NATIONAL RESEARCH FOUNDATION

LIST OF AWARDED CENTRAL GAP FUND PROJECTS ADMINISTERED BY NRF

Title	Project Lead	Host Institution	Domain*	Technology Areas
Automated Continuous Post-surgical Monitoring of Vascularized Grafts using Electrochemical Metabolite Detector	Ong Yee Siang	SGH	HHP	Medtech
Product development and verification of a revolutionary solution for the treatment of glue ear	Jasmine Qiu	SGInnovate	HHP	Medtech
SPEEDCARGO	Thomas Aulig, Suraj Nair	TUM CREATE	MTC	Robotics/ Automation
Satellite Quantum Key Distribution: A UK-Singapore Joint Mission	Alexander Ling Euk Jin	NUS	USS	Quantum
Innovative Hybrid Super Absorbent-Indirect Evaporative Water-Based Cooling System for All-Weather Air-Conditioning Without Compressors and Chemical Refrigerants	Ernest Chua	NUS	USS	Sustainability
Green catalytic oxidation for industrial wastewater treatment and manufacturing processes	Yang Kun-Lin	NUS	USS	Waste Management
Soft robotic sock for robot-assisted ankle-foot mobility in chronic bedridden patients	Yeow Chen Hua, Raye	NUS	HHP	Medtech
New Silicon ICs	Kenneth E Lee	SMART LEES	MTC	Electronics
Manufacturing readiness and clinical validation of a novel synthetic tendon graft	Thian Eng San	NUS	HHP	Medtech
Probiotic beer to enhance gut health and immune system function	Liu Shao Quan	NUS	HHP	Foodtech
Disruptive products in camera technology using prism optics	Mark Breese	NUS	MTC	Lasers and Optics
Bioprocessed okara for value-added, diabetic-friendly health food products	Liu Shao Quan	NUS	HHP	Foodtech

* Manufacturing, Trade and Connectivity (MTC), Human Health and Potential (HHP), Smart Nation and Digital Economy (SNDE), Urban Solutions and Sustainability (USS)

Title	Project Lead	Host Institution	Domain*	Technology Areas
WIND: Product development and verification of a non-invasive solution for treatment and management of airway secretion diseases	Simon Gordon	SGInnovate	HHP	Medtech
AITachnology (AIT) – Giving robots a sense of human touch (Product development of AI-enabled tactile skins for perceptive robotics)	Suchitra Narayan	SGInnovate	MTC	Robotics
Multi-column Ebeam Wafer Inspection using Graphene Coated Cold Field Emission Source	Anjam Khursheed	NUS	MTC	Precision Engineering
Printed Micro and Nanoscale Bio Sensor Systems using 2D materials	Antonio Helio Castro Neto	NUS	MTC/ HHP	Advanced Materials
A novel limb cryocompression system for prevention of Chemotherapy Induced Peripheral Neuropathy (CIPN)	Raghav Sundar	NUH	HHP	Medtech
TriSail™: A Percutaneous Triscuspid Valve Repair Device	Yeo Khung Keong	NHCS	HHP	Medtech
DCWiz: A Cloud AI Platform for Data Centre Digital Transformation	Wen Yonggang	NTU	SNDE	Digital/AI
A portable acoustic shearography system for defect imaging	Zhang Lei	IMRE	MTC	Inspection
Lead Optimisation Platform for a Cardiac Gene Therapy	Colin Stewart	IMB	HHP	Medtech
Data-driven Transformations in Healthcare	Wen Yonggang	SBIC	SNDE	Digital/AI
Automated system to surveillance unauthorized excavations using distributed acoustic sensing and data-driven machine learning models	Vuong Nhu Khue	I2R	MTC	Inspection/ AI
“SingValve” – First naturally designed, personalised, stentless, Heart Valve Bioprosthesis	Theodoros Kofidis	NUS	HHP	Medtech
Manufacturing of atmospheric water and antiviral air delivery system	Ho Ghim Wei	NUS	USS	Sustainability

Title	Project Lead	Host Institution	Domain*	Technology Areas
Development of the most advanced ion microscope for proton beam writing in the world	Jeroen Anton van Kan	NUS	MTC	Precision Engineering
A comprehensive SERS platform technology for real-time detection of greenhouse gases for onshore and offshore applications	Ling Xing Yi	NTU	MTC	Laser and Optics

Automated Continuous Post-surgical Monitoring of Vascularized Grafts using Electrochemical Metabolite Detector

Executive Summary

Flap (vascularized graft) transfers are used to surgically reconstruct a patient's body using his/her own skin and muscle (i.e. **auto-transplantation**), after trauma or cancerous tissue removal. However, post-surgical complications like vessel thrombosis (clotting) and ischemia can cause flap failures, requiring urgent surgical re-intervention within 8 hours, when the flap may still be salvaged. It is therefore essential to detect flap failures early. The current gold standard is manual observation, where junior surgeons or nurses inspect the flap hourly for the first 48 hours post-operatively for clinical signs of flap failure, then every 4 hours for the rest of the patient's stay. This is labour-intensive and subjective.

Using a prior NHIC I2D grant, we have developed the critical part of our solution to detect early flap failure: a **patch-like biocompatible sensor** assessing an identified combination of metabolites, which studies have shown are an accurate proxy for predicting flap viability.

Currently, a variety of flap monitoring methods are available, but they are not widely used due to cost, inconvenience, high learning curve, and/or low efficacy. Our device is **affordable**, automated, rapid, and **accurate**. It has been validated in benchtop and animal studies.

With the Central Gap Fund, we plan to optimize the sensor for high-volume production, refine and test the back-end system, run a first-in-man trial, and prepare for regulatory submissions. We plan to **spin out a company to commercialise** the product within two years.

Product development and verification of a revolutionary solution for the treatment of glue ear

Executive Summary

Glue ear, or otitis media effusion ("OME"), is an inflammation and excessive fluid build-up in the middle ear space for months or recurrently. It is a leading cause of children visits to doctors and hearing loss in children worldwide. Patients with 3 or more recurring episodes of OME in a year will undergo surgical procedure, which involves an incision in the eardrum followed by an insertion of a grommet tube into it to drain and aerate the middle ear.

In the US, Europe, China and South-east Asia, approximately 5.9 million grommet tube placement surgical procedures are performed every year, more than 90% are in children. In US alone, the estimated annual health care cost for grommet tube placement is more than USD 5 billion. Children undergoing this procedure require general anaesthesia (GA) which not only is costly but is associated with health risks to children. In Dec 2016, the USFDA warned that repeated or lengthy GA and sedation drugs used in children younger than 3 years of age may affect the development of children's brains and functions.

We aim to develop a hand-held, automated "point & click" grommet deployment applicator (CLiKX) that provides a quick, safe and consistent single-step grommet insertion procedure without the need for GA. The short procedural time of less than 1 second in deploying the grommet coupled with removing the reliance on GA means that the procedure can be shifted out of the operating theatre to the office or clinic of an ENT surgeon. This will reduce the economic burden on the patients and improve the allocation of hospital resources for more critical procedures. It is estimated that direct treatment cost saving ranges from 30% to 60%, depending on the types of healthcare institution, health economic and reimbursement in particular country. More critically, the success of this procedure will allow parents of young children to receive treatment without having to worry over the negative effects of GA.

Our device also has the potential to insert grommets using just a simple eye-loupe for visualization, without the need for a surgical microscope. This could increase the uptake of the treatment tremendously and allow many more disadvantaged patients in underprivileged areas, with limited access to proper health care infrastructure, to have the chance to receive quality and timely care. The market potential of our solutions for glue ears is significant, as it benefits many more paediatric patients by helping them to hear again.

There are competitors developing devices for the same intended use. But unlike the competitive devices, which are fully mechanical and significantly dependent on the surgeon's hand manipulation during the procedure, our system is automated and sensor-controlled, minimizing contact time with the eardrum to reduce trauma or discomfort, potentially allowing the procedure to be done under local anaesthesia (LA) only. Furthermore, our system can deliver existing commercial grommets, without requiring unique custom-made grommets to go with the delivery device. This will allow our system to have a higher adoption rate among physicians.

This project will focus the resources on developing the key technology and innovation of a compact, cable-less, safe handheld automated CLiKX system to address the unmet market needs, with the aim of bringing the technology to complete human trials and subsequently be

ready for product registration and commercialization in targeted markets such as the US, Europe, Southeast Asia and China.

SPEEDCARGO

Executive Summary

Problem

Figure 1 Manual labour packing aviation cargo pallets. Image Source: CAAS

The aviation sector in Singapore is experiencing rapid growth and therefore rapid expansion of its infrastructure and operations. In addition, with the global boost in e-commerce, cargo operation volumes are experiencing a sharp increase. This increase in the global air freight market is not only limited to the shipper-to-customer traffic, but also has opened a new market in terms of shipments being returned back from the customer-to-shippers (e.g. amazon, eBay, etc.). While Singapore strives to become the leader in global aviation, acquiring manpower for daily operations is becoming more and more challenging. As a result intelligent automation is becoming increasingly attractive. In the foreseeable future, given the fact the number of people wanting to do such arduous jobs is reducing, intelligent automation will become a necessity.

Solution

TUMCREATE has developed **SPEEDCARGO** - the world's first AI-powered robotics system that automates the build-up and breakdown of air cargo pallets. A high 'Technology Readiness Level (TRL)' automation system which combines sensor based robot technology, novel mechatronics and advanced control has been developed as a part of TUMCREATE's efforts for automating aviation cargo handling process. The integrated system consists of:

- Sensing system for measurement of incoming cargo (dimension, weight, centre of gravity, material and labels)
- Planning system for generating an optimal packing plan for the cargo where every requirement/constraint is met
- Gantry robot system with advanced gripping technology for precise manipulation of cargo

A key design aspect is the modularity of the hardware and software components, which ensures scalability in terms of different operation environments. At present, there is no robotic system in the world that can handle high-mix cargo in terms of weight, dimension and volume. Our system goes beyond the state of the art and will be the first deployable robotics system for cargo handling.

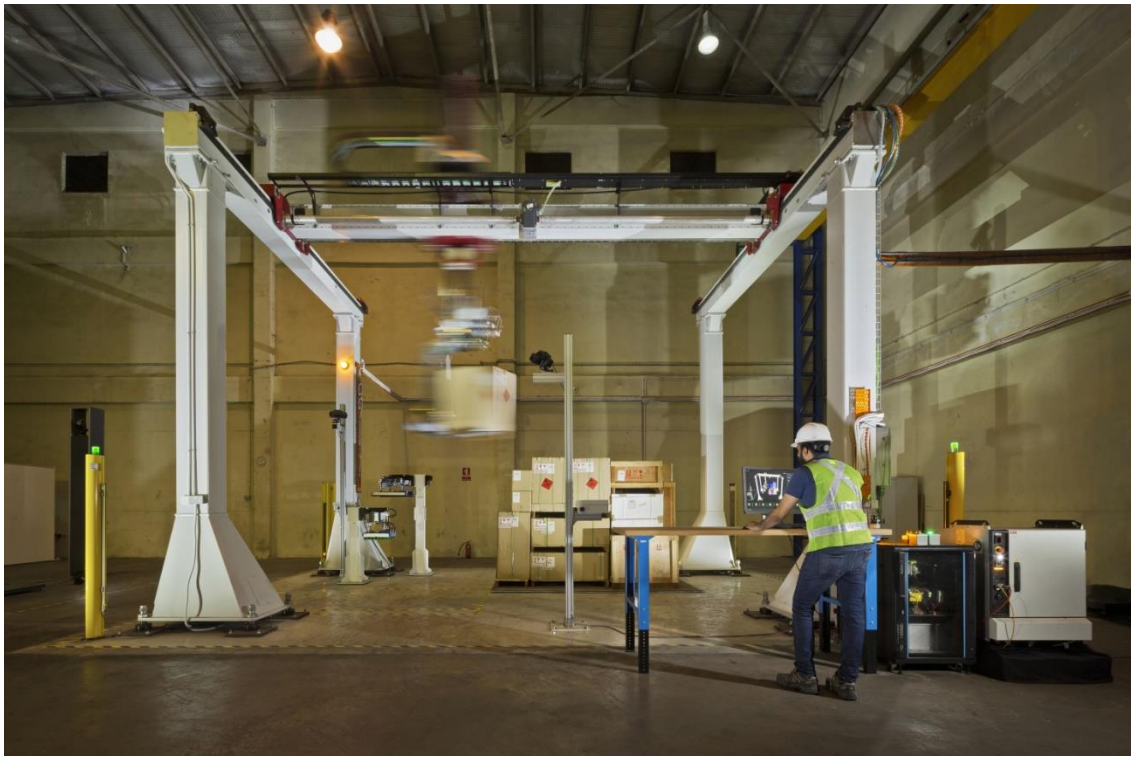


Figure 2 Current working prototype

Prototype to Product

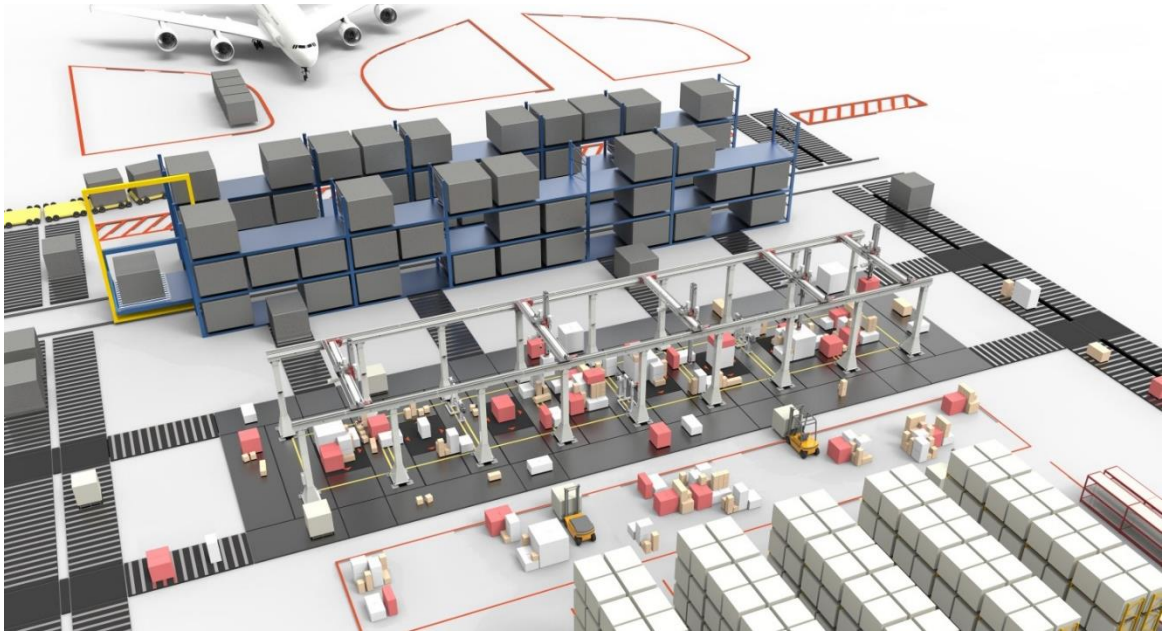


Figure 3 Vision of SPEEDCARGO powered Airfreight Terminal

Going forward our primary objective is to transform the existing working prototype to a product which can be deployed at cargo handling facilities in Singapore and worldwide. Using this technology and knowhow we would like to establish a Singaporean company specializing in air cargo process automation technology. With Singapore as its base, the company shall provide technology and services to air cargo handling facilities worldwide.

The Central Gap Fund will enable us to develop the technology and business required for the transformation of the existing SPEEDCARGO prototype to a robust and marketable product. The existing prototype was developed adhering to the strict specification of the Aviation Challenge. These specifications were framed around the general challenge statement and are limited in capturing ground level operations and complexities. Through a structured product and technology development cycle, we will accelerate the prototype from TRL7 to TRL9 by developing an optimized turnkey system integrated into the workflow of actual operations at the Changi Airfreight Terminal (AFT). In addition, the exiting software will go through a series of optimisation and industry standard test cycles for production quality code. It will also be interfaced with the existing partial automation and IT systems at the AFT. The focus will be on meeting operational requirements such as yield, speed, efficiency and usability of the system. In order to quantify and validate the value proposition of our system, the final test cycles will be conducted under real environmental conditions. Having achieved this upgrading, the optimized system will be able to produce the first robot packed airfreight pallet, leaving in a freighter aircraft from Singapore.

Satellite Quantum Key Distribution: A UK-Singapore Joint Mission

Executive Summary

Securing our networks from space: A UK-SG satellite QKD mission

The global telecoms market is estimated at USD1.1T (2015), rising at 2.2% PA. These international networks will require secure communications in the era of quantum computers when powerful computing techniques will render existing encryption schemes obsolete. Quantum Key Distribution (QKD) provides a means of securing communications, both space-based and terrestrial. QKD technology is computationally unbreakable and will remain so against all possible future improvements in computing (forward security). Satellite-based QKD will enable the secure distribution of cryptographic keys over globe-spanning distances, overcoming existing range limits for ground-based distribution. The work outlined in this proposal will support the translation of research at the Centre for Quantum Technologies (CQT) into high-value products and services and build capacity within Singapore's emerging quantum and space industry.

The United Kingdom (UK) and Singapore (SG) have established a collaboration to develop and fly a satellite QKD test-bed. This collaboration is aimed to take prime-mover advantage in this emerging QKD market, building on both countries' efforts to grow the space and quantum technologies sectors. This test-bed will comprise QKD receiving stations in the UK and SG, and a QKD transmitter from a small satellite platform. This bilateral collaboration is the broader context in which this proposal sits.

CQT seeks a total of SGD3M under this proposal towards a bilateral mission of total value SGD18M. The UK STFC will contribute SGD9M. The GAP funding will support the development of CQT's quantum light source for the bilateral mission. CQT will seek the remaining SGD6M from sources as outlined in the budget. This proposal outlines a work-package valued at SGD3M, towards designing and developing the quantum transmitter and detector apparatus that will enable satellite QKD. The remaining SGD6M for designing and establishing the optical station by which QKD signals will be relayed between satellite and ground, as well for supporting Singapore-based mission control. The quantum apparatus that will be developed in this proposal is broadly useful for all types of free-space QKD implementations, and not strictly confined to the Singapore-UK project.

The commercial landscape surrounding QKD is rapidly evolving. Much of this change has been driven by the exquisite Chinese Micius satellite which has successfully implemented several quantum communication protocols from space. While these proof-of-principle experiments are important milestones, the QKD demonstration is not commercially viable due to its significant costs. The Singapore-UK proposal follows the New Space approach of using small cost-effective spacecraft that can be used to build a constellation for servicing global locations, enabling Singapore to play a role in setting international standards for satellite quantum communications.

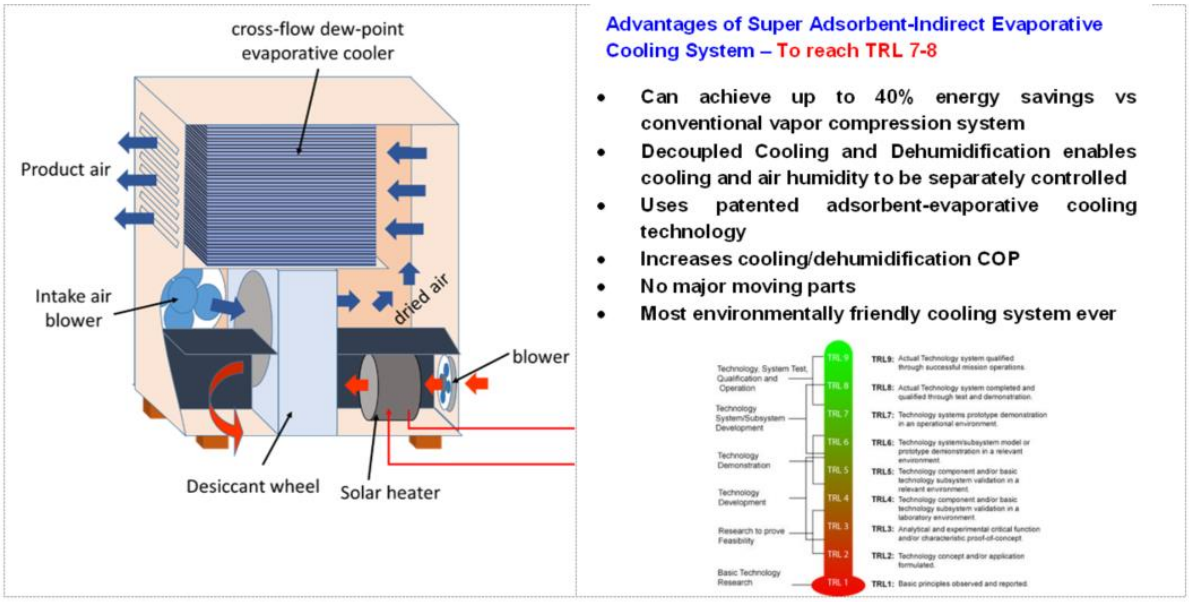
Singapore has a competitive advantage in this field by being the first country to demonstrate a quantum light source in space (launched Dec 2015 on the nanosatellite Galassia). This project will support the translation of CQT technology towards commercial deployment while building advanced capabilities in the satellite and quantum technology ecosystem.

Innovative Hybrid Super Absorbent-Indirect Evaporative Water-Based Cooling System for All-Weather Air-Conditioning Without Compressors and Chemical Refrigerants

Executive Summary

In Singapore's hot and humid climate, the energy consumed by Heating, Ventilation and air-conditioning (HVAC) typically comprises up to 50% of total energy consumption in a building. Of which, 55% of HVAC's energy consumption is for the chiller. This highlights the importance of improving energy efficiency of the air-conditioning and its impact on the environmental well-being.

