Optimal control of fed-batch fermenters

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Fermentors are often run in a fed-batch manner to avoid the formation of overflow metabolites. At a high growth rate, the most efficient metabolic pathway(s) of certain microorganisms become saturated resulting in overflow metabolite production. These by-products are undesirable since their accumulation in the reactor may be inhibitory and the productivity of biomass and growth-associated products is reduced. The ideal way to run such fed-batch fermentation is to grow the cells in the reactor at the critical growth rate, *i.e.*, the point at which overflow metabolite production begins. However, since this value changes from run to run, or even during a given fermentation, its identification is not trivial. A simple way to overcome this difficulty is to maintain a very small, but constant overflow metabolite concentration in the reactor, ensuring that most of the substrate is consumed efficiently. However due to exponential cell growth, standard controllers can maintain a constant concentration only for a limited time period.

In this work an adaptive control strategy to maintain a constant overflow metabolite concentration in fed-batch fermentation is presented. The proposed approach requires the knowledge of only two system parameters: the yield coefficient, expressing the relation between overflow metabolite and substrate, and the instantaneous concentration of the overflow metabolite.

Baker's yeast fed-batch experiments were performed with the objective of maximizing biomass productivity and minimizing ethanol production. Mid-infrared spectroscopy was used to measure the ethanol concentration that was provided on-line to the controller. The results from numerous experiments have demonstrated the effectiveness of the proposed control strategy. The specific growth rate was maintained constant, at a value close to the critical point, until oxygen transfer limitation occurred. Then, the controller automatically reduced the feed rate to prevent excess ethanol production. The biomass increased from 0.5 to 65 grams per liter during the exponential growth phase. Simulation results based on this control strategy show its applicability to other overflow metabolite organisms, such as *Escherichia coli*.