IDMxS
INSTITUTE FOR DIGITAL MOLECULAR ANALYTICS & SCIENCE

IDMxS 2nd Symposium

"Technologies for Molecular Detection"

Date: Friday, 5 Jan 2024
Time: 8:30 am to 6:30 pm
Venue: SBS Foyer & SBS Classroom 1

Time	Programme
8:30 AM - 9:00 AM	**Registration & Breakfast**
9:00 AM - 9:05 AM	**Opening Address by acting director Peter TÖRÖK**
9:05 AM - 9:50 AM	**Plenary 1: David DUFFY** Digital Detection of Proteins
9:50 AM - 9:55 AM	**Detection cluster introduction: Atul N. PARIKH**
9:55 AM - 10:25 AM	**Keynote 1: Anderson H.C. SHUM** Assembly at Phase-Separating Aqueous Systems
10:25 AM - 10:40 AM	**SUN Simou** Emergent Biomolecular Systems for Digital Bioassays
10:40 AM - 10:55 AM	**Joey DEGRANDCHAMP** Powering Accessible Molecular Diagnostics through Nanoparticle Imaging
10:55 AM - 11:15 AM	**Coffee / Tea break**
11:15 AM - 11:20 AM	**Analytics cluster introduction: Thorsten WOHLAND**
11:20 AM - 11:50 AM	**Keynote 2: SHEN Zuowei** Mathematics in Data Science
11:50 AM - 12:05 PM	**YIN Yueming** Predicting Molecular Drug Efficacy through Molecule Graph Models: A Perspective from AI Data Analysis
12:05 PM - 12:20 PM	**KIM Hyuneil** Generalized Likelihood Ratio Test Methods for Nanoparticle Imaging Assays
12:20 PM - 1:20 PM	**Lunch**
1:20 PM - 1:25 PM	**Transduction cluster introduction: Peter TÖRÖK**
1:25 PM - 1:55 PM	**Keynote 3: CHEN Wei Ting** Metasurface Optics: Fundamentals, Applications, and Commercialization
1:55 PM - 2:10 PM	**Xiao-Liu CHU** Lensless Imaging Based Nanoparticle Assays
2:10 PM - 2:25 PM	**YOW Ai Ping** The Use of AI in Optical Design: Learning to Design
2:25 PM - 2:45 PM	**Coffee / Tea break**
2:45 PM - 2:50 PM	**Translation cluster introduction: Eric YAP**
2:50 PM - 3:20 PM	**Keynote 4: TAN Boon Huan** Solutioning the Next Pandemic
3:20 PM - 3:35 PM	**James HO Chin Shing** Reconstituting Living Interfaces: Tear Film
3:35 PM - 3:50 PM	**XIAO Yi** Interferometric Scattering Microscopy for Precision Digital Molecular Analytics
3:50 PM - 4:35 PM	**Plenary 2: Daniel A. FLETCHER** Expanding the Reach of Image-Based and Molecular Diagnostics
4:35 PM - 5:30 PM	**Posters presentation**
5:30 PM - 6:30 PM	**Reception - End of symposium**

Oral presentation

Plenary 1
David DUFFY
CTO & VP (Research), Quanterix Corp, USA

Digital Detection of Proteins

The digital detection of proteins—which has improved the analytical sensitivity of protein tests from picomolar to attomolar concentrations—has emerged as a key tool for the understanding, diagnosis, and treatment of devasting diseases, such as Alzheimer's disease (AD). We will describe how single molecule detection initially enabled digital immunoassays and the subsequent explosion in innovative digital methods. Digital bead assays (DBA)—based on the capture and labeling of proteins on beads, optically identifying "on" and "off" beads, and quantification using Poisson statistics—have enabled highly sensitive, robust protein detection leading to unique measurements in clinical research and diagnostics. DBA have been used to develop "blood tests for the brain" that have had profound effects on the diagnosis and treatment of neurological diseases, e.g., allowing AD to be diagnosed 16 years before symptoms and catalyzing the approval of a therapy for amyotrophic lateral sclerosis based on measuring a neurological protein biomarker in blood. We end by considering technical innovations needed for the mass adoption of digital protein methods that would maximize their impact on society.