The conventional work-driven compressor air conditioning systems have a thermodynamic limit of 0.45 kW/Rton at a standard rating condition where the outlet temperature of chilled water and inlet cooling water temperature are 12.2o C and 29.4°C, respectively. Additionally, there have been big concerns about ozone depletion and greenhouse effect caused by HCFC/CFC refrigerants. Recently, we developed a dew-point evaporative cooling system without the need to use mechanical compressors. It is based on the evaporative potential of water to cool the supply air. It is capable of achieving temperatures below wet bulb temperature. Without the use of compressors and CFC refrigerant, the energy efficiency ratio (EER) of our evaporative cooling system is attainable to be as high as 40 and the electricity consumption is up to 90% less than the conventional air conditioners. The Technology Readiness Level (TRL) of our innovative dew-point cooler is around 4-5.



In general, evaporative coolers have been widely used in industrial and domestic cooling systems, especially in arid climate conditions. However, they do not perform well in tropical countries like Singapore, where the air is highly humid. It is because, the evaporative cooling potential decreases at higher supply air humidity. In order to enlarge the evaporative cooling potential, we have recently developed a dehumidification technology. It is based on a newly developed super absorbent. Compared with commercial silica-gel, our super absorbent has much high water sorption capacity and can be regenerated at lower temperature. This thermal source for the regeneration can be obtained from solar collectors or low quality waste heat. Presently, our absorbent is deemed to have a TRL of 4-5.

In this proposal entails the development of an operating hybrid prototype comprising our dew-point evaporative cooler and super absorbent-based dehumidifier. By using this hybrid system, the locality limitation of the evaporative cooler is overcome. The supply air is firstly dry by the dehumidifier and then sensibly cooled by the cooler. The dehumidifier not only dramatically reduces humidity of the supply air to the human-thermal comfort level, but also synergistically enhances the evaporative cooling potential for the cooler. With the help of the dehumidifier, the evaporative cooler is widely suitable for all-weather conditions. The key objective of this proposal is to realize a world's first commercial game-changing air-conditioning system with a TRL of 7-8. Additionally, the design of the prototype is highly versatile such that it has the option to be operated with and without solar-assisted powered. It can be used as a mobile aircon unit for outdoor uses (e.g. in a NEA designated hawker centre), which is highly in demand for outdoor activities in Singapore.

Green catalytic oxidation for industrial wastewater treatment and manufacturing processes

Executive Summary

Singapore must be able to reach water self-sufficient before the long-term water supply agreement with Malaysia expiring in 2061. Meanwhile, water demand in Singapore is expected to double from 380 to 760 million gallons per day between 2010 and 2060, according to an official forecast. The increase is expected to come from industrial water usage, which will account for 70% of water demand by 2060. Therefore, it is important to develop advanced wastewater treatment technology for industrial wastewater. In a worldwide context, the total market size for industrial wastewater treatment is reaching $11 billion per year (by 2020) and growing fast (7.5% a year).

The main objective of the projects is further development of catalytic oxidation processes for industrial wastewater treatments and manufacturing processes through pilot studies. The oxidation process is based on peroxidase-inspired, copper-based catalysts and related technologies disclosed under two Non-Provisional Singapore patent applications (No. 1021708774Q and 1021708769R). The catalysts are able to activate hydrogen peroxide under a broad range of pH and oxidize pollutants quickly to benign products (e.g. CO2). The process is ideal for the reduction of chemical oxygen demand (COD) and colours in industrial wastewaters, especially recalcitrant organic compounds. Compared to advanced oxidation processes (AOPs), the catalytic oxidation process is a homogenous reaction and it can be used to degrade pollutants more efficiently than traditional AOPs on a large scale. It will be a cost-saving, environmental-friendly treatment technology that can be broadly applied to different kinds of industrial wastewater and manufacturing processes in Singapore and other countries.

In addition, the catalytic oxidation process can also be used in a wide range of applications, including laundry, fabric bleaching, waste reduction, soil remediation and manufacturing processes, etc. We will work with our partners to scale up and test the feasibility of the catalytic oxidation processes in real applications.

Soft robotic sock for robot-assisted ankle-foot mobility in chronic bedridden patients

Executive Summary

Chronic bedridden patients are highly susceptible towards developing ankle joint contracture and deep vein thrombosis (DVT). Current treatment methods are able to mitigate deep vein thrombosis with some side effects, but not ankle joint contracture, which can eventually lead to poor ankle mobility post-stroke and reduced quality of life. These patients usually have to rely on regular physiotherapy sessions that provide therapist-assisted ankle exercises to prevent ankle joint contracture and reduce the risk of DVT. However, given growing manpower constraints and a greying global population, there is an increasing workload on physiotherapists, resulting in insufficient time to complete their physiotherapy routines.

Our soft robotic sock (TRL-6) provides an automated robot-assisted ankle exercise solution that can save time, cost and effort for physiotherapists in preventing ankle joint contracture and reducing DVT risk, without specialized physiotherapy training.

Building on our prior pilot clinical trial and interview feedback, we seek to refine the capability of the soft robotic sock system through sensor integration and data visualization. We will also conduct a multi-site clinical trial on 100 chronic bedridden patients across different healthcare institutions, so that we can establish the efficacy of our soft robotic system in preventing ankle joint contracture and reducing DVT risk, and investigate the effect of our system on the potential time-cost savings and workload reduction for the physiotherapists.

New Silicon ICs

Executive Summary

SMART LEES has developed a CMOS + III-V integration platform ("Platform") to enable the integrated circuits of the future. The genesis of the technology was a US$65M DARPA COSMOS grant to prove that CMOS + III-V integrated circuits were realisable, and possessed significant performance and functional advantages. The efforts in LEES were funded by NRF to converge research on the right methods of process integration and on demonstrating the most needed "lowest-hanging-fruit" chip applications. LEES operates at initial wafer scale to build "test chips" showing the attributes of this Platform. Initial steps towards commercialization have been taken, with the SMART Innovation Centre having funded one Innovation and three Ignition Grants to design test chips using the Platform.

SMART LEES' Platform enables the creation of advanced IP-rich lighting, photonic and wireless integrated circuits and electronic systems with minimal additional CapEx required over existing semiconductor manufacturing infrastructure in Singapore. The technology has been proven at the lab-scale (low-10s of wafers/year) using a combination of: a) semiconductor processing equipment in local and foreign research institutes and universities; and b) volume production manufacturing facilities in commercial wafer fabs in Singapore and overseas.

However, the semiconductor industry relies on scale and high-yield volume manufacturing to reach low chip costs and profitability. Numerous wafers and design/test cycles are necessary to transition to a commercial production phase. As an example, commercial products by wafer fabs such as GlobalFoundries require volumes in excess of 10,000 wafers/year to be viable.

There is therefore a critical need for LEES to build a Development Supply Chain (DSC) that can produce 100s to 1000s of wafers/year so that market-specific prototype chips can be manufactured in sufficient quantity for multiple design/test cycles to build commercial confidence in the Platform. Recognising this, LEES' Scientific Advisory Board strongly recommended that LEES seek additional funding to build the DSC and use it to exercise the Platform (see attached reference letter), which would be a key step towards the commercialisation of LEES' research output, at a cost which is effectively incremental to the amount of R&D investment used to develop the Platform.

This Central Gap Funding proposal will enable 2-3 market-specific chips (with customer input and feedback) to be designed and tested, resulting in the Platform being proven to scale to production in a commercially reliable manner. This will bridge the gap towards scaling to full commercial production in partnership with CMOS foundries such as GlobalFoundries. It will also allow capital to be raised so that a new company can be built in Singapore based on the Platform, which will herald the rebirth of a new silicon industry anchored in Singapore.

Manufacturing readiness and clinical validation of a novel synthetic tendon graft

Executive Summary

TendonRegen is conceived to address the issue of Achilles tendon ruptures. Every year, 18 out of 100,000 patients suffer from this common tendon pathology, making this an addressable market size of 1.3 million patients worldwide. Unresolved Achilles tendon ruptures can result in a complete inability to mobilise the affected leg, rendering the patient handicapped. This has tremendous impact on both the individual and society in terms of quality of life and loss of work productivity. Hence, there exists a great unmet need for solutions which can enable the restoration of torn tendons to its pre-injury state whilst shortening recovery time in a manner which is safe, effective, and affordable.

The gold standard of treatment is currently surgical end-to-end tenorrhapy (suturing) of the ruptured tendon. Subsequently, the tendon is left to heal naturally. As such, the effectiveness of such treatments are highly variable, and dependent on factors such as surgical technique, size of tear, and patients' characteristics. There is general agreement that end-to-end tenorrhaphy alone is inadequate for ruptures with gaps of more than 3 cm in the tendon as it has a high re-rupture rate.

Artificial implants currently available include reinforcement patches and synthetic tendon grafts. Reinforcement patches are typically made of acellularized collagen sheets, which are wrapped around the end-to-end anastomosis, in an attempt to relief forces on the primary suture. However, these patches do not provide adequate strength and stiffness to reduce re-tear rates as the torn ends still experience significant strain. Through repeated physiological loads imposed at these sites, long-term implant failure can result. The interface between impant and tissue may also weaken through time, thus leading to dysfunction and injury regression. Thus, majority of patients who have had tendon ruptures never regain full functionality and performance of their affected limbs.

The team has successfully designed and fabricated a tubular tendon graft (TendonRegen), which not only recreates the complex three-dimensional (3D) architecture of the tendon to serve as a scaffold for tissue regeneration, but also possesses mechanical properties similar to that of the native tendon.

TendonRegen's core-shell design not only allows tenocytes to migrate into the graft for regeneration, but also provides the required mechanical strength and stiffness to withstand forces whilst the regeneration process is on-going. This combination of properties gives it higher utility as compared to existing solutions.

To-date, the team has successfully designed and fabricated TendonRegen, with an international patent application filed under the Patent Cooperation Treaty (PCT), and is currently undergoing national phase entry. An in-vitro was conducted, confirming enhanced and directed tenogenesis, with no cytotoxicity. In collaboration with PWG Genetics Pte Ltd, a pilot in-vivo study involving micropigs was also conducted. The study indicated presence of tendon regeneration, with no adverse effects. Full functionality of the injured limb could be observed after 2 months post-implantation.

Probiotic beer to enhance gut health and immune system function

Executive Summary

The global beer industry faces its greatest challenge in 50 years. All at once, there is falling consumer demand, increasingly competitive products, heightened requirements by retailers and consumers, and tougher market access. Industry players are faced with challenges such as demographic changes, the increasing supply and emergence of alternative beverage categories like wine, cider and health-oriented drinks as well as tighter regulatory and taxation measures. The industry in general is categorised by low technological changes as well.

In spite of the challenges, there has been a growing trend towards functional and fortified beverages. As such we have developed a process that can guarantee at least one billion live probiotics into every 100 ml of beer, at the end of the shelf life period. For probiotics to have health benefits, the International Scientific Association for Probiotics and Prebiotics recommends a minimum of one billion probiotics per serving. The probiotic strain we have managed to incorporate into our beer is known as Lactobacillus paracasei L26, which can neutralise toxins and viruses in the body, while boosting immunity and improving gut health.

