2023 MIT Health Science Technology Conference

April 4, 2023 9:00 am - 5:00 pm

8:00 AM - 9:00 AM

Registration with Breakfast

9:00 AM - 9:15 AM

Welcome and Introduction John Roberts Executive Director (Interim), <u>MIT Corporate Relations</u>



John Roberts Executive Director (Interim) MIT Corporate Relations

John Roberts has been Executive Director of MIT Corporate Relations (Interim) since February 2022. He obtained his Ph.D. in organic chemistry at MIT and returned to the university after a 20-year career in the pharmaceutical industry, joining the MIT Industrial Liaison Program (ILP) in 2013. Prior to his return, John worked at small, medium, and large companies, holding positions that allowed him to exploit his passions in synthetic chemistry, project leadership, and alliance management while growing his responsibilities for managing others, ultimately as a department head. As a program director at MIT, John built a portfolio of ILP member companies, mostly in the pharmaceutical industry and headquartered in Japan, connecting them to engagement opportunities in the MIT community. Soon after returning to MIT, John began to lead a group of program directors with a combined portfolio of 60-80 global companies. In his current role, John oversees MIT Corporate Relations which houses ILP and MIT Startup Exchange.

Sheryl Greenberg Program Director, MIT Industrial Liaison Program



Sheryl Greenberg Program Director MIT Industrial Liaison Program

Sheryl Greenberg initiates and promotes the interactions and development of relationships between academic and industrial entities to facilitate the transfer of new ideas and technologies between MIT and companies, and has created numerous successful partnerships. By understanding the business, technology, and commercial problems within a company, and understanding the technologies and expertise of MIT researchers, Greenberg identifies appropriate resources and expertise to foster new technology applications and collaborative opportunities.

Prior to MIT, Greenberg created and directed the Office of Technology Transfer at Brandeis University. In the process of managing intellectual property protection, marketing, and licensing, she has promoted the successful commercialization of technologies as diverse as new chemicals and manufacturing, biotechnology, food compositions, software, and medical devices. She facilitated the founding and funding of new companies, as well as creating a profitable technology transfer program. She also facilitated the patenting, marketing, and licensing of Massachusetts General Hospital technologies. In addition to her cellular, biochemical, and genetic research experience in academic and corporate environments, she has also created intellectual property for medical uses. Greenberg has been an independent intellectual property and business development consultant, is a U.S. Patent Agent, and has previously served the Juvenile Diabetes Research Foundation as Co-Chair of the lslet Research Program Advisory Committee and grant reviewer. She currently also mentors startup companies and facilitates partnering them with large life science and healthcare companies.

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Accelerating Manufacturing and Translation of Biologic Medicines Using Alternative Hosts J. Christopher Love

Raymond A. (1921) and Helen E. St. Laurent Professor, <u>MIT Department of Chemical Engineering</u>, Member, Koch Institute for Integrative Cancer Research at MIT,

Associate Member, <u>Broad Institute of MIT and Harvard</u>, Associate Member, <u>Ragon Institute of MGH, MIT, and Harvard</u>



J. Christopher Love

Raymond A. (1921) and Helen E. St. Laurent Professor, <u>MIT Department of Chemical Engineering</u>, Member, <u>Koch Institute for Integrative Cancer Research at MIT</u>, Associate Member, <u>Broad Institute of MIT and Harvard</u>, Associate Member, Ragon Institute of MGH, MIT, and Harvard

J. Christopher Love is Professor of Chemical Engineering and a member of the Koch Institute for Integrative Cancer Research at MIT. He is also an Associate Member of the Broad Institute, and an Associate Member at the Ragon Institute of MGH, MIT, and Harvard. Love earned a BS in chemistry from the University of Virginia and a PhD in physical chemistry at Harvard University under the supervision of George Whitesides. Following completion of his doctoral studies, he extended his research into immunology at Harvard Medical School with Hidde Ploegh from 2004-2005, and at the Immune Disease Institute from 2005-2007. Dr. Love has been named a W.M. Keck Distinguished Young Scholar for Medical Research (2009), a Dana Scholar for Human Immunology (2009), and a Camille Dreyfus Teacher-Scholar. Prof. Love served as a Distinguished Engineer in Residence at Biogen from 2015-2016. He has co-authored more than 100 manuscripts and is an inventor on multiple patents.

Professor Love is co-founder of OneCyte Biotechnologies, HoneyComb Biotechnologies, and Sunflower Therapeutics. He serves as an advisor to SQZ Biotechnologies, Repligen, QuantrumCyte, and other companies.

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Biopharmaceuticals and vaccines traditionally relies on linear stages of development from discovery to translational readiness and manufacturing design (CMC) to manufacturing. Alternative concepts like agile development are common in other industries like software. Holistic approaches leveraging alternative 'fast' expression systems offer unique advantages to integrate design cycles for rapid design and testing and production. This talk will explore examples of how the workflow from discovery to production could be transformed through the use of simple engineered production hosts like those developed in the MIT Alternative Host Consortium.

9.50 AM - 10.25 AM

Moving On Up: Combining Soft Robots With Dynamic Organs and Biological Systems Ellen Roche Latham Family Career Development Professor, MIT Department of Mechanical Engineering



Ellen Roche Latham Family Career Development Professor MIT Department of Mechanical Engineering

Ellen Roche is the Latham Family Career Development Professor at the Department of Mechanical Engineering and the Institute for Medical Engineering and Science at MIT. She directs the Therapeutic Technology Design and Development Lab. She completed her PhD at Harvard University School of Engineering and Applied Sciences. Her research focuses on applying innovative technologies to the development of cardiac devices. Her research includes development of novel devices to repair or augment cardiac function using disruptive approaches such as soft robotics. Ellen was employed in the medical device industry for over five years as a research and development engineer and employs her understanding of the medical device industry and the regulatory pathways to medical device commercialization in her academic research. Her work has been published in Nature Biomedical Engineering, Science Translational Medicine, Science Robotics, Advanced Materials among others. She is the recipient of multiple awards including the Fulbright International Science and Technology Award, the Wellcome Trust Seed Award in Science, a National Science Foundation CAREER Award, an NIH Trailblazer Award, a Charles H. Hood Award for Excellence in Child Health Research, the LabCentral Ignite Golden Ticket and the inaugural Future Founders Grand Prize.

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Cvclical dynamic expansion and contraction are essential to the life-sustaining function of organs, exemplified by the heart and lungs. These continuous movements coupled with complex tissue architecture and composite mechanical properties pose considerable challenges to augmenting impaired organ function. My research is providing paradigmshifting approaches to overcome those challenges, by blending principles of pathophysiology, biomechanics and mechanical engineering with state-of-the-art materials and robotics. In this talk I will speak about three interrelated research streams (i) augmenting the remaining native function in failing organs and biological systems to restore functionality, (ii) introducing technologies to replace or repair focal deficits in tissues and deliver therapy and (iii) developing physiologically realistic in vitro, in vivo, ex vivo and in silico approaches suitable for testing cardiac or pulmonary technologies. I will review my group's overarching approach to designing these technologies, and how these endeavors have opened up possibilities for further understanding of the biomechanics associated with their targeted organ systems. I will illustrate exemplary work from each research strand with specific vignettes. Finally, I will discuss the potential impact of our work, and how co-designing multimodal simulation models with clinical and industrial partners can not only lead to enhanced implantable device design and testing, but also to further understanding of the fundamental mechanical influencers of pathophysiology and intervention strategies.

10:25 AM - 10:55 AM

Networking Break

10:55 AM - 11:30 AM

Does Cell State Matter in Cancer? Alex K. Shalek Core Member of IMES, Associate Prof of Chemistry, and Extramural Member of the KI, MIT Institute Member of the Broad Institute Member of the Ragon Institute



Alex K. Shalek Core Member of IMES, Associate Prof of Chemistry, and Extramural Member of the KI, MIT Institute Member of the Broad Institute Member of the Ragon Institute

Alex K. Shalek is currently the Pfizer-Laubach Career Development Associate Professor at MIT, as well as a Core Member of the Institute for Medical Engineering and Science (IMES), an Associate Professor of Chemistry, and an Extramural Member of The Koch Institute for Integrative Cancer Research. He is also an Institute Member of the Broad Institute, an Associate Member of the Ragon Institute, an Assistant in Immunology at MGH, and an Instructor in Health Sciences and Technology at HMS. His research is directed towards the creation and implementation of new approaches to elucidate cellular and molecular features that inform tissue-level function and dysfunction across the spectrum of human health and disease. This encompasses both the development of broadly enabling technologies as well as their application to characterize, model, and rationally control complex multicellular systems. Dr. Shalek received his bachelor's degree summa cum laude from Columbia University and his Ph.D. from Harvard University in chemical physics under the guidance of Hongkun Park, and performed postdoctoral training under Hongkun Park and Aviv Regev (Broad/MIT).

