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RIE NEWS

SG GUIDE TO TECHNOLOGY, INNOVATION AND ENTERPRISE

FEATURE

AN AI
FOR DETAIL

CONVERSATION

3D-PRINTING PRO
PROF CHUA CHEE KAI

SPECIAL

SPOTLIGHT ON
INNOVATION

COMMENTARY

PARSING THE
PANDEMIC

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SPOTLIGHT ON INNOVATION

We look at technological innovations that have emerged out of the COVID-19 pandemic

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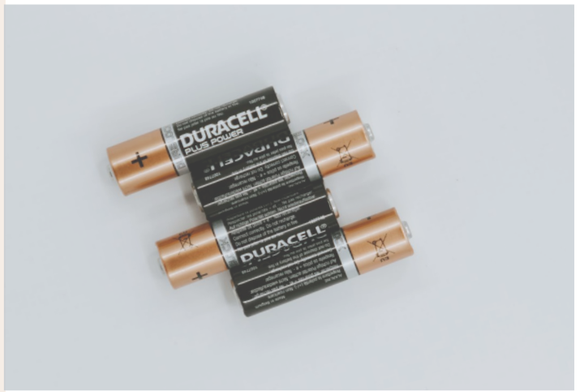
RESEARCH ROUNDUP

ENHANCING SINGAPORE'S ELECTRICITY NETWORK RESILIENCE

SP Group will be embarking on S$30 million in research and education initiatives with NTU, to enhance the resilience of Singapore's electricity network, improve the reliability and efficiency of supply to consumers, and nurture experts for the energy sector. The collaboration will also launch a SP Group-NTU Joint Laboratory to explore energy-related projects in the areas of asset management and network operations. Located at the university, the joint lab will house 60 researchers, 85 undergraduate and postgraduate students, and serve as a training platform for SP's engineers. In addition, SP is contributing S$10 million to set up two endowment funds at the university to support and groom next-generation experts in Singapore's energy sector.



PEELING OUT THE OLD WITH THE NEW

NTU scientists have developed a new method of using fruit peel to turn old batteries into new ones. Through a special process, researchers used fruit peel waste to extract and reuse precious metals from spent lithium-ion batteries in order to create new batteries. This "waste-to-resource" approach tackles both food waste and electronic waste. The new lithium-ion batteries produced using the recovered materials showed a similar charge capacity to commercial ones. The team is now finding ways to optimise the charge-discharge cycling performance of these new batteries.


Image: NUS

60-SECOND COVID-19 TEST WITH A SINGLE BREATH

Researchers from NUS have developed a breath test to detect COVID-19 within a minute. The test, which detects volatile organic compounds (VOC) in a person's breath, achieved more than 90 per cent accuracy in a clinical trial with NCID involving 180 patients. The exhaled breath is analysed using a mass spectrometer and a machine learning software, which generates results in less than a minute. Developed by NUS startup Breathonix, it offers a fast and convenient solution to identify COVID-19 infections. Clinical trials are ongoing and more tests are required to further improve the accuracy of the technology.

SINGAPORE RESEARCHERS WORKING ON COVID-19 VACCINE CANDIDATE TRIALS

Duke-NUS and United States pharmaceutical company Arcturus Therapeutics have received approval for clinical trials for their vaccine candidate 'Lunar-COV19'. The vaccine candidate works by triggering the body's cells to begin producing a protein similar to the COVID-19 virus, enabling the body to learn and fight it. Approval for trialling the vaccine in Singapore was given in July and the first phase involving young healthy volunteers, each getting one injection of varying doses, started in August. The second phase will comprise of people up to the age of 80, with each participant given two doses of the vaccine. Both parties aim to end the trial in December and complete the overall study of the process by January 2021.

3D PRINTING, WITH A HEART

Researchers from the SUTD have used additive manufacturing or 3D-printing to control stem cell differentiation into embryoid bodies that replicate heart cells. They 3D-printed several micro-scaled physical devices with finely tuned geometries which helped to direct the differentiation of stem cells by forming embryoid bodies. Through this process, they successfully regulated the parameters for enhancing the production of 'cardiomyocytes' – cells which are found in the heart. This proves that 3D-printing can be used as a method to control cell growth in a lab, similar to in-vivo conditions.

TWO VIRUSES WITH ONE STONE

Researchers at NTU's Lee Kong Chian School of Medicine have developed a new way to find out if a person is infected with COVID-19 in just 36 minutes. Known as 'direct-PCR', the researchers' method uses a series of commercially available enzymes and reagents. By mixing them together with patient swab samples in a test tube, researchers are able to perform the test on the sample directly, producing accurate results in a shorter time. The method works on the dengue virus as well, producing results in an even shorter 28 minutes, and it can also be deployed outside of a laboratory using a machine known as a portable thermocycler.

CONVERSATION

PRINTING AN ARSENAL OF PANDEMIC PREPAREDNESS

Think 3D printing in Singapore, and the first name that will probably come to mind is **SUTD's Professor Chua Chee Kai,** one of the world's leading experts in the area. We speak to him about his thoughts on how the COVID-19 pandemic has impacted the field of additive manufacturing, and how it will continue to influence it in the years to come.

Images: SUTD

The COVID-19 pandemic has placed unprecedented strain on supply chains worldwide. Demand for healthcare supplies has skyrocketed, but lockdowns around the globe has brought manufacturing to a near standstill.

