Microbial Cell Factories

BioMed Central

Poster Presentation

Automated fed-batch cultivations using base consumption for real time biomass determination during production of heterologous proteins

Markus Ganzlin*, Benjamin Gerwat and Philipp Garbers

Address: Global Protein Science & Supply, AstraZeneca, Macclesfield, UK
* Corresponding author

from The 4th Recombinant Protein Production Meeting: a comparative view on host physiology
Barcelona, Spain. 21–23 September 2006

Published: 10 October 2006

Microbial Cell Factories 2006, **5**(Suppl 1):P27 doi:10.1186/1475-2859-5-S1-P27

Background

Automation can improve efficiency for fast development of reproducible bioreactor processes required for drug discovery. Target protein production in bioreactors can also benefit from online biomass determination, since the problem of undefined maximum specific growth rates for a high through-put of newly-designed recombinant *E.coli* strains can be addressed. In order to realise online biomass monitoring a variety of different technical approaches are commercially available. Some of them are quite complex and expensive. In contrast to this an effective method of real time biomass monitoring for *E.coli* fed-batch cultivations was described previously [1].

Results

A software tool was programmed in MATLAB® and linked to the SCADA system MFCS/win® via an OPC Client. Using this tool with user-friendly graphical interfaces, automated induction and exponential increasing mass feeding strategies were carried out successfully. A reproducible automated batch end detection was implemented and successfully validated for twenty cultivations. The batch end detection triggered the automatic start of an exponential increasing feed strategy. During the development of the detection method a suitable set of logical conditions based on online cultivation data was determined. These conditions were used for a loop algorithm, which ensured that all conditions were true for a period of three minutes, which eliminated interference of outlier online signals. For all fed-batch cultivations a good linear correlation between base (NH_3) consumption and biomass production was determined. The biomass yield coefficient with respect to ammonia was constant during the course of cultivation and remained the same after protein production was induced. The same yield coefficient ($Y_{X/NH3}$ = 5.9 g g^{-1}) was determined for five different feeding strategies. These bioprocesses used a feed forward strategy aiming at a different constant growth rate (μ_{SET1} = 0.04 h^{-1}, μ_{SET2} = 0.06 h^{-1}, μ_{SET3} = 0.09 h^{-1}, μ_{SET4} = 0.12 h^{-1} μ_{SET5} = 0.14 h^{-1}).

Conclusion

The implementation of a reproducible automated batch end detection significantly reduced the requirements for out of hours working time. Using the online base consumption signal as an indicator for biomass production improved the quality of decision making during running time.

References

1. Schmidt M, Viaplana E, Hoffmann F, Marten S, Villaverde A, Rinas U: **Secretion-dependent proteolysis of heterologous protein by recombinant Escherichia coli is connected to an increased activity of the energy-generating dissimilatory pathway.** *Biotechnol Bioeng* 1999, **66**:61-67.