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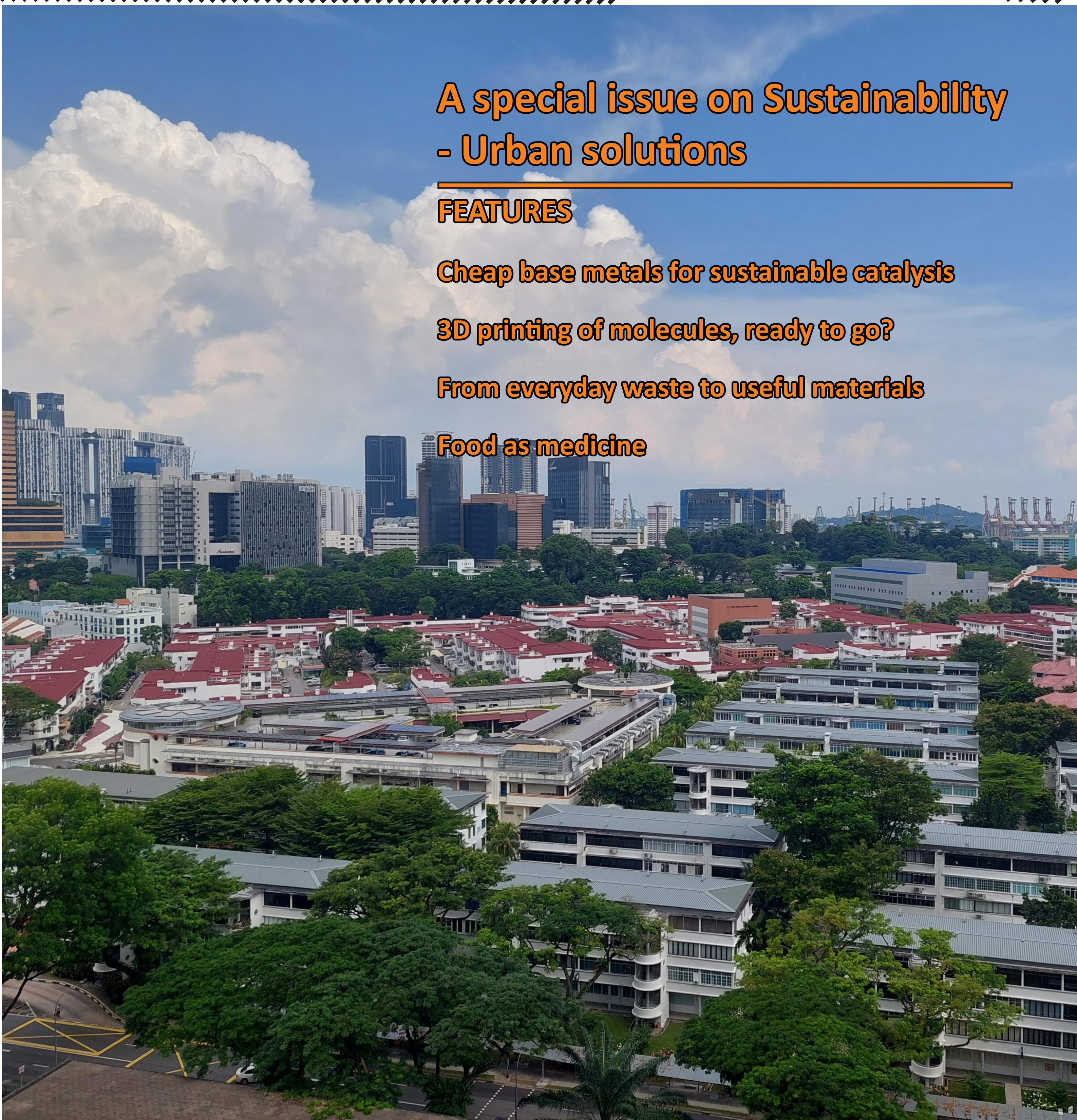

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Editor: SOH Kok Hoe (kok.hoe@nus.edu.sg)
Deputy Editor: Janice QUAH (janice.quah@nus.edu.sg)
Consultant: Giorgia PASTORIN (scipg@nus.edu.sg)

Dean's Office, Faculty of Science
National University of Singapore
Blk S16, Level 5, Science Drive 2
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On the cover: Photograph of pre-war flats against a backdrop of new modern buildings. With the urbanisation of cities, there lies opportunities for scientific advances to create and develop green services and solutions for urban sustainability.

Cheap base metals for sustainable catalysis

Multi-tasking and energy-efficient nickel catalysts upgrade abundant feedstock alkenes to high-value chemicals

Introduction

Chemical manufacturing is one of the central pillars of the global economy and plays a key role in society. Catalysis is an indispensable process that drives chemical reactions to enable access to various categories of chemicals, ranging from fine chemicals to polymeric materials. This process leverages a catalyst, which is a substance that accelerates chemical reactions without itself being consumed. Despite advances made in this field, many reactions still rely on catalysts derived from precious metals (such as palladium) which are rare and expensive. Given the rapidly dwindling supply of such metals, this approach cannot continue much longer. Many industries have started an earnest search for sustainable and cost-effective alternatives that are not subject to devastating fluctuations caused by price speculation, a well-known attribute of the precious metals market.

Furthermore, many precious metal-derived catalysts can only mediate a narrow range of chemical reactions. As a result, longer synthetic sequences often have to be employed to convert a starting material to the desired target product. Unfortunately, every step in a chemical synthesis process consumes energy, resources and time, and generates waste (spent carbon-based solvents and other byproducts) that has to be treated or incinerated. Based on the National Environment Agency's statistics, millions of litres of spent solvents are collected annually in Singapore and subsequently used as supplementary fuel for toxic waste incinerators. Consequently, this leads to more carbon dioxide and other toxic emissions that contribute to a series of negative repercussions on our environment. A lengthy and inefficient chemical synthesis process also means that manpower costs inevitably rise due to a greater demand for workers to carry out the tasks.

