Scientific Paper:

Biotechnol. Prog., 2010, Vol. 26, No. 5, 1259 - 1270

Microfluidic Reactor for Continuous Cultivation of *Saccharomyces cerevisiae*

Astrid Edlich[1], Veronika Magdanz[1], Detlev Rasch[1], Stefanie Demming[2], Shobeir Aliasghar Zadeh[3], Rodrigo Segura[4], Christian Kähler[4], Rolf Radespiel[5], Stephanus Büttgenbach[6], Ezequiel Franco-Lara[7], Rainer Krull[7]
[1]Institute of Biochemical Engineering, TU Braunschweig, 38106 Braunschweig, Germany
[2]Institute of Microtechnology, TU Braunschweig, 38106 Braunschweig, Germany
[3]Institute of Fluid Mechanics, TU Braunschweig, 38106 Braunschweig, Germany
[4]Institute of Fluid Mechanics and Aerodynamics, Universität der Bundeswehr München, 85577 Neubiberg, Germany
[5]Institute of Fluid Mechanics, TU Braunschweig, 38106 Braunschweig, Germany
[6]Institute for Microtechnology, TU Braunschweig, 38106 Braunschweig, Germany
[7]Institute of Biochemical Engineering, TU Braunschweig, 38106 Braunschweig, Germany

Abstract:

A diffusion-based microreactor system operated with a reaction volume of 8 µL is presented and characterized to intensify the process understanding in microscale cultivations. Its potential as screening tool for biological processes is evaluated. The advantage of the designed microbioreactor is the use for the continuous cultivation mode by integrating online measurement technique for dissolved oxygen (DO) and optical density (OD). A further advantage is the broaden application for biological systems. The bioreactor geometry was chosen to achieve homogeneous flow during continuous process operation. The device consisted of a microstructured top layer made of poly(dimethylsiloxane) (PDMS), which was designed and fabricated using UV-depth and soft lithography assembled with a glass bottom. CFD simulation data used for geometry design were verified via microparticle-image-velocimetry (µPIV). In the used microreactor geometry no concentration gradients occurred along the entire reaction volume because of rapid diffusive mixing, the homogeneous medium flow inside the growth chamber of the microreactor could be realized. Undesirable bubble formation before and during operation was reduced by using degassed medium as well as moistened and moderate incident air flow above the gas permeable PDMS membrane. Because of this a passive oxygen supply of the culture medium in the device is ensured by diffusion through the PDMS membrane. The oxygen supply itself was monitored online via integrated DO sensors based on a fluorescent dye complex. An adequate overall volumetric oxygen transfer coefficient k_La as well as mechanical stability of the device were accomplished for a membrane thickness of 300 µm. Experimental investigations considering measurements of OD (online) and several metabolite concentrations (offline) in a modified Verduyn medium. The used model organism *Saccharomyces cervisiae* DSM 2155 tended to strong reactor wall growth resembling a biofilm.
Key-words: microreactor, screening, microfluidics, yeast, cell density, bioreactor