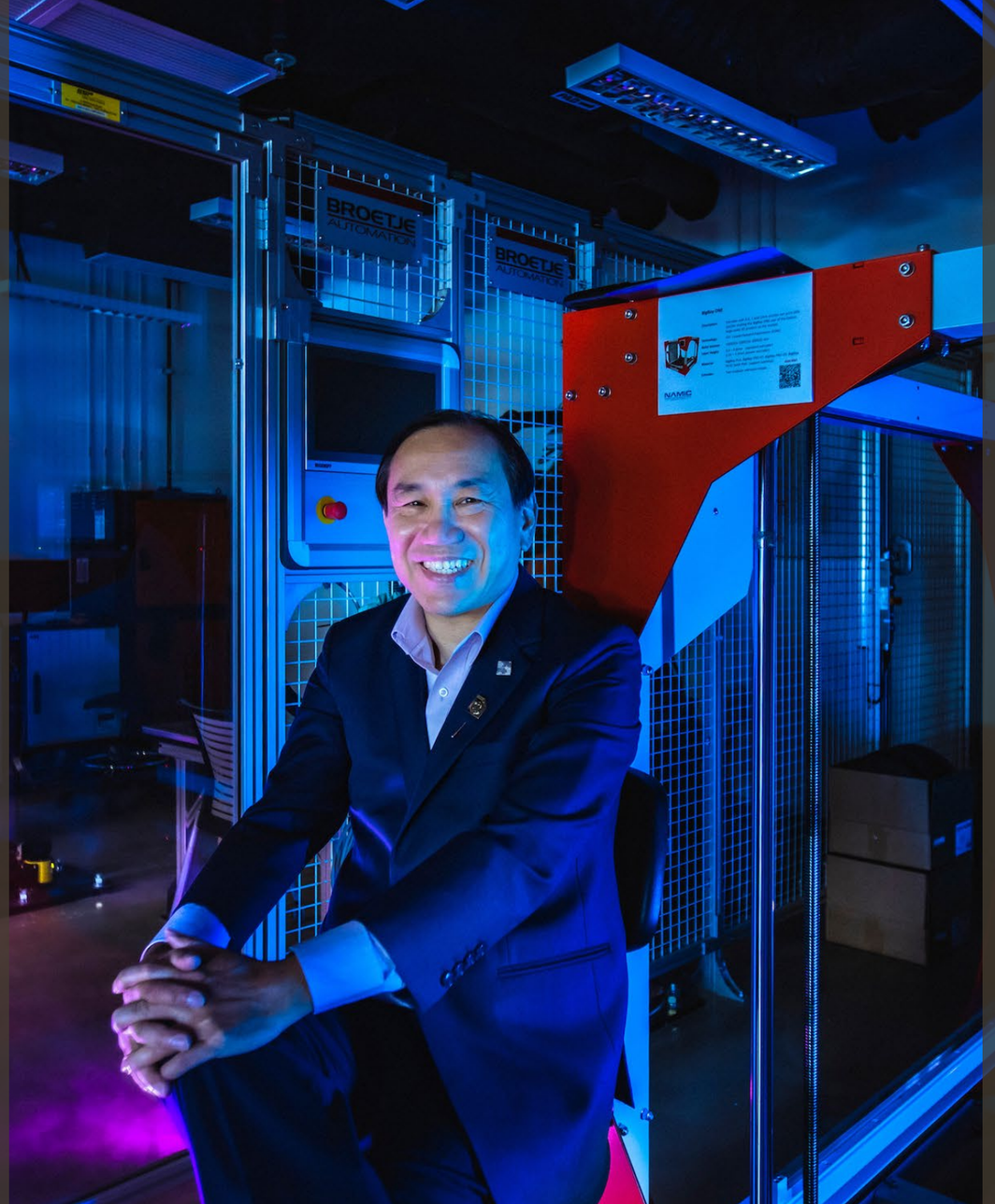
This predicament has placed a fresh spotlight on the world of additive manufacturing, also known as 3D printing. The technology has been around for decades, but while it has gained much traction in many industries, the biomedical field has not been one of them. However, its unique ability to produce important supplies on demand has highlighted just useful it can be in global emergencies such as this.

Enter Professor Chua Chee Kai, who heads Engineering Product Development at the Singapore University of Technology and Design (SUTD). The most published and most cited scientist in 3D printing, Prof Chua's experience in additive manufacturing spans around 30 years, making him the foremost expert in Singapore in the field.

Recently, Prof Chua published a piece in prestigious academic journal Nature about the rise in 3D printing during the pandemic. In an interview with RIE NEWS, he shares his thoughts about this trend, and what lies in the future of 3D printing.

You wrote a piece in Nature about the rise in 3D printing during the pandemic. What do you think led to the rise in interest in 3D printing? Are there any needs that the technology is uniquely well-placed to meet, for instance?

The rise of interest in 3D printing is dependent on many factors. For instance, the flexibility and fast prototyping of 3D printing allows for quick deployments and rapid responses to



emergencies. In addition, critical parts can be readily manufactured on-demand by any 3D printing facility amid severe disruptions in supply chains. These characteristics have enabled 3D printing technology to play a significant role in mitigating this global health crisis.

What was your personal experience like, observing the rapid rise in interest in 3D printing technology?

In times of crisis, we have seen many people collaborating and contributing selflessly. The 3D printing technology has become a rallying point for communities to freely share ideas, designs, know-how, knowledge and resources to help one another.

It is always comforting to know that people from different parts of the world stand together on a united front to fight against the COVID-19 virus. For instance, we previously came upon a news article stating that Northwell Health (New York's largest healthcare provider) was willing to share their 3D printed nasal swabs design files with other institutions. We contacted them and they readily shared their design files of the 3D printed nasal swabs and technical know-how with us. I hope that this kind of collaboration will still remain strong even after the pandemic.

How about locally and within South-east Asia? How has the regional 3D printing community responded to this trend?

In an effort to join hands with professional communities to fight COVID-19 pandemic, SUTD supported Tan Tock Seng Hospital (TTSH) in enhancing their new face shield frame design using cutting edge 3D-printing technologies. In addition, utilising our in-house design capabilites, we

have been working closely with TTSH to improve the original design to increase its strength and durability.

SUTD alumni also came together to 3D-print ear guards (a plastic tension release band worn at the back of the head, designed to hold the elastic straps of surgical masks and bring relief from discomfort around the ears) for COVID-19 healthcare workers.

Outside of SUTD, Singapore-based companies Creatz3D and AuMed have used the 3D printing technology to fabricate life-sized medical manikins. These medical manikins complement existing training materials and allow healthcare workers to practice COVID-19 swab testing procedures with standard medical-grade swabs. I always feel a strong sense of pride when I see Singaporeans contributing innovatively and selflessly in this fight against the COVID-19.

How do you think the pandemic will impact the future of 3D printing, as well the medical device manufacturing field as a whole? What are your hopes of what the community and technology will look like in the next pandemic?

While 3D printing bodes an exciting future, the acceleration in 3D printing is also being driven by the change in the production-consumption model due to social, ecological, and technological megatrends, coupled with externalities such as COVID-19.

The 3D printing landscape is changing rapidly in response to COVID-19. However, 3D printing facilities and 3D printed parts for the medical industry both need to meet stringent medical regulations in order to be certified safe for use. Regulations often have the tendency to lag behind innovation, thus causing serious bottlenecks in the mass adoption of 3D printed medical devices. I believe that strong regulatory frameworks must be established first in order to gain greater confidence and wider adoption of 3D-printed medical devices.

I hope that the next pandemic does not come. Even the next pandemic does come, international and scientific communities will take the threat of pandemics more seriously. More resources will also be invested in technology for detecting and responding to outbreaks in better preparing the world for the next pandemic. The healthcare industry may have more accepting attitudes towards 3D printing technologies in the future, as the COVID-19 pandemic situation has raised awareness of how 3D printing technologies can fit in and complement the current healthcare system. Hospitals hopefully will begin to take more ownership of their supply chain, where 3D printers can be brought in to ease critical shortages.

Despite it getting more attention recently, 3D printing has been around for a long time, and it's a very established technology. Are there any breakthroughs in 3D printing technology we can look forward to, or that you're hoping to see?

Yes, 3D printing has been around for more than three decades. The technology was initially used for prototyping purposes and hence, it was widely known as 'rapid prototyping' in the 1980s.

In recent years, it has has been getting more established and reliable as the technology for printing process and printable materials advances significantly. We will start to see more companies exploring, accepting, and adopting 3D printing technology for parts manufacturing in the near future. Due to the expiry of several leading 3D printing patents, prices of 3D printers have also come down, leading to greater adoption.

One exciting area to look out for is generative design with 3D printing. 3D printing technologies usually offer large amounts of design freedom, enabling the fabrication of complex geometries in a cost-effective manner. Coupling generative design with 3D printing technologies can bring us many benefits – for instance, parts can be printed with increased functionality and performance, while reducing waste, material, and weight. In addition, generative design can also reduce the need for companies to maintain huge inventories by 'printing on demand'.

