



## Optimization of fed-batch fermentation processes using the Backtracking Search Algorithm



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### ARTICLE INFO

#### Article history:

Received 8 November 2016

Revised 19 June 2017

Accepted 22 July 2017

Available online 24 August 2017

#### Keywords:

Fed-batch fermentation

Backtracking Search Algorithm

Evolutionary algorithms

Wastewater treatment

Feeding trajectory optimization

Sewage sludge

### ABSTRACT

Fed-batch fermentation has gained attention in recent years due to its beneficial impact in the economy and productivity of bioprocesses. However, the complexity of these processes requires an expert system that involves swarm intelligence-based metaheuristics such as Artificial Algae Algorithm (AAA), Artificial Bee Colony (ABC), Covariance Matrix Adaptation Evolution Strategy (CMAES) and Differential Evolution (DE) for simulation and optimization of the feeding trajectories. DE traditionally performs better than other evolutionary algorithms and swarm intelligence techniques in optimization of fed-batch fermentation. In this work, an improved version of DE namely Backtracking Search Algorithm (BSA) has edged DE and other recent metaheuristics to emerge as superior optimization method. This is shown by the results obtained by comparing the performance of BSA, DE, CMAES, AAA and ABC in solving six fed batch fermentation case studies. BSA gave the best overall performance by showing improved solutions and more robust convergence in comparison with various metaheuristics used in this work. Also, there is a gap in the study of fed-batch application of wastewater and sewage sludge treatment. Thus, the fed batch fermentation problems in winery wastewater treatment and biogas generation from sewage sludge are investigated and reformulated for optimization.

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### 1. Introduction

The diverse applications of optimization which range from manufacturing and engineering to business and medication have attracted many researchers to explore the field. Since the mid-20th century, researchers have developed a number of high performance optimization methods by taking inspiration from biology, physics, social and cultural behaviour, neurology and other disciplines. For instance, particle swarm optimization (PSO) (Kennedy & Eberhart, 1995) is a bio-inspired metaheuristics which is based on the metaphors of social interaction and communication (e.g., fish schooling and bird flocking). These algorithms are classified as a branch of optimization techniques called swarm intelligence metaheuristics. These metaheuristics use a process of trial and error to discover the solution of a problem and consists of certain trade-off of randomization and local search. They have a unique feature where more than one solution is evaluated simultaneously in a single iteration. Their most appealing characteristics are

their derivation-free mechanisms, relatively simple structures and stochastic nature. This enables faster convergence and less expensive computation as compared to deterministic method.

The field of biotechnology, which is considered as one of the important knowledge-based “economy” contains many problems that can take advantage of the optimization process by using metaheuristics. One such problem is the fermentation problem. In fermentation problem, the maximization of yield in a bioreactor is often regarded as the main goal. The yield efficiency is defined as the ratio of product against substrate. In the context of fed-batch fermentation, the timing and the amount of substrate input can directly affect the production of a bioreactor. As the complexity of the chemical reaction process is high along with high experimental cost, an automated system is needed to quickly calculate the optimal input profile that will optimize the yield. In order to obtain proper simulation of the process, usually differential equations that model the mass balances of various state variables are formulated. To this end, an expert system that combines swarm intelligence-based metaheuristics with simulation models of fed-batch fermentation problem is simplest yet effective in optimization of fed-batch problem.

In fermentation and bioprocess technology, the utilization of fed-batch operation is considered common. In biological

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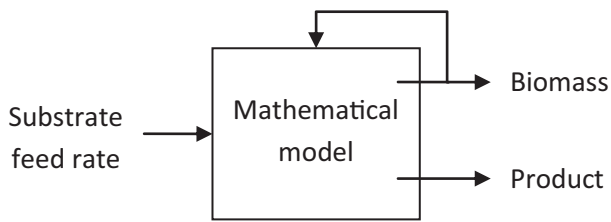


Fig. 1. Schematic illustration of a fed-batch fermentation process simulation.

wastewater treatment however, batch mode is still dominantly used and fed-batch is regarded as a relatively new technique (Montalvo et al., 2010). In a basic process of fed-batch wastewater treatment, the wastewater is fed slowly into the aerated bioreactor to reduce the chemical oxygen demand (COD) in the aeration tank. The disposal of sludge is one of the major problems in municipal wastewater treatment, and constitutes up to half of the operating costs of a Waste Water Treatment Plant (WWTP) (Baeyens, Hosten, & Van Vaerenbergh, 1997). Though different methods for sludge disposal exist, anaerobic digestion is one of the preferred routes (Appels, Baeyens, Degrève, & Dewil, 2008). The anaerobic digestion kinetics for methane fermentation of sewage sludge was proposed by Sosnowski, Klepacz-Smolka, Kaczorek, and Ledakowicz (2008). However, the proposed model was only designed for batch mode operation. Considering the advantages of fed-batch process in various fermentation problems, it is appropriate to convert this model into fed-batch mode. The utilization of fed-batch technique can increase the output of desirable products such as protein and bio-fuel in various fields of biotechnology and hence contribute to the development of renewable energy production and sustainable science.

The optimization of fed-batch fermentation process was intensively studied in recent years. Chen, Nguang, Chen, and Li (2004) proposed the optimization of a fed-batch bioreactor using a cascade recurrent neural network (RNN) model and modified genetic algorithm (GA). They applied their method in the fed-batch fermentation of a common yeast species in food technology, *Saccharomyces cerevisiae*. Levišauskas and Tekorius (2005) investigated various fed-batch fermentation processes optimization using the feed-rate time profile approximating functions and the parametric optimization procedure. In their work, four types of time functions namely constant feed-rate, ramp-type function, exponential function and a network of radial basis functions are compared. The parametric optimization problems were solved using chemotaxis random search algorithm. Liu, Gong, Shen, and Feng (2013) proposed a new nonlinear dynamical system to formulate the fed-batch fermentation process of glycerol bioconversion to 1,3-propanediol (1,3-PD). Peng et al. (2014) studied the fed-batch fermentation process of an antibiotic, iturin A using an artificial neural network-genetic algorithm (ANN-GA) and uniform design (UD).

In fed-batch fermentation simulation, a key variable in the optimization process is the substrate feed rate. The unit of substrate feed rate is defined as the volume per unit time ( $V/t$ ). This variable provides the feeding profile for the bioreactor to provide a certain amount of input at a certain time during the fermentation process. Fig. 1 shows the schematic illustration of a typical simulated fed-batch fermentation model. The substrate feed rate is given as an input to the system. A mathematical model consists of some ordinary differential equations describing the relationship between operating parameters that includes inputs, intermediary and outputs. The biomass and product form the output of the system. The biomass is continuously used by the substrate to produce yield. The most suitable optimization strategy is the use of numerical methods which depend on the use stochastic algorithms.

This is because complexity involved in analytical approaches will increase with the increasing number of state and control variables. Deterministic algorithms also have a high computational overhead as well as have a tendency of premature convergence towards local optima.

Stochastic algorithms or metaheuristics have been previously applied on various bioprocess optimization problems. Evolutionary algorithms (EA) have been utilized on the bioprocess of protein production with *E. coli*, and they have been compared with first order gradient algