POC-2-kierzek-C1net-public-summary-application

Metabolic modelling to support synthetic biology in C1Net organisms.

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Gas fermentation is a process where microbial cells use gases as a carbon source and convert them into other chemicals. The C1Net is a community of researchers who create processes where microbial gas fermentation is harnessed to convert gases discharged in other industrial processes, such as petroleum refining and steel milling into valuable products. Members of C1Net use a Synthetic Biology approach where microbial cells are genetically engineered to efficiently convert carbon dioxide, carbon monoxide, methane and hydrogen to more valuable products for the chemical industry. Synthetic Biology adopts the engineering approach of developing biological parts that can be assembled in different configurations within host microorganism (chassis) to implement a wide range of bioprocesses. One of the hallmarks of engineering, widely adopted in well-established industries, is design and verification of products by computational modelling before implementation. In this project we will create the first computer model of the metabolic network of a C1 fermenting microorganism. This model will serve as blueprint for Synthetic Biology designs made by C1Net partners. Experts in genetic engineering and bioreactors will be able to test their designs before implementing them. While some predictions of the model will be wrong due to the incomplete knowledge about cellular metabolism, application of computer simulation will significantly reduce the number of alternative designs that will have to be tested. The use of the model by researchers without a modelling background will be supported by Simulocyte: the online simulation tool. The users will be given accounts in the social network environment where they will be able to access the model and share model modifications and simulation results. The software will further support understanding of the biological system by providing 3D visualization of the metabolic network and simulation results.

This proof of concept project will be delivered by collaboration of two C1Net partners having long standing experience in modeling of genome scale metabolic networks. The groups of Mark Poolman and David Fell at Oxford Brookes University will apply their ScrumPy network reconstruction pipeline which has been recently used to build network of rice and Salmonella typhimurium. Simulocyte is an interface to SurreyFBA tools developed by Andrzej Kierzek at the University of Surrey. The SurreyFBA software has been developed during projects focused on bacterial pathogens: Mycobacterium tuberculosis and Nisseria meningiatis. The first reconstruction of the M. tuberculosis network was also the first model published in an online simulation environment. Recently, Kierzek equipped SurreyFBA with a new algorithm called Quasi Steady State Petri Net, which enables integration of dynamic processes with models of metabolic flux. This algorithm will be used here to couple the metabolic model to the model of nutrient concentration changes in a bioreactor environment.

The model of the target organism will be published and made available to the public both through Simulocyte and distribution of a standard model exchange file in public databases.