspired by classical signal processing techniques, a new approach to fine-tuning AI models helps reduce irrelevant computing while maintaining performance.

Like the human brain, many modern artificial intelligence (AI) models often feature multiple information processing layers, each containing millions or even billions of parameters. These tiny internal settings are what enable large language models (LLMs) such as ChatGPT and Claude to produce complex text outputs.

However, this scale comes at a cost; massive models need massive amounts of computing memory and power, making them difficult to deploy on everyday hardware such as smartphones, medical devices or industrial sensors.

According to Kaixin Xu, a Senior Research Engineer at the A*STAR Institute for Infocomm Research (A*STAR I²R), many parameters are developed during a model's training, but aren't actually critical to its overall performance. Hence, to streamline a model, researchers often 'prune' it, identifying and removing redundant parameters while maintaining its capabilities.

Conventional pruning generally relies on post-training methods that apply simple rules, such as deleting parameters with the smallest weights in a layer. While such methods are easy to implement, Xu noted that they often failed to account for how

changes in a specific layer might negatively impact the rest of the model.

In a recent work, Xu and A*STAR I²R colleagues, including Principal Scientist Min Wu and former Principal Scientist Xiaoli Li, worked with collaborators at Nanyang Technological University, Singapore, to address two optimisation challenges in model pruning: finding the link between specific parameters and overall model performance, and minimising the 'cost' of the pruning process itself.

Drawing inspiration from rate-distortion theory—a concept in signal processing traditionally used to find the best balance between data compression and quality in image and sound files—the team developed a holistic pruning method that focused on how much the model's final output changes after pruning.

"Instead of guessing which layers can tolerate more pruning, we directly measure how pruning affects the model's final output, and then choose pruning levels across all layers together in a coordinated way," Xu explained.

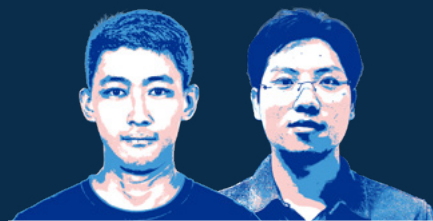
Putting their method to the test, the team found that it could be solved through two proposed algorithms, one of which could run very quickly even

without graphics processing units (GPUs): specialised and increasingly costly components for AI hardware. This efficiency could be critical for deployment-constrained environments where memory and power consumption are primary bottlenecks.

"Our method works during the post-model training stage and can be guided by practical targets such as computation cost," Xu said. "This makes it easier to adapt large, high-quality models for deployment without needing specialised hardware or complex training pipelines."

The researchers were also heartened by their success in adopting aspects of classical information theory for their pruning approach, given the relative complexity of deep neural networks today. "This encourages future research to borrow more ideas from the field, instead of relying mainly on trial-and-error pruning rules," Xu added.

Looking ahead, Xu and colleagues are exploring how they could apply their pruning approach to LLMs and their visual counterparts, while also developing hardware-side optimisations to unlock their algorithms' full potential. ★



Researchers
Kaixin Xu and Min Wu,
A*STAR I²R

IN BRIEF

By coordinating simultaneous changes to different neural network layers, a new AI model pruning technique helps reduce memory and power requirements without sacrificing performance, supporting high-quality model deployment on resource-constrained edge devices.

1. Xu, K., Wang, Z., Huang, R., Geng, X., Lin, J., *et al.* Efficient distortion-minimized layerwise pruning. *IEEE Transactions on Pattern Analysis and Machine Intelligence* **47** (10), 9298–9315 (2025).

ARTIFICIAL INTELLIGENCE

Tuning AI to local news beats

Bigger models are not always better, as A*STAR researchers show how a targeted AI model can beat global, general-purpose models in summarising multilingual regional news.



In the newsroom, headlines are constructed to distil the gist of a story in one glance, appealing to readers with limited time on their hands. However, relying solely on headlines can lead to a partial or skewed understanding of events. A similar limitation appears in general-purpose large language models (LLMs) such as GPT-4, particularly when summarising vast troves of multilingual news articles from local sources.

