SENSOR CDT

SENSORS DAY 2021

OCTOBER 13

SENSORS, HEALTHCARE, GLOBAL HEALTH

UKRI Engineering and Physical Sciences Research Council

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Klaus Schönenberger - *Director of EssentialTech*

Science and technology for development, humanitarian action and peace promotion.

Abstract: Technologies designed and deployed in high-income countries are often unable to deliver their full potential when transposed to Low and Middle-Income Countries (LMICs). The health sector is a key example where donated or purchased medical devices such as oxygen concentrators, neonatal incubators, anesthesia machines or diagnostic X-ray systems are generally short-lived in those contexts. The case of diagnostic X-ray imaging is particularly striking: 126 years after its invention, up to two thirds of the world population still does not have access to radiology services, according to the World Health Organization. Yet X-ray radiology is a crucial instrument for diagnosing health issues ranging from trauma to tuberculosis. The mismatch between needs and available solutions originates from the inappropriateness of both the technology and the business models.

This presentation will explore how science and technology that accounts for the context can be mobilized to address the unmet need for "essential" technologies and thereby support development. Our approach relies on three crucial pillars: cooperation, interdisciplinarity and entrepreneurship with a long-term sustainability perspective. The case of x-ray imaging is presented through a practical real-world example, wherein an innovation designed for the context has led to the creation of a spin-off company. We also note that these unmet needs are a result of poverty, but also, in many LMICs, due to humanitarian disasters and conflicts. The presentation will provide additional reflections on how science and technology can support humanitarian action and promote peace.

Biography: Klaus Schönenberger obtained an MSc in Microengineering (1993), followed by a PhD (1996) from the Swiss Federal Institute of Technology in Lausanne (EPFL). After a post-doctoral fellowship at Lawrence Livermore National Laboratory in California, he spent more than 11 years in the medical devices industry in leading positions, including as Vice-President of Worldwide R&D in a $100m company and Global Vice-Resident of Research and Technology in a $1bn company.

Motivated by concern about the huge imbalance in access to medical technology in industrialized versus low and middle-income countries, he left the industry in 2009 and co-founded the EssentialMed Foundation, an innovative non-profit venture. In 2011, after realizing that both technology and business models needed a profound rethinking for true impact, he joined EPFL, where he launched EssentialTech. Initially, this was a university-wide program aiming to develop innovative technologies and business models to support sustainable development in low and middle-income countries.

Several major Humanitarian actors such as the ICRC and MSF took notice of the unique approach proposed, which led to collaborations starting in 2015-16. In May 2017, Klaus directed and launched a MOOC (Massive Open Online Course) entitled "Technology Innovation for Sustainable Development" to help spread the methodology worldwide. In 2018, Pristem SA, the first spin-off company created thanks to this new approach, was launched. This award-winning

company will deploy an innovative digital x-ray imaging system, specifically designed for low-income contexts. In December 2018, the EPFL presidency announced the creation of the EssentialTech Centre, where Klaus is now the Director. The Centre's mission is to harness science and technology to drive sustainable development, support humanitarian action and foster peace. In 2020, HMCare, EssentialTech's second spin-off company was created to bring a transparent surgical mask to market.

Solomzi Makohliso - *Deputy Director of EssentialTech*

Exploring Advanced Local Manufacturing Prospects in Africa

Abstract: The recent Covid-19 has exposed how fragile the international supply chains can potentially become and has highlighted the importance of local manufacturing for certain key supplies, especially medical supplies. Already prior to that, the World Health Organisation has been highly vocal on the need to establish local manufacture of appropriate, affordable, quality medicines and medical devices in low-resource settings. Lack of local advanced manufacturing opportunities is also a major hindrance towards the full realisation of many technological innovations emanating from these regions. In this talk, we will explore the challenges these regions face towards realising local production of essential medical products, such as vaccines, pharmaceuticals and medical devices, with a particular focus on sub-Saharan Africa. We will also discuss some promising initiatives and prospects towards the realisation of this goal.

Biography: Dr. Soli Makohliso is an international entrepreneur with over 20 years of experience in the US, Switzerland and southern Africa, some of which involved the development of biosensors for in vtiro diagnostics. His current professional interests are in innovation and entrepreneurship for sustainable impact, with a particular interest in health. He currently serves the Deputy Head of the EssentialTech Centre at the Swiss Federal Institute of Technology (EPFL), where he is actively involved in harnessing cutting-edge research to develop technology innovations that can leapfrog the development and drive sustainable impact, support humanitarian action and foster peace in low- and middle-income countries. He recently served as a member of the Ministerial Task Team in Technology Innovation aspects for the South African government. Previously, he has held various advisory positions in the past in biotechnology innovation, and for the implementation of the South African Nanotechnology Strategy. He also served as the advisor to the Swiss government for the bilateral strategy with South Africa in science, technology & innovation. Soli received his B.Sc. and M.Sc. in Biomedical Engineering at Brown University in the US and his Ph.D. at the Swiss Federal Institute of Technology in Lausanne (EPFL).

Krathika Parchani - *Partnerships Manager at Simprints*

Biometrics for global health and development

Abstract: Numerous governments, businesses, and NGOs have committed to the sustainable Development Goals (SDGs) “zero” targets, such as ending preventable deaths of newborns, and ending epidemics of a number of diseases. However, these targets are impossible to achieve if we have no idea who we have reached – and who we have missed. Compounded by poor infrastructure and weak national ID schemes, the inability to identify people costs lives, wastes resources, and prevents millions from escaping poverty. A growing body of evidence demonstrates that biometrics has huge potential to bridge this gap, building solid ID systems in short periods of time, improving distribution of medical interventions, reducing fraud, and simplifying monitoring and reporting processes. However, existing solutions often fall short of meeting the needs of the last mile - Simprints was built to address this gap and provides digital ID solutions that are fit-for-purpose for these settings.

Biography: Krathika works as a partnerships manager at Simprints, where she is responsible for private sector partnerships and grant and innovation funding. Previously, as Analyst to the CEO at Simprints, Krathika helped establish Simprints' Board of Directors, and managed annual strategy reviews. She holds a BA (Hons.) in Economics from Ashoka University, Delhi.

Themis Prodromakis – *Director of the Centre for Electronics Frontiers*

Practical Applications of Memristive Technologies in Sensory Systems

Abstract: A novel nano-electronic technology, known as the memristor, proclaims to hold the key to a new era in electronics, being both smaller and simpler in form than transistors, low-energy, and with the ability to retain data by 'remembering' the amount of charge that has passed through them – akin to the behaviour of synaptic connections in the human brain. In his lecture Themis Prodromakis will present the attributes of memristive technologies that make them attractive for a variety of emerging applications with a focus on Sensory Systems.

Biography: Themis is Professor of Nanotechnology and Director of the Centre for Electronics Frontiers at the University of Southampton, UK. His work focuses on developing metal-oxide Resistive Random-Access Memory (memristor) technologies and related applications. He holds an RAEng Chair in Emerging Technologies and is an Adjunct Professor at UTS Australia. In 2015, he established ArC Instruments Ltd that delivers high-performance testing infrastructure for automating characterisation of novel nanodevices. His contributions in the field have brought this emerging technology one step closer to the electronics industry for which he was recognised as a Blavatnik Award UK Honoree in Physical Sciences and Engineering.

Lara Allen - *CEO of Centre for Global Equality*

The Challenges and Opportunities of Inclusive Innovation – some insights from the Sensor CDT community

Abstract: Can advanced science really make a positive difference to the lives of poor people living in countries with developing and emerging economies? Can cutting edge technology really be made available to that half of the world's population that lives on less than $4 a day? A group of researchers, innovators and practitioners based at the Centre for Global Equality hold that the answer to these questions has to be yes and have evolved an approach to make this possible: inclusive innovation. Inclusive in both purpose and method, the research and innovation undertaken mobilises advanced science and technology to enhance the wellbeing and economic development of the world's rising billions, without harming the environment or the interests of future generations. Core to the approach is the co-creation of potential solutions with the people they are intended to benefit.

Genuine collaboration and effective co-creation are, however, more easily aspired to than achieved. Capabilities need to be built and ecosystems strengthened before equitable dialogues can take place. Received notions of expertise and knowledge need to be examined. Partnerships between people from academia, civil society, government, and business need ongoing attention to ensure they remain mutually beneficial and productive.

Drawing on initiatives ongoing in the Sensors CDT community, this presentation explores some of the challenges faced, and opportunities made possible, when taking an inclusive approach to contributing to sustainable development through research and innovation.

Biography: In her role as CEO, Lara has led the evolution of the Centre for Global Equality's approach to Inclusive Innovation. This approach entails facilitating productive collaborations between academic researchers and key actors in civil society, government and business to ensure that innovations stemming from research are appropriate for the intended end-users and their contexts, and are diffused and scaled effectively. Lara also leads the Inclusive Innovation Programme at the Department of Chemical Engineering and Biotechnology, University of Cambridge. She has twelve years of experience as an international development practitioner working as an employee, consultant and volunteer with grassroots Community Based Organisations and national and international NGOs in South Africa, Kenya, Ireland and the UK. Prior to this she was an academic with nine years of post-PhD experience at the University of Cambridge and the University of the Witwatersrand in South Africa.

Jenny Molloy - *Founder and Director-Open Bioeconomy Lab*

Open-source technologies for molecular diagnostics in the global South

Abstract: Access to diagnostics and biosensing technologies has long been a challenge in low- and middle-income countries. The COVID-19 pandemic has highlighted challenges in designing useful technologies for molecular diagnostics in resource limited settings and also the importance of expanding manufacturing capabilities for reagents, sensors and devices. This talk will draw on examples from the explosion of innovation in molecular diagnostics in the last two years to explore effective engineering approaches to sensor technologies for molecular diagnostics in the global South, mechanisms to increase and accelerate access through open source sharing and ways to engage with policy, regulation and global partners to increase opportunities for technologies to generate positive impacts within health systems.

Biography: Jenny is the Founder and Director of the Open Bioeconomy Lab. She is also a Shuttleworth Foundation Research Fellow in the Department of Chemical Engineering and Biotechnology at the University of Cambridge, studying the role and impact of open approaches to Intellectual Property for a Sustainable and Equitable Bioeconomy. Her work focuses on better understanding problems facing researchers accessing biological research tools in low-resource contexts, particularly Latin America and Africa. Jenny has been analyzing existing innovative solutions and the potential for local, distributed manufacturing of enzymes to improve access and build capacity for biological research. The broader aim of her research is to contextualize “open source” approaches to biotechnology within current narratives of innovation and the bioeconomy policy agenda.

Student Talks: Francesca W. van Tartwijk

The influence of FUS protein variants on axonal architecture and local protein synthesis

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FUS is a phase-separating RNA-binding protein, which forms ribonucleoprotein granules to regulate gene expression. Though FUS is predominantly nuclear, it also localises to the cytoplasm, where its functions are less well-studied. In neurons, its presence in neurites may allow regulation of local protein synthesis (LPS) [1], which is known to affect axonal development and structure [2].

Certain mutations of FUS mutants are associated with amyotrophic lateral sclerosis (ALS) and frontotemporal dementia. These mutations can make FUS mislocalise to the cytoplasm or enhance its self-association, altering its phase state. However, it remains unclear how these variants cause neurodegeneration. As neurons with long axons are affected in ALS, we hypothesised that LPS and hence axonal structure may be perturbed [1].

Here, we investigated the effects of four protein constructs on axonal development, using developing Xenopus laevis retinal ganglion cell axons: GFP, FUS(wild-type)-GFP, FUS(P525L)-GFP, and FUS(16R)-GFP. FUS(P525L) is a patient-derived variant that mislocalises to the cytoplasm, FUS(16R) is an artificial aggregation-prone mutant. Using a range of imaging techniques, we quantified the variants' effects on axonal morphology, RNA transport, cytoskeletal stiffness, and LPS. We found that FUS(P525L) reduces axonal arbour complexity and growth cone stiffness, indicating it affects the function of the actin cytoskeleton.

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Student Talks: Ben J Woodington

The Dark Side of the Spine: Using Bioelectronics to Interface with the Spinal Cord

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Implantable bioelectronic devices for diagnosing and treating disease are emerging as a prominent component of modern healthcare. However, there remains several technical and clinical barriers within the development of new tools to interface with the central nervous system (CNS). Overcoming these barriers could improve the lives of people suffering from conditions such as Parkinson's, chronic pain, and paralysis as well enabling better neuroscientific research and prognostics.

We present thin, flexible, and shape adaptive implants which can be used to interface with the CNS. The devices are fabricated from biocompatible materials and can be used to stimulate and sense the tracks of the spinal cord. The technology is fabricated using scalable manufacturing techniques in order to create a conformable interface which is up to 100 times thinner than commercially available spinal cord devices, allowing larger coverage than previously possible, whilst minimising risk during implantation.

After showing our technology can be used as a minimally invasive interface for classical spinal cord stimulation in the treatment of drug refractory pain [1], we are now moving forward to take this interface further and elucidate the dark side of the spinal cord.

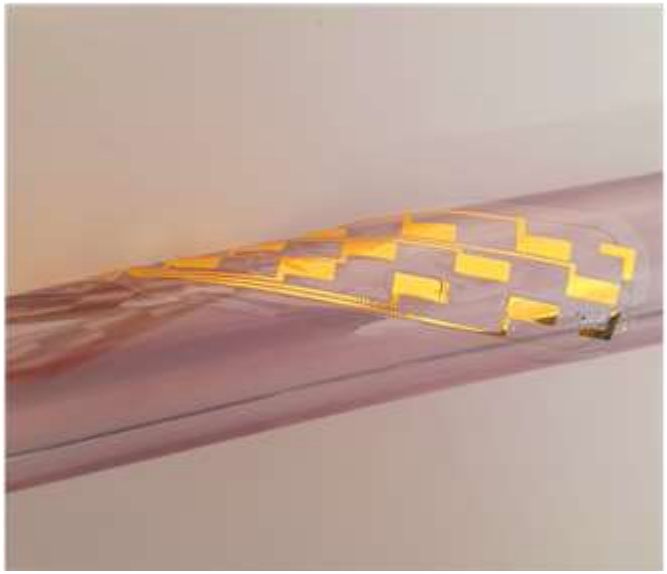

Figure 1. The minimally invasive spinal cord stimulator (MI-SCS) wrapped around a spinal analogue

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Student Talks: Sarah L Barron

Developing bioelectronics for monitoring cell cultures at the air liquid interface

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The respiratory epithelium is one of the first lines of physical and immunological defence in the body. However, a dysfunctional respiratory barrier may lead to chronic lung diseases and infection, which are among the leading causes of death worldwide.1 Thus, having in vitro models which accurately reflect the complexity found in vivo, is fundamental to enhancing therapeutic delivery and treatment of these conditions. Although over the past decades, advances have been made in developing biomimetic and 3D cell cultures, there remains a limited capacity in sensor technologies which can continuously and non-invasively monitor these systems.2 Additionally, air-interfaced (ALI) cultures, pose further challenges such as the necessity of measuring in the air, rather than submerging the system in an electrolyte for electrode operation. To address this issue, the work presented highlights the fabrication and characterisation of novel, conformable microelectronic devices, as well as conducting polymer scaffolds. Furthermore, these bioelectronic sensing systems have been interfaced with 2D and 3D lung cultures, for the continuous and non-invasive measurement of cell growth and barrier disruption.

