Project title: Genome-scale metabolic modelling and optimizing medium for biomass production of *Intestinimonas butyriciproducens AF211*

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Expected starting time: from September 2019 onward

Goal: Build model and find optimum medium for biomass production

Project description:

Intestinimonas butyriciproducens AF211 is a gram-positive, spore forming, non-motile and strictly anaerobic rod-shaped bacterium (Bui et al., 2015, Bui et al., 2016). This strain was isolated from stool of a healthy individual. It's able to ferment many different substrates to form butyrate that is known as energy source for epithelial cells (Hamer *et al.*, 2008). Gut bacteria are known to produce butyrate mainly from carbohydrate degradation while amino acid/protein fermentation is often referred as unfavorable process which leads to the formation of detrimental compounds. To date, this bacterium is the only intestinal isolate that is capable of converting amino acid lysine and fructoselysine to butyrate and it has the entire machinery to perform this reaction. This fermentation has been elucidated via proteome and genome analysis (Bui *et al.*, 2015). Interestingly, fructoselysine is one of abundant Amadori products that are formed in cooked food during thermos treatments and this compound has been associated with several diseases (Uribarri *et al.*, 2005, Wang *et al.*, 2012, West *et al.*, 2014). Hence, *Intestinimonas butyriciproducens* AF211 is proposed as potential therapeutics for preventing these diseases. To do that it's important to produce a large amount of cell biomass that can later be used for animal or human studies. Lots of physiological and genomic characterization have been done for this strain but the condition that this strain can grow best is not yet known.

A rational approach to screen the optimal medium is to use genome scale model (GEM). A GEM is manually curated repository describing the metabolic capabilities of an organism. It combines available metabolic knowledge of an organism in a consistent and structured way that allows prediction and simulation of metabolic phenotypes. The main components of these models are metabolites, metabolic reactions, enzymes and the corresponding encoding genes.

The construction of a GEM includes three main steps (Thiele, I. & Palsson, B.Ø, 2010; Overbeek, R. *et al.,* 2016). First, the genome of the organism considered is functionally annotated in order to identify enzymes and the associated reactions and metabolites. Second, the list of enzymes and reactions is converted into a mathematical model, a so-called draft model, in the form of a stoichiometric matrix to which constraints are added to account for reaction reversibility and uptake and secretion of metabolites. Last, the model is manually curated using experimental data (such as growth data), information from literature and/ or expert knowledge.

Tasks:

1. Build model
    a. Draft model – metabolic functions are collected from genome annotation
    b. Curate model – Simulate biomass formation and fill gaps if there is any
    c. Validate model – compare *in-silico* and *in-vitro* growth and/or other known metabolic characteristics
2. Find optimum medium for biomass production
3. Write report
4. Give presentations (1 midterm and 1 final)

Timeline

1st month: literature research to get familiar with GEMs concept, model construction and simulation methods. In addition, learn to use COBRA-TOOLBOX in Matlab or COBRApy in Python.
2nd month: task (1a) and (1b)
3rd month: task (1b) and give midterm presentation
4th and 5th month: task (1b), (1c) and (2)
6th month: submit report and give final presentation

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