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Recent advances in high throughput genomic sequencing technologies have led to a detailed understanding of the genetic alterations that underlie human tumors. However, evidence increasingly indicates that using mutations alone to assign therapies has its limitations, even for cancers with actionable mutational heterogeneity. The advent of singlecell genomic technologies has confirmed extensive mutational heterogeneity in human tumors but also revealed that the complexity of cancer extends to variation in cell transcriptional state. Deciphering whether transcriptional variation informs treatment response heterogeneity represents a new but poorly understood frontier in cancer therapeutics. In pancreatic ductal adenocarcinoma (PDAC), clinically relevant RNA expression states exist but our understanding of their drivers, stability, and relationship to therapeutic response is limited. To examine these attributes systematically, we profiled metastatic biopsies and matched organoid models at single-cell resolution. We identify a new intermediate PDAC transcriptional cell state and uncover distinct site- and state-specific tumor microenvironments. Moreover, we reveal strong organoid culture-specific biases in cancer cell transcriptional state representation and nominate critical factors missing from the ex vivo microenvironment. By adding back specific factors, we restore in vivo expression state heterogeneity and show plasticity in culture models, demonstrating that microenvironmental signals are critical regulators of cell state. Importantly, we prove that non-genetic modulation of cell state can significantly influence drug responses and uncover state-specific vulnerabilities. Our work provides a broadly applicable framework for mapping cell states across in vivo and ex vivo settings, identifying drivers of transcriptional plasticity, and manipulating cell state to target its associated vulnerabilities.

11:30 AM - 12:30 PM

Startup Lightning Talks Catarina Madeira Director, MIT Startup Exchange



Catarina Madeira Director MIT Startup Exchange

Catarina has been working with the Cambridge/Boston startup ecosystem for over 10 years and joined Corporate Relations with a solid network in the innovation and entrepreneurial community. Prior to MIT, she was part of the team that designed and launched the startup accelerator IUL MIT Portugal, which was later rebranded as Building Global Innovators. She was based in Lisbon and worked in direct relation with the Cambridge team. She held positions including Operations Coordinator, Program Manager, and Business Developer. The accelerator soon achieved steady growth in large part due to the partnerships that Catarina led with regional and global startup ecosystems. After that, she worked at NECEC, leading a program that connects cleantech startups and industry. In this role, she developed and built a pipeline of startups and forged strong relationships with both domestic and European companies. She has also held positions in Portugal and France, including at Saboaria e Perfumaria Confiança and L'Oréal as Technical Director and Pharmacist. Catarina earned her bachelor's in chemistry and pharmaceutical sciences in Portugal. She went on to earn her Master of Engineering for Health and Medicines in France.

Benjamin C. Williams VP of Corporate Development & Co-Founder 4M Therapeutics

Rick Pierce CEO Decoy Therapeutics

Ho-Jun Suk Co-Founder & CEO DxLab

Erez Kaminski Founder and CEO Ketryx Corporation

Matt Mulvey SVP and Chief Technology Officer Replay Holdings

Laura Crowell Director of R&D Sunflower Therapeutics

Greg Ekchian Co - founder and CEO Stratagen Bio

Jasdave S. Chahal Co-Founder and Chief Scientist Tiba Biotech

Maureen Deehan Chief Executive Officer <u>Vivtex</u>

12:30 PM - 1:30 PM

Lunch With Startup Exhibit

1:30 PM - 2:05 PM

Single-Cell Biology via Perturbation Profiling at Scale Paul Blainey Associate Professor of Biological Engineering, <u>MIT Biological Engineering</u>



Paul Blainey Associate Professor of Biological Engineering MIT Biological Engineering

Paul Blainey is a core member of the Broad Institute of MIT and Harvard and an associate professor in the Department of Biological Engineering at MIT. An expert in microanalysis systems for studies of individual molecules and cells, Blainey is applying such technologies to advance understanding of functional properties of molecules and cells and the mechanisms underlying these properties. Broadly, research in the Blainey group integrates molecular, optical, microfluidic, and computational tools to understand and engineer cellular activities related to a wide range of health challenges.