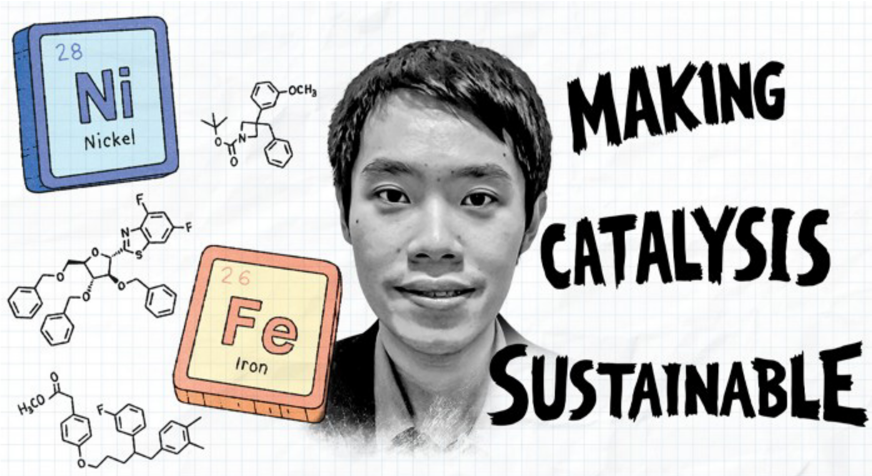


Figure 1: Sustainable catalysis helps to shrink synthetic chemistry's environmental footprint. [Credit: Chemical and Engineering News (C&EN)]

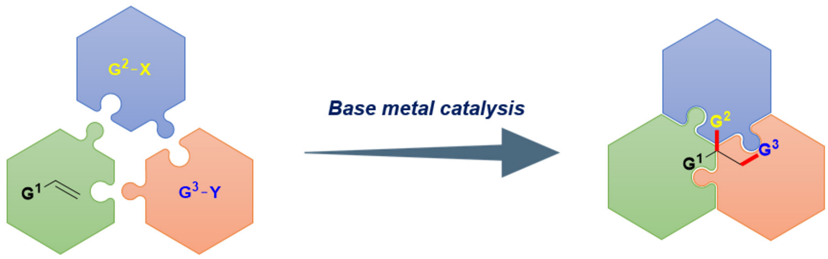


Figure 2: Multicomponent alkene functionalisation reactions catalysed by base metal complexes generate molecular complexity and diversity rapidly and shorten synthetic routes.

Why cheap base metals?

Base metals such as nickel are earth-abundant, inexpensive and less toxic, making them attractive candidates to prepare cheap and environmentally friendly catalysts for chemical manufacturing. For example, nickel is 5,000 times more abundant and at least 2,000 times cheaper than palladium, one of the most extensively used precious metals in the industry. In addition, base metals possess unique properties and exhibit distinct reactivity and selectivity profiles compared to precious metals, enabling them to mediate new chemical transformations that provide new opportunities to assemble molecules in a cheaper and faster fashion. Therefore, base metal catalysis has tremendous potential to drive sustainable chemical production beyond the limits of traditional precious metal catalysts.

Although base metal catalysis has seen substantial progress in recent years, the developments in this area and its utility in chemical synthesis still pale in comparison with those of the more established precious metals. This owes to the lack of suitable ligands as well as mechanistic knowledge to tune the activity and selectivity of base metal complexes, which can be overcome with focused research efforts. In the last five years, our group has built a program on sustainable catalysis (see Figure 1) where we

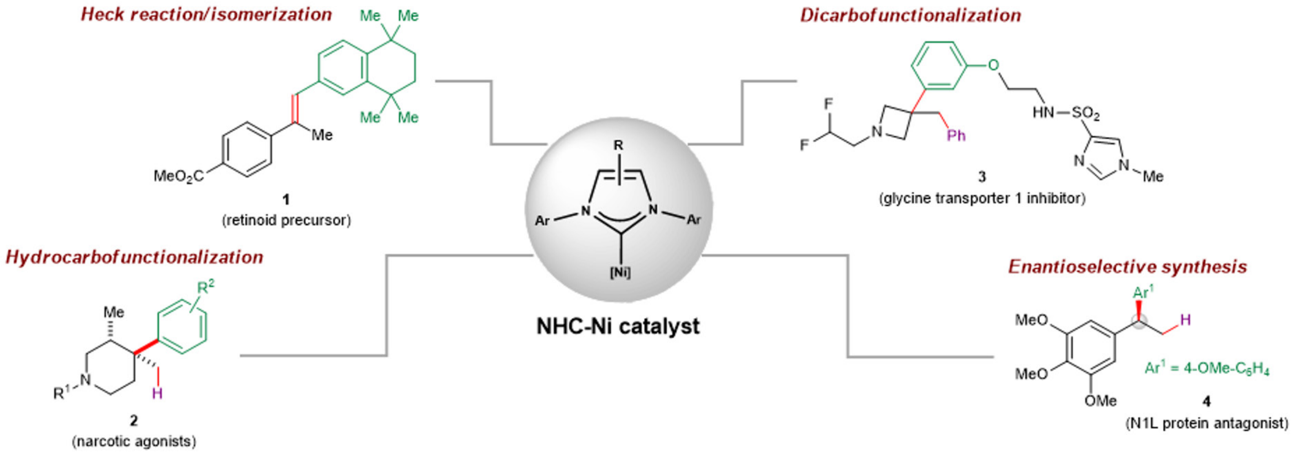


Figure 3: NHC-nickel catalysis as an enabling platform to access various classes of useful compounds for fine chemical synthesis.

developed new multitasking and energy-efficient base metal catalysts that mediate unprecedented chemical reactions, significantly enhancing the efficiency and shortening the steps required to make a target product. We employ these catalysts in innovative approaches to transform cheap and abundant feedstock chemicals to value-added chemicals with a lower carbon footprint.