Leveraging on the NRF Central Gap Fund, we intend to scale up our current production in preparation for full scale production, marketing, sale and licencing of our Probiotic Beer and production process.

Disruptive products in camera technology using prism optics

Executive Summary

The advent of the digital age has seen many advances, most notably in the miniaturization of components, an exponential increase in the speed, computational power and the evolution of smart devices. Cameras and optics play a key role in this evolution. The products and inventions described in this proposal show how our patented technologies, comprising various geometric forms and materials of reflective prism optics, along with other hardware and software which we have developed, can be a key contributor in driving this change.

First, the use of prism-based optics allows multiple cameras to function together, each providing a separate direction of view which is defined by a small reflective prism. When such cameras are combined the overall field of view is increased without any distortions or aberrations.

Second, a revolutionary invention allows a single camera to have an electrically-driven change in its direction of view. This invention is based on the development of a range of cube (and non-cube) beam splitters (called “PrizmCubes”), combined with suitable liquid crystal-based optical shutters. Two (or even three) fields of views from different directions simultaneously enter the PrizmCube. The viewing direction entering the camera is selected by turning on/off the relevant light shutter on timescales of milliseconds, with no need for any mechanical motion. Any new or existing camera, whether it is embedded in a drone, or a security/facial recognition camera, can be fitted with this technology and used for rapid switching of the viewing direction. The opportunities offered by this invention are vast, some relying on there being no mechanical motion, others relying on the rapid switching times between different directions.

Third, we extend our inventions in prism optics into medical endoscopes and industrial borescopes. These inventions are based on a similar but miniaturized range of cube beam splitters as described above, to provide two directions of view entering the single miniature camera at the tip of an endoscope or borescope. Selection of the viewing direction is made solely by altering the direction or polarization of illumination, allowing rapid changes of view with no mechanical motion. Given the small operating volumes in which these devices typically function this has the potential to radically alter the whole way in which endoscopes and borescopes are operated, leading the development of these devices across a wide range of applications.

Camera technologies are continuously being expanded with new functions and smart devices are being expanded with camera qualities. Our inventions promise to disrupt all industries using miniaturized camera modules, including Consumer Electronics, Security, Defence, automotive, Smartphones and Medical.

When these technologies are deployed into commercial products, there are five distinct applications:

a. Smartphones: wide angle photos and videos
b. 180° view with 2 cameras for automotive, video conferencing, security and PTZ
c. 180° capture with miniaturized cameras suitable for IOTs, wearables
d. Prism Cube with switchable direction of view with one camera, extending applications into drones, security cameras
e. Prism Cube with switchable direction of view in a miniature format for endoscopes and borescopes.

Bioprocessed okara for value-added, diabetic-friendly health food products

Executive Summary

Okara (soybean pulp) is a food processing by-product from soymilk and tofu manufacture. About 30 tonnes of okara are produced in Singapore daily, and most soy food companies have to pay an external vendor for okara disposal at the landfill or to use in animal feed (low-value use). Although okara is still edible, it is highly perishable, not palatable and largely indigestible.

Currently, in Singapore, okara has been used to make various vegetarian products and cereal snacks. In these cases, okara is used directly or after physical processing; these methods do not significantly change the flavour and nutritional profile of okara. The high amount of insoluble fibre in okara remains; this limits the amount of okara that can be added into foods as it gives a gritty mouthfeel. Yet, from another perspective, these examples demonstrate the feasibility of using okara in food products, and the industry potential and willingness to adopt these practices.

On the other hand, the incidence of type 2 diabetes mellitus (T2DM) is increasing worldwide, especially in Asia. Consequently, the demand for diabetic-friendly packaged foods has also increased. The global diabetic food market size was valued at USD 7.0 billion in 2015, with Asia Pacific accounting for over 22.0% of overall revenue. Asia Pacific is also expected to witness the fastest growth at a CAGR of 6.0% from 2015 – 2025.

Soluble fibre and free isoflavones in okara have been shown to improve the risk of T2DM in animal studies. Our lab has demonstrated that bioprocessing of okara using enzymes and/or microorganisms boosted the amounts of these nutrients. Moreover, the changes in okara composition also make it suitable for wider food applications. The bioprocessed okara (subsequently referred to as “bio-okara”) is a potential functional, diabetes-friendly food ingredient that is more palatable and may help manage T2DM.

Hence, this project aims to:

(1) Demonstrate the technical feasibility of the bioprocessing of okara on a pilot- and industry-scale;

(2) Apply the bio-okara into food products such as baked goods (biscuits, breads, cakes etc.), noodles, probiotic beverages, or be consumed directly as a food product suitable for the elderly and diabetics;

(3) Assess the effects of consuming this bio-okara food product on blood glucose and insulin levels in middle-aged and older adults in a pioneer clinical study, providing robust evidence to support the beneficial effects of bio-okara.

The success of this proposed project will convince and incentivise food producers to utilise okara and, therefore, potentially mitigate the negative environmental effects resulting from the disposal of this food processing by-product.

WIND: Product development and verification of a non-invasive solution for treatment and management of airway secretion diseases

Executive Summary

Bronchiectasis is a chronic respiratory disease affecting at least 57 million globally. The disease results in patients chronically overproducing mucus resulting in many problems related to mucus, breathing, infection, and hospitalisations. Patients with difficult to clear mucus experience lifelong clinical, social, and economic impact in the form of increased mortality, poor quality of life (QoL) and loss of workdays.

Respiratory conditions often overlap, and this is the case with bronchiectasis. Of the 170+ million people with COPD, 57 million suffer from both bronchiectasis and COPD overlap syndrome (BE COPD OS). The burden of COPD has been much better studied than bronchiectasis. We know that in Singapore and the USA, the costs to payors exceeds USD 120 million and USD 49 billion, respectively. Data shows that a patient with BE COPD OS will cost the US healthcare system 250% more than a patient with just COPD or bronchiectasis. Although bronchiectasis patients only represent around 30% of total COPD patients, they may be responsible for more than half of the costs.

To avoid mucus build ups and associated costly exacerbations regular Airway Clearance Therapy (ACT) has become the Standard of Care to mobilize mucus. Patients are administered chest physiotherapy by a third party (either a physiotherapist or a caregiver) where a person slaps different areas on the patient's chest to loosen and mobilize the mucus so it can be coughed up. This therapy is required at least twice each day for 30 minutes a session. It is incredibly lifestyle-invasive and uncomfortable resulting in high non-compliance (>50%) and poor patient outcomes.

This Project aims to develop a solution for patients to effectively and easily treat and manage their disease. The solution combines a hardware treatment device with a mobile app for chronic disease management (CDM) using AI. The hardware treatment device utilises acoustic intrapulmonary vibrations to vibrate the airway and shake mucus free. The automated, non-invasive solution enables the patient to administer this therapy daily without the help of a third party. The mobile app will monitor patient symptoms using artificial intelligence to allow doctors to intervene before costly and damaging exacerbations. Overall, we expect the device to improve patient outcomes and lower the disease burden to payors.

A proof of concept hardware device showing the acoustic intrapulmonary vibrations has undergone bench testing and cadaver testing showing that it produces a similar effect to FDA approved acoustic devices. Although the mechanism of acoustic intrapulmonary vibrations is moderately complex there is significant effort required to optimise the combination of components used in creating, directing and transmitting the acoustic waves to vibrate various patient's airways. With this design effort, we believe the system can be optimised to be more efficacious than the current Standard of Care in a wide variety of patients while other devices in the market have only sought to be as effective as this questionable treatment for patients. This device will also be suitable for all severities of bronchiectasis while current devices largely focus on early to moderate-stage bronchiectasis rather than the more costly and impactful moderate to severe-stage patients.

This Project will focus resources on further developing the key technology and innovation of an automated wearable, wireless, safe system, and its companion mobile application. Over the course of the project, we will mitigate technical risks, design risks, system integration risks

and confirm performance specifications in preparation for clinical validation in targeted markets such as the US, Europe, and Asia.

AITachnology (AIT) – Giving robots a sense of human touch (Product development of AI-enabled tactile skins for perceptive robotics)

Executive Summary

The increasing demand for process automation, pressure on corporate margins and need for customer centricity is driving the need for robotic augmentation of human capability. Moreover, increasing worldwide needs for addressing aging populations further drives demand for assistive robots that can support humans, automate processes, and act as caregivers, especially in a myriad of environments. In fact, the robotics technology market is forecast to be valued US$ 82.7 billion in 2020 and is expected to register a CAGR of 10.11% over the forecast period of 2020-2027.

Robots today largely work in highly structured environments, typically carrying out simple repetitive manipulation/assembly tasks. Although "Vision" is being used to augment capability of these robots, dynamic tasks that requires real time feedback and learning in unstructured environments remain challenging without a robust touch feedback capability. "Touch" enables the robot to deal with uncertainties about an object's physical properties, especially during dynamic contacts. These limitations make vision-only approaches inadequate in unstructured environments, especially when the object is partially or fully obscured.

Enabling next generation robots, AITacnology (AIT) is developing a breakthrough, enabling platform technology that gives robots a human-like sense of touch, filling an unmet need and technological gap.

AIT aims to integrate "Touch" into robots and address three specific unmet technological gaps and automation pain points –

1. Real-time manipulation and object grasping: The sense of "Touch" will provide "Vision" augmented robots with critical information about the curvature of the object, the temperature of the object, the force exerted and the surface texture.
2. Contact inference: Contact with objects or humans can happen either accidentally or as the robot searches for support in dynamic movements. "Touch" is critical for determining contact and for the robot to react effectively and immediately post contact. This will enable robot's ability to work with more closely with humans.
3. Speed, latency and sensor density: Current tactile sensors designed to solve this problem transmit the tactile information from sensors serially, resulting in readout latency bottlenecks and complex wiring as the number of sensors increases.

Leveraging on ACES, the patent-pending Asynchronously Coded Electronic Skin parallel edgesensing system developed at the National University of Singapore (NUS), and synergistically combining it with leading machine learning classification algorithms, AIT will offer toolkits for a complete 'Sensing System'. Inspired by a neuro-mimetic architecture, our sensing system is highly scalable and provides ultra-fast somatosensory perception for robots, enabling more than a 10X increase in sensing speed and density scalability compared to commercial touch sensing systems that operates serially and struggle with the trade-off between speed and sensor density.

While the ACES achievements are promising, these prototype arrays and transmissions were conducted in a lab environment and in part simulated. It is critical that the sensing system is developed further through this GAP project to attain performance reliability and stability when used outside the lab environment.

Primary applications include end effectors (claws, grips, and clampers etc.), robotic surface areas, as well as neuro-prosthetics for dexterous object manipulation and somatosensory perception. Because AIT presents a paradigm shift in achieving tactile perception, we have a strong value proposition in a developing and nascent market where competitors are limited. We seek the resources required to develop market sampling ready prototypes in preparation for large-scale venture-backed commercial launch in 2022.

