1st FEBS Advanced Lecture Course on
Systems Biology:
From Molecules & Modeling to Cells

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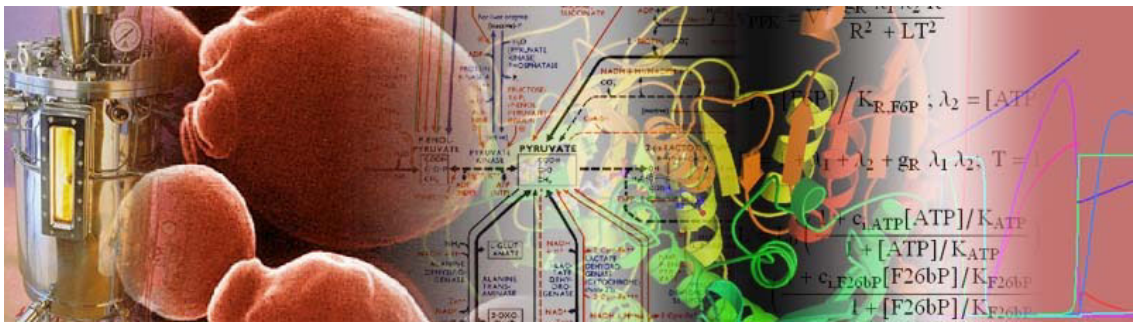

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U-P20 A Systems Biology approach for the optimization of recombinant protein production in *E. coli*

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Escherichia coli has been the organism of choice for the production of many recombinant proteins with high therapeutic value. However, while the research on molecular biology has allowed the development of very strong promoters, there are still several phenomena associated with this process that have hampered the full use of that promoter strength, namely the aerobic acetate production associated with high specific growth rates. The presence of acetate is known to reduce both biomass yield on the chosen carbon source and protein productivity while totally inhibiting growth when present at high concentrations due to its toxic effect. While there have been several studies covering the recombinant protein production process with the bacterium Escherichia coli, including genome-scale analysis of the transcriptome, proteome, fluxome or metabolome, there has been a lack of an integrative approach that is able to combine genomic and physiological information about those processes with high-throughput analysis.
Also, the existence of genome-scale models that cover both stoichiometry and regulation of some pathways has not been taken into account in genome-scale data analysis and for the consequent formulation of hypothesis and development of new strategies for improving the performance of the process.
In our group, a high-cell density fed-batch process for recombinant protein production in *E. coli* is being studied, giving particular relevance to acetate production. A systematic approach is being used, by first compiling the existing knowledge about this phenomenon, extending existing genome-scale models to accommodate that knowledge, derive hypothesis in silico that are then tested by using genome-scale analysis of the omes. A reliable fermentation process was developed to be able to reproducibly study this phenomenon in different strains in order to reduce external variances to a minimum.