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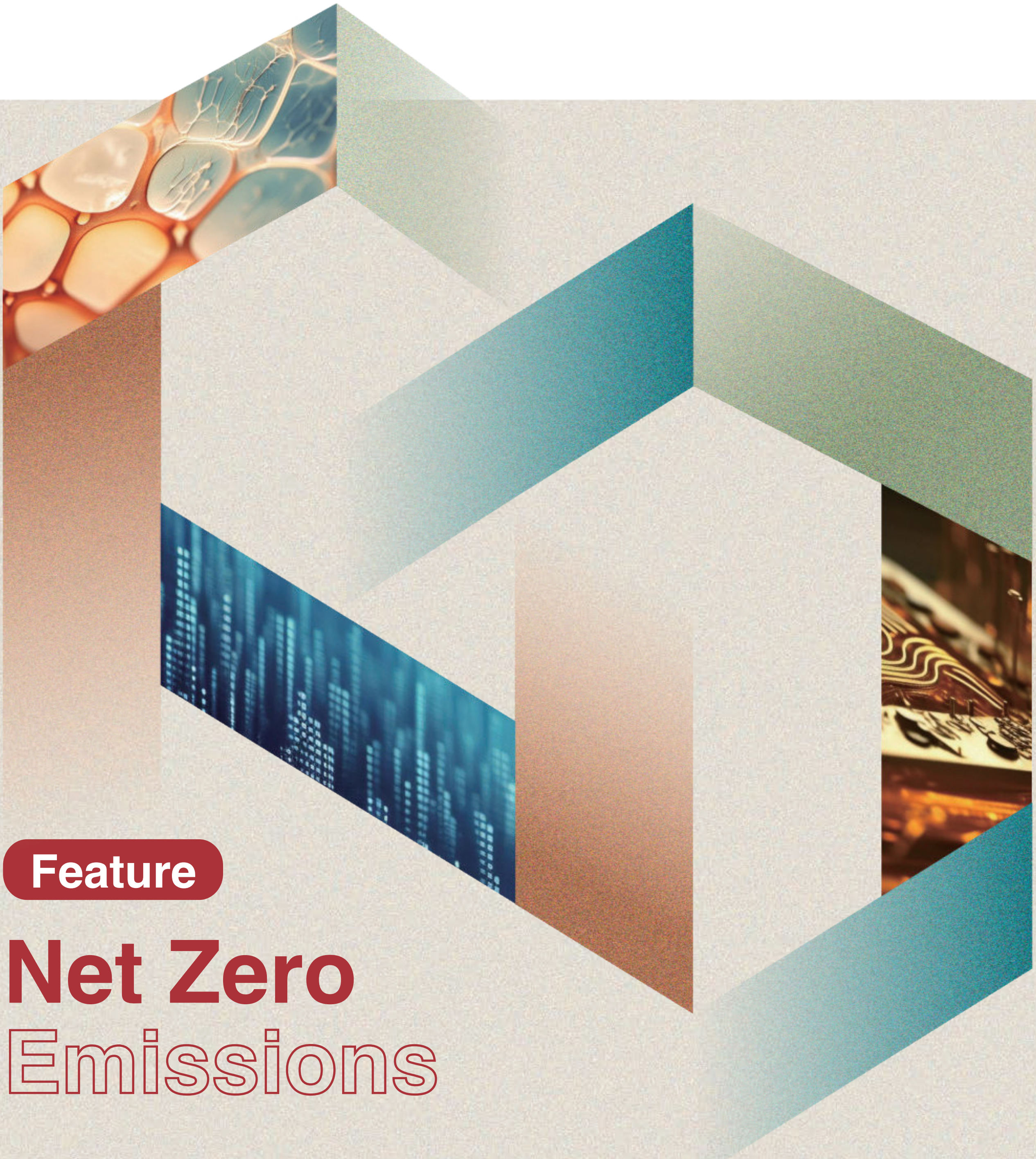
NATIONAL CHENG KUNG UNIVERSITY

RESEARCH DIGEST



Feature

Net Zero Emissions

Issue 2

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Entropied Green Hydrogen

From Photosynthetic Carbon Capture to SuperLubricants

Dr. Yeau-Ren Jeng
University Chair Professor
National Cheng Kung University

Professor Yeau-Ren Jeng is a renowned scholar specializing in Tribology. He brings Tribology to manufacturing, metrology, biomaterial, and nano-mechanics through multi-scale and interdisciplinary approaches. He serves as a University Chair Professor at National Cheng Kung University in Biomedical Engineering. Currently, he focuses on SDG (Sustainable Development Goal) issues with mechanochemistry and mechanobiology approaches, including biodiversity, carbon capture and utilization, and green manufacturing.

As a leader in university-industry collaborative research, he has significantly benefited multiple industries, including automotive, electronics, material, manufacturing, electronic, and nano-related industries. He has successfully led several interdisciplinary, multinational research projects sponsored by funding agencies worldwide. Professor Jeng was on the advisory board of the university administration of several eminent universities in Taiwan.

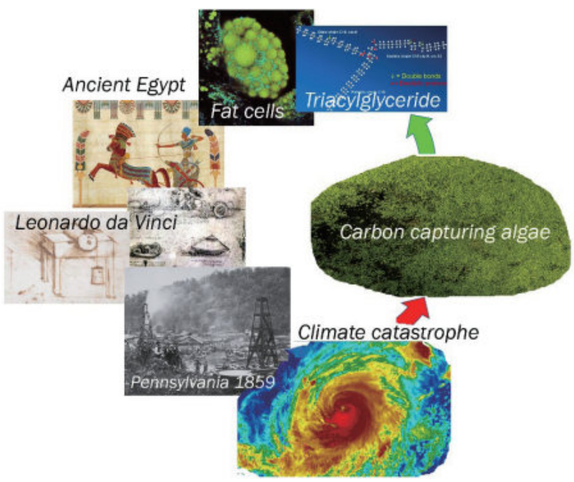
Yeau-Ren Jeng,
University Chair Professor

Humanity has been using lubricants for millennia to make our world run smoothly. For example, in ancient times, plant-oil lubricants were used to ease the movement of megalithic blocks to make some of the iconic structures, like The Pyramids, which still stand and inspire us today. On a smaller scale, animal fats with calcium salts were used to grease the axles of ancient chariots.

Even Leonardo da Vinci turned his thoughts to understanding lubricants, no doubt to harness them for use in his architectural building plans or for helping his war machines to operate.

In these early days of the development of the lubricant industry, the most available source of oil and grease was the triacylglycerides that animals and plants produce as a form of long-term energy storage that living organisms can later consume to maintain life. Triacylglycerides are so fundamental that they are even used by bacteria, such as deadly TB bacilli, to sustain long-term survival in a victim's lungs, ready to re-emerge and strike when the victim is in an immunocompromised state. The takeaway is that triacylglycerides can usually be found where there is life. When they are located, humans have been able to use them to smooth the running of their world as fuels and lubricants.

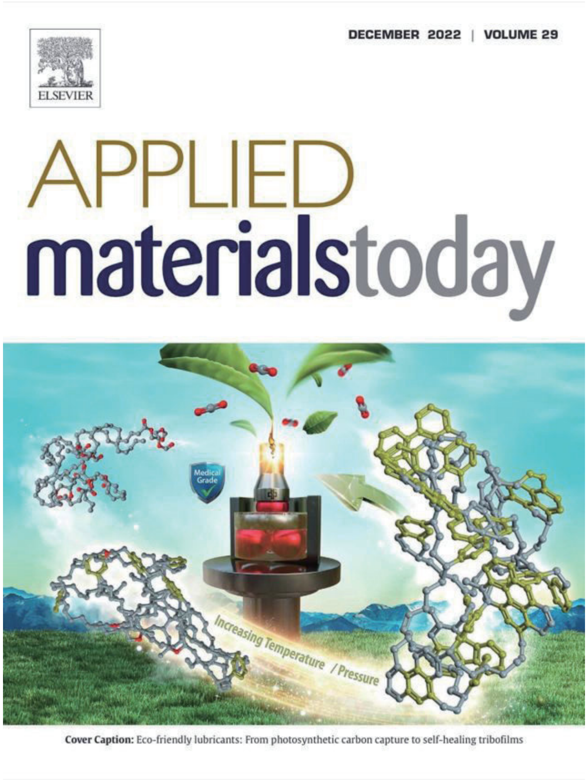
In the millennia of lubricant use, a momentary blip was the discovery of large reserves of mineral oils, starting with the repositories in Pennsylvania in 1859. From this time on, large-scale extraction of mineral oils occurred to supply industrial demands, with such large volumes being exhumed that lubricants and fuels have evolved into the environmental disaster of climate change and extreme weather. The central part of the global economy's current ecological problems stems from discovering and exploiting mineral oil reserves, so we realize that we must stop extracting and burning off our fossil oils for fuels and lubricants. However, we still need the energy that can be extracted from fats, and we still need the lubricants. Hence, we need to find another way to supply these requirements. One way that was explored was to use terrestrial plant-based sources of oil, such as palm oils. But this leads to the destruction of rainforests to plant oil palms. Furthermore, land-based oil-producing plantations compete with food production, causing inflationary effects in global food markets and further pegging food prices with fuel prices.



A more recent and less problematic solution is to take the triacylglycerides production offshore by growing oil-producing algae, which capture carbon already in the atmosphere and photosynthesize it into carbon biomass, including valuable oils for fuels and lubricants. In this way, we hope that the lubrication industry can come full circle and again use the ancient oils produced offshore on a modern industrial scale, returning us to a carbon-neutral state that avoids us burning off our fossil hydrocarbon supply.

Of course, there are some problems to overcome, and that is where our research comes in. The significant issues that we encounter are historical rather than technological. The modern industrial age developed alongside fossil fuel technologies. Hence, the additives we have developed to enhance our oils for the demands of contemporary industry are all specifically designed to work with mineral oils and synthetic analogs. But the current markets are evolving, and the motors driving our economy are changing. This had happened before as we changed from coal-fired steam-driven engines to diesel and gasoline-fired internal combustion engines. We are changing to electric vehicles again, so we have to reconsider our lubricant options. The time is perfect to re-examine triacylglycerides to see if they can be made to operate as high-performance lubricants for the modern age of electric motors and solar power.

Two triacylglyceride problems must be overcome, and we are on the way to solving these. Firstly, they are chemically unstable and tend to react at their chain double bonds. So, we need to slow down these reactions with antioxidant additives. Secondly, tribofilm-forming additives for triacylglycerides are unavailable to form protective films on rubbing surfaces. Historically, the available film-forming additives have all been developed for mineral oils. But once again, we can take our inspiration from ancient Asian cooking skills handed down through time. Every matriarch in Asia knows how to condition a wok to generate a non-stick property suitable for cooking. Well, this working conditioning technology relies on the reactivity of the conditioning oils to form carbon networks due to heat-initiated reactions of the triacylglycerides chain double bonds. Triacylglycerides can create protective tribofilms by thermal reactions caused by heat or friction. The research we are conducting is to optimize these film-forming reactions while suppressing the decomposition rate so that the useful life of the oils is optimized. We are developing our oil formulations for triacylglycerides derived from carbon-capturing algae that can grow offshore. This kind of research is essential to reverse the effects of climate change while supporting the lubricant needs of the modern era.



Toward Carbon Neutrality and Obtain High-Value Chemical Using Synthetic Biology Technology

—— I-Son (Grace) Ng, Professor

Professor I-Son (Grace) Ng currently serves in the Department of Chemical Engineering at National Cheng Kung University. She is a top scholar in synthetic biology research and has led NCKU students to achieve 7 iGEM gold medals and the world championship in 2019. Her group focused on CRISPR gene editing technology to modify microalgae and microbial metabolic pathways, which is dedicated to the development of high-value chemicals for carbon neutrality. She has received the University Innovation and University Social Responsibility Teaching Excellence Awards for four consecutive years (2020, 2021, 2022, 2023), NCKU College of Engineering Research Excellence Award (2021), the Outstanding Female Chemical Engineer Award from the Taiwan Institute of Chemical Engineers (2022), and the Outstanding Female Chemical Engineer Award from the Biotechnology and Biochemical Engineering Society of Taiwan (2023).

With the rise of Sustainable Development Goals (SDGs), chemical engineering has entered a new era of “green manufacturing”, representing an opportunity to embrace the Fourth Industrial Revolution. In response to climate change and the greenhouse effect, achieving net-zero emissions and carbon-neutral technology has become a globally prominent and critical issue in recent years.

Professor Ng's Functional Genes and Proteomics Lab is dedicated to exploring new genes, optimizing gene pathways, and developing new technologies to attain carbon-neutral production of high-value chemicals. Within this, synthetic biology technology provides as the core methodology, employing the"Design-Build-Test-Learn" cycle for continuous improvement. This process enables the bottom-up construction of engineered strains, leading to the creation of more precise and efficient intelligent cell factories (as shown in Figure 1). These advancements can be applied across various aspects such as biomedicine, fine chemicals, food ingredients, bioenergy, biomaterials, biosensors, environmental restoration, and other areas, addressing a wide range of needs in daily life.

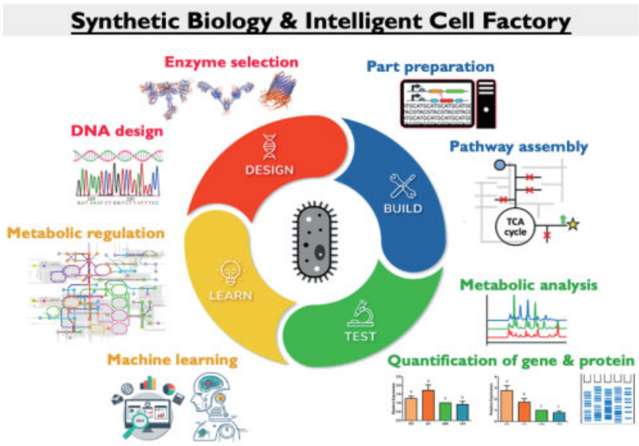


Figure1 Design and Application of Intelligent Cells Using Synthetic Biology

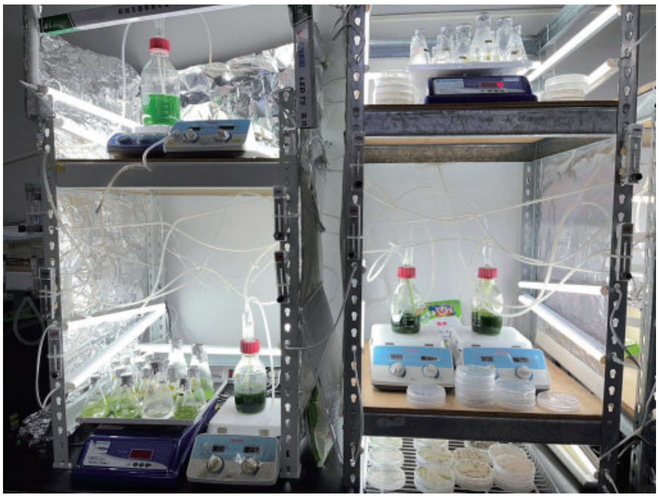


Figure 2 Cultivation of Microalgae in Shake Flasks and Autotrophic Device.

Figure 3 Cultivation of Microalgae Using Direct Air Capture and Wavelength Effects of Light.

In pursuit of the national goal of net-zero carbon emissions by 2050, Professor Ng has integrated the research and development capabilities of the Department of Chemical Engineering at our university, the discipline of Industrial Hygiene and the Institute of Environmental Medicine, as well as the Department of Biotechnology and Food Technology at Southern Taiwan University of Science and Technology. Under the theme of "Innovative Microalgae Engineering Technology for Direct Air Carbon Capture and Usage & High-Density Cultivation Process Development," Professor Ng has secured the project from the Engineering Division of the National Science and Technology Council (NSTC) focused on Net Zero Emissions. The objective is to promote technological synergy, foster research innovation, and cultivate top-notch experts in carbon neutrality. This initiative aims to establish a strong link between academia and industry, realizing the social responsibilities of both universities and businesses.

Due to its rich composition of compounds, including carbohydrates, pigments, lipids, and proteins, microalgae biomass has become one of the raw materials for biofuels and renewable substitute chemicals, owing to its high growth rate, high lipid productivity, and carbon sequestration capabilities. Currently, the algal species available for bioenergy include

Chlamydomonas, Scenedesmus, Chytrid algae, Chlorella species, and cyanobacteria. Compared to other biofuels, microalgae offer the advantage of not competing with food crops or arable land, thriving in seawater, industrial, or domestic wastewater [1]. Therefore, microalgae are considered environmentally friendly resources that effectively mitigate greenhouse gas emissions, estimated to account for 40% of global carbon sequestration.

Based on microalgae carbon capture technology, Professor Ng's team has developed over 20 native and genetically modified microalgae strains over the past nine years, focusing on three core areas: (1) circular economy and carbon-neutral technology, (2) CRISPR/Cas9 gene editing, and (3) synthetic biology technology for green biomanufacturing. Notably, CRISPR/Cas9 technology received the Tang Prize in 2016 and the Nobel Prize in Chemistry in 2020, making it the most effective gene-editing technology today. In 2017, her team successfully completed the first CRISPRi gene interference in *Chlamydomonas reinhardtii*, marking the first application of CRISPRi for gene regulation in *Chlamydomonas* both domestically and internationally, resulting in a 174% increase in lipid content [2]. In 2019, her team further applied CRISPR/Cas9 technology to complete the gene editing in *Chlorella,* enhancing the efficiency of carbon sequestration and protein yield [3]. Currently, the team is selecting suitable algal strains from their accumulated library, adjusting airflow rates and employing strategies involving different wavelengths to further advance negative carbon capture and utilization through direct air capture methods.

A significant global challenge is how to mitigate greenhouse gas emissions. The goal of achieving net-zero carbon emissions requires the establishment of carbon footprint control and negative carbon emission technologies. The final destination is to gradually reduce carbon dioxide from the current atmospheric concentration of 420 ppm to levels below 300 ppm.

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Entropied Green Hydrogen

Dr. Siang-Yun Li
Jyh-Ming Ting
Distinguished Professor

Dr. Siang-Yun Li

Prof. Jyh-Ming Ting

Author Introduction

Dr. Siang-Yun Li is a postdoctoral researcher at Prof. Jyh-Ming Ting's lab in the Department of Materials Science and Engineering, National Cheng Kung University. Dr. Li's research expertise spans nanocomposite materials, thin films, green energy, and high-entropy materials. Employing Sophisticated techniques like magnetron sputtering, he fabricates various nanomaterials and films, delving into the microstructure, growth mechanism, and physicochemical properties to unlock the hindered potential and broaden the applications.

Prof. Jyh-Ming Ting possesses extensive knowledge of various metals, oxides, nitrides, sulfides, and phosphides. In recent years, he has pioneered the development of innovative high-entropy materials, encompassing both alloys and oxides, with particularly noteworthy results in high-entropy catalysts.

Moving forward, Professor Ting's team is ardently dedicated to enhancing energy efficiency, energy storage, and sustainable energy infrastructure, laying a strong foundation for continued research and innovation.

This article

Energy holds a pivotal position to be a crucial driving force for human societal progress. For a long time, traditional fossil fuels have been the primary source of energy, leading to several severe issues. On one hand, traditional fossil fuels, being non-renewable, cannot meet the sustainable development needs of human society. On the other hand, excessive fossil fuel consumption emits greenhouse gases, which have detrimental effects on the global ecological environment. Thus, the development of clean and efficient renewable energy technologies to achieve human sustainability has become a consensus among nations worldwide. Energy transition is an essential choice for sustainable socio-economic development. Enhancing the proportion of renewable energy and vigorously promoting the development of wind and solar power are vital measures for achieving a green energy transition and low-carbon development. However, both wind and solar energy are discontinuous and unstable, making them difficult for direct integration into the grid. To effectively utilize the dispersed and low-density energy sources, developing large-scale electrical energy conversion and storage technologies holds strategic importance.

The global demand for hydrogen exceeded ninety million tons in 2021, and it's projected to grow to five hundred to six hundred and eighty million tons by 2050. Currently, 96% of hydrogen is sourced from steam methane reforming or coal gasification, resulting in significant carbon dioxide emissions. To achieve the goal of zero emissions by 2050, the development of environmentally friendly and sustainable alternative energy technologies to produce green hydrogen is of paramount importance. Electrolysis of water, powered by renewable energy sources, offers a promising emission-free method for producing green hydrogen. Electrolysis or electrochemical water splitting is a process that uses electricity to transform water ($H2O$) into oxygen ($O2$) and hydrogen ($H2$). This involves two half-cell reactions: the oxygen evolution reaction (OER) at the anode and the hydrogen evolution reaction (HER) at the cathode. These reactions can be achieved through various methods such as high-temperature electrolysis (HTE), photoelectrochemical electrolysis (PECE), conventional alkaline water electrolysis (AWE), proton exchange membrane water electrolysis (PEMWE), and anion exchange membrane water electrolysis (AEMWE).

OER has a pivotal role in renewable energy technologies, such as hydrogen-oxygen electrolyzers, solar fuel cells, and rechargeable metal-air batteries. Due to its sluggish kinetics, OER becomes the bottleneck in electrochemical water splitting. While noble metal oxides like $IrO2$ and $RuO2$ are recognized as the state-of-the-art OER electrocatalysts, their scarcity, high cost, and limited durability pose significant constraint their applications. A pressing challenge remains to find alternative precious-metal-free and cost-effective catalysts that exhibit high OER activity and stability. It's understood that OER is a heterogeneous process, taking place on the catalyst surface. To improve the OER activity, one of the most effective strategies involves altering the surface electronic structure. Doping a primary material has proven to be an effective method for this aim. Consequently, multi-metal materials, particularly high entropy materials, have garnered considerable interests, as they offer a vast range of characteristics and potential for improved catalytic performance. Based on these reasons, Dr. Li and Prof. Ting have used high entropy alloys to develop a new type of thin film catalyst," As reported in "Sputter-deposited high entropy alloy thin film electrocatalyst for enhanced oxygen evolution reaction performance. Table of contents (TOC) as show in Figure 1. [S. Y. Li, T.X. Nguyen, Y.H. Su, C.C. Lin, Y.J. Huang, Y.H. Shen, C.P. Liu, J.J. Ruan, K.S. Chang, and J.M. Ting, "Sputter Deposited High Entropy Alloy Thin Film Electrocatalyst for Enhanced Oxygen Evolution Reaction Performance." Small, 2106127, (2023).]

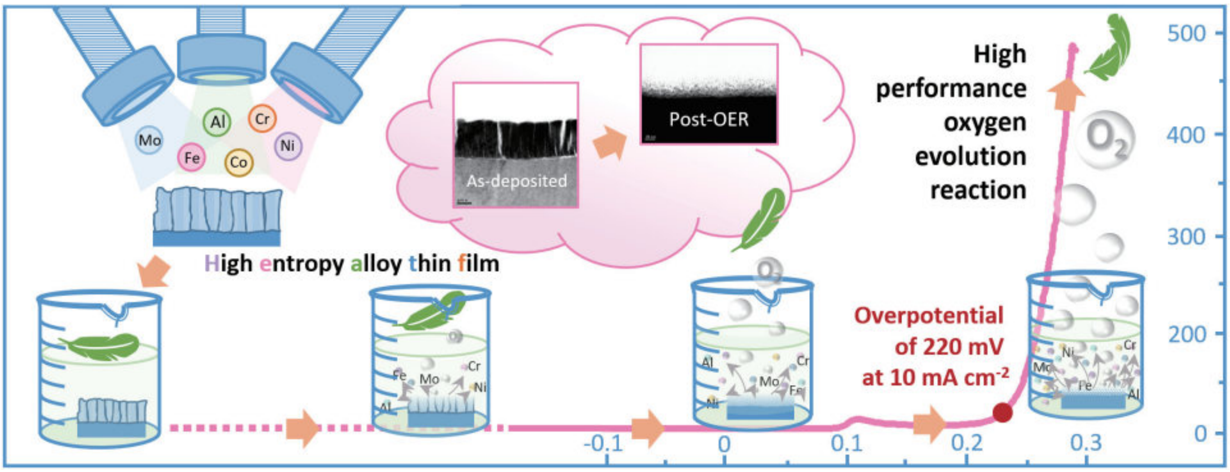

Figure 1. Paper table of contents. (Paper 摘要圖)

In this study, a thin film catalyst with its unique morphology, provides notable benefits over conventional catalyst particles in gas evolution reactions. Leveraging the merits of sputter deposition, Dr. Li presents a high entropy alloy (HEA) thin film as an electrocatalyst for OER. He has investigated the characteristics of the HEA catalyst, examined the catalysts throughout the OER process, either in-situ or ex situ. In the study, they also prepared and assessed unary, binary, ternary, and quaternary thin film catalysts for a comprehensive comparison. Modifications in the surface electronic structure due to metal addition were analyzed both experimentally and theoretically (density function theory calculation). Dr. Li found that the sputtered quinary HEA thin film showcases OER performance that surpasses other known HEA catalysts, giving a low overpotential of 220 mV at 10 mA cm-2 and excellent electrochemical stability at different constant current densities of 10 and 100 mA cm-2 for 50 h (Figure 2). Quinary HEA is the best alloy catalyst and displays consistent electrocatalytic activity and exceptional electrochemical stability.

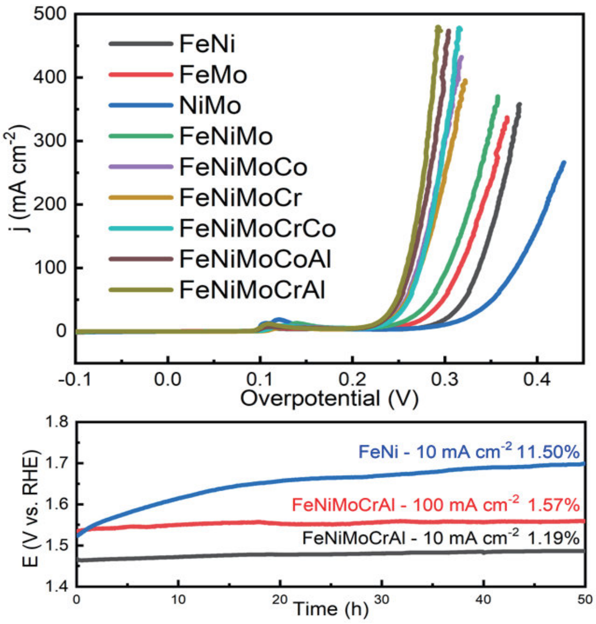

Figure 2. LSV curves and long-term durability tests of FeNi at 10 mA cm-2 and FeNiMoCrAl at 10 mA cm-2 and 100 mA cm-2. (FeNi 在 10 mA cm-2 下以及 FeNiMoCrAl 在 10 mA cm-2 和 100 mA cm-2 下的 LSV 曲線和長期耐久性測試)

Moreover, Dr. Li studied the microstructural chnages during the OER for better understanding of the mechanism involved for the HEA electrocatalyst. As shown in

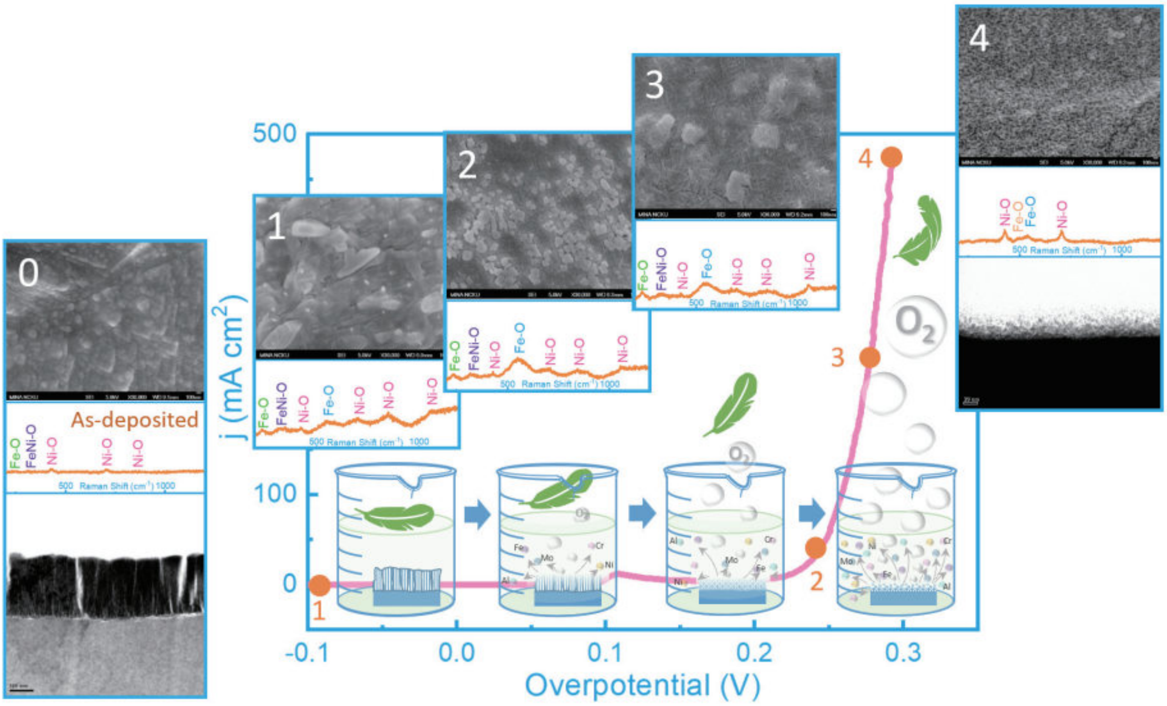

Figure 3. Phase transformation and structural evolution during OER. (OER 反應中的相變和結構演化)

Figure 3, the initially deposited amorphous quinary thin film shows a columnar structure, consisting of nodulate-like grains. Additionally, there are noticeable surface oxides of Ni and Fe at this stage (Stage 0). When a potential is applied (Stage 1), these nodulate-like grains begin to stretch, and an increase in oxides is seen, as evidenced by the SEM image and Raman data. Just after reaching the on-set voltage (Stage 2), these elongated grains fracture into smaller particles, accompanied by a surge in oxide formation. This discovery holds promise for advancements in catalyst design in the future.