Multi-column Ebeam Wafer Inspection using Graphene Coated Cold Field Emission Source

Executive Summary

The goal of this project is to design and manufacture an innovative field emission source array for a world's first high density multi-column SEM for applications, in biology, material science and the semiconductor industry. The key competitive advantage of this commercial multi-column unit is based on the innovative high brightness graphene source development under the current NRF CRP project (NRF-CRP13-2014-04). The output of this project targets a field emission gun unit of multi-source, because the source unit market offers high value and high margin. Our strategy is to leverage on the innovative electron source development carried out in the CRP project which will provide critical components for a competitive edge in a large market. The final product will be fully automated with software interface compatible to industry standards, so that it will be ready for customer engagement and commercialization steps after the GAP project.

A multi-column SEM system with 100 columns will provide 100X faster data acquisition speed compared to a single column SEM system for the same area under investigation. Graphene coated cold field emission tips offers a much higher electron beam brightness, which will further increase the electron beam current linearly on the sample to up to 3X. 3X higher beam current will allow 3X faster imaging speed at the same imaging signal to noise ratio. When using graphene cold field emission source for a multi-column SEM with 100 columns, the overall imaging throughput will increase up to 300 times. This high throughput imaging SEM fits into the demands of semiconductor Fabs for R&D and process control purposes. The project can also leverage on collaboration agreements that have been already been made with international electron beam instrument manufacturers, and form the basis of a working relationship for the future.

Current CRP project has validated many principles, and reported promising scientific results, but industrial applications require automated, repeatable, and a reliable engineering performance. Results in CRP project need further development for commercialization standards, and central GAP fund will support the transformation from promising research work to a viable industrial product.

Printed Micro and Nanoscale Bio Sensor Systems using 2D materials

Executive Summary

A new disruptive nanoscale printing technology for making sensors and nanoelectronics based on 2D materials will be leveraged to develop biological and chemical sensor system platform. This new additive a sustainable technology will enable making sensors systems at a very low cost. This is accomplished by utilizing a new directed assembly based-printing of 2D materials that enables the printing of electronics and sensors. A key to the success of this technology is taking advantage of the unique and novel properties of 2D materials and the world leading research and technology developed at the *Center of Advanced 2D materials* (CA2DM) at NUS. We propose to use this technology to make a sensor system platform that could be used to make bio and chemical sensors.

We propose to focus on developing sweat based noninvasive sensors for the detection of glucose, lactate and urea. Diabetes is a chronic metabolic disorder that affects more than 400 M people worldwide according the World Health Organization and more than 500,000 adults in Singapore. It can lead to serious health problems such as cardiovascular disease hypoglycemic events that could lead to coma and even death. Treating diabetes requires 24/7 management and monitoring the glucose concentration. However, all commercial sensors today are invasive and expensive. We will, in less than two years, produce a non-invasive inexpensive wearable wireless sensor platform that can monitor glucose and lactate continuously and communicate the results to the patient's smart phone and/or doctor.

The proposed printed sensor platform can also be used to print environmental sensors for the detection of contaminants indoors or outdoors. During the first year, the team will start with a hybrid printing system that will integrate printed sensor and circuit components with conventional electronic chips on flexible substrates to accomplish a fully functional sensor. This will be used to test the sensor and develop measurements protocol in collaboration with medical personnel, allowing early validation of the electronics and early testing and verification of the sensor systems to identify any challenges while the monolithic printing of the entire systems is being developed.

The proposal has a significant commercial and societal impact in Singapore and globally. On the one hand, Singapore has invested heavily in 2D materials in the last decade and the results achieved here will vindicate that investment. On the other hand, glucose sensor market is worth billions of dollars globally, the China glucose biosensor market alone will reach two billion US dollars by 2022 while wearable sensors global market will reach USD$ 20 billion by 2024 with CAGR of 31% while medical sensors have a CAGR at 21%. The environmental sensors market will reach over USD$ 17 billion this year. We will also make significant

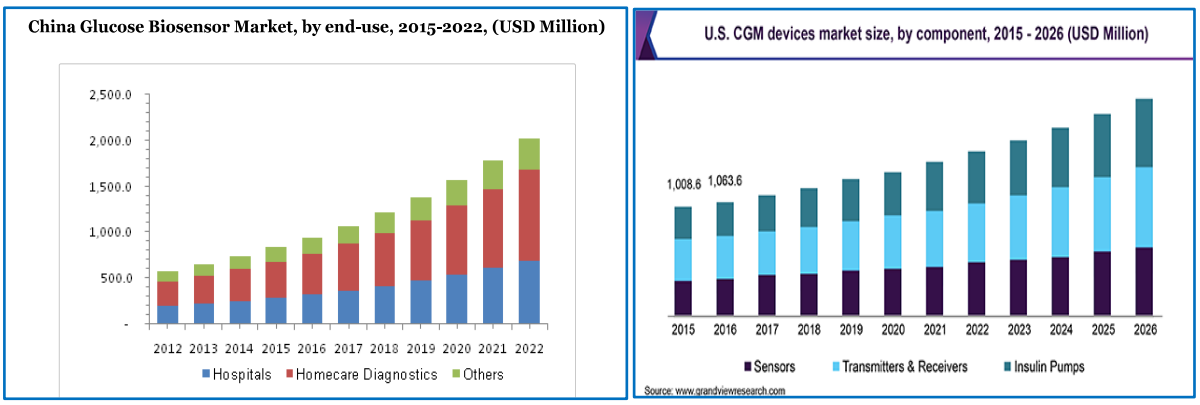


Figure 1. US and China glucose sensor market.

contribution to the Internet of Things (IoT) which relies on embedded sensors, electronics and connectivity with an estimated market of USD$ 4-11 trillion by 2025. See Figure 1.

This proposal will leverage the nanomaterial science and technology created by the *CA2DM* using 2D material innovations to enable sensor and electronics superior performance, flexibility and wearability and the nanoscale printing technology created at the NSF Center for high-rate nano-manufacturing (CHN) in the USA. Singapore will be the first country where this new scalable nano-printing technology using nanomaterials will be utilized to make commercial products serving as a model to other countries that can no longer afford conventional CMOS electronics fabrication plants that cost US$17 B to build and US$ 1 B per year to operate.

A novel limb cryocompression system for prevention of Chemotherapy Induced Peripheral Neuropathy (CIPN)

Executive Summary

A graphical representation of the executive summary is depicted in below figure.

Overview of the project depicting "Clinical unmet need"/problem of chemotherapy-induced peripheral neuropathy (CIPN), Proposed technology solution – portable limb cryocompression system specifically designed for cancer patients undergoing chemotherapy and existing approaches and their pain points which the proposed solution mitigates.

Chemotherapy-induced peripheral neuropathy (CIPN), an unmet and increasing clinical need, is a severe dose-limiting side-effect of chemotherapy for cancer treatment. CIPN causes progressive often irreversible pain/sensitivity in hands and feet and affects cancer survival rates as it can cause delays and discontinuation of chemotherapy, affecting almost 1.4 million cancer patients annually worldwide (Park et al. 2013). CIPN contributes to long- term morbidity for patients and significantly increasing economic burden in terms of healthcare costs estimated to be US$17,000 more in cancer patients with CIPN than those without CIPN and patient work-loss (productivity loss of 50 days with usual care) (Seretny et al. 2014) (Molassiotis et al. 2020).

Several pharmacological agents have been developed to prevent and treat CIPN, yet none have proven effective in large-scale clinical trials (Loprinzi 2017). Non-pharmacological approaches, specifically cryotherapy for preventing CIPN symptoms have gained prevalence. A study involving frozen gloves worn during chemotherapy, in a controlled trial, demonstrated

reduction in incidence of CIPN (Hanai et al. 2018). However, the frozen gloves currently used to administer limb cryotherapy to cancer patients is not user-friendly, delivers unstable cooling and can cause severe frostbite. The gloves used in the trial by Hanai et al were eventually withdrawn from the market for incidences of frostbite. In pilot clinical trials in Singapore, we have demonstrated that cryocompression (addition of low dynamic pressure to cooling) produces a similar cooling profile to frozen gloves but with significantly improved tolerability (Sundar et al. 2018) (Bandla et al. 2019) (Bandla et al. MASCC 2018). Our studies have also been cited in clinical guidelines for prevention and management of chemotherapy-induced neurological side-effects by 2 leading clinical societies – American Society of Clinical Oncology (ASCO) and European Society for Medical Oncology (ESMO) (Loprinzi, Lacchetti, et al. 2020, Jordan et al. 2020). The guidelines state that cryotherapy is a promising intervention for CIPN prevention, and more proof of evidence is required as currently available modalities are prone to causing frost bites and unsuitable for use in cancer patients.

Existing cooling technology, mainly developed for sports medicine and orthopedic indications, are generally class I and either bulky, manpower intensive, energy inefficient, or do not cater for use in preventing CIPN in cancer patients. Specifically, none of these devices offer accessories which allow for concomitant administration of chemotherapy and cryotherapy. This means that patients will be unable to undergo cryotherapy in the cannulated arm in which the chemotherapy is administered and hence exposing it to a risk of CIPN. There is also a trade-off between stable thermoregulation and size of device – smaller devices require the user to manually add ice at regular intervals throughout the therapy, causing unstable temperatures; on the other hand, the device which offer good thermoregulation are bulky and not convenient for placement in chemotherapy suites. There is an urgent need for a class II medical device specifically developed for cancer patients to be administered in a chemo suite by delivering stable cooling, tolerable over the entire duration of the chemotherapy.

In collaboration with Paxman Coolers Ltd, world-leaders in scalp cooling for prevention of hair loss due to chemotherapy, we aim to design, develop and test a portable limb cryocompression class II system specifically targeting prevention of CIPN in cancer patients. This device will be tested in cancer patients undergoing CIPN-causing chemotherapy and the efficacy of prevention will be monitored using various clinical and patient-reported outcomes. Paxman bring to the collaboration extensive expertise in design, development, manufacture, regulatory approval, and commercialisation of medical cooling devices. Paxman's route to market is also well established and operate in 54 countries with the channels and infrastructure to successfully launch this product to its own customer base and growing distribution network. These factors (including Paxman's established route to market, extensive regulatory experience, the project's systematic clinical trial validation and the class II regulatory classification) have taken a considerable time (~20 years) to achieve, making Paxman a trusted player, and present a significantly high barrier to entry into market.

Overall, this project will have a significant and broad impact. Primarily, by preventing/reducing CIPN the health and quality of life of cancer patients will be significantly enhanced, during-and-after chemotherapy. Economically, a CIPN preventative treatment will alleviate the associated heavy-and-increasing economic burden generated by CIPN ($2200/CIPN-at-risk-patient (Pike et al. 2012b)). Socio-economically, preventing CIPN will reduce patient work-loss through accelerated return to work.

We have already filed 2 provisional patents with the NUH Innovations Transfer Office and which will be followed by design registrations. On successful completion of the project, joint IP will be filed between Singapore-Paxman teams within 2 years of the project's successful outcomes. A Centre of Excellence (COE) will be setup in Singapore, for Training and R&D in South East Asia (SEA) attracting local talent and collaboration. This COE and training hub will also support Singapore as the "world-class" regional hub for medical tourism. This is coupled with a fast, local medical device registration timeline with HSA where patients can have access to the latest innovation without a significant delay observed in many other countries.

