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New Milliliter-Scale Stirred Tank Bioreactors for the Cultivation of Mycelium Forming Microorganisms

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Abstract:

A novel millilitre-scale stirred tank bioreactor was developed for the cultivation of mycelium forming microorganisms on a 10 milliliter-scale. A newly designed one-sided paddle impeller is driven magnetically and rotates freely on an axis in an unbaffled reaction vessel made of polystyrene. A rotating lamella is formed which spreads out along the reactor wall. Thus an enhanced surface-to-volume ratio of the liquid phase is generated where oxygen is introduced via surface aeration. Volumetric oxygen transfer coefficients (kLa) > 0.15 s^{-1} were measured. The fast moving liquid lamella efficiently prevents wall growth and foaming. Mean power consumption and maximum local energy dissipation were measured as function of operating conditions in milliliter-scale stirred tank bioreactor (V = 10 mL) and compared to a standard laboratory-scale stirred tank bioreactor with six-bladed Rushton turbines (V = 2,000 mL). Mean power consumption increases with increasing impeller speed and shows the same characteristics and values on both scales. The maximum local energy dissipation of the milliliter-scale stirred tank bioreactor was reduced compared to the laboratory-scale at the same mean volumetric power input. Hence the milliliter impeller distributes power more uniformly in the reaction medium. Based on these data a reliable and robust scale-up of fermentation processes is possible. This was demonstrated with the cultivation of the actinomycete Streptomyces tendae on both scales. It was shown that the process performances were equivalent with regard to biomass concentration, mannitol consumption and production of the pharmaceutical relevant fungicide nikkomycin Z up to a process time of 120 h. A high parallel reproducibility was observed on the milliliter-scale (standard deviation < 8%) with up to 48 stirred tank bioreactors operated in a magnetic inductive drive. Rheological behavior of the culture brot h was measured and showed a highly viscous shear-thinning non-Newtonian behaviour. The newly developed one-sided paddle impellers operated in unbaffled reactors on a 10 milliliter-scale with a magnetic inductive drive for up to 48 parallel bioreactors allows for the first time the parallel bioprocess development with mycelium forming microorganisms. This is especially important since these kinds of cultivations normally exhibit process times of 100 h and more. Thus the operation of parallel stirred tank reactors will have the potentialto reduce process development times drastically.

Key-words: Milliliter bioreactor; Streptomyces tendae; nikkomycin Z; power consumption; maximum energy dissipation; surface aeration