Online Biomass Monitoring of Shake Flask Cultures via an optical multisensory Platform

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Introduction

Shake flask cultivation represents an easy method to perform proliferation of microorganisms for different purposes. The focus is on screening routines and the heterologous production of proteins in R & D. Estimation of the culture condition needs a continuous analysis of biomass data, growth rate, oxygen concentration at a pH. The aim is a fast response to critical developments during the cultivation process.

Process Monitoring

In the context of this work, a multisensory platform was evaluated by monitoring of three basic cultivation parameters (pH, pO₂, biomass). The biomass sensor was calibrated for a couple of selected microorganisms. Influences on the measuring signal were revealed. By online monitoring of metabolic phenomena, sensitivity of the signal has shown to be superior.

Principle of Measurement

The non-invasive measurement of biomass is performed by detection of 180° scattering light at a dominance wavelength of 625 nm. The included acceleration sensor triggers each measurement at the moment of maximum liquid level (synchronized) (Fig. 1). The measuring interval can be reduced to 7 s. pH value and O₂ saturation are measured optically by special sensor spots (Fig. 3).

Calibration

Calibration of the light scattering signal against basic cultivation measurements (OD₆₀₀, BTM) can be described by the Bleasdale-Nelder function with most of the applied organisms. Reproducibility of the calibrations was proved by three independent cultivations with a RMSEP < 0.5 for OD₆₀₀nm±.

Conclusion

The 180° scattering light sensor for online biomass monitoring of shake flask cultures proved to be suitable especially for homogenous cell suspensions. System specific calibrations feature a good reproducibility. One of the system's biggest advantages is the high sensitivity of the scattering light signal beyond the lag-phase. The combination of information regarding all three measurand's offers a solid analysis of critical changes and limitations during the cultivation process.

Sponsorship

This project was supported in the context of the ZIM-initiative (BMWi).