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Miniature bioreactors for automated high-throughput bioprocess design (HTBD): reproducibility of parallel fed-batch cultivations with Escherichia coli

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Abstract:

To verify the reproducibility of cultivations of *Escherichia coli* in novel milliliter-scale bioreactors, fully automated fed-batch cultivation was performed in seven parallel-operated ml-scale bioreactors with an initial volume of 10 ml/reactor. The process was automatically controlled by a liquid-handling system responsible for glucose feeding, titration and sampling. Atline analysis carried out (externally of the reaction vessel with a short time delay) comprised automated pH and attenuance measurements. The partial pressure of oxygen (pO2) was measured online by a novel fluorimetric sensor block measuring the fluorescence lifetime of fluorophors immobilized inside the milliliter-scale bioreactors. Within a process time of 14.6 h, the parallel cultivation yielded a dry cell weight of 36. 9 ± 0.9 g l^{-1}. Atline pH measurements were characterized by an S. D. of < 1.1 % throughout the process. Computational-fluid-dynamics simulation of single-phase flow yields a mean power input of 21.9 W l^{-1} at an impeller speed of 2800 rev./min corresponding to a power number (N_P) of 3.7.

Key-words: aerobic process, automation, bioprocess design, fed-batch cultivation, high throughput, oxygen transfer