CENTRE OF BIOLOGICAL ENGINEERING
UNIVERSIDADE DO MINHO

INSTITUTE FOR BIOTECHNOLOGY AND BIOENGINEERING

Investigating metabolic responses in recombinant *E. coli* cultures using metabolomics and fluxomics data

Sónia Carneiro, Rafael Carreira, Eugénio C. Ferreira, Isabel Rocha

IBB-Institute for Biotechnology and Bioengineering, Centre of Biological Engineering, University of Minho, Campus de Gualtar, 4710-057 Braga, Portugal

During recombinant processes the host-cell metabolism endures severe alterations in order to adjust to the additional drain of biosynthetic precursors, energy and other cellular resources required for protein production. This, ultimately, results in reduced cellular growth and recombinant protein yields. The identification of metabolic bottlenecks can help in the understanding of cellular imbalances occurring during these recombinant processes and further assist rational engineering strategies.

Recently, analytical platforms, like fluxomics and metabolomics, have been used to measure and monitor the metabolic variation between different states of biological systems [1]. In particular, fluxomics can be used to quantify fluxes in the entire metabolic network of an organism, by tracing the transition path of the isotopic labels between metabolites (substrates/products). The abundance of those metabolites can also be determined in a high-throughput manner through metabolomics, which in combination allows a detailed analysis of the intracellular dynamics of cellular metabolism. These analytical methods can be used to identify metabolic bottlenecks in recombinant systems and thereby to provide useful information to support effective strategies for biotechnology applications.

At present, only few attempts have been made to tackle relevant metabolic bottlenecks in recombinant productivity using both fluxomics and metabolomics approaches [2]. In this work, a combination of metabolomics and fluxomics analyses was applied to study the recombinant *E. coli* system producing AcGFP (i.e., a green fluorescent protein derived from the jellyfish *Aequorea coerulescens*).

References

[1] Carneiro S, Villas-Boas SG, Ferreira EC, Rocha I, “Metabolic footprint analysis of recombinant *Escherichia coli* strains during fed-batch fermentations” (2011) Mol Biosys. 7**:** 899-910.

[2] Wittmann C, Weber J, Betiku E, Kromer J, Bohm D, Rinas U, “Response of fluxome and metabolome to temperature-induced recombinant protein synthesis in Escherichia coli” (2007) J Biotech 132: 375-384.