

## WORKFLOW FOR MINING PROCESS RELEVANT KNOWLEDGE FROM TRANSCRIPTOMICS

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Understanding the effect of different perfusion process parameters, such as feed amino acid composition and cell specific perfusion, would allow more knowledge-based process optimization and control strategies. Different \*omics approaches, such as transcriptomics, have been used to shed light onto the mechanism explaining the differences arising from process parameters. However, obtaining mechanistic information from the transcriptome remains challenging. Here we highlight a systematic workflow for mining mechanistic data from transcriptomic measurements. The workflow is demonstrated on perfusion cultures with varying amino acid feed composition and cell specific perfusion rate, while limiting the effect of glucose via targeted feeding (TAFE)[1].

For this work, a perfusion process was carried out to collect data on the effect of cell specific perfusion rate. This was followed by a set of perfusion runs while varying amino acid feed composition. Transcriptomic data was collected from both sets of experiments. Next, the transcriptomics data was transformed and mapped to a reaction network to obtain mechanistic metabolic insight. We observed that the perfusion rate and amino acid composition had an effect on the lactate, ammonium and amino acid metabolism. Additionally, the effect on different subsystems of protein and biomass production were assessed. We observed both perfusion rate and amino acid composition dependent changes.

In conclusion, the presented workflow provides tools for capturing process relevant biological mechanisms from transcriptomic data.

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References:

[1] Zhang, L., Schwarz, H. et al. 2021. Metabolic engineering, 65, 135-145