In the diverse space of entropy and countless changes in electronic structure, disorder is a result of returning to nature. Without external intervention, chaos is eternally stable. Lastly, let's use a lighthearted poem to guide everyone in understanding the essence of high entropy materials and green hydrogen.

Green energy guards our Earth's song,
Sustainable visions, globally strong.

Transitioning, cutting carbon, policies in line,
Pure power advances, with green hydrogen prime.

Entropy swirls, in an endless dance,
With green hydrogen's catalyst, taking its chance.

Alloys so potent, entropy's reign,
In entropy's vast world, no bounds remain.

- Entropied Green Hydrogen / Siang-Yun Li-

SPECIAL REPORTS

Ta-You Wu Memorial Award From National Science and Technology Council

Yen-Chin Chen, Associate Professor

Pei-Fen Kuo, Associate Professor

Ting-Yuan Tu, Associate Professor

Sleep Disturbances are common complains in the Older Population

Yen-Chin Chen,
Associate Professor

AUTHOR INTRODUCTION

Dr. Yen-Chin Chen is associated with National Cheng Kung University (NCKU) Hospital, currently serving as the Chief of Research, Innovation, and Evidence-Based Practice within the Nursing Department. Furthermore, Dr. Chen holds the position of Clinical Assistant Professor in the NCKU Nursing Department. Her expertise spans various domains, including adult nursing, infectious disease care, evidence-based healthcare, sleep nursing, and oral health. She earned her doctoral degree from the International Doctoral Program in Nursing (IDPN) at National Cheng Kung University in 2018. She received a scholarship from the Taiwan Ministry of Education's Taiwan Scholarship Program, allowing her to engage in a one-year academic exchange at the department of Engineering, University of Pittsburgh in the United States during 2016-17. Dr. Chen has contributed significantly to the sleep care field through her numerous high-quality academic research publications, which have found practical applications in clinical care.

Sleep Disturbances are common complains in the Older Population

Aging is often accompanied by changes in sleep structure and physiological rhythms. Frequent brief awakenings and early morning awakenings are the most common sleep disorders reported by older adults [1]. According to a comprehensive meta-analysis finding that included 47 studies, 35.9% (30.6-41.2%) of older adults have experienced sleep difficulty including sleep onset or maintenance [2]. In Taiwan, 53.14% of older people has reported poor sleep quality based on Chinese version of Pittsburgh sleep quality index greater than 5 points and equal [3]. Several potential factors contribute to declining sleep quality in older individuals, including multimorbidity, polypharmacy, and psychosocial factors [4].

Practical Guidelines for Non-Pharmacological Interventions to Improve Sleep in Older Adults Still Lacking

In the quest for swift relief from insomnia, older adults often resort to sedative-hypnotic medications to facilitate sleep onset. According to Nguhen KL (2020), findings from the 2011 National Health and

Aging Trends Study (NHATS) revealed that 30.18% of Americans aged 65 and older use hypnotic medications [5]. A study conducted by Mokhar et al. (2018) investigated a random sample of 340 older adults covered by one health insurance plan who had received prescriptions for benzodiazepines (BZDs) and z-drug within the past 12-month. The finding revealed that commonly used substances among older people in Germany were zopiclone (38.1%), oxazepam (18.1%, and lorazepam (13.8%) [6]. Despite the prevalance of pharmacological treatments in managing sleep difficulties [7], prolonged use of sedative-hypnotic medications not only contributes to memory impairment and delirium in older adults but also elevates the risk of accidents such as falls and fractures [5; 8].

Numerous studies have explored non-pharmacological interventions, including exercise [9], cognitive-behavioral therapy [10], aromatherapy [11], massage [12], acupressure [13], foot baths [14], and more, as effective means to alleviate insomnia in older adults. However, a comprehensive clinical care guideline for non-pharmacological approaches remains deficient. Moreover, there is a lack of empirical evidence regarding their practical implementation in clinical settings.

Academic Research Outcomes

In response to the aging population, under the recommendation of senior mentors, I took on the role of convener for the Sleep Health Group in 2021. Subsequently, we integrated multidisciplinary physicians, including sleep medicine center, otolaryngology, pulmonology, family medicine, psychiatry, neurology, and rehabilitation medicine, to establish a comprehensive care team for sleep care in the older adults (see Figure 1).

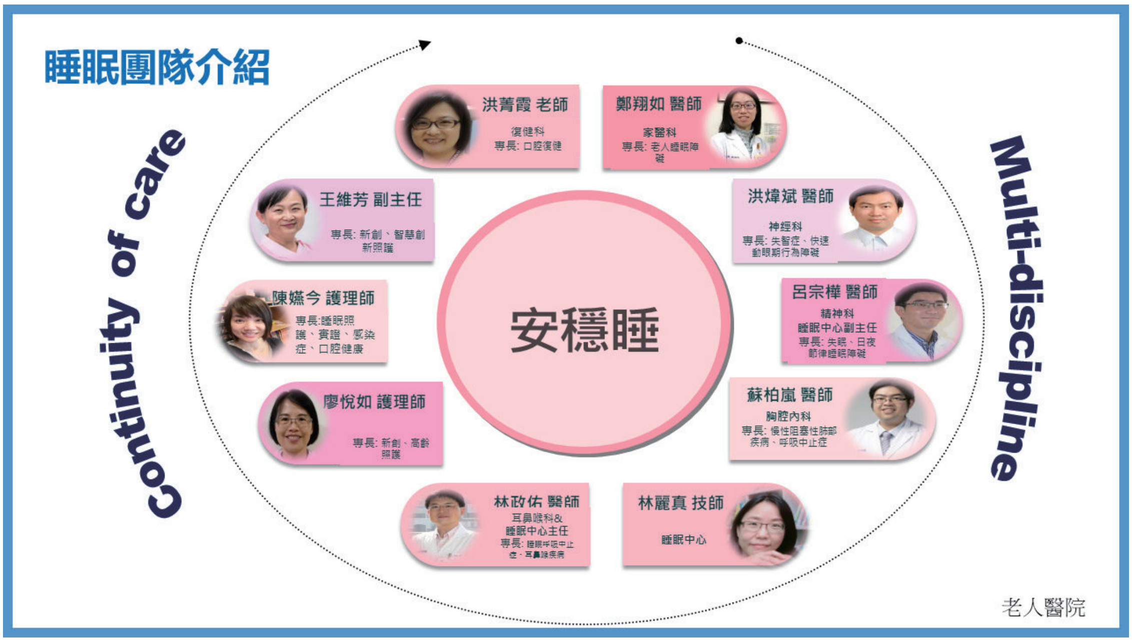

Figure 1. Sleep care team for older adults with sleep disturbances

We also conducted a rigorous systematic review method to develop clinical practice guidelines for non-pharmacological interventions in the management of sleep disturbances in older adults [15]. These guidelines were applied to general internal medicine wards, providing guidance to healthcare professionals on understanding the causes of sleep disorders and how to implement non-pharmacological interventions, such as massage and music therapy. The content of practice guideline has also been translated into a sleep health education leaflet for older adults (see Figure 2).

Figure 2. Sleep health education leaflet for older adults

A nurse-led sleep health education and consultation clinic operates within the outpatient department, catering to older adults who experience sleep disturbances. Recognizing that older individuals often bear the burden of poly pharmacy and comorbidities. We initiated the development of non-pharmacological intervention strategies. These strategies included a simplified 4-week behavioral intervention program implemented in the clinical setting, which is founded on a comprehensive systematic review [16] (see Figure 3). To date, this non-pharmacological sleep health education and counseling clinic has provided services to over a hundred and fifty patients. Our preliminary clinical trial results (Protocol ID: A-ER-112-175) indicated that a four-week brief behavioral intervention could reduce the severity of insomnia from an average of 15.54 points to 10.54 points on the insomnia severity scale (F= 6.753, p=