Harnessing nickel and N-heterocyclic carbenes to drive alkene functionalisation

A powerful class of reactions that we have developed using base metal catalysis involves alkene functionalisation (see Figure 2). Alkenes are one of the most abundant classes of raw materials in organic chemistry. They serve as lynchpins to merge two or more components together to form a more complex scaffold. This enables us to generate a diverse range of complex molecules rapidly, and the resulting products are drug-like building blocks that can be further elaborated to important compounds of interest such as pharmaceuticals, agrochemicals and other fine chemicals.

In this field, the direct installation of carbon-based functional groups across alkene (carbofunctionalisation) has traditionally been a significant challenge, relying heavily on impractical directing groups that diminish efficiency and produce unnecessary waste. To address this problem, we harnessed a class of ligands known as *N*-heterocyclic carbenes (NHCs) which are electron-rich, sterically bulky and readily accessible. NHCs form complexes with nonprecious nickel to give NHC-Ni catalysts that are effective in promoting site-selective carbofunctionalisation reactions (see Figure 3). These reactions reduce the number of synthetic steps required to generate useful molecules with desirable biological activities, such as **1**, **2** and **3** [1], [2].

All chiral molecules exist in pairs (called enantiomers) which are mirror images of each other. Generally, the two enantiomers have different biological function or toxicity. Thus, the ability to access enantiomers selectively through enantioselective catalysis is vital in pharmaceutical and agrochemical development. However, related strategies that employ chiral base metal catalysts are extremely rare. Recently, we showed that chiral NHC-Ni catalysts are capable of mediating the formation of enantiomerically pure compounds such as **4** [3]. This potentially facilitates countless applications in natural product synthesis and drug discovery.

Besides the above nickel-catalysed methods that simplify the synthesis of fine chemicals, we have an ongoing project in which we leverage nickel catalysis to upcycle polyolefin plastic waste to functional polymers by reaction with greenhouse gases. This venture provides a viable route to sustainable waste plastic and greenhouse gas valorisation in Singapore.

For more details, please visit: https://www.mjkohgroup.com/

KOH Ming Joo is a President's Assistant Professor with the Department of Chemistry, NUS. He received his Ph.D. degree from Boston College in 2017 and carried out post-doctoral studies in the same institution. In 2018, he joined the Department of Chemistry at NUS. His current research focuses on developing sustainable and practical catalytic solutions that address critical challenges in chemical synthesis through base metal catalysis and radical chemistry.

References

[1] Wang H; Liu C; Martin RT; Gutierrez O*; Koh MJ*, "Directing-group-free catalytic dicarbofunctionalization of unactivated alkenes" NATURE CHEMISTRY DOI: 10.1038/s41557-021-00836-6 Published: 2022.

[2] Liu C; Wang H; Martin RT; Zhao H; Gutierrez O*; Koh MJ*, "Olefin functionalization/isomerization enables stereoselective alkene synthesis" NATURE CATALYSIS DOI: 10.1038/s41929-021-00658-2 Published: 2021.

[3] Liu C; Wang Z; Luo X; Lu J; Ko, CHM; Shi S*; Koh MJ*, "Synthesis of tri- and tetrasubstituted stereocentres by nickel-catalysed enantioselective olefin cross-couplings" NATURE CATALYSIS DOI: 10.1038/s41929-022-00854-8 Published: 2022.

3D printing of molecules, ready to go?

On-demand end-to-end synthesis of organic molecules can lead to more effective and efficient development processes

Introduction

Organic small molecules are the fundamental building blocks for drug development. Their unique structures and properties enable the discovery of lead molecules that may possess potential bioactivity towards specific biotargets. This discovery process typically involves screening up to 15,000 different molecules, followed by the creation of around 500 derivatives based on the lead molecule to optimise its effectiveness. When a promising drug candidate has been identified, it needs to be synthesised at a large scale, typically ranging from kilogram to ton-gram quantities, for clinical trials and eventual commercial production.

Despite the crucial role of organic synthesis in drug development, the process remains largely manual and labour-intensive, with the added challenge of optimising, purifying and scaling-up the drug molecule. As a result, the entire process can be incredibly time-consuming, with a significant amount of waste generated due to the repetitive nature of the development cycle.

With a similar concept to three-dimensional (3D) printing, 3D molecule printing allows for the automated synthesis of molecules with specific functions, making it easier for non-specialists to conduct chemical reactions. By incorporating different building blocks as needed, 3D molecule printing can speed up the process of developing potential drug candidates. Additionally, it can be used to create larger amounts of the required molecules. This transition from manual synthesis to automated 3D printing can led to improvements in efficiency, safety, reproducibility and cost savings. It can also help address issues with supply chain shortages.

Continuous-flow synthesis provides a promising platform for automated synthesis of molecules

Contrary to traditional batch-wise synthesis where reactions occur in separate batches, continuous flow synthesis is a method in which chemical reactions occur continuously in a flow reactor. In continuous flow synthesis, the reactants are continually fed into the reactor, and the product is continuously collected as it flows out of the reactor. Batch-wise synthesis involves adding reagents, stirring, heating, cooling and filtering, which is time-consuming and requires frequent human intervention. In comparison, continuous-flow can be easily automated using pumps, valves and sensors. The progress of the reaction can be monitored in real-time and the flow rate of the reactants precisely regulated based on reaction conditions. This provides a high degree of precision, consistency and reproducibility in the synthesis process, a feature which is essential for the development of new drugs and other high-value chemicals.

Despite its potential, the use of continuous-flow synthesis in the pharmaceutical industry is still limited due to several reasons. Firstly, solid reagents and slow reactions are not well-tolerated by this technology, which means that only certain types of reactions can be performed. Secondly, there are compatibility issues between the reagents and solvents used in each step of the process, which requires extensive optimisation and strict quality control to achieve continuous purification. These challenges make it difficult to achieve end-to-end multistep synthesis of diverse pharmaceutical molecules using flow synthesis. As a result, most flow synthesis is limited to one or two steps, significantly restricting the molecular diversity that can be accessed.

