From Strain to Product: A fast approach in bioprocess development for recombinant protein expression in Pichia pastoris

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Background and Motivation

Pichia pastoris is one of the most important host organisms for recombinant protein production in industrial biotechnology. To date, strain specific parameters, which are needed to set up feeding profiles for fed batch production processes, are determined by time-consuming continuous experiments or consecutive fed batch cultivations, operated at different parameter sets. Due to the current advances in genetic manipulation and the resulting emerging number of various host strains, faster quantification methodologies for strain characterization and bioprocess development are needed.

The present study aimed at establishing a novel strain quantification method to set up efficient fed batch production processes for recombinant Pichia pastoris strains.

Experimental strategy

Batch cultivations - Methanol pulses were used to determine the adaptation time, the specific substrate uptake rate during the adaptation and the maximum specific substrate uptake rate of the used strain.

Fed Batch cultivations - Data from batch cultivations were used to set up feeding strategies based on \( q_s \). Different dynamic feeding profiles were tested to find an optimized operation point regarding productivity.

Results and Discussion

The study presents a fast and easy to do method to determine strain specific data of P. pastoris expression systems:

- The scalable and novel process parameter \( q_s \) was successfully transferred from batch into fed batch production systems for various strains.
- A dynamic feeding strategy based on \( q_s \) in a single substrate system resulted in the highest specific productivity \( q_p \) compared to other strategies tested.
- Additional information of physiological interactions during mixed substrate assimilation were revealed by applying the novel strategy to a mixed feed environment.

Dynamic feeding profiles turned out to be a valuable tool to boost specific productivity and increase process understanding.

References:

