CAMBRIDGE
CARES

cares.cam.ac.uk

A research collaboration platform:
University of Cambridge
and Singapore

Biannual Research Report October 2025 - March 2026

COVER IMAGE

CARES' Chief Operating Officer Elizabeth Macrae presenting at our first hybrid event "Cambridge in Singapore–Who CARES?", held as part of Cambridge Festival, the University of Cambridge's largest annual science festival

PRODUCED BY

CAMBRIDGE CENTRE FOR ADVANCED RESEARCH AND EDUCATION IN SINGAPORE LTD.

Registration No. 201302109Z

1 Create Way, #05-05 CREATE Tower

Singapore, 138602

enquiries@cares.cam.ac.uk

www.cares.cam.ac.uk

CLIC, HYCOMBS, SM_3, and HD_4 are supported by the National Research Foundation, Prime Minister's Office, Singapore under its Campus for Research Excellence and Technological Enterprise (CREATE) programme.

PIPS Automated Evaluation of Environmental Impacts of Pharma Manufacturing Processes, and Building a Capability in Magnetic Resonance Methods for the Pharmaceutical and Agrochemical Secitor within PIPS is supported under the Pharmaceutical Innovation Programme Singapore.

LCER is supported by the National Research Foundation, Prime Minister's Office, Singapore under its Low-Carbon Energy Research (LCER) Phase 2 programme.

Content Page

Foreword 2

About Us 4

Programme Updates

CLIC 6

HYCOMBS 12

SM_3 24

HD_4 36

PIPS 44

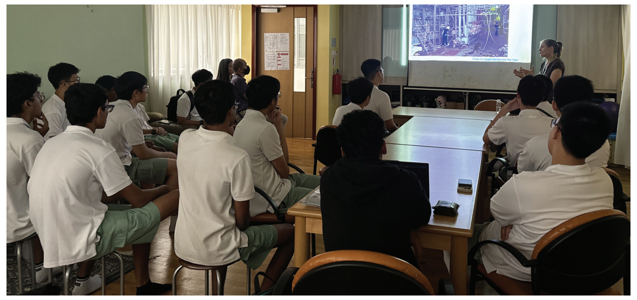
LCER PHASE 2 48

Publications 51

Foreword

CARES has been actively working with Cambridge to explore new public engagement ideas. A joint event that brings Cambridge and CARES together adds a new dimension for audiences to learn about opportunities to study with Cambridge and to work with CARES throughout their education and career.

As a recent example, a Cambridge Admissions representative visited Singapore for a series of education fairs and planned a school counsellor networking session in the CREATE building. CARES contributed a Visiting Cambridge Professor, Assoc Prof Ewa Marek, as a guest speaker to provide her perspective on the admissions process as an interviewer. The valuable session initiated two invitations for Assoc Prof Marek to speak to students about chemical engineering at NUS High and Tanglin Trust. The opportunity for unique activities such as this creates a thriving ecosystem at CARES where research grows in parallel with nurturing the next generation of young learners.



Assoc Prof Ewa Marek presenting to students at NUS High.

As a publicly funded research centre, CARES bears the responsibility to share the work we do to the public. In the past six months, we've explored more creative approaches and leveraged our connections with the British Council and Cambridge to reach wider audiences.

CARES @ Cambridge Festival 2026

CARES joined Cambridge Festival, the University of Cambridge's largest annual science festival, for the first time in 2026 to share our decarbonisation research to a younger schooling audience. The hybrid event for both Singapore and UK audiences (online) drew an incredible response of over 150 attendees from 30 different schools. Our researchers shared their day-to-day work with engaging quizzes and questions, and talked about their career journeys. The incredible feedback and response from students who stayed behind to speak with our researchers and operations team has made it clear that there is an appetite for scientific events.

HD_4 and Science Centre's Community of Practice Day

The Health-driven design for cities (HD_4) programme led a successful Community of Practice Day aimed at local educators, in collaboration with Science Centre Singapore. The session considered the different drivers of choice and behaviour in daily decisions, such as making healthy food choices, with the groups role-playing as different stakeholders debating the opening of a fast food outlet near a school. HD_4's work at the nexus of health and environment stood as the backdrop with Prof Marie Loh explaining how HD_4 studies the urban environment as a factor in shaping our daily choices and healthy outcomes.

Attendees at the Science Centre's Community of Practice Day with HD_4.

CLIC research benefits from CREATE connections

The unique social collaboration of the CREATE ecosystem has enhanced our lifelong learning research programme, CLIC. Adult students attending French language classes hosted by CNRS@CREATE will have the option to join CLIC's research recruitment, studying the effects of language on cognitive flexibility.

Welcoming our largest-ever UK Higher Education Delegation

We were pleased to host senior leaders from leading UK universities, in partnership with the British Council Singapore, as part of a visit to explore Singapore's education and research ecosystem. We showcased research from CLIC and HD_4, demonstrating how our projects leverage Singapore's urban environment and population to advance human health and potential. We even connected the delegates with the National Research Foundation Singapore to share insights on RIE 2030 and emerging collaboration opportunities. Such engagements place CARES as a key player in strengthening UK–Singapore partnerships.

We are delighted that our research and outreach teams have been working together to curate these unique engagement opportunities for the public. It is a testament to the proverb that "Rome wasn't built in a day", as many of the networks we have cultivated have taken time, patience, and effort.

Please get in touch with us if you would like to know more about our work or have ideas for collaboration.

About Us

Cambridge CARES is the University of Cambridge's presence in Singapore

The Cambridge Centre for Advanced Research and Education in Singapore (CARES) is a wholly-owned subsidiary of the University of Cambridge. Cambridge CARES is funded by the National Research Foundation (NRF) as part of CREATE (Campus for Research Excellence and Technological Enterprise). We have a number of research collaborations between the University of Cambridge, Nanyang Technological University, the National University of Singapore, industrial partners, and other universities in Japan, France, Norway, and Switzerland.

The first programme administered by CARES, the Cambridge Centre for Carbon Reduction in Chemical Technology (C4T), wrapped up in October 2025 after 12 years. The motivation for C4T was to provide a rich pipeline of scientific insight and technological innovation with high potential for positive results within the decarbonisation agenda if deployed by appropriate industry and government parties.

The C4T programme is a world-leading partnership between Cambridge and Singapore, with the first five-year research phase focused on assessing and reducing the carbon footprint of the integrated petro-chemical plants on Singapore's Jurong Island.

The programme received a further five years of funding for Phase 2, which commenced in November 2018 and ended on October 2025. This second phase considered that decarboisation must be addressed at all levels — from fundamental science to the development of low-carbon alternatives of key technologies, to identifying deployment opportunities, and exploiting synergies across research groups.

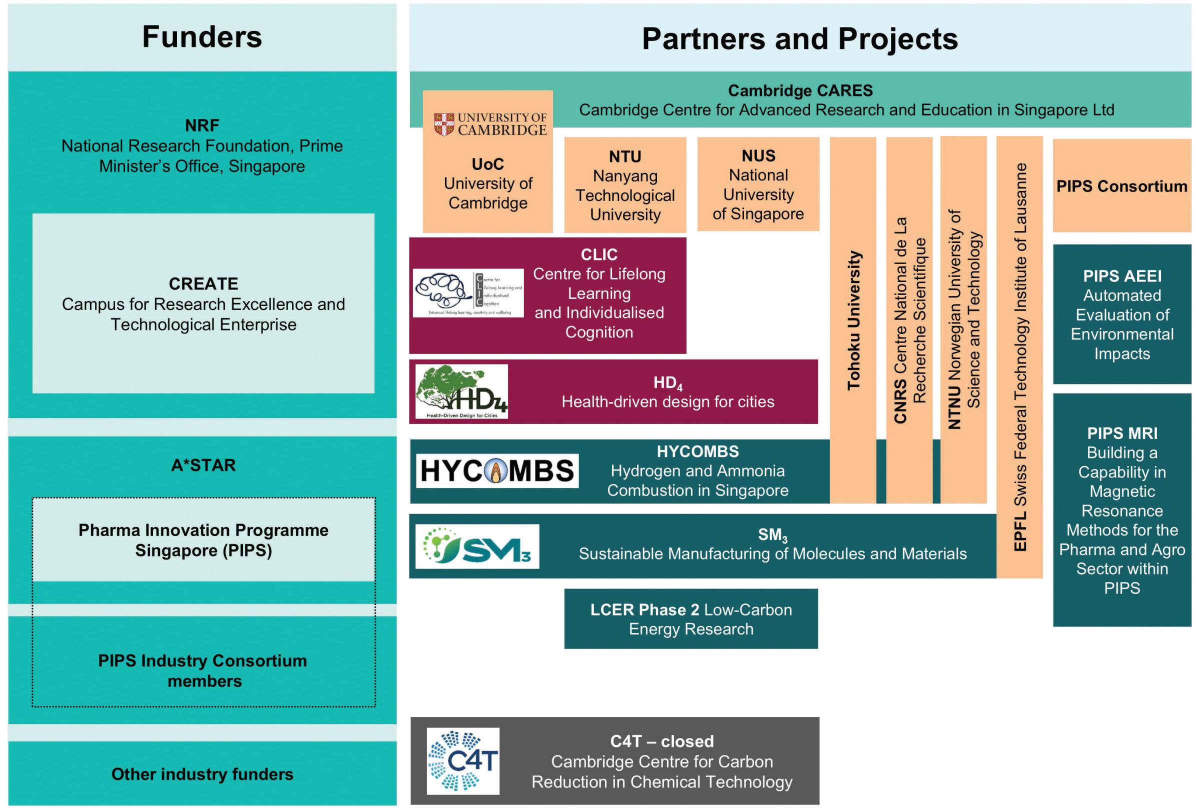
C4T's impact and contribution to fundamental research (726 papers and an H-index of 106 to date), technology development (36 invention disclosures, 52 patent filings and 4 licenses), and translational impact (6 spin-off companies), is evident. The programme has also hosted 47 PhD students, some with matched industry funding through the Cambridge-CARES studentship scheme. As C4T ends, we celebrate the programme's legacy and platform for kickstarting our new decarbonisation projects.

In July 2024, NRF announced a new SGD$90m Decarbonisation programme. The two CARES-hosted project under this initiative are Hydrogen and Ammonia Combustion in Singapore (HYCOMBS), and Sustainable Manufacture of Molecules and Materials in Singapore (SM$_3$). New collaborators on these projects include Tohoku University, CNRS, the Norwegian University of Science and Technology, and the Swiss Federal Technology Institute of Lausanne.

AMPLE (An Accelerated Manufacturing Platform for Engineered Nanomaterials), funded by the Central Gap Fund, also had its final phase at CARES. AMPLE grew from research within the C4T programme and is bringing products to commercialisation via the spin-off company, Accelerated Materials, which have recently completed their seed round campaign in April 2025.

CARES embarked on a new research area called the Centre for Lifelong Learning and Individualised Cognition (CLIC) in October 2020. CLIC is a collaboration between the University of Cambridge and NTU and focuses on the neuroscience of learning. CLIC has received confirmation of a further three years of funding, extending the programme to September 2026.

The Health-driven design for cities (HD$_4$) programme commenced in October 2024, contributing to CARES' building portfolio on human health and potential. HD$_4$ will use data from the SG100K study to investigate the relationships of the built environment on the behaviour and health outcomes of Singaporean residents.



There are currently two ongoing streams under the Pharmaceutical Innovation Programme Singapore (PIPS); one stream focuses on using data-driven solutions to rapidly identify environmental impacts in the chemical supply chain, the other stream will use magnetic resonance imaging to optimise operating conditions for heterogeneous hydrogenation reactions in continuous-flow microscale trickle-bed catalytic reactors.

CARES is also contributing to two projects in the Low-Carbon Energy Research (LCER) Phase 2 Programme, one hosted by NUS and one hosted by NTU.

CARES celebrated its first decade in Singapore in 2023 with a Scientific Showcase highlighting achievements in Digital Transformation, Chemical Technologies and Processes, From Emissions to Solutions, and Lifelong Learning. The scientific content from the event and highlights from 2023 can be viewed on our website.

This report is a summary of our last half-year of research progress. It includes scientific updates and external engagements from each of our researchers, along with a list of recent publications.

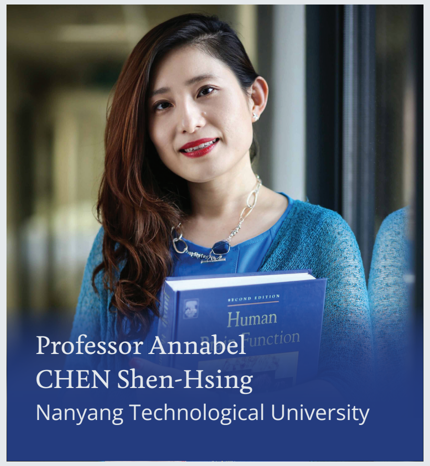


CLIC

CENTRE FOR LIFELONG LEARNING AND INDIVIDUALISED COGNITION

The Centre for Lifelong Learning and Individualised Cognition (CLIC) is a programme within the Science of Learning initiative, harnessing advancements in neuroscience to develop lifelong learning programs. CLIC is dedicated to enhancing lifelong learning and cognitive flexibility through pioneering interdisciplinary research, with the goal of developing educationally relevant cognitive flexibility paradigms that inform future interventions across the lifespan.

Directors



Professor Annabel CHEN Shen-Hsing
Nanyang Technological University

Professor Zoe KOURTZI
University of Cambridge

The Centre for Lifelong Learning and Individualised Cognition (CLIC) has continued to build strong momentum across Work Packages 1-3, with steady progress in research quality, translational alignment, and research output. The team has focused on strengthening methodological rigour while ensuring our work remains closely aligned with educational and policy priorities.

In the last six months, we have been working on incorporating valuable recommendations from the Scientific Advisory Committee into the development of an enhanced Structure Learning (SL) task. The full task battery has now been centralised onto a unified NTU-hosted platform, and comprehensive quality assurance and user testing are currently underway, with completion targeted for mid-March. An upcoming staff training workshop will introduce the new Cognitive Testing Hub to ensure procedural consistency and readiness for the next phase of data collection.

The adolescent cognitive assessment has also been thoughtfully redesigned in consultation with the Ministry of Education (MOE) and the National Research Foundation (NRF). The revised framework integrates Structure Learning assessments to better characterise the effects of cognitive flexibility (CF1) and CF2. This refinement aligns with the Critical, Analytical, and Inventive Thinking (CAIT) within the MOE framework, enhancing the translational value of our findings.

The pre-post MR imaging protocol has been successfully piloted and optimised with reduced scan time and improved data quality. Cross-team collaboration has further strengthened integration across behavioural and MRI codebases, alongside ongoing HPC infrastructure development and SOP preparation. All the above contribute to WP1 efforts.

Work Package 2 (WP2) continues to advance intervention research in language learning, social framing, and career adaptability, with ongoing data collection and IRB-approved studies progressing as planned. Meanwhile, Work Package 3 (WP3) has deepened collaboration with the Singapore Examinations and Assessment Board (SEAB), validating CAIT against CLIC indices and refining adolescent models of cognitive flexibility. Regular engagements with MOE and NRF ensure continued policy alignment, while sustained school outreach supports meaningful knowledge translation.

Taken together, these developments reflect a coordinated and forward-looking programme of research. CLIC is well-positioned to deliver sustained scientific contributions alongside tangible educational and policy impact.

Professor Annabel Chen Shen-Hsing
Director of CLIC, NTU

Professor Zoe Kourtzi
Director of CLIC, CAMBRIDGE

WORK PACKAGE 1

CLIC is ramping up preparations to commence with the Structure Learning-based Cognitive Flexibility Training Suite (SLiCX) adult intervention study by end March 2026. Preparations include centralising and hosting the cognitive task battery on an NTU-hosted platform, completing the gamification components for the Structure Learning task on iABC, and at the same time, refining the active control task (All You Can E.T.) on DREAM which is a collaborative effort with New York University (NYU). The SLiCX team will be conducting comprehensive quality assurance checks and user testing to ensure stability and smooth performance of all tasks before participant rollout. The team aims to have all preliminary checks completed by mid-March. In parallel, preparations are underway for a staff training workshop to familiarise the team with the protocols for the SLiCX adult study. The workshop will also introduce additional tasks not included in Phase 1, such as Maggie's Farm, the Cambridge Gambling Task, and the Iowa Gambling Task. The workshop will also serve as a refresher course for all staff involved in data collection, ensuring procedural consistency and readiness ahead of the next stage of the study.

Building on recommendations from the Ministry of Education (MOE) and the National Research Foundation (NRF), the adolescent testing paradigm has been comprehensively revamped. These refinements are designed to advance understanding of the development of cognitive flexibility (CF1) and CF2 in adolescents, particularly in relation to structure learning (SL). The revised plans incorporate SL assessments alongside cognitive profiling components, allowing the team to characterise students' levels of cognitive flexibility. The updated adolescent task battery is structured to clarify the relationship between cognitive flexibility and other related constructs, strengthening construct validity and interpretability. In alignment with the MOE framework, the battery is also designed to examine how structure learning and cognitive flexibility contribute to the development of Critical, Analytical, and Inventive Thinking (CAIT) skills, thereby enhancing the translational relevance of WP3's research for educational contexts.

Since the previous progress update, the full pre–post MR imaging protocol has been piloted with adult and adolescent participants. The protocol was further optimised by implementing no-gap resting-state fMRI scans and replacing model-free Diffusion Spectrum Imaging (DSI) with model-based Constrained Spherical Deconvolution (CSD) diffusion imaging. These refinements have reduced the total scan time to approximately 70 minutes while enhancing data quality output and enabling advanced downstream analysis. Pilot neuroimaging and SL data have passed initial quality checks. Automated pipelines for BIDS structuring, MRIQC-based multi-modality quality reporting, and standardised preprocessing for resting-state fMRI and diffusion MRI has been established. Phase 1 resting-state preprocessing and analyses are currently underway to ensure procedural and analytic alignment with Phase 2 protocols.

Cross-team collaboration is ongoing to develop a centralised SL task codebase spanning both the iABC platform and the MRI scanner environment for Phases 1 and 2, alongside the adaptation of analysis scripts for MRI-based SL tasks. The MRI team is also supporting high-performance computing infrastructure setup, including secure data storage and scalable pipeline design to support large-scale analyses. Standard operating procedures for data collection, management, and backup are currently in preparation. Phase 2 of the adult main study is tentatively scheduled to commence on 23 March 2026, with a training workshop planned for study personnel and student assistants.

The WP1 team has also made significant progress across several research fronts, marked by the preparation of multiple manuscripts and the development of new study protocols. A key manuscript examining the structure of cognitive flexibility and how different CF elements relate to essential real-life outcomes like reading, mathematics, and creative thinking has been submitted. A second manuscript, exploring how stress and anxiety may interfere with a person's cognitive flexibility and its real-world translation, is currently undergoing internal review and is expected to be submitted for publication in the coming months. Related findings have already been accepted for presentation at the International Association for Child and Adolescent Psychiatry and Allied Professions (IACAPAP) 2026 congress.

In parallel, WP1 is collaborating with the CLIC school team to design and refine new assessment protocols for cognitive flexibility by May 2026. This work addresses a critical practical challenge in educational settings: existing cognitive assessments are often too lengthy and resource-intensive for routine school implementation. The promising finding that early performance in structure learning tasks can reliably predict a person's broader cognitive flexibility profile offers a potential path toward brief, scalable tools that can be realistically deployed in classrooms, enabling faster identification of students who may benefit from targeted support without placing undue burden on schools. Taken together, these efforts reflect a productive and increasingly collaborative research programme, with active manuscript preparation and protocol development laying the groundwork for continued impact in education, mental health, and intervention design.

Beyond SLiCX, CLIC continues to explore the emergence of cognitive flexibility across the lifespan and how this relates to creativity and school readiness. A small study is underway with children aged 12 to 48 months, integrating EEG and ECG measures to examine the neural and physiological mechanisms associated with early emerging cognitive flexibility and creativity skills and the social contexts that positively facilitate these.

WORK PACKAGE 2

Steady progress has been made across several ongoing intervention studies investigating language learning, social framing, and career development. Data collection is in progress for the **Language Learning** study, with 99 young adult participants recruited to date. The team is also reaching out to external collaborators such as CNRS@CREATE to recruit working adult participants enrolled in a language course.

The **Social Framing** study investigates how cooperative and competitive social framing influences task performance within a structure-learning paradigm, and how these effects are moderated by individual differences in trait social orientation. This study has been approved by the Institutional Review Board (IRB), and current efforts are focused on programming the experimental task and developing the data analysis scripts.

The **Career Study** has made significant progress in developing the intervention design and questionnaires aimed at examining how cognitive flexibility, career adaptability, and related competencies influence decision-making. The research design continues to be refined through ongoing literature review and conceptual development in collaboration with SkillsFuture Singapore.

A manuscript examining measurement issues in the Big Five Inventory has been invited for revision and resubmission to the *European Journal of Personality*. Two additional papers are also currently under review: 1) a manuscript on behavioural game theory tasks submitted to *Behaviour Research Methods*, and 2) a study evaluating the Career Construction Model of Adaptation (CCMA; Savickas & Porfeli, 2012) with *Frontiers in Psychology*.

In addition, a collaborative paper with Work Package 3 examining the relationship between multilingualism and cognitive flexibility across adolescent and adult populations has also been accepted for presentation at the upcoming 28th Biennial Meeting of the International Society for the Study of Behavioural Development (ISSBD) in Incheon, South Korea.

The team is also concurrently preparing three other manuscripts. These papers aim to examine: 1) the relationship between language entropy and cooperativeness, 2) the association between receptiveness to opposing views and trust, and 3) how cognitive flexibility moderates the relationship between career adaptation dimensions and income among working adults in Singapore.

WORK PACKAGE 3

Work Package 3 (WP3) has continued its collaboration with the Singapore Examinations and Assessment Board (SEAB). In November 2025, the team met with SEAB to discuss ongoing analyses aimed at validating SEAB's Critical, Analytical, and Inventive Thinking (CAIT) assessment against CLIC's cognitive flexibility indices. The teams exchanged ideas on next steps for analysis, including the development of design principles for strengthening the assessment framework for CAIT.

Between November to December 2025, the team conducted a re-analysis of WP01 data to further validate the cognitive flexibility model for adolescents. Preliminary analyses were also completed for the Scientific Thinking/CAIT tasks and the Crossing Valley Task. With contributions from WP1, the team identified structural differences between adult and adolescent models of cognitive flexibility, suggesting that strategy flexibility continues to develop and consolidate into adulthood. These findings were first presented to the SAC in November 2025.

