Shake Flask Monitoring and Control using a Multisensory Platform in Combination with a Scale-Down Control Unit

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Introduction
pH control in shake flask has not established due to the lack of a practical combination of online sensor system and an appropriate control unit. The objective of this investigation was to develop a minimum scale dosage apparatus (shake flask controller “SFC”) incl. control algorithm, which is able to control the pH during a complete microbial cultivation. A well evaluated optical, non-invasive, multisensory platform prototype for online biomass, pO₂- and pH-measurement was used as sensor.

Function & Calibration
The SFC working principle is based on a tank (11.5 mL, reservoir) connected to a piezoelectric micropump (mp6), which is pumping the liquid through a nozzle into the shake flask (Fig. 2A). Through calibration the controller is converting a volume command [µl] into the pulse count of the mp6 piezo elements (Fig. 2B).

Online pH control
E. coli K12 was cultivated in LB medium (+10 g·L⁻¹ glucose), once without active pH control (Fig. 3A) and once controlled by the SFC in combination with an adaptive P controller (Fig. 3B). In comparison the pH could be controlled precisely over the full cultivation time (19 h). The pH control resulted in a significantly advanced growth and a longer active growth phase. A growth rate of at least 0.2 h⁻¹ was maintained over the whole cultivation time.

Conclusion
The combination of an optical sensor platform and a compact cap-integrated actuator offered a comparatively inexpensive and simple way to run processes in small scale with a bioreactor like process control system. Thus, shake flask cultivations are valorized to be more comparable to bioreactor cultivations.

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