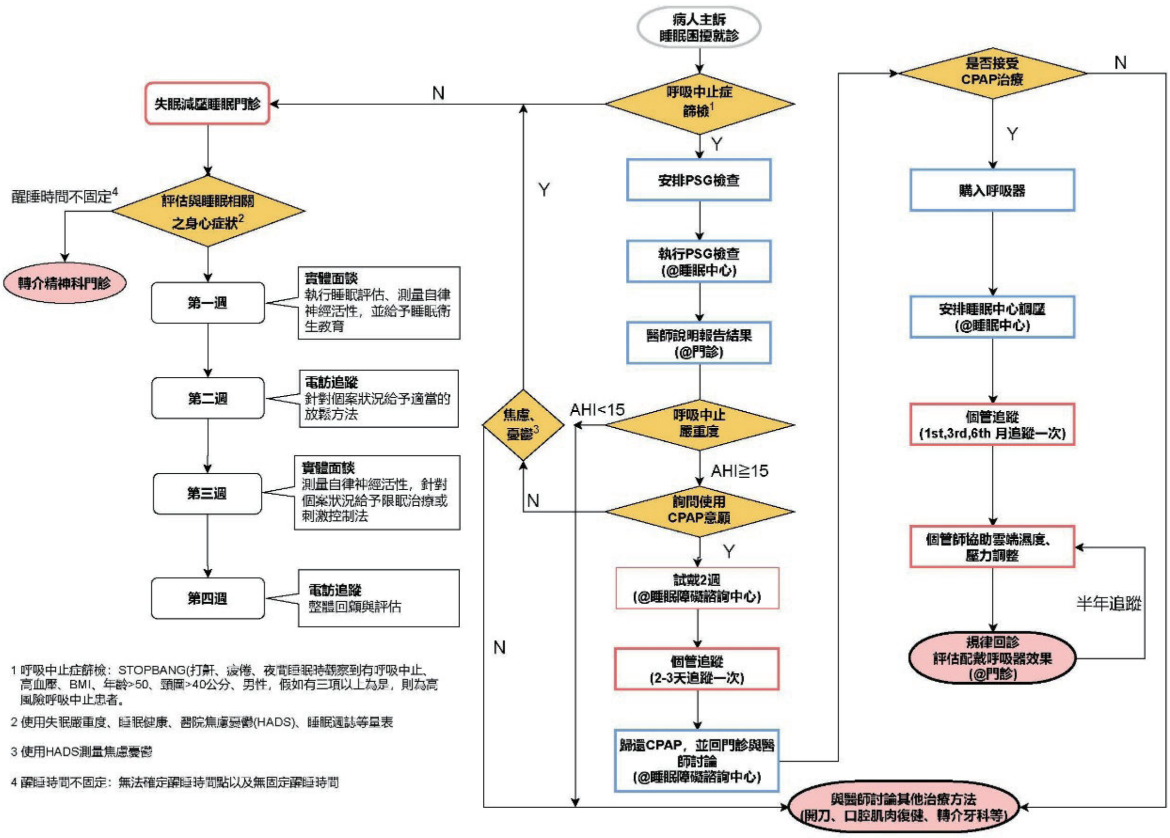

Figure 3. Clinical sleep care protocol

0.001). Furthermore, there was a significant decrease in the mean anxiety score over the four weeks, declining from 8.67 to 6.17 points (F= 3.622, p= 0.023). However, there was no significant difference observed in the depression measure (F= 0.455, p= 0.716).

Addressing concerns about potential addiction to sleep pills among patients, our clinic conducts sleep assessments to identify core issues and gradually improve sleep conditions through non-pharmacological strategies. Our achievements have been published in the NCKU Hospital e-newsletter [17] and various promotional platforms. Additionally, we have been featured in TVBS interviews [18].

Conclusions

We maintain ongoing collaborations with multidisciplinary professionals, including physicians, rehabilitation therapists, and technologist of sleep medicine center, to align with the evolving care needs of the older population. Our objective is to gradually standardize and systematize sleep care practices. The ultimate goal is to expand these initiatives to satellite hospitals affiliated with NCKU Hospital, such as Douliu Hospital (斗六醫院) PUZI Hospital (朴子醫院) and Kao General Hospital (郭綜合醫院). In the future, non-pharmacological interventions will be prioritized as the first-line approach for addressing sleep problems in older adults.

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National Cheng-Kung University - Spatial Social Science Lab

Bio

Pei-Fen Kuo, Ph.D., is an Associate Professor in the Department of Geomatics at National Cheng Kung University in Taiwan. She has been awarded the 2023 Ta-You Wu Memorial Award from the National Science Council. Dr. Kuo's research centers on applying spatial statistics, GIS, and data mining in the realms of traffic safety, crime data analysis, and policy evaluation. Over the past five years, she has served as the Principal Investigator (PI) and Co-Principal Investigator (Co-PI) for more than 20 research projects in Taiwan. The total research funding is nearly 20 million NTD.

Dr. Kuo earned her Ph.D. in the Transportation Engineering Program at Texas A&M under the supervision of Dr. Dominique Lord. Furthermore, she worked as a postdoctoral researcher for the Texas Department of Transportation (TxDOT) and collaborated with Dr. Mohamed Abdel-Aty at the University of Central Florida.

—— Pei-Fen Kuo,
Associate Professor

In our lab, we are dedicated to exploring spatial data, spatiotemporal techniques, and cutting-edge technology to unravel the intricate interactions between human spatial behavior and their environment. Our primary mission is to enhance both traffic safety and efficiency through our research endeavors.

Over the past five years, our research has covered a diverse range of topics, including traffic safety, human travel behavior, movement patterns, spatiotemporal crime trends, and strategies to mitigate air pollution. We employ various sophisticated research methodologies, including spatial statistical models, spatiotemporal data analysis, and trajectory data examination.

Our innovations can be categorized into three fundamental areas:

Perspective Innovation: We have shifted from macro-level to micro-level analysis by utilizing raw disaggregated accident data, increasing precision, and eliminating aggregation errors often associated with the Modifiable Area Unit Problem (MAUP).

Methodology Innovation: We continuously seek to enhance existing methodologies by drawing from other research fields and pioneering their application in traffic safety.

Application Innovation: We prioritize

producing visual and quantitative results with practical implications that can be applied in real-world situations.

Our research contributions include the use of micro-level data for precise analysis, refinement of existing methodologies to quantify spatial relationships, and the provision of clear definitions for problem hotspots through visual representations.

Let's delve into some recent research endeavors:

Spatial Colocation[1]: This study investigates the spatial proximity of accident sites with varying degrees of injury severity. We employ the Colocation Quotient to examine the spatial proximity of accident sites sharing the same severity level from a micro-level perspective. This research marks the first application of this method in the context of traffic safety, departing from its previous use in different contexts. The results reveal a pattern where accident sites with equivalent injury severity levels tend to cluster together, providing valuable insights for future traffic engineering enhancements.

Spatial Variation[2]: Our second paper explores the correlation between accident-prone areas and environmental factors, specifically focusing on incidents related to drunk driving, crimes, and the presence of drinking establishments. We employ kernel density maps and color addiction theory overlay to identify shared hotspots for these incidents, enhancing our understanding of their spatial variations. This research represents a pioneering advancement in traffic safety analysis, extending the analysis from two variables to three, encompassing a broader spectrum of uncertainty and risk factors.

Point pattern[3]: The third paper investigates how the spatial distribution of fatal traffic accidents has changed before, during, and after economic recessions. We employ the Spatial Point Pattern Test (SPPT) to assess the spatial similarity of traffic fatalities across these economic periods. This innovative approach offers new insights into the relationship between economic recessions and fatal accidents, enabling precise identification of specific locations where these changes occur.

Beyond focusing on traffic safety, our laboratory applies spatial analysis methods to examine human transportation behavior. We have made significant contributions to innovative target analysis and methodological innovations in diverse research areas, including assessing the impact of virtual reality activities on transportation usage and gathering pandemic data through web scraping.

Innovative Target Analysis: We have transitioned from traditional point data to origin-destination (OD) traffic flow data, providing more information closely aligned with the real world. Our applications include assessing the impact of virtual reality activities like Pokémon GO on real transportation usage and gathering pandemic data through web scraping, including the arrival times of the first COVID-19 cases in various countries and the structures of airline networks.

Methodological Innovations: We adapt and enhance methods borrowed from diverse fields to address old questions with new solutions. Our applications include employing causal analysis techniques such as the Difference-in-Differences (DID) approach from economics and combining specialized methods, including effective distance measurement in road networks (graph theory), random spreading modeling (public health), point clustering (data mining), and statistical testing (statistics).

Spatial Causality[4]: The fourth paper utilizes the Difference-in-Differences method to examine the changes in travel behavior during and after the Pokémon GO event by analyzing shared bicycle card data for trip origins and destinations in Tainan City. The primary objective of this study is to employ GIS statistics and causal analysis (DID) to infer the actual impact of large-scale tourist events on the utilization of shared bicycles. The contribution is the integration of the virtual and physical realms, assessing how mobile virtual reality gaming activities influence real shared bicycle usage before and after the event. The research addresses the common issue of overestimation caused by many game account registrations, enabling the flexible relocation of bicycles to popular stations before the event begins.

In conclusion, our lab operates at the intersection of multiple fields, combining expertise in civil engineering, transportation, criminology, and spatial information. Our interdisciplinary approach equips us to tackle complex challenges and devise effective solutions. Our central mission revolves around harnessing spatial data, spatiotemporal analysis techniques, and advanced scientific technology to enhance the safety and efficiency of transportation systems. Our commitment to innovation and adaptability drives us to define the next generation of road users, particularly in response to evolving transportation landscapes. Our current project focuses on elderly pedestrian walking safety and autonomous vehicle driving risk (Figure 1). We invite you to explore our research and collaborate with us on our journey toward safer and more efficient transportation systems.

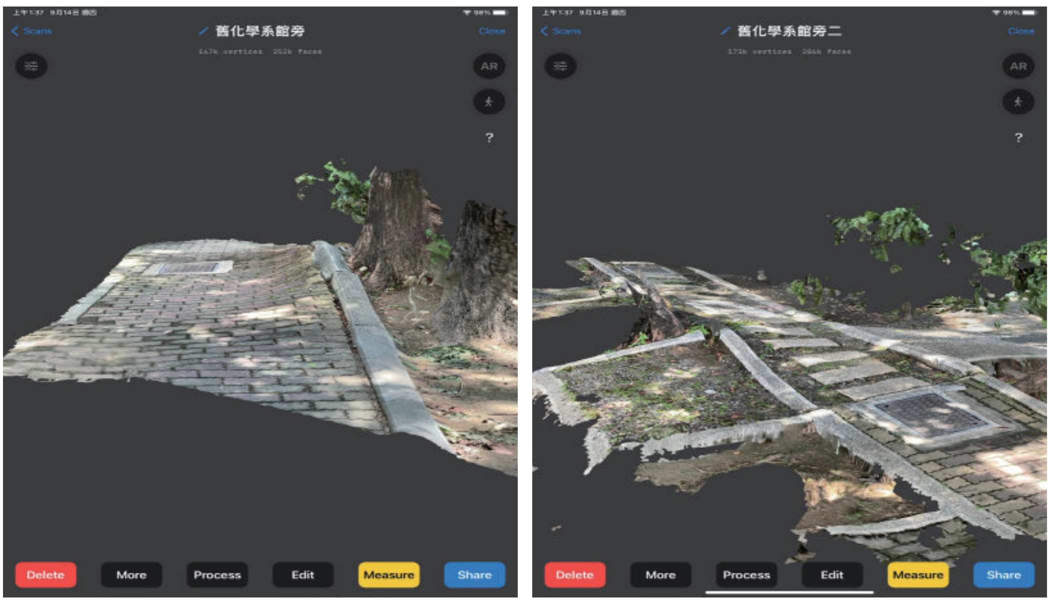

Figure 1 (a) Scanning results of sidewalks with uneven pavement on the NCKU campus.

