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Bioreactor process optimization of *Pichia pastoris* high-level secretion strains under methanol-induced as well as glycerol-driven conditions

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Pichia pastoris is being increasingly embraced by the biopharmaceutical industry as an expression system for therapeutic proteins, next to its usage as highly efficient producer of enzymes. In controlled bioreactors, this recombinant host´s strength is good growth to and at high cell densities (up to 600 g/L wet cell weight) and concomitant expression/secretion of heterologous proteins to high levels. VTU Technology´s versatile AOX1 promoter library for fine-tuned expression enables production of recombinant proteins in gram quantities per liter culture supernatant under methanol-induced conditions, as well as with sub-repressive concentrations of glycerol/glucose leveraging unique 2nd generation AOX1 promoters for regulation of gene expression.

Methanol-driven bioreactor cultivations can be optimized with respect to the fed-batch phase on glycerol (non-productive event) and methanol-induced production phase. As the requirements of individual strains producing recombinant proteins at high levels are different for each particular case, a thorough understanding of the general process is a key to success. Over 1000 fermentations per year in 1 L bioreactors laid the foundation for sophisticated parameter setting in order to quickly optimize customized processes for any production strain.

Special process understanding is particularly needed for recombinant protein production under sub-repressive glycerol concentrations: The balance of potential repression of protein production with too high carbon source supply and suboptimal conditions for cellular maintenance with too low supply must be met. This presentation features case studies to both cultivation regimes with strains secreting recombinant proteins at very high levels from the therapeutic as well as the industrial enzyme field.

Biography

Roland Weis completed his Ph.D. in molecular biotechnology at Graz University of Technology, Austria in 2004. After a post doctorate at Graz University of Technology in a bilateral project with Pasadena, US-based BioCatalytics, Inc., he acted as authorized representative and scientific director of BioCatalytics Europe GmbH in Grambach, Austria. In 2007, he joined VTU Technology to head the operational team for protein production with *Pichia pastoris*.

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