



ESAB Webinar

Synthetic Biology and Metabolic Engineering Tools and Methodologies

Friday, 25th June 2021 at 10:00 – 12:00 CET

Welcome Address: Willi Meier, DECHEMA

Chairs: Frangiskos Kolisis, School of Chemical Engineering, National Technical University of Athens

Roland Wohlgemuth, Lodz University of Technology, Chair ESAB

PROGRAMME

**10.00 Prof. Dr. Gregory Stephanopoulos, Department of Chemical Engineering, MIT
Cambridge, MA 02139, USA**

Engineering Microbes for Fun and Profit

Biotechnology is rapidly coming of age as enabling technology for the production of biofuels and biobased chemicals. In this task, it is aided by critical advances in Metabolic Engineering that engineers microbes into little chemical factories capable of converting renewable feedstocks to a variety of products. While in earlier years this application was limited to specialized chemicals and pharmaceutical products, recent advances in metabolic engineering and synthetic biology have expanded the portfolio of biotechnological applications beyond specialty products and into the domain of commodity chemicals. As the latter have been traditionally the realm of the chemical process industry using fossil fuels as feedstocks, we are witnessing a process of creative destruction whereby one manufacturing technology based on chemistry is gradually being replaced by another based on biology. Process and product sustainability is a major driver of this development.

Engineering microbes, however, for real industrial applications requires more than just the assembly of the genes comprising a biosynthetic pathway. The capacity of the pathway must be assessed vis-a-vis alternative routes, along with its thermodynamics and kinetic bottlenecks, and its performance in bioreactor environments evaluated. In this context, alternative feedstocks should be evaluated to identify the one that can be fully utilized for the production of the target product with minimal byproduct formation. These concepts and tools constitute the essence of metabolic engineering as will be illustrated in this talk with an example from the engineering of oleaginous yeast for lipid (biodiesel) and alkane production. In another example, the synthesis of isoprenoid products used as flavors, fragrances, vitamins and pharmaceuticals will be presented. I will then expand on the parameters that will define the winners and losers of the antagonism between chemistry and biotechnology ultimately leading to efficient processes for the sustainable manufacturing of fuels and chemical products.

10.30 Prof. Dr. Victor de Lorenzo, Environmental Synthetic Biology Laboratory, National Center for Biotechnology, Spanish National Research Council, Madrid

What is a Synthetic Biology chassis and what it takes to become one

The notion of biological chassis is now central to the challenge of developing useful and safe forward-engineered bacteria for industrial or environmental biocatalysis. The optimal one would in most cases involve a genome encoding a limited number of basic biological functions for self-maintenance and growth, but deleted of many other structures and signal processing components which, under natural circumstances, allow microorganisms to interact with their environment. A proper definition of chassis can ease regulatory roadmaps to industrial and regulatory acceptance. The need to come up with a good definition of a SynBio chassis in fact stems from demands by regulatory bodies. As deeply engineered agents leave the laboratory for potential use in industry and the environment, they start falling under the radar of agencies that provide risk assessment advice on products used for the agri/food/feed chain e.g. the European Food Safety Authority (EFSA) and even have regulatory authority e.g. the US Food and Drug Administration (FDA). The soil bacterium *Pseudomonas putida* will be discussed as an example of the roadmap that one environmental isolate may go through to become a bona fide SynBio chassis and the many possibilities opened once a standardized platform is put in place.

11.00 Prof. Dr. Paul Freemont, Centre for Synthetic Biology & Innovation, UK Innovation & Knowledge Centre for Synthetic Biology, Imperial College, London

Cell-Free Expression: A Strategy for Prototyping Genetic Parts, Building Biosynthetic Pathways, and Making Novel Xenobiotics

Cell-free transcription/translation systems (known as CFPS or TX-TL) have recently been re-evaluated as a promising platform for enabling synthetic biology research and applications. In particular CFPS has been shown to provide a reproducible prototyping platform for regulatory elements where measurements in vitro are in part consistent with similar measurements in vivo. The advantage of being non-GMO allows rapid automated assays for characterizing parts and genetic circuit designs for pathway engineering, natural product discovery and biosensor designs. My lab has been interested in exploring cell free extracts from different organisms and I will present our recent studies on combining in vitro geno-chemetic strategies to allow rapid access to xenobiotic compounds which may provide improved therapeutic activity. By focusing on the violacein biosynthesis pathway and using seven different substrate analogues, we have been able to generate 66 new to nature analogues of violacein. Furthermore, 20 new derivatives were generated from brominated analogues via Suzuki-Miyaura cross-coupling reaction directly using the crude extract without prior purification.

11.30 Prof. Dr. Matthew Chang, NUS Synthetic Biology for Clinical and Technological Innovation and Wilmar-NUS Corporate Laboratory, National University of Singapore

Engineering microbes to rewire host-microbiome interactions

The wealth of knowledge on the human microbiota composition and its roles in health and disease has recently spurred the development of novel therapeutic strategies. Moreover, with an array of genetic tools that are readily available, programmable genetic circuits can be designed, genomes can be edited and rewritten, and cells can be reprogrammed to foster novel microbiota-based interventions. In this talk, our recent work on engineering gut-resident microbes as versatile platforms equipped with clinically relevant functionalities will be presented. A particular emphasis will be placed on our efforts to transform gut microbes into live biotherapeutics with prophylactic and therapeutic efficacy against pathogenic infections and chronic metabolic diseases. This work provides a strong foundation for engineering microbes to modulate host-microbiome interactions and supports the use of live biotherapeutics as a viable strategy for clinical intervention.

ABOUT THE SPEAKERS

Greg Stephanopoulos is the W.H. Dow Professor of Chemical Engineering and Biotechnology at MIT, and Instructor of Bioengineering at Harvard Medical School (1997-). He received his BS from the National Technical University of Athens, MS degree from the U. of Florida and PhD from the U. of Minnesota, all in Chemical Engineering. He taught at Caltech between 1978-85, after which he was appointed Professor of ChE at MIT. His current research focuses on metabolic engineering, the engineering of microbes for the production of fuels and chemicals. He has co-authored or –edited 5 books, more than 425 papers and 55 patents and supervised more than 130 graduate and post-doctoral students. He co-founded the journal *Metabolic Engineering*, and is presently co-editor-in chief of *Current Opinion in Biotechnology*. He serves on the Editorial Boards of 10 scientific journals and the Advisory Boards of 5 ChE departments. For his research and educational contributions, Prof. Stephanopoulos has been recognized with numerous awards, such as: Dreyfus award, Excellence in Teaching Award-Caltech, AIChE Technical Achievement Award, PYI from NSF, AIChE-FPBE Division Award, Marvin Johnson Award of ACS, Merck Award in Metabolic Engineering, the R.H. Wilhelm Award in Chemical Reaction Engineering of AIChE, Amgen Award in Biochemical Engineering. In 2003 he was elected to the National Academy of Engineering (NAE) and in 2005 he was awarded an honorary doctorate degree (doctor technices honoris causa) by the Technical University of Denmark. In 2007 he won the C. Thom Award from SIM and the Founders Award from AIChE and in 2010 the ACS E. V. Murphree Award in Industrial and Engineering Chemistry and the George Washington Carver Award of BIO. In 2011 he was selected as the Eni Prize winner for Renewable and non-Conventional Energy and was also elected as Corresponding Member of the Academy of Athens. He is a ASSS and AIChE Fellow. He was the 2014 recipient of the 2014 Walker award from AIChE. In 2013 he was awarded the John Fritz Medal of the American Association of Engineering Societies, in 2016 he won the Eric and Sheila Samson \$1 Prime Minister Prize (Israel) and was awarded an honorary doctorate by the Technical University of Athens and in 2017 we was recognized with the Novozymes Prize. Professor Stephanopoulos has served the professional organization of Chemical Engineers as chairman of Division 15, member of the Board of Directors and Chairman of the AIChE Society for Biological Engineering. In 2014, he was elected as 2016 President of AIChE. Professor Stephanopoulos has taught undergraduate and graduate courses of the core of Chemical Engineering and Biotechnology at Caltech and MIT and co-authored the first textbook on *Metabolic Engineering*. He is presently directing a research group of approximately 15 researchers who work on applications of metabolic engineering for the production of fuels and chemicals.