TriSail™: A Percutaneous Triscuspid Valve Repair Device

Executive Summary

Tricuspid regurgitation (TR) is a common valvular heart disease worldwide affecting ~5% of the elderly population and, when its severity reaches moderate to severe, is an independent predictor of increased mortality. Approximately 7.2 million people suffer from moderate to severe TR in the U.S and Europe alone, and this number is growing by more than 0.5 million each year. In these patients, medical therapy restricted to diuretics and heart failure medication is frequently ineffective.

Currently, surgery is the only treatment option for patients who remain symptomatic on medical therapy. However, Tricuspid Valve (TV) surgery is associated with an unacceptably high risk of operative mortality and poor outcomes and hence only ~0.5% of patients with moderate to severe TR currently undergo surgical intervention. Consequently, a percutaneous and minimally invasive approach to treat TR represents an attractive solution to this highly significant global unmet clinical need.

Several transcatheter technologies are currently in various stages of development underscoring the significant market interest and clear opportunity to commercialize a safe and effective solution. Given the many underlying mechanisms resulting in TR, it is expected that eventually a few different technologies most suitable for different patient segments will succeed commercially. Current percutaneous options have several drawbacks such as the use of a bulky device and technically complicated procedures, requiring advanced imaging and disruptions to the normal anatomy.

In this project, we propose the development of a highly innovative technology TriSail™, a percutaneous tricuspid valve repair device, which consists of a transcatheter delivery system and an implant. Compared to competition, TriSail™ is highly differentiated and innovative in multiple ways – It uses a simple yet robust and significantly less bulky single neo-leaflet flap which enhances coaptation of the native leaflets to effectively reverse TR. TriSail™ has been designed to accommodate various valvular anatomies, requires a vastly less complicated deployment process without the need for advanced imaging, minimizes the risk of damage to the native structures as it does not use sutures, pledgets or barbs for anchoring to the tricuspid valve and is easily retrievable and repositionable if needed peri-operatively.

The project team is comprised of accomplished professionals with decades of experience in clinical, scientific, product development and commercialization of class III medical devices. The technology is protected by a strong IP portfolio consisting of two patent families (filed in ~15 countries), a third patent family in the process of filing, and is being primed to be commercialized through the creation of a local start-up company.

With the ongoing technology development TriSail™ will be completing device efficacy and large animal acute safety) studies using existing funds. In this gap fund proposal, the team aims to further advance the technology, make it scientifically more robust and accelerate its commercialization by a) completing large animal chronic safety studies; b) generating advanced computational fluid-structure modelling to simulate the device's safety and performance characteristics in patients over a long duration; c) completing device biocompatibility safety testing and mechanical characterization including FEA and d) conducting First-in-Human studies in Singapore and Australia.

DCWiz: A Cloud AI Platform for Data Centre Digital Transformation

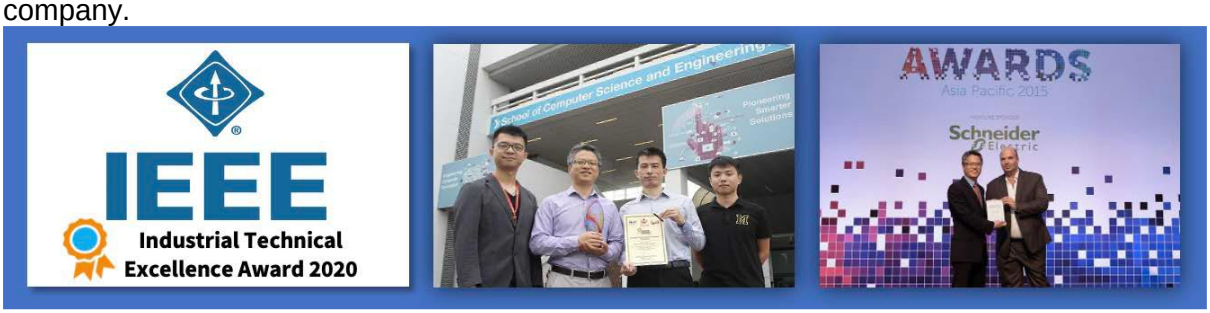
Executive Summary

The data centre (DC) industry is growing exponentially in recent years at the expense of high energy consumption and carbon emission. It is estimated that by 2025, DCs of the world will consume 1/5 of Earth's power. Energy cost has evolved to be the most pressing issue, contributing to 50% of DC life cycle operating cost. Meanwhile, Singapore has become arguably the most attractive DC market in the Asia-pacific region, with an expected DC market size of USD 2.5 billion in 2025 and an annual growth rate of over 4% from 2020 to 2025. Efficiency and sustainability are becoming more and more critical for economic and environmental reasons.

Against this backdrop, the DC management today remains by and large a best practice-based manual process with pain points of risk-averse mindset, silo-ed operations, and staff turnover, which cumber the industry by poor energy efficiency and high maintenance costs. Recent progress in AI technology has provided an unprecedented opportunity for automating DC management. However, most emerging AI-based solutions require installing myriad physical sensors and use over-provisioning as a fallback mechanism, leading to high device costs and long model training time.

To tackle these challenges, we propose a cloud-based industrial AI platform, DCWiz, that integrates digital twins with AIoT into a one-stop solution for DC management and operations. The industry-grade digital twins provide an accurate yet intuitive 3D simulation platform that covers the DC layout, thermal dynamics, and airflow directions, allowing for quick detection of hot spots and anomalies. The high-fidelity digital twins can also synthesize a massive amount of data for AI algorithms with high quality and diversity within a relatively short period, avoiding excessive sensor deployment. During actual operations, the digital twins work synergistically with the AIoT component, allowing the AI-recommended actions to be first validated in cyber-space before actual physical applications, to assure the safety and alleviate the prevalent risk-averse mindset. The cloud-based integrated solution will transform how DC is managed and operated, similar to the proven approach of how Meraki transformed enterprise WIFI management.

So far, we have successfully conducted the Proof of Concept (PoC) trial in the data centre of Alibaba Group. The results confirmed the feasibility of optimizing data hall energy consumption using digital twin technology with an industrial level accuracy (within 1oC) while involving minimum physical sensors. Alibaba has reported in their media release that the tested solution can potentially reduce up to 90% of its Capital Expenditure (CAPEX) in IoT deployment for DC monitoring. The system also shortened the testing duration from 1 month to merely 1 week. Well recognized in the industry, the DCWiz technology concept has won the 2020 IEEE TCCPS Industrial Technical Excellence Award. With the Central Gap Fund, we plan to further develop a minimum viable product (MVP) that completes all the essential components of DCWiz and integrates them into a cloud-based platform. A series of Proof of Value (PoV) trials with local partners will also be conducted, followed by its commercialization by a spin-off company.



Award-winning technology components of DCWiz: the 'Digital twin + AIoT' technology winning the 2020 IEEE TCCPS Industrial Technical Excellence Award (Left), and the Cloud3DView technology winning the Gold Medal of 2016 ASEAN ICT Award (Middle) and the 2015 Datacentre Dynamics Awards, the 'Oscar' award of Data Centre Industry (Right).

A portable acoustic shearography system for defect imaging

Executive Summary

Defect detection is widely requested in many industrial sectors ranging from microelectronic components to huge infrastructures. Although there are many defect imaging methods available, there is a persistent need to request for a faster, low cost and universal defect imaging tool. Acoustic shearography is a new and disruptive defect imaging technology developed at IMRE, A*STAR, by integrating laser shearography with acoustic wave excitations. The technology has combined advantages of fast and full-field imaging of optical methods and deep penetration of acoustic waves. The technology is suitable for fast imaging of both surface and deep subsurface defects in any solid materials and it has broad applications for nondestructive defect imaging in multiple industries. Currently, the technology has been demonstrated in lab based on multiple interconnected bulky components. To bring the technology closer to commercial market, a portable acoustic shearography system is to be developed. The objective of this project is to develop a prototype of a portable acoustic shearography system suitable for industry deployment and adoption.

Lead Optimisation Platform for a Cardiac Gene Therapy

Executive Summary

LMNA dilated cardiomyopathy (DCM) is a cardiac disease caused by mutations in the LMNA gene with a younger onset and worse outcome than other DCMs. DCM is characterized by reduction in pumping capacity and thinning of the walls of the heart. Treatment options are very limited, and the only cure is a heart transplant. At an estimated prevalence of up to ~1:12500, LMNA DCM is a rare disease that benefits from laws promoting drug development for so-called orphan diseases, such as a Phase 3 trial as small as 160 patients.

AAV (adeno-associated virus) gene therapies promise one-time treatments for rare diseases. AAV gene therapy has proven commercially viable, being sold at US$850,000 – US$2.1 million. Several AAV biotechs were acquired in 2018-19 for between US$109 million – US$8.7 billion. Some, like Myonexus, treat patient populations that are up to 40x smaller than LMNA DCM. LMNA DCM therefore seems ripe for a AAV gene therapy, but its autosomal dominant genetics requires a more sophisticated approach than typical gene replacement. We have established proof-of-concept in a LMNA DCM mouse model using AAV to suppress the function of a group of proteins known as the LINC complex, which potentiates the negative effects of LMNA mutations. We inhibit the LINC complex by overexpressing a mutant form of the Sun1 protein known as Sun1DN (dominant negative).

To make the therapy safer, we express Sun1DN only in the heart. If priced at a reasonable US$1 million, the sizeable LMNA DCM population implies an addressable market size of ~$50 billion in the developed world. A small molecule drug is in Phase 3 clinical trials for LMNA DCM, but does not address the underlying cause of the disease. Other AAV approaches relying on CRISPR gene editing, for example, are not
commercially viable due to the multitude of LMNA mutations, each requiring a specially tailored gene editing drug. With no other competition, our one-size-fits-all gene therapy is a first-in-class product.

In this proposal, we seek to extend ongoing pre-clinical studies on our AAV gene therapy to bring the product closer to an IND (investigational new drug) application, which is required for clinical trials to commence. There are 3 major experimental aims: (1) optimizing the product, and performing animal experiments to determine (2) the dose response, and (3) the treatment window. We will genetically engineer the current AAV gene therapy so that we reduce safety risks due to aberrant immune responses, and improve gene expression, a key performance attribute of the therapy. We will select a final clinical design, and test multiple dosages in a mouse model of disease to determine the appropriate dosages to use in patients. We will also test the therapy at early, mid and late stages of disease progression in a mouse disease model, to determine the appropriate time point for intervention in patients. By thus bringing the product closer to clinical trials, Esco Ventures X will be able to attract a strong investment syndicate for seed and Series A funding of Nuevocor Pte Ltd.

Data-driven Transformations in Healthcare

Executive Summary

Current patient journey still sees 2 significant issues from hospitals to homes, with respect to use of data.