Let's talk a bit about SUTD. Are there any projects or research work ongoing in SUTD that is related to COVID-19, or infectious diseases as a whole? Perhaps highlight one or two that you find particularly interesting or impactful.

To date, there are 19 projects and research work (and counting) ongoing in SUTD that are related to COVID-19 by faculty, staff, researchers, students and alumni. Associate Professor Ye Ai's research work is one of the projects that I find particularly impactful. His research team is developing a gentle cell purification technology and working to develop an antibody treatment for combating COVID-19 and other coronaviruses.

Currently, peripheral blood mononuclear cell (PBMC) samples from recently recovered COVID-19 patients are collected for performing single cell antibody sequencing assays. This is to identify B cells that will generate antibodies targeting the SARS-CoV-2 virus. However, the existing purification method of B cells from PBMC can cause too much cell damage that will adversely affect the B cell antibody sequencing assays.

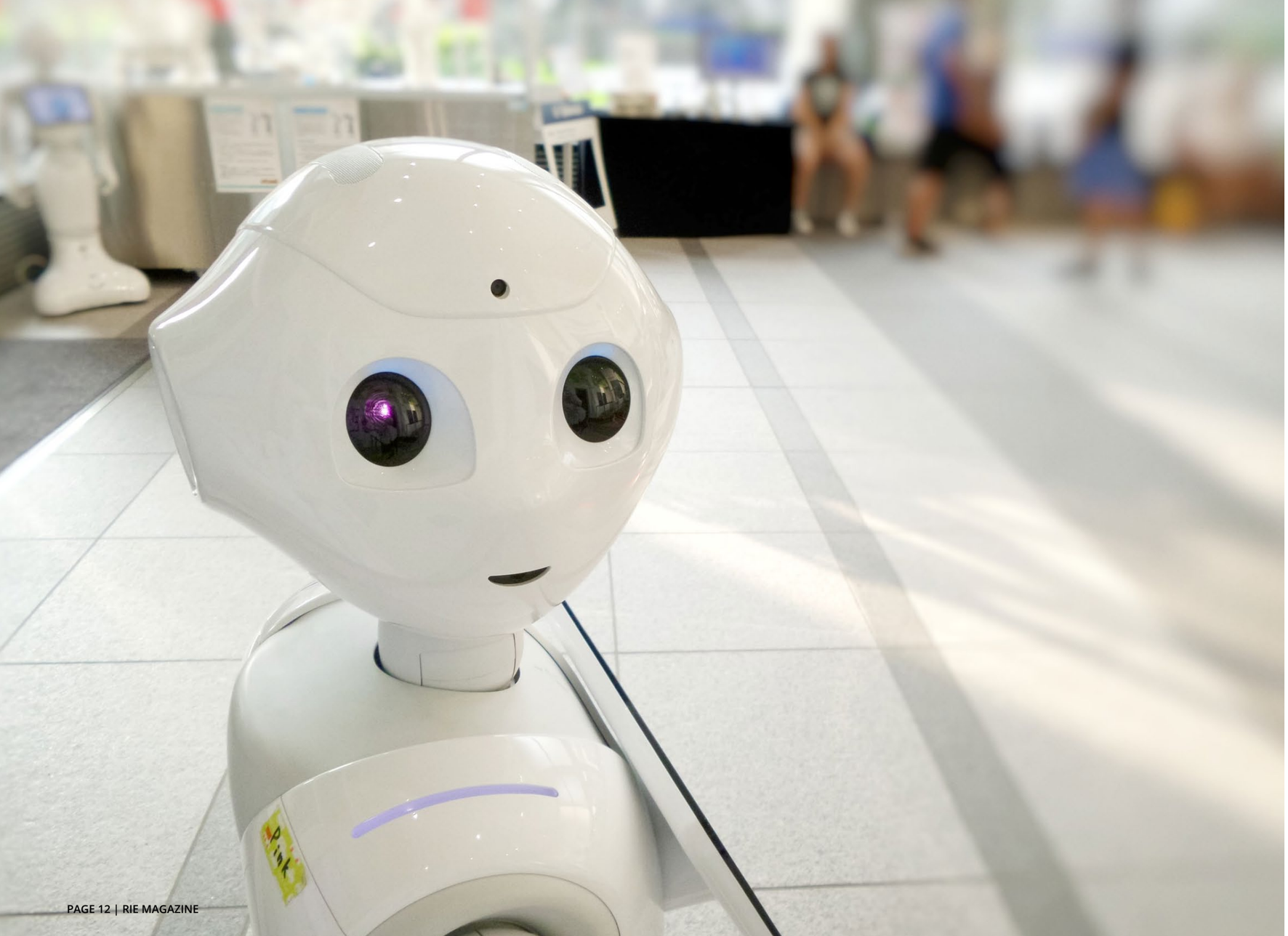
Dr Ye Ai's acoustic cell sorting technology can isolate target B cells with high purity and no cell damage to assist the development of antibody treatment for COVID-19. Currently, they are still testing their acoustic cell sorting technology. The current standard is about 50 per cent, so half of the cells, which may be the target B cells generating antibodies again SARS-CoV-2 virus, will be lost.

Preliminary results have proven that their technology can maintain over 95 per cent cell viability after sorting, which is significantly better than the current standards. Once the whole validation is complete, their cell sorting can be a routine cell purification step to develop antibody treatments for other infectious diseases.

What do you think young or aspiring researchers in the 3D-printing field should take away from this pandemic? Do you have any advice for them?

From this pandemic, young or aspiring researchers in the 3D printing field should take away this quote: "In the midst of every crisis lies great opportunity". This pandemic may change the way we live, work, and play, but it doesn't limit our creativity and innovative thinking.

As young aspiring researchers, they should always keep a keen eye on finding innovative ways to improve the current situation so that the society can move forward as a whole. 3D printing has proven itself to be a handy tool to turn creative ideas into a tangible reality in a short time.



FEATURE

AN AI FOR DETAIL

One local startup has found a way to humanise the way computers think. We speak to **Lexikat** founder **Jennifer Dodgson** to find out more.

With the onset of Internet-of-Things and other digital technologies, computing has taken on a new meaning with the power of artificial intelligence (AI). AI and machine learning have been hot topics as they increasingly find their way into everything digital, from the "inner voice" on smartphones via the Google Assistant on Android and Siri on iPhones, to high-speed quantum computing systems.

They also form the basis of most big data analytical platforms that process large amounts of data for specific tasks, especially market research and surveys. Even today, these still comprise the bread-and-butter of most enterprises such as retail, to stay connected with ongoing trends on the ground and to ensure their businesses remain relevant to current needs.

One local company is aiming to advance this with the power of AI by making it more natural and human-like. Enter Lexikat, a start-up founded by researchers from the National University of Singapore (NUS), which is developing AI-assisted topic modelling and natural language processing.

"The question, 'What if you could analyse data from human opinions effortlessly?' was a key inspiration for our business," said Jennifer Dodgson, founder of Lexikat Pte. Ltd.

"Manually going through huge amounts of data is impossible for any human, and even using simple AI would not be feasible as qualitative data is much more complex than a quantitative one," she added.