Víctor de Lorenzo (Madrid, 1957) is a Chemist by training and current holds a position of Research Professor in the Spanish National Research Council (CSIC) after working in Paris (I. Pasteur), UC Berkeley, Univ of Geneva and the GBF in Braunschweig. He currently heads the Laboratory of Environmental Synthetic Biology at the National Center for Biotechnology. He is a member of the EMBO (European Molecular Biology Organization) and the American and European Academies of Microbiology, and he has co-chaired with Drew Endy the EC-US Working Group on Synthetic Biology.

At present, his work explores the interface between Synthetic Biology and Environmental Biotechnology (see <https://vdl-lab.com/> for details).



Professor Paul Freemont is the co-founder of the Imperial College Centre for Synthetic Biology and Innovation and co-founder and co-director of the National UK Innovation and Knowledge Centre for Synthetic Biology (SynbiCITE; since 2013) and co-director of the London BioFoundry (since 2016) at Imperial College London. He is also currently the Head of the Section of Structural and Synthetic Biology in the Department of Infectious Diseases at Imperial College. He was previously the Head of the Division of Molecular Biosciences and Centre for Structural Biology having joined Imperial from Cancer Research UK London Research Institute (now known as the Crick Research Institute) where he was a Principal Investigator and Head of Group. His recent research interests are focused on developing synthetic biology foundational tools, automation and biofoundries and cell-free systems for specific applications including biosensing and metabolic engineering. Recently he has pivoted his research to develop, establish and validate modular automated workflows for Sars-CoV-2 clinical diagnostics, working closely two London hospitals. He is author of over 270 scientific publications (H-index 82-GS) and is an elected member of European Molecular Biology Organisation and Fellow of the Royal Society of Biology, Royal Society of Chemistry and Royal Society of Medicine and is an Honorary Fellow of the Royal College of Art. He was a co-author of the British Government's UK Synthetic Biology Roadmap and was a recent member of the Ad Hoc Technical Expert Group (AHTEG) on synthetic biology for the United Nations Convention for Biological Diversity (UN-CBD).



Matthew Chang is Dean's Chair Associate Professor of Biochemistry and Synthetic Biology in the Yong Loo Lin School of Medicine at the National University of Singapore. He is also Director of the Singapore Consortium for Synthetic Biology (SINERGY), Wilmar-NUS Corporate Laboratory (WIL@NUS) and NUS Synthetic Biology for Clinical and Technological Innovation (SynCTI). His research focuses on studying the engineering of biology to develop autonomous, programmable cells for biomedical and bio-manufacturing applications. His scientific contributions have been recognised with honours and awards, including the National Research Foundation of Singapore Investigator-ship Award, NUHS-Mochtar Riady Pinnacle Research Excellence Award, the Korean Federation of Science and Technology Societies Presidential Award and the Scientific and Technological Achievement Award from U.S. Environmental Protection Agency. He co-led the establishment of the Asian Synthetic Biology Association (ASBA) and the Global Biofoundry Alliance (GBA), and serves on the World Economic Forum's Global Future Council on Synthetic Biology. <http://SynCTI.org/>



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Schedule and Topics of next ESAB webinars:

30 July 2021, Biocatalysis and

Functional Genomics

August 2021, Joint US-European Webinar on

Biocatalysis and Bioeconomy

Education

3 Sept. 2021, Standards for Reporting Biocatalysis

14.00-16.00 Experiments

CET organized by Peter Halling

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The aims of ESAB are to promote initiatives in areas of growing scientific and industrial interest of importance within the field of Applied Biocatalysis. Further information can be found on the ESAB website www.esabweb.org

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