A first analysis of the central carbon pathway of *Bacillus subtilis:*

Integration of both genetic and enzymatic levels in regulations

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A challenging problem in systems biology consists in understanding the regulation and the global coordination of metabolic pathways of bacteria in response to environmental changes, at the cell scale. Recently we identified the main regulation structures of metabolic pathways through the manually curated reconstruction of the regulatory networks of *Bacillus subtilis* [1]. We noticed a strong interplay between the metabolic pathways and the genetic regulations: 13% of 456 metabolites are involved in genetic regulations and 53% of the genes involved in metabolic pathways are directly regulated by a genetic regulator under the control of a metabolite. Surprisingly, few studies centred on metabolic pathways have considered this coupling between the genetic and metabolic regulatory networks [2-3]. Using a mathematical dynamic model, we illustrate the necessity of integrating both genetic and metabolic regulations, through the study of glycolysis, during exponential growth on glucose. Some interesting results are presented in this talk:

- Identification of the key steps of glycolysis,
- Identification of the key metabolites which determine the pathway behaviour,
- Prediction of the behaviour of the enzymes and metabolites concentrations, of the fluxes and validation in simulation,
- The respective role of genetic and enzymatic regulations.

References: