CONTROL OF BIOREACTOR WITH ADAPTIVE NEURAL NETWORK SYSTEM

RAJIB NAYAK

DEPARTMENT OF BIOCHEMICAL ENGINEERING & BIOTECHNOLOGY

INDIAN INSTITUTE OF TECHNOLOGY, DELHI

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By

RAJIB NAYAK

Department of Biochemical Engineering & Biotechnology

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Dedicated to….

My Baba (Mr. Anil Kumar Nayak)
and
Maa (Mrs. Sandhya Nayak)

My idol, inspiration and who gave me every opportunity to realize and fulfill my dreams.

CERTIFICATE

This is to certify that the thesis entitled **"Control of Bioreactor with Adaptive Neural Network System"**, being submitted by **Rajib Nayak** 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.

Dr. James Gomes
Associate Professor,
School of Biological Science,
Indian Institute of Technology, Delhi,
New Delhi – 110016
India.

ABSTRACT

Bioprocess engineering has seen distinct improvement in techniques of monitoring, modeling and control over the last two decades. Further, with the rapid improvement in biotechnological research has lead to the continuing development and discovery of new clinically and industrially important biomolecules everyday, there are a host of variables that always need to be determined indirectly due to lack of reliable and robust on–line hardware and / or bio–sensors. Since bioprocesses are characterized by inherently nonlinear, time varying, considerably slow in response and endure phenomenological model uncertainty, employing neural network based "intelligent" software sensors systems is an attractive technique for innovative bioprocess control development.

The main focus of this research work concerns the search and study of ensemble of neural networks methodologies aiming at a more precise and robust estimation of state variables to develop innovative bioprocess monitoring and control strategies. In this respect, Sequential Adaptive Networks (SAN) based 'soft sensor' for state estimation and one sampling step ahead prediction of key state variables is developed. SAN is an assembly of chronologically ordered single neural networks, with one sub–network assigned to each sampling interval, so that feature memory is distributed. Each of these networks in turn is adapted to changing process conditions based on on–line measurement that guide the entire ensemble along the evolution of the process. The information of the metabolic state of the process obtained from *DO* measurement is used to update the weights of the SAN, enabling an on–line adaptation to changing process dynamics.

Two bioprocesses, yeast production by *Saccharomyces cerevisiae* and methionine production by *Corynebacterium lilium* were employed to evaluate the performance of the SAN based control strategies. Sonnleitner & Käppeli model was used to describe the yeast production. The model developed for methionine production contains an exponential kinetic structure for describing the nonlinearities and metabolic switching function for describing oxygen dependency. In order to appraise the developed model, six different statistical analyses were carried out.

Three SAN based control strategies were designed for yeast production system. The control objectives were biomass concentration tracking at a predefined slope and maximization of biomass production while keeping yeast concentration at a minimum value. For methionine production process, two control objectives were defined. First control objective was methionine concentration tracking along a linear profile and a SAN assisted mechanistic feed forward controller was designed to achieve the objective. In the second control strategy, an objective function was defined to optimize the methionine production. A statistical framework was developed by combining the objective function, model equations and operational constrains on state variables to get the range of controller parameters for optimum methionine production.

A cubic data domain with different combination of state variables and parameters for each control strategy was constructed for training, validation and implementation of SAN. The SAN was trained for an average threshold Root Mean Square Error (RMSE) per data point of 10^{-5} for all the control strategies. The recall profiles matched the training dataset profiles with recall RMSE of the order of 10^{-5}. Cross validation was done to evaluate the accuracy of the SAN prediction. Data sets for validation were farthest distance from the training data sets. Results showed that the overall Normalized Root Mean Square Error (NRMSE) for each data sets of each control strategy was in the order of 10^{-3} to 10^{-4}.

In case of implementation, SAN based control strategies were tested in three different simulated process environments namely, ideal case, up to 10% noise in measured variable (*DO*) and process parameters uncertainty. In ideal case, results showed that overall NRMSE in the order of 10^{-3} to 10^{-4} for all the data sets with periodic adaptation of SAN. To simulate actual process conditions, the *DO* output of the process model was combined with 5% and 10% white noise and presented to SAN. The results showed that the prediction error was increased for both the cases and NRMSE reached in the order of 10^{-3} for 5% noise and 10^{-3} to 10^{-2} for 10% noise. The parameters defining specific growth rate were randomly varied up to ±40%, to generate a truly parameter uncertain environment. The results showed that the overall NRMSE for prediction was of the order of 10^{-3} and the performance of SAN controlling under condition of model–plant mismatch was acceptable.

In simulated environment, the final concentration of methionine achieved for SAN feed forward controller and SAN hybrid controller was 4.8 g L^{-1} and 6.9 g L^{-1} respectively compared to 1.8 g L^{-1} when no control action was taken. The SAN assisted all the developed controller is steady, robust and exhibited stable tracking of control objective in different simulation environment. It is perceived that it can be used for on–line real time implementation in fed-batch bioprocesses.

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Rajib Nayak

Rajib Nayak

CONTENTS