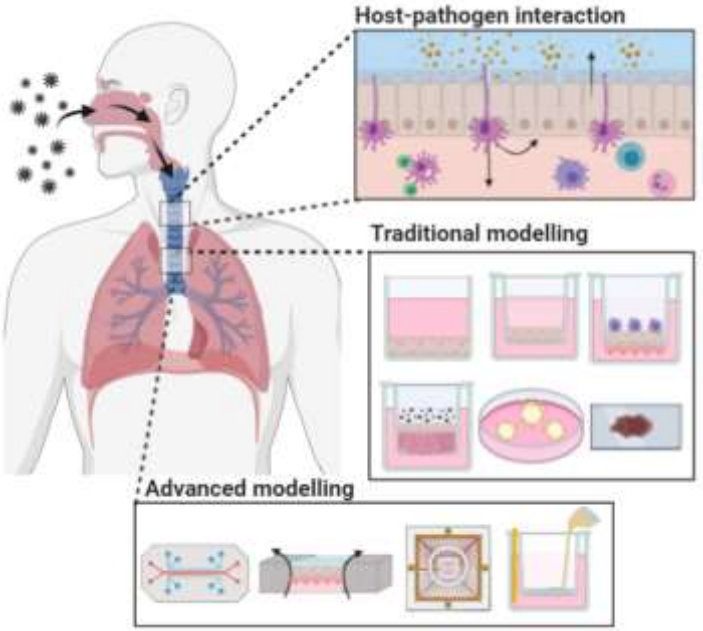

Figure 1: Advanced modelling and monitoring of in vitro lung cultures at the Air Liquid Interface using soft microelectronics.

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Student Talks: Johanna Kölbel

In-situ Observation of the Structure of Crystallising Magnesium Sulfate Solutions

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Magnesium sulfate hydrates have recently received a lot of attention. When choosing appropriate concentrations, crystallisation at room temperature is easily achieved within minutes, making it an ideal candidate for experimental studies of crystallisation processes.

Terahertz time-domain spectroscopy (THz-TDS) is a very useful tool to distinguish between polymorphs and to study crystallisation processes [1]. By utilising a custom-built cell, terahertz spectra are acquired during the crystallisation while the progress is monitored with an attached optical imaging probe. The temperature is precisely controlled with a circulating water bath. The current setup can be applied to investigate a system between 4 and 90 ℃ without modification, while circulating another liquid cooled with dry ice will further expand the temperature range.

First experiments investigated the crystallisation of MgSO4•7H2O between 6 and 20℃, and the results were reproducible. The terahertz spectrum of crystalline MgSO4•7H2O as received from Sigma Aldrich shows a pronounced feature at 1.6 THz. The onset of crystal growth in the crystallisation cell is clearly observed when the peak at 1.6 THz starts to emerge (Figure 1). Careful spectral investigation allows to extract information about the amorphous phase before and during the crystallization as well. A stagnant system was studied in the first experiments, and the use of an additional syringe pump will facilitate solution flow through the cell during measurements.

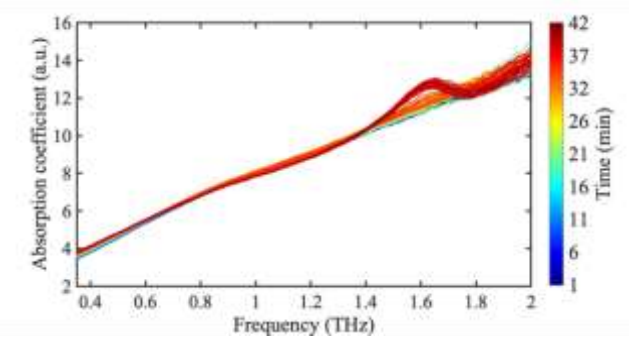

Figure 1: Absorption during crystallisation. With increasing time, the baseline drops and a peak appears at 1.6 THz.

