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Growth and recombinant protein expression with Escherichia coli in different batch cultivation media

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Abstract:

Parallel operated milliliter-scale stirred tank bioreactors were applied for recombinant protein expression studies in simple batch experiments without pH titration. An enzymatic glucose release system (EnBase), a complex medium, and the frequently used LB and TB media were compared with regard to growth of *Escherichia coli* and recombinant protein expression (alcohol dehydrogenase (ADH) from *Lactobacillus brevis* and formate dehydrogenase (FDH) from *Candida boidinii*). Dissolved oxygen and pH were recorded online, optical densities were measured at-line, and the activities of ADH and FDH were analyzed offline. Best growth was observed in a complex medium with maximum dry cell weight concentrations of 14 g L^{-1}. EnBase cultivations enabled final dry cell weight concentrations between 6 and 8 g L^{-1}. The pH remained nearly constant in EnBase cultivations due to the continuous glucose release, showing the usefulness of this glucose release system especially for pH-sensitive bioprocesses. Cell-specific enzyme activities varied considerably depending on the different media used. Maximum specific ADH activities were measured with the complex medium, 6 h after induction with IPTG, whereas the highest specific FDH activities were achieved with EnBase medium at low glucose release profiles 24 h after induction. Hence, depending on the recombinant protein, different medium compositions, times for induction, and times for cell harvest have to be evaluated to achieve efficient expression of recombinant proteins in *E. coli*. A rapid experimental evaluation can easily be performed with parallel batch operated small-scale stirred tank bioreactors.

Key-words: milliliter stirred-tank bioreactor, protein expression, optical sensors, alcohol dehydrogenase, fromate dehydrogenase, batch cultivation