“Like someone who only listens to the loudest voices in the room, LLMs often ignore crucial, nuanced details in favour of the most repeated statements,” said Longyin Zhang, a Research Scientist at the A*STAR Institute for Infocomm Research (A*STAR I²R). “They also struggle to maintain accuracy regarding local entities and cultural nuances, sometimes confusing timelines and making up facts based on outdated information.”

Zhang and colleagues designed CLUST-Multi-lingual, Cross-lingual and

Multi-documents Summarisation (CLUST-McMs), a two-stage artificial intelligence (AI) pipeline designed to produce more accurate and context-aware summaries of multilingual regional news. In its first stage, CLUST-McMs dynamically categorises articles based on specific events—such as an election period or the passage of a new law—rather than broad topical groupings typically used by general-purpose LLMs.

The pipeline’s second stage applies a data sharpening technique to guide the summarisation process. By balancing the volume and diversity of input information, the model filters out repetitive content and prioritises dense, information-rich sentences, helping to reduce bias in the final summary.

The team also introduced a localisation step to better capture cultural and contextual nuances, akin to the judgement of a local editor. “We train the AI through

specific question-answering tasks to strictly cite facts and timestamps directly from the local source texts,” Zhang explained.

Using a specially curated dataset of news from Southeast Asia, the team reported that CLUST-McMs significantly outperformed GPT-4, effectively synthesising overlapping articles across multiple languages into a single, concise English-language summary. Based on three evaluation metrics, their smaller, targeted model delivered more accurate coverage and stronger fidelity to the original sources, highlighting the importance of smart data sharpening and localisation over relying solely on large, general-purpose models.

Moving forward, the team hopes to expand their work and localise multimodal models to understand regional news shared not just in written form, but also in audiovisual formats.

“The AI community needs to shift its focus from merely scaling up model sizes to making AI highly faithful to real-world facts and deeply culturally aware in localised contexts,” said Zhang. “Our goal is to mitigate the cultural biases inherently embedded in global models, ensuring the AI correctly interprets local visual cues, dialects and nuances.” ★



Researchers

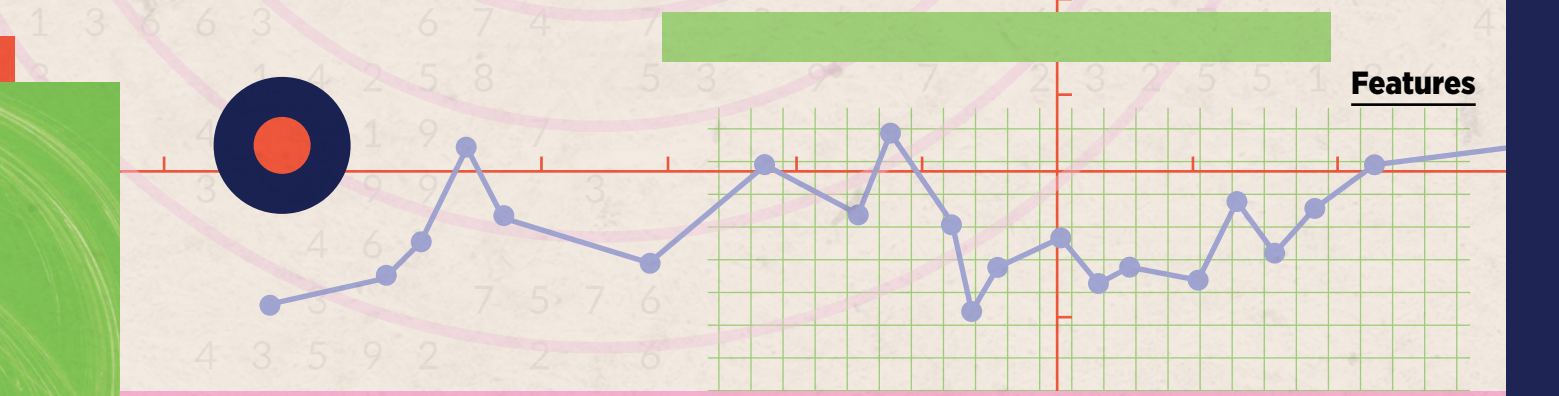
Longyin Zhang and Ai Ti Aw,
A*STAR I²R

IN BRIEF

By integrating event-centric clustering, data sharpening and localisation techniques, an AI pipeline can better extract local facts and cultural nuances from regional news sources, producing more contextually grounded summaries with reduced bias compared to global models.