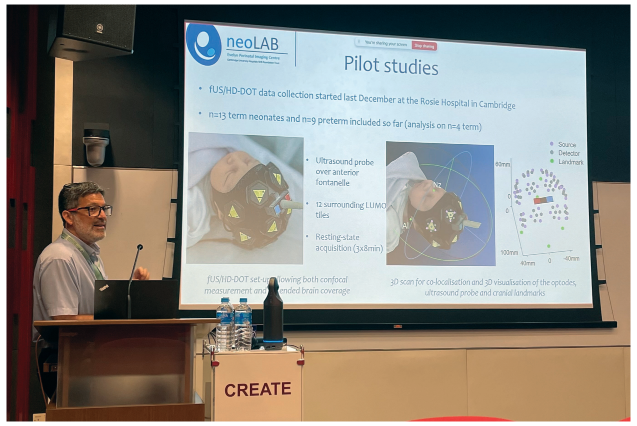
A follow-up discussion was subsequently held in January 2026 with Dr Teh Laik Woon and Dr Goh Sao Ee, both from the Ministry of Education in Singapore, focusing on the translational work in WP3 to ensure continual alignment with policymakers. The feedback from this discussion informed improvements to adolescent data collection plans, which were presented to Dr Teh, Dr Goh and Prof Subodh Mhaisalkar from the National Research Foundation in February 2026. The quarterly meeting between CLIC, MOE and NRF, was initiated in October 2025 and was established to ensure continued alignment of WP3's research efforts and expected pedagogical impact. WP3 emphasised the commitment to translational work for school settings—elaborating on upcoming plans for validating structure learning in adolescents, including a data-driven, compacted task battery to improve motivation and engagement for adolescent participants.

WP3 has also maintained active engagement with the secondary schools that have partnered with CLIC. With more analyses emerging from the 2025 data collection, the team has begun visiting the schools to share updated findings. These engagements are expected to continue through March and April 2026.

In addition, three manuscripts, the first, an empirical study on CF and creativity in adolescents, the second, a scoping review on creativity and CF in adolescents, and the third, a cross-cultural validation of a new assessment targeted at examining general cognitive abilities, are currently under review and are expected to be published by the end of 2026.

OTHER ACTIVITIES AND ACHIEVEMENTS

During this period, CLIC sustained active engagement with the academic and educational communities. During his residency in Singapore, Cambridge PI, Prof Topun AUSTIN delivered a talk titled Sleep, Touch & Making of The Human Brain on 27 November 2025 at CREATE. The session drew participants from CARES, Early Mental Potential & Wellbeing Research Centre (EMPOWER), CRADLE@NTU, along with other CREATE entities. The talk covered his work in investigating the relationship between sleep and brain connectivity, neural synchrony, and how these processes lay the foundation for learning from childhood through to later life.

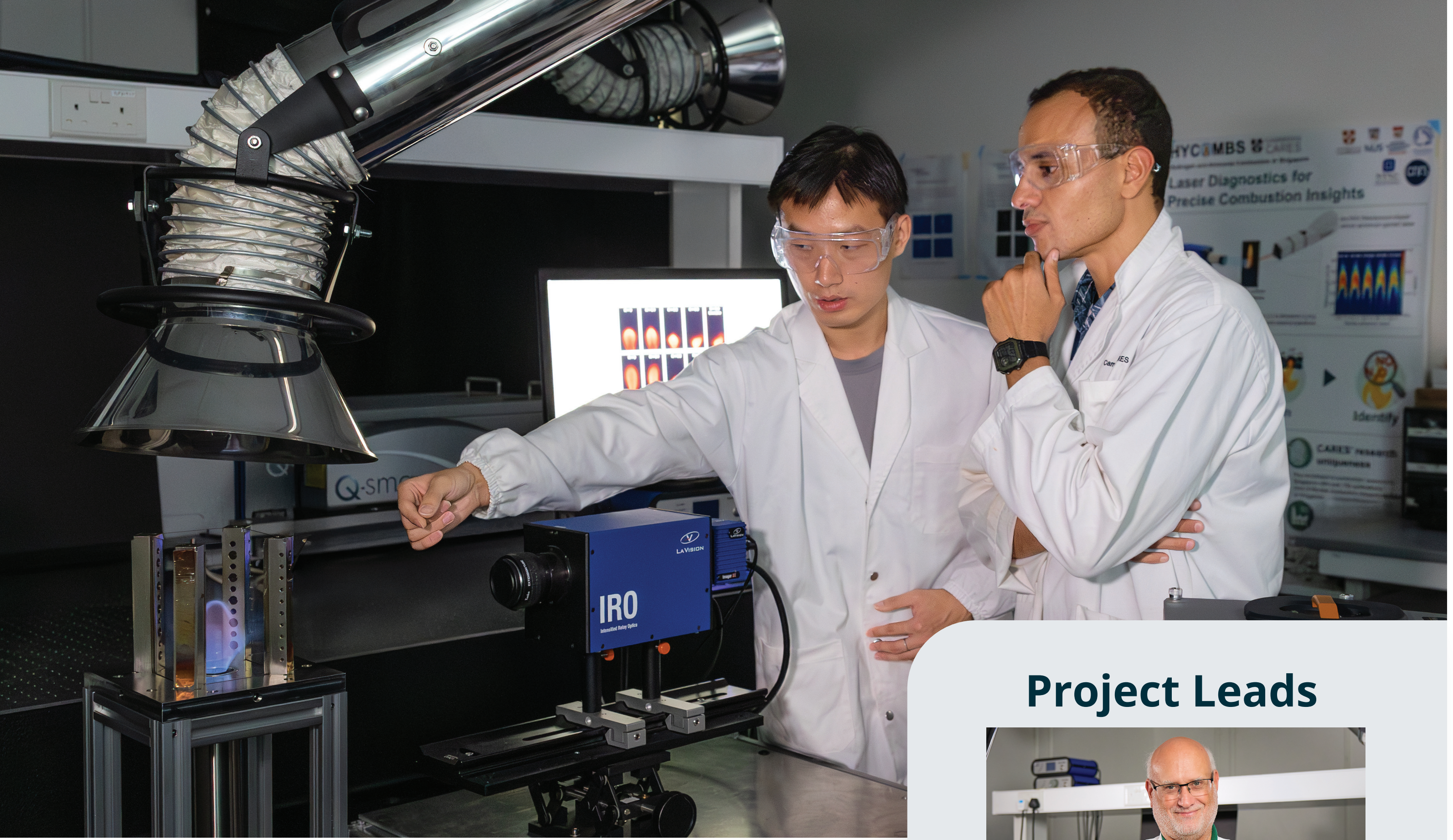


Prof Topun Austin at his CREATE seminar.

Dr Rui WANG (Research Fellow, NTU) and Dr Ke TONG (Research Fellow, NTU) presented the goals of CLIC's research in Singapore and the ongoing school collaborations to a visiting delegate from the British Council on 30 January 2026. The visit was part of a learning journey hosted by the British Council Singapore to bring over 10 senior representatives from various UK universities to learn about Singapore's education and research ecosystem and to explore collaboration opportunities.

Dr Wang and Dr Tong spoke to the delegate in CLIC's new office in CREATE.

Assoc Prof Georgios CHRISTOPOULOS (PI, NTU) is preparing a research proposal with SkillsFuture Singapore to incorporate CLIC's intervention design into the agency's work.

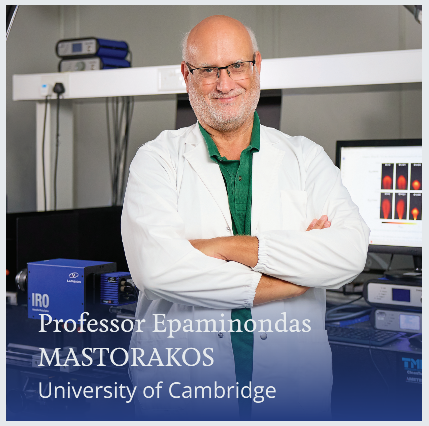


HYCOMBS

HYDROGEN AND AMMONIA COMBUSTION IN SINGAPORE

HYCOMBS focuses on the combustion fundamentals of hydrogen, ammonia, their blends, and their blends with hydrocarbon fuels. The knowledge acquired in this project will enable the penetration of zero-carbon fuels in the Singapore energy system and this will benefit Singaporean industries and residents.

Project Leads



Professor Epaminondas MASTORAKOS
University of Cambridge

Assoc Professor Fei DUAN
Nanyang Technological University

Professor Kaoru MARUTA
Tohoku University

WP1: CHEMICAL KINETICS

Work Package 1 focuses on investigating the fundamental chemistry governing the combustion of hydrogen, ammonia, hydrocarbons, and their blends. Achieving this objective requires both a deep theoretical understanding of reaction mechanisms and the acquisition of high-quality experimental data to develop, validate, and refine chemical kinetic models. Our approach integrates experimental measurements using the Micro Flow Reactor (MFR) with advanced computational simulations to provide comprehensive insights into ammonia and hydrogen oxidation chemistry.

Experimental Rig Development

Significant progress has been made in establishing our experimental capabilities. We have finalised the design of the MFR and commenced assembly of its core systems, with particular attention to the ultra-low flow rate control and gas sampling systems that are critical for precise measurement of reaction products. The MFR heating furnace, currently under fabrication at our partner facility in Tohoku, Japan, is scheduled for delivery to CARES in March 2026. Upon installation, this system will enable detailed investigation of reaction kinetics under well-controlled temperature and residence time conditions.

Computational Framework and Mechanism Evaluation

Parallel to our experimental efforts, we have implemented numerical simulations for reactive-diffusive flows within the MFR geometry. These simulations utilise ammonia chemical kinetic mechanisms sourced from recent literature, enabling us to model ammonia/hydrogen oxidation. A key focus of our current computational work is identifying specific conditions where significant discrepancies exist among various published kinetic mechanisms. These critical points, where model predictions diverge, will be prioritised for subsequent experimental validation. By systematically comparing mechanism predictions and identifying sources of uncertainty, we aim to guide the development of more accurate and comprehensive kinetic models for ammonia-based fuels.

Additionally, we have conducted initial comparisons between computational results and available experimental data for neat ammonia oxidation. Based on these comparisons, we are currently evaluating specific elementary reactions for potential updates. This process is supported by an ongoing literature review and uncertainty quantification of rate constants. Reactions exhibiting high sensitivity and large uncertainty intervals will be designated as priority candidates for high-level ab initio calculations to ensure the research output is maximised.

Mechanism Validation Against Flame Data

To assess the predictive capabilities of existing kinetic models for flame conditions, we have conducted extensive testing of literature mechanisms against experimental data for partially cracked ammonia in partially premixed diffusion flame configurations (KAUST Flame D). This validation process reveals important insights into the performance of the mechanisms.

Our analysis (see Figure 1.1) shows that all tested mechanisms recover qualitatively similar behaviour with increasing strain rates, leading to comparable predictions of extinction strain rates. However, significant quantitative differences emerge in the prediction of NO_x concentrations within the flame core. These variations depend strongly on the level of mechanism detail: detailed mechanisms incorporating 40+ species and 250+ reactions show different NO_x predictions compared to lighter mechanisms with approximately 20 species and 70 reactions. This sensitivity highlights the importance of nitrogen chemistry sub-mechanisms in determining pollutant formation.

Additionally, we have compared promising light mechanisms against experimental strain diffusion flame data obtained from Tohoku University. While the lighter mechanisms systematically underpredict extinction strain rates compared to experimental measurements, even the most detailed mechanisms fail to perfectly recover the experimental data across all tested conditions. This observation indicates that current kinetic descriptions, while sophisticated, still require refinement, particularly regarding the interaction between transport processes and chemical kinetics in strained flame configurations.

Additionally, we have compared promising light mechanisms against experimental strain diffusion flame data obtained from Tohoku University. While the lighter mechanisms systematically underpredict extinction strain rates compared to experimental measurements, even the most detailed mechanisms fail to perfectly recover the experimental data across all tested conditions. This observation indicates that current kinetic descriptions, while sophisticated, still require refinement, particularly regarding the interaction between transport processes and chemical kinetics in strained flame configurations.

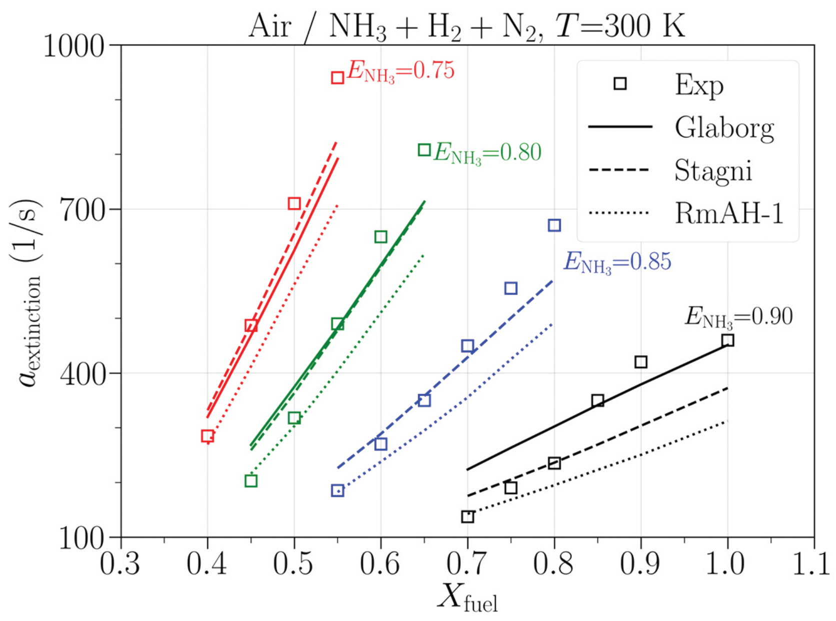


Figure 1.1: Extinction strain rates of N_2-diluted NH_3/H_2 blend diffusion flames in air at 300K. The data includes experimental results from Tohoku University alongside numerical simulations (combining reproductions of prior Tohoku University data with new numerical results from the present study).

Advanced Numerical Methods for Micro-Scale Combustion

To complement our experimental MFR studies, we have implemented PeleLMeX, *i.e.* an adaptive-mesh, low-Mach-number hydrodynamics code specifically designed for reacting flows. This advanced numerical framework will enable detailed 2D modelling of flame dynamics in narrow heated channels, capturing the essential physics of micro-scale combustion systems.

We are working to include the continuous development of the solver and conditions to model the MFR. Validation of results based on known experimental and numerical results, to confirm accuracy of the solver and developed setup. Sample of the results can be found in Figure 1.2.

Development of new data for ammonia and hydrogen fuels, with a focus on the physics of FREI (flame repeated extinction and ignition). Comparison of results in various state-of-the-art chemical kinetic models for Ammonia (to date, Polimi 2020, KAUST 2023, NUIG 2023).

Figure 1.2 shows the dynamics of FREI, reproduced in methane using a reduced (DRM19) mechanism in a microflow reactor for an inlet velocity of 15 cm/s. This dynamic behaviour matches past experimental results. Varying the inlet velocity, the code also accurately reproduced other solutions (stable normal flame, stable weak flame).

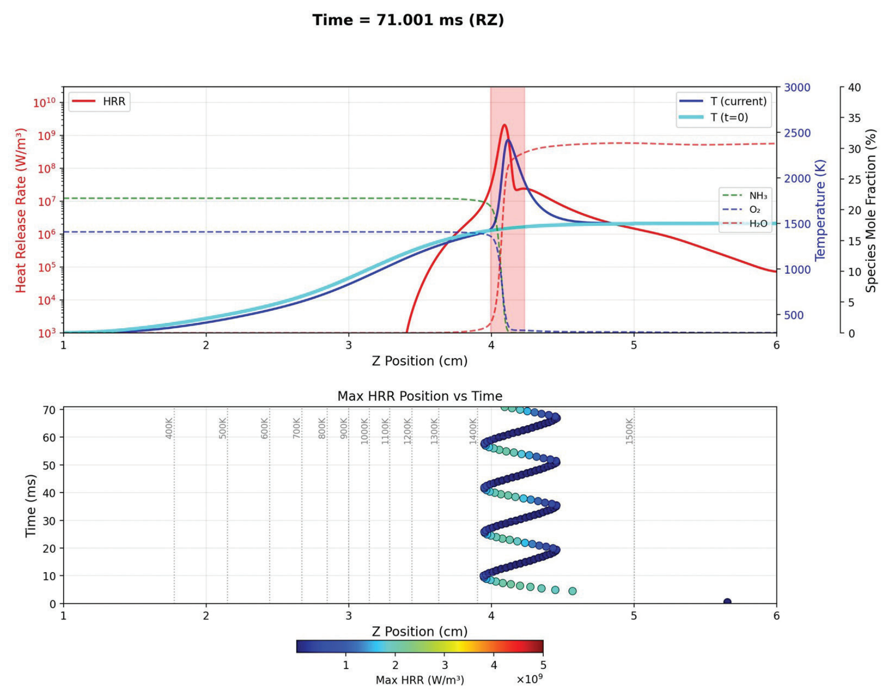


Figure 1.2: Centreline results of the simulation in methane. Top shows heat release rate (HRR - red), wall temperature (cyan), gas temperature (blue) as well as mass fractions of CH_4, O_2 and H_2O (dashed lines). Red area represents the flame position at current time. Bottom shows an x-t diagram showing maximum HRR position in the domain every 0.5 ms.

WP2: FLAMES

Work Package 2 investigates fundamental laminar and turbulent flames of increasing complexity, focusing on turbulence effects on reaction zones and novel stabilisation concepts for gas turbines and ignition mechanisms for engines. Laminar flame experiments reveal how pulsation, strain, and curvature affect hydrogen-ammonia flames. Turbulent flame experiments examine how staging influences stability and structure, while exploring novel stabilisation and ignition schemes.

Computational Flame Modelling

Research on computational fluid dynamics, numerical solver optimisation, and advanced post-processing of turbulent combustion data progressed in parallel.

First, mesh optimisation for the Cambridge Swirl Burner enhanced simulation predictive capabilities. Refining grid topology and orthogonality enabled higher-order numerical schemes while maintaining computational stability, fundamental for accurately capturing complex flow-flame interactions.

Second, collaboration with Sapienza University of Rome advanced an explicit solver integration into the 0D-CMC (Conditional Moment Closure) code. This development targets the most computationally expensive component of simulations: chemical kinetics calculation. Stability and performance benchmarking indicate significant potential to reduce CPU time for CMC-based simulations, enabling more complex chemical mechanisms in practical engineering applications.

Third, a scientific visit to Kyoto University in January 2026 initiated comprehensive post-processing of Direct Numerical Simulation data for a turbulent jet flame (KAUST Flame D). Analysis focuses on sub-grid modelling of differential and preferential diffusion in LES equations, and evaluating chemical markers to identify reaction zones in premixed and non-premixed regimes. This framework establishes foundations for forthcoming NO_x formation pathway analysis.

Turbulent H_2/NH_3 Flames

Experimental diagnostics captured OH-PLIF and OH*/CH* chemiluminescence images for premixed methane flames with premixed and non-premixed hydrogen addition. These measurements provide fundamental insight into flame structure modifications induced by hydrogen blending. Averaged OH-PLIF images present as Figure 1.3 below showing a very different OH distribution when changing the hydrogen injection locations. Instantaneous OH-PLIF images can be used for further quantitative analyse for these flames, such as flame surface density, curvature, etc.

Laminar H_2/NH_3 Flames

A laminar burner based on the design of Kagaya was successfully installed in the CARES laboratory on a three-axis automated translation stage, enabling precise

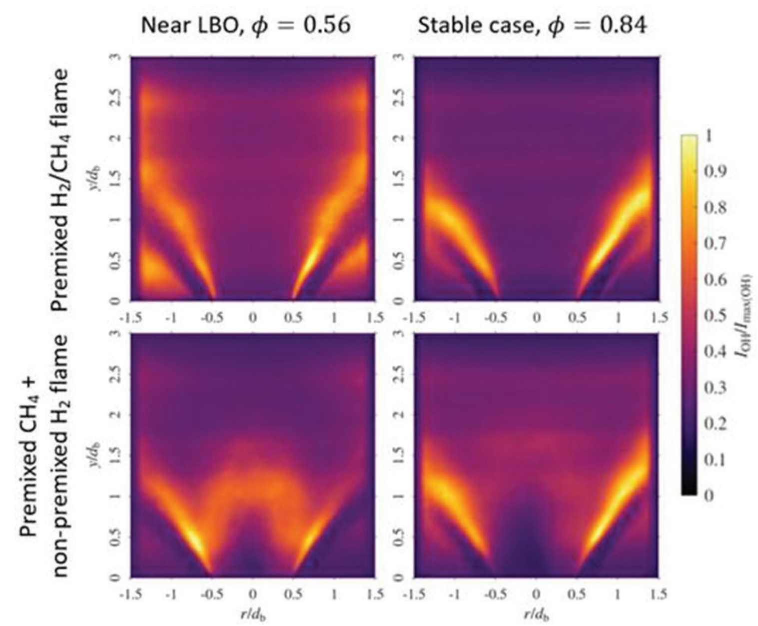


Figure 1.3: Normalised average OH-PLIF images of premixed CH_4-air flame with premixed and non-premixed H_2 injection at 15 m/s at near and far away from (stable) lean blow-off conditions.

positioning during experimental campaigns, as shown in Figure 1.4. Full system commissioning included a chiller for controlled wall temperature, fabricated gas supply manifold for multiple fuel types, and installation of a tuneable diode laser absorption spectroscopy (TDLAS) system for line-of-sight temperature and H_2O concentration measurements.

Preliminary methane flame experiments validated temperature and H_2O concentration measurements. A collaborative experimental campaign with Prof Nicolas MINESI (PI, CNRS) and Prof Sébastien DUCRUIX (PI, CNRS) was conducted in February 2026. The immediate priority is validating laser-based measurements against reference diagnostics, i.e., known flame conditions for H_2O mole fraction and thermocouple temperature measurements.

Experiments under self-sustained thermoacoustic instability conditions demonstrated successful capture of relative temperature and H_2O concentration fluctuations using the laser diagnostic. Following validation, three objectives follow: cross-checking fluctuations against conventional photomultiplier tube chemiluminescence measurements; mathematically correlating measured temperature and H_2O fluctuations with heat-release-rate fluctuations; and mapping the burner for carbon-free ammonia-hydrogen flames.