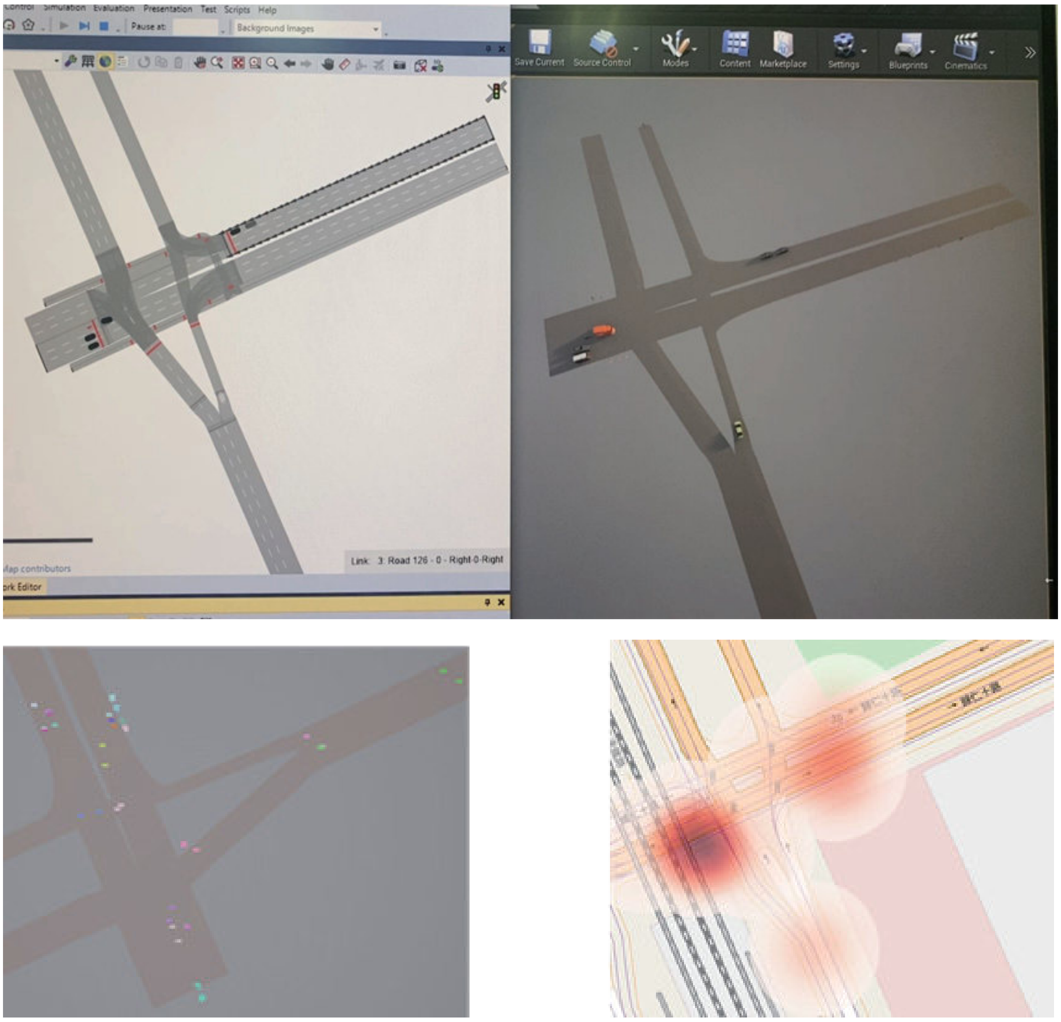

Figure 1 (b) autonomous vehicle simulation and cash risk hotspots based on high dimension (HD) map

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Investigating Tumor Spheroid Invasion in a Microfluidic Platforms: Interfacial Stiffness and Deep Learning Image Analysis

Dr. Ting-Yuan Tu currently serves as an Associate Professor in the Department of Biomedical Engineering at National Cheng Kung University. His research focuses on utilizing in vitro tumor models along with three-dimensional co-culture microfluidic platforms to simulate the tumor microenvironment. This approach enables the understanding of basic invasive behaviors of cancer cells and the screening of anti-metastatic drugs.

—— Ting-Yuan Tu,
Associate Professor

In the context of cancer metastasis, interactions with interstitial microenvironments between tissues are inevitable. However, prior research, both in vitro and in vivo, has rarely explored the physiological and behavioral responses of cancer cells within such interstitial microenvironments. Led by Dr. Ting-Yuan Tu from the Department of Biomedical Engineering at National Cheng Kung University (NCKU), Taiwan (referred to as 'the team') and in collaboration with Prof. Roger Kamm from the Department of Mechanical and Biological Engineering at Massachusetts Institute of Technology, USA, have utilized microfluidic chips and extracellular matrix (ECM) to establish a simulated tissue interstitial microenvironment for investigating the process of cancer metastasis.[1]

Within this setup, glass and polydimethylsiloxane (PDMS) with varying degrees of curing ratios are employed as substrates for three-dimensional cell spheroid culture. Surface modifications of these substrates are achieved using three biocompatible molecules: Pluronic F127, Poly-D-lysine (PDL), and Glutaraldehyde (GA). These modifications aim to study the impact of interfacial hardness and surface topography (i.e., adhesion between the substrate and the ECM) on the invasiveness of cancer cell spheroids.

The team examined the invasive behavior of MDA-MB-231 breast cancer spheroids embedded within soft collagen scaffolds, positioned over platforms with different stiffness levels (Figure 1): glass, PDMS (10:1), and PDMS (30:1) (arranged from highest to lowest Young's modulus). This design created a so-called 2.5D artificial microenvironment, mimicking the soft-hard tissue transitions observed in living organisms. Notably, the tumor spheroids displayed significant outgrowth, primarily from their lower hemisphere near the interface between the matrix and the platform. It was observed that platforms with higher Young's modulus, contributing to increased interface stiffness, could facilitate the detachment of individual cells from the interface and enhance their migration speed. The heightened interface stiffness also appeared to induce a change in the shape of detached cells, trending towards an elongated-mesenchymal phenotype. Interestingly, in certain cases, spheroids

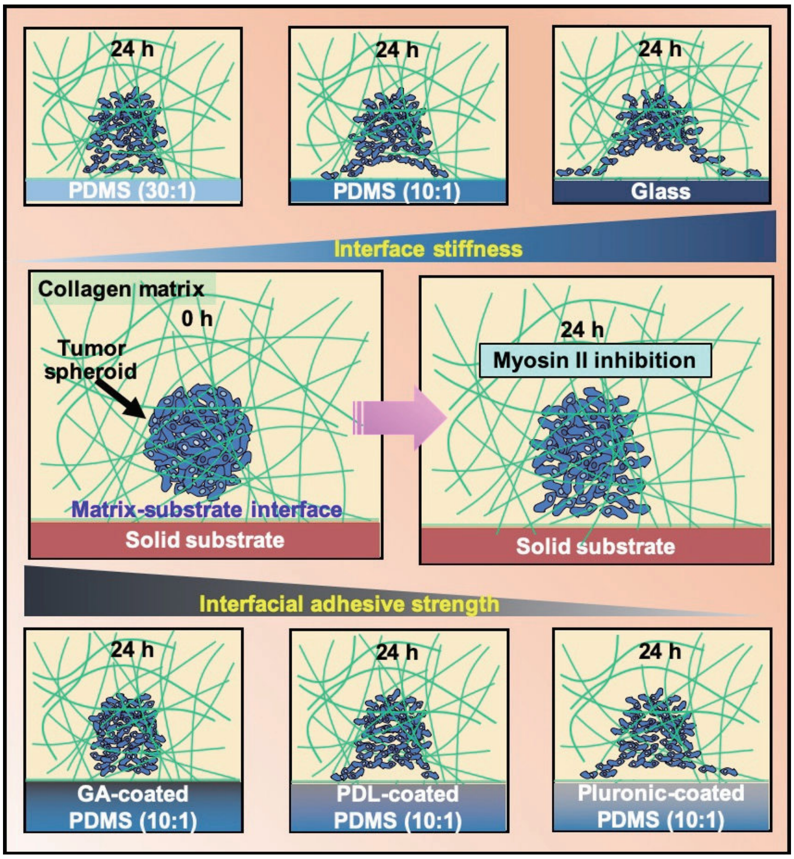

Figure 1 The investigation of MDA-MB-231 breast cancer spheroid invasion in a interfacial microenvironment. Glass and PDMS substrates with different stiffness levels (varying Young's modulus) are used for spheroid cultures, modified with biocompatible molecules (Pluronic F127, PDL, GA) to study effects of interfacial hardness and surface topography on spheroid invasiveness.

positioned above these interfaces exhibited a dome-like void beneath their lower halves, a phenomenon also influenced by the stiffness of the platform. However, despite the influence of interface rigidity on the aforementioned interfacial invasion and cell migration, the team suggests that the presence of an interface is a ‘necessary and sufficient’ condition for initiating invasive outgrowth, single-cell detachment, and guiding detached cells to migrate towards the interface, irrespective of its elastic modulus. In more precise terms, the team introduced the term ‘diepafitaxis’ (formed from ‘interface’ in Greek and ‘orientation in response to an external stimulus’) to describe this distinctive interface-mediated tropistic behavior. Additionally, the team has provided mechanistic evidence confirming the role of myosin II-mediated cell contraction, in comparison to matrix metalloproteinases, in governing the invasiveness of cell spheroids within the interstitial microenvironment.