Figure 1: Stepwise decoration of the silicon atom using the $RSiH_3$ molecule in an on-demand and automated manner. In each step, one of the hydrogen atoms bonded to the silicon atom is replaced with a functional group.

Think out of the box: Overcoming limitations in flow synthesis

Rooted on flow chemistry, my group has developed several innovative technologies over the past seven years to overcome the limitations encountered in continuous flow synthesis in pursuit of 3D molecule printing and on-demand synthesis. We achieved stepwise on-demand functionalisation of multihydrosilanes based solely on eosin Y-based hydrogen atom transfer photocatalysis in continuous flow micro-tubing reactors. This results in excellent selectivity as opposed to batch reactors whereby a mixture of products was obtained. By exploiting this strategy, we realised preferable hydrogen abstraction of silicon-hydrogen (Si–H) bonds in the presence of more active carbon-hydrogen (C–H) bonds, diverse functionalisation of hydrosilanes (for example, alkylation, vinylation, allylation, arylation, deuteration, oxidation and halogenation), and highly selective monofunctionalisation of di- and trihydrosilanes [1] (see Figure 1).

In 2021, we developed a compact solid-phase synthesis (SPS) flow platform for the production of prexasertib and its derivatives in a continuous and automated manner. Equipped with a computer-based chemical recipe file (CRF), this platform facilitates on-demand early- and late-stage modification of the lead compound [2]. The SPS-flow circumvents the need for tedious intermediate isolation and purification procedures by using simple filtration through automation. This approach offers a simpler and more compact system for the automated multistep synthesis of pharmaceutical compounds.

As the drug synthesis method is digitally stored with this approach, the automated production process is able to respond to a sudden change in the demand for specific pharmaceutical compounds. Also, the generated chemical recipe files can be adopted directly for the automated synthesis of drug derivatives, facilitating late- and early-stage diversification. With these advantages, this approach reduces the cycle time of drug discovery and expands the chemical space for *de novo* drug design/ optimisation and synthesis.

Moreover, we have also developed a high-speed circulation microflow (HSCF) synthesis platform that overcomes solid sedimentation, prevents clogging and enhances mixing efficiency. This facilitates large-scale heterogeneous photocatalytic reactions. As a proof-of-concept, we have successfully conducted up to kilogram-scale heterogeneous

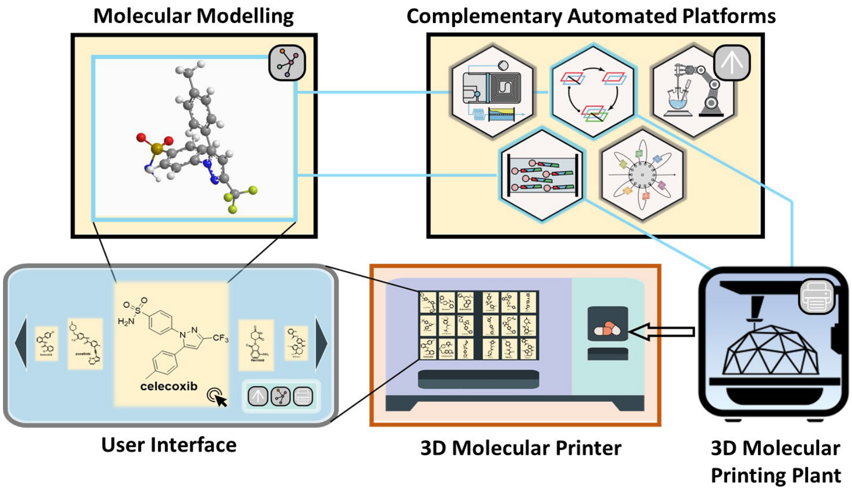


Figure 2: A future platform for on-demand synthesis of drug molecules.

photocatalytic cross-coupling reactions in an automated fashion with the HSCF platform. The HSCF platform represents a crucial advancement toward automated synthesis of organic molecules as it tolerates both slow reactions and solid-involved reactions that are challenging to achieve in continuous-flow synthesis.

What is the next step?

On-demand end-to-end synthesis of organic molecules has several benefits, including customisability, efficiency, accessibility, speed and flexibility. These benefits can have a significant impact on various fields and lead to more effective and efficient production processes. However, organic molecules can have, in principle, infinite diverse structures, each with different combinations of atoms, functional groups and bonding arrangements. Therefore, it seems nearly impossible to find one single platform that can produce all these molecules in an automated manner. However, iterative synthesis, robotic chemists and flow synthesis have each contributed a big step toward this goal. Flow synthesis is especially beneficial to automated synthesis due to the nature of its simple control of valves, pumps and sensors for automation. We anticipate that, by introducing SPS-flow and high-speed circulation flow, much more reactions can be tolerated in a flow mode.

The future efforts toward automated synthesis will largely be focused on developing advanced technologies and techniques, such as robotics, machine learning, flow chemistry, in situ analysis and 3D printing. With careful consideration of suitable platforms or combinations of technologies, molecules with various functions can eventually be synthesised in a “push-button” manner (see Figure 2). Although there is still a long way to go, I believe it is only a matter of time before this goal is achieved, allowing chemists to save time and focus their efforts on innovation.

For more details, please visit:
https://www.wujiegroupnus.com/

WU Jie is an Associate Professor with the Department of Chemistry, NUS. He pursued his Ph.D. study with Prof James S. PANEK at Boston University working on natural product total synthesis. In his postdoc research at the Massachusetts Institute of Technology with Prof Timothy JAMISON and Prof Alan HATTON, he has been exposed to the fundamentals of continuous flow chemistry. Since joining NUS in 2015, his research group has been focusing on new synthetic methodology development using photocatalysis assisted by advanced flow technologies.