In the hospital-setting, a sandwich class of patients in general care exhibit “code-blue” or MET (medical emergency team) activations and do not have access to continuous monitoring and advanced analytics for early intervention. At any day, approximately 3 “codeblue” activations are made and that can result in ICU transfers at S$ 12,000 per stay. Early prediction of 1 ICU transfer, can result in significant accumulated savings. There have been companies making ingress into this market. Early Sense uses bed-sensors to track MET and provide analytics. The limitation lies in its mobility to deploy in alternate sites. ViSi leverages on vital sign monitoring in general care but lacks predictive analytics. Philips Biosensor is a ECG patch that measures basic vitals but the cost of the non-reusable patch may be a limitation for scale. The fundamental generic limitation is the lack of validated prospective Asian based models and that are continuously-integrated and applicable to general care. Most models are based on ICU and are Western phenotypic, namely, MIMIC. Furthermore, models are NOT integrated into continuous monitoring in general wards.

In the home-setting, there is interest on use of remote-monitoring. Benefits include pre-empting readmissions, providing care to patients that need them less in hospitals and reducing risk of infection. While several companies e.g. Biofourmis, Philips and Spry Health etc. have provided good products in this space, the key limitations are 3-fold. Firstly, such platforms require mobile interfaces and synchronizations that impacts compliance (proven limitation). Secondly, there is a lack of primary vitals, Asian cohort specific data models, integration into hospitals from home and lastly, lack of usability or form factor. KOLs have provided feedback. Biofourmis has a large form factor, is not validated on primary vitals e.g. respiratory rate for COPD and has analytics that are to be validated in an Asian cohort.

Philips has an ECG patch but lacks oxygen saturation in addition to direct respiratory rate for monitoring worsening. Spry has the ability to measure direct oxygen saturation but lacks in direct respiratory rate measurement. Like the hospital aspect, home-care models lack the robust prospective validation needed in an Asian phenotypic cohort with integration into work-flow processes.

In this project, we aim to systematically and methodically develop, validate and integrate predictive analytics for general care code-blue prediction and home-care exacerbation prediction into continuous monitoring systems provided by Respiree©.

We structure retrospective and prospective validations, model development, UI integrations and clinical workflow adaption processes via user-interfaces. The key is to prospectively validate this fully integrated system and to ensure that the relevant flags and alarms have been co-developed by nursing and primary care with workflow integration. What we do envisage also is to top up the system with an all-integrated UI that registers the patient in hospital (general care) and is able to transit the patient for home-care (when the patient is discharged) while making use of baseline conditions and familiarity from hospitals.

Automated system to surveillance unauthorized excavations using distributed acoustic sensing and data-driven machine learning models

Executive Summary

This project aims to build and deploy an automated system to detect unauthorized excavations in the vicinity of optical fiber systems in Singapore. Unauthorized excavations may cause damage to fiber infrastructure and interruption of internet supply which results in economic losses and poses threats to national security.

This project is a continuation of a previously completed GAP project titled “Intelligent Software-Defined Multifunctional Optical Interrogator” in which we successfully developed the DAS interrogator that employs optical fibers to measure vibrations from activities such as moving vehicles, industrial operations, excavation activities and reports these vibrations. We have additionally employed the vibration signals measured by the DAS interrogator to perform the proof-of-concept trial of detecting 3 events involved in an excavation activity including cutter, hammer, digging. The preliminary results show that signals collected by DAS interrogators can aid to detect excavation activities.

In this project, we further focus on developing data-driven algorithms that can recognize excavation activities from the sensed vibration signals provided by the DAS interrogators so as to provide an online real-time alarm management of unauthorized excavations. To the best of our knowledge, there is no system available in the market to perform real-time management of unauthorized excavations. Offline algorithms to classify excavations exist in the literature but the experimental setup is far from being a realistic scenario in terms of robust environmental settings and rigorous experimental design.

There are two key challenges to actualize an online excavation detection system leveraging on DAS infrastructure. First, the huge number of sensed positions in the entire fiber system makes concurrent processing and analysis of all acoustic traces infeasible due to computation limit and communication throughput restrictions. Second, vibrations created by sounds from excavation activities are non-stationary and affected by various environmental settings. They are also dependent on temporal and spatial elements such as time of the day or road traffics. To resolve these issues, we propose a two-step algorithm in which the first step will scan acoustic traces using a predefined threshold to identify possible locations along the fiber optical cables where excavation activities may occur and the second step will further process vibration signals at these possible locations using the to-be-developed data-driven machine learning models. We plan to carry out data collection at 6 common environmental settings in Singapore including residential areas, public roads, factories, schools, working places, and nearby MRT (mass rapid transit) lines at different timings so as to capture the variance and characteristics of vibrations caused by excavations. The intensive data collection will help select suitable cut-off threshold and develop robust data-driven machine learning models catering to various settings.

Therefore, this project concentrates on building machine learning models to recognize excavation events and integrating data-driven models with DAS interrogators to provide optical fiber infrastructure owners with a continuous, high-performance, cost-effective surveillance system to monitor large areas. The detected events will be sent to system owners to verify whether or not excavations at a particular location are authorized based on the list of approved activities available in their systems.

“SingValve” – First naturally designed, personalised, stentless, Heart Valve Bioprosthesis

Executive Summary

The purpose of this project is to develop and test a disruptive Class III implant, a Heart Valve prosthesis, with unique differentiators, in Singapore, and bring it to clinical practice.

This prosthesis’s differentiators are aimed to have disruptive features, which will elicit benefits to patients worldwide. So far, the project has matured since 2017, from a “napkin design” to successful chronic animal experiments, space allocation for cleanroom, development of an individualized design template, acquisition of a USPTO patent, successful FDA pre-submission, and preliminary in vitro tests in our wetlab.

Through the Central Gap Funding, we aim to execute the remaining crucial stages of the R&D and transition to commercialization: these steps include, GLP-level preclinical studies, in vitro studies, freeze of the prototype, advance regulatory matters, setting up of resourcing, design verification, chemical and biological treatment, and QA processes, and the First-in-Man clinical trial. Our heart valve prosthesis, which we call “The SingValve” was entirely designed and developed in Singapore and Proof-of-Concept experiments have been carried out both at NUS as well as IMMR, Paris.

The first key differentiator of our valve to any other existing heart valve on the market is that it is the first in the world with a Human-like, biomimicry design, as will be explained and illustrated below. It features a natural shape and is composed of materials already used in FDA-approved applications. It is superior to the available commercial counterparts as it is fashioned to resemble the natural valve not only in design but also in functionality, hence offering better hemodynamic performance and potentially better outcomes for the receiving patient.

The second differentiator of our prosthesis is the Personalized / Individualized design and production process, also unique to our valve prosthesis. We developed a formula, which permits us to customise it to the individual patient recipient, using his pre-operative scans. This promises further functional and marketing advantages.

The global market for heart valves is already in the Billions, and growing, particularly in the developing world, while there is only a small number of key players. The market is expected to increase due to the rise of relevant heart valve disease that demands valve replacement, and growing access to modern heart surgery, around the globe. This provides a hospitable niche for an innovative product that is customisable and more physiological in its function, than anything so far marketed. Singapore has herewith an attractive opportunity to position herself as a MedTech hub in this arena.

We request for a full consolidated funding of 2 years, to conduct the necessary R&D as well as “1st in Man (FIM)”, which will pave the way towards a Startup and commercialisation of the SingValve.

Manufacturing of atmospheric water and antiviral air delivery system

Executive Summary

Owing to climate and pandemic crises, clean air and water shortages/pollution are the greatest emerging global threats. We are now living in the water stress and air viral contaminated era, which becomes the defining health and wellbeing issues. Hence, it is imperative to look to nature-based solution for these urgent water-air challenges so as to meet the demand in a way that does not exacerbate negative impacts on ecosystems.

It is known that atmospheric water is an abundant source of fresh water, accessible everywhere and naturally renewed by the hydrological water cycle. Ideally, its harvest can be realized as continuous
freshwater delivery, and at minimal energy/infrastructure cost. Also, it is recognized that airborne microorganisms, residing in the air as aerosols can build up over time in enclosed spaces and transmitted over greater distances. Recent reports revealed that the coronavirus is transported not only through tiny droplets but also airborne transmission. Various precautions, such as air purifier and increasing ventilation indoors are recommended to reduce the risk of infection.

In this proposal, we are offering an innovative solution to render clean air and water modular portable/large-scale systems to suit household and industries needs. We designed an atmospheric water delivery strategy, on a continuous basis, that captures air moisture and delivers liquid water directly. It does so at minimum external energy expenditure uniquely without ancillary condensers. Continuous sorption-desorption is maintained through the reversible hydrophilic-hydrophobic transitions and direct release of weakly-bound water clusters that support the uninterrupted hydro-active sites regeneration. In parallel, we devised an antiviral air purifier membrane constructed using our invention disclosure Localized Phase Transition Ordering (LoPTO) technique to manufacture advanced photon-thermal anisotropic 3D membrane. The 3D porous and aligned nanofillers gel shows enhanced light trapping, thermal insulation and mass transport. The anisotropic membrane enables light scattering (haze of ~90%), resulting in uniform light absorption, insensitivity in light direction and directionally confined heat flow. The supramolecular disulfide membrane possesses antimicrobial/antivirus properties embedded with Ag/Cu nanowires biocidal agents. Aside from their inherent antibacterial properties, the nanowires demonstrate efficient photon-to-thermal energy conversion with precision in nanoscale heat modulation, without heating up the entire bulk medium. Due to the localized surface plasmon resonance (LSPR), the localized heat can reach up to 85 °C. Recent studies demonstrated heat inactivation/disinfection of SARS-CoV-2 viremia at 56°C-30 min or 65°C-10 min, and MHV virus at 80°C-1 min. Moreover, photoredox can trigger endothermic stimulated dynamics of UV-induced charge carriers to significantly enhanced biocidal reactive oxygen species (OH* radicals and H2O2) energetics.

Finally, we will fabricate a modular/portable atmospheric water and antiviral air delivery system made up of 3 lamellae namely the passive pre-filter, active antiviral membrane and a hydrophobic membrane to disinfect the air. Subsequently, the clean humid air is drawn into the water absorber gel at the water collection chamber. A pulsed LED inter-switches hydrophilic-hydrophobic states of the water absorber gel to steadily release clean water. This product is designed to deliver efficient airborne water supply, indoor dehumidification and antiviral clean air supply at minimal energy cost.

Development of the most advanced ion microscope for proton beam writing in the world

Executive Summary

Objectives and scope: We plan to build up the best Ion Microscope for Proton Beam Writing (PBW) in the world capable of proton beam imaging and nanofabrication below 10nm, based around our patented ion source. We have the best PBW technology in the world and there is demand for our technology, ranging from industry, academia and hospitals.

Our system will revolutionize four technological areas: 1) Failure Analysis (FA) 2) Nanolithography 3) Deterministic ion implantation 4) Improvement of cancer treatment with fast protons.

Here we will focus on the first two as they are our Beach Head Market.