Today, we investigate and interpret the biology of human cells and their roles in disease through a "cell state" paradigm. We often parameterize cell state via high-content, single-cell molecular profiling. The need to expand this paradigm to include the response of cells to perturbations, the local context of the cells, and additional profiling data modes is clear. Less clear, however, is how we should navigate the expanding panoply of technologies to generate interpretable data at large scales in the most relevant human biological model systems in ways that are relevant to disease. Many available technologies are currently hobbled by high costs or limited applicability to sample types of interest. My group has developed optical pooled screening (OPS), an in situ genomic approach for profile-based screening of the effects of genomic perturbations in human cells at massive scales. Image-based phenotyping provides access to valuable cellular phenotypes complementary to sequencing-based methods and currently provides routine throughputs of tens of millions of cells at modest cost. I will describe the OPS technology and review several recent large-scale applications. I will also speak to ongoing efforts to expand the performance and applicability of OPS in collaboration with industrial partners.

2:05 PM - 2:40 PM

Mammalian Synthetic Biology and Programmable Organoids Ron Weiss Professor, Biological Engineering Director, MIT Synthetic Biology Center



Ron Weiss Professor, Biological Engineering Director, MIT Synthetic Biology Center

Ron Weiss is Professor in the Department of Biological Engineering and in the Department of Electrical Engineering and Computer Science at the Massachusetts Institute of Technology, and is the Director of the Synthetic Biology Center at MIT. Professor Weiss is one of the pioneers of synthetic biology. He has been engaged in synthetic biology research since 1996 when he was a graduate student at MIT and where he helped set up a wet-lab in the Electrical Engineering and Computer Science Department. After completion of his PhD, Weiss joined the faculty at Princeton University, and then returned to MIT in 2009 to take on a faculty position in the Department of Biological Engineering and the Department of Electrical Engineering and Computer Science. The research pursued by Weiss since those early days has placed him in a position of leadership in the field, as evidenced both by publications from his lab as well as a variety of awards and other forms of recognition. He pursued several aspects of synthetic biology, including synthesis of gene networks engineered to perform in vivo analog and digital logic computation. The Weiss lab also published seminal papers in synthetic biology focused on programming cell aggregates to perform coordinated tasks using engineered cell-cell communication with chemical diffusion mechanisms such as quorum sensing. Several of these manuscripts were featured in a recent Nature special collection of a select number of synthetic biology papers reflecting on the first 10 years of synthetic biology. While work in the Weiss lab began mostly with prokaryotes, during the last 5 years a majority of the research in the lab shifted to mammalian synthetic biology. The lab focuses both on foundational research, e.g. creating general methods to improve our ability to engineering biological systems, as well as pursuing specific health related applications where synthetic biology provides unique capabilities.

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Mammalian synthetic biology has recently emerged as a field that is revolutionizing how we design and engineer biological systems for diagnostic and medical applications. In this talk, we will describe our integrated computational / experimental approach to engineering complex behavior in mammalian cells with applications to Programmable Organoids derived from hiPS cells. In our research, we apply design principles from electrical engineering and other established fields. These principles include abstraction, standardization, modularity, and computer aided design. But, we also spend considerable effort towards understanding what makes synthetic biology different from all other existing engineering disciplines by discovering new design and construction rules that are effective for this unique discipline. We will present Programmable Organoids, a new platform for drug discovery that enables rapid and effective drug screening. Based on programmed differentiation into synthetic mammalian tissues having multiple cell type architectures that are similar to human organs, Programmable Organoids mimic the response of a target organ to both positive and negative effects of drug candidates. Factors that can be non-destructively measured include cell state, viability, and function. Because they are synthetic, Programmable Organoids can host a large array of live-cell biosensors, built-in to one or more cell types, providing a rapid and realtime spatial readout of pathway-specific biomarkers including miRNAs, mRNAs, proteins, and other metabolites. Organoids programmed with both general and disease specific sensors then provide detailed information that can be used to identify candidates for further analysis. We envision a programmable common platform that can be shared among multiple drug candidates.