References

[1] Fan XZ; Zhang ML; Gao YJ; Zhou Q; Zhang YB; Yu JJ; Xu WG; Yan JM; Liu HW; Lei ZX; Ter YC; Chanmungkalakul S; Lum YW; Liu XG; Cui GL, Wu J*, “Stepwise on-demand functionalization of multihydrosilanes enabled by a hydrogen-atom-transfer photocatalyst based on eosin Y” NATURE CHEMISTRY Volume: 15 DOI: 10.1038/s41557-023-01155-8 Published: 2023.

[2] Liu CG; Xie JX; Wu WB; Wang M; Chen WH; Idres SB; Rong JW; Deng LW; Khan SA*; Wu J*, “Automated synthesis of prexasertib and derivatives enabled by continuous-flow solid-phase synthesis” NATURE CHEMISTRY Volume 13 DOI: 10.1038/s41557-021-00662-w Published: 2021.

From everyday waste to useful materials

Repurposing waste hair into sustainable material – from hiding messages in plain sight to being a water pollutant detector

Introduction: Why is it interesting/ Why is it important?

Reduce, reuse and recycle. These are the three "R"s that have long been instilled in most of us from a very young age to inculcate the good habit of reducing the amount of waste we produce. Reduce means to minimise consumption so that less waste is generated. Reuse focuses on finding new ways of using the things that would otherwise have to be discarded. Recycle transforms old and useless items into something new and useful.

However, there is a question that is always at the back of our minds – what if the waste is inevitably produced every day as humans go about their daily activities? One such example is human hair. An average person is likely to shed between 50 to 100 strands of hair daily. Over time, this material ccumulates into a sizeable amount of waste. While it can be reused and made into hair wigs, are there any other possibilities to utilise this seemingly inconspicuous waste? This would add a fourth "R" – Repurpose, in addition to the three "R"s – to unlock and open new potential applications .and turn this waste material into "treasure".

Human hair is considered one of the most abundant biological wastes on earth. With its slow biodegradability, putting it in landfills will inevitably occupy a sizeable amount of land space. This is not a valid option, especially in Singapore, where land is scarce. Alternatively, such waste could be incinerated. However, when waste hair is subjected to direct incineration, toxic gases such as ammonia and sulphur dioxide could be produced and this may cause environmental pollution. For long-term sustainability, the best way to address this is to develop alternative applications which utilise waste hair as a resource. Apart from reducing waste, it may also contribute to, and benefit the economy.

Research focus

Human hair has a unique property. It emits a blue fluorescence under a wood lamp or when subjected to ultra-violet (UV) light excitation. However, the root cause of this fluorescence effect in human hair is not clearly understood at this point in time. Despite a limited understanding of its fluorescence property, human hair has already been used as an indicator in certain instances. For example, in forensic studies, the presence of traces of arsenic detected in human hair is frequently used to determine possible arsenic poisoning during the course of an investigation. In the medical field, the changes to human hair optical properties due to the invasion of hyphae into a hair follicle offers a simple way to detect a fungal presence with a wood lamp. We foresee that with a better understanding of the fluorescence properties of human hair, this material can potentially be tailored for use as a chemical/ biological sensor that comes with a visual indicator element.

Making human hair glow!

We recently discovered that human hair could be made to glow brightly under UV light illumination through a simple heating process!

Human hair has a multi-layered structure comprising the outer layer, the cuticle, the mid-section, or cortex, and the core, or medulla (see Figure 1(a)). Contained within these layers are various chemical compounds, namely the keratin backbone found in the medulla, melanin within the cortex, and other scarce particles such as tryptophan.

On a macroscopic scale, the entire strand of a human hair emits a dim royal blue fluorescence under UV light excitation. With a simple concept akin to using a magnifying glass to focus sunlight into a tiny spot of intense heat, a laser beam can be readily focused onto the surface of the human hair. By manipulating the laser beam, microscopic patterns such as musical notes or other designs can be created on it. These patterns will have a cyan fluorescence under UV light but cannot be seen under normal lighting conditions (see Figure 1(b-c)). The introduction of heat treatment by the laser beam changes the chemical nature of human hair and modifies its fluorescence property. This allows information to be imprinted on, or encoded using the material which becomes visible only under UV lighting conditions. Apart from using the laser beam, the fluorescence property of human hair can also be activated by annealing it using a hotplate under room conditions. As shown in Figure 1(d), an array of original and heated human hair is arranged to form the word "NUSHS". Under UV excitation, the word "NUS", created using heated human hair, glows a bright cyan colour, distinguishing it from the original "NUSHS" wordings and showing the steganographic capability of this unique material.

Application

The heated human hair is not limited to such steganographic applications. It also exhibits an enhanced detection capability towards water pollutants such as methylene blue. Under the same heating conditions, white hair has been shown to exhibit greater fluorescence enhancement when compared to black hair. It is also found to be sensitive to a substance called