Keynote 1
Anderson H.C. SHUM
Associate Vice-President (Research and Innovation), Department of Mechanical Engineering, The University of Hong Kong

Assembly at Phase-Separating Aqueous Systems

In Nature, water is a major component of living matters. The emergence of complicated hierarchical structures from water is fascinating. Biological cells represent an important and illustrative example where liquid droplets in the form of membraneless organelles play significant roles in numerous biological processes. Such sophistication in structure and functions in all-aqueous environments has yet to be comprehensively understood, let alone replicated, in synthetic systems. In this talk, I will introduce our works studying how phase separation and physico-chemical processes can co-exist in all-aqueous systems, and how their interplay can lead to hierarchical structures with properties and features different from one-phase aqueous system and two-phase oil-water-based systems. The talk will conclude with discussions on implications of these synthetic aqueous systems for biomimetic materials and biotechnological applications.

SUN Simou
Research Fellow, IDMxS, Nanyang Technological University

Emergent Biomolecular Systems for Digital Bioassays

Digital bioassays, such as Digital ELISA and Digital PCR, have catalyzed a paradigm shift in molecular diagnostics. As an approach that is particularly effective for measuring analytes with low concentrations, it presents significant opportunities in biomedical applications, along with certain technical challenges. In this talk, I will introduce three emergent biomolecular systems with the potential to address these challenges and discuss how they can also be applied to explore the frontiers of traditional disciplines. The highlighted systems include switch-like signal amplification with protein condensation phase transitions, compartmentalized microreactor droplet arrays with aqueous two-phase systems, and multidimensionally labeled single-extracellular-vesicles arrays.

Joey DEGRANDCHAMP
Research Fellow, IDMxS, Nanyang Technological University

Powering Accessible Molecular Diagnostics through Nanoparticle Imaging

The current generation of portable diagnostics is currently dominated by cheap but insensitive rapid antigen tests (lateral flow assays) and responsive but expensive isothermal nucleic acid amplification tests (eg. RT-LAMP). The Institute for Digital Molecular Analytics and Science (IDMxS) envisions an emergent class of biosensing technology based on optical imaging and analysis, utilizing the unique expertise of our interdisciplinary Detection, Transduction, Analytics, and Translation clusters. I will introduce the Detection arm of our concept for an affordable nucleic acid detection platform based on the imaging of DNA-functionalized gold nanoparticles and their target-induced clustering. Using optical imaging, we can spatially discretize clusters or even single particles to access a wealth of hidden information as well as remove noisy elements. We can additionally collect dynamic data to utilize particle motion for further analysis. Particle clustering by traditional crosslinking inherently limits signal generation, so we have also begun development of amplification strategies. We hope to achieve an optimal regime wherein detection is possible with simple optical systems, enabling sufficiently economical but accurate diagnostic tests.

Keynote 2
SHEN Zuowei
Vice Provost (Graduate Education & Special Duties), National University of Singapore

Mathematics in Data Science

We are living in the era of big data. The discovery, interpretation and usage of the information, knowledge and resources hidden in all sorts of data to benefit human beings and to improve everyone's day to day life is a challenge to all of us. The huge amount of data we collect nowadays is so complicated, and yet what we expect from it is so much. This provides many challenges and opportunities to many fields, especially, the field of mathematical science. In this talk, we will show by examples how mathematics has been playing important roles in the era of big data. We will further discuss how mathematics can move the frontier of data science and what kind of challenges mathematicians face in this era of big data.

YIN Yueming
Research Fellow, IDMxS, Nanyang Technological University

Predicting Molecular Drug Efficacy through Molecule Graph Models: A Perspective from AI Data Analysis

In AI-based drug discovery, molecules are often modeled as graphs, and graph neural networks are used to extract structural and chemical information from these graphs to predict drug efficacy. Drug efficacy is typically measured by biological activity, the minimum concentration (mol/L) of a molecule needed, along with a drug target protein, to complete a specific biological process. Biased data collection based on human decisions poses challenges for AI data analysis. We utilize family information of protein molecules, annotation data on small molecule-protein activity, and employ transfer learning to mitigate data biases, significantly improving real drug screening performance. Furthermore, employing adversarial learning generally enhances the AI model's generalizability in handling molecular graph data, universally improving the predictive performance of various mainstream AI models on molecular bioactivity prediction. Finally, we utilize generative adversarial techniques to optimize molecules and obtain new molecules with higher drug efficacy. We hope that detecting molecular activities in the physical world will help us understand the process through which molecules generate drug efficacy, opening new perspectives for modeling molecular drug efficacy.

