

Evaluating Evolutionary Algorithms and Differential Evolution for the Online Optimization of Fermentation Processes

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Abstract. Although important contributions have been made in recent years within the field of bioprocess model development and validation, in many cases the utility of even relatively good models for process optimization with current state-of-the-art algorithms (mostly offline approaches) is quite low. The main cause for this is that open-loop fermentations do not compensate for the differences observed between model predictions and real variables, whose consequences can lead to quite undesirable consequences. In this work, the performance of two different algorithms belonging to the main groups of *Evolutionary Algorithms* (EA) and *Differential Evolution* (DE) is compared in the task of online optimisation of fed-batch fermentation processes. The proposed approach enables to obtain results close to the ones predicted initially by the mathematical models of the process, deals well with the noise in state variables and exhibits properties of graceful degradation. When comparing the optimization algorithms, the *DE* seems the best alternative, but its superiority seems to decrease when noisier settings are considered.

Keywords: Fermentation processes, Online optimization, Differential Evolution, Real-valued Evolutionary Algorithms.

1 Introduction

In recent years, many efforts have been devoted to the optimization of processes in bioengineering as a number of valuable products such as recombinant proteins, antibiotics and amino-acids are produced using fermentation techniques. A problem that has received special attention is the dynamic optimization of fed-batch bioreactors. This process has traditionally been conducted on the substrate feed rate as key manipulated variable in operation. The optimization problem is therefore solved before the beginning of the fermentation process (open-loop optimal control) and consists on finding an expression or a sequence of values for

the feeding rate that maximizes an objective function that represents the process productivity, subject to the constraints represented by a dynamical model.

Several optimization methods have been applied to solve this kind of problem. It has been shown that for relatively simple bioreactor systems, which are expressed in differential equations models, the optimization problem can be solved analytically from the Hamiltonian function by applying the Minimum Principle of Pontryagin [14]. However, in the majority of the cases reported, determination of the optimal feed rate profile has a problem of singular control.

Numerical methods make a distinct approach to dynamic optimization. The gradient algorithms are used to adjust the control trajectories in order to iteratively improve the objective function [3]. In contrast, dynamic programming methods discretize both time and control variables to a predefined number of values. A systematic backward search method in combination with the simulation of the system model equations is used to find the optimal path through the defined grid. However, in order to achieve a global minimum, the computational burden is very high [3].

An alternative comes from the use of algorithms from the *Evolutionary Computation (EC)* field, which have been used in the past to optimize nonlinear problems with a large number of variables. These techniques have been applied with success to the optimization of feeding or temperature trajectories [8][1], and, when compared with traditional methods, usually perform better [12][5].

However, even when the mathematical models used for open-loop optimization are reliable and validated by experimentation, in a real environment several sources of noise can contribute to changes in the observed values of the state variables. These issues are of particular importance when dealing with recombinant high-cell density fermentations, as the process, besides the nonlinearities exhibited, tends to change dramatically upon some events, like induction. Also, it is likely that there exists a time-variance of both yield and kinetic parameters not contemplated in most process models. These scenarios have an important impact on the experimental results that end up being worse than the ones predicted after running the offline optimization.

An alternative to cope with model inaccuracies is the use of online optimization algorithms that periodically generate new solutions as the process is running, making use of the measurement of relevant state variables for update of the internal model. Indeed, unlike the previously stated alternatives where the optimization is conducted prior to the experimental process, in this case, the optimization is performed simultaneously, taking into account values of the state variables measured by sensors within the fermentation process.

In this work, the performance of two different algorithms belonging to the main groups of *Evolutionary Algorithms (EA)* and *Differential Evolution (DE)* is compared in this task of online optimization. These methods were the ones that performed better in offline optimization, in a previous study [6]. Three case studies were taken from literature in order to test the performance of both algorithms. These are used to perform an offline optimization and then a simulation of a real-world fermentation is conducted. The relevant state variables are, in