SynCTI SEMINAR SERIES

NUS Synthetic Biology for Clinical and Technological Innovation (NUS SynCTI)
Member of Singapore Consortium for Synthetic Biology (Sinergy)

Professor Paul Freemont

Centre for Synthetic Biology and Innovation,
Department of Medicine, Imperial College London, UK

Rapid acquisition and model-based analysis of cell-free transcription-translation reactions from non-model bacteria

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 (1,2). 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 (3). My lab has been interested in exploring cell free extracts from different organisms (4,5) and I will present our most recent work on cell-free systems (6). Here, we have developed a rapid automated platform for measuring and modelling in vitro cell free reactions and have applied this to B. *megaterium* to quantify a range of RBS variants and previously uncharacterized endogenous constitutive and inducible promoters. To provide quantitative models for cell-free systems, we have also applied a Bayesian approach to infer ordinary differential equation model parameters by simultaneously using time course data from multiple experimental conditions. Using this modelling framework, we were able to infer previously unknown transcription factor binding affinities and quantify the sharing of cell-free transcription-translation resources (energy, ribosomes, RNA polymerases, nucleotides, and amino acids) using a promoter competition experiment. This allows insights into resource limiting-factors in batch cell-free synthesis mode. Our combined automated and modelling platform allows for the rapid acquisition and model-based analysis of cell-free transcription-translation data from uncharacterized microbial cell hosts as well as resource competition within cell-free systems, which potentially can be applied to a range of cell-free synthetic biology and biotechnology applications.

(1) Chappell J, Jensen K, Freemont, PS Nucleic Acid Research, 41: 3471 (2013)

(2) Moore SJ, Hung-En Lai, Kelwick R, Chee SM, Bell D, Polizzi KM, Freemont PS. ACS Synth Biol, DOI: 10.1021/acssynbio.6b00031 (2016)

(3) Wen KY, Cameron L, Chappell J, Jensen K, Bell DJ, Kelwick R, Kopniczky M, Davies JC, Filloux A, Freemont PS, ACS Synth Biol, 6 :2293 (2017)

(4) Kelwick R, Webb AJ, MacDonald JT, Freemont PS. Metabolic Engineering DOI 10.1016/j.ymben.2016.09.008 (2016)

(5) Moore SJ, Hung-En Lai, Needham H, Polizzi KM, Freemont PS. Biotechnology Journal DOI: 10.1002/biot.201600678 (2017)

(6) Moore SJ, MacDonald JT, Wienecke S, Ishwarbhai A, Tsipa A, Aw R, Kylilis N, Bell, DJ, McClymont DW, Jensen K, Polizzi KM, Biedendieck R, Freemont, PS. Proc. Natl. Acad. Sci USA in press (2018)

2nd May 2018, Wednesday | 2 pm
Centre for Translational Medicine, MD6-04-01A
CeTM SMART CLASSROOM
syncti.org | sinergy.sg
Hosted by: A/P Yew Wen Shan

NUS National University of Singapore | SynCTI Synthetic Biology for Clinical & Technological Innovation

Sinergy Singapore Consortium for Synthetic Biology