KIM Hyuneil
Senior Research Fellow, IDMxS, Nanyang Technological University

Generalized Likelihood Ratio Test Methods for Nanoparticle Imaging Assays

The precise detection of target analytes in samples is crucial for advancing diagnostic capabilities, particularly in low-abundance and high-noise scenarios. Overcoming these challenges is key for detecting biomarkers, previously elusive at critical timings or relevant environments. Here, we introduce a framework that applies the Generalized Likelihood Ratio Test (GLRT) to image data analysis in nanoparticle assays, aiming to approach the detection limits.

In contrast to heuristic or machine-learning methods, our approach leverages detection and information theory to systematically extract mathematical and statistical insights from image data. The application of GLRT to simulated image datasets not only demonstrates the effective identification of particle presence but also yields critical metrics such as the probability of false positive rates and false discovery rates. These metrics establish a robust framework for assessing the reliability of analysis results.

Our findings indicate that GLRT-based methods offer a parameter-free, interpretable, and training-free framework for image analysis in nanoparticle assays that will complement machine-learning methods effectively. The framework will further be extended across a wide range of assay schemes, offering a solid mathematical basis for data interpretation in precision analytics.

Keynote 3
CHEN Wei Ting
CTO, SNOChip Inc. USA

Metasurface optics: fundamentals, applications, and commercialization

Imagine a world where all optical components are reduced to less than a millimeter in thickness and seamlessly integrated with semiconductor sensors. This vision is being brought closer to reality through metasurface optics built by optical elements consisting of sub-wavelength nanostructures. Over the past few years, the development and application of these metasurface optical components have shifted from laboratory concepts to mass production. The momentum is driven by the potential for semiconductor foundries to not only produce semiconductor sensors but also these advanced meta-optical elements using deep ultraviolet lithography. In this presentation, I will introduce the fundamental principle and applications of metasurface optics, detail the journey of metasurface optics from research innovation to commercial application, contrast its distinctive features in comparison with traditional refractive and diffractive optics, and highlight the latest significant advancements.

Xiao-Liu CHU
Research Fellow, IDMxS, Nanyang Technological University

Lensless Imaging Based Nanoparticle Assays

Within the context of diagnostic testing through imaging technology, the imperative lies in achieving exceptional sensitivity across an expansive sample volume. Conventional COVID lateral flow tests for example, while including the entirety of the provided sample, often fall short in terms of sensitivity. The main challenge in enhancing sensitivity within imaging technology thus resides in extending this crucial attribute across a wide field of view in a cheap and compact manner. In this research, we employ a combination of metallic nanoparticles tethered to our target molecules, alongside the use of straightforward imaging methods such as dark field and interferometric scattering microscopy. We complement these techniques with computational tools designed to discern the presence of singular target molecules. Furthermore, we explore the realm of lensless imaging technology, aiming to overcome the limitations imposed by conventional optical lenses, thereby extending the field of view to several millimeters while preserving a resolution at the sub-micron scale. These improvements hold significant promise in advancing existing diagnostic instruments, all the while remaining cost-effective and compact in their design.