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Student Talks: Chiara Barberio

3D Conducting polymer/ECM scaffolds for the maintenance and differentiation of human neuronal cells in vitro

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Compared to two-dimensional (2D) cell culture, which are overall too simplistic and lacking most of the cell-cell and cell-environment interaction occurring in the *in vivo* milieu, three-dimensional (3D) cell culture modelling can resemble the tissue microenvironment in a more biomimetic manner[1]. Scaffold-based systems integrating natural and/or synthetic materials are extensively employed in tissue engineering to develop tissue-specific architecture for better supporting cell survival and outgrowth[2]. Using a freeze-drying technique, we engineered porous 3D composite scaffolds consisting of poly (3,4-ethylene-dioxythiophene) doped with polystyrene sulfonate (PEDOT:PSS), containing ECM-derived proteins (i.e., Collagen, Hyaluronic Acid and Laminin) for hosting neural 3D cell culture. The highly porous microstructure of these scaffolds was characterised optically by scanning electron microscopy (SEM) along with confocal microscopy, and their conducting properties via electrochemical impedance spectroscopy (EIS). The resulting scaffolds exhibited remarkable mechanical stability and water uptake capacity, directly proportional to the increasing collagen/HA content. Furthermore, we observed that the presence of ECM proteins within the 3D backbone seems to support cell viability and propensity to differentiate into mature neurons, which generated 3D neural networks *in situ*. In conclusion, these cell-laden hybrid scaffolds could be customised for a variety of more complex yet highly mimetic tissue engineering applications.

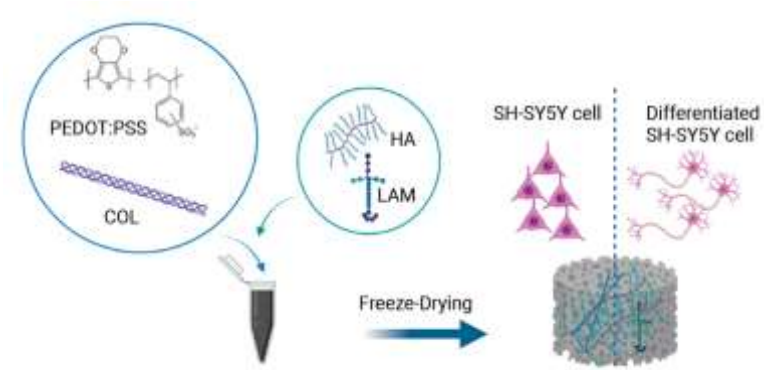

Figure 1: Schematic diagram showing the components and fabrication steps of the 3D PEDOT:PSS/ECM composite scaffolds engineered in this study

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Student Talks: Elena Schäfer

Bioremediation: Developing robust systems to identify and evolve novel PET degrading enzymes

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Polyethylene terephthalate (PET) is ranking fourth on the world plastic consumption list.[1] However, due to the lack of appropriate technologies in place to date only 30 % of the material is recycled, which leads to an accumulation of PET in landfills[2].

A promising way of sustainably combating the PET crisis lies in bio-catalysis. Enzymatic degradation of PET was first described in 2005[3] and is both greener than current recycling methods and results in higher quality products. Multiple efforts have been made to increase the efficiency of yet inefficient PET degrading enzymes yielding moderate success only.[4,5,6]

