Understanding the organization of the metabolism in *Bacillus subtilis*

**Background information:**
*Bacillus subtilis* is the major model organism of the prokaryotic kingdom beside *Escherichia coli*. A wealth of information is available of physiology, metabolism and signaling pathways in that organism. *B. subtilis* is an important organism used by biotechnological companies for recombinant protein production and medical applications. A new European research project aims to improve our knowledge on central carbon core and nitrogen metabolism. Our partners in this project found that many enzyme in the metabolism have varying affinities for other enzymes in the metabolic path. The questions are: why are there low to medium affinities between enzymes, and how is the metabolic flux improved?

**Goals:**
The objective of the student position is to built a model of *B. subtilis* central carbon core and nitrogen metabolism. This model need to be able to reproduce metabolic fluxes published in literature as well as generated in the partner laboratories.
The scientific question that we want to answer with these models is how much regulation is of transcriptional or post-translational nature, and for which circumstances which regulation is optimal.

**Work procedure:**
A literature survey has to be performed to identify reactions of central carbon core and nitrogen metabolism. Reaction rate constants for most reactions will be available in databases. Existing models of the metabolism (also derived from published *E. coli* models) are then adapted to fit experimental data.
The models will be based on ordinary differential equations. A sensitivity and metabolic flux analysis is necessary to detect critical reactions for optimal performance of the metabolism. These analyses techniques will detect reactions that are suitable hubs for regulation on either the transcriptional or allosteric level. Predictions for the reaction hub regulation will be validated using literature and possibly experiments by our partner laboratories.

**Skills you learn:**
Knowledge of bacterial metabolism
Scientific literature surveys
Modelling and simulation with Matlab
Formulation of model based predictions
Design of experimental tests and analysis of data

**We offer:**
Expertise on prokaryotic metabolism
International group
Insight into the organization of a European research project