By combining AI and natural language processing, Dodgson and her team came up with a solution that does just that. "The way people think is basically categorising things to similar connections within a specific context. That is where Lexikat's AI-powered solution comes in. It uses a special text analysis algorithm that groups similar words with each other to spot significant trends in the data," she explained.

She added, "The essence of surveys is basically qualitative research, which is a very tough element for AI because it includes specific nuances that require a human-like mode of thinking and connecting things to other things."

The AI-powered topic modelling and natural language processing software makes sifting through huge chunks of data a breeze. It looks at a much larger context to group similar words together, much like how humans would do.

"Imagine going through hundreds of legal documents, a thousand academic papers or even a million tweets – it is almost impossible to pick out key themes or trends. Using natural language processing and AI, our solution provides topic modelling that is fully customisable, and the algorithms will quickly find the key themes through a few clicks of the mouse," Dodgson shared.

The human-ness in AI lies in natural language processing

Natural language processing combines the subfields of linguistics, computer science, and AI, which are focused on the interactions or relationships between computers and human language, and process and analyse large amounts of natural language data.

It is the basis of speech recognition that is a common feature in most smartphones or smart home devices that does specific tasks based on simple verbal commands.

The Lexikat team (left to right): Daniel Tablan (intern), Jennifer Dodgson (CEO), Zhang Shaorong (Project Manager) and Pei Junjie (CTO)

Dodgson said that the AI firstly has to calculate on some form of probability. "It is the same as asking what time the next bus will be arriving, which is typically derived from some form of calculability." She added that it is also similar to natural language and conversations where there is some form of relationship and interconnectivity, or what is known as 'embedding'.

"Take for example the word 'iPhone', which is also used very much in sentences in which iPod or even the generic word, apple, is used," explained Dodgson. "So, these words are tangled up with each other and is part of natural language processing."

The most comprehensive language generator is owned by Google known AS GPT-3, which is the largest language model ever created and is used in platforms such as Google Assistant and Google Translate to name a few.

"When you ask the Google Assistant or even Siri for that matter, to find or to do certain things, the command goes into a large database of information and finds those related words and categorisations based on probability and generates the answer you need," said Dodgson. "This would easily take days to weeks for a human to do, but just a few seconds for AI."

Lexikat's software solution can process English, Chinese, and even Bahasa Indonesia languages through a partnership with an Indonesian university. Dodgson and her team hope to create a better database of language processing for the internet. "The Internet is archaic actually as search engines still rely on specific words on a literal basis. The idea is to create a more reliable and convincing categorisation system that allows for a more human-like internet, similar to talking a person behind the screen."

"Starting a business has been an interesting experience; I expected it to be a lot more stressful than it was. Even though our development process was affected by the coronavirus pandemic, it still has not been as difficult as I was expecting – it's a reflection of how good Singapore's innovation ecosystem is which supports emerging technologies and businesses."

CONVERSATION

FISHY BUSINESS

In August this year, there was another infectious disease in Singapore that briefly made the news – Group B Streptococcus. We find out more about the bacterial disease from **Dr Swaine Chen**, group leader at the **Genome Institute of Singapore**, **A*STAR**.

Group B Streptococcus (GBS) is a common bacterium found in the human gut and urinary tract of 15 to 30 per cent of adults without causing disease. However, it occasionally causes invasive infections of the skin, joints, heart and brain.

Back in 2015, it was behind a large outbreak of fish-borne blood poisoning in Singapore. Then, the GBS strain – identified as ST283 – caused more than 160 people to be hospitalised with fever and invasive infections, such as meningitis, after they consumed raw freshwater fish.

This July, public hospitals reported a sudden spike in the number of ST283 GBS cases and in August, the Ministry of Health issued a public health advisory on the consumption of ready-to-eat raw fish. Investigation found no trace of GBS in fish samples.

We speak to Dr Swaine Chen, group leader in Bacterial Genomics at the Genome Institute of Singapore (GIS), Agency for Science, Technology and Research (A*STAR), about GBS. Chen was involved in decoding the genetic blueprint of the bacteria. Subsequent genomics work after the outbreak revealed that ST283 is not unique to Singapore, but widespread throughout Southeast Asia. These findings are important in guiding medical teaching about GBS and education about food handling and food preparation.

High density modern aquaculture farms are breeding grounds for bacteria transmission

What are the latest findings on the ST283 GBS strain?

After publishing the findings that revealed ST283 GBS was widespread throughout Southeast Asia, we have been working on understanding why it causes foodborne disease. This taps on my lab's expertise in bacterial genetics and animal model systems for infectious disease. Understanding what makes ST283 stand out from other GBS strains may give us clues about treatment and prevention.

Currently, we know from the Singapore outbreak that the transmission was definitely (at least) through eating food contaminated with ST283 GBS. It remains an open question as to whether that was unique to Singapore or if it is happening in the rest of Southeast Asia. These are questions that require additional research.

Is ST283 GBS only a foodborne disease?

For ST283, it certainly can be transmitted by the foodborne route. Other GBS strains are not thought to be foodborne, but they cause infections through external exposure (as with wounds) or due to weakened immunity (allowing GBS that is normally present in many people to get into the bloodstream).

There is every expectation that ST283 GBS can cause disease the way other GBS do, in addition to foodborne disease, but again we have only started doing research on the pathogenesis of ST283 GBS. If I had to speculate, I would venture to say that ST283 GBS is likely able to cause disease both through foodborne and non-foodborne routes.

But the foodborne route is the one that's most important to understand; it would be very dangerous if other GBS could become foodborne as well, because non-ST283 GBS is so common throughout the rest of the world.

Is ST283 GBS a widespread threat around the world?

Since discovering that ST283 GBS was widespread throughout Southeast Asia, we have gotten the attention of the Food and Agriculture Organization of the United Nations (FAO). Together, Tan Tock Seng Hospital, GIS of A*STAR, and FAO are organising a risk assessment specifically for ST283 GBS.

This assessment will involve FAO specialists as well as international food safety experts to examine the data on ST283 GBS, its distribution, and its risk to fish in aquaculture and the food supply for humans. One possible outcome of this risk assessment meeting will be distribution of the report to UN member nations, which might spur additional data collection in other countries so we can better answer the question about how widespread the threat is.

One possible outcome of this risk assessment meeting will be distribution of the report to UN member nations, which might spur additional data collection in other countries so we can better answer the question about geographical extent.

Images: GIS

*Dr Swaine Chen, group leader in Bacterial Genomics at the Genome Institute of Singapore, A*STAR , decoled the genetic blueprint of the Group B Streptococcus ST283 bacteria strain*

What do researchers need to understand better about the disease in order to prevent an outbreak in future?

We are very interested in the pathogenicity question; answering why ST283 is special among GBS strains in being able to cause foodborne disease will allow us to understand how ST283 evolved to be so virulent.

As my lab specialises in bacterial genetics and genomics, one of the bigger goals, of this research is to understand how ST283 emerged only in the last 30-40 years. This question is critical because it would help us figure out whether other non-ST283 GBS (or other bacteria) could similarly evolve to cause new infections that we are unprepared for.

