F3: *Silicon Technologies in the Fight Against Pandemics – From Point of Care to Computational Epidemiology*

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COVID-19 resulted in massive human casualties and an economic collapse across the globe. To prepare for the future, this Forum introduces the key challenges with detection and prevention of pandemics and highlights some potential opportunities for employing silicon technologies to quickly diagnose, treat, and prevent diseases. IC technologies that enable point-of-care diagnostics, continuous health monitoring, and lab-on-chip RNA detection continue to revolutionize healthcare. Further, high-performance computing (HPC) accelerates drug discovery, vaccine development, as well as real-time tracking of the spread of diseases and their socio-economic impacts. This Forum will address a wide spectrum of topics at the intersection of circuit/system design and bio-engineering.

Silicon for Pandemics: The Role of Point-of-Care Diagnostics in COVID-19 and the Future

Jennifer Lloyd, *Analog Devices, Santa Clara, CA*

The global coronavirus pandemic of 2019 created a major disruption to the world, in terms of both human casualties and economic impact, challenging the very core of sustainability. Globally, our fundamental way of life changed almost overnight, as lockdowns and other government interventions to contain the spread of the virus were implemented. At the same time, the medical system was stretched beyond its limits as countries and communities incorrectly assessed the rate at which the disease spread. What diagnostic technology was leveraged to assist in the identification, diagnosis and management of the COVID-19 disease? What recent advancements in point-of-care diagnostics were critical? What technology gaps did we discover? What will be the role of technology in combatting or even preventing future pandemics, and what direction will this take us in new applications of integrated circuit technology? What will that require? In this introductory talk, I will explore these questions to start the Forum.

Jen Lloyd received S.B., S.M., and Ph.D. degrees in EECS from the Massachusetts Institute of Technology. She started her career as an analog designer at Analog Devices in the High-Speed Converter group, and has contributed to various ADC, DAC and SerDes products for which she holds 9 US patents and several publications. She served on the technical program committee for both the IEEE Custom Integrated Circuits Conference and the IEEE Symposium on VLSI Circuits. She is currently a member of the ISSCC IMMD subcommittee. Jen has led several technology and market segment businesses at ADI, including Healthcare, Consumer, and Instrumentation. Dr. Lloyd is now Vice President for the Precision Technology and Platforms Group, in which she drives market-leading products and solutions across ADI's franchises in amplifiers, converters, and isolation.

Single-Molecular Bioelectronics

Kenneth Shepard, *Columbia University, New York, NY*

Experimental techniques that interface single biomolecules directly with microelectronic systems are increasingly being used in a wide range of powerful applications, from fundamental studies of biomolecules to ultra-sensitive assays. In talk, we review several technologies that can perform electronic measurements of single molecules in solution, including ion channels, nanopore sensors, carbon nanotubefield-effect transistors, electron tunneling gaps, and redox cycling. We discuss the shared features among these techniques that enable them to resolve individual molecules, and discuss their limitations. Recordings from each of these methods rely on similar electronic instrumentation, and we discuss the relevant circuit implementations and potential for scaling these single-molecule bioelectronics interfaces to high-throughput arrayed sensing platforms. The advantages that these systems are bringing and can bring to molecular diagnostic applications in the era of pandemic infectious diseases will be discussed.

Kenneth Shepard received the B.S.E. degree from Princeton University and the M.S. and Ph.D. degrees in electrical engineering from Stanford University. From 1992 to 1997, he was a Research Staff Member and Manager with the VLSI Design Department, IBM Thomas J. Watson Research Center, Yorktown Heights, NY, where he was responsible for the design methodology for IBM's G4S/390 microprocessors. He was the Chief Technology Officer of CadMOS Design Technology, San Jose, CA, which he co-founded, until its acquisition by Cadence Design Systems in 2001. Since 1997, he has been with Columbia University, New York, NY, where he is currently the Lau Family Professor of Electrical Engineering and Biomedical Engineering and the co-founder and the Chairman of the Board of Ferric (New York), which is commercializing technology for integrated voltage regulators, and Quicksilver Biosciences, which is commercializing single-molecule bioelectronics diagnostics. His current research interests include power electronics, biophysics, and CMOS bioelectronics