While the interfacial tumor spheroid invasion model has provided insights into potential mechanistic contributions to the metastasis process, this image-based assay presents challenges due to the need for concurrent image processing and analysis during the assay period. Manually processing and analyzing a large number of time-lapse brightfield differential interference contrast (DIC) images is a time-consuming task. Furthermore, distinguishing between cell-cell boundaries and cell-ECM contacts can be challenging, even with the assistance of digital drawing boards or manual segmentation tools.

Therefore, through a collaborative effort provided by the Alliance of Southeast Asia and Taiwan Universities (SATU) at NCKU and in partnership with Dr. Saw Shier Nee from the Department of Artificial Intelligence at the University of Malaya, Malaysia, a deep learning-based image processing pipeline has been developed to analyze tumor spheroid invasion using DIC microscopic images (Figure 2).[2] By automatically learning and extracting relevant features from image data, these deep learning models have the potential to improve the accuracy of semantic segmentation, eliminating the need for manual annotation and enabling efficient generation of analytical results and predictions. The team employed an encoder-decoder architecture to create a deep learning-based image segmentation pipeline, allowing for the effective analysis of time-lapse imaging data and the characterization of invasive and migratory behaviors exhibited by various cancer cell types (e.g., breast cancer and melanoma) under various conditions, without human intervention. The insights derived from post-processing and analysis of image data, facilitated by the developed deep learning-based automated segmentation models, align with those obtained through manual analysis in the aforementioned study. Specifically, increased interface stiffness and decreased interfacial adhesive strength can enhance the invasiveness of tumor spheroids. Moreover, these models demonstrate their effectiveness in accurately and reliably segmenting spheroids and individual cells within a three-dimensional context, even in the presence of environmental interferences.

In conclusion, the team’s research findings

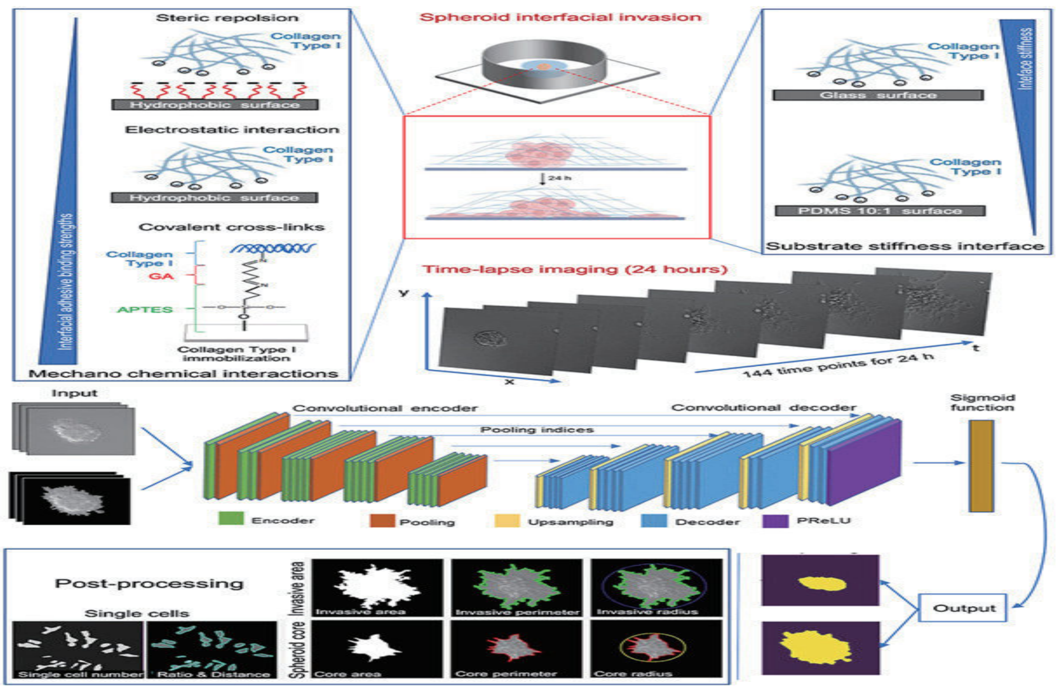

Figure 2 A deep learning-based image processing pipeline developed for analyzing tumor spheroid invasion using differential interference contrast (DIC) microscopic images. An encoder-decoder architecture was employed allowing for the effective analysis of time-lapse imaging data and the characterization of invasive and migratory behaviors exhibited by spheroid invasion.

suggest that when cancer cells or spheroids encounter interstitial microenvironments, stiffer interfaces or microenvironments with weaker interfacial forces may enhance the migratory abilities of cancer cells, potentially leading to their diffusion along interfaces in a two-dimensional manner. The validity and robustness of the proposed deep learning-based models for spheroid and single-cell segmentation have been confirmed through a comprehensive series of assessments. It is our hope that by continuing to construct and utilize such in vitro models, various patterns of cancer metastasis can be simulated and understood, ultimately making significant contributions to cancer metastasis research and potentially paving the way for innovative treatment strategies.

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UNIVERSITY RESEARCH CENTERS

Intelligent Manufacturing Research Center

The Center for Innovative FinTech Business Models

Intelligent Manufacturing Research Center

Director's Profile

Professor Fan-Tien Cheng has dedicated himself to applying the technologies of Information and Communication Technology (ICT) and Artificial Intelligence (AI) to both high-tech and traditional industries so as to exceed Industry 4.0 and reach the goal of Industry 4.1, which is the state of Zero Defects of all products. To realize Zero Defects of Industry 4.1, Professor Fan-Tien Cheng established the Intelligent Manufacturing Research Center (iMRC) in National Cheng Kung University (NCKU), and he has been serving as the Director of iMRC since then.

According to the academic research performance analysis report done by Scopus, Elsevier and SciVal in August 2022, Professor Cheng ranks Top 1 both domestically and internationally under the category of "Run; Metrology; Exponentially Weighted Moving Average" during 2012~2021. In addition, per the survey done by Clarivate in September 2023, Professor Cheng is the main inventor of AI related patents; he has the most AI patents in Taiwan, R.O.C., and his patent strength score is also the best domestically. Professor Cheng has won numerous awards and honors since his research power and achievements are highly acknowleged and praised not only in Taiwan but all over the world. The major honors and awards he received domestically and internationally include: the 2011 Award for Outstanding Contributions in science and technology from the Executive Yuan; Outstanding Research Awards from National Science Council (NSC) for three times (2006, 2009, and 2013); National Invention and Creation Award from Ministry of Economic Affairs (MoEA) for three times (2011, 2012, 2018); the 2013 IEEE Inaba Technical Award for Innovation Leading to Production; IEEE ICRA Best Automation Paper Award for two times (1999 and 2013); IEEE CASE 2017 Best Application Paper Award; the Chinese Institute of Automation Engineers (CIAE) Award in 2022; the Merit National Science and Technology Council (NSTC) Research Fellow in 2023. In addition, he has been the Chair of IEEE CASE Steering Committee on a 6-year term Since August 2020; and he served as the first Taiwan, R.O.C. Senior Editor of the IEEE T-ASE from 2017 to 2022.

Intelligent Manufacturing Research Center (iMRC) was established aiming to realize the goal of manufacturing with Zero Defects of Industry 4.0. iMRC developed the intelligent factory automation (iFA) system via incorporating the cross-university and cross-domain research resources, and successfully implemented it into 10 major industries with a total of more than 18 companies/institutes, including semiconductor, TFT-LCD, solar cell, aerospace, carbon fiber, machine tool, blow molding machine, metal additive manufacturing, Stick'N, pulp and paper industry, etc. Integrated with cloud intelligent manufacturing services such as Automatic Virtual Metrology (AVM), Intelligent Predictive Maintenance (IPM), and Intelligent Yield Management (IYM), the iFA system has been assisting the manufacturing industries to realize the vision of intelligent manufacturing with Zero Defects; which generates a total amount of technology transfer contract fee exceeding NTD$ 219,701,231 by far. The implementation of the iFA system benefited the Innolux Kaohsiung fab be selected as a Global Lighthouse in 2021, and ASE Kaohsiung fab a Global Lighthouse in 2023 certified by the World Economic Forum; assisted ChumPower Machinery to win the “Intelligent Machine Award” in TAIPEI PLAS 2018; and helped Chung Hwa Pulp Corporation to win the Digital Transformation Award (Intelligent Manufacturing Division) held by the Harvard Business Review in 2023. The success of the iFA system also contributed to NCKU’s ranking 1st in 3 consecutive years on SDG 9: “Industrialization, Innovation and Infrastructure” of the Times Higher Education (THE) Rankings. In addition, NCKU ranks 1st in Taiwan, R.O.C. and 24th globally on 2023 THE World University Rankings. iMRC made an exclusive licensing technology transfer contract of NTD $ 20,000,000 entitled “Intelligent Predictive Maintenance based on Container Technology (IPM_C)” with Mirle Automation Inter Co., Ltd. in April 2022. Related research results had been written by Director Cheng and iMRC’s research team into an English textbook entitled: “Industry 4.1: Intelligent Manufacturing with Zero Defects,” which was officially published worldwide by Wiley-IEEE Press in October 2021. Meanwhile, the English-taught course "Industry 4.1: Zero-Defect Smart Manufacturing" has been launched in NCKU to cultivate master's and PhD students to become the talents of intelligent manufacturing industries by combining theories and practice, in hopes to accelerate the digital intelligent transformation, achieve Industry 4.1 of Zero Defects, and enhance industrial competitiveness. Authorized by Wiley-IEEE Press, the traditional Chinese version of this book was officially published by NCKU Press in January 2023. Based on the iFA system, an intelligent AM framework called IAMA was proposed to online monitoring of the AM manufacturing process for better surface quality, density, and tensile strength. IAMA was shortlisted for the 2021 “Future Technology Award”.

