ALTERNATIVE CONTROL STRATEGIES FOR BIOPROCESSES

by

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Dedicated

To

My Papa & Mummy...

CERTIFICATE

This is to certify that the thesis entitled **"Alternative control strategies for bioprocesses"**, being submitted by **Mr. Amalendu Prakash Ranjan** to the Indian Institute of Technology, Delhi, for the award of the degree of "Doctor of Philosophy" is a record of the bonafide research carried out by him, which has been prepared under my supervision and guidance in conformity with rules and regulations of the "Indian Institute of Technology, Delhi". The results described in it have not been submitted in part or full to any other University or Institute for the award of any Degree / Diploma.

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ABSTRACT

This thesis documents a comparative study of the performance of alternative control strategies applied to the fed-batch production *L*–methionine. Since the synthesis of methionine requires seven ATPs per molecule, the metabolic pathway leading to its synthesis is strictly regulated at the cellular level to conserve energy. Apparently, regulation at the cellular level results is highly nonlinear state-time profiles used to characterize bioprocesses. Processes exhibiting a certain degree of nonlinearity due to inherent complexity are not easy to predict or control. In such circumstances, special attention must be devoted during the design and implementation of controllers. Fed-batch methionine production possesses an appropriate degree of nonlinearity so that designing a satisfactory controller for this process presents a challenge. Consequently, by solving the control problem for this process in turn becomes equivalent to providing a solution for a range of bioprocesses. A systems-based methodology was followed to ensure that the strategies proposed and results obtained would be applicable to other similar processes, with at the most, minor modifications.

A model for fed-batch methionine production was first developed. This model was examined from a systems perspective to ensure that it possessed the correct structure in terms of controllability and observability. Its parameters were computed using existing experimental data. To describe the dynamics of cell mass, residual glucose and methionine concentration, an exponential kinetic term was used in combination with a metabolic switching function and a term for describing the dependence methionine reutilization on residual glucose concentration was incorporated. The model was validated using five different statistical measures and its prediction of states was verified against experimental data.

Using this model a decoupled input-output linearizing controller (DIOLC) was developed. This controller split the control system into two separate loops – substrate controlled by substrate feeding rate and dissolved oxygen controlled by airflow rate. The performance of DIOLC was benchmarked against the performance of a PI controller using five test cases that were categorized under high oxygen demand regime, low oxygen demand regime and methionine production. In addition, parametric uncertainty conditions are simulated to test the robustness and noise rejection capability of the designed controllers. Although, the PI controller was accurately tuned using the Astrom and Rivera criteria, it performed poorly compared to DIOLC because the PI controller was not designed to eliminate the interaction between the inputs and outputs.

Since the development of a structurally correct model possessing acceptable features that enable accurate prediction of nonlinear dynamics is demanding, a different strategy was sought that did not have a strong dependence on the quality of the model. Therefore, the suitability of an adaptive control methodology was examined but with a systems flavor. Borrowing some of the principles of decoupling used for DIOLC, a decoupled adaptive controller (DAC) was designed. This controller was evaluated under the same test conditions used for the DIOLC and PI controllers. Results showed that in comparison to DIOLC, DAC performed better in controlling substrate concentration but poorly in controlling the dissolved oxygen concentration. It was also observed that the DIOLC performs better in the high oxygen demand condition while the DAC performs better under low oxygen demand conditions. As a result, a combination of strengths of both these controller was used to develop the third control strategy.

The third control strategy, called the DAC-DIOLC controller is constructed on a decoupled system description of the methionine process. The substrate concentration – feed rate loop is controlled using DAC while the dissolved oxygen concentration – airflow rate loop is controlled using the DIOLC. The performance of the DAC-DIOLC displays an improvement over the performance of the individual controllers. The parametric uncertainty studies were carried out in conjunction with noise in the measurements of process outputs. The state-time and input-time profiles of DAC-DIOLC exhibit marked improvement. A comparison of these results are presented and discussed.

Finally, an enhancement of the DAC-DIOLC controller was constructed by splitting the control of dissolved oxygen between the airflow rate and agitation speed as a dual inputs. The design and development of such a dual inputs control is using principles of systems theory is presented for the first time. This design is based on a correlation between the oxygen mass transfer coefficient, airflow rate and agitation speed that was derived in course of the development of the previous controllers. Using a set of heuristic arguments, the Dual Input- DAC-DIOLC was implemented with airflow rate as the primary input and the agitation speed as the secondary input. The performance of the Dual Input DAC-DIOLC controller was benchmarked against the performance of the other developed control strategies, namely, DIOLC, DAC and DAC-DIOLC. Overshoot, rise time and decay ratio were used to characterize the controlled outputs and the deviation of the control action with respect to the mean obtained in the absence of noise or parametric variation (ground case) was used to characterize quality of control inputs. The results established without ambiguity that the Dual Input- DAC-DIOLC was the best among the four designed control strategies.

The exhaustive theoretical work embodies the development of alternative control strategies that would be easily applicable to other similar bioprocesses. The information contained herein will be invaluable to the control and process engineer. More importantly, this work has created innumerable leads that may be picked up for initiating new research.

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