Analyze the Patient, Engineer the Therapy

Liesbet Lagae, *imec, Leuven, Belgium*

The exponential growth of the semiconductor industry has shown value for consumers by increasing performance while scaling down the cost. The result of that is the highest standard in precision and volume production of nanoelectronics based chip and sensor solutions. Over the past 10 years, imec has used their experience in semiconductor process and design technologies for building out a health-oriented activity that uses single-use silicon biochips and microfluidics for DNA sequencing, cell sorting, DNA synthesis, single-cell gene editing and biosensing. These chip solutions have until now mainly served the diagnostic market. But we need to go further. Similar technology building blocks can solve challenges in personalized healthcare by following trajectories of individual patients and by adapting the therapies. The latest generation of therapies uses not only individual information from the patient, but also patient material such as immune cells from the patient, which can be genetically modified to build powerful new types of personalized treatments. These innovative therapies come with very new challenges in relation to cost, logistics and quality, and todays infrastructure and healthcare systems are not adapted for this. We will explain how the same chip-based building blocks can help to overcome important challenges for these new set of immune therapies. These chips will help to give patient access to more personalized and adapted treatments and save lives.

Liesbet Lagae, Ms. E. E., Phd is IMEC fellow and is currently program director of IMEC Life Sciences. In this role, Liesbet is the scientific leader of a multidisciplinary team of >50 researchers working on miniaturization of biochips, microfluidics and integration of bio-assays. By leveraging those chip-based sensor solutions, she builds the tools for next-generation sequencing, cytometry, cell sorting, genomics, implantables and bioreactors. Liesbet Lagae (born 1975, Leuven, Belgium) received her PhD degree from KU Leuven, Belgium for her work on Magnetic Random Access Memories in 2003. She has pioneered life-science technologies based on silicon biochips at IMEC, Belgium. She created a successful growing business line for how smart silicon biochips could be tailored to the needs of our customers in the medical community. She was appointed as a KU Leuven part-time Professor in nanobiophysics as a consequence of these early career achievements. Liesbet has (co-) authored more than 300 publications. She holds 16 patents. She coordinated several EU and regional projects. She holds a prestigious ERC Consolidator Grant that deals with an innovative cell sorter-on-chip technology. She is or has been promotor of >20 PhD students.

CMOS Ion-Sensing Arrays Enabling Rapid Diagnostics and Surveillance for Infectious Diseases: Addressing COVID-19

Pantelis Georgiou, *Imperial College London, United Kingdom*

In this talk, I present how my lab is advancing rapid diagnostics for infectious diseases through the design of CMOS-based Lab-on-Chip systems using Ion-Sensitive Field Effect Transistor (ISFET) arrays. I will showcase Lacewing, our handheld molecular diagnostic system which is able to rapidly identify bacterial and viral infections, communicating results in real-time to the cloud for epidemiological surveillance. Results from our latest trials for detection of Malaria and bacterial-related drug-resistant infections will be discussed in addition to our most recent efforts in tackling the COVID-19 outbreak. We have achieved the detection of SARS-CoV-2 from clinical samples in under 20 minutes with high sensitivity and specificity. This constitutes the first handheld rapid molecular test for COVID-19 which can now be deployed for real-time testing and surveillance in the community.

Pantelis Georgiou currently holds the position of Reader (Associate Professor) at Imperial College London within the Department of Electrical and Electronic Engineering. He is the head of the Bio-inspired Metabolic Technology Laboratory in the Centre for Bio-Inspired Technology, a multi-disciplinary group that invents, develops and demonstrates advanced micro-devices to meet global challenges in biomedical science and healthcare. His research includes ultra-low-power micro-electronics, bio-inspired circuits and systems, lab-on-chip technology, and application of micro-electronic technology to create novel medical devices. Application areas of his research include new technologies for treatment of diabetes such as artificial pancreas, novel Lab-on-Chip technology for genomics and diagnostics targeted towards infectious disease and antimicrobial resistance (AMR), and wearable technologies for rehabilitation of chronic conditions. Dr. Georgiou graduated with a 1st-Class Honours MEng Degree in Electrical and Electronic Engineering in 2004 and Ph.D. degree in 2008 both from Imperial College London. He then joined the Institute of Biomedical Engineering as Research Associate until 2010, when he was appointed Head of the Bio-inspired Metabolic Technology Laboratory. In 2011, he joined the Department of Electrical and Electronic Engineering, where he currently holds an academic faculty position. He has made significant contributions to the development of integrated chemical-sensing systems in CMOS for Lab-on-Chip applications. He has pioneered the development of the Ion-Sensitive Field Effect Transistor, an integrated pH sensor which is currently being used in next-generation DNA sequencing machines and rapid-diagnostic systems for detection of infectious diseases. Dr. Georgiou is a Senior Member of the IEEE and IET, and serves on the BioCAS and Sensory Systems Technical Committees of the IEEE CAS Society. He is an Associate Editor of the IEEE Sensors and TBioCAS journals. He is also the CAS representative on the IEEE Sensors Council. In 2013, he was awarded the IET Mike Sergeant Achievement Medal for his outstanding contributions to engineering and development of the bio-inspired artificial pancreas. In 2017, he was also awarded the IEEE Sensors Council Technical Achievement Award. He is an IEEE Distinguished Lecturer in Circuits and Systems.

