Scientific Paper:

Wiley Periodicals, Inc., DOI 10.1002, bit. 20352, 2005

Development, Parallelization and Automation of a Gas-Inducing Milliliter-Scale Bioreactor for High-Throughput Bioprocess Design (HTBD)

R. Puskeiler[1], K. Kaufmann[2], D. Weuster-Botz[1]
[1]Lehrstuhl für Bioverfahrenstechnik, Technische Universität München,
Boltzmannstrasse 15, 85748 Garching, Germany;
telephone: ++49-89-28915729; fax: ++49-89-28915714;
e-mail: r.puskeiler@lrz.tum.de
[2]H & P Labortechnik AG, Oberschleissheim, Munich, Germany

Abstract:

A novel milliliter-scale bioreactor equipped with a gas-inducing impeller was developed with oxygen transfer coefficients as high as in laboratory and industrial stirred-tank bioreactors. The bioreactor reaches oxygen transfer coefficients of >0.4 s^{-1}. Oxygen transfer coefficients of >0.2 s^{-1} can be maintained over a range of 8- to 12-mL reaction volume. A reaction block with integrated heat exchangers was developed for 48-mL-scale bioreactors. The block can be closed with a single gas cover spreading sterile process gas from a central inlet into the headspace of all bioreactors. The gas cover simultaneously acts as a sterile barrier, making the reaction block a stand-alone device that represents an alternative to 48 parallel-operated shake flasks on a much smaller footprint. Process control software was developed to control a liquid-handling system for automated sampling, titration of pH, substrate feeding, and a microtiter plate reader for automated atline pH and atline optical density analytics. The liquid-handling parameters for titration agent, feeding solution, and cell samples were optimized to increase data quality. A simple proportional pH-control algorithm and intermittent titration of pH enabled Escherichia coli growth to a dry cell weight of 20.5 g L^{-1} in fed-batch cultivation with air aeration. Growth of E. coli at the milliliter scale (10 mL) was shown to be equivalent to laboratory scale (3 L) with regard to growth rate, μ, and biomass yield, YXS.

Key-words: Bioprocess design, high troughput, gas-inducing impeller, parallel bioreactor, automation