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A System of Miniaturized Stirred Bioreactors for Parallel Continuous Cultivation of Yeast With Online Measurement of Dissolved Oxygen and Off-Gas

Tobias Klein, Konstantin Schneider, Elmar Heinzle
Biochemical Engineering Institute, Saarland University, Saarbrücken, Germany

Abstract:

Chemostat cultivation is a powerful tool for physiological studies of microorganisms. We report the construction and application of a set of eight parallel small-scale bioreactors with a working volume of 10 mL for continuous cultivation. Hungate tubes were used as culture vessels connected to multichannel-peristaltic pumps for feeding fresh media and removal of culture broth and off-gas. Water saturated air is sucked into the bioreactors by applying negative pressure, and small stirrer bars inside the culture vessels allow sufficient mixing and oxygen transfer. Optical sensors are used for non-invasive online measurement of dissolved oxygen, which proved to be a powerful indicator of the physiological state of the cultures, particularly of steady-state conditions. Analysis of culture exhaust-gas by means of mass spectrometry enables balancing of carbon. The capacity of the developed small-scale bioreactor system was validated using the fission yeast *Schizosaccharomyces pombe*, focusing on the metabolic shift from respiratory to respiro-fermentative metabolism, as well as studies on consumption of different substrates such as glucose, fructose, and gluconate. In all cases, an almost completely closed carbon balance was obtained proving the reliability of the experimental setup.

Key-words: continuous cultivation, dissolved oxygen, *Schizosaccharomyces pombe*, steady state, respiratory quotient, carbon balance