There are many other questions we have about this disease. Imagine, we are still learning about diseases like tuberculosis or malaria, which have plagued humanity for tens of thousands of years. We have only had five years since the discovery of foodborne ST283 GBS disease, so we're working hard to do the research to catch up.

How can genomics play a role in infectious disease control?

We are interested in using genomics to do continuous monitoring for both known and unknown food pathogens. Genomics has advanced so fast that this is now economically feasible. In addition, genomics is the first technology we have that can allow us to detect previously unknown potential pathogens.

Having such a genomic monitoring system in place would really keep Singapore at the cutting edge of food safety, and I think it would allow us to catch the initial outbreaks and subsequent resurgences like those we have seen for ST283 GBS much sooner.

SPOTLIGHT ON INNOVATION

In the light of the COVID-19 pandemic, a number of innovators have taken action to address the new challenges that have arisen. In this issue, we spotlight two technologies that have caught our eye.

ROBOT SWABBERS A SHOT IN THE ARM

Nasopharyngeal swabs are unpleasant affairs. Although their unsurpassed ability to pick up viral load has made them the backbone of Singapore's COVID-19 testing strategy, they are frightening to patients and pose a significant threat to healthcare workers involved in the swabbing process as well.

The SwabBot, an automated swabbing device, hopes to make swabbing safer and more comfortable. We speak to **Duke-NUS's Dr Rena Dharmawan**, principal investigator of the SwabBot project, to find out more.

Image: Duke-NUS

Images: Duke-NUS

The SwabBot automates the process of swabbing, making it gentler and safer

The idea started in April, when Dr Rena Dharmawan was rostered for swabbing duties along with a few of her colleagues.

"My colleague, Dr Tan Ngian Chye, and I were having a chat about swabbing. We thought that the process could and should be automated to reduce the exposure of healthcare workers to potentially COVID-19-positive patients, reduce manpower, and also improve the standard and quality of swabs done," explains Dr Dharmawan, who holds double appointments as a surgeon in the National Cancer Centre Singapore (NCCS) as well as a clinical innovator at Duke-NUS.

"The vision was kind of like 'going to the optometrist for an eye check-up', where all you need to do is to fix your head to a robot or device and get your nasopharyngeal swab done."

Nasopharyngeal (NP) swabs are the primary weapon in Singapore's COVID-19 testing arsenal. Compared to their saliva, oropharyngeal, or nasal counterparts, NP swabs are currently the gold standard for

swabbing worldwide. However, they are also risky – invasive and uncomfortable, they may cause patients to cough or sneeze during the process, potentially exposing healthcare workers to the virus.

In hopes of coming up with a better method, Dr Dharmawan was introduced to Mr Sim Kok Hwee, chief executive officer of medtech firm Biobot Surgical Pte Ltd. The pair partnered with colleagues from NCCS, Singapore General Hospital, and Biobot Surgical, and eventually came up with the idea for an automated swabbing device. The device was then developed under the SingHealth-Duke-NUS Joint Centre for Technology and Development (JCTeD), a first-of-its-kind health innovation accelerator in Singapore.

Just three months later, the robot was completed. "The progress was extremely fast, from idea to market, and for good reasons with COVID-19 innovation," says Dr Dharmawan.

"It was a fantastic example of great team work and importance of synergy between the clinical and engineering teams – from identifying the unmet clinical need, to brainstorming possible solutions to solve that need, to prototyping and refining the prototypes quickly to ensure that we have a safe product that works."

"I have to give it to the Biobot team, they came up with the first-generation prototype in just 6 weeks since we started collaborating!" she adds.

Even though the process took such a short time, the team faced plenty of challenges, including administrative work, team and people management, and clinical trial design. The short timeline was also an obstacle that the team needed to overcome in order to ensure that the product would be timely and not "miss the boat" on the COVID-19 pandemic, says Dr Dharmawan.

Medtech with meaning

The made-in-Singapore robotic device allows swabbing to be conducted at a distance. This reduces the exposure of healthcare workers to the virus, and frees up healthcare-trained personnel to be deployed elsewhere. It also standardises the process by removing factors such as worker fatigue or varying skill levels, ensuring that swabs collected are of good quality every time.

Importantly, the SwabBot is also fully patient controlled, gentler, and more precise, which means that it is both less intimidating and more comfortable for patients.

While other countries have produced swabbing devices of their own, the SwabBot is much less complicated and technically lighter than those, says Dr Dharmawan. As a result, healthcare workers are more easily able to deploy the device.

Currently, SingHealth is working with Biobot Surgical to protect the invention with a patent filing, and to commercialise and deploy the product locally and globally. The SwabBot has also already been registered with the Health Sciences Authority as a Class A medical device.

"I hope SwabBot will be able to help in increasing the efficiency of mass swabbing operations in Singapore and beyond," says Dr Dharmawan. "This includes the higher risk group populations who require regular swabs, like migrant workers, or in airports, where travellers are required to be tested prior to getting on a plane."

A SMART MASK THAT DOES IT ALL

Using flexible electronics and digital technologies, researchers from **A*STAR** and **NTU** have developed a 'smart mask' that safely monitors COVID-19 patients while enhancing the safety of healthcare workers.

As masks become the norm worldwide, tech companies and researchers around the world are leveraging technology to advance the humble mask towards into a robust device capable of combating the pandemic.

In Singapore, local scientists have developed an integrated monitoring system that can be easily attached to any face mask.

Led by Professor Loh Xian Jun from the Agency for Science, Technology and Research (A*STAR) and Professor Chen Xiaodong from Nanyang Technological University (NTU), the new 'smart mask' comes with multiple sensors that monitor the wearer for health indicators associated with COVID-19.

The researchers had been working on the smart mask quickly since the circuit-breaker period earlier this year, exploring a plethora of sensors. They ended up developing a thumb-sized sensor system that uses pulses of light and electrochemical sensing to monitor patients' vitals. These include picking up skin temperature, blood oxygen saturation, blood pressure and heart rate – all of which are parameters associated with coronaviruses.

"The new smart mask was an inspiration that sparked during the circuit-breaker period when mask wearing was a necessity, especially for healthcare workers," said Prof Loh, who is the executive director at A*STAR's Institute of Materials Research and Engineering. "We looked at ways to help healthcare workers, by combining key diagnostic elements into a single, streamlined device and we thought, the humble mask could be the perfect platform."

The prototype was developed very quickly and is currently in its fourth iteration. "One thing that we always strived to achieve was how to make the prototype smaller, lighter, and more convenient to the wearer," said Prof Chen, who is the President's Chair Professor in Materials Science and Engineering at NTU. "We worked very closely with healthcare practitioners and conducted clinical trials with healthy volunteers to streamline and optimise

the prototype into its current state. Ultimately, we wanted the smart mask to conduct continuous monitoring of vitals, and take into consideration conditions unique to patients at the individual level."

Bending the rules of innovation through flexible and biodegrable electronics

Hooking up a variety of sensors onto a conventional fabric mask would mean discomfort for the user because of the bulkiness. The researchers also observed that healthcare workers had to drag large and bulky equipment from room to room to monitor the conditions of the COVID-19 patients, and wondered if there was a better way to conduct such activities safely.

"Many of these frontline workers are exposed to patients when they are taking their vital signs," said Prof Loh. "Instead of them having to lug the equipment into the isolation rooms, we thought, why not incorporate them into the patients' masks?"