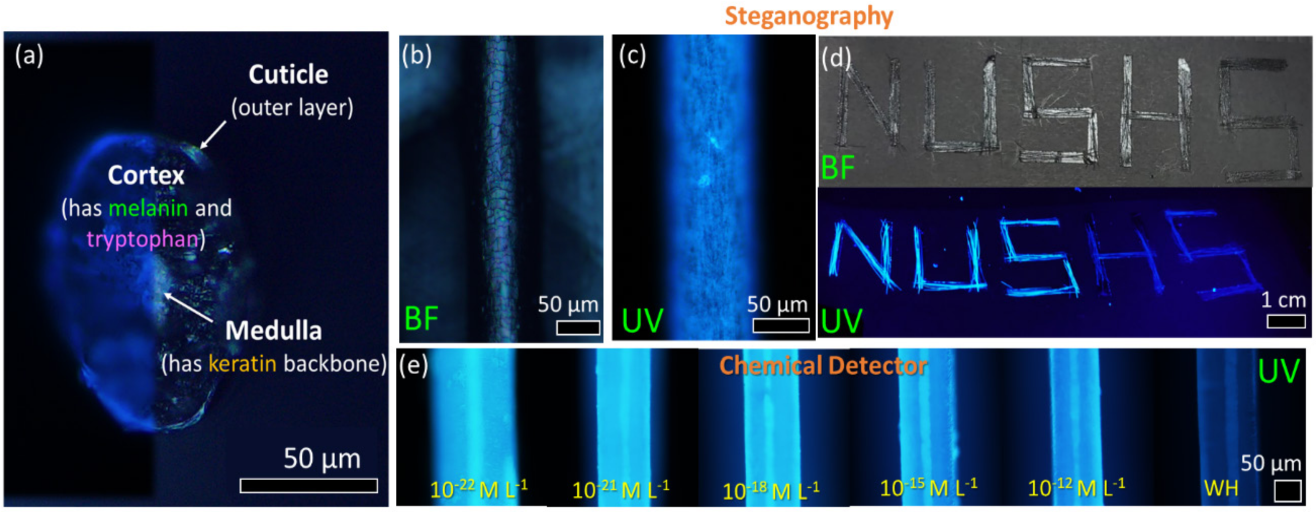


Figure 1: (a) Cross-sectional view showing the different regions of a strand of human hair. (b-c) Controlled laser patterned "musical note" on human hair under normal light and UV excitation. (d) An array of human hair forming the word "NUSHS" with "NUS" comprising of human hair with heat treatment and "HS" made of original human hair. (e) Visuals showing a strand of white hair immersed in different concentrations of methylene blue. Heat treatment of white human hair increases its chemical detection capabilities. When in contact with methylene blue pollutants, it glows brightly under ultraviolet light.

methylene blue. Methylene blue is a chemical dye commonly used in the textile industry, and often discharged untreated into water bodies in developing nations, polluting them. The ability of white waste hair, after heat treatment, to glow brightly under UV light when it comes into contact with methylene blue pollutants, opens up an affordable way to detect them without using complicated and expensive analytical tools (see Figure 1(e)).

We believe that our discovery is only the tip of the iceberg of the many possibilities in repurposing waste human hair. There are more questions to be addressed and more applications to be investigated with this material - Can these heated and original human hair be developed into ink for printing hidden messages in text or other surfaces? Can these human hair detectors be recovered? What other properties of waste human hair await to be discovered? These are some interesting yet highly important questions waiting to be investigated.

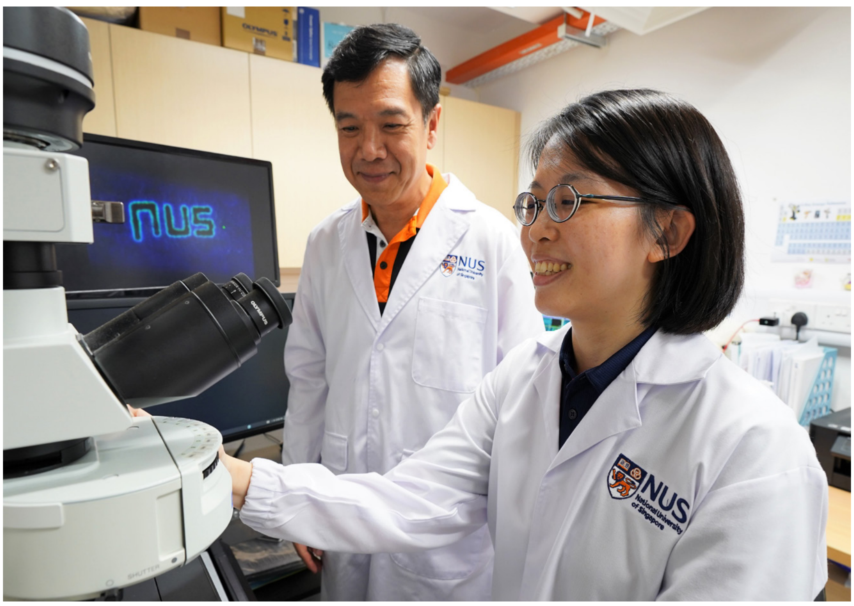
Collaboration

The research work presented in this article is achieved through a collaborative effort between scientists from NUS and the Agency for Science, Technology and Research (A*STAR), together with a student from NUS High School (NUSHS).

For more details, please visit: https://phyweb.physics.nus.edu.sg/~physowch/NanoLab/

SOW Chorng Haur (left) is a Professor with the Department of Physics, NUS. His laboratory works on all kinds of nanomaterials and nature-based materials with a keen interest to investigate how a focused laser beam can engineer interesting physical properties on these materials.

Sharon LIM Xiaodai (right) is a senior research fellow with the Department of Physics, NUS. Her interest lies in exploring carbon nanomaterials and nature derived materials, with special interest in liquid assisted assembly and laser induced optical effects.



Reference

[1] Sow MMG; Lim SX*; Zhang Z; Sow C H*, "Microstyling of Biofluorescence in Human Hair as Sustainable and Functional Waste" ADVANCED PHOTONICS RESEARCH DOI: 10.1002/adpr.202200161 Published: 2022.

Food as medicine

Agri-food side streams can be converted into nutraceuticals and provide food and nutritional security to global population growth accompanied with aging society

Introduction

Humanity is now facing unprecedented challenges. By the year 2050, the global human population is projected to reach 10 billion and it will be challenging to produce enough food to feed everybody. By then, more than one fifth of the world's population would also be older than 60 years.
Increasing food production by 60% by the year 2050 is a suggested way to address these challenges. However, there is limited agricultural land and the cost of production for urban farming remains a constraint. Simpler solutions are needed. If we can resolve the global food wastage problem, it could be possible to at least partially address these challenges. According to the Food and Agricultural Organization (FAO), global food wastage leads to economic losses of US$2.6 trillion per year.

Food wastage occurs throughout the different stages of food production, including agriculture, postharvest, food processing, distribution and consumption. On average, 30% of food is wasted worldwide. This gives rise to a potential opportunity to develop a "biorefinery" to convert agricultural biomasses into value-added nutraceuticals – agriceutical products for human health promotion.