1. Zhang, L., Zou, B. and Aw, A. Enhancing event-centric news cluster summarization via data sharpening and localization insights. *Proceedings of the 63rd Annual Meeting of the Association for Computational Linguistics (Volume 1: Long Papers)*, 16412–16426 (2025).

TRACKING ORDER IN QUANTUM CHAOS



Bridging theory and experimentation, Bo Xing is developing the computational approaches needed to predict the complex quantum dynamics of many-body systems.

Calculating the path of one billiard ball across an empty table is mathematically straightforward. But strike a full rack of balls, each instantly colliding and altering the others' paths, and the table rapidly descends into chaos. Factor in the messy realities of the real world—felt friction, microscopic dents, tiny imperfections in the equipment—and you'll likely need a computer's help.

Quantum physicists face the same problem at a much greater scale when predicting what happens to groups of quantum particles in quantum systems, thanks to the strange and random behaviours of matter at a quantum level. Heat, vibrations and other environmental noise can disrupt these delicate systems instantly, scrambling the valuable information they contain. Yet, interactions between them and their surrounding environment are often unavoidable, and when multiple quantum particles are involved, their collective behaviour can rapidly become too complex for even the most powerful conventional computers to simulate.

Bo Xing, an A*STAR International Fellowship (AIF) scholar and postdoctoral fellow at the Massachusetts Institute of Technology (MIT), has shaped his career around this challenge—developing computational approaches that track how information moves through complex many-body quantum systems as they interact with their environments, bridging the gap between idealised models and experimentally realistic conditions. Such tools would enable more accurate predictions of how quantum systems behave, opening the door for more robust quantum technologies in precision sensing and information processing.

In this A*STAR Research feature, Xing reflects on his journey into quantum physics, discusses how scientific understandings of quantum entanglement have evolved, and shares his perspectives on the future of quantum computation.

Q: TELL US ABOUT YOUR JOURNEY INTO SCIENCE.

My interest in physics and engineering began in my first year of junior college, thanks to a charismatic and devoted physics teacher. In one lecture, he showed the class a slow-motion video of his son tripping and falling, then turned it into a lesson on dynamics by tracing his son's centre of gravity with free-body diagrams. It was a humorous and illuminating lecture, and it shaped my impression of physics as something fun, intriguing and deeply connected to everyday life.

Motivated by the desire to better understand the physical world around us, I enrolled at the Singapore University of Technology and Design (SUTD), initially choosing engineering because I wasn't sure pure physics was the right fit. There, I worked with Dario Poletti on many-body quantum systems out of equilibrium. The unintuitive yet elegant nature of quantum physics immediately captivated me; because many-body quantum systems are often too complex to solve analytically, I became increasingly drawn to computational physics as a tool with which to understand complex quantum phenomena.

Q: HOW HAS THAT JOURNEY SHAPED YOUR DEVELOPMENT AS A RESEARCHER?

My trajectory was not strictly predetermined, but on hindsight, it formed a coherent progression. I obtained an engineering degree, pursued a theoretical PhD degree in many-body quantum systems, and am now a theory postdoctoral fellow in an experimental group at MIT, supported by the AIF.

Features

One reason I chose SUTD was its collaboration with MIT, though I didn't expect that connection to become personally meaningful later.

SUTD's multidisciplinary curriculum and its focus on hands-on, project-based learning exposed me to both theory and the practical applications thereof. While I'm more drawn to the former, this exposure gave me a deeper appreciation for how applied work grounds and guides theoretical thinking. It shaped my problem-solving approach and encouraged me to think carefully about how to bridge experiment and theory. This perspective naturally motivated and eased my transition into a theory-focused role within an experimental group; a transition that would have been much more challenging without that foundation.

Q: TELL US ABOUT A PIECE OF RESEARCH YOU'RE ESPECIALLY PROUD OF.

I'm particularly proud of our recent paper on how quantum entanglement behaves when a system interacts with its environment. In recent years, researchers have discovered that a quantum system 'measured' by its environment can undergo an entanglement phase transition when the rate of that measurement crosses a critical threshold. Below that threshold, the system can remain highly entangled even under observation. This has major implications for quantum error correction; the threshold tells us how much we can monitor a quantum system before its quantum properties are lost.

