Batch-to-Batch Iterative Learning Control of a Fed-Batch Fermentation Process

Abstract

In this work, Iterative Learning Control on a fed-batch fermentation process using linearised models has been studied. The repetitive nature of batch processes enables ILC to obtain information from a previous batch in order to improve the performance of the current batch such that the product quality converges asymptotically to the desired trajectory. The basic batch to batch ILC law presents the control action of a current batch as a summation of the control action from the previous batch and the deviation of the output trajectory from the desired reference trajectory incorporation with a learning rate. In a bid to address the issue of the process non-linearity, the control policy and the output trajectory were linearised around their respective nominal trajectories. The linearised models were then identified using Multi Linear Regression (MLR), Principal Component Analysis (PCR) and Partial Least Squares (PLS). In order to curb the effects of plant-model mismatches and process variations, the linearised models were reidentified after each batch operation. This was done by selecting the immediate previous batch as the nominal batch and then adding the recently obtained process data into the historical data batch on completion of the current batch run. The weighting matrices in the objective function were carefully selected taking into consideration that they have a major influence on the robust performance of the process. In using PLS and PCR models the issue of process collinearity was effectively addressed. The proposed batch to batch ILC strategy was applied to a simulated fed-batch fermentation process for the production of secreted protein. The results of the optimal control policy were comparable to that obtained in using full mechanistic model. ILC, a simple but yet an effective optimal control strategy has demonstrated to be a viable option in complex processes such as batch processes where mechanistic models are difficult to develop.

Keywords- Iterative Learning Control, batch process, fed-batch fermentation, batch to batch ILC, control policy.

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List of Nomenclature

d_k	Model disturbance sequence
e_{k-1}	Error from previous run
f_p	Protein expression rate
G_s	Linearised model
h	Sampling time
k	Batch index
L	ILC learning gain
m	Glucose concentration of the feed stream, g/l
N	Sampling interval
P_M	Amount of secreted protein on a unit culture volume basis
P_T	Total amount of protein on a unit culture volume basis
q	Feed flow rate, l/h.
Q, R	Positive-definite matrices
S	Culture glucose concentration, g/l
t	Time for kth batch run
U_k	Control input for the previous batch
U_{k+1}	Control input of the current batch
U_s	Nominal input trajectory
V	Culture Volume, l
v_k	Vector of measurement noises
w_k	Matrix of model errors
X	Culture cell density, g/l
Y	Yield of glucose (g)/cell mass (g)
Y_d	Desired output trajectory

Y_k	Output for previous batch
Y_s	Nominal output trajectory
ϕ	Protein secretion rate
μ_x	Specific growth rate of the host cell

List of Acronyms

CAFNN	Control affine Feed Forward Neural Network
FNN	Feed Forward Neural Network
IDP	Iterative Dynamic Programming
ILC	iterative learning control
KICR	Kernel Independent Component Regression
MLR	multiple linear regression
MPC	model predictive control
ODE	ordinary differential equation
OS-ELM	Online Sequential Extreme Learning Machine.
PCR	principal component regression
PID	proportional–integral–derivative
PLS	partial least square
RC	Repetitive control
R2R	Run to run
SHRO	Shrinking Horizon Re-Optimization
SQP	Sequential Quadratic Programming
SVR	Support Vector Regression

Chapter 1 : INTRODUCTION

1.1 Introduction

Fermentation is a chemical process in which organic substances are transformed into simpler compounds by the action of enzymes produced by micro-organisms (William and Akiko, 2004). This process has been in existence since 6000 B.C. and in every civilization, at least one or two products from fermentation has been found in its heritage (Gutierrez-Correaa and Gretty, 2010). Fermentation which started with local production of alcoholic beverages, through series of scientific researches, found its way into food processing, chemical, agricultural and pharmaceutical industries in later years. Improvements on fermentation process have been noted which started with making of alcoholic beverages down to food processing and drug production. A fermentation system is bound to a bioreactor providing the environment so that the specific biological and technological demands are met. (Gutierrez-Correaa and Gretty, 2010).

Fermentation process is industrially divided into three distinct types, continuous, batch and fed-batch fermentation. Continuous fermentation involves the addition substrate continuously into the bioreactor at a fixed rate. Simultaneously, an equivalent amount of the product is also harvested. In a batch process, the fermentation process is carried out with the addition of substrate or removal of the products during the course of the process. However, oxygen, an antifoam agent, and acid or base is added to control the ph. On completion of the batch run, the products are taken out and the reactor is cleaned out for another run. Fed-batch fermentation is an extension of the batch process. It involves the injection of nutrients into the bioreactor during fermentation in which the product(s) remain in the bioreactor till the batch run ends (Yamanè and Shimizu, 1984). In a fed-batch process the medium is supplemented with nutrients that are depleted or that may be needed for the terminal stages of the culture. Following that there is no withdrawal of liquid, the volume of the reactor increases till the final batch time. The difference between fed-batch and batch operation is that in the former feed is continuously supplied. An obvious advantage of fed-batch operation is that nutrient levels are continuously varied to achieve favorable growth conditions without significant risk of culture contamination (Henson, 2006). Over the years, fed batch process has been preferred over the normal batch process in the manufacturing industry. Production of by-product is a major threat in any production process. Fed batch fermentation limits the production of bye products by controlling the growth limitation of substrate.