YOW Ai Ping
Senior Research Engineer, IDMxS, Nanyang Technological University

The Use of AI in Optical Design: Learning to Design

IDMxS's optical transduction devices are designed using over a century old optical design theory and knowledge and so the success of our lens design relies significantly on the expertise and experience of human designers, coupled with their familiarity with design software. Designers have been actively seeking AI-based methods that can automatically suggest good initial designs for faster optimization. However, existing approaches are data-driven and require meticulous curation of design databases with specific specifications. The pressing question is whether a lens design generation approach can be devised solely based on first-order optics principle, without the explicit need for a predefined reference database. In our pursuit of an answer to the question, we delved into reinforcement learning (RL), a technique that has proven effective in domains like autonomous driving and robotics. The use of RL in lens design generation remains largely unexplored. In this talk, we share how the implementation of RL approach enables machines to learn autonomously without explicit theories or prior knowledge, explore the design landscape and generate initial designs based on desired specifications. This exploration has the potential to usher in a paradigm shift in lens design, moving away from conventional design strategies while offering tangible practical benefits.

Keynote 4

TAN Boon Huan
Distinguished Scientist, DSO National Laboratories

Solutioning the next pandemic

On May 2023, when WHO announced that the COVID-19 global health emergency was over, everyone breathed a sense of relief. However, the question lingering at the back of everyone's mind is when will the next pandemic emerge? Where will it originate? Who will be the most at-risk population? How are we going to prevent the emergence, and worse, the escalation?

The presentation aims to trace the lessons Singapore learnt from the first SARs crisis that took place in 2003, highlight the technical capability development that had taken place at the national level since then, and relate how Singapore transformed to cope with the second and current SARs crisis.

As the second crisis unfolded in Singapore and globally around the world, it saw scientists and clinicians, and many others outside the healthcare industry coming together to integrate different expertise to manage the crisis. Now that COVID-19 is endemic, surely there must be lessons that Singapore can learn to better herself to cope with the next pandemic. The presentation will end with a review of the preparedness plan that Singapore will put in place. One of the requirements of this plan is the development of the next generation of diagnostics, and hopefully this presentation will facilitate some discussion on collaborative research in biodetection.

James HO Chin Shing
Senior Research Fellow, IDMxS, Nanyang Technological University

Reconstituting Living Interfaces: Tear Film

The tear film lipid layer (TFLL) is the direct interface of our eyes and the external environment. The multifunctional, multilayer structure of the tear film prevents excessive evaporation of the underlying aqueous layer, ensures optical transparency to light, and minimizes microbial assaults. This window to the outside world may become susceptible to invasive chemicals, for instance those present in various consumer products, and loses its structural integrity. Moreover, when the chemical composition of the TFLL deviates from the normal range, it can show enhanced sensitivity to those chemicals. To minimize contact of our eyes with invasive chemicals, regulatory bodies use an arsenal of in vivo and in vitro cell-based models to screen for such molecules. However, many of these methods are time consuming, lack accuracy in predicting outcomes in physiological conditions, and may not provide mechanistic insights. To overcome these limitations, we define a minimal chemical system that reproduces the general structural characteristic and molecular organization of the TFLL. Current efforts in translating the chemical and biophysical response into digital ones for high throughput screening are presented.

XIAO Yi
Research Fellow, IDMxS, Nanyang Technological University

Interferometric Scattering Microscopy for Precision Digital Molecular Analytics

Conventional bioassays can only report average behaviour of a population of molecules. For such ensemble measurements, subtle information and heterogeneity at the molecular level are lost, and the sensitivity of detection is limited. Digital molecular analytics has recently emerged to tackle these issues by constructing individual micro/nano-scale partitions and incorporating signal amplification mechanisms based on enzymatic reactions. However, these methods suffer from tedious workflows, time-consuming and heterogeneity-ignoring. Recently, interferometric scattering microscopy (iSCAT) offers unique opportunities for ultrasensitive detection and analysis of single molecules with high spatiotemporal resolution. Our project aims to develop precision digital molecular analytic platforms based on iSCAT, which is able to detect low presence and heterogeneous properties (e.g., binding kinetics) of cancer-related biomarkers (e.g., nucleic acids, proteins). Such goal can be achieved by new optical system design, detection strategy design and microfluidic system construction. Our efforts will offer unprecedented possibilities for disease diagnosis and fundamental studies of biomolecules.