Advanced Flame Modelling

Numerical simulations of KAUST partially cracked ammonia diffusion flames (see Figure 1.5) required modifications to the Conditional Moment Closure approach. A validated modification for canonical counterflow flames now accounts for differential diffusion of H and H_2 species, critical for accurate flame structure and strain response predictions. Initial Large Eddy Simulations have commenced with a completed cold flow simulation; full burning flame simulation is ongoing.

Hydrogen-Enriched Flame Stability

Research focused on structure and stability of lean premixed swirl flames fuelled by methane and hydrogen-enriched methane, relevant to low-carbon gas turbine combustion. Laboratory-scale experiments examined how hydrogen enrichment and swirl intensity influence flame morphology and heat release distribution using 10 Hz OH* chemiluminescence diagnostics.

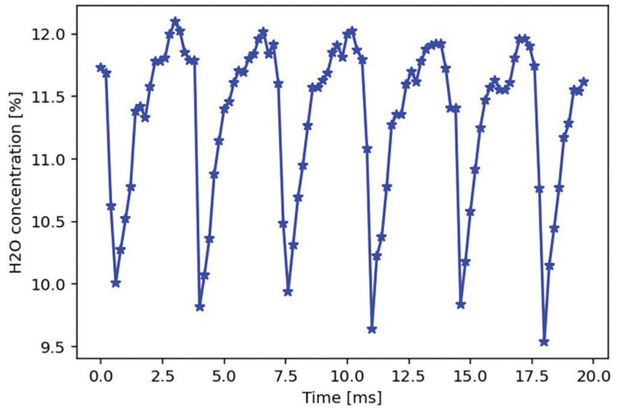


Figure 1.4: (Top) Up-close view of the burner/TDLAS. (Bottom) Fluctuation of H_2O concentration along the line of sight at the condition of self-sustained thermoacoustic instability.

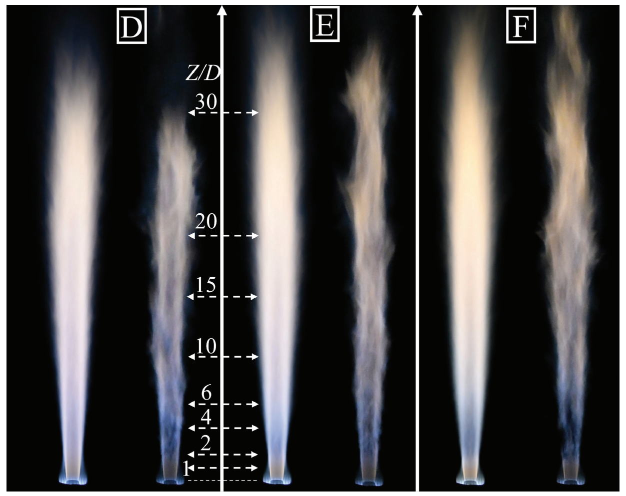


Figure 1.5: Instantaneous and time-averaged photographs of the KAUST partially cracked ammonia flames (figure taken from Hao Tang et. al., Combustion and Flame (2025) 279).

Figure 1.6 shows that hydrogen addition significantly modifies flame structure under lean conditions (ϕ = 0.8). Hydrogen-enriched flames exhibit more compact, spatially concentrated high-OH regions compared with pure methane, indicating enhanced reactivity and localised heat release. These modifications improve flame anchoring and stabilisation in swirl-stabilised flow, highlighting hydrogen blending's potential to extend lean operability while maintaining stable combustion. These findings provide fundamental understanding of flame stabilisation in fuel-flexible combustors.

Future work will extend diagnostics to OH-PLIF for investigating hydrogen enrichment effects in ammonia flames, enabling higher-resolution analysis of unsteady flame dynamics including flame surface density, curvature effects, and flame-vortex interactions across broader hydrogen fractions and operating conditions.

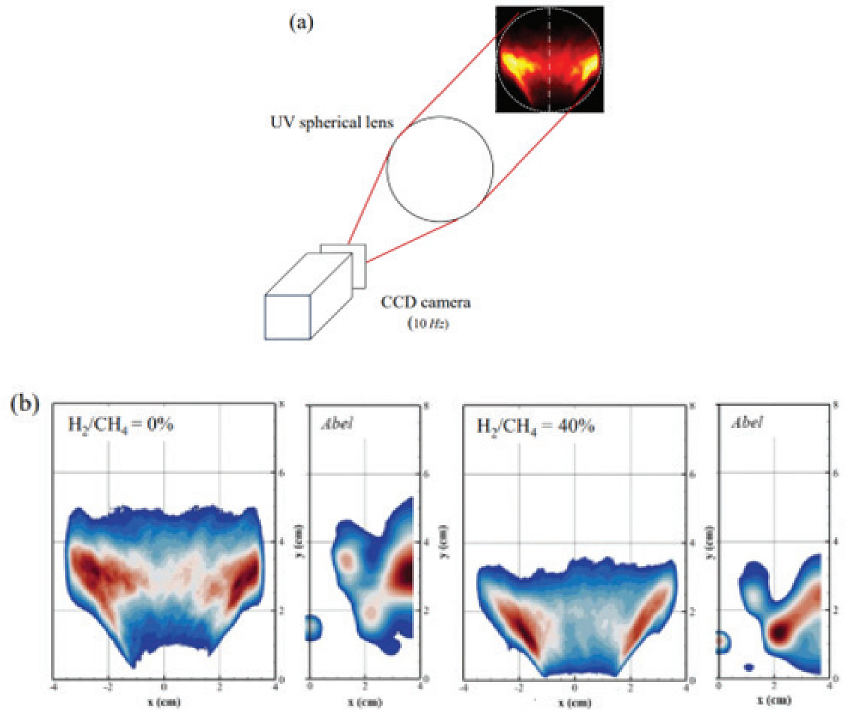


Figure 1.6: (a) Schematic of the chemiluminescence setup used to infer the time-resolved flame shape. (b) Averaged OH chemiluminescence normalised to the maximum value (I_{OH*}/I_{max}) and their inverse Abel transform for each case at ϕ=0.8.*

WP3: NOVEL COMBUSTION SYSTEMS FOR GAS TURBINES

Work Package 3 focuses on understanding the combustion behaviour of ammonia-hydrogen blends in gas turbine configurations, bridging the gap between fundamental flame studies and practical application, and providing essential data for model validation and practical combustor design. A new modular bluff-body stabilised flame rig with swirl will be designed and commissioned at CREATE, drawing on experience from previous hydrogen-ammonia combustors at NTNU. The rig will feature a secondary jet-in-crossflow combustion zone downstream to enable studies of axial staging for investigations on combustion instability and emissions in fuel-flexible gas turbines. Systematic testing will explore a wide range of operating conditions, fuel blends, and power staging ratios between primary and secondary flame zones, with variable jet configurations to control mixing and momentum ratios.

Experimental Rig Development

Significant progress has been made on a new experimental combustion setup, capable of staged operation and independent acoustic excitation of primary and secondary stages. Preliminary design work has been completed for a new modular combustion rig capable of staged operation with independent acoustic excitation of both primary and secondary flame zones. Detailed engineering drawings have been finalised (see Figure 1.7), and the team is currently engaged with manufacturing partners to fabricate the design.

In parallel, substantial upgrades to the laser laboratory infrastructure are underway to accommodate higher flow-rate turbulent flames with precise reactant metering. Critical diagnostic and control equipment has been procured and is now being integrated into the facility, including high-speed cameras, PIV systems, photomultiplier tubes, data acquisition hardware, mass flow controllers, amplifiers, and microphones. The acoustic forcing system is currently being specified and will be ordered shortly to enable comprehensive thermoacoustic characterisation of the combustor.

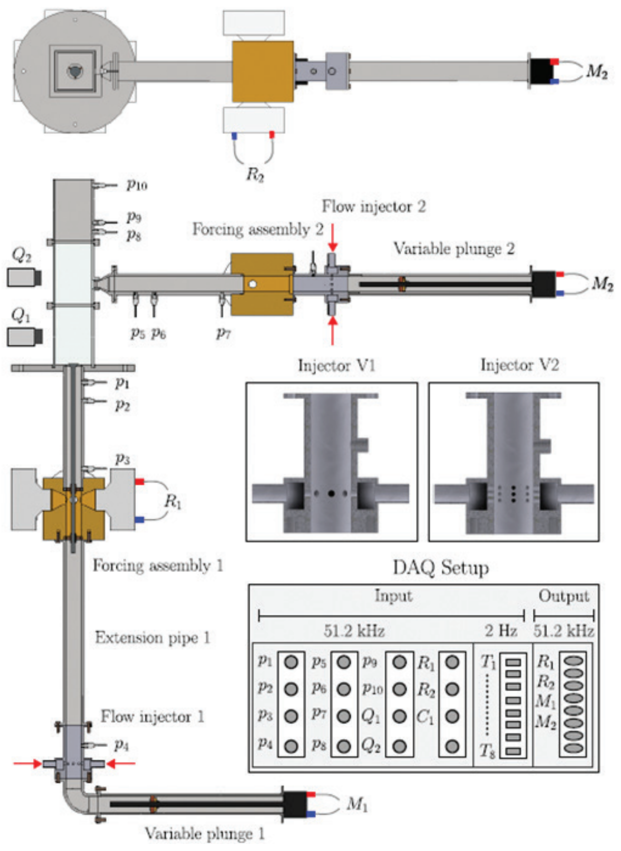


Figure 1.7: Schematic of the staged burner.

WP4: NOVEL COMBUSTION SYSTEMS FOR RECIPROCATING ENGINES

Work Package 4 addresses the unique challenges of combusting ammonia, hydrogen, and their blends in reciprocating engines. Unlike gas turbines, reciprocating engines operate under transient, high-pressure conditions that demand robust ignition systems and careful control of combustion phasing. Our approach combines two complementary strategies: optical diagnostics in a new high-pressure constant volume combustion chamber to visualise flame structures and ignition processes, and emission measurements in single-cylinder engines to understand scale effects and generate validation data for models.

System Validation and Commissioning

A major milestone has been achieved with the successful construction of a high-temperature, high-pressure optical constant volume combustion chamber (CVCC). The CVCC comprises of a fuel boosting system capable of pressurising ammonia and hydrogen gases to the required test conditions and a cooling system to maintain thermal stability during extend operation.

In December 2025, we conducted a comprehensive site acceptance test at the CVCC supplier's facility to evaluate system functionality and safety performance. This rigorous testing protocol identified several areas requiring corrective action, which were formally communicated to the supplier. All specified modifications have now been successfully implemented, and the complete CVCC have been shipped to Singapore. Commissioning in the NTU laboratory is scheduled for April 2026, at which point full experimental operations will commence.

Preliminary Experimental Results

Despite the system still being in transit, preliminary experiments have already been conducted using temporary facilities to investigate key phenomena relevant to ammonia-fuelled reciprocating engines. Figure 1.8 presents the morphology of premixed ammonia laminar flames across different equivalence ratios (Φ). These visualisations reveal that the equivalence ratio exerts a profound influence on flame propagation behaviour. At lean conditions (Φ = 0.8), the flame surface exhibits pronounced wrinkling accompanied by significant upward drift, indicative of thermo-diffusive instability and buoyancy effects. As the mixture becomes richer (Φ = 1.2), the flame surface progressively smoothens, the overall flame shape becomes more spherical, and the upward drift is substantially reduced. This transition demonstrates how mixture composition fundamentally alters flame stability characteristics.

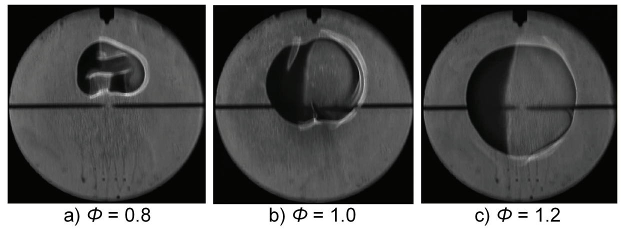


Figure 1.8: Ammonia premixed laminar flames at different equivalence ratios.

Figure 1.9 compares passive and active pre-chamber jet ignition of ammonia-hydrogen mixtures. The images reveal distinct flame propagation and diffusion characteristics between the two ignition strategies. High-temperature gases from the pre-chamber into the main combustion chamber exhibit markedly different penetration depths, ignition kernel development, and subsequent flame front evolution depending on the ignition mode employed. These differences can have important implications for combustion phasing, cyclic variability, and overall engine performance.

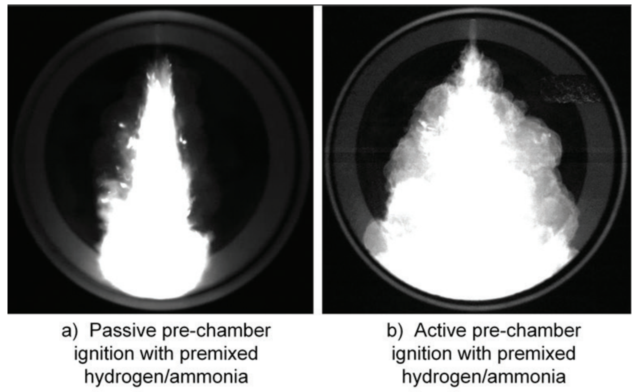


Figure 1.9: Active/passive pre-chamber ignition.

WP5: DEPLOYMENT

Work Package 5 translates fundamental science from previous work packages into industrially deployable technologies. This includes developing reduced-order models to complement complex CFD approaches, assessing detonation and ignition risks for safe hydrogen deployment, and comprehensive training programmes.

Shock-Induced Mixing and Ignition

Richtmyer–Meshkov (RM) instability occurs when a perturbed interface between fluids of different densities is impulsively accelerated by a shock wave, progressing from linear growth through nonlinear development to turbulent mixing. While extensively studied in inertial confinement fusion and scramjet applications, the combined effects of chemical reactions and azimuthal mode number on reactive double-layer gas cylinders under convergent shocks remain poorly understood.

As shown in Figure 1.10, numerical investigations of bubble evolution, hydrodynamic instability, and ignition characteristics reveal that increasing azimuthal mode number (from Figure 1.10(a) to 1.10(b)) significantly modifies interface geometry. This produces a reflected transmitted shock (RTS) where the jet head behind the RTS propagates outward, deforming the inner interface and generating outward-directed jets in spike regions, as shown in Figure 1.10. Interaction between the transmitted shock (TS_1) and perturbed inner interface deposits substantial baroclinic vorticity at higher mode numbers, accelerating RM instability growth. More transverse waves and reflections introduce stronger pressure perturbations and additional baroclinic vorticity, enhancing interfacial deformation and pre-ignition mixing.

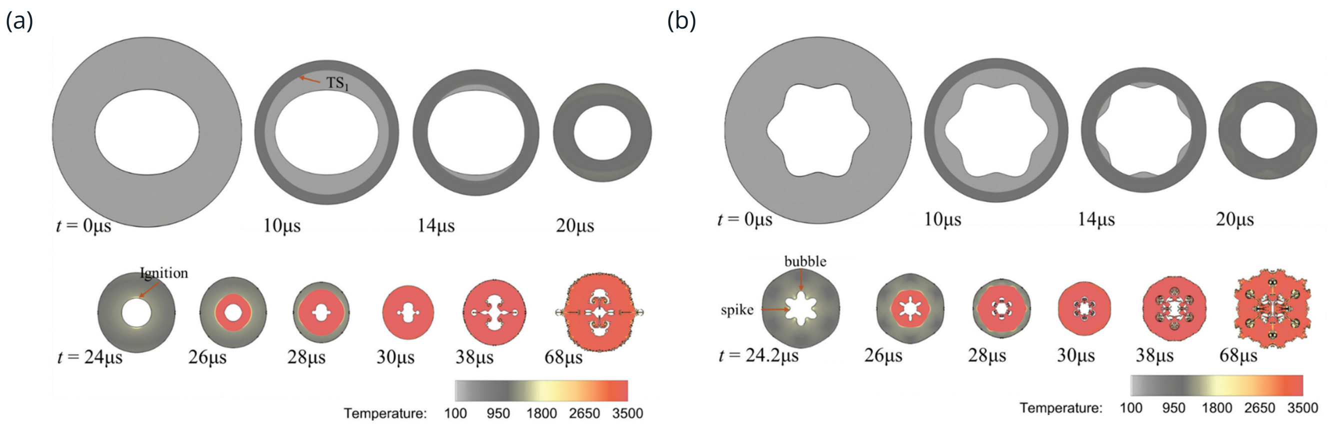


Figure 1.10: Time sequence of temperature contours showing shock-induced mixing and ignition in reactive double-layer gas cylinders for different azimuthal mode numbers. (a) Azimuthal model number, n = 2. (b) Azimuthal model number, n = 6.

Hotspots originate from localised compression following transverse-wave interactions, elevating temperature and pressure in spike regions to trigger ignition and outward-propagating detonation. Post-detonation, reflected rarefaction waves interacting with the inner interface induce Rayleigh–Taylor instability, further enhancing deformation and mixing at higher mode numbers. Future work will apply Chemical Explosive Mode Analysis to identify dominant species and reactions responsible for ignition.

Detonation-Vortex Interactions

The interaction between detonation waves and vortices is a fundamental issue in detonation combustion dynamics. Early numerical studies by Lasseigne et al. [1] reveal that heat release effects can significantly influence the interaction of intensity with vorticity perturbations. Recent advances have established a four-quadrant mechanism map for detonation-turbulence interactions, providing a theoretical framework that guides the optimal design of propulsion systems such as rotating detonation engines [2].

We have conducted numerical simulations on the interaction between normal detonation waves and Gaussian vortices to elucidate the flow field evolution and the underlying influence mechanisms of key factors. Numerical simulations were conducted by using PeleC on GPU platform, with the flow fields at different times shown in Figure 1.11.

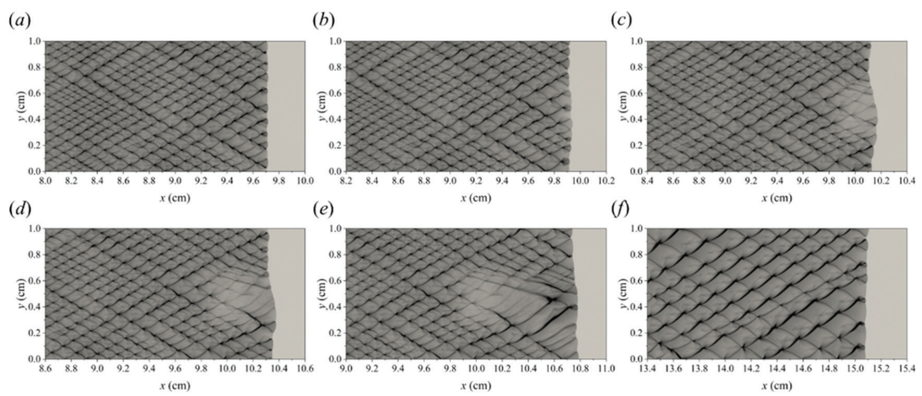


Figure 1.11: Numerical simulations were conducted by using PeleC on GPU platform, with the flow fields at different times (a) 43 μs, (b) 44 μs, (c) 45 μs, (d) 46 μs, (e) 48 μs, and (f) 69 μs.

Due to the variations in incoming flow velocity induced by the vorticity field, the regular cellular detonation transitions into a multi-segmented, curved detonation structure, significantly enhancing the vorticity within the flow field as shown in Figure 1.12. The vorticity is mainly concentrated behind the incident curved detonation wave, whereas almost no vorticity is observed downstream of the Mach stem. In strongly disturbed regions, vorticity is markedly amplified in both strength and spatial extent, while the lower part of the flow field remains essentially unaffected. The intensified pressure and velocity gradients resulting from the interaction lead to enhanced shear layers and jet formations. A larger vortex radius and greater vorticity intensity markedly increase the degree of detonation deformation, whereas the position of the vortex has a relatively insignificant effect on the interaction intensity.

Thus far, a manuscript has been compiled and submitted to the World Hydrogen Energy Conference (WHEC) 2026. In future, researchers will focus on the influence of vorticity on detonation wave deformation, such as the intensity of vortices required to extinguish the detonation wave.

[1] D. G. Lasseigne, T. L. Jackson, M. Y. Hussaini, Physics of Fluids (1991), 3(8): 1972–79.

[2] Eric Loth, Journal of Propulsion and Power (1995), 11(3): 529-34.

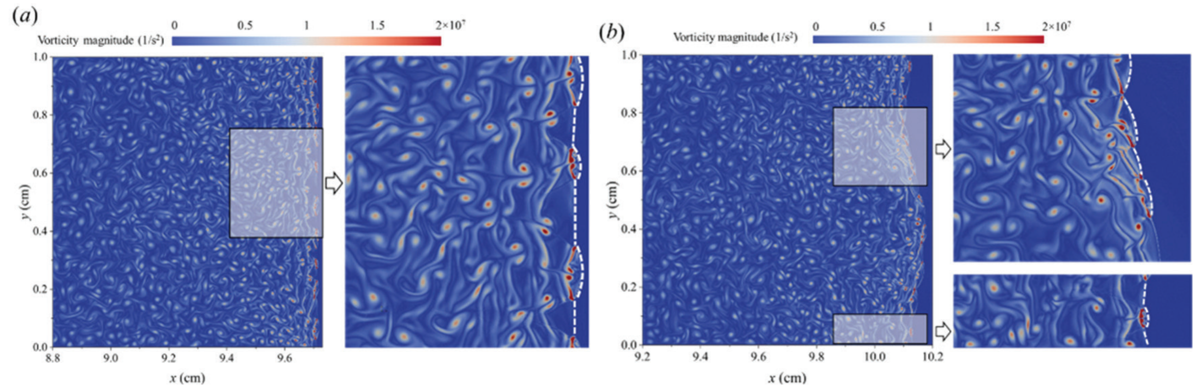


Figure 1.12: The vorticity of the flow field: (a) cellular detonation mode before interaction, (b) curved detonation mode after interaction.

Onboard Hydrogen Production for Maritime Decarbonisation

Previous work demonstrated thermodynamic feasibility and efficiency advantages of onboard natural gas reforming with pre-combustion carbon capture (Pre-CCS) as a maritime decarbonisation pathway. Subsequent investigation of combined-cycle gas turbine architectures showed further efficiency improvements through integrated power generation.

