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Master Thesis Project:

Mycoplasma pneumoniae genome annotation and constraint-based metabolic modelling for growth rate optimization

Description

Mycoplasmas infect not only humans, but a wide range of hosts including pets and farm animals. For most Mycoplasma infections, there is no effective commercial vaccine, which would help preventing diseases, lesions and economic losses.

The *MycoSynVac* project, starting in 2015, is a collaborative European Project for engineering *Mycoplasma pneumoniae,* a human respiratory tract pathogen, as a global broad-spectrum animal vaccine. The different goals of the project involve the optimization of large-scale production, the chassis engineering and the vaccine design.

The thesis project focuses on the optimization of large-scale production of the vaccine: *Mycoplasma pneumoniae* and *Mycoplasma hyopneumoniae* are difficult to grow in axenic culture, requiring a complex media that includes animal serum. The constraint-based metabolic model will be able to identify and study the effects of candidates for the new medium components to enhance the growth rate into a minimal chemically-defined medium.

The thesis project is divided in two main parts:

1. *Mycoplasma pneumoniae* Genome Annotation and Genome-Scale Metabolic Model updating. The existing genome-scale model from 2013 (*Wodke et al.*), which exists in SBML format, requires to be updated in terms of content of reactions, reversibility of reactions, lower and upper bounds of reaction fluxes and annotation of metabolites and reactions, with links to the main existing databases. An updated and well-annotated genome-scale model is essential for an efficient constraint-based modelling procedure.
2. Constraint-based Metabolic Modelling for Growth Rate Optimization. The metabolic fluxes indicated in the Genome-Scale model will be simulated through a Flux Balance Analysis approach. Possible applications of the method are growth rate optimization and antigen production optimization.

Methods

Programming skills (Python is recommended) and a basic understanding of the principles of metabolic modelling and constraint-based modelling (Flux Balance Analysis) are required.

References

- Project overview, partners and publications can be found on the website www.mycosynvac.eu.
- Reference for the existing genome-scale metabolic model: Wodke J.A.H. et al. (2013). "Dissecting the energy metabolism in Mycoplasma pneumoniae through genome-scale metabolic modelling". *Molecular Systems Biology 9, 653*.
- What is Flux Balance Analysis: Orth J.D. et al. (2010). "What is flux balance analysis?". *Nature Biotechnology 28, 245-248*.
- The COBRA toolbox: Becker S.A. et al. (2007). "Quantitative prediction of cellular metabolism with constraint-based models: the COBRA Toolbox". *Nature Protocols 2, 727-738*.
- Examples of constraint-based metabolic modelling of *Escherichia coli*: Reed J.L. and Palsson B.O. (2003). "Thirteen Years of Building Constraint-Based in Silico Models of *Escherichia coli*". *Journal of Bacteriology, 185, 9*.