However, trying to experimentally determine this threshold usually requires tracking every measurement

event and obtaining the same measurement outcomes. As quantum mechanics is inherently random, this forces researchers to repeat experiments and discard most of their data, a major obstacle known as postselection. On the other hand, numerical studies of these thresholds often rely on approximations that restrict the validity of their results in different scenarios.

In our work, we introduced a new perspective to studying such problems without relying on those approximations. Instead, we treat the combined evolution of a quantum system and its environment as a single deterministic process. Conceptually, our protocol challenges the way we view quantum information in systems interacting with an environment; even when the system appears completely devoid of its quantum features, the transition can still be found hiding within the environment itself. Our protocol also bypasses the postselection problem, giving experimentalists a practical way to study these problems in the lab.

Q: HOW DOES YOUR MIT RESEARCH BUILD ON PAST WORK?

The fundamentals are similar. But while my central goal remains using numerical methods to understand many-body systems, my research focus has shifted from the intrinsic physics of those systems to accounting for their experimental imperfections. One phrase I've come to appreciate is: "In theory, theory and practice are the same. In practice, they are not." It captures the gap I routinely confront between idealised models and real-world constraints.

An interesting material I'm now studying is one my wife is also fond of: diamonds. But rather than the clear and pure types prized as gemstones, I'm more intrigued by the 'dirty' ones filled with defects, particularly nitrogen-vacancy

"Rather than optimising every decision in an uncertain landscape, it's more important to explore broadly and maintain a positive outlook."

— Bo Xing, A*STAR International Fellowship scholar and Massachusetts Institute of Technology postdoctoral fellow

(NV) centres, which are emerging as powerful platforms for precision measurement, quantum information processing and quantum simulation.

While often idealised as simple quantum defects, NV centres exist within a rich, interacting environment of nuclear spins, defects and lattice degrees of freedom. Capturing this interplay is essential to understanding decoherence mechanisms and designing protocols that better preserve and control quantum information. To address this, I'm currently developing numerical methods to simulate the complex many-body quantum dynamics between NV centres and their environment. Ultimately, I aim to build computational tools that enable more accurate predictions and more robust quantum technologies.

Q: WHERE WILL COMPUTATIONAL APPROACHES TO QUANTUM SYSTEMS MAKE THE BIGGEST IMPACT?

In recent years, quantum simulators have risen to challenge classical numerical ones, especially for certain classes of many-body quantum problems. As these experimental platforms improve, they offer a more native way to realise and study quantum dynamics that are increasingly difficult for classical computers to simulate efficiently. This has led to suggestions that classical computers may gradually become less central in the study of quantum systems.

Yet, classical computation is also advancing rapidly, driven by better algorithms, improved numerical techniques, as well as increasingly sophisticated hardware. The rise of artificial intelligence is accelerating this progress. Advances in machine learning, numerical optimisation and algorithm design are creating a constructive competition between classical and quantum approaches in many areas.

Classical simulations offer unmatched flexibility and controllability, as well as the ability to systematically probe parameters and approximations. They allow controlled benchmarking, interpretation and validation of experimental results, which remain essential even with quantum hardware. I expect computational approaches to make their biggest practical impact in the modelling and control of noisy intermediate-scale quantum (NISQ) systems; as quantum hardware scales, these developments will also lay the groundwork for hybrid quantum-classical methods.

Q: WHAT ADVICE WOULD YOU GIVE TO ASPIRING RESEARCHERS?

My own trajectory has been far from optimised—I've always had broad interests, tending to explore different topics every few years. Ironically, as a computational physicist, I spend my time optimising numerical methods for efficiency, but I don't think this mindset should guide broader research decisions: you could say that in the latter case, the objective function is far less well-defined than with numerical problems.

Rather than optimising every decision in an uncertain landscape, it's more important to explore broadly and maintain a positive outlook. If you genuinely enjoy learning, the process becomes meaningful. The things that feel like inefficient detours at the time may turn out to be exactly the experiences that give you a broader, more versatile skill set later on. ★



Bo Xing

A*STAR
International
Fellowship scholar

BIOCHEMICALS

A metabolic highway to citrus scents

Researchers successfully engineer microbes to take a metabolic ‘fast lane’ to producing a commercially valuable citrus-scented compound.

