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A New Microfluidic Concept for Parallel Operated Milliliter-Scale Stirred Tank Bioreactors

Gabi Gebhardt[1], Ralf Hortsch[1], Klaus Kaufmann[2], Matthias Arnold[3], and Dirk Weuster-Botz[1]

[1]Institute of Biochemical Engineering, TU Munich, Germany
[2]2mag AG, Munich, Germany
[3]DASGIP AG, Jülich, Germany

Abstract:

Parallel miniaturized stirred tank bioreactors are an efficient tool for "high-throughput bioprocess design". As most industrial bioprocesses are pH-controlled and/or are operated in a fed-batch mode, an exact scale-down of these reactions with continuous dosing of fluids into the miniaturized bioreactors is highly desirable. Here, we present the development, characterization, and application of a novel concept for a highly integrated microfluidic device for a bioreaction block with 48 parallel milliliter-scale stirred tank reactors (V = 12 mL). The device consists of an autoclavable fluidic section to dispense up to three liquids individually per reactor. The fluidic section contains 144 membrane pumps, which are magnetically driven by a clamped-on actuator section. The micropumps are designed to dose 1.6 µL per pump lift. Each micropump enables a continuous addition of liquid with a flow rate of up to 3 mL h^{-1}. Viscous liquids up to a viscosity of 8.2 mPa s (corresponds to a 60 % v/v glycerine solution) can be pumped without changes in the flow rates. Thus, nearly all feeding solutions can be delivered, which are commonly used in bioprocesses. The functionality of the first prototype of this microfluidic device was demonstrated by double-sided pH-controlled cultivations of *Sacharomyces cerevisiae* based on signals of fluorimetric sensors embedded at the bottom of the bioreactors. Furthermore, fed-batch cultivations with constant and exponential feeding profiles were successfully performed. Thus, the presented novel microfluidic device will be a useful tool for parallel and, thus, efficient optimization of controlled fed-batch bioprocesses in small-scale stirred tank bioreactors. This can help to reduce bioprocess development times drastically.

Key-words: millilitre bioreactor, process control, high-throughput, microfluidic, scale-down