The thumb-sized sensors on the inside of a mask would make it uncomfortable for use, so the team integrated them into an artificial skin-like substrate using flexible electronics. This would also allow the sensors to conform to the flexibility of the mask and human skin.

Prof Chen, who is also an expert in flexible electronics and the director of Innovative Centre for Flexible Devices at NTU, said, "The benefits of using flexible electronics are multifold. For example, using a special silicon polymer means it is not only lightweight, but also does not induce any allergy-related problems with the user. By integrating the chip into the elastic material, it allows the wearer to feel more comfortable while also allowing more accurate readings to be obtained."

The extremely flexible and durable material is also water-resistant, which protects the sensors and electronics within, enabling it to be reused, added Prof Chen. The device can be incorporated into the cheek area of any conventional reusable mask or even a disposable one.

The researchers are also exploring using biodegradable materials to develop the overall 'smart mask' system, which includes magnesium, basic metals, and biomass.

Prof Chen said that overall sensor system is simple to produce and materials can be sourced locally. Under current lab-scale conditions, it costs about S$50 to produce a set, but this could cost S$20 or less if it is scaled up for mass production.

Enhancing safety and convenience through digitalisation

To improve convenience and safety of the healthcare workers, the researchers added a Bluetooth device that allows data to be transmitted to a smartphone in real-time. This could ensure real-time monitoring of all patients.

The technology could also be hooked up to a unified platform complementing existing telemedicine efforts, in order to monitor health trends in communities like migrant worker dormitories or nursing homes.

"By leveraging digital technologies, we can deliver better healthcare solutions to overcome the COVID-19 challenges as we support Singapore's fight against the pandemic," said Prof Loh.

"Telemedicine is set to become a key feature of Singapore's healthcare landscape and it offers greater convenience and improved accessibility to medical support and medication through new digital self-help options."

Telemedicine could also enable cloud-based computing that could aggregate personalised or randomised data, paving the way to even more comprehensive and personalised healthcare solutions, added Prof Loh.

Image: NTU

Prof Chen Xiaodong (left) and Prof Loh Xian Jun (right) unveil the 'smart mask' which contains a bluetooth device that allows data to be transmitted to a smartphone in real-time

Moving forward, both researchers and their teams are looking at adding additional sensors to the face mask to detect particles in saliva droplets. They also aim to make it even smaller and more lightweight, to improve overall comfort and convenience, and even incorporate sustainable materials such as recyclable batteries.

As their prototype development has demonstrated, the researchers highlight that science and research need not be a phenomenon likened to sitting atop an ivory tower.

Prof Loh highlighted that the collaboration focused on use-inspired basic research (UIBR) in their earlier collaborations. "During the pandemic, we were able to quickly harness our respective knowledge to develop a prototype in a month.

"The essence of UIBR is to be grounded with inputs and feedback from stakeholders and partners, to create something that improves the conditions of living and overcomes challenges that society faces."

CONVERSATION

A STING OPERATION

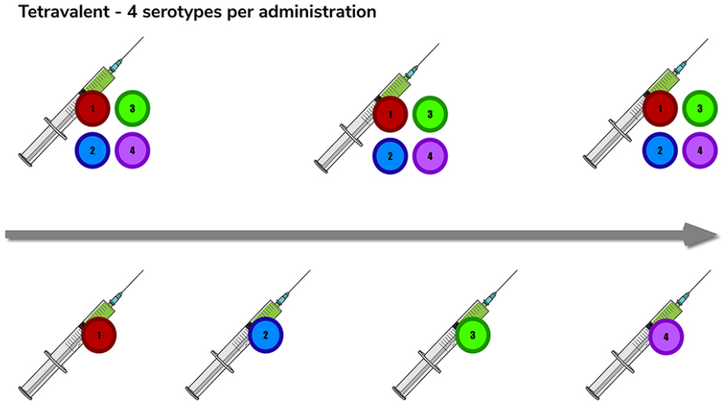
While most will remember 2020 for the COVID-19 pandemic, another virus has been posing a serious threat to public health here – dengue.

A year-round risk in Singapore, 2020 has seen a record high of reported cases. A vaccine against the dengue virus has been notoriously challenging to develop, but there is some good news from the **Singapore-MIT Alliance for Research and Technology**. Scientific director, **Dr Megan McBee,** tells us more.

Dengue is a viral infection caused by four serotypes of viruses (DENV1-4). The viruses are transmitted through the bite of infected female aedes mosquitoes – pesky things that feed during the day and thrive in urban areas with standing water. Singapore, with its perennially rainy disposition, is an endemic hot spot.

This year (and with two more months to go), the dengue virus has already infected over 30,000 people in Singapore, a historic high that has broken the previous 2013 record of over 22,000 cases. Twenty people have died. The need for a safe and effective vaccine has never been more pressing.

Researchers from the Singapore-MIT Alliance for Research and Technology (SMART) have recently made inroads into vaccine development for the virus. Using proof-of-concept studies, they have found a practical way to induce immunity to the dengue virus through sequential immunisation (or one serotype per dose). Dr Megan McBee, scientific director at the SMART Antimicrobial Resistance Interdisciplinary Research Group, explains more.



Sequential immunisation – one dose per serotype – promises a broad and strong response to all four dengue serotypes

The number of recorded dengue virus (DENV) cases so far in Singapore this year is over 30,000 – already surpassing the previous annual record of about 22,000 in 2013. What is a possible reason for this huge increase?

There could be two contributing reasons for the increase. Firstly, there is a higher prevalence of serotype 3 virus, which has not been circulating widely in Singapore for a couple of decades. Thus, fewer people are immune to it. Secondly, environmental factors related to the SARS-CoV-2 pandemic could be another reason. With people spending more time inside their homes, there have been increased chances for transmission. The reduced landscaping island-wide might also have created more breeding grounds for mosquitos.

The dengue virus has been around for a long time. Why hasn't a vaccine that can be universally applied to everyone at risk of dengue been successfully developed?

Multi-valent vaccines, such as the influenza and HIV vaccines, are more difficult to develop. Additionally, vector-borne infections such as dengue or malaria create more challenges. Knowing what endpoints or level of protection is necessary for prevention has also been a major challenge for successful vaccine development.

For DENV, understanding the biology, both of the virus and how people respond, has been important to developing a vaccine. Singapore is a major hotspot for dengue research and many key breakthroughs have occurred in recent years with more advanced research tools.

What are the challenges that scientists face in developing a dengue vaccine?

The key challenge is getting the human immune system to generate a broad and strong response to all four serotypes that is sufficient to protect against any of the four. It turns out that each serotype can induce different responses from our bodies.

One main concern for dengue is infection with a second serotype. Generally, the first time one gets a DENV infection, the disease is more likely to be mild. The body then produces antibodies that only protects against that serotype. Antibodies that cross-react with the other serotypes do develop – but this is actually dangerous, as these antibodies can potentially enhance DENV infection instead. This results in higher viral load which leads to over-reactive immune responses from the body to cause severe dengue. Developing a vaccine that produces immune responses that not only prevent dengue but also avoid the risk of enhancing DENV infection is challenging.