Analog Front-End Design Techniques for Robust Health Monitoring and Biosensing

Minkyu Je, *KAIST, Daejeon, Korea*

Analog front-end circuits play a critical role in health monitoring and biosensing systems by directly interfacing with various types of electrodes and sensors. Although providing the basic functionality of reading out the analog signals from the electrodes and sensors is simple and straightforward, realizing robust readout interfaces is extremely challenging due to the presence of diverse disturbing factors such as powerline interferences, motion artifacts, stimulation artifacts, and sensor variations, depending on the application and usage scenario. In this talk, advanced analog front-end design techniques developed to address such challenges are introduced and discussed.

Minkyu Je received the M.S. and Ph.D. degrees, both in Electrical Engineering and Computer Science, from Korea Advanced Institute of Science and Technology (KAIST), Daejeon, Korea, in 1998 and 2003, respectively. In 2003, he joined Samsung Electronics, Giheung, Korea, as a Senior Engineer and worked on multi-mode multi-band RF transceiver SoCs for GSM/GPRS/EDGE/WCDMA standards. From 2006 to 2013, he was with Institute of Microelectronics (IME), Agency for Science, Technology and Research (A*STAR), Singapore. He worked as a Senior Research Engineer from 2006 to 2007, a Member of Technical Staff from 2008 to 2011, a Senior Scientist in 2012, and a Deputy Director in 2013. From 2011 to 2013, he led the Integrated Circuits and Systems Laboratory at IME as a Department Head. In IME, he led various projects developing low-power 3D accelerometer ASICs for high-end medical motion-sensing applications, readout ASICs for nanowire biosensor arrays detecting DNA/RNA and protein biomarkers for point-of-care diagnostics, ultra-low-power sensor node SoCs for continuous real-time wireless health monitoring, and wireless implantable sensor ASICs for medical devices, as well as low-power radio SoCs and MEMS interface/control SoCs for consumer electronics and industrial applications. He was also a Program Director of NeuroDevices Program under A*STAR Science and Engineering Research Council (SERC) from 2011 to 2013, and an Adjunct Assistant Professor in the Department of Electrical and Computer Engineering at National University of Singapore (NUS) from 2010 to 2013. He was an Associate Professor in the Department of Information and Communication Engineering at Daegu Gyenogbuk Institute of Science and Technology (DGIST), Korea from 2014 to 2015. Since 2016, he has been an Associate Professor in the School of Electrical Engineering at Korea Advanced Institute of Science and Technology (KAIST), Korea. His main research areas are advanced IC platform development including smart sensor interface ICs and ultra-low-power wireless communication ICs, as well as microsystem integration leveraging the advanced IC platform for emerging applications such as intelligent miniature biomedical devices, ubiquitous wireless sensor nodes, and future mobile devices. He is an author of 5 book chapters and has more than 300 peer-reviewed international conference and journal publications in the areas of sensor interface IC, wireless IC, biomedical microsystem, 3D IC, device modeling and nanoelectronics. He also has more than 50 patents issued or filed. He has served on the Technical Program Committee and Organizing Committee for various international conferences, symposiums and workshops including IEEE International Solid-State Circuits Conference (ISSCC), IEEE Asian Solid-State Circuits Conference (A-SSCC) and IEEE Symposium on VLSI Circuits (SOVC). He is currently working as a Distinguished Lecturer of the IEEE Circuits and Systems Society.

