

Technical University of Denmark



## Design and optimization of sustainable process technologies

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**Programme****DTU Biosustain Annual Seminar 2017****Day 1**

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09:30 - 10:00

**Registration and coffee**

Please collect your name tag (includes the programme) when arriving at the seminar room

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09:30 - 10:00

**Accommodation**

Our venue team will be present to help store luggage until access cards are available

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10:00 - 10:10

**Welcome by Bo Skjold Larsen, COO**

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10:10 - 10:30

**'Towards 2020' by Bernhard Palsson, CEO and Scientific Director**

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10:30 - 10:35

**Moderator / Recapitulation: Alex T. Nielsen, Professor**

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10:30 - 10:50

**Petter Holland, Postdoc: Correlating transcription factor binding to functional outcomes for improved understanding and engineering of yeast metabolism**

Petter Holland<sup>1</sup>, David Bergenholm<sup>1</sup>, Christoph S. Boerlin<sup>1</sup>, and Jens Nielsen<sup>1\*</sup>

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Keywords: Transcription factors, transcriptional regulation, metabolism, yeast

We have mapped the interaction of 21 transcription factors (TFs) in *Saccharomyces cerevisiae* to DNA using state-of-the-art chromatin immunoprecipitation ChIP-exo under four distinct metabolic conditions. Experiments were performed in nitrogen-, glucose-, ethanol- and oxygen-limited chemostats to cover a broad range of states of yeast metabolism. From this dataset, we have explored general characteristics of TF binding such as position relative to transcription start site and overlap between TF binding and nucleosome occupancy. By mapping the TFs that are known to be most enriched on central carbon metabolism genes, we aim to get a system-level overview of transcriptional regulation of yeast metabolism. A major goal for the project is to correlate TF binding to transcript levels and other aspects of yeast metabolism to describe single TF or combinations of several TF binding events that are highly correlated to functional outcomes.

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10:50 - 11:10

**Irina Borodina, Senior Researcher**

14:30 - 14:50

### **Solange Mussatto, Group Leader: Design and optimization of sustainable process technologies**

Solange I. Mussatto\*, Fen Qin, Celina K. Yamakawa, Ignacio S. Moguel, and Marco Cassano

Biomass Conversion and Bioprocess Technology Group, DTU Biosustain, Lyngby, Denmark

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Keywords: Biomass conversion, Fermentation, Process performance, Optimization

The development of sustainable processes and innovative strategies that can accelerate the transition to a bio-economy is one of the main goals of the current society in order to have a future less dependent on oil and with lower carbon emissions. The use of biomass as a feedstock for bioprocesses has been then considered a key point to achieve such purposes, being also able to result in potential environmental, economic, and social benefits. In this sense, the Biomass Conversion and Bioprocess Technology Group (BCBT) has been working on the development of new strategies for the use of biomass in bioprocesses, covering the different aspects of the whole biomass conversion chain, since the feedstock until the final product. Our research efforts aim to identify the optimal exploitation of such resources according to sustainability principles and obtain an improved process performance. In this sense, process design and optimization is one of our main tools as it involves the simultaneous optimization of several parameters (e.g. suitable carbon and nitrogen sources, and process variables such as pH, temperature, dissolved oxygen, agitation, among others), by performing a minimal number of experiments, minimizing the costs and maximizing the efficiency and productivity. Once the optimal conditions are identified, the process scale-up can be then evaluated. This could be translated in a faster time to market for new process technologies.

14:50 - 15:10

### **Morten Nørholm, Senior Researcher: Evolution of the cAMP receptor protein CRP with a single codon toggle switch**

Emil C. Fischer<sup>1</sup>, Sofie Wendel<sup>1</sup>, Agnieszka Sekowska<sup>2</sup>, Ida Lauritsen<sup>1</sup>, Pernille Frendorf<sup>1</sup>, Silvia Capucci<sup>1</sup>, Cassandre Hellensberg<sup>1</sup>, Antoine Danchin<sup>2</sup>, and Morten H. H. Nørholm<sup>1\*</sup>

<sup>1</sup> Microbial Evolution and Synthetic Biology Group, DTU Biosustain, Lyngby, Denmark

<sup>2</sup> Institute of Cardiometabolism and Nutrition, CHU Pitié-Salpêtrière, Paris, France

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Keywords: Experimental evolution, adaptive mutations, CRP, global transcription factor

How do bacteria generate adaptive mutants? Over a period of two months, we isolated on ageing bacterial colonies outgrowing mutants able to use a new carbon source, and sequenced their genomes. Most mutations were located in just a few hotspots, while over time, the mutations increasingly originated from 8-oxo-guanosine, formed exclusively on the transcribed strand. This provides strong support for retromutagenesis as a general process creating adaptive mutations during ageing. CRP, the cAMP receptor protein, was a major mutational hotspot in the experiment and new results indicate that a single codon in *crp* acts an evolutionary toggle switch by activating and deactivating this global transcription factor in response to cAMP availability.

15:10 - 15:30

### **Jie zhang, Researcher: Combinatorial and model-guided pathway optimization for aromatics production in yeast**

Jie Zhang<sup>1\*</sup>, Søren Dalsgård Petersen<sup>1</sup>, Quanli Liu<sup>2</sup>, Benjamin Sánchez Barja<sup>2</sup>, Yun Chen<sup>2</sup>, Dushica Arsovska<sup>1</sup>, Kasper R. Pedersen<sup>1</sup>, Jens Nielsen<sup>1,2</sup>, Samuel Deutsch<sup>3,4</sup>, Michael K. Jensen<sup>1</sup>, and Jay D. Keasling<sup>1,5-8</sup>

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Metabolic engineering is an enabling technology for cell factory optimization. However, our ability to rationally engineer a biological system is often challenged by its complex regulations and poor characterization. Here, I will present how we apply a combinatorial approach to tackle major challenges in the pathway optimization, using tryptophan overproduction as an example. A combinatorial library is constructed by direct assembly of multiple genes involved in the precursor supply and various promoters with different strengths and conditionality. The landscape of the library is analysed both by a tryptophan biosensor we developed in this study and sequencing of the assembled gene clusters. Strategies of using machine learning to correlate these genotypic vs. phenotypic data and predict further improved genetic designs will also be discussed.

15:30 - 16:00

### **Coffee break**

15:30 - 16:00

### **Accommodation**

Participants who have booked accommodation will receive their access card during the coffee break

16:00 - 17:00

### **Poster Session**

Kai Blin;