What if the molecule behind the zesty aroma of lemons could be brewed by microbes, similar to how yeast ferments sugars into wine? *Escherichia coli* bacteria, for example, can be engineered to carry the production engine for limonene, a citrus-scented biochemical found in fragrances and medicines.

This engine, the limonene synthase (LS) enzyme, is normally found in plant cells and enables the conversion of a compound called geranyl pyrophosphate (GPP) into limonene. However, the bacteria’s native metabolic pathways quickly consume GPP to produce other compounds, leaving LS without sufficient substrate.

“We were motivated to find an alternative that could essentially give *E. coli* a dedicated lane on the highway leading only to limonene production, instead of competing with many other metabolic routes,” said Clement Scipion, a Scientist at the A*STAR Singapore Institute of Food and Biotechnology Innovation (A*STAR SIFBI).

For Scipion, Group Leader Xixian Chen and A*STAR SIFBI colleagues, this alternative came in the form of neryl pyrophosphate (NPP), which consists of the same elements as GPP but differs slightly in structure.

In collaboration with the Campus for Research Excellence and Technological Enterprise (CREATE) programme under the National Research Foundation, Singapore; the National University of Singapore; and the Toulouse Biotechnology Institute in France; the researchers screened public sequence databases for LS-like enzymes that could use GPP or NPP.

While these enzymes were expected to naturally use GPP as the main substrate, the ArLS enzyme derived from *Agastache rugosa*, the Korean mint plant, showed an 11.5-fold faster reaction using NPP.

“Our broad screening strategy identified ArLS to perform particularly well with NPP, revealing a hidden diversity that would likely have been missed if we had only tested GPP,” Chen said.

To optimise limonene production, the researchers compared the sequences of ArLS against a GPP-preferring LS. Despite carrying identical active sites—the main reaction engine—the enzymes had subtle differences in surrounding ‘second shell’ regions. By targeting these areas, the researchers designed LS mutants with alterations that could influence how substrates enter, sit in and move within the enzymes’ active sites.

“We did not redesign the engine itself,” said Chen. “Instead, we fine-tuned the parts around it so that the fuel is delivered more efficiently and consistently.”

Taking this metabolic detour, the best-performing mutant increased limonene production by 4.8-fold and 1.9-fold via the GPP and NPP pathways, respectively.

The researchers have since filed a patent in Singapore for their work and hope to continue developing strategies that fine-tune second shell regions, given their importance in influencing enzymatic reactions.

“The most powerful strategy is an integrated one: redesigning the pathway to channel resources more effectively, while engineering the enzyme to use those resources with greater efficiency and selectivity,” said Scipion. ★



Researchers

Clement Scipion and Xixian Chen,
A*STAR SIFBI

IN BRIEF

Targeted modifications of second shell regions in the limonene synthase enzyme lead to stronger substrate preference and increased limonene production efficiency, allowing engineered *Escherichia coli* bacteria to generate the sought-after aromatic compound.

1. Scipion, C.P.M., Esque, J., Borkar, S., Seah, C., Bozonnet, S., *et al.* Exploring natural diversity of limonene synthases and molecular determinants involved in substrate specificity in *Escherichia coli*. *Journal of Agricultural and Food Chemistry* **73** (22), 13722–13735 (2025).

Photo credit: Dan Gold / Unsplash

POLYMERS AND PLASTICS

Breaking barriers in polystyrene waste

A molecular reshuffling strategy allows access to otherwise blocked sites on polystyrene's structure, enabling the transformation of a major form of plastic waste into a new class of high-value chemicals.

Polystyrene is everywhere, from takeaway food containers to test tubes in labs. Once discarded, this familiar plastic becomes one of the most persistent forms of waste. To transform this waste into industrially relevant chemicals, existing upcycling approaches can derive simple molecules such as benzoic acid. But within its very structure, polystyrene carries a yet untapped—or rather, blocked—potential for generating higher-value products.

Polystyrene's phenyl rings, which consist of carbon and hydrogen bound together in a hexagonal structure, offer several molecular sites where atoms can be added to create new chemicals. "However, these rings are partially blocked by their attachment to the polymer backbone, making some positions difficult for chemical reactions to reach and hindering the production of more valuable multi-substituted chemicals," explained Jason Y. C. Lim, a Principal Scientist at the A*STAR Institute of Materials Research and Engineering (A*STAR IMRE).

Imagine these phenyl rings as a row of cars tightly parked side-by-side, facing a wall. As each car's hood is blocked by the wall, and its doors by its neighbours, the only access to its interior is through the trunk. Likewise, phenyl rings in polystyrene have limited access points for conventional reactions due to how they're normally 'parked' against the polymer backbone.

Together with Research Scientist Albert Ong and A*STAR IMRE colleagues, the team devised a strategy to unlock a more valuable class of compounds by altering the link between polystyrene's phenyl groups and its polymer backbone. The team's approach was inspired by previous work that showed how to reorganise the polymer structure into one where the rings are fused into indane units.

"In this polyindane arrangement, the rings are linked to the backbone at two adjacent positions, rather than a single point," Lim said. "This structural change effectively circumvents the problem of site accessibility on the aromatic ring previously blocked by the polymer backbone. The two attachment sites created a geometric shift, like parking cars at a new angle that affords greater accessibility."

Once these links were altered, the researchers could then introduce an oxidation reaction to free up phenyl rings from the backbone. Oxygenating not one but two positions led to the production of 1,2-disubstituted compounds such as phthalic

acid and phthalic anhydride, which are used in pharmaceuticals, energy storage devices, dyes and other advanced materials.

"The global market for phthalic anhydride is worth billions of dollars annually and is several times larger than that of benzoic acid," Lim said, adding that their strategy can also contribute to supply chain resilience by offering an alternative production route for these high-value chemicals.

After filing a patent application, the researchers next aim to improve the efficiency and scalability of their approach as well as expand its use cases. "We believe that applying this strategy to different polystyrene derivatives can yield an even larger family of high-value aromatic specialty chemicals, further enhancing the value of polystyrene as a feedstock," said Lim. ★

Researcher
Jason Y.C. Lim,
A*STAR IMRE



IN BRIEF

By rearranging the backbone of polystyrene into polyindane, researchers induce oxidation and substitution reactions on key adjacent positions on phenyl rings, producing industrially relevant phthalic acid and phthalic anhydride compounds that have been previously inaccessible from polystyrene.

1. Ong, A., Zhang, Z., Teo, J.Y.Q., Lee, Y.H. and Lim, J.Y.C. Upcycling of polystyrene to 1,2-disubstituted oxygenated aromatics through backbone rearrangement and oxidation reactions. *Angewandte Chemie International Edition* **64** (44), e202515072 (2025).



GREEN ENERGY

Cracking methane's carbon problem

An in-depth investigation of how graphene catalysts split methane molecules offers a cleaner route to hydrogen fuel production with near-zero CO₂ emissions.

Every time you light up your gas stove to cook, it releases a powerful greenhouse gas into the air. Known as methane, this carbon-based fuel is burned in stoves, engines and power plants worldwide, but also has a global warming effect projected to be 28 to 80 times that of carbon dioxide.

Now, researchers aim to craft a cleaner-burning fuel from methane: hydrogen gas. One promising method is methane 'cracking' or pyrolysis, which breaks methane into hydrogen and solid carbon. However, many metal-based catalysts being explored for methane cracking tend to quickly stop working as they get clogged up with carbon deposits.

Jia Zhang, a Principal Scientist at the A*STAR Institute of High Performance Computing (A*STAR IHPC), and Lili Zhang, Division Director of

Emerging Technologies at the A*STAR Institute of Sustainability for Chemicals, Energy and Environment (A*STAR ISCE²), are studying how carbon itself might do a better catalytic job, particularly when shaped as graphene: orderly sheets of carbon only one atom thick.

