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Poster Presentation

Two-compartment bioreactor as a scale-down model to study the effect of glucose overflow and anaerobiosis on large-scale recombinant protein production processes

Jaakko Soini*[1], Ulla Pajulampi[1], Janne Sandqvist[1], Arne Matzen[2] and Peter Neubauer[1]

Address: [1]Bioprocess Engineering Laboratory, Department of Process and Environmental Engineering, University of Oulu, Oulu, Finland and [2]Sanofi-Aventis, Germany

* Corresponding author

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Background

In high-cell density fermentations the host cells are often subjects of transient changes in microenvironment around them. This is true especially in large-scale bioreactors. The changes can be for example substrate gradient, differences in oxygen availability and pH variations. Our aim is to obtain more information about physiological changes of *E.coli* W3110 and its recombinant variants in such conditions for better understanding of the bottlenecks in recombinant protein production processes.

To mimic the conditions in large-scale fermentations, we have set-up a two-compartment bioreactor [1], in which cells are circulated between a regular stirred tank reactor (STR) and a plug-flow reactor (PFR) using a peristaltic pump. The glucose is fed into the bottom of the plug-flow reactor with the aim of maintaining the glucose limitation in the STR part.

The advantage of the model is that the conditions of the zones where the changes occur can be measured. We take samples from 4 positions A, B, C and D (See Fig 1) of the PFR and additionally from 1 sample position of the STR. The normal process parameters such as pH, DOT and temperature are measured from the STR and additionally we have placed DOT and pH sensors in two positions of the PFR (S1 and S2).

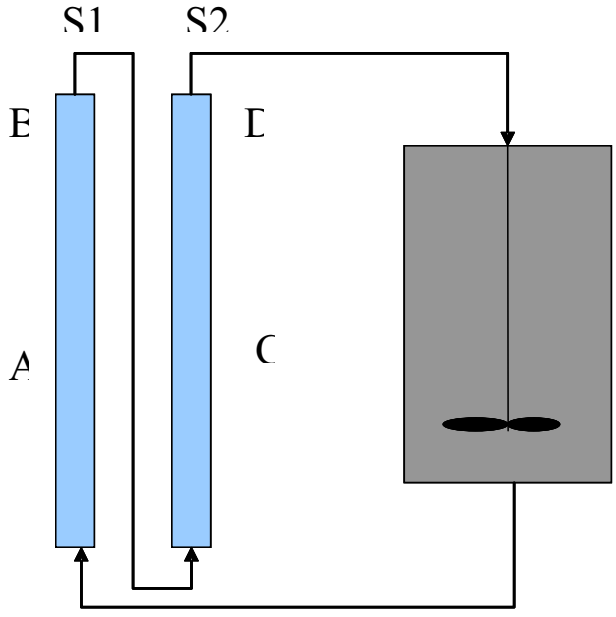

Figure 1
Schematic figure of the STR-PFR reactor and its sampling points.

Results

From the initial fermentation experiments in the STR-PFR reactor we have seen that the model is a good simulator for conditions in large-scale fermentors. When the STR part only was monitored, no signs from anaerobic conditions or pH variations were observed. However, in the PFR part glucose was measured and the highest value was obtained close to the feeding point decreasing then towards the end of the plug-flow reactor. Rapid formate accumulation was observed and 150 mg/L of formate was produced in few minutes. Low amounts of oxygen was monitored from PFR before the feed start but after it variable dropped down to zero at both measuring points. Also pH decreased more than 0.5 units in the plug-flow compartment.

References

1. George S, Larsson G, Enfors SO.: **A scale-down two-compartment reactor with controlled substrate oscillations *Saccharomyces cerevisiae*.** *Bioprocess Engineering* 1993.