A Systems Biology approach for the characterization of metabolic bottlenecks in recombinant protein production processes

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The purpose of this project is to derive strategies for increasing the productivity of recombinant protein production processes by applying a systems biology perspective to the phenomena occurring in the recombinant cell. This will specifically involve the use of genome-scale analysis of the transcriptome, proteome and fluxome. Escherichia coli have been the organism of choice for the production of many recombinant proteins with high therapeutic value. However, there are still some associated phenomena that decrease the process performance, like the stringent response that usually occurs when very high levels of heterologous protein production. In this work, the high-cell density fed-batch recombinant protein production process in E. coli will be studied, giving particular relevance to stringent response. The approach is intended to be systematic, by first compiling the existing knowledge about this phenomenon, extending existing genome-scale models to accommodate that knowledge, and derive hypothesis *in silico* that will then be tested by using genome-scale analysis of the transcriptome.