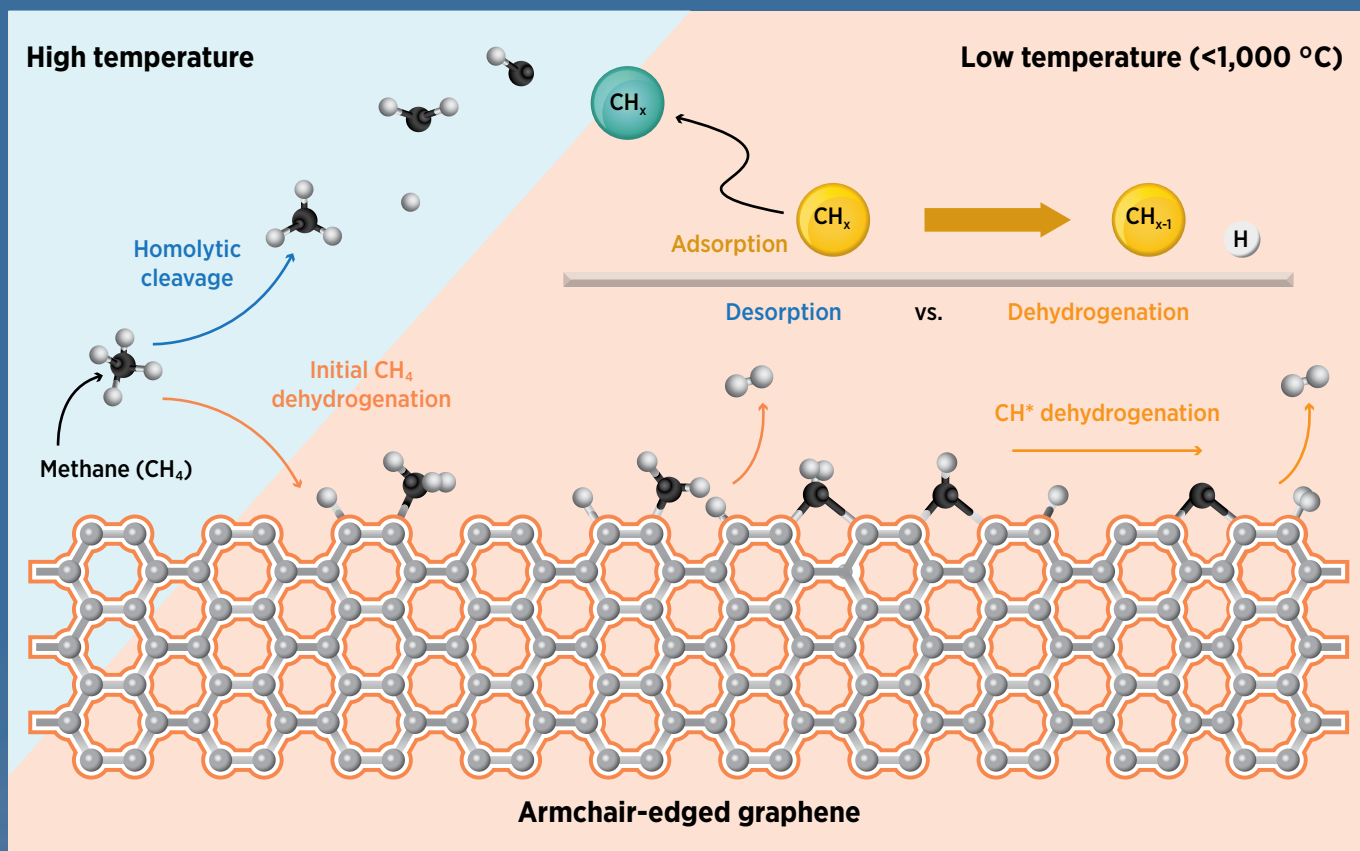
"Graphene is not only good at catalysing methane pyrolysis reactions, but can also guide the formation of solid carbon into valuable byproducts for electronics, batteries and strong lightweight

materials, making the process more economically attractive," said Lili Zhang.

In a recent collaboration between A*STAR IHPC, A*STAR ISCE² and ExxonMobil Technology and Engineering, Jia Zhang, Lili Zhang and colleagues explored the atomic-level mechanics of methane pyrolysis on armchair-edged graphene. The team aimed to identify fundamental bottlenecks in the process and guide meaningful improvements to boost the catalyst's commercial viability.

"It was not clear if or how graphite deposition during methane pyrolysis plays an active role in catalysis, or changes the catalyst's behaviour under different conditions," said Jia Zhang. "A systematic theoretical study allowed us to look at and better understand what happens at the atomic level."