Fermentation process depends on an adequate optimization which should be done during the development of the process to ensure process stability, inhibit the influence of disturbance, minimise cycle batch time and for maximum production and profit. The fed-batch processes presents the greatest challenge in optimal control (Zhang, 2004). Due to the ever-increasing market competition and need for high value added products, there is a growing need to develop optimal control strategies in the manufacturing industry. Lot of researchers have made efforts to come up with different optimal control strategies each with its success and limits. In order to come up with a good optimal strategy, the dynamics of the process involved have to be well understood. According to Van Impe and Bastin (1995), the design of high-performance model-based control algorithms for batch processes is limited by two major problems. Firstly, due to the complexity of these processes, their kinetics are poorly understood nonlinear functions coupled with the parameters that are generally time-varying. Secondly, there is a limitation of reliable online sensors suitable for real-time monitoring of the process variables. This calls for an adequate optimal solutions. Attempts have been made in the use of mechanistic models to describe these processes. However due to their complex nature developing mechanistic models can be time consuming, costly and at the end can turn up being unrealistic. A lot of researchers have deemed it wise to resort to data based methods to solve this growing need. Data based methods are empirical methods that develops a relationship between the measured inputs to the outputs that describe the process response to changes in inputs (Cinar *et al*, 2003). An important objective of batch processes lies in improving the performance of the process from batch to batch. Due to the repetitive nature of these processes, information from the previous batches can provide an insight on how to improve subsequent batches. Most learning control strategies utilize this set of information. Iterative learning control is one of such promising methods.

Iterative Learning Control (ILC) is an optimal control strategy that tries to address the problem of transient response performance for systems that operate in a repetitive manner. (Moore, 2006). It adjusts the process feed rate based on the errors observed from past operation. (Moore, 2006). ILC overcomes the shortcomings posed by the need for a complete and accurate knowledge on the process model before a desired product quality is achieved. Utilizing the information on the control policy and error on the previous batch, it iteratively updates the input from trial to trial till the desired reference trajectory is achieved. In order to avoid plant model mismatches and unknown disturbances, the basic approach to ILC is to linearise the process around a fixed nominal control trajectory. However significant batch to batch variation could lead to the optimal control strategy becoming prone to error and failing in its principal objective of achieving the desired trajectory. To overcome this limitation, the linearised models are preferably updated after each batch operation. In doing this, the non-linear behaviour of processes such as fermentation is fully addressed.

ILC has relatively become well established in the area of optimal control. With its origin in robotics industries, ILC has successfully moved into other industries such as electrical systems, rotary systems, biomedical systems, mechanical systems, aerodynamics system and process systems.

1.2 Aims and Objectives

The aims of this work is listed below;

- To develop an ILC strategy for a fed batch bioreactor for the production of secreted protein to address model-plant mismatches and unknown plant disturbances.
- To generate and compare the performance of different linearised models used in developing the batch to batch ILC strategy. The model parameters will be generated using Multiple Linear Regression (MLR), Partial Least Square (PLS) and Principal Component Regression (PCR).
- To compare batch to batch ILC performance based on fixed and updated model parameters, control policy and product quality.

1.3 Summary

ILC is a form of an intelligent control which overcomes the shortcomings of traditional controller design. Its application is mostly found in complex systems which operate in a repetitive manner. With issues of non-linearity and complexity mostly associated with batch processes, ILC has become a good optimal control option for most batch related industries due to its ability to address these issues.

1.4 Work Layout

This work is arranged in the following way. Chapter 2 presents a literature review on Iterative Learning Control of a fed batch fermentation process. Discussion on fermentation and its optimization is presented. ILC and its concept followed by its application, advantages, and limitation, and integration with other controllers are looked into. This is followed by a review on past work done on batch to batch ILC. A brief summary on regression models and their mathematical representation is given and finally, the mathematical development of the batch to batch ILC law used in this work which were subsequently coded in MATLAB is presented.

Chapter 3 presents the kinetics and dynamic models and simulation of the fed batch reactor for the production of secreted protein. A brief introduction on production of secreted protein is given. The simulation result for this models through series obtained through series of MATLAB coding are used as a case study for this work.

Chapter 4 presents a step by step algorithm of the proposed control scheme.

Chapter 5 presents the results of the batch to batch ILC strategy on the fed batch reactor. Comparisons on the outcomes of the fixed and updated batch to batch ILC control on the different linear regression methods used are discussed.

Chapter 6 gives a conclusion on the work done and outlines suggestions for future work.