Planned laboratory experiments will combust reformate blended with methane across 0–100% range to analyse emission profiles (CO, CO_2, NO_x) as a function of fuel composition. Results will develop and validate a reactor network combustion model for gas turbine emissions simulation under varying fuel blends and operating conditions, ultimately integrating with financial models for techno-economic optimisation.

A parallel financial model for onboard hydrogen production has been coupled with a stochastic framework evaluating investment risks under fuel price, emissions surplus, and carbon pricing uncertainties, which is applicable to Singapore's maritime sector. Additional activities include biofuel route planning for low-carbon vessel operations and LIBS testing for biofuel authentication.

Hydrogen Detonation Inhibition

Hydrogen's low ignition energy and high flammability pose explosion risks that limits its widespread adoption. Hence, we explore the use of a chemical inhibitor, i.e., trifluoroiodomethane (CF_3I), to understand its detonation suppression effect, doping proportion and mechanism, which in turn enable the assessment of its feasibility as a chemical inhibitor for detonation. This investigation has been carried out through numerical simulation. Specifically, by analysing the steady reaction zone structure and critical initiation energy.

The Zeldovich-von Neumann-Doering (ZND) model analysis (see Figure 1.13(a)) of stoichiometric hydrogen-air mixtures with up to 10^5 ppm CF_3I reveals dual behaviour: small additions (~10^3 ppm) enhance reaction and shorten reaction length, reducing critical initiation energy; conversely, ~10^4 ppm doping produces strong inhibition, increasing critical initiation energy by several orders of magnitude. To facilitate the unsteady modelling of hydrogen detonation and its chemical inhibition, a GPU-CPU hybrid detonation solver was developed (see Figure 1.13(b)) to accelerate chemical reaction modelling, demonstrating significant speed-up over CPU-only simulation.

Future work will apply this solver to unsteady detonation initiation modelling, revealing dynamics under CF_3I sensitisation or inhibition to provide theoretical guidance for hydrogen safety enhancement.

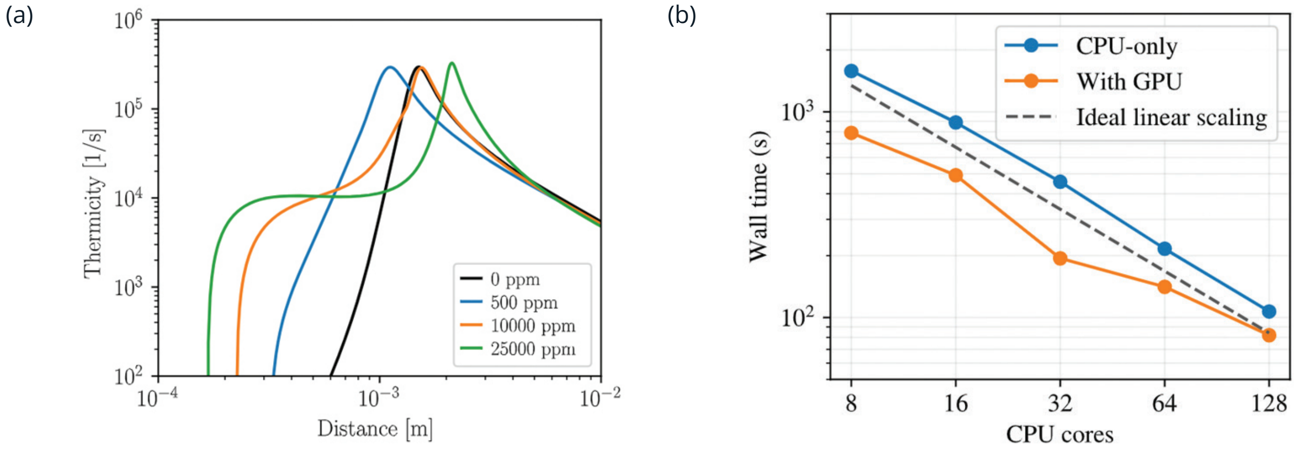


Figure 1.13: (a) Thermicity profiles for CF_3I at different doping levels through the Zeldovich-von Neumann-Doering (ZND) model analysis. (b) GPU-CPU Hybrid Solver Performance.

OTHER ACTIVITIES AND ACHIEVEMENTS

The conference participation by HYCOMBS is listed below:

- Dr Hao SHI (Research Fellow, CARES) and Dr Victor LAFAURIE (Research Fellow, CARES) attended the International Conference on Flow Dynamics (ICFD) from 10 - 13 November 2025 in Sendai, Japan.
- Prof Epaminondas MASTORAKOS (Programme Lead, CAM) presented research on behalf of Dr B HARIKRISHNAN (Research Fellow, CARES) for "Incompletely Stirred Reactor Low-Order Modelling for Gas Turbine Combustors" at the International Conference on Flow Dynamics (ICFD) from 10 - 13 November 2025 in Sendai, Japan.
- Dr Francesco D'ALESSIO (Research Fellow, CARES), Dr Victor LAFAURIE (Research Fellow, CARES) and Dr Ahmed ELBANNA (Research Fellow, CNRS) attended the 1st Singapore Section Combustion Institute Annual Combustion Meeting on 9 December 2025 in NUS, Singapore.
- Dr Ahmed ELBANNA (Research Fellow, CNRS), Dr Tong SU (Research Fellow, CARES), Dr Francesco D'ALESSIO (Research Fellow, CARES), Dr Yong Ren TAN (Research Fellow, CARES), and Dr Hao SHI (Research Fellow, CARES) attended the Annual Decarbonisation Scientific Symposium on 29 October 2025 in CREATE, Singapore.

Programme leads Prof Epmaninondas Mastorakos (left side of banner) and Prof Kaoru Maruta (right side of banner) with HYCOMBS PI Asst Prof Youhi Morii (third from left) and researchers Dr Hao Shi (second from left) and Dr Victor Lafaurie (third from right) in Sendai, Japan.

Dr Li Chin LAW (Research Fellow, CARES) was invited as a speaker to the Smart Maritime Network event in Singapore on 25 November 2025. Dr Law sat on a panel for "Green Solutions & Decarbonisation" to share her work on fuel data analysis in collaboration with Laskaridis Shipping and METIS Cybertechnology.

Dr Tan and Dr Law were selected to participate in the Global Young Scientists Summit (GYSS). The 2026 edition welcomed its largest cohort yet, with over 400 young researchers from 57 countries gathering in Singapore to interact with Nobel Laureates and other researchers from a wide range of disciplines.

Dr Law at the Smart Maritime Network 2025 event.

Left: Dr Law standing with Prof Brian Schmidt, a Nobel prize winner in Physics, and Prof Kae Nemoto, the Director of the Okinawa Institute of Science and Technology's Center for Quantum Technologies. Right: Dr Tan attending a GYSS seminar.

Dr Tan, Dr Su, and Dr Marc LE BOURSICAUD (Research Fellow, CARES) joined CARES' first participation in Cambridge Festival, the University of Cambridge's largest annual science festival, with a hybrid event "Cambridge in Singapore–Who CARES?" on 18 March 2026.

The public engagement event was targeted for a younger, schooling audience from secondary school and older, drawing over 150 attendees at the in-person venue in Singapore and online, from over 30 schools and universities.

The CARES researchers reframed the importance of decarbonisation for the younger audience, drawing on examples in their personal lives. The presentations shared the current work at CARES and their own research journeys. The successful event has inspired CARES to explore more public engagement opportunities in the future.

Left: Dr Su sharing her journey in science with the audience. Top: Dr Tan (left), Dr Marc Le Boursicaud (middle) and Dr Su (right) in a panel answering questions from the audience. Bottom: Dr Le Boursicaud giving an overview of HYCOMBS.

Project Leads

SM3

SUSTAINABLE MANUFACTURE OF MOLECULES AND MATERIALS IN SINGAPORE

SM3 will aim to shift the chemical manufacturing industry to a more circular, sustainable, and resilient model. This project will address systemic challenges, including the integration of regionally available resources and the development of scalable, flexible technologies for local manufacturing.

THEME 1: NOVEL SYNTHETIC STRATEGIES

WP1. Novel Synthesis Methods

Prof Ning YAN (NUS)
Dr Jiong CHEN (NUS)

Our work focused on developing stereoretentive transformations of biomass-derived substrates toward chiral hub molecules. The synthesis of high-value molecules bearing chiral centers traditionally relies on asymmetric catalysis, often requiring expensive chiral catalysts and ligands. Biomass represents the most abundant natural reservoir of chirality; however, most existing biomass conversion strategies overlook this intrinsic stereochemical value, typically resulting in achiral or racemic products. Developing transformation strategies that preserve native stereochemistry is therefore essential for the efficient generation of chiral hub molecules and downstream value-added compounds.

We developed two distinct stereoretentive strategies. The first approach is based on strengthening catalyst–substrate interactions to suppress competing racemisation pathways. Specifically, strong interactions between Ag single atoms and monosaccharide substrates were leveraged to significantly increase the energy barrier for keto–enol tautomerization (Figure 2.1a). In parallel, Ag clusters promoted efficient O_2 activation. Through the synergistic effect of the designed Ag single atom–cluster catalyst, stereoretentive oxidation of monosaccharides was achieved, affording optically pure organic acids with ee values exceeding 99% and yields up to 96% (Sci Adv 11(47):eadz4136(2025)). The second strategy relies on thermodynamic control at the product level. Hydrogenative dehydroxylation of monosaccharide-derived lactones was achieved over ReO_x catalytic sites. Owing to ring strain constraints in the product, only the cis-hydroxyl group in 6,3-lactones undergoes selective removal, whereas the hydroxyl group in 1,4-lactones remains unreactive (Figure 2.1b). This selective transformation afforded chiral vicinal diols with diastereomeric ratios exceeding 99:1 and ee values above 99%. In addition, a pronounced support effect was observed, with catalytic performance significantly enhanced by tuning the degree of graphitisation of the carbon support, yielding up to 99%.

In parallel, we advanced our studies on C-N bond formation from renewable biomass feedstocks toward N-containing hub molecules. Using lignin-derived substrates as representative examples, a designed Pd–M bimetallic catalyst enabled the conversion of phenol and hydroquinone to aniline, diphenylamine, and p-phenylenediamine in yields of 72%, 66%, and 81%, respectively. Ongoing efforts will integrate theory-guided catalyst design (WP5, AI for Chemistry) to further optimise the catalytic system, aiming to achieve more efficient and milder lignin amination processes for the synthesis of aromatic amines.

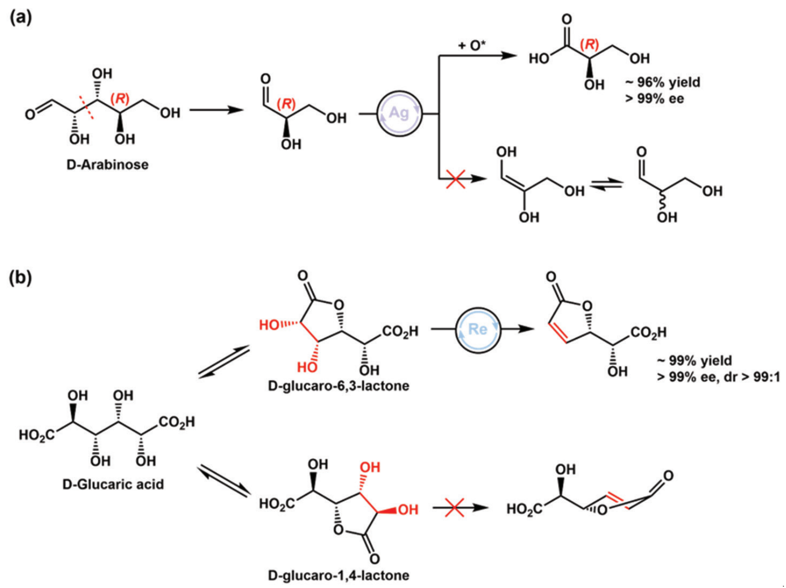


Figure 2.1. Chirality-retention pathways: (a) substrate–catalyst interactions suppress racemisation (b) product configurational restriction.

Assoc Prof Ming Joo KOH (NUS)
Dr Jun WU (NUS)

Deoxygenated carbohydrates feature prominently in bioactive natural products and are promising targets for therapeutic studies. However, access to these sugar residues remains the bottleneck due to the difficulty of site-selective deoxygenation in the presence of multiple hydroxyl groups of similar reactivity. Here, we report a photocatalytic lock-and-cut strategy that enables direct and selective deoxygenation of unprotected and minimally protected sugars in Figure 2.2. By employing benzaldehyde dimethyl acetal as a molecular lock, this approach directs hydrogen atom abstraction to the most reactive benzylic position, triggering site-selective deoxygenation and hydrogen atom transfer. The orchestrated sequence of oxidation, C–O bond scission, and reduction mimics enzymatic deoxygenation and simultaneously installs a benzoate protecting group, facilitating downstream transformations to assemble complex glycans. This method offers streamlined access to structurally diverse mono- and dideoxy sugars without extensive synthetic manipulations. Utility is highlighted through the simplified syntheses of important deoxysugars, including the repeating tetrasaccharide unit of the O-chain from a general phytopathogenic agent.

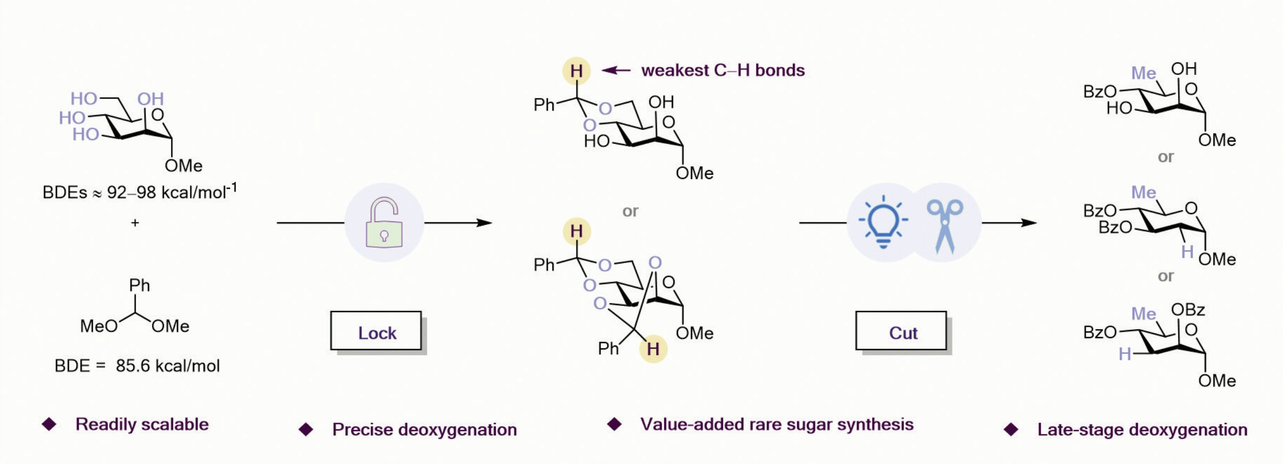


Figure 2.2: Strategy for late-stage deoxygenation reactions.

Prof Shunsuke CHIBA (NTU)
Dr Taku WAKABAYASHI (NTU)

A new type of heteroarene skeletal-editing via photo-induced single-electron-transfer (SET) process was discovered (Figure 2.3). This pyrimidine-to-pyrrole transformation may offer a new synthetic route for utilising pyrimidine analogues in the set of hub molecules. Availability of the hub molecules is currently under investigation.

This reaction may shortcut the synthesis of drug molecules/candidates and encourage the use of pyrimidine-based bio-renewable compounds; see potential starting molecules with a pyrimidine ring in Figure 2.4.

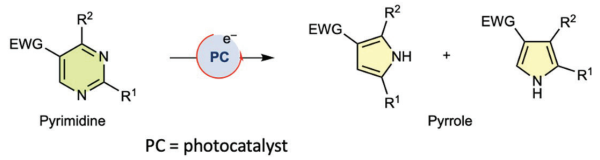


Figure 2.3: Scheme of pyrimidine-to-pyrrole transformation.

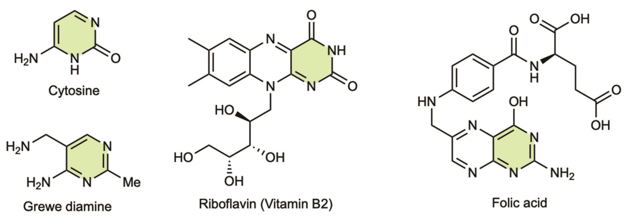


Figure 2.4: Examples of potential starting materials with pyrimidine ring.

Dr Wakabayashi learnt more about high-throughput experimentation while visiting Prof Matthew GAUNT's (PI, CAM) laboratory in Cambridge for 6 weeks in the start of 2026. He acquired HTE techniques and confirmed it's applicability for photo-induced SET chemistry, see Figure 2.5 and Figure 2.6. He is currently working on the installation of HTE facility in Prof Chiba's laboratory in NTU.

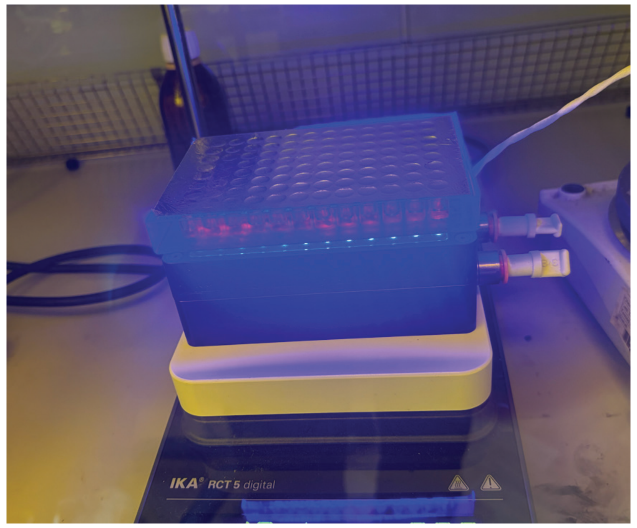


Figure 2.6: An image of a photoreaction reaction using a 96-well plate.

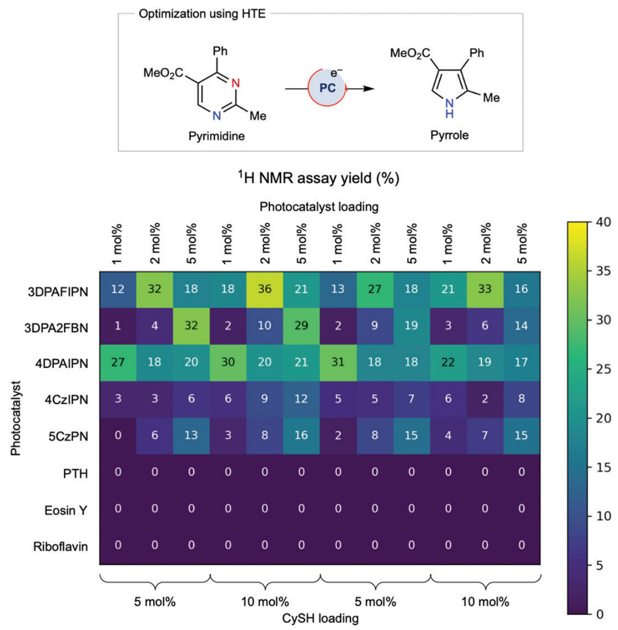


Figure 2.5: High-throughput set-up for performing pyrimidine-to-pyrrole reaction screening.

WP2. Reaction Networks and Project Targets

Prof Alexei LAPKIN (CAM)
Dr Raudah LAZIM (CARES)

We designed and implemented an automated workflow (Figure 2.7A), which integrates a unified reaction network graph, the Isolation Forest algorithm and centrality-derived features, to predict hub molecules. In this updated workflow, features were selected through systematic analysis of their distributional properties to avoid degeneracy in unsupervised learning. Network centrality metrics of reaction networks often exhibit zero-inflation, heavy tails and saturation effects. To mitigate these issues, we introduced a feature-specific preprocessing module that transforms raw features based on their distributional patterns. For example, betweenness, PageRank and HITS hub are strongly zero-inflated and heavy-tailed, as shown in Figure 2.7B (left) by their extreme position in the kurtosis-skewness plot (see red arrow). We addressed this by decomposing each metric into a binary indicator (non-zero vs zero) and a log-transformed continuous component for non-zero values. This transformation yields features that more closely approximate normal distributions in Figure 2.7B (right), which is important for Isolation Forest as feature distributions directly influencing tree-splitting during outlier isolation.

Additionally, the feature space was expanded by decomposing degree centrality into five components, namelyin-degree(production),out-degree(consumption), total degree (overall reaction participation), degree ratio (production-consumption bias) and balanced degree (symmetry between production and consumption). Although these components are derived from the same underlying degree centrality metric, they exhibit low pairwise correlation (Figure 2.7C, red box). This indicates that each component captures a distinct attribute of the network topology, thus enabling the model to encode subtle patterns of chemical reactivity rather than a simple reflection of overall reaction connectivity.

To enhance the robustness of hub prediction, we implemented an ensemble strategy in which Isolation Forest was executed N times (N=100), and molecules were ranked by anomaly score in each run. The final top K (K=2000) candidates were defined by consensus, retaining molecules that appeared within the top K in the majority of the runs. When fewer than K stable candidates were identified, remaining slots were filled with molecules with the highest mean anomaly score across runs. Compared to a single Isolation Forest run, the ensemble framework reduces sensitivity to random initialisation and tree construction by prioritising consensus vote stability and anomaly strength, thus resulting in more reproducible anomaly estimates and hub prediction.

While Isolation Forest identifies molecules with unusual feature combinations as outliers, directly equating these data points with hubs may lead to misclassification. To address this, we incorporated a role-classification module that distinguishes structurally significant hubs from spurious outliers by evaluating coreness, embeddedness and source-sink balance. True hubs typically exhibit: (i) high coreness, indicating residence within densely connected network cores, (ii) high embeddedness, reflecting strong integration within local clusters rather than peripheral associations and (iii) source-sink balance, indicating symmetric production and consumption patterns.

To validate the prediction workflow, we performed shortest-path analysis on 3570 start-target pairs (70 biomass-derived feedstocks x 51 target molecules from WHO Essential Medicines List), constraining paths to pass through predicted hubs or matched decoy hubs (324 molecules each). Decoy hubs were selected to match predicted hubs in total degree and molecular weight, serving as structurally comparable controls. By comparing the path lengths from start to target via predicted and decoy hubs, we can evaluate the ability of predicted hubs to improve synthetic route efficiency.