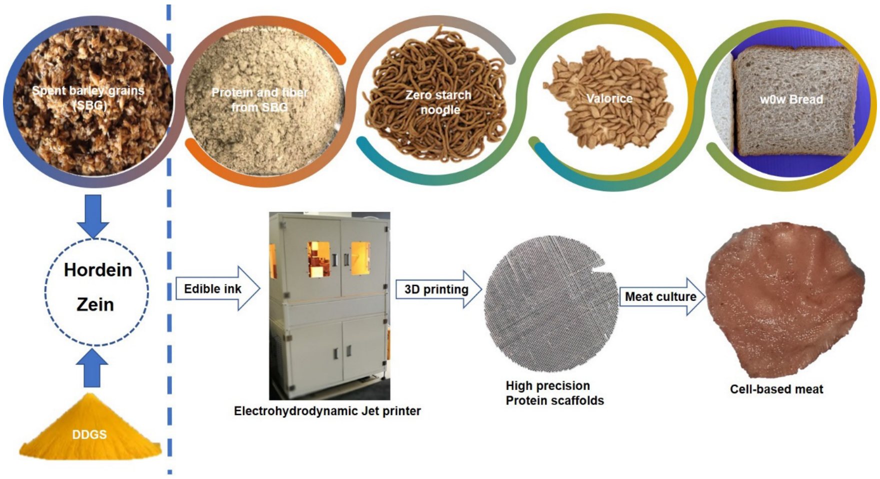


Figure 1: From trash to treasure: making good use of spent barley grains (SBG) and distiller's dried grains with solubles (DDGS) for future food products such as cell-based meat.

From trash to treasure – Converting spent grains into future foods

The traditional food manufacturing industry is generally wasteful. For example, in the production of alcoholic beverages such as beer, starch in malted barley grains is extracted (by a process called mashing) through enzymatic digestion (mostly starch hydrolases) to convert starch into fermentable sugars that are needed to generate alcohol. In this process, only limited amounts of proteins are digested into soluble peptides and amino acids as nutrients. After mashing, the resulting wort is filtered and the solid materials are discarded as spent barley grains (SBG) while the remaining liquid is further processed into beer. The beer manufacturing industry in Singapore generates about 75,000 tonnes of SBG per year. In addition, a comparable amount of SBG is generated from plants involved in manufacturing malt extracts. The SBG contains over 20% proteins (on a dry weight basis). This is much higher than the initial barley grains because starch is stripped off in the mashing process. Apart from proteins, the SBG also contains fibres and lipids. From a nutritional perspective, SBG is a nutrient-rich material but frequently ends up as animal feed or landfills because it spoils easily due to its high moisture content. By extracting the proteins and fibres from it, the resultant powder can potentially be used for making food products with low or no starch content.

Besides SBG, corn-based bioethanol manufacturing plants extract starch, which is fermented to produce bioethanol. The distiller's dried grains with solubles (DDGS), which represent a by-product of the bioethanol fermentation process, are destarched and contain high protein content (over 20%), fibres and lipids. DDGS have a poor amino acid profile and this limits its use as animal feed. We have extracted prolamin (alcohol soluble protein) zein from DDGS and applied it as ink materials for high precision three-dimensional (3D) printing. We also developed a patented technology for printing scaffolds with tuneable pore sizes and shapes. The resulting scaffolds have found applications in 3D cell culture as well as cell-based meat culture [1]. Every year, 44 million metric tons of DDGS are produced in the United States. By refining them into proteins and fibres or zein, we can up-value the materials for sustainable production of novel foods such as cell-based meat (see Figure 1).

Agriceuticals- Reclaiming active nutraceutical ingredients from agricultural by-products

A large amount of crop biomass is generated in agriculture. These fibrous materials, which include stems, leaves and roots are normally discarded in the field or, sometimes, burnt. In addition, part of the fruits and seed shells is discarded when crops undergo postharvest processes as they are not edible. Yet, these plant tissues contain nutrients (e.g. leaf proteins) and a wide range of phytochemicals with complex structures and bioactivity for to promote health. Our laboratory has been developing green extraction methods to obtain these nutrients and phytochemicals that show promise for health promotion activities. Figure 2 highlights a few successful examples.

Peanut shells contain a good amount of luteolin, a common flavone with anti-inflammatory and antioxidant activity. Luteolin is produced commercially by extracting it from peanut shells. In the process of studying the antioxidant action mechanisms of luteolin, we serendipitously discovered that luteolin could undergo oxidative coupling, mediated by oxygen as a limiting reagent, under mild (and food grade) conditions to form dimers, trimers and cyclic trimers. By using this food grade synthetic approach, we have obtained about 100 flavone dimers and trimers which possess intriguing properties such as starch hydrolase inhibitors (alpha-amylase), anti-microbial activity [2]. Our finding opens an avenue to exploit these flavone dimers and oligomers as active ingredients in nutraceuticals and pharmaceuticals.

Another example involves sweet potato leaves and stems. By applying a high throughput screening assay, we found that vegetables belonging to the morning glory family, such as sweet potato and kangkong, contain resin glycosides that can inhibit pancreatic lipid activity. This inhibitory action is also the target of the synthetic pharmaceutical agent called Orlistat.