Plenary 2

Daniel A. FLETCHER

EAB member, Department of Bioengineering, University of California Berkeley

Expanding the reach of image-based and molecular diagnostics

The goal of making diagnostic testing available for all is hampered by two major challenges. The first is determining what biological marker or signature is the best indicator of a disease. Advances in understanding the mechanistic underpinnings of disease have revealed new molecular biomarkers and opportunities for diagnostic assays, though better signatures are still needed for early detection and disease progression. The second challenge is developing diagnostic technology that is simple, rapid, and accessible. Most diagnostic testing remains centralized in diagnostic laboratories, even though populations most in need are far from hospitals and medical centers with modern equipment and disease experts. This talk will address progress on both challenges, with a focus on new molecular assays using Cas enzymes and portable diagnostic technology aimed at reaching underserved populations.

Poster abstracts

Afu FU, IDMxS, Nanyang Technological University

Polyubiquitination-Induced Phase Separation (PIPS) Enables Biosensing of Low-Abundant Disease Biomarker for Human Health

Detecting diseases early, like infection, cancer, or neurodegenerative diseases, can greatly improve patient outcomes. However, the challenge lies in detecting low abundant signal molecules that are masked by highly abundant proteins in clinical samples. To address this, various techniques have been developed to detect the analytes and enrich the signals. We are developing the ubiquitin system, a robust intracellular protein recognition system for selectively degradation, to be novel biosensing tools for low abundant proteins. Excitingly, recent study revealed that polyubiquitinated proteins was able to induce the liquid-liquid phase separation (LLPS) by ubiquitin-scaffolding protein with precision control. In light of these findings, our study aims to develop the ubiquitination system as a specific tool for sensing low abundant proteins, utilizing LLPS as a signal amplification system. In a prototype design, we employ synthetic biology methods to generate fusion proteins incorporating nanobodies and specific degrons, along with their cognate E1, E2, and E3 enzymes. Additionally, we use fluorescence-labelled ubiquitin system components for detection and signal amplification using recombinant proteins. Our on-going technology development will generate a ubiquitination fingerprint bank for specifically detecting and enhanced-sensing broader protein targets.

Xiangfu GUO, CCEB, Nanyang Technological University

2D protein condensation enrichment on negative membrane curvature

Two-dimensional (2D) protein condensation plays an essential role in various biological processes, including immune reaction, cell adhesion and synapse formation. On T cell membrane, the condensation of LAT, Grb2, and Sos1 facilitate the formation of T cell receptor (TCR) clusters. TCRs are enriched on the tip of microvilli, which are highly curved plasma membrane protrusions with diameters ranging from 50-350 nm. This distinctive distribution hints at potential preferences for specific membrane topographies. However, whether the membrane topography influences the protein condensation is an intriguing yet challenging question to study as the dimension of the microvilli is around the diffraction limit of light and hard to manipulate precisely. Here, we harnessed nanofabrication techniques to replicate microvilli geometry in vitro and study the impact of membrane topography on the condensation of LAT/Grb2/SOS1 system. Specifically, we created "nano-channels" with varying sizes (from 50 to 950 nm in diameter) and distinct shapes (curved tips and straight grooves) on quartz chips. The formation of supported lipid bilayers (SLBs) over the entire nanochannel surface results in diverse membrane topographies. We observed that upon introducing Grb2 and SOS1 in the solution, SLB-anchored LAT exhibited a pronounced tendency to cluster at the curved tips of nanochannels, and the signal on the tips was higher than that on the straight grooves. This finding indicates that the topography of nano-channel enriched the condensation of LAT/Grb2/SOS1 system at the curved tip. We further characterized the impact of protein density, protein mobility, cluster diffusivity and cross-linking strength on the topography sensitivity. Overall, our study introduces membrane topography as a novel dimension in the exploration of membrane-associated protein condensation.

James HO, IDMxS, Nanyang Technological University

Reconstituting Living Interfaces: Tear Film

The tear film lipid layer (TFLL) is the direct interface of our eyes and the external environment. The multifunctional, multilayer structure of the tear film prevents excessive evaporation of the underlying aqueous layer, ensures optical transparency to light, and minimizes microbial assaults. This window to the outside world may become susceptible to invasive chemicals, for instance those present in various consumer products, and loses its structural integrity. Moreover, when the chemical composition of the TFLL deviates from the normal range, it can show enhanced sensitivity to those chemicals. To minimize contact of our eyes with invasive chemicals, regulatory bodies use an arsenal of in vivo and in vitro cell-based models to screen for such molecules. However, many of these methods are time consuming, lack accuracy in predicting outcomes in physiological conditions, and may not provide mechanistic insights. To overcome these limitations, we define a minimal chemical system that reproduces the general structural characteristic and molecular organization of the TFLL. Current efforts in translating the chemical and biophysical response into digital ones for high throughput screening are presented.