Figure 2.7D shows the distribution of path length differences for routes passing through decoy and predicted hubs ($\Delta L = L_{decoy} - L_{hub}$). The distribution of median ΔL across the 3570 start-target pairs is zero-inflated, indicating substantial redundancy in shortest-path in the reaction network topology (74% identical outcomes). The redundancy could be attributed to the use of all-to-all wiring scheme during network construction. Nevertheless, when alternative pathways exist, the predicted hubs produce shorter routes in 26% of the cases, with no cases favouring the decoy hubs (binomial test, $p << 0.001$). The pronounced positive asymmetry observed in ΔL indicates that the hub molecules identified by the automated workflow occupy chemically productive and structurally advantageous positions within the reaction network, serving as critical intermediates that ameliorates synthetic efficiency when pathway flexibility permits. This experiment will be repeated under alternative wiring schemes (mixed and one-to-one wiring) to assess the robustness of predicted hubs and compare their impact on reaction efficiency.

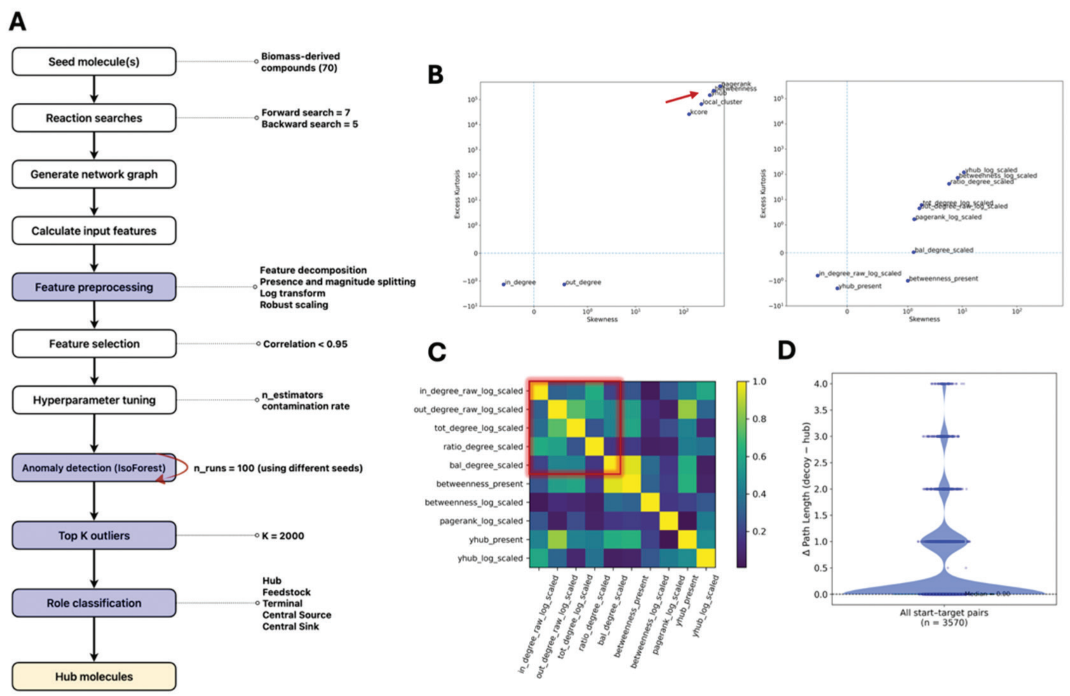


Figure 2.7: (A) Flowchart summarising the automated workflow for hub prediction. Blue boxes indicate newly added modules. (B) Kurtosis-skewness plots of features used in previous (left) and current (right) hub prediction workflow. In the current workflow, feature distributions shift closer to (0, 0) indicating improved approximation to normal distribution. (C) Correlation matrix of the feature space. The red box highlights features from degree centrality decomposition. (D) Violin plot showcasing the distribution of path length differences ($\Delta L = L_{decoy} - L_{hub}$) for reaction routes constrained to pass through decoy and predicted hubs for 3570 start-target pairs.

Prof Ruth WEBSTER (CAM)
Dr Miguel CHACON-TERAN (CARES)

The team focused on the topic of access to nitrogen and useful scaffolds from waste aminoacids. The rapid growth of the dairy industry has created a major environmental bottleneck in the form of acid whey, a high-volume byproduct with a chemical oxygen demand (COD) of up to 62,400 mg/L, nearly 70 times above municipal discharge limits (~900 mg/L). Rather than treating acid whey as a costly waste stream, this project redefines it as a zero-cost, nitrogen-rich platform feedstock for a distributed biorefinery model. The vision is to unlock its full carbon and nitrogen value by converting it into polymer-grade L-glutamic acid and subsequently into advanced C4 and C5 bio-based monomers, enabling the production of high-performance bioplastics while reducing environmental burden at the source.

An extensive literature and feasibility assessment identified acid whey as the most promising high-protein waste stream among evaluated alternatives, based on volume, environmental pressure, operational accessibility, and diversification potential, see Figure 2.8. A technological roadmap demonstrates full-stream valorisation: lactose can be converted via established fermentation routes into lactic acid and PLA, while the protein fraction rich in β-lactoglobulin, α-lactalbumin, and glycomacropeptide can be hydrolysed into a free amino acid mixture with glutamic acid as a major component. This positions glutamic acid as a strategic nitrogen-containing platform molecule capable of controlled upgrading into C4 and C5 intermediates, including routes toward polyamides, polyurethanes, polyesters, and polyglutamic acid. The concept establishes acid whey as a scalable biochemical infrastructure rather than a disposal liability.

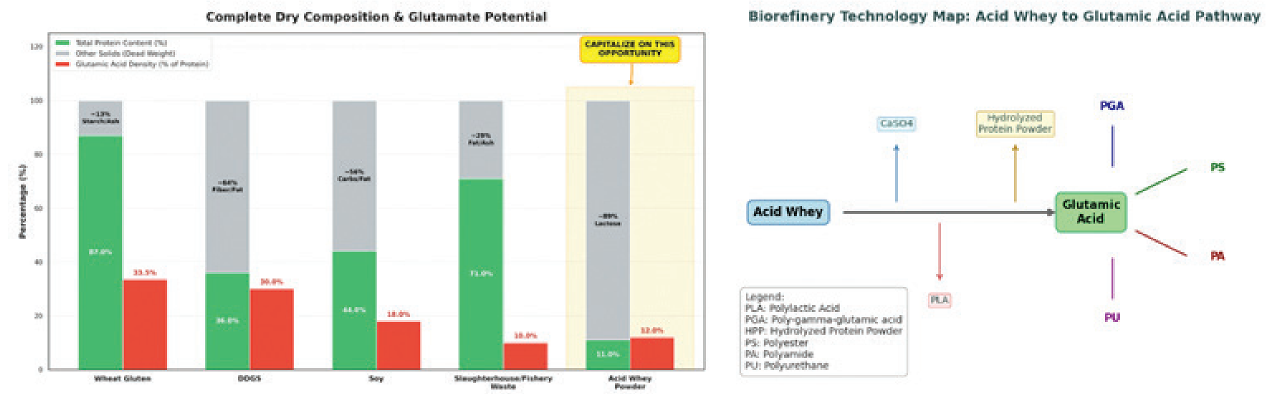


Figure 2.8: Comparative glutamate yield potential across selected bio-based waste streams (left) and projected valorisation pathways of acid whey within the proposed biorefinery model (right).

THEME 2: SCALABLE AND SUSTAINABLE TECHNOLOGIES

WP3. Novel Scalable Synthesis Technologies

Prof Saif KHAN (NUS)
Fangyuan ZHANG (NUS)
Yi Wei LEE (NUS)

The current focus of WP3 is to develop a dedicated scale-up workflow for novel synthesis technologies. Compared with conventional thermal-based synthesis platforms, emerging technologies, particularly those involving the deployment of alternate energy (electricity/light), are far less explored and therefore face unique scale-up challenges. Key obstacles include the absence of established scale-up rules and a limited understanding of how process performance evolves across the chemical parameter space. In addition, SM_3 requires alignment across the entire industrial pipeline—from molecule discovery to production—which introduces multiple, simultaneous objectives and constraints during scale-up.

To address these challenges, we propose a three-stage scale-up workflow consisting of:

1. Virtual kg-scale reactor design and fabrication
2. Operational regime mapping
3. Intra-regime optimisation

1. Virtual kg-scale reactor design and fabrication. Kg-scale reactor designs will first be developed virtually using modelling tools such as computational fluid dynamics (CFD). By optimising key characteristics, such as minimising dead zones and maximising mixing efficiency, within a fully digital environment, we eliminate the costs associated with physical prototyping. Once an optimal design is achieved, the reactor can be fabricated using advanced manufacturing methods such as additive manufacturing to create atypical reactor designs.

2. Mapping the operational regimes of the kg-scale reactors. After fabrication, we will map the operational regimes of the reactor within the relevant parameter space. Parameters include reactant concentrations, temperature, pressure, residence time, among others. This step aims to delineate regions of similar reaction outcomes, such as yield, selectivity, and side-product profiles, using our in house developed 'regime cartography' framework. The regime cartography framework is a machine-learning-driven framework that efficiently uses experimentally obtained data to partition the reactor's parameter space into regions exhibiting similar reaction outcomes, thereby generating a 'regime map.' An illustration of a regime map is provided in Figure 2.9, where each coloured region represents a distinct reactor operating regime. The regime map enables clear comprehension of the reactor's behaviour across various operational parameters, which enables informed decisions to be made in the third stage of this workflow. The boundaries and constraints of the parameter space will be informed by computational models developed in WP 8, which incorporate data from lab-scale experiments conducted in Theme 1.

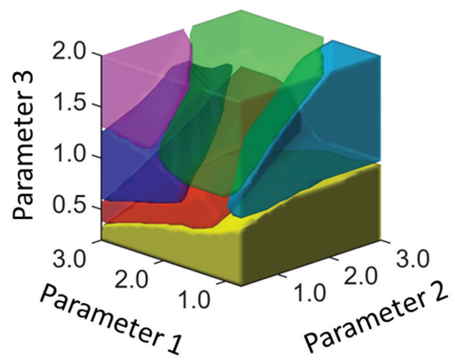


Figure 2.9: An illustration of a regime map within a parameter space. Each coloured region represents an operational regime in which the reactor exhibits similar reaction outcomes.

3. Intra-regime optimisation. Once the parameter space has been partitioned into distinct operational regimes, we will collaborate with other groups in Theme 2 to identify the regime offering the best technoeconomic and environmental performance. Within that selected regime, we will conduct fine-scale optimisation to determine the most suitable conditions for operating the kg-scale reactor systems.

This proactive workflow is expected to significantly accelerate the future scale-up of lab-scale reactions identified in Theme 1. While we await suitable reactions from the upstream work packages, we have initiated a stress test of the proposed workflow by scaling up a model reaction. Specifically, we selected an electrochemical flow reactor performing an amination reaction. The overall reactor design is shown in Figure 2.10a. It has been developed to accommodate potential light augmented , photoelectrochemical processes—one of the synthesis technologies that may be deployed within the SM_3 project. We are currently executing the first stage of the workflow, which focuses on the electrode design for the electrochemical flow reactor. Specifically, we have applied CFD to design a new electrode geometry that offers improved reactive surface area, enhanced bulk mixing, and superior mass transfer characteristics. The final electrode geometry selected through this process is presented in Figure 2.10b. Fabrication of these electrodes is currently underway, after which they will undergo experimental characterisation to validate the simulation results.

In the coming months, our efforts will shift to the next stage of the workflow. This will involve implementing the regime cartography framework to map the reactor's operational regimes as a function of key processing parameters, such as current and reagent concentration.

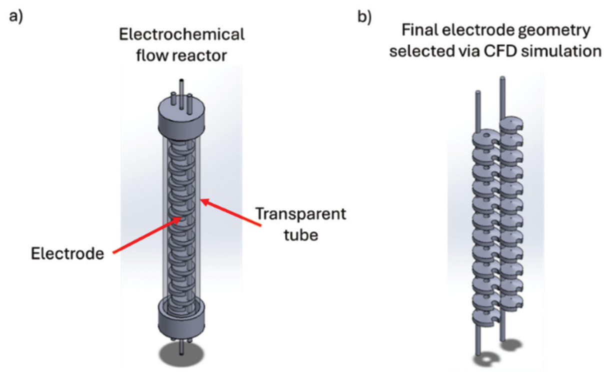


Figure 2.10: (a) Overall design of the electrochemical flow reactor. (b) Final electrode geometry selected via CFD simulation.

Prof Tej CHOKSI (NTU)
Dr Karam HASHEM (NTU)
Christopher Kevin WIJAYA (NTU)

This section of WP3 focuses on assessing the suitability of ultrasound irradiation for chemical synthesis of relevance to SM_3. In the last six months, we developed quantitative relationships between rates of free-radical initiators of green chemistry with properties of ultrasound waves and the solutions in which they propagate. These relationships (Figure 2.10a and Figure 2.10b) reveal how tuning reaction conditions causes 5-10x increases in rates of free-radical initiator generation relative to baseline scenarios, suggesting significant room for improvement of the energy efficiency of sonochemical reactors, a key consideration for scalability. These relationships are established via a fundamental understanding of mass, momentum, and energy transfer during cavitation, advancing the empirical understanding that has thus far dominated the state-of-the-art. This work is under revision in *Reaction Chemistry and Engineering*. This project was started by a former Research Fellow in Prof Tej CHOKSI's (PI, NTU) group and has been taken over by Dr Karam HASHEM (Research Fellow, NTU) since Feb 2026. Ultrasound waves generate hotspots under nominally ambient conditions, with these hotspots being the sites where free-radical initiators are generated. From a chemical synthesis standpoint, a key question is whether the lifetime of these hotspots is sufficiently short to prevent unselective pyrolysis chemistry of reactants. Figure 2.11c maps the temperature outside the cavitation bubble by modelling the rate of energy dissipation into the solution. Our findings reveal that under standardised conditions for ultrasound irradiation, hot spots (temperature > 680 K) have a lifetime of < 2 nanoseconds and a diameter of < 1 micrometer. The rate of energy dissipation is 10x faster than the rate at which free radical initiators react with non-volatile reactants, indicating that non-volatile reactants will not be unselectively degraded within these hotspots.

This first-of-a-kind quantification of the hotspot in ultrasonic reactors indicates that ultrasonic cavitation can perform radical-mediated chemistry of relevance to pharmaceutical manufacturing, without driving unselective pyrolysis of reactants. In the coming months, we will leverage this understanding to outline specific reactions of relevance to SM_3 (Theme 1) where ultrasonic cavitation presents greener alternatives to the state-of-the-art.

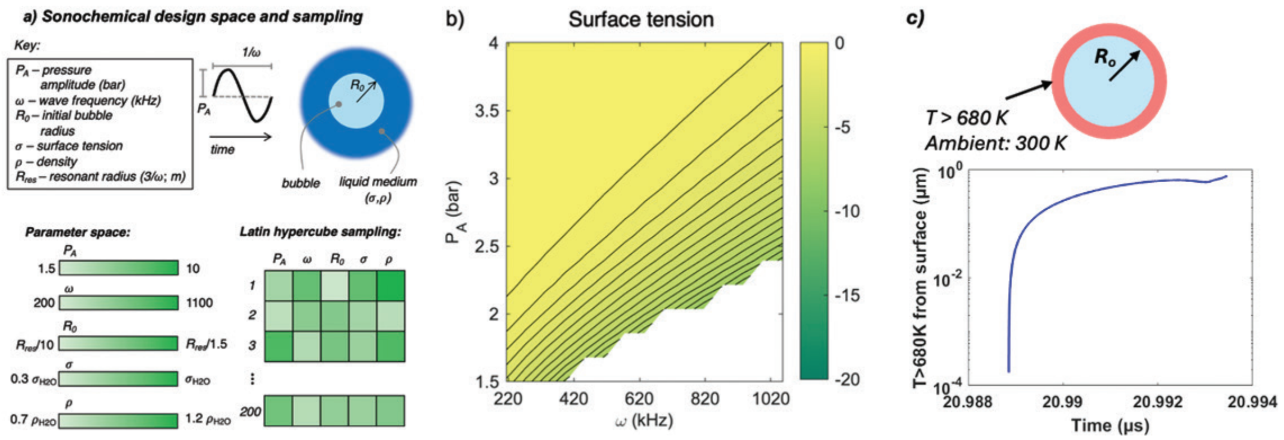


Figure 2.11: (a) Design space of the sonochemical reactor showing considered ranges in acoustic variables and solution phase properties. (b) Small changes in surface tension of the solution (~1%), can cause between 5-10x increases in the rates of free radical production (heat map). This sensitivity to the rates of free radical production is plotted as a function of the amplitude and frequency. (c) Modelling the temperature distribution outside a micron-sized cavitation bubble. The distance from the centre where the temperature exceeds 680K, is plotted as a function of simulation time. Conditions: frequency: 26.5 kHz, amplitude: 1.3 atm., density, surface tension and viscosity of liquid water.

WP4. Technology Mapping and Value Chain Analysis

Prof Alexei LAPKIN (CAM)
Dr Pavlos GKINIS (CARES)

Progress has been achieved within the SM_3 library of models through the development of a semi-mechanistic ball mill reactor model for mechanochemical processing. The framework has evolved from a simplified energy-based representation to a fully coupled mechanochemical model capable of simultaneously predicting Particle Size Distribution (PSD), temperature dynamics and reaction conversion. A Population

Balance Model (PBM) [1] has been implemented with size and specific energy dependent selection and breakage functions [2] that construct the breakage matrix, ensuring mass conservation and enabling PSD prediction over time. This allows dynamic monitoring of surface area development and size-dependent process behaviour.

Representative results showing the temporal evolution of particle size reduction and the final PSD for different grinding times are presented in Figure 2.12a-b. The PBM is coupled with a transient energy balance accounting for mechanical power dissipation, impact energy conversion to heat and heat losses through natural convection and radiation, thus enabling dynamic prediction of temperature evolution. Optional jacket and microwave modules have been incorporated, including microwave penetration depth and absorbed power calculation based on the dielectric properties of the grinded material throughout the milling process. Additionally, an adjustable mechanochemical reaction kinetics module has been integrated using a stress-dependent Arrhenius formulation.

The effective activation energy is reduced via a mechanical activation term including collision stresses estimated through Hertzian contact mechanics. This computes reaction conversion under tumbling neat grinding conditions, providing quantitative insight into the influence of reactor design, operating conditions and grinding media properties on reaction rates. Figure 2.12c-d illustrates the significantly higher sensitivity of mechanochemical reaction conversion to changes in rotational speed compared to overall grinding performance. Whereas particle size reduction depends primarily on total specific energy input over time, mechanochemical reactions are highly sensitive to impact frequency and intensity, leading to stronger dependence on rotational speed.

Overall, the model provides a physics-based predictive framework for mechanochemical reactor performance, supporting process optimisation, operating window identification and future scale-up analysis. Forthcoming work will extend the framework to planetary and vibratory mill configurations, add liquid-assisted grinding effects and perform further parameter calibration as experimental data become available from respective work packages in SM_3, in parallel with the development of an electrochemical reactor model.

[1] Austin, L. G., Klimpel, R. R., & Luckie, P. T. (1984) Process Engineering of Size Reduction: Ball Milling. Society of Mining Engineers, AIME.

[2] Herbst, J. A., & Fuerstenau, D. W. (1980) Scale-up procedure for continuous grinding mill design using population balance models. International Journal of Mineral Processing, 7(1), 1–31.

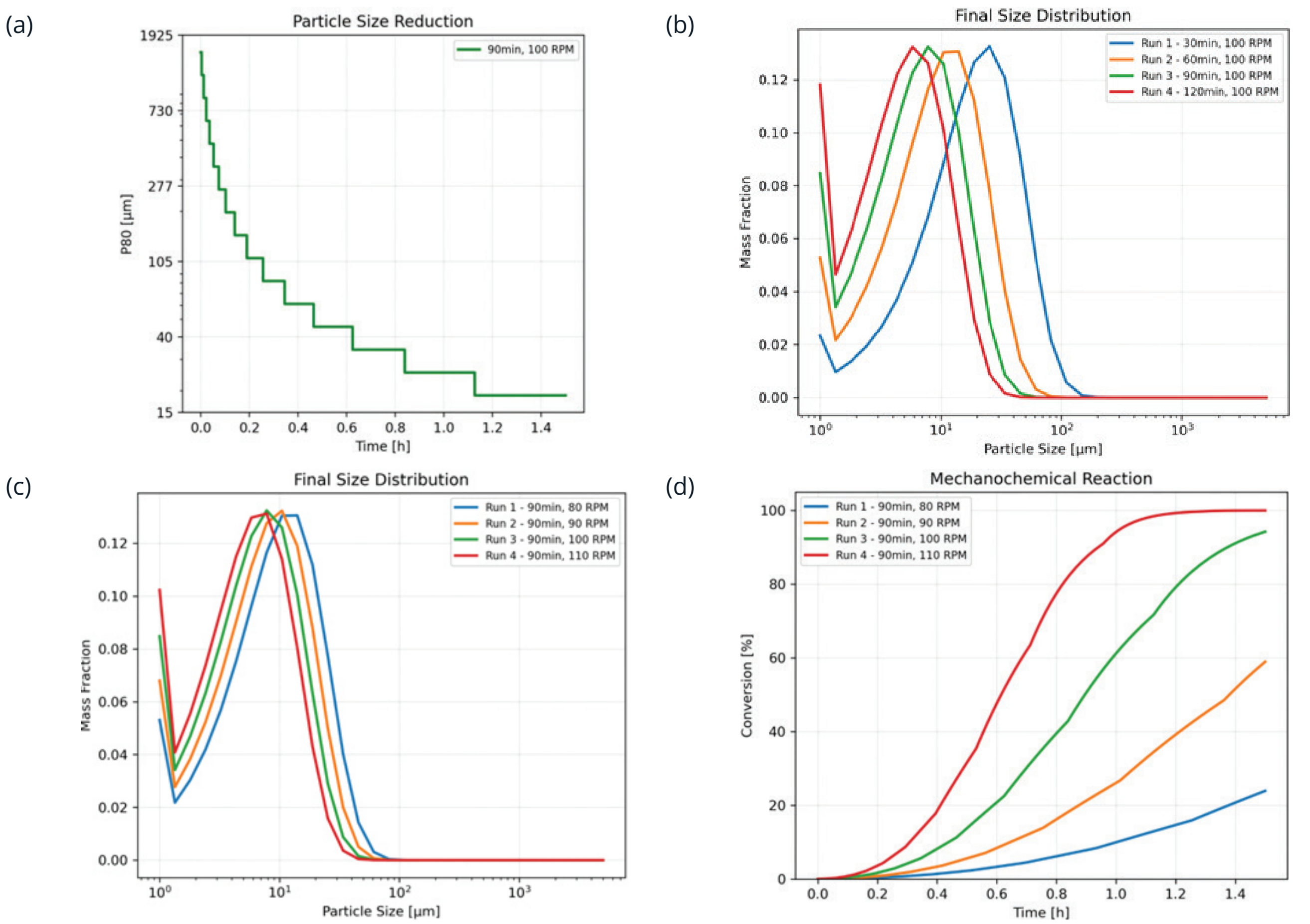


Figure 2.12: (a) Particle size reduction over grinding time (90min) at 100RPM. (b) PSD comparison at different grinding times. (c) PSD comparison at different rotational speeds. (d) Mechanochemical reaction conversion of "toy" kinetics at different rotational speeds over time (final mill temperature: 30, 32.1, 34.7, 37.7°C respectively, ambient 25°C).