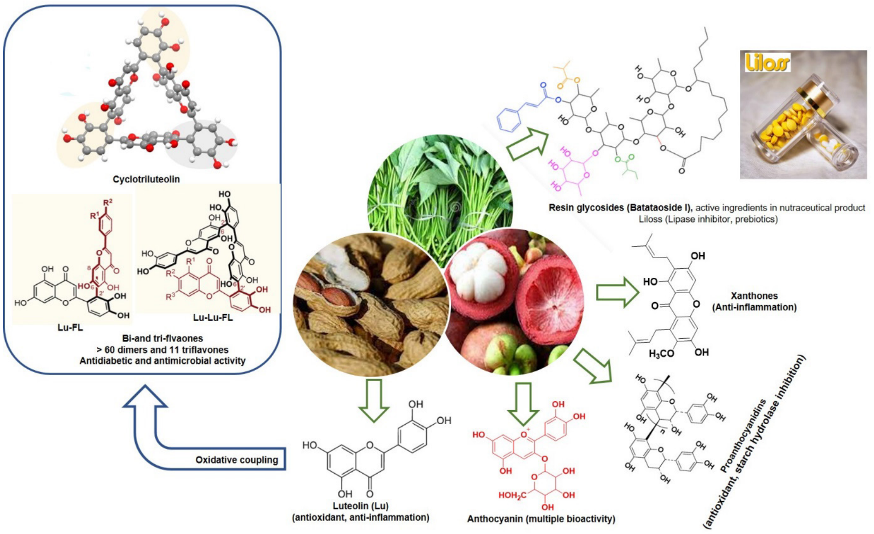


Figure 2: Examples of utilising three different agricultural by-products for manufacturing bioactive molecules for use as ingredients for nutraceuticals or pharmaceutical products for human health promotion.

Globally, sweet potato production is reported to reach close to 90 million metric tons in 2021. The aerial part of the sweet potato plant, including the stems and leaves, contain a good amount of soluble fibre, proteins and resin glycosides, which can be extracted and applied as active nutraceutical ingredients. The soluble fibre (mostly pectin) can help reduce the glycemic index of starchy foods while both the resin glycosides and fibre can be used as active ingredients for functional food products associated with body weight control.

As the queen of tropical fruits, mangosteen has a thick pericarp that weighs up to two-thirds of the whole fruit. The discarded pericarp contains a good amount of fibre and phytochemicals including anthocyanins, proanthocyanidins and xanthones. These phytochemicals are useful as antioxidants and anti-inflammatory agents.

Summary

In summary, the agri-food industry produces a great deal of biomasses that has not been fully utilised. Traditional food processing methods are wasteful and predominantly focus on only one component in the raw material while the rest is wasted. If we are able to effectively tap into the rich resource of agricultural by-products for commercial scale production of dietary fibres, proteins and agriceuticals for health promotion and disease prevention, we can potentially achieve food and nutritional security and sustainability.

For more details, please visit: https://www.fst.nus.edu.sg/our_people/faculty-members/huang-dejian/

HUANG Dejian is a Professor with the Department of Food Science and Technology, NUS. His research interests include chemistry of food bioactive molecules (flavonoids, organosulfides and resin glycosides), 3D printing application for scaffolds for cell-based meat culture and 3D cellular model for cancer cells and monolayer tissues, alternative proteins (plant proteins and microalgae proteins) as seafood and egg mimics, and valorisation of agri-food by-products and side streams for nutraceuticals and functional foods.

References

[1] Su LS; Jing LZ; Zeng XJ; Chen T; Liu H; Kong Y; Wang X; Yang X; Fu CL; Sun J; Huang DJ*, “3D-Printed Prolamin Scaffolds for Cell-Based Meat Culture” ADVANCED MATERIALS Volume: 35 Issue: 2 DOI: 10.1002/adma.202207397 Published: 2023.

[2] X Yang, et. al., “Oxygen mediated oxidative couplings of flavones in alkaline water” NATURE COMMUNICATIONS Volume: 13 Issue: 1 Article Number: 6424 DOI: 10.1038/s41467-022-34123-w Published: 2022.

Research Centre on Sustainable Urban Farming (SUrF)

The indoor farming research facility at the Research Centre on Sustainable Urban Farming (SUrF) is equipped to grow plants under different coloured lights. These lights help the plants achieve different growth patterns.

Singapore imports more than 90% of its food from various sources. This leaves the nation's food supply vulnerable to supply chain disruptions, which could be caused by factors such as climate change or pandemics. As part of its efforts to build a more resilient food future, Singapore is seeking to increase its agricultural output with the aim of producing 30% of its nutritional needs locally by 2030. As Singapore has less than 1% of its land available for farming, modernised agricultural methods such as indoor vertical farming are novel solutions which could be explored to overcome this constraint.

Although, indoor farming requires the use of less land area compared to traditional agriculture, it comes with several unique challenges. Firstly, the direct application of previously proven methods in traditional farming to modern farming becomes challenging as the shift from soil-based to water-based agricultural approaches alters several factors, including the growth requirements and conditions for optimal crop growth. Also, in order for the indoor farming business to become profitable and sustainable over the longer term, various issues such as high energy consumption, light source optimisation and automation need to be addressed as part of the solution.

The Research Centre for Sustainable Urban Farming (SUrF) at the Faculty of Science, NUS was established in 2022 to develop sustainable indoor farming solutions that address major scientific and technological gaps associated with the three stages of food production, namely, the pre-production, production and post-production phases. These issues are often multifaceted, requiring a diverse range of expertise for in-depth investigation and eventual conceptualisation of the potential solutions.

With this in mind, SUrF brings together a multidisciplinary team of experts from the domains of Science, Engineering and Computing whose expertise covers a wide research scope ranging from plant and food science to genomics, sensor technology and artificial intelligence. The coalescence of these diverse but complementary sciences has kindled multidisciplinary research that otherwise would not have been possible with a single discipline. For example, researchers well-versed in plant sciences and sensor technology are developing "wearable" sensors for plants that are grown in indoor farm conditions. The data collected is expected to help in optimising the growth conditions of plants and enhance the overall sustainability of indoor farming.

Furthermore, SUrF recognises that for solutions to be economically viable, there has to be an element of business acuity and, towards that purpose, it is actively involved in collaborations with several local industrial partners. Additionally, SUrF also organises workshops to facilitate discussions and nucleate multidisciplinary projects among NUS faculty members, businesses and other established research partners in the ecosystem.

For more details, please visit:
https://www.dbs.nus.edu.sg/surf/

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