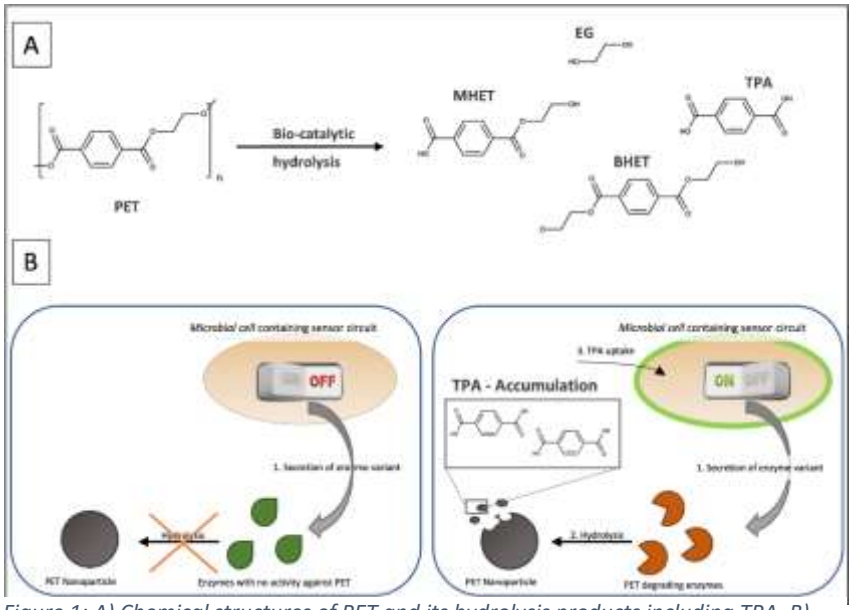

Figure 1: A) Chemical structures of PET and its hydrolysis products including TPA. B) Whole cell biosensor setup for terephthalate sensing. Left: the microbial biosensor secretes enzymes with no PET degrading activity. The PET particle stays intact. Right: The microbial biosensor secretes enzymes with activity against PET, leading to its degradation and the accumulation of TPA. TPA is sensed by the microbial cell and triggers the expression of a green fluorescent reporter molecule

One of the main obstacles in successfully identifying or evolving PET hydrolases originates from the lack of appropriate assays. Thus, this work focuses on the development of a robust synthetic genetic circuit that links the degradation of PET to enzyme activity by sensing the accumulation of the degradation product terephthalic acid (TPA). The assay is compatible with an ultra-high throughput screening platform and is to be used for the subsequent evolution and identification of novel PET biocatalysts from an environmental sample using microfluidics.

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Student Talks: Charlie Wedd

Mapping Gene Expression to Host Fitness in Single Bacterial Cells

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Microorganisms can be engineered to perform useful functions for applications in production, healthcare, agriculture, environmental remediation, and sensing. The workhorse of these applications is the synthetic gene circuit: a gene or group of genes engineered to perform a desired function when expressed by the host cell (figure 1a). However, the utility of synthetic gene circuits is almost universally impaired by the parasitic interaction between synthetic circuits and their host cells. Microorganisms possess a limited pool of cellular resources for their growth and maintenance, and a synthetic circuit will compete with the host for these resources, placing a burden on the host cell (figure 1b,1c). This burden reduces the fitness of the host cell. A consequence of reduced host cell fitness is that the functional strain will quickly be outcompeted by any non-functional mutants which arise. In this work, we aim to precisely quantify the fitness cost to Escherichia coli cells from both dynamic and steady state gene expression. Preliminary results from single cell time-lapse microscopy images indicate reduced growth rates while gene expression is activated. Understanding the fitness costs of gene expression will allow for the design of synthetic circuits with improved evolutionary stability and functional performance.