THEME 3: SUSTAINABILITY, SYSTEMS AND AI

WP5. AI for Chemistry

Prof Philippe SCHWALLER (EPFL)
Dr Ka Lok CHAN (CARES)

We are developing a Large Language Model (LLM) agent that operates computational chemistry software through user prompts. This agent provides theoretical validations, mechanistic explanations for novel reactions, and suggestions for designs of potential reactants. In this work, we integrate the LLM agent with an existing molecular generative model. The LLM agent acts as an oracle, generating computational chemistry outcomes, including optimised structures and desired computed chemical properties. The molecular generative model would suggest candidate molecules in SMILES format.

Several key features have been implemented in this prototype. First, the molecular generative model is modified to include a substructure filter that uses SMARTS patterns. This filter assigns a reward of zero to SMILES outputs that do not meet the specified requirements, thereby discouraging the generation of similar molecules in subsequent iterations. Additionally, tools have been developed to manipulate molecular geometries. These tools enable conformer generation, atom removal, and structural transformations, including translation and rotation of entire molecules. Moreover, the LLM agent can also operate with medium-sized language models when provided with additional chemical information.

Prof Tej CHOKSI (NTU)
Dr Neeru CHAUDHARY (NTU)
Dr Chunchu BALAJI (NTU)

The team are focused on predicting the energetics of catalysts involving multi-functional molecules using machine learning. The chemical transformations in Theme 1 entail large multi-functional molecules that react on low-symmetry active sites of catalysts. Despite advances in machine learning to predict catalytic properties including by Meta (e.g., OC20 models), these models are not applicable to the complex chemistry of relevance to SM_3. Figure 2.13 shows that bespoke, physics-based machine learning models trained on small datasets (order of 100) were 30% more accurate in predicting reaction energies than off-the-shelf foundational models that were trained on large datasets (100 million).

This analysis encompassed catalysts and reactions relevant to both SM_3 and the AxCIS lab, through a collaboration with Prof Kedar Hippalgaonkar in A*STAR. This work was shared at the American Institute of Chemical Engineers Annual Meeting 2025, a flagship international conference for chemical engineers, and is currently being prepared for publication. More recently, we have retrained the MACE interatomic potential, an equivariant message passing neural network, that can also accurately predict the energetics of surface reactions involving multifunctional molecules relevant to SM_3. This progress shows how density functional theory, physical models, and foundational interatomic potentials can be synergistically used for catalyst design, balancing accuracy, speed, and physical insights.

In the coming months, we will apply these learnings to provide atomistic insights into the mechanisms driving entantio-selective catalysts (Theme 1, Figure 2.1), and perform a high-throughput virtual screening to identify Pt-based alloys for C-N bond formation reactions (Theme 1, Figure 2.1), both of which are collaborations with Prof Ning YAN (PI, NUS). Furthermore, the quantum chemistry calculation approaches will be integrated within the Chemical Data Intelligence LAB environment for seamless use across the project.

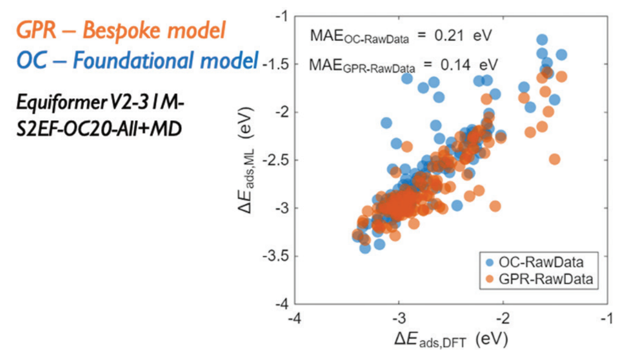


Figure 2.13: Comparisons of dehydrogenation energies on Pt-bimetallic nanoclusters (< 1 nm diameter) as predicted by a bespoke machine learning model trained on small data sets (GPR, orange), and foundational machine learning model trained on large data sets (OC, blue). The bespoke model is 30% less accurate than the foundational model.

WP6. Metrics and Systems

Assoc Prof Ewa MAREK (CAM)
Dr Lek Hong LIM (CARES)

The team are focused on integrating large language models in the automated techno-economics workflow. Data-driven workflows typically require large amounts of consolidated, structured data for the construction of decently accurate models. The absence of such comprehensive databases remains one of the key challenges in producing accurate estimates in techno-economic analyses (TEA) of chemical plants.

In this research stream, we are leveraging the recent advancements in AI, such as in the contextual understanding of code and reasoning in large language models (LLMs), as well as optical character recognition. These improvements allow the implementation of some level of automation for integrating old and new literature data within the modular cost estimation framework that we have developed. The utilisation of multiple methods for costing will, when combined with statistical analysis and industrial data, allow for more accurate estimates and better representation of uncertainties in TEAs.

Recently, a semi-functional new costing method was implemented using a short and crude prompt, hinting at the potential of creating a fully functional module with a single, specific and structured prompt. Apart from increasing the total number of equipment cost datasets in our database from ~150 to ~240, this test also serves as a proof of concept confirming the potential for LLMs to build upon our framework to accelerate the database construction process.

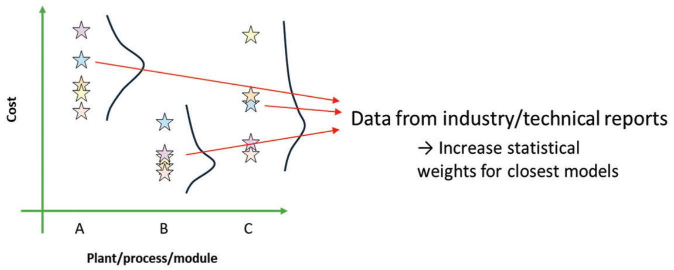


Figure 2.14: Illustration of how estimating costs with multiple methods will reveal the extent of underlying uncertainties in a single method study, and how industry data can influence the final cost model.

Another aspect of AI integration within the automated TEA workflow is to exploit the potential for contextual awareness in LLMs in process synthesis. We have been testing the current capabilities of LLMs in extract information from the literature to evaluate the "performance" of industrial processes. Thus far, it has shown promising results in terms of deriving comparison strategies and presenting logic for ranking processes according to factors such as the projected economics, efficiencies and scalability, based only on the process descriptions. To address the hallucination and fake citation issues plaguing LLM-assisted literature search, which would be critical in AI-assisted process synthesis, we are developing a tool that integrates application programming interfaces (API) from academic publishers and databases within the process evaluation protocol to dynamically verify the cited claims and sources.

Prof Markus KRAFT (CAM)
Dr Kumaran ELUMALAI (NTU)

SM_3 leverages digital twins of high-throughput experimentation (HTE) to enable predictive, interoperable, and sustainability-aware workflows. A modular ontology stack captures laboratory infrastructure, equipment, scheduling, documentation, maintenance, and spatial allocation, reusing existing ontologies where possible and introducing domain-specific extensions only as needed. The partial ontology structure, see Figure 2.15, combined with underlying chemical knowledge, enables fully machine-interpretable representations of laboratory assets and workflows. Although the physical HTE infrastructure is still being expanded and metadata collection is ongoing, the digital backbone for its twin representation is already under active development. Implemented within The World Avatar (TWA) ecosystem, this framework provides the semantic foundation for seamless integration of experimental data streams, process models, and sustainability metrics, establishing a robust platform for digital-twin–enabled discovery.

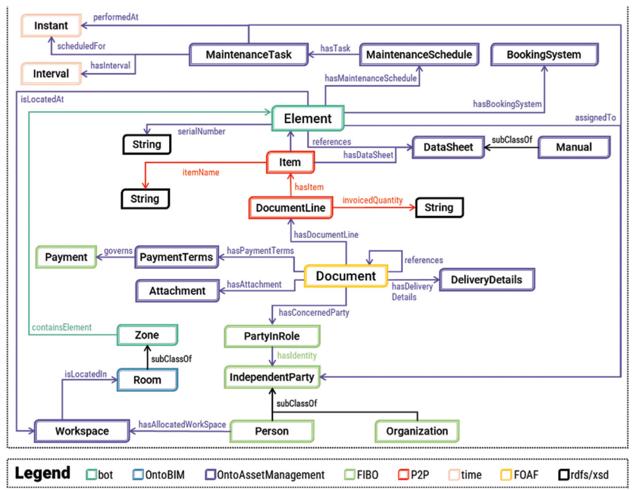
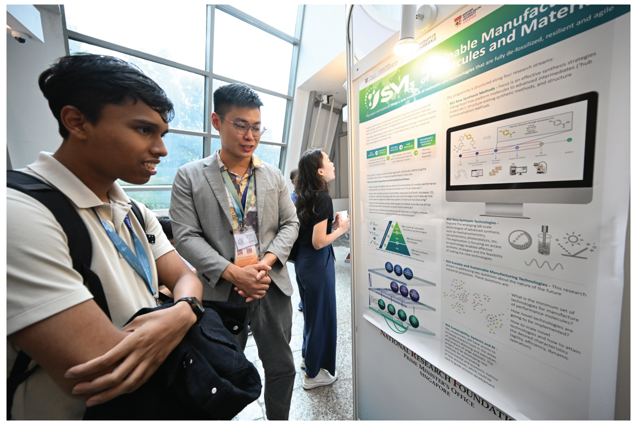


Figure 2.15: Snippet of the ontology landscape in TWA describing lab equipment.

[1] Bai, J.; Mosbach, S.; Taylor, C.J.; Karan, D.; Lee, K.F.; Rihm, S.D.; Akroyd, J.; Lapkin, A.A.; Kraft, M. Nature Communications 2024, 15, 462. https://www.nature.com/articles/s41467-023-44599-9#citeas

OTHER ACTIVITIES AND ACHIEVEMENTS



Dr Lim presenting his poster during the GYSS poster presentation session.

Dr Lek Hong LIM (Research Fellow, CARES) was selected to participate in the Global Young Scientists Summit (GYSS). The 2026 edition welcomed its largest cohort yet, with over 400 young researchers from 57 countries gathering in Singapore to interact with Nobel Laureates and other researchers from a wide range of disciplines.

Dr Lim joined CARES' first participation in Cambridge Festival, the University of Cambridge's largest annual science festival, with a hybrid event "Cambridge in Singapore–Who CARES?" on 18 March 2026. The public engagement event was targeted for a younger, schooling audience from secondary school and older, drawing over 150 attendees at the in-person venue in Singapore and online, from over 30 schools and universities. Dr Lim reframed the importance of decarbonisation for the younger audience and shared his research journey through schooling and proactively reaching out for PhD opportunities.

CARES and the University of Cambridge have signed a contract through which Chemical Data Intelligence (CDI) Pte Ltd has committed to co-fund a PhD student within the SM_3 project. Furthermore, CDI has fully funded a PhD student at the University of Cambridge to work on an additional research question, relating to scalability of novel synthesis technologies. Pfizer is actively engaging with the project by providing data and taking part in the project's face-to-face workshops. The project has also engaged with Andrew Rutter through his company rutterdesign, to work together on a technology mapping for SM_3.

Dr Lim presenting at Cambridge in Singapore–Who CARES?

SCIENTIFIC OUTPUT

The following are the CREATE-acknowledged publications generated by the SM3 programme during the reporting period.

Peripheral Aryl Group Transposition on Pyridines Using Photoredox Catalysis

Tan, Eugene Yew Kun, Tian-Yu Peng, Taku Wakabayashi, and Shunsuke Chiba, Nature Synthesis, ahead of print

https://doi.org/10.1038/s44160-026-01023-6

Single Atom-Cluster Synergy in Ag Catalysts Enables Chiral Glyceric Acid from Biomass

Xu, Shuguang, Jianmei Li, Jiong Cheng, et al., Science Advances

https://doi.org/10.1126/sciadv.adz4136

Photocatalytic Coupling of Unprotected Sugars and N-Heteroarenes

Zhou, Qian-Yi, Daniel Zhi Wei Ng, Jun Wu, et al., International Journal of Multilingualism, Nature Synthesis, ahead of print

https://doi.org/10.1038/s44160-025-00980-8

HD4

HEALTH-DRIVEN DESIGN FOR CITIES

HD$_4$ brings together researchers from Nanyang Technological University, the National University of Singapore, and the University of Cambridge to investigate how urban environments shape health. The programme integrates environmental data with health and behavioural information from the SG100K cohort study, a national research initiative that has recruited 100,000 participants across Singapore.

People living in cities face growing challenges to their health and wellbeing, including heat, noise, air pollution, and limited opportunities to eat healthily and be physically active. As urban populations grow, understanding how the design and organisation of cities influence health has become an increasingly important public health priority.

Singapore provides a unique setting for this research. With ambitious public health goals, rich data resources, and a strong commitment to evidence-informed urban planning, Singapore offers an exceptional opportunity to study how urban environments influence health. Working in partnership with government agencies, HD4 aims to generate insights that can help guide future strategies for designing healthier cities.

Research Objectives

HD$_4$ will undertake research in the following areas:

- Characterising features of the Singapore environment that potentially impact health
- Understanding the links between environmental factors, individual behaviour and health outcomes
- Observing the impact of environmental change on health in Singapore
- Working with government agencies to explore the development of useful public health tools

Research Team

The HD$_4$ team was delighted to be joined by researchers Dr Lucia SEGOVIA DE LA REVILLA, Dr Mutian MA, Dr Tomas GONZALES and PhD student Xu TANG at CARES, alongside researcher Fumiaki IMAMURA in Cambridge and researchers Xiaoxi FU, Palak SHARMA, Penny TEO and Ruixin CHI, and Associate Professor Konstadina GRIVA, who are co-located in the SG100K offices at the Lee Kong Chian School of Medicine at Nanyang Technological University.

Deputy Programme Lead Prof Ronita BARDHAN and investigators Prof James WOODCOCK, Dr Tom BURGOINE and Dr Belen ZAPATA-DIOMEDI have been resident at CARES in recent months, moving the research forward at pace and contributing to the HD$_4$ Seminar Series.

Research Plan

HD$_4$ is working in partnership with SG100K to understand how Singapore's urban environment shapes behaviour and health. By linking detailed environmental information with lifestyle and clinical data collected from participants across SG100K, HD$_4$ is creating a platform for investigating how features of cities influence health risks and outcomes.

HD$_4$ will proceed in two phases. The critical contribution of the current phase of HD$_4$ – Phase 1 – is to test feasibility and deliver proof-of-concept analyses to establish a foundation for subsequent research. This will pave the way for Phase 2, which will identify how changes in the environment and people's intersection with it can lead to improvements in the health of Singaporeans.

During Q4 of 2025 and Q1 of 2026, the programme has made substantial progress in building the scientific foundations needed for this work. Researchers have used existing environmental data sources to derive spatial datasets describing environmental exposures across Singapore, including indicators of greenspace and accessibility to parks and recreational areas. At the same time, analyses of behavioural data from SG100K participants have begun to characterise patterns of physical activity, sleep, diet, and fitness across the population.

Important progress has also been made in linking participant data with electronic health records, enabling researchers to examine how environmental conditions and lifestyle behaviours relate to disease risk and health outcomes. In parallel, HD$_4$ is piloting new approaches to measuring environmental exposures and behaviours more dynamically, including methods that capture how individuals move through the city in their daily lives.

Project Leads


Professor Nick WAREHAM
University of Cambridge


Professor John CHAMBERS
Nanyang Technological University


Professor Rudi STOUFFS
National University of Singapore


Professor Ronita BARDHAN
University of Cambridge

SCIENTIFIC UPDATES

Urban environmental exposures for SG100K participants

Leads

Prof Ronita BARDHAN (CAM)

Assoc Prof Rudi STOUFFS (NUS)

This research area focuses on developing the environmental data that underpin the analyses undertaken by HD_4. By linking data describing Singapore's urban environment with individual participants in the SG100K cohort, HD_4 is creating the foundation for investigating how environmental conditions influence behaviour and health. Over the past six months, the team has advanced the environmental exposure framework and begun generating new spatio-temporal data for linkage with SG100K.

A central focus has been the development of new indicators of urban greenspace that capture how greenery is available, visible, and accessible. In Q4 2025 the team moved from early proof-of-concept metrics to preparing multi-year datasets ready for linkage with SG100K. Following advice from government agencies at the HD_4 Scientific Advisory Group meeting in August 2025, a framework has been developed that distinguishes between physical access to green space and the visibility of greenery in the urban environment. A ten-year series of satellite-derived greenness indicators has been generated, producing annual maps of vegetation across Singapore. These data were supplemented with OpenStreetMap information to identify different types of green space. Automated methods are being used to classify physical access to green space at scale, combining rule-based approaches with large-language-model tools to better identify parks, informal green spaces, and other vegetation features. In parallel, the team is developing indicators of visual exposure to greenery, incorporating building height and residential patterns to better estimate how greenery is experienced in everyday settings.

Work is progressing on indicators that capture how people access green spaces through the urban transport network. Earlier proof-of-concept analyses in the Clementi area examined walking and cycling accessibility to parks using network-based methods. This work is now being expanded across Singapore, with walking and cycling networks derived from OpenStreetMap data. Additional information about the street environment is being incorporated to allow more realistic modelling of accessibility. The resulting indicators are being prepared for linkage with SG100K and will support analyses examining how access to parks and sports facilities influences physical activity.

Progress has been made in developing indicators of exposure to heat and humidity. The team is developing an exposure index based on the Universal Thermal Climate Index (UTCI), combining physical modelling of radiation and heat exchange with machine-learning predictions of local weather conditions. These analyses draw on high-resolution information about Singapore's built environment, including models of building and canopy heights that allow indicators such as sky view factor to be calculated. An automated analytical workflow integrates multiple environmental data, including building characteristics, green infrastructure, road networks, biophysical indicators, and meteorological observations, to estimate heat and humidity exposures across the city.

HD_4 stakeholder workshop with representatives from the Health Promotion Board, Singapore Food Agency, National Environment Agency, Housing & Development Board, and the Urban Redevelopment Authority, February 2026.

In addition to green space, mobility, and humid-heat exposures, the programme is examining other environmental features that may influence health. A systematic review of the retail food environment in Singapore has been completed, helping identify research gaps and priorities for future analyses. In February 2026, a stakeholder workshop brought together representatives from government agencies, including the Health Promotion Board, Singapore Food Agency, National Environment Agency, Housing & Development Board, and the Urban Redevelopment Authority. Discussions clarified the availability of relevant data and helped shape research questions on how neighbourhood food environments may influence dietary behaviours.

The environmental data developed through this work are now being shared across the HD_4 programme. The first green space and accessibility indicators have been provided to teams examining links between environmental characteristics, health behaviours, and clinical outcomes within the SG100K cohort. Over the coming months, these data will be expanded and refined to support analyses across the cohort, helping build an evidence base on how urban environments shape health in Singapore.

Relationship between environments and health-related behaviours

Leads

Asst Prof Marie Chiew Shia LOH (NTU)

Dr Louise FOLEY (CAM)

Dr Jenna PANTER (CAM)

Understanding how lifestyle behaviours vary across the population is an essential step in examining how urban environments influence health in Singapore. This strand of the HD_4 programme focuses on characterising key health-related behaviours within the SG100K cohort and preparing the analytical foundation for investigating how these behaviours may be shaped by environmental conditions.

In Q4 of 2025 and Q1 of 2026, the team has made substantial progress in analysing behavioural data from the first 20,000 participants in SG100K. These analyses provide a detailed epidemiological baseline across several major domains of health behaviour, including physical activity, sleep, diet, and cardiorespiratory fitness. Together, these measures offer a comprehensive picture of lifestyle patterns within Singapore's multi-ethnic population and provide an important foundation for subsequent analyses linking behaviour with environmental exposures and health outcomes.

Initial analyses have examined how physical activity varies across different population groups, including differences in participation across activity domains and intensity levels. These findings highlight how physical activity is accumulated through daily routines and reveal important variations across sociodemographic groups. Sleep health has also been examined in depth, considering multiple dimensions of sleep quality such as duration, latency, efficiency, disturbances and daytime functioning. The analyses indicate a high prevalence of short sleep duration and difficulties with sleep onset, with some groups disproportionately affected, including women, individuals experiencing mental health symptoms, and those with lower socioeconomic status.

Dietary patterns have been characterised using information on macronutrient intake, food groups, and overall dietary quality. These analyses show clear differences in dietary habits by age, sex, and ethnicity, alongside evidence of modest changes in dietary quality over time. Cardiorespiratory fitness has been assessed using estimates of maximal oxygen consumption, revealing differences between population groups that appear to be largely explained by variations in adiposity. These findings reinforce the importance of fitness as both a marker and potential determinant of metabolic health.

Building on this descriptive work, the team is developing analyses that link these behavioural measures with the environmental exposure data generated within HD_4. The first green space exposure indicators and measures of accessibility to parks via walking and cycling networks have already been shared and two collaborative analysis proposals are being developed to examine how these environmental characteristics relate to self-reported physical activity and cardiorespiratory fitness. Additional analyses focusing on diet and sleep are also in preparation and will be undertaken as the environmental indicators become available, for example measures of heat or neighbourhood food environments.

Looking ahead, the analyses will be expanded across the full SG100K cohort to strengthen statistical power and improve representation across Singapore's diverse population. These resources will support more detailed investigations of how environmental conditions shape lifestyle behaviours and contribute to health inequalities in Singapore, including objective physical activity measurements, neighbourhood-level indicators, and linked electronic health records.