Cardiovascular Disease Detection, Analysis, and Evaluation System-On-Chip and Platform

Shuenn-Yuh Lee, *National Cheng Kung University, Tainan, Taiwan*

There are several medical devices that are made to monitor the heart to avert heart disease. Moreover, body sensor network (BSNs) based applications or wearable devices have become more acceptable to people for monitoring their real-time health information, such as in electrocardiogram (ECG) and phonocardiogram (PCG). In order to enable early detection and diagnosis, a low-power wireless system on a chip (SoC) stuck on the body or as a wearable/portable device for heart disease diagnosis is required. In this Forum talk, a bio-signal acquisition SoC and platform with low power consumption, wireless transmission, on-time monitoring and diagnosis with artificial intelligence (AI), will be presented. Moreover, it is efficient to electrically generate neural action potential to control dysfunctional organs. Therefore, integrated circuits for telemetry will be required because they can transmit or receive data to or from according to an implantable body sensor network. In this forum, a closed-loop implantable micro-stimulator system on chip (IMSoC), which possesses the capabilities of sensing a physiological signal, disease identification, micro-stimulation, and wireless data/command transmission, will be also presented.

Shuenn-Yuh Lee received the B.S. degree from the National Taiwan Ocean University, Keelung, Taiwan, in 1988, and the M.S. and Ph.D. degrees from the National Cheng Kung University, Tainan, Taiwan, in 1994 and 1999, respectively. He is currently a Professor at the Department of Electrical Engineering, National Cheng Kung University, Tainan, Taiwan. From 2013 to 2016, he served as the Chairman of the IEEE Solid-State Circuits Society Tainan Chapter. From 2016 to 2017, he served as the Vice Chairman of the IEEE Tainan Section. He is an Associate Editor for the IEEE Transactions on Biomedical Circuits and Systems (2016-2021). His present research activities involve the design of analog and mixed-signal integrated circuits, biomedical circuits and systems, low-power and low-voltage analog circuits, and RF front-end integrated circuits for wireless communications.

AI/ML-Aided Diagnosis of Biomarkers

Bruno Michel, *IBM Research, Zurich, Switzerland*

Wearables and home sensors that continuously acquire medically relevant vital parameters facilitate treatment optimizations and shorten hospitalizations, thus improving quality of life of patients. We demonstrate an architecture that combines wearables, nearables, edge, and cloud computing to provide optimal user interaction and analytics on multi-stream time-based IoT data. A home-based lung disease management system that objectively tracks the disease progress during the daily life of patients was developed. Other systems were created for stress monitoring in firemen and to support elderly to live longer independently at home. A large effort was devoted to combine components into a functioning system that identifies anomalies by deep learning. We reduce system-level complexity and ease the process of extracting insights out of time-based sensor data. The COVID-19 pandemic has shown the need for more telehealth solutions to quickly detect onset of worsening in people with a positive test, but also to monitor the recovery of people sent home from hospital.

Bruno Michel received a Ph.D. degree in biochemistry and computer engineering from the University of Zurich and joined IBM Research to work on scanning probe microscopy and soft lithography. Later, he improved thermal interfaces and miniaturized convective cooling and demonstrated improved efficiency and energy re-use in sustainable datacenters, and photovoltaic thermal solar concentrators. He developed microfluidics, 3D packaging with interlayer cooling and electrochemical chip power supply to trigger a density roadmap to replace Moore’s law. Most recently he has focussed on integration of IoT and wearable devices with efforts spanning from sensing principles over edge computing to multi- sensor data fusion and cognitive computing. Areas of particular interest are sustainable edge intelligence and Green AI. He is an IEEE Fellow as well as a member of the US National Academy of Engineering and the IBM Academy of Technology.

Towards Scalable Real-Time Computational Epidemiology to Support COVID-19 Response

Madhav Marathe, *University of Virginia, Charlottesville, Viginia, VA*

The COVID-19 pandemic represents an unprecedented global crisis. Its global economic, social and health impact is already staggering and will continue to grow. Increased urbanization, global travel, climate change and a generally older and immuno-compromised populations continue to make the problem of pandemic planning and control challenging. Computation, and more broadly, computational thinking, plays a multi-faceted role in supporting global real-time epidemic science, especially because controlled experiments are impossible in epidemiology. High-performance computing, data science, and new sources of massive amounts of data from device-mediated interactions have created unprecedented opportunities to prevent, detect, and respond to pandemics. In this talk, using COVID-19 as an exemplar, I will describe how scalable computing, AI, and data science can play an important role in advancing real-time epidemic science.

Madhav Marathe a Distinguished Professor in Biocomplexity, the division director of the Networks, Simulation Science and Advanced Computing Division at the Biocomplexity Institute and Initiative, and a Professor in the Department of Computer Science at the University of Virginia. His research interests are in network science, computational epidemiology, AI, foundations of computing, socially coupled system science and high-performance computing. Before joining UVA, he held positions at Virginia Tech and Los Alamos National Laboratory. He is a Fellow of the IEEE, ACM, SIAM, and AAAS.

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