With the above-mentioned advantages of various technologies and research results that we developed for pursuing the Industry 4.1 vision of Zero Defects, iMRC will utilize the advanced ICT (including container virtualization, IoT, cloud computing, edge computing, real-time streaming, 3D modeling, virtual/augmented reality, blockchain, information security, etc.), intelligent manufacturing technologies (such as AVM, IPM, IYM, and IDS, Digital Twins, etc.) and green metal AM technology to develop a so-called Industry 4.2 with Green Intelligent Manufacturing System (I4.2-GiM) in the future. I4.2-GiM offers digitalized, intellectualized, and energy-saving & carbon-reducing advanced technologies, including systematic carbon emission management (e.g. carbon disclosure, carbon neutrality) and intelligent energy management (e.g. energy consumption forecast, intelligent facilities energy management, and intelligent virtual power plant). I4.2-GiM can help Taiwan, R.O.C.’s manufacturing industries

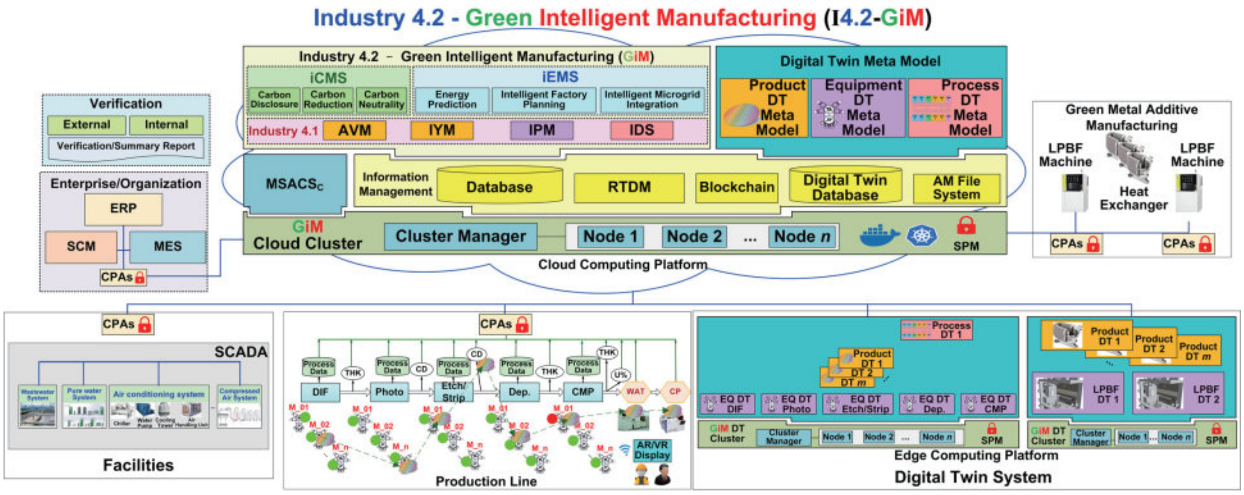

Figure 1. I4.2-GiM Architecture

to meet the needs of digital transformation and intelligent manufacturing while also achieving energy conservation and carbon reduction for moving towards the goal of Net Zero in 2050, and thereby enhancing international competitiveness and sustainable development.

The R&D of I4.2-GiM comprises of 3 research divisions. (1) Information and Communication Platform (ICP) Division—in charges of "the development and promotion of green intelligent advanced intelligent and communication platform;" (2) Green Manufacturing (GM) Division—responsible for the development and promotion of the green intelligent manufacturing system with energy saving and carbon reduction; (3) Additive Manufacturing (AM) Division—takes care of the development and promotion of green metal additive manufacturing system with digital twins.

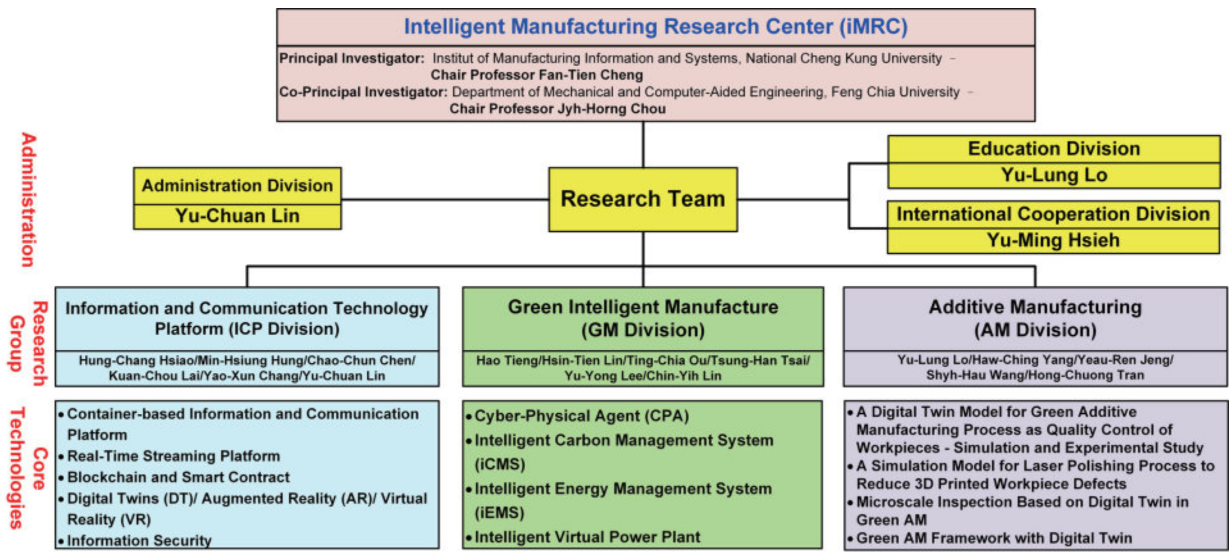

Figure 2. iMRC Organization and I4.2-GiM Research Group

The Center for Innovative FinTech Business Models

Director's Profile

Dr. Yeu-Shiang Huang is currently a Distinguished Professor in the Department of Industrial and Information Management at NCKU, where he also serves as Dean of the School of Management, Director of the Center for Innovative FinTech Business Models, Chair of the Sustainable FinTech Alliance, Convener of the NSTC Management II Discipline, and Chairman of the Board of Directors of the Chinese Professional Management Association of Tainan. He specializes in green supply chain management and enterprise sustainable management strategies, and is committed to promoting industry-academia cooperation links and talent cultivation in Taiwan's fintech innovation and sustainable strategy management. He was awarded the title of Fellow of the Chinese Society for Management Of Technology.

The Center for Innovative FinTech Business Models has been established since 2018 and was upgraded to a university-level research center of NCKU in 2020. The Center has nine laboratories and specializes in the in-depth research of various core technologies (ABCDM), such as Artificial Intelligence, Blockchain, Big Data Analysis, Cloud Computing, Data Mining, Machine Learning, and Mobile Payment, etc. It also actively integrates professional knowledge in business administration and law to develop various innovative financial business models or new convergent economic ecosystems. Through cross-disciplinary cooperation, the Center translates research results into forward-looking patented technologies, and promotes them to different industries through industry-academia cooperation or technology transfer to operate and validate them in various fields, responding to the national policy of the Ministry of Economic Affairs (MOEA) and the Financial Supervisory Commission (FSC) to promote the transformation of digital empowerment of industries, and to strengthen the resilience of Taiwan's industries to compete in the global supply chain.

The Center effectively integrates the strengths of the Management, Social Science, Electrical Engineering and Information teams to actively channel the seven core technologies and patented achievements into the local financial industry. To date, the Center has assisted more than 10 financial institutions (more than one-third of the financial industry) in possessing their own R&D capabilities in digital finance, and has promoted the international visibility and competitiveness of financial technology in Taiwan (SDGs.8 & SDGs.9). In view of the booming development of digital financial services and products in Taiwan, the lack of general knowledge about digital finance has given rise to a large number of digital financial frauds and caused serious social problems in recent years. Therefore, the Center has cooperated with FinTechSpace to set up the Fintech Digital Sandbox P.O.C Base in 2022 to accelerate the cultivation of more digital financial innovation and financial security talents in Taiwan. Moreover, the Center has organized the largest international conference and practical forum on sustainable fintech and regulatory compliance in the south-central part of Taiwan for four consecutive years since 2020, which not only contributes to the international linkage and academic influence, but also provides a platform for representatives from the government, industry, academia and overseas experts and scholars to exchange information on the latest development and application of global financial technology, besides creating an opportunity for teachers, students and the public to know more about the innovative knowledge of digital finance and technology popularization (SDGs.4 & SDGs.16).

In the light of the growing importance of global sustainability initiatives and the international trade impact of global carbon management on industries, the Center has established the Sustainable FinTech Alliance (SFTA) with the support of the National Science and Technology Council (NSTC) in 2023. SFTA will actively promote the Center's forward-looking sustainable and intelligent risk assessment and management technologies, as well as carbon management solutions or strategies to SMEs in Taiwan. Also, SFTA will assist financial institutions to accelerate the design or development of locally tailored sustainable credit or investment frameworks and technologies, with a view to strengthening the competitive advantages and operational resilience of the supply chain of various industries under the global sustainability initiative, enhancing the international visibility of the sustainable financial services framework in Taiwan. Meanwhile, the Center has been co-organizing the Enterprise Sustainability Management Profession Training Course with the Taiwan Institute for Sustainable Energy (TAISE) from 2022 onward to cultivate more industry experts in sustainability management for Taiwan. The Center will also co-organize the Climate Change Response Profession International License Training Course in the coming year to accelerate the training of professionals who are in line with the international sustainability industry, aiming to satisfy the industry management and analytical talents demands for the Taiwan Carbon Solution Exchange, which will be launched soon in Taiwan.

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Opening Ceremony of the Sustainable FinTech Alliance (SFTA) and FinTech Digital Sandbox P.O.C Base 2023

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