There is an existing dengue vaccine in the market – Dengvaxia – but it has not been able to vaccinate the population against DENV. What are its limitations?

Dengvaxia vaccine is a tetravalent vaccine. Each dose is composed of all four serotypes of dengue virus. As mentioned, it turns out that our body responds differently to each strain. Exposing the body to DENV1-4 at the same time does not give a broad and strong response to each serotype.

Dengvaxia has thus not shown equal efficacy in protecting against dengue by each of the four serotypes of DENV. Consequently, anyone without a prior episode of DENV infection has shown increased risk of severe dengue after vaccination. Therefore, Dengvaxia can only be given to those who test positive for prior DENV infection. These limitations have severely affected the utility of the vaccine.

Can you explain how the sequential immunisation would work to protect against dengue?

Sequential immunisation mimics the natural exposure in a faster time-scale. Each serotype is given one at a time, however, as it is a vaccine, the reactions that result in dengue fever or dengue haemorrhagic fever do not occur. We might be able to induce a sufficiently robust and cross-reactive response from 2 serotypes that would only require two doses rather than four. The sequential immunisation results in both broad and strong responses to all four serotypes, and also induces higher levels of neutralising antibodies to all four serotypes.

If successful, what does this mean for the general population? Would it be an annual vaccination, much like the flu jab?

One would be fully vaccinated against all four serotypes. Hence, it would likely be similar to longer lasting vaccines, such as many childhood vaccines. Perhaps once every 10+ years, but this would be determined in follow-up clinical trials. It would also be available to a larger demographic including young children and the elderly, if deemed safe. That is the goal.

COMMENTARY

PARSING THE PANDEMIC

Despite all the attention on medical innovations and revolutionary therapies, one of humanity's best weapons to tackle the pandemic might be something as simple and complex as data.

Prof Lim Sun Sun, who heads the humanities and social sciences department at **SUTD**, writes about how computational social science can be harnessed to staunch the spread of COVID-19.

In mere months, COVID-19 has charted a veritable path of destruction marked by widespread infection, premature deaths, battered economies and fractured societies. But it has also left a trail in its wake – a digital trail, to be precise. Unlike previous outbreaks such as the Spanish flu or SARS, COVID-19 has emerged in an intensely digitalising world where multiple data streams can help us understand its spread.

The Big Data we generate in our hyperconnected world provide unprecedented insights into the movement of people, objects and by extension, disease. This wealth of data can unlock valuable insights for contact tracing and disease containment for the near term, but also epidemiological research that will inform our strategies for tackling future pandemics.

What are these different sources of data, and how can computational social science leverage this flood of information for the advancement of knowledge, policymaking, governance, and design?

In societies with a high level of technology penetration, the shift towards digitalisation provides an unprecedented raft of data that can be used to analyse population movements and interactions. The proliferation of smartphones alone constitutes a robust scaffold for a dynamic and informative Internet of Things (IoT). Augmenting that is a slew of other IoT-connected devices such as traffic and security systems, power grids, weather stations, vehicles, appliances, thermostats and more. Together, these devices – collect a rich diversity of information – which, if suitably anonymised and systematically analysed, afford us penetrating insights into human mobility, behaviour, preferences and even emotions.

This trend towards 'datafication' holds significant promise, albeit not without its pitfalls. Datafication, as defined by Viktor Mayer-Schoenberger and Kenneth Cukier in their book on the big data revolution, is the process of transforming social action into online quantified data, thus facilitating real-time tracking and predictive analysis. Processes and activities that were previously ephemeral and invisible are now recorded, streamed, and converted into data for collation, tracking, analysis and optimisation.

Therein lies the many opportunities for transformative research, especially in computational social science. This explosion of data needs to be optimised with scalable computational tools that are integrated with social science insights to lend depth to analysis. Ceaseless refinement in computational techniques has also given a significant boost to social scientists' ability to distil meaningful insights from large-scale demographic, behavioural and network data.

With COVID-19 impacting all aspects of our everyday lives considerably, computational social science efforts can be geared towards answering a wide variety of critical questions. These include changes in work patterns and commuting behaviour, shifts in consumption habits, influence on physical and mental health, responses to public health communication, and adaptations in information sharing and social interaction.

In urban areas in particular, computational social science can be applied to urban analytics data to manage population density and pandemic preparedness. Principally, the design of residential, commercial and recreational spaces must take into account the possibility of future disease outbreaks and strike a balance between space optimisation and optimal human density, as well as physical and social structures for directing human movement flows during health crises.

Nevertheless, before we exult too enthusiastically at the prospects of tackling disease through such quantification and computation, we must also be cognisant of some pitfalls in this turn towards the datafication of disease. As the vociferous concerns around contact tracing apps and their modest adoption rates have demonstrated, people have fears about surveillance that cannot be disregarded.

Issues of privacy and confidentiality in data must be squarely addressed with robust safeguards and strict adherence to ethical principles. Once these best practices are put in place, provisions for data sharing must ensure that leading research teams are granted access to the data for its utility to be maximised.

To further jumpstart relevant research, governments and other benefactors should offer grants with rapid review processes and institutional ethical review boards can also introduce fast-track approval channels for COVID-19 related research. This practice has already been adopted by leading institutions and international peer-reviewed journals.

Through such facilitation and the application of cutting edge computational social science techniques, we can fully optimise insights from Big Data to build vital social and physical structures for pandemic preparedness.

Image: SUTD

SUTD's Prof Lim Sun Sun talks about how data can be harnessed to fight the pandemic

Images: 3SC

COMMENTARY

MAPPING THE WAY TO ACTION

The emergence of COVID-19 has highlighted the importance of public health efforts in combating infectious disease spread. **Singapore-ETH Centre** researcher **Miya Irawati**, who is part of a team that is studying the spatial distribution of infected cases in Jakarta, shares about how mapping the vulnerable areas to COVID-19 can lead to useful insights for rapid response.

The far-reaching impacts of the COVID-19 pandemic demand urgent action on many fronts. A medical response is, of course, the most immediate need. This is followed by the gathering and analysing of data – an often challenging task, in view of how data and the process of data collection is often fragmented and imperfect.

Although the world has experienced global pandemics as far back as the Plague of Justinian (541 AD – 750 AD) and the Black Death (1346-1353), the mapping of infected cases did not begin until the early 1600s. The 1854 cholera outbreak in London further popularised these efforts, and John Snow, the father of modern epidemiology, further illustrated the power of mapping by tracing cholera infections in Soho . While miasmas (or obnoxious gases) was previously believed to be the cause of cholera, Snow mapped the spread of infections and traced the disease back to a public water pump. The discovery of this relationship between water contamination and cholera has shaped planning of modern-day water infrastructure in London and most cities.

In Indonesia, one of the world's most populous countries , the Future Cities Laboratory (FCL) has been conducting rapid-response studies in the form of mapping the COVID-19 pandemic in Makassar and Jakarta areas to support policymakers in pandemic management by using 'ur-scape' as a practical planning support tool. Since 2016, FCL has used this tool to help local governments in Indonesia, including Bandung, Palembang, and Semarang, in spatial planning and policy-making decisions . However, there are challenges involved in mapping a fast-moving phenomenon such as COVID-19 – for instance, obtaining reliable spatial data in a timely fashion.