We propose to commercialize our technology with a business development specialist. Our plan focuses on Technical & Business development areas and consists of 3 Phases:

- Prototype Phase, (First 2 Years)
- Commercialization Phase: (3 -5 Year)
- Business Expansion Phase (6-10 Year)

There is market need for these 4 technologies

1) More accurate characterization techniques capable of imaging smaller nanostructures in 3D are needed. Currently there is no credible technique that can image ICs in 3D with sub-10nm resolution also precise ion sputtering with Focus Ion Beam (FIB) technology with smaller beam spot size and reduced sample damage through a wider variety of ions is needed.
2) More accurate nanolithographic techniques, capable of producing smaller nanostructures are needed. Currently there is no credible technique that can produce tall high density sub-10nm nanostructures*.
3) Large scale fabrication of quantum computers through more accurate deterministic ion implantation.
4) Analysis tools will enable medical groups to be able to understand and improve cancer treatment with fast protons.

Existing competitive techniques:

In FA, optical and electron based techniques are used for 3D imaging of working IC circuits and sputtering is used in FIB with Ga ions for destructive FA. Electron beam lithography (EBL) is used for nanolithography.

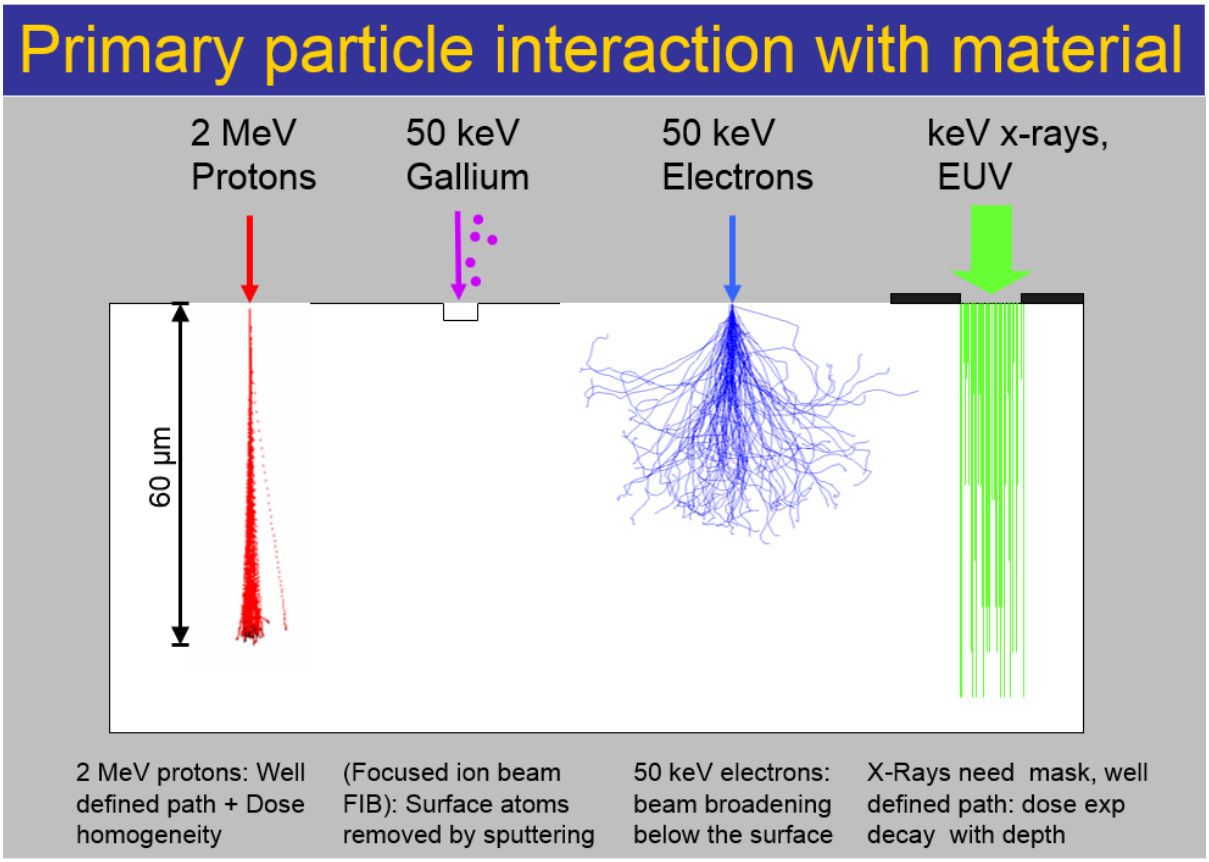
- Current FA techniques have resolutions of ~100 nm in 3D imaging of working ICs.
- FIB technologies have shown isolated features below 10nm but suffer from: contamination, damage due to sputtering and blistering.
- EBL, can produce high quality nanostructures through direct-write technology at nanodimensions. Isolated features of ~2nm, 30nm apart have been shown, EBL lacks the capability to produce reliably sub-10nm lines and spaces due to proximity effects.

Currently companies that provide FA and EBL solutions, are our potential competitors.

Developing an ion Microscope that can break the 10nm barrier is in high demand, by industry and academia to improve their resolution.

Advantage of our technology compared with competitors (See Figure below):

- Proton microscopy can provide reliable sub-10nm resolution in 3D without proximity effects, facilitating 3D imaging at the nano scale and high quality nanolithography!
- High sensitivity
- Even energy deposition in material
- No sputtering



Proposed solution

- Our Ion Microscope for protons (5-400 keV) will meet the needs of our existing customers as it is the best proton microscope for 3D FA of IC circuits and the best nanolithography system featuring sub-10nm resolution.
- Our Ion Microscope can perform sputtering as well as implantation with nanometer accuracy for a wide variety of ion species. This solution is extremely powerful in FIB for FA as well as for quantum device fabrication.
- Our system will enable hospitals to test cancer cell response to fast protons and decide how “expensive proton therapy” can be best applied in cancer treatment.

Therefore, we need enough funding to realise our goal.

Outcome

Commercialization of our ion microscope will start at the end of this project with an initial revenue of S$ 19M based on existing customers. We will create a brand new industry, jobs and a positive contribution to the economy with an expected total turnover exceeding S$50M after 5 years. After 10 years we expect a total turnover of more than S$ 600M.

**D Fishman, Senior FA engineer and Technical Leader at Intel in Quora 4 Jan 2017*

A comprehensive SERS platform technology for real-time detection of greenhouse gases for onshore and offshore applications

Executive Summary

Rapid detection of gases is vital to safeguard the lives of people because toxic gas can cause mass-disaster by easily entering the respiratory system to effect instantaneous harm. Furthermore, these gases can spread easily and linger in the air, making it difficult to contain them. Despite these dangers, hazardous gaseous chemicals such as carbon monoxide, chlorine, ammonia can be released into the environment as industrial by-products or during leakages. These gases are highly toxic, corrosive and/or flammable which needs to be detected rapidly so that remediation efforts can be performed as soon as possible. Notably, such gas leakages are not uncommon, even within Singapore. As recent as October 2020, Jurong Island reported the death of one worker in a pipe maintenance project due to accidental hydrogen sulfide gas leakage. In another incident, an ammonia leak in 2016 resulted in > 100 people evacuated, and several sent to the hospital, while the HazMat specialists had to be activated for a full day to perform decontamination and to trace the source of leakage. Furthermore, in the national security point of view, the detection of these gases is vital because they can be easily used as chemical warfare agents for mass casualties.

Hence, there have been intensive global efforts **to develop advanced techniques and technologies to monitor and regulate the emissions of hazardous gases. Specifically, it is imperative to develop an on-site gas sensor that can detect the real-time emission of various hazardous gases from industrial plants for timely decontamination**. The growing importance of gaseous surveillance is evident in the burgeoning international gas sensor market which is expected grow to USD 4 billion in 2025,1 within which excessive demand comes from major (petro)chemical, transportation, and environmental industries. However, current gas sensors rely heavily on classical electrochemical methods are highly prone to false signals and interferences and often fail to perform large-volume detection of multiple samples. Hence, we foresee that our technology can create an attractive market niche that stands out from current solutions.

Herein, we propose the development of a **surface-enhanced Raman scattering (SERS)-based sensor for the real-time and on-site monitoring of hazardous gas chemicals and volatile organic compounds (VOCs), namely chlorine, ammonia, carbon monoxide, formaldehyde, ethylene oxide, bromine, phosphine, fluorine, aziridine, in both industrial plants and at security checkpoints** (Figure 1). Our group has successfully designed a powerful SERS-based gas sensing technique that offers molecular-specific information even at trace (parts-per-billion, ppb) concentration and remote distances,2 as featured on Channel News Asia, TODAY and top global technology sites.3-6 Our invention involves the use of SERS, which utilizes plasmonic Ag particles as signaling particles to enhance the unique molecular Raman vibrational fingerprints for identification and quantification of analytes, achieved within a mere 10 s. Our invention has been proven to address the limitations of commercial electrochemical and infrared-based gas sensing devices, such as their poorer detection/quantification limit (higher than parts-per-million), long response time and/or susceptibility to false positive response due to the lack of molecular specificity/recognition. Importantly, our highly versatile SERS chips are small and can be easily coupled with remote, portable or handheld Raman devices to enable onsite detections. This multitude of benefits therefore allows the development of a superb gas sensor capable of detecting various greenhouse gases at the molecular-level with sensitivities below permissible exposure limit (PEL).

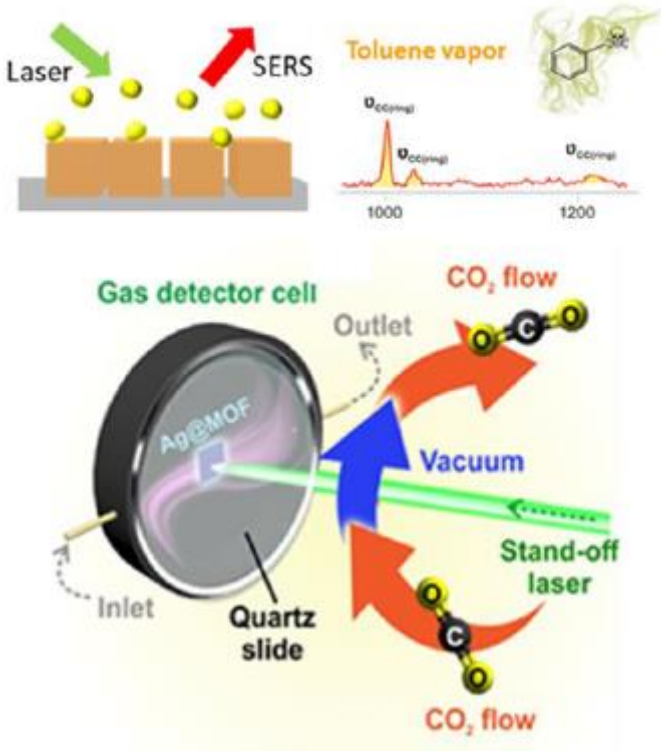


Figure 1. Scheme of our proposed SERS sensing system for hazardous gas/VOCs detection in designated plants.