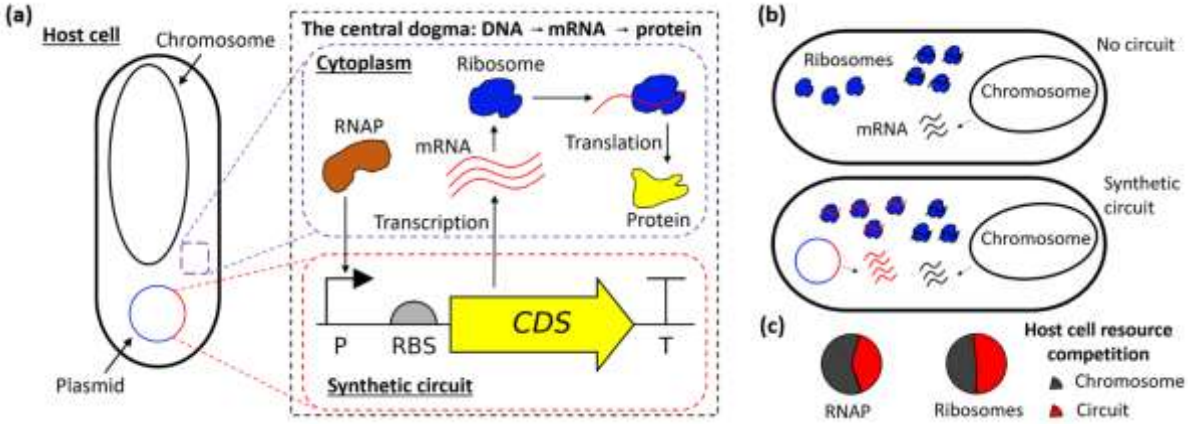

Figure 1: (a) A synthetic gene circuit in the context of its host cell. Transcription and translation of the synthetic gene leads to expression of the functional protein. (b) The synthetic circuit competes for host cell resources, placing a burden on the host. (c) A synthetic circuit can use a large fraction of host resources, incurring a significant fitness cost to the host. RNAP = RNA polymerase, mRNA = messenger RNA, P = promoter, RBS = ribosome binding site, CDS = coding sequence, T = terminator.

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Team Challenge 2021: Open Ventilator System Initiative (OVSI)

Presented by: Anne-Pia Marty, Ned Wills, Sarah Sibug-Torres, Nuzli Karam, Liam Self, Matthew Ellis.

The Oxygen and Ventilator System Initiative (OVSI) is a project started in 2020 by a collaboration made of the Centre for Global Equality, the University of Cambridge, Cambridge Precision Ltd., the University of Nairobi, the Bahir Dar Institute of Technology (BiT, Ethiopia) and many others. This project was designed to be a context-appropriate answer to shortages in ventilator and oxygen supply in low- and middle-income countries (LMICs) due to the COVID-19 pandemic. Over the summer 2021, the 10 students from Sensor CDT 2020 cohort worked on this system to bring this project closer to market. The team worked to make it more compliant to medical standard, publish it under an open source licence, and conducted a comprehensive market analysis to plan how OVSI could meet its target users. This talk presents the results of three months of work: we will discuss the need for ventilation in LMICs, the technical development we brought to the system, our recommendations for the way forward of this project, and we will end the talk with the public release of OVSI as an open source project.

EPSRC Centre for Doctoral Training in Sensor Technologies for a Healthy and Sustainable Future

The EPSRC Centre for Doctoral Training in Sensor Technologies for a Healthy and Sustainable Future (Sensor CDT) delivers an interdisciplinary and research focussed training programme to students who have the aspiration as well as the academic and technical skills to become world leaders in the field of sensors.

Students are taught and supervised by academics and researchers from around 20 departments across the University of Cambridge. This allows them to sample a broad variety of research environments and gain hands-on experience in the use and capabilities of state-of-the-art research instruments and techniques.

The first year of the Sensor CDT programme is an MRes course, consisting of a balanced mix of taught and research components. Lectures introduce our students to the science that underpins sensor design and applications. Research projects and a team challenge provide key skills to carry out cutting edge sensor research in experimental design, project management, data handling, dissemination of research outcomes and teamwork.

This is followed by three years of PhD research during which the students continue to learn from leading experts and each other during our monthly Sensors Café workshops and seminars.

Thank you to our official sponsors and partners

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