Photo credit: Anne Nygård / Unsplash



Schematic of methane decomposition at high versus low temperatures in the presence of armchair-edged graphene. (Adapted from Zhao *et al.* 2025)

“Graphene is not only good at catalysing methane pyrolysis reactions, but can also guide the formation of solid carbon into valuable byproducts.”

By combining quantum-mechanical computer simulations with experimental validation, the team mapped out, step by step, how graphene helps split methane into hydrogen and carbon products. The simulations helped them calculate how individual atoms interact during the process, and how stable the different intermediate chemicals are under real temperature and pressure conditions.

“Our study helped identify which reaction steps are the most difficult under different process conditions,” said Jia Zhang. “This helps pinpoint which elementary reactions need to be accelerated and provides clear guidance on how catalysts should be improved to target those steps.”

Among the study’s insights were that graphene edges are far more reactive than the material’s flat interior: simulations revealed that edges effectively lowered the activation energy needed to break methane’s carbon-hydrogen bonds at low temperature. “Our experimental results mirror the theoretical trend,” Jia Zhang added.

The study’s findings provide new guidance for the directed design of graphene catalysts for more energy-efficient methane pyrolysis, providing an alternative to trial-and-error approaches, noted the researchers. “Understanding how carbon atoms attach, rearrange, and grow at specific sites also helps in designing better

processes for producing graphene, graphite, carbon nanotubes and other advanced carbon materials,” added Lili Zhang. ★



Researchers

**Lili Zhang, A*STAR ISCE²
and Jia Zhang, A*STAR IIPC**

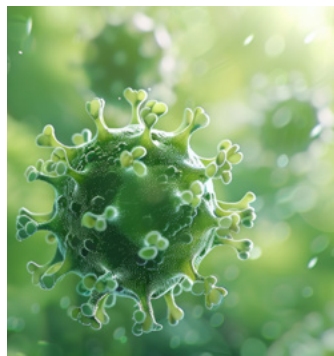
IN BRIEF

Quantum-mechanical simulations and thermodynamic calculations coupled with experimental validation enable atomic-level mapping of the complete reaction mechanism of methane decomposition on armchair-edged graphene, revealing new insights for optimising reactions and producing valuable carbon byproducts.

1. Zhao, P., Poh, C.K., Gao, J., Zeng, J., Abubakar, S., *et al.* CH₄ decomposition over carbon for CO₂-free hydrogen production: A combined DFT and experimental investigation on the role of carbon. *ACS Catalysis* **15** (18), 16333–16343 (2025).

SNEAK PEEK

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



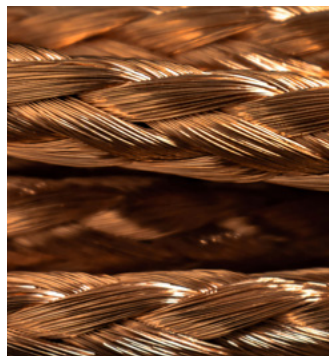
DRUG DISCOVERY **A COMMON AGENT AGAINST CORONAVIRUSES**

A novel broad-spectrum drug candidate stalls replication of several SARS-CoV-2 variants and other coronaviruses, with the potential to boost preparedness against future pandemics.



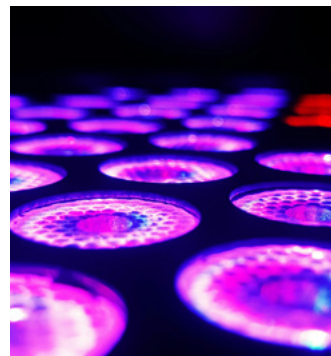
COMPUTER VISION **FRESH AI EYES FOR ODD OBJECTS**

A comprehensive study reveals how tiny differences in process settings can affect the structure and performance of 3D-printed titanium alloys.



SUSTAINABLE CHEMISTRY **SCULPTING COPPER FOR CARBON CONVERSION**

Behavioural studies reveal how surface-shaping reactions help copper catalysts capture carbon dioxide.



PHOTONICS **IT TAKES TWO TO RESONATE**

A hybrid platform for manipulating deep ultraviolet light in semiconductor materials opens new possibilities for next-generation ultraviolet photonic devices.



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