Giora MOROZOV, IDMxS, Nanyang Technological University

Recombinant TLR molecules for biosafety and translational medicine

We are going to express and purify recombinant soluble TLR and use it to detect traces of viruses and prokaryotes in pharmaceutical and biotherapeutic products.

Parenteral medications must be free of bacterial and viral compounds that may induce life-threatening systemic reactions. Traditionally, quality control tests to determine pyrogens were the Rabbit Pyrogen Test, established in 1912; the Gram-Negative Bacterial Endotoxin Test, known on the market since 1977; and the Monocyte Activation Test, introduced in 2010. The recombinant TLR pyrogen detection system we are going to develop has significant advantages over existing tests in terms of spectrum of action and reliability.

Aswani NATARAJAN, IDMxS, Nanyang Technological University

Electromagnetic modelling of grating-based substrates for optical imaging applications

Imaging of nanoparticle aggregates is a critical task in medical diagnostics. Dark field and interferometric scattering (iSCAT) microscopy techniques can be used to image nanoparticles with high sensitivity. However, the complex and bespoke optics that these methods involve pose a barrier to their adoption at scale for viable diagnostics. To surmount this, diffraction grating structures are being investigated as an easily fabricable and affordable option for imaging of nanoparticle aggregates. Moreover, by virtue of their ability to manipulate light at the nanoscale, diffraction gratings represent a good candidate substrate to enhance nanoparticle imaging.

In this work, rigorous electromagnetic modelling of a diffraction grating-based nanostructured substrate is performed using COMSOL Multiphysics software. Additional scattering of electromagnetic waves by

gold nanoparticles placed on a grating substrate is also simulated. Our numerical simulation uses an electromagnetic frequency domain finite element analysis framework. A grating-based nanoparticle substrate is designed and optimized for visible wavelengths under normally incident illumination. Geometrical parameters such as shape, period, thickness, and the duty cycle of the grating are optimized so as to enhance sensitivity to scattering from perturbing nanoparticles through minimizing background illumination.

Kamal Kant SHARMA, Department of Biological Sciences, National University of Singapore

Finding antibodies based on single virus fusion dynamics of enveloped viruses

The recent pandemic caused by Sars-CoV-2 has shown the potential of emerging/neglected enveloped viruses. Therefore, now is more than ever urgent need to understand the functioning of these viruses for finding potent viral therapeutics. Here, we are finding novel monoclonal antibodies based on dynamic traits of enveloped viruses with advanced spectroscopy methods. A neutralizing antibody can disrupt the viral lifecycle usually involves binding to the viral glycoprotein, which can then disrupt entry by blocking one or more of the processes. We have established a dengue virus-model membrane fusion assay to monitor disruptions during virus fusion and obtained fusion kinetics of dengue virus.

Tan Ching Hai, LKCMedicine, Nanyang Technological University

Digitization of bacterial isolation and culture on an open low-cost automated platform

Antimicrobial Resistances (AMR) are responsible for a larger number of deaths globally due to the rise of antibiotic resistance genes. In fact, AMR is predicted to be responsible for 10 million deaths by 2050, exceeding that of even cancer. Existing methods of bacterial isolation, classification and characterisation are too slow and expensive, requiring either large amounts of manpower or expensive machines and algorithms to carry out these processes, making them inaccessible in addition to generating large amounts of plastic waste. Hence, a new process was formulated through designing and printing custom grids using reusable and sterilisable materials, an open-source liquid handler (Opentrons-2) and custom-written protocols to maximise the number of environmental samples which could be processed simultaneously. To make the process more user-friendly, a user-interface was developed so they would not have to adjust the source code.

Results showed that automating the bacterial culturing process on the OT-2 resulted in significantly higher throughput than the traditional method of streaking. Additionally, this process and be scaled up based on the number of machines available. Given the relative success of this automation processes, it could be adapted for other microbiological experiments such as antibiotic resistance testing or other fields of biology such as cell-culturing.

Future improvements could include granting the OT-2 imaging capabilities and linking it to a server to process the images to obtain qualitative and quantitative information about the bacterial growth in real-time.

Jianwu WANG, IDMxS, Nanyang Technological University

Integrated Electrochemical Sensing Platform for Brain-Machine Interface (BMI)

Brain-machine interfaces (BMI) rely on electrophysiological signals to interpret and transmit neurological information, while neurons communicate through synapses using neurotransmitters. To effectively communicate with biological neurons, bioelectronics must possess three key functionalities: neurotransmitter recognition, synaptic plasticity, and action potential firing. However, current neuromorphic devices only respond to electrical or physical signals, leading to inadequate interpretation of neuron information.

Our report introduces a chemically mediated artificial neuron for bidirectional communication in a BMI, enabling it to both receive and send chemical information using neurotransmitters as messengers.

WEE Soon Keong, LKCMedicine, Nanyang Technological University

Profiling Urban Microbes in Asia: Initial analysis of 211 whole genome sequences of environmental Acinetobacter for digital molecular analysis

Acinetobacter baumannii is one of the ESKAPE pathogen listed by World Health Organisation (WHO) to be of global concern given its rise of multi-drug resistance. It is capable of causing hospital-acquired and community-acquired infections, but little is known about its extra-hospital environmental reservoirs. Current strain typing methods involve the use of multi-locus or whole genome sequencing which would not be suitable for rapid genomic epidemiology applications. This study aims to isolate and characterise A. baumannii in the urban environment and develop a molecular-based strain typing approach. Briefly, soil and water field sampling was conducted through Project Profiling Urban Microbes in Asia (PUMA) to isolate and characterise environmental A. baumannii isolates. A. baumannii (n = 197, A. nosocomialis (n = 11) and A. pittii (n = 3) were isolated and sequenced in this study. The large pangenome consisting of 18,625 cloud genes was observed in our environmental A. baumannii isolates. The blaOXA-51 gene (825 nt), an intrinsic resistance gene present in all A. baumannii, were found to be highly polymorphic, with more than 65 known types and as many as 39 untyped novel sequences in our isolates. It demonstrated concordance when present MLST and SNP clustering typing approaches and is a potentially cost-effective target for probe development for resequencing and strain typing applications. The development of an efficient molecular-based strain typing tool targeting such single locus polymorphic region would enable high throughput environmental and clinical surveillance studies.

Yi XIAO, IDMxS, Nanyang Technological University

Computational interferometric scattering microscopy for precision digital molecular analytics

Digital molecular analytics has recently emerged to tackle these issues by constructing individual micro/nano-scale partitions and incorporating signal amplification mechanisms based on enzymatic reactions. However, these methods suffer from tedious workflows and are incapable of true single-molecule analysis. This work aims to develop precision digital molecular analytic platforms based on computational interferometric scattering microscopy (iSCAT), which can detect low presence (even down

to the single-molecule level) and properties (e.g., hydrodynamic radius, binding affinity with antibodies) of cancer-related biomarkers (e.g., nucleic acids, proteins) from small-volume biofluids. Such goal can be achieved by new optical system design (high-speed wide-field off-axis mode), detection strategy design (characterizing biomolecules on surfaces or tracking their three-dimensional trajectories in motion), microfluidic system construction, and artificial intelligence (AI) for image processing. Our efforts will offer unprecedented possibilities for disease diagnosis and fundamental studies of biomolecules.

Junqi Yi, IDMxS, Nanyang Technological University

Water-responsive Supercontractile Polymer Films for Bioelectronic Interfaces

Connecting electronics is easy with rigid, standardized interfaces. Linking biological tissues with electronic devices, however, is challenging owing to the softness of tissues and their arbitrary shapes and sizes. Stimulus-responsive films offer a solution by contracting to fit, resembling industrial shrink wrapping. An innovative water-responsive, supercontractile polymer film, inspired by spider silk, allows the construction of soft, stretchable and shape-adaptive tissue–electronic interfaces.