2:40 PM - 3:15 PM

De Novo Mutations in the Skin Microbiome Tami Lieberman Assistant Professor of Institute for Medical Engineering and Science, Assistant Professor of Civil and Environmental Engineering, MIT Civil and Environmental Engineering



Assistant Professor of Institute for Medical Engineering and Science, Assistant Professor of Civil and Environmental Engineering

MIT Civil and Environmental Engineering

Professor Lieberman studies microbial evolution in real time, including the evolution of antibiotic resistance and evolution during infection. Her lab is interested in understanding the molecular determinants of colonization success in complex environments and enabling the precise manipulations of microbiomes in the clinic and the environment.

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A new generation of rationally designed, durably colonizing, microbial therapeutics has yet untapped potential to sustainably treat disease and promote wellness. Fecal transplants are famously effective in treating people with recurrent *Clostridium dificile* infections. Recurrent urinary tract infections have been treated with asymptomatic bacteria that outcompete pathogens. Even for diseases that are not caused by bacteria, microbiome-based therapies may one day improve drug metabolism, supply vital nutrients, and modulate the immune system (including for cancer therapy). Probiotics for the skin may one day improve wound healing, protect skin from UV damage, or outcompete *Staphylococcus aureus* to manage atopic dermatitis. I will share a few stories from the lab that demonstrate the potential of the microbiome to treat disease and improve wellness, and the particular value in tracking the microbiome at the level of individual bacteria mutations for understanding *in vivo* mechanism.

3:15 PM - 3:45 PM Networking Break

3:45 PM 4:20 PM

Molecular Technologies for Genome Editing and Cell Control

Jonathan Gootenberg Fellow <u>MIT McGovern Institute</u>

Omar O. Abudayyeh Fellow MIT McGovern Institute

As we further understand the complexity and diversity of cellular states, it is becoming necessary for a cellular engineering toolbox, consisting of molecular tools that allow control over cell states and types. Drawing from a combination of natural discovery and rational engineering, we will discuss our lab's recent work in this area. We will cover RNA, DNA, and cell targeting approaches, including the novel CRISPR effector, Cas7-11, that can be used to target transcripts in mammalian cells for degradation, with reduced toxicity; a new genome insertion system, PASTE, that enables efficient, programmable insertion of large DNA segments into the genome without limitations of previous genome editing approaches; and a new approach for control of cell states, RADARS, that can sense and react to transcript levels in cells. These technologies form the basis or new approaches to manipulate and understand cellular states, with implications in basic biology, diagnostics, and therapeutics.

From Genomics to Therapeutics: Single-Cell Dissection and Manipulation of Disease Circuitry Manolis Kellis Member, Broad Institute of MIT and Harvard Professor, MIT Computer Science and Artificial Intelligence Lab



Manolis Kellis Member, Broad Institute of MIT and Harvard Professor MIT Computer Science and Artificial Intelligence Lab

Manolis Kellis is a professor of computer science at MIT, a member of the Broad Institute of MIT and Harvard, a principal investigator of the Computer Science and Artificial Intelligence Lab at MIT, and head of the MIT Computational Biology Group (compbio.mit.edu). His research includes disease circuitry, genetics, genomics, epigenomics, coding genes, noncoding RNAs, regulatory genomics, and comparative genomics, applied to Alzheimer's Disease, Obesity, Schizophrenia, Cardiac Disorders, Cancer, and Immune Disorders, and multiple other disorders. He has helped lead several large-scale genomics projects, including the Roadmap Epigenomics project, the ENCODE project, the Genotype Tissue-Expression (GTEx) project, and comparative genomics projects in mammals, flies, and yeasts. He received the US Presidential Early Career Award in Science and Engineering (PECASE) by US President Barack Obama, the Mendel Medal for Outstanding Achievements in Science, the NIH Director's Transformative Research Award, the Boston Patent Law Association award, the NSF CAREER award, the Alfred P. Sloan Fellowship, the Technology Review TR35 recognition, the AIT Niki Award, and the Sprowls award for the best Ph.D. thesis in computer science at MIT. He has authored over 280 journal publications cited more than 148,000 times. He has obtained more than 20 multi-year grants from the NIH, and his trainees hold faculty positions at Stanford, Harvard, CMU, McGill, Johns Hopkins, UCLA, and other top universities. He lived in Greece and France before moving to the US, and he studied and conducted research at MIT, the Xerox Palo Alto Research Center, and the Cold Spring Harbor Lab. For more info, see: compbio.mit.edu

