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Development and Investigation of Efficient Substrate Feeding and Dissolved Oxygen Control Algorithms for Scale-Up of Recombinant E. coli Cultivation Process

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Abstract : The paper deals with model-based development and implementation of efficient control strategies for recombinant protein synthesis in fed-batch E.coli cultivation processes. Based on experimental data, a kinetic dynamic model for cultivation process was developed. This model was used to determine substrate feeding strategies during the cultivation. The proposed feeding strategy consists of two phases – biomass growth phase and recombinant protein production phase. In the first process phase, substrate-limited process is recommended when the specific growth rate of biomass is about 90-95% of its maximum value. This ensures reduction of glucose concentration in the medium, improves process repeatability, reduces the development of secondary metabolites and other unwanted by-products. The substrate limitation can be enhanced to satisfy restriction on maximum oxygen transfer rate in the bioreactor and to guarantee necessary dissolved carbon dioxide concentration in culture media. In the recombinant protein production phase, the level of substrate limitation and specific growth rate are selected within the range to enable optimal target protein synthesis rate. To account for complex process dynamics, to efficiently exploit the oxygen transfer capability of the bioreactor, and to maintain the required dissolved oxygen concentration, adaptive control algorithms for dissolved oxygen control have been proposed. The developed model-based control strategies are useful in scale-up of cultivation processes and accelerate implementation of innovative biotechnological processes for industrial applications.

Keywords : adaptive algorithms, model-based control, recombinant E. coli, scale-up of bioprocesses
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