Yueming YIN, IDMxS, Nanyang Technological University

Predicting Molecular Drug Efficacy Through Molecule Graph Models: A Perspective from AI Data Analysis

In AI-based drug discovery, molecules are often modeled as graphs, and graph neural networks are used to extract structural and chemical information from these graphs to predict drug efficacy. Drug efficacy is typically measured by biological activity, the minimum concentration (mol/L) of a molecule needed, along with a drug target protein, to complete a specific biological process. Biased data collection based on human decisions poses challenges for AI data analysis. We utilize family information on protein molecules, annotation data on small molecule-protein activity, and transfer learning to mitigate data biases, significantly improving real drug screening performance. Furthermore, employing adversarial learning generally enhances the AI model's generalizability in handling molecular graph data, universally improving the predictive performance of various mainstream AI models on molecular bioactivity prediction. Finally, we utilize generative adversarial techniques to optimize molecules and obtain new molecules with higher drug efficacy. We hope that detecting molecular activities in the physical world will help us understand the process through which molecules generate drug efficacy, opening new perspectives for modeling molecular drug efficacy.

Jing YU, IDMxS, Nanyang Technological University

Spatiotemporal Oscillation in Confined Epithelial Motion upon Fluid-to-Solid Transition

Fluid-to-solid phase transition in multicellular assembly is crucial in many developmental biological processes, such as embryogenesis and morphogenesis. However, biomechanical studies in this area are limited, and little is known about factors governing the transition and how cell behaviours are regulated. Due to different stresses present, cells could behave distinctively depending on the nature of the tissue.

Here we report a fluid-to-solid transition in geometrically confined multicellular assemblies. The confinement size-dependent surface tension regulates actin fibre assembly, cellular force generation, and cell polarization.

Shixing YUAN, IDMxS, Nanyang Technological University

Imprinting of Photonic Components on Soft Materials for Spectrometers

To fulfill the requirements of real-world applications, there are growing demands and interests in the demonstration of miniaturized, compact, and low-cost spectrometers, which will act as a powerful tool in a wide range of research areas. Based on the advantages such as high resolution, compatible with different materials, and low cost, imprinting technology is a promising method to fabricate the photonic components for compact spectrometers. We aim to design and demonstrate a compact spectrometer, in which photonic devices (such as gratings and waveguides) are proposed to be fabricated by imprinting technology. Specifically, thermal and UV imprinting technologies are explored to fabricate structures such as free space gratings and planar components on soft materials, which will lay a foundation for investigating photonic devices and spectrometer systems.

Ming ZHU, IDMxS, Nanyang Technological University

A Mechanically Interlocking Strategy for Soft Packaging of Stretchable Electronics

Stretchable electronics incorporating critical sensing, data transmission, display and powering functionalities, is crucial to emerging wearable healthcare applications. To date, methods to achieve stretchability of individual functional devices have been extensively investigated. However, integration strategies of these stretchable devices to achieve all-stretchable systems are still under exploration, in which the reliable stretchable interconnection is a key element. Here, solderless stretchable interconnections based on mechanically interlocking microbridges are developed to realize the assembly of individual stretchable devices onto soft patternable circuits toward multifunctional all-stretchable platforms. This stretchable interconnection can effectively bridge interlayer conductivity with tight adhesion through both conductive microbridges and selectively distributed adhesive polymer. Consequently, enhanced stretchability up to a strain of 35% ($R/R0 \leq 5$) is shown, compared with conventional solder-assisted connections which lose electrical conduction at a strain of less than 5% ($R/R0 \approx 30$). As a proof of concept, a self-powered all-stretchable data-acquisition platform is fabricated by surface mounting a stretchable strain sensor and a supercapacitor onto a soft circuit through solderless interconnections. This solderless interconnecting strategy for surface-mountable devices can be utilized as a valuable technology for the integration of stretchable devices to achieve all-soft multifunctional systems.