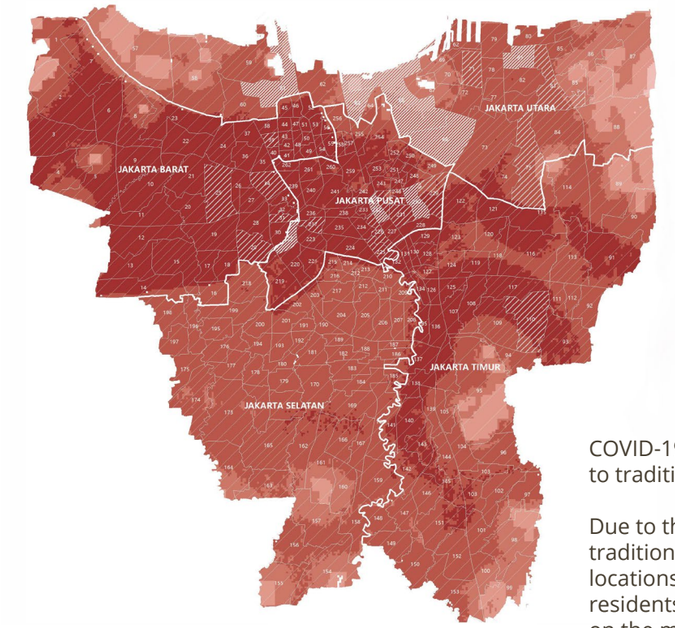
Mapping the unfolding of the pandemic

In Jakarta, we use spatial analysis to map the vulnerability of kelurahan (hamlets) in the urban communities to support the government in planning and setting priorities. These inputs, which are mostly provided by governments and other independent institutions, include the number of COVID-19 cases reported in each kelurahan, population density, urban morphology, and the location of public facilities, such as traditional markets and public transportation hubs.

The first COVID-19 case in Indonesia was announced on 2 March 2020. Consisting of 262 kelurahan within five administrative cities, including mixed middle-class settlements and denser urban kampung enclaves, the Jakarta province was unsurprisingly the worst hit .

As of 31 March, a month after the announcement of the first COVID-19 case in Indonesia, only 13 kelurahans reported high number of COVID-19 cases, with the highest number of cases at just 19. In the early days of case reporting, efforts were centralised in the Ministry of Health under the central government. There were questions of whether there were unreported cases, and whether delays in understanding the reality on the ground were hindering mitigation efforts and the implementation of safety measures for Jakarta's communities.

However, once authority was given to the local governments and more laboratories were established, local governments have been able to publish daily COVID-19 data, thereby reducing the delay in case reporting and allowing for timely action. By 31 July, the numbers of reported COVID-19 cases were more realistic – 40 kelurahan reported over 70 confirmed daily cases, especially those with dense urban morphologies.



This map shows the population density and the number of COVID-19 cases in each area, allowing the researchers to detect patterns in the spread of disease. The darker the shade of red, the denser the population living there

Revealing patterns: zooming in to the traditional markets

Jakarta is littered with markets of varying types and scales – wholesale markets, traditional (food) markets, and smaller community markets. Spatial analysis shows that kelurahan with high numbers of COVID-19 daily cases were mostly in close proximity to traditional markets.

Due to the absence of strict health protocols, traditional markets are considered high-risk locations for the spread of COVID-19. This makes residents who live nearby and those who depend on the markets for their livelihoods particularly vulnerable. Unfortunately, in the early days, members of the public – such as residents and traders – were not involved at the forefront together with the authorities to help implement and monitor compliance of COVID-19 protocols in the markets.

From mapping to action

In addition to revealing vulnerable hamlets, spatial analysis provides information specific to local conditions to support preventative measures at the local level, such as updated numbers of elderly and people with chronic diseases who are at high risk of being infected with COVID-19. By forming

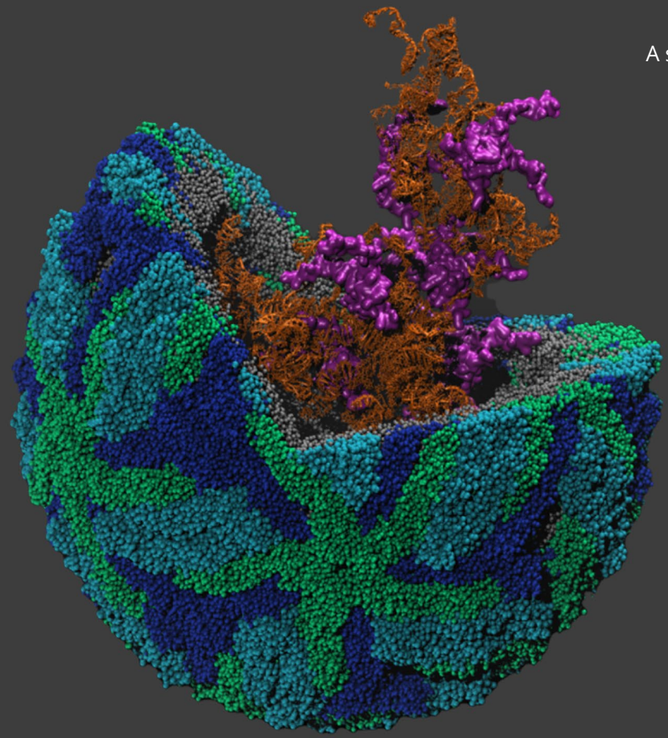
community groups and involving the public, each hamlet was able to reinforce mitigation measures and monitoring for the health and safety of its respective community.

At the local level, empowering residents also enabled them to contribute COVID-19-related data in a ground-up manner as open data, thereby improving the quality of data. At a time when a rapid response is crucial, a challenge of such magnitude is most effectively tackled as a joint effort by governments together with the community.

Examining epidemiology with spatial dimensions can also contribute to urban spatial planning and design, and thereby benefit societies in two ways. First, it contributes to infrastructure planning in cities, especially for clean water and waste management. Second, epidemiology is increasingly integrated into web-based Geographic Information Systems (GIS) to support spatial analysis across scientific disciplines.

As urbanisation increasingly leads to higher urban density, the threat of the spread of diseases also grows correspondingly. Looking at urban planning and design through the lens of epidemiology is helping planners to rethink design in a way that safeguards the health and well-being of residents. Conversely, a spatial understanding of the activity patterns of residents will provide important insights on the vulnerability of areas to diseases and possible mitigation strategies.

A VIEW ON SCIENCE



A schematic representation of mature and infectious dengue virus. Scientists from the Agency for Science, Technology and Research's (A*STAR) Genome Institute of Singapore (GIS), together with scientists from Duke-NUS Medical School and A*STAR's Bioinformatics Institute (BII) have mapped out the structures of four dengue and four Zika viruses.

The research studied the viruses' activities and vital parts to identify portions of the viruses' genetic materials that could be targeted for treatments. Understanding the biology of these viruses – as well as their corresponding functions – will enable scientists to design better drugs and treatments. This is a significant step forward towards targeted therapeutics to tackle both mosquito-borne infections, which can be deadly. Additional research is necessary to better understand how the viruses' structural mutations reduce the effect of treatments.

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