Relationship between environments, behaviours, and health

Leads

Prof John CHAMBERS (NTU)
Assoc Prof Xueling SIM (NUS)
Prof Nita FOROUHI (CAM)

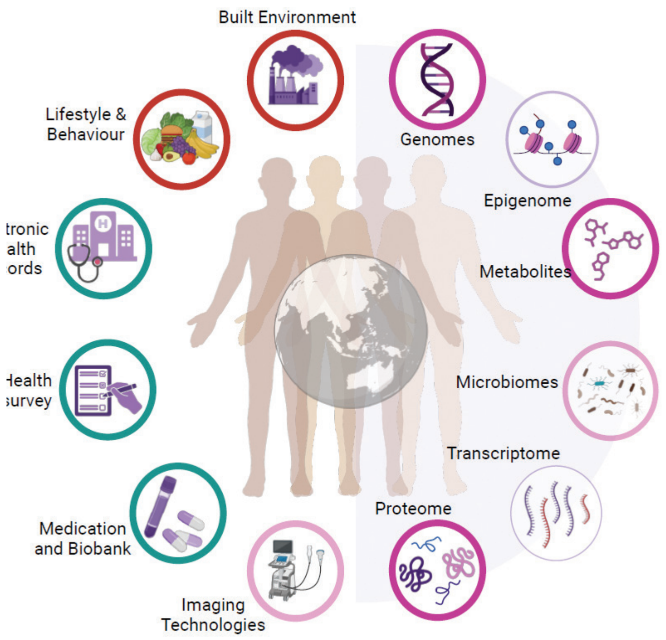
HD_4 seeks to understand how environmental conditions influence health by shaping lifestyle behaviours and disease risk. Achieving this requires the integration of complex data sources, including environmental indicators, behavioural data, and clinical outcomes. In Q4 of 2025 and Q1 of 2026, the team made significant progress in building the data infrastructure needed to support these analyses within SG100K.

A major milestone during this period has been the consolidation of the research phenotype data used for epidemiological analyses. Data collection, curation, and quality checks have been completed for a wide range of clinical and metabolic traits, together with the coding of prevalent health conditions based on linked health records. These developments provide a robust foundation for examining patterns of disease and health risk across the cohort.

Alongside these efforts, substantial work has been undertaken to organise and document behavioural data collected in SG100K. The data have been systematically catalogued, and an inventory of key health behaviours, particularly diet and physical activity, has been developed to support consistent analysis across the programme. Dietary intake data have been processed and coded into food groups and macronutrients, enabling the derivation of widely used dietary quality indicators. These developments improve the efficiency, comparability and reproducibility of analyses across research teams.

Progress has been made in processing objective physical activity data. The Health Informatics Group at the NTU Lee Kong Chian School of Medicine, working with the University of Cambridge, has processed more than 25,000 raw seven-day accelerometer data, with expected release by Q3 2026. These measurements provide detailed information about participants' daily activity patterns, including how activity levels vary throughout the day and week. Such data allow researchers to identify different behavioural profiles, for example, individuals who are consistently active compared with those who concentrate activity into short periods, enabling more precise analyses of the relationship between physical activity and health outcomes.

Another important milestone has been the successful linkage of SG100K participants to electronic health records through the Ministry of Health's TRUST platform. To date, 50,000 participants have been linked to their health records, providing detailed information on diagnoses and clinical outcomes. These linked data are now available for analysis and strengthen the capacity to investigate disease risk and long-term health outcomes. Linkage of the full cohort of 100,000 participants is expected later this year.



SG100K research phenotypes for epidemiological analyses ready for analysis in HD_4. (Created in BioRender. Chambers, J. (2026) https://BioRender.com/um2dxec).

The HD_4 team has also begun integrating the environmental exposure indicators developed by HD_4 with these behavioural and clinical data. The first greenness exposure metrics and proof-of-concept indicators of walking and cycling accessibility have been incorporated into the analytical framework, enabling researchers to begin exploring how environmental characteristics relate to behaviour and health within the SG100K cohort.

In Q2 of 2026, the focus will shift toward large-scale analyses examining how lifestyle behaviours contribute to disease risk and how environmental factors may influence these relationships. By combining detailed environmental data with behavioural and clinical information, HD_4 is creating a powerful platform for understanding how Singapore's urban environment shapes health across the population.

Novel approaches for improving assessment of person-level environmental and behavioural exposures

Leads

Dr Søren BRAGE (CAM)
Assoc Prof Falk MÜLLER-RIEMENSCHNEIDER (NUS)
Assoc Prof Jason Kai Wei LEE (NUS)

A key ambition of HD_4 is to develop new ways of measuring how people interact with their environment in daily life. Traditional epidemiological studies of the environment often rely on residential addresses, which can miss how people move through the city and experience different environments. This research area focuses on testing innovative methods that capture these exposures more continuously and at greater resolution.

To explore the feasibility of these approaches, the team has designed a pilot study of remote assessment involving 200 participants drawn from the SG100K cohort. Participants attending their baseline SG100K clinical assessments will be invited to take part in this add-on digital study, which will allow the research team to build on existing study procedures while minimising disruption for participants.

Several complementary technologies are being developed and tested as part of this work. One area of focus is location and movement tracking using smartphones. Systems have been established to collect GPS data from both iOS and Android devices, enabling the characterisation of participants' daily travel patterns and the environments they encounter throughout the day. The study will also explore the potential to access historical physical activity information recorded on participants' smartphones, providing additional insights into behavioural patterns over time.

The team is also developing new approaches for assessing physical fitness remotely. Early testing showed that smartphone-based heart rate measurements can be unreliable across different phone designs. The study design has therefore been adapted to incorporate smartwatch-based monitoring. Some participants will use their own heart rate-enabled smartwatches, while others will be provided with a Garmin smartwatch for the duration of the study. This approach will allow the team to test different models for collecting remote physiological measurements and to explore effective incentives for participation in digital health studies.

Another component of the study focuses on the indoor environment, recognising that people spend a large proportion of their time inside buildings. Participants will receive two small sensors, one for the living room and one for the bedroom, to measure aspects of indoor air quality. Data from these sensors will be transmitted remotely to the research team through newly established data pipelines.

The team is also developing digital tools that allow participants to review and annotate their own location and activity data. These tools will help capture additional contextual information, such as travel modes or activities undertaken during different parts of the day, enriching the interpretation of the sensor and GPS measurements.

Together, these developments will help establish practical and scalable methods for measuring environmental exposures and behaviours in real time. Insights from this pilot study will inform the design of future data collection approaches that could be applied more widely within SG100K in Phase 2 of the HD_4 programme.

Making an impact through engagement

Leads

Dr Thomas BURGOINE (CAM)

Dr Yih Yng NG (NTU/NUS)

Asst Prof Bernett LEE (NTU)

Assisted by Specialist Collaborator Oliver FRANCIS (CAM)

Engagement with government agencies and other partners is central to HD_4's mission to translate research into real-world impact. Alongside generating new scientific insights, the programme aims to build strong collaborative relationships with organisations involved in urban planning, public health, and environmental management in Singapore. These partnerships help ensure that the research addresses policy-relevant questions and supports evidence-informed decision-making.

In Q4 of 2025 and Q1 of 2026, HD_4 expanded and strengthened its stakeholder network. Following recommendations from the programme's Stakeholder Advisory Group, additional organisations have joined the group to broaden the range of perspectives informing the research. The Agency for Integrated Care and the Land Transport Authority have recently become members, complementing the existing representation from agencies involved in planning, health, and environmental management.

The second meeting of the Stakeholder Advisory Group took place in February 2026, providing an opportunity for agency partners to review progress across the programme and to offer feedback on emerging research priorities. Discussions highlighted opportunities for closer collaboration, including potential data sharing arrangements and joint exploration of new analytical approaches.

In parallel with these formal advisory structures, HD_4 has continued to build relationships across government through ongoing dialogue and targeted engagement activities. The programme's Knowledge Broker plays a key role in maintaining connections between researchers and policy partners, helping to identify opportunities for collaboration and ensuring that insights from the research are communicated effectively. These efforts are also helping to strengthen connections between agencies and creating new opportunities for cross-sector collaboration on urban health challenges.

A number of engagement activities have taken place during this reporting period. In November 2025, HD_4 representatives visited the Urban Redevelopment Authority to view the Draft Master Plan Exhibition and discuss potential areas of collaboration. HD_4 has continued to strengthen its public profile. The programme now maintains an active presence on LinkedIn, sharing updates on research progress and events. The HD_4 Seminar Series resumed in January 2026 following its initial run in 2025, providing a platform to showcase emerging research and foster collaboration across institutions. HD_4 researchers have contributed to national and international events, including the Singapore Scientific Conference and the Urban Solutions and Sustainability Research & Innovation Congress hosted by the Urban Redevelopment Authority.

These engagement activities are helping to build a strong foundation for translating HD_4's research into practical insights for policy and practice. Over the coming months, the programme will continue to deepen these partnerships and explore opportunities for co-developing research that can support healthier urban environments in Singapore.

URA tour of Draft Master Plan Exhibition, November 2025.

CONFERENCE PRESENTATIONS

Team members have presented HD_4 work at local, national and international events.

- "*HD_4 – Health-driven design for cities*" was presented as a research poster by researchers Dr Jielin CHEN, Dr Wubin XIE, Dr Theresia MINA, Dr Mutian MA and Sharyl CHIN at the Singapore Scientific Conference from 8 - 11 December 2025.
- Prof John CHAMBERS was invited as a speaker to present "The SG100K Longitudinal Population Study: Unravelling Genes and Environment for Better Health Outcomes in Singapore" at the Leveraging Science and Technology for Healthy and Regenerative Cities breakout session of the Urban Solutions and Sustainability Research & Innovation Congress organised by URA, Singapore on 6 February 2026.
- Asst Prof Marie LOH, Dr Theresia MINA, Dr Wubin XIE, and Dr Lucia SEGOVIA DE LA REVILLA hosted a Science Centre Community of Practice Event to local educators on 6 March 2026 at CREATE. The event received enthusiastic feedback with one participant remarking, "Health driven design for cities is related to urban planning in Sec 2 and Sec 3 Geography Topics. I could get students to discuss on social and economic sustainable development on real life issues in Singapore."
- Assoc Prof Rudi STOUFFS and Dr Theresia MINA delivered "Linking Built Environment, Lifestyle and Population Health" as an oral presentation at the Symposium for World Demographics and Ageing Forum organised by the Singapore-ETH Centre on 12 March 2026.
- "*Ultra-Processed Food Intake and Cardiometabolic Outcomes: A Cross-Sectional Analysis in a Multi-Ethnic Asian Population in Singapore*" was presented as a research poster at the EPI Lifestyle Scientific Sessions from 17 - 20 March 2026 in Boston, USA.

HD_4 team at the Singapore Scientific Conference, December 2025.

PUBLISHED PAPERS

The following publications with contributions from the HD4 team were published in the scientific literature during this reporting period.

The Health for Life in Singapore (HELIOS) Study: Delivering precision medicine research for Asian populations

X. Wang, T. Mina, N. Sadhu, et al., Nature Communication

doi: 10.1038/s41467-025-65774-0

Adversity, adiposity, nutrition and metabolic well-being in multi-ethnic Asia

T. H. Mina, P. R. Jain, N. G. Forouhi, and J. C. Chambers, Nature Metabolism

doi: 10.1038/s42255-025-01441-4

Impacts of building height and local climate zones on the performance of the In-VEST Urban Cooling model

Y. Wang, P. Hamel, E. E. Ramsay, P. Liu, and R. Stouffs, Earth and Environmental Science

doi: 10.1088/1755-1315/1554/1/012047

Find out more: www.cares.cam.ac.uk/research/hd4-project

Contact: HD_4 Knowledge Broker Sharyl Chin, sharyl.chin@cares.cam.ac.uk

PIPS

PHARMA INNOVATION PROGRAMME SINGAPORE

PIPS is an industry-led platform coordinated by Singapore's Agency for Science, Technology and Research (A*STAR). PIPS aims to synergistically and strategically bring together public sector research capabilities and domain expertise of the pharmaceutical industry to enhance the productivity and operational efficiency within Singapore's pharmaceutical sector through leveraging novel manufacturing technologies and data analytics.

Project Leads


Professor Alexei LAPKIN
University of Cambridge


Professor Dame Lynn
Lynn GLADDEN
University of Cambridge


Professor Mick MANTLE
University of Cambridge


Dr Ann CHOW
A*STAR

SCIENTIFIC UPDATES

Automated Evaluation of Environmental Impacts of Pharma Manufacturing Processes

The three-year project that started in July 2023 is funded by the Pharma Innovation Programme (PIPS 2) programme and led by Prof Alexei LAPKIN (CAM). The project involves creating physical and machine learning based model libraries for upstream, downstream, wastewater treatment operations in pharma manufacturing processes, automatically assembling the models for a given target molecule, calibrating the models based on process needs, solving the models, and finally estimating the environmental impact of the process for a given production scale.

In the last six months of development, the project is focusing on delivery of a demonstration of calculation of environmental impacts for example processes. The target application of this technology will be in predicting life cycle assessment impacts at the early R&D stages, and focusing on developing chemical processes in speciality chemicals and small molecules pharmaceuticals. The tool will specifically focus on synthesis technologies, on treatment of waste from chemicals manufacture and on energy use in process plants. The project team is planning to present the outcomes of the project at conferences and events in Singapore and globally after project completion in June 2026.

Dr Dogancan KARAN (Research Fellow, CARES) has been focusing on environmental impact prediction of the upstream processes. In particular, Dr Karan has been working on the thermodynamic engine of the pipeline to solve the equation of the state to predict bulk liquid properties, solid and slurry handling. In addition, he has developed a language model (LLM) based tool and database schema to ingest information from text documents which contain detailed information about the chemical process of interest whose environmental to be predicted. Finally, Dr Karan has also developed a recipe-based task manager framework where ingested information with LLM is converted into a series of executable code which can be run by the simulation environment he developed over the past year. In the next 6 months, he will be working on generating the life cycle inventory of the upstream processes from the ingested documents by the LLM tool and estimating the carbon footprint of the chemical processes from the life cycle inventory data.

Building a Capability in Magnetic Resonance Methods for the Pharmaceutical and Agrochemical Sector within PIPS

The PIPS project commenced in July 2025 led by Dr Ann CHOW (A*STAR), Prof Mick MANTLE (CAM), and Prof Dame Lynn GLADDEN (CAM). Significant progress has been made by the Cambridge team with the appointment of Dr Andy YORK (PDRA, CAM) as the project's postdoctoral research associate, starting 2 February 2026. Dr York brings extensive experience in heterogeneous catalysis and magnetic resonance methods.

Experimental NMR/MRI studies on carbon spheres imbibed with methanol were conducted during the period October 2025 to January 2026. These studies included 1H spectroscopy, T1–T2 and D–T2 relaxation correlation measurements, and three-dimensional magnetic resonance imaging (MRI) with an isotropic voxel resolution of 79 µm. Figure 3.1 shows example two-dimensional 1H MR images obtained from the middle section of a packed bed of Kureha A-BAC SP 400 µm carbon spheres imbibed with methanol.

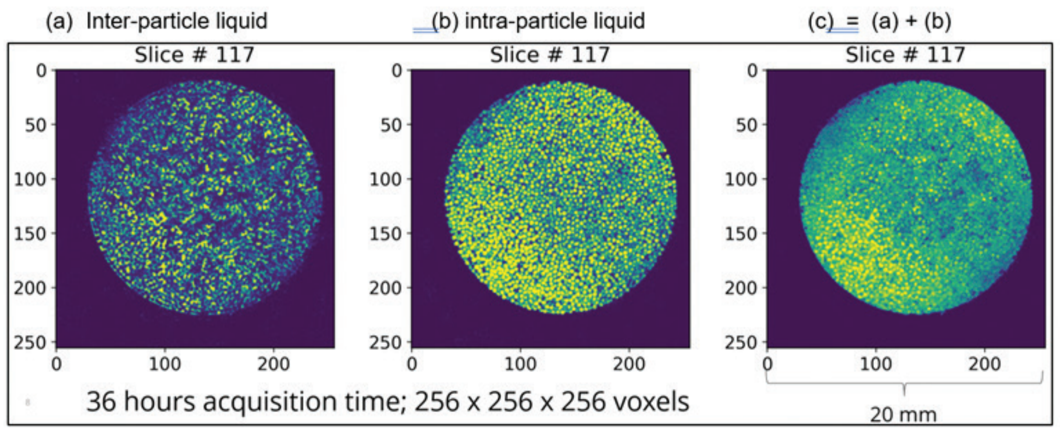


Figure 3.1: 2D 1H MRI slices taken from a 3D MRI data set at a voxel resolution of 79 µm.

New chemically selective three-dimensional MRI pulse sequences were developed to enable selective imaging of both the inter-particle methanol solution and the intra-particle methanol solution, allowing these regions to be distinguished within a single 3D MRI dataset.

Standard 1H spectroscopy was also applied to several samples, and the results highlight the conductive nature of the carbon supports. Figure 3.2 shows a 1H spectrum obtained from Kureha A-BAC SP 400 µm carbon spheres imbibed with methanol, in which two peaks are clearly visible: (i) the left-hand peak is attributed to inter-particle methanol and (ii) the right-hand peak to intra-particle methanol. In non-conducting systems these signals would typically overlap and would not be spectrally resolved.

The 1H spectral behaviour observed for conducting carbon spheres can potentially be exploited to obtain unambiguous information from both the inter- and intra-particle regions of a packed catalyst bed in a micro trickle-bed reactor. Preliminary T2 measurements further show that the intra-particle methanol peak (right-hand peak) has a significantly shorter T2 value. This difference may allow NMR relaxation-editing techniques to be used to simplify spectra under real catalytic reaction conditions.

Building on this understanding of the conductive nature of carbon-based supports, 1H chemically selective D–T2 relaxation correlation pulse sequences were developed to demonstrate the transferability of chemical selectivity to other NMR methodologies. Figure 3.3 shows the results of these newly developed D–T2 experiments performed on Kureha A-BAC SP 400 µm carbon spheres imbibed with methanol.

Finally, Prof Mantle visited Singapore in December 2025 to transfer the relevant NMR methodologies to the Bruker NMR instruments available on Jurong Island and at Neuros. Prof Mantle performed the initial experiments with a team from the A*STAR Institute of Sustainability for Chemicals, Energy and Environment (A*STAR ISCE^2).

The ISCE^2 team attempted to process the T1–T2 and D–T2 datasets provided by CARES using the Bruker Dynamics Centre software but encountered challenges likely stemming from data formatting incompatibilities. These issues were subsequently resolved during Prof Mantle's visit to Singapore in December 2025, where the Python-based data-processing scripts were transferred to ISCE^2, allowing the datasets to be processed successfully.

During the same visit, significant progress was made on the experimental setup and instrument readiness. Pulse calibration, image profiling, diffusion measurements and T1–T2 experiments were established on both the JI and Neuros NMR spectrometers at ISCE^2. Additional pulse sequences, including D–T2, soft spin-echo, and T2–T2 exchange, were also implemented on the Neuros spectrometer. These sequences are still undergoing development for deployment on the more advanced TopSpin 4.5 platform used on the JI spectrometer.

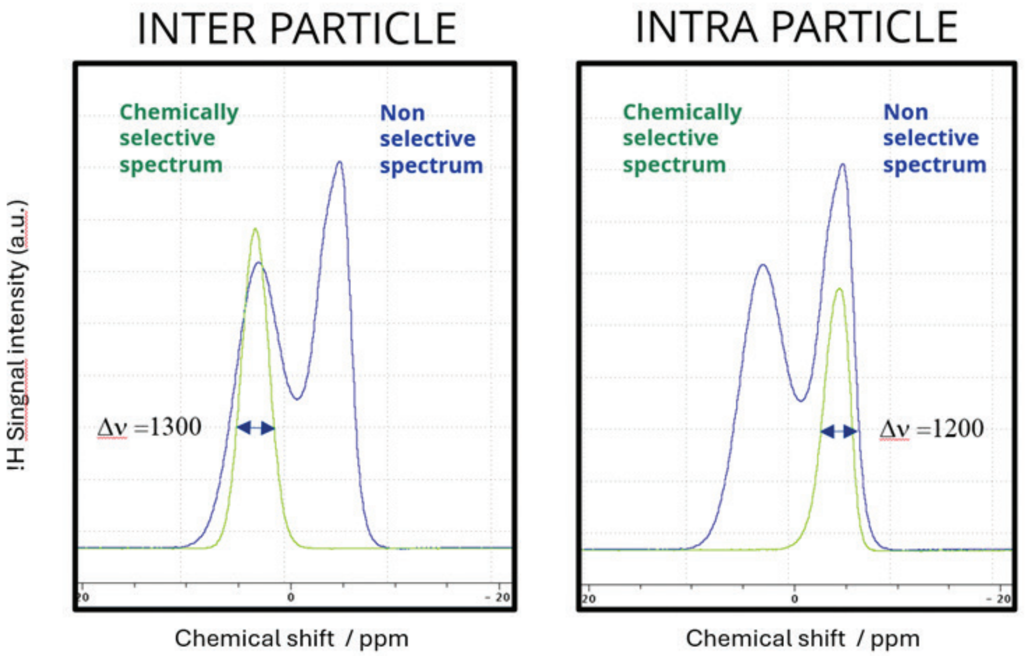


Figure 3.2: 1H NMR spectra from Kureha A-BAC SP 400 µm carbon spheres imbibed with methanol. The blue trace shows a non-chemically selective 1H NMR spectrum, displaying two peaks attributed to inter-particle (left) and intra-particle (right) methanol. The green traces correspond to chemically selective 1H spectra obtained from the respective regions, demonstrating excellent discrimination between the two environments together with reduced overall linewidths.

The transferred and newly implemented pulse sequences were successfully validated using various solvents, both in pure form, mixture and in systems containing catalyst particles composed of silica, alumina and activated carbon, demonstrating continuity and expansion of the work initiated previously.