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Disease-associated variants lie primarily in non-coding regions, increasing the urgency of understanding how gene-regulatory circuitry impacts human disease. To address this challenge, we generate comparative genomics, epigenomic, and transcriptional maps, spanning 823 human tissues, 1500 individuals, and 20 million single cells. We link variants to target genes, upstream regulators, cell types of action, and perturbed pathways, and predict causal genes and regions to provide unbiased views of disease mechanisms, sometimes re-shaping our understanding. We find that Alzheimer's variants act primarily through immune processes, rather than neuronal processes, and the strongest genetic association with obesity acts via energy storage/dissipation rather than appetite/exercise decisions. We combine single-cell profiles, tissue-level variation, and genetic variation across healthy and diseased individuals to map genetic effects into epigenomic, transcriptional, and function changes at single-cell resolution, to recognize cell-type-specific disease-associated somatic mutations indicative of mosaicism, and to recognize multi-tissue single-cell effects. We expand these methods to electronic health records to recognize multiphenotype effects of genetics, environment, and disease, combining clinical notes, lab tests, and diverse data modalities despite missing data. We integrate large cohorts to factorize phenotype-genotype correlations to reveal distinct biological contributors of complex diseases and traits, to partition disease complexity, and to stratify patients for pathwaymatched treatments. Lastly, we develop massively-parallel, programmable and modular technologies for manipulating these pathways by high-throughput reporter assays, genome editing, and gene targeting in human cells and mice, to propose new therapeutic hypotheses in Alzheimer's, ALS, obesity, cardiac disease, schizophrenia, aging, and cancer. These results provide a roadmap for translating genetic findings into mechanistic insights and ultimately new therapeutic avenues for complex disease and cancer.

4:55 PM - 5:30 PM

Machine Learning Enabled Label-Free Live-Cell Optical Identification Loza Tadesse Brit (1961) & Alex (1949) d'Arbeloff Career Development Professor in Mechanical Engineering, MIT Department of Mechanical Engineering



Loza Tadesse Brit (1961) & Alex (1949) d'Arbeloff Career Development Professor in Mechanical Engineering

MIT Department of Mechanical Engineering

Loza Tadesse is the Brit (1961) & Alex (1949) d'Arbeloff Career Development Assistant Professor in Mechanical Engineering at MIT and an associate member of the Ragon Institute of MGH, MIT and Harvard. She received her PhD in Bioengineering from Stanford University in 2021 and previously was a medical student at St. Paul Hospital Millennium Medical College in Ethiopia. She also did a postdoctoral training at the University of California, Berkeley. Tadesse's research program at MIT develops next generation point-of-care diagnostic devices using spectroscopy, optical, and machine learning tools for application for extreme environments such as developing nations, military sites, and space exploration. Tadesse has been listed as a 2022 Forbes 30 Under 30 in healthcare, received many awards including the Biomedical Engineering Society (BMES) Career Development Award, the Stanford DARE Fellowship and the Gates Foundation \$200K grant for SciFro Inc., an educational non-profit in Ethiopia, which she co-founded.

Label-free live-cell monitoring is ideal for research and clinical applications; however, it presents unique challenges. In this talk, I will discuss how Raman spectroscopy can enable such a platform using bacteria identification as a case study. Current infection diagnostic methods are slow and costly, due to the long bacterial culturing steps. We demonstrate that Raman spectroscopy enables rapid culture-free, sensitive, and specific bacterial identification and antibiotic susceptibility testing. To this end, I will present three major milestones that bring Raman closer to clinical application by using machine learning and nanophotonics. First, we achieve high (>99%) species level classification accuracies across 30 major disease-causing bacterial species. Second, we showcase the first of its kind demonstration of a versatile and antibiotic co-incubation free susceptibility testing. Third, we develop a simple liquid well setup for clinical sample handling with uniform Raman spectral enhancement using gold nanorods. I will conclude with remarks on enabling widespread clinical translation of Raman spectroscopy and its vast potential for label-free live-cell studies with implications for both diagnostics and therapeutics.

5:30 PM

Adjournment with Networking Reception