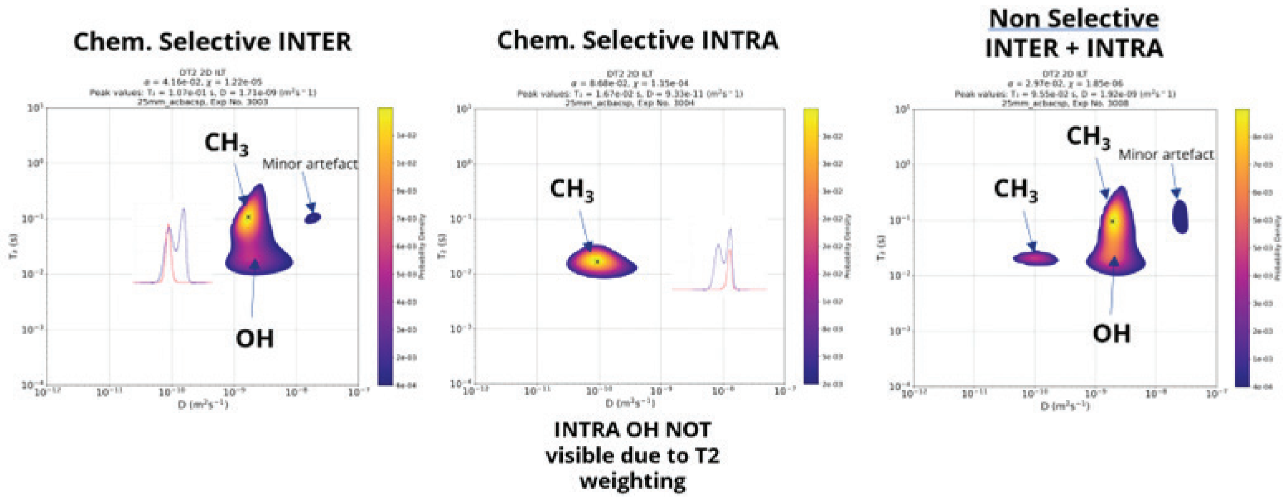


Figure 3.3: Chemically selective 1H 2D D-T2 correlation plots for methanol imbibed in Kureha A-BAC SP 400 µm carbon spheres.

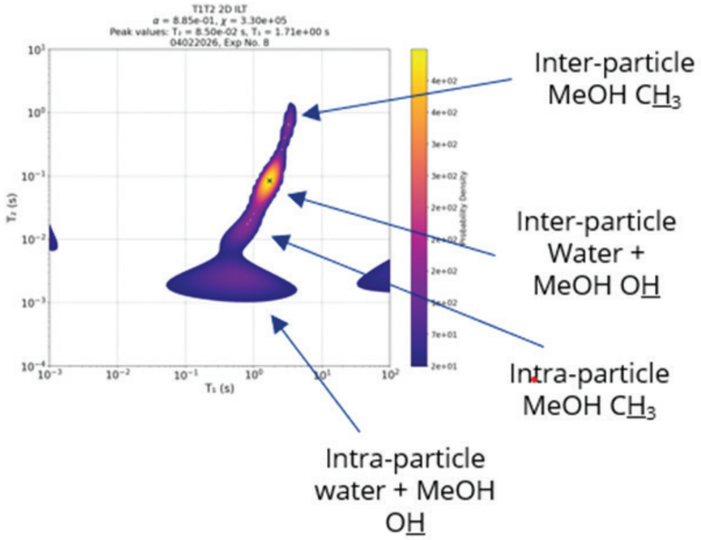


Figure 3.4: T1-T2 distribution of methanol-water imbibed within activated carbon.

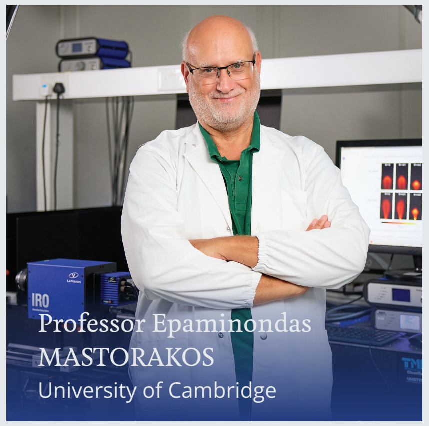
LCER Phase 2

Low-Carbon Energy Research Phase 2

The Low-Carbon Energy Research (LCER) Programme is an initiative funded by Singapore's National Research Foundation (NRF) and hosted by the Agency for Science, Technology and Research (A*STAR) to support research, development and demonstration projects to advance low-carbon technologies, and enable decarbonisation of the power and industry sectors.

CARES is contributing to two projects under Phase 2 of the LCER Programme which fall under the remit of LCER's Directed Hydrogen Programme.

CARES researchers



Professor Epaminondas MASTORAKOS
University of Cambridge

Professor Adrian FISHER
University of Cambridge

Dr B HARIKRISHNAN
Cambridge CARES

Dr B. HARIKRISHNAN (Research Fellow, CARES) has been working on the application of the low-order Incompletely Stirred Reactor Network (ISRN) model for partially cracked ammonia combustor and the validation with existing experimental data. The mixing field statistics required for performing ISRN are obtained by performing Large Eddy Simulation – Conditional Moment Closure (LES-CMC) simulations, which are reference conditions of ammonia decomposition ratios: 0.50 and 0.90. Figure 4.1 shows the mixture fraction and its sub-grid scale variance. The pressure for this case is 5 bar and the fuel/air temperature is 563.15 K. The primary zone is in stoichiometric condition. The power for both cases is fixed to be at 50.2 kW.

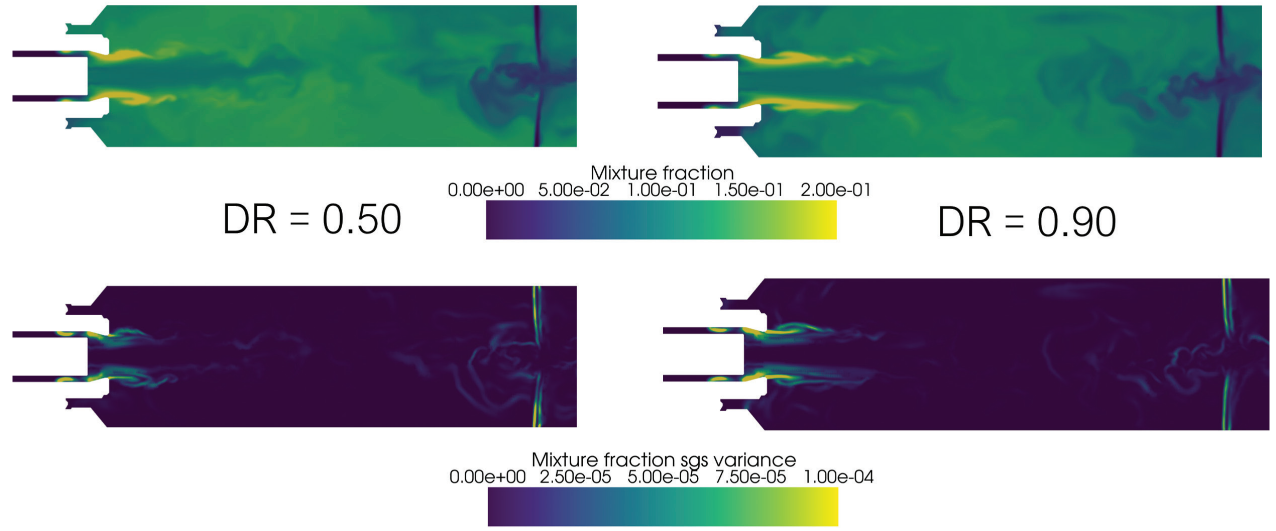


Figure 4.1: Instantaneous mixture fraction and its sub-grid scale variance

Figure 4.2 shows the NO mass fraction for the LES-CMC cases. The primary zone NO production is high due to the stoichiometric condition. But the cooling air significantly reduces the NO production for the case of DR=0.90. Figure 4.3 shows that the exit NOx emissions are comparable against the experimental results of Ditaranto and Saanum (2024). The research will further continue on validating the ISRN results with the extracted mixing field statistics.

Currently, work is underway on coupling ISRN with the CFD code STARCCM+ for collaborative work with SIEMENS Energy, where emission predictions will be performed on an industrial cracked ammonia burner.

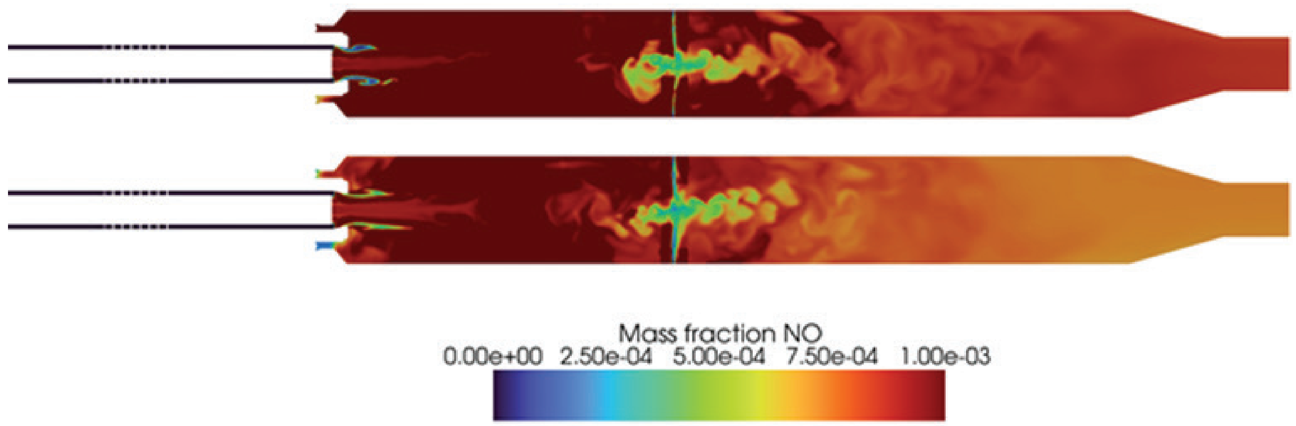


Figure 4.2: NO mass fraction for DR = 0.50 and DR = 0.90

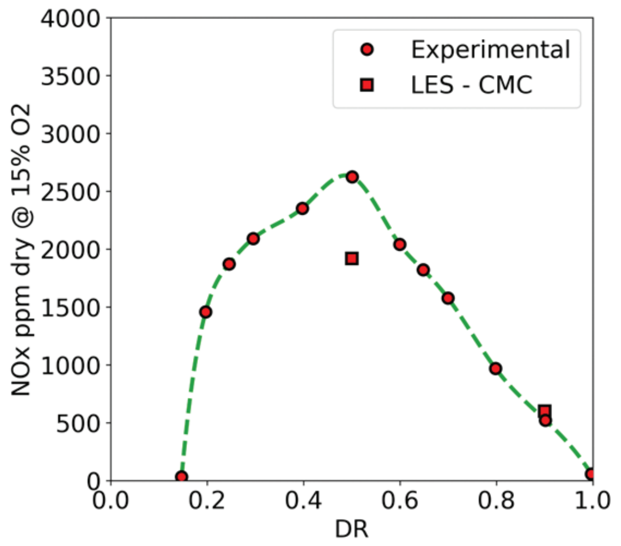


Figure 4.3: Exit NOx emissions for LES-CMC compared against the experimental results.

OTHER ACTIVITIES AND ACHIEVEMENTS

Dr B. HARIKRISHNAN (Research Fellow, CARES) presented “Modelling Ammonia Combustion to Power the Next Generation of Clean Energy” at the Singapore Scientific Conference on 9 December 2025.

Dr Harikrishnan was selected to participate in the Global Young Scientists Summit (GYSS). The 2026 edition welcomed its largest cohort yet, with over 400 young researchers from 57 countries gathering in Singapore to interact with Nobel Laureates and other researchers from a wide range of disciplines.

Dr Harikrishnan, top left, pictured with other international GYSS attendees.

SCIENTIFIC OUTPUT

The following are the CREATE-acknowledged publications generated by LCER Phase 2 during the reporting period.

Large Eddy Simulation of Dual-Fuel Swirl Flames

Harikrishnan, B., Savvas Gkantonas, and Epaminondas Mastorakos, Combustion Theory and Modelling

https://doi.org/10.1080/13647830.2026.2631715

Publications

ALL PUBLICATIONS WITH CREATE ACKNOWLEDGEMENT

Newly added publications for this reporting period are coloured in red. For a full record of earlier publications, please visit our Publications page on the CARES website

Centre for Lifelong Learning and Individualised Cognition (CLIC)

Friedman, N. P.; Robbins, T. W. The Role of Prefrontal Cortex in Cognitive Control and Executive Function. *Neuropsychopharmacol.* 2022, *47* (1), 72–89. https://doi.org/10.1038/s41386-021-01132-0.

Lee, L. Y.; Healy, M. P.; Fischer, N. L.; Tong, K.; Chen, A. S.; Sahakian, B. J.; Kourtzi, Z. Cognitive Flexibility Training for Impact in Real-World Settings. *Current Opinion in Behavioral Sciences* 2024, *59*, 101413. https://doi.org/10.1016/j.cobeha.2024.101413.

Leong, V.; Raheel, K.; Sim, J. Y.; Kacker, K.; Karlaftis, V. M.; Vassiliu, C.; Kalaivanan, K.; Chen, S. H. A.; Robbins, T. W.; Sahakian, B. J.; Kourtzi, Z. A New Remote Guided Method for Supervised Web-Based Cognitive Testing to Ensure High-Quality Data: Development and Usability Study. *J Med Internet Res* 2022, *24* (1), e28368. https://doi.org/10.2196/28368.

Melia, N.; Christopoulos, G.; Wigdorowitz, M.; Vassiliu, C.; Feng, S.; Abraham, A.; Chan, Y. N.; Lee, L. L.; Yap, H. S.; Robbins, T.; Sahakian, B.; Kourtzi, Z.; Leung, V.; Cheng, A.; Hendriks, H.; the CLIC Phase 1 Consortium. Validation of the CILD-Q for Measuring Contextual Linguistic Diversity in Singapore. *International Journal of Multilingualism* 2025, 1–18. https://doi.org/10.1080/14790718.2025.2570205.

Michael, E.; Covarrubias, L. S.; Leong, V.; Kourtzi, Z. Learning at Your Brain’s Rhythm: Individualized Entrainment Boosts Learning for Perceptual Decisions. *Cerebral Cortex* 2022, bhac426. https://doi.org/10.1093/cercor/bhac426.

Teo, L. Z.; Leong, V. Age-Appropriate Adaptation of Creativity Tasks for Infants Aged 12–24 Months. *MethodsX* 2024, *12*, 102655. https://doi.org/10.1016/j.mex.2024.102655.

Tong, K.; Fu, X.; Hoo, N. P.; Kean Mun, L.; Vassiliu, C.; Langley, C.; Sahakian, B. J.; Leong, V. The Development of Cognitive Flexibility and Its Implications for Mental Health Disorders. *Psychol. Med.* 2024, 1–7. https://doi.org/10.1017/S0033291724001508.

Vassiliu, C.; Leong, V.; Hendriks, H. The Influence of Multilingual Experience on Executive Function and Structure Learning: Effects in Young Adults in the UK and Singapore. *Languages* 2024, *9* (4), 136. https://doi.org/10.3390/languages9040136.

Yu, J.; Fischer, N. L. Asymmetric Generalizability of Multimodal Brain-behavior Associations across Age-groups. *Human Brain Mapping* 2022, 1–12. https://doi.org/10.1002/hbm.26035.

Yu, J.; Fischer, N. L. Age-specificity and Generalization of Behavior-associated Structural and Functional Networks and Their Relevance to Behavioral Domains. *Human Brain Mapping* 2022, *43* (8), 2405–2418. https://doi.org/10.1002/hbm.25759.

Registered Studies

Feng, Shengchuang, George Christopoulos, Henriette Hendriks, Nadhilla Melia, Yoke Sam, Hui Shan Yap, Ke Tong, et al. 2022. ‘Social Decision-Making and Its Association with Cognitive Flexibility in Healthy Young Adults’, July. https://doi.org/10.17605/OSF.IO/JB38T.

Melani, Irene, George Christopoulos, Henriette Hendriks, Shengchuang Feng, Yoke Sam, Nadhilla Melia, Hui Shan Yap, et al. 2022. ‘Cognitive Flexibility and Its Association with Linguistic Preferences, Decision-Making, Tolerance of Uncertainty and Perceived Social Support’, August. https://doi.org/10.17605/OSF.IO/AY9GR.

Melia, Nadhilla, George Christopoulos, Henriette Hendriks, Shengchuang Feng, Yoke Sam, Hui Shan Yap, Ke Tong, et al. 2022. ‘Tolerance of Uncertainty, Perceived Social Support, and Their Association with Structure Learning and Cognitive Flexibility in Healthy Young Adults’, August. https://doi.org/10.17605/OSF.IO/SCJMP.

Sam, Yoke, George Christopoulos, SH Chen, Shengchuang Feng, Irene Melani, Nadhilla Melia, Henriette Hendriks, et al. 2022. ‘Cognitive and Social

Aspects of Career Transition and Adaptation', August. https://doi.org/10.17605/OSF.IO/N352U.

Tong, Ke, Ryutaro Uchiyama, Shengchuang Feng, Xiaoqin Cheng, Kastoori Kalaivanan, Victoria Leong, George Christopoulos, et al. 2022. 'Assessing Cognitive Flexibility, Other Executive Functions, and Learning in Healthy Young Adults', August. https://doi.org/10.17605/OSF.IO/6RC9H.

Uchiyama, Ryutaro, Nastassja Fischer, Phillis Fu, Timothy Lee, Xiaoqin Cheng, Shengchuang Feng, Irene Melani, et al. 2022. 'Assessing Cognitive Flexibility, Other Executive Functions, and Learning in Healthy Adolescents', August. https://doi.org/10.17605/OSF.IO/MD4TV.

Research Protocol papers

Liu, Chia-Lun, Xiaoqin Cheng, Boon Linn Choo, Min Hong, Jia Li Teo, Wei Ler Koo, Jia Yuan Janet Tan, et al. 2023. 'Potential Cognitive and Neural Benefits of a Computerised Cognitive Training Programme Based on Structure Learning in Healthy Adults: Study Protocol for a Randomised Controlled Trial'. *Trials* 24 (1): 517. https://doi.org/10.1186/s13063-023-07551-2.

Tong, Ke, Yuan Ni Chan, Xiaoqin Cheng, Bobby Cheon, Michelle Ellefson, Restria Fauziana, Shengchuang Feng, et al. 2023. 'Study Protocol: How Does Cognitive Flexibility Relate to Other Executive Functions and Learning in Healthy Young Adults?' Edited by Avanti Dey. *PLOS ONE* 18 (7): e0286208. https://doi.org/10.1371/journal.pone.0286208.

PhD thesis

Sam, Yoke Loo. 'Socio-Cognitive Aspects of Career Transition'. Nanyang Technological University, 2024. https://hdl.handle.net/10356/184212.

Health-driven design for cities (HD_4)

T. H. Mina, P. R. Jain, N. G. Forouhi, and J. C. Chambers, "Adversity, adiposity, nutrition and metabolic well-being in multi-ethnic Asia," Nature Metabolism, vol. 8, no. 1, pp. 16–26, 2026. doi: 10.1038/s42255-025-01441-4.

X. Wang, T. Mina, N. Sadhu, et al., "The Health for Life in Singapore (HELIOS) Study: Delivering precision medicine research for Asian populations," Nature Communications, vol. 17, no. 1, 2025. doi: 10.1038/s41467-025-65774-0.

Xu, Lei, Ronita Bardhan, Hao Mei, Srilalitha Gopalakrishnan, Xing Zheng, and Thomas Schroepfer. 'Harnessing Street Shade to Mitigate Heat Stress: An in-Situ Parallel Investigation under Extreme Heat Conditions in Tropical Singapore'. *Science of The Total Environment* 958 (January 2025): 177864. https://doi.org/10.1016/j.scitotenv.2024.177864.

Y. Wang, P. Hamel, E. E. Ramsay, P. Liu, and R. Stouffs, "Impacts of building height and local climate zones on the performance of the In-VEST Urban Cooling model," IOP Conference Series: Earth and Environmental Science, vol. 1554, no. 1, p. 012 047, 2025. doi: 10.1088/1755-1315/1554/1/012047

Sustainable Manufacture of Molecules and Materials in Singapore (SM_3)

Tan, Eugene Yew Kun, Tian-Yu Peng, Taku Wakabayashi, and Shunsuke Chiba. 2026. 'Peripheral Aryl Group Transposition on Pyridines Using Photoredox Catalysis'. *Nature Synthesis*, ahead of print, March 4. https://doi.org/10.1038/s44160-026-01023-6.

Xu, Shuguang, Jianmei Li, Jiong Cheng, et al. 2025. 'Single Atom–Cluster Synergy in Ag Catalysts Enables Chiral Glyceric Acid from Biomass'. *Science Advances* 11 (47): eadz4136. https://doi.org/10.1126/sciadv.adz4136.

Zhou, Qian-Yi, Daniel Zhi Wei Ng, Jun Wu, et al. 2026. 'Photocatalytic Coupling of Unprotected Sugars and N-Heteroarenes'. *Nature Synthesis*, ahead of print, January 19. https://doi.org/10.1038/s44160-025-00980-8

PIPS

Hao, Zhimian, Magda H. Barecka, and Alexei A. Lapkin. 2022. 'Accelerating Net Zero from the Perspective of Optimizing a Carbon Capture and Utilization System'. *Energy & Environmental Science*, March, 10.1039. D1EE03923G. https://doi.org/10.1039/D1EE03923G.

Jeraal, Mohammed I., Simon Sung, and Alexei A. Lapkin. 2020. 'A Machine Learning-Enabled Autonomous Flow Chemistry Platform for Process Optimization of Multiple Reaction Metrics'. *Chemistry–Methods* 1 (1): 71–77. https://doi.org/10.1002/cmtd.202000044.

Karan, Dogancan, Guoying Chen, Nicholas Jose, Jiaru Bai, Paul McDaid, and Alexei A. Lapkin. 2024. 'A Machine Learning-Enabled Process Optimization of Ultra-Fast Flow Chemistry with Multiple Reaction Metrics'. *Reaction Chemistry & Engineering* 9 (3): 619–29. https://doi.org/10.1039/D3RE00539A.

LCER Phase 2

Harikrishnan, B., Savvas Gkantonas, and Epaminondas Mastorakos. 2026. 'Large Eddy Simulation of Dual-Fuel Swirl Flames'. *Combustion Theory and Modelling*, February 22, 1–23. https://doi.org/10.1080/13647830.2026.2631715

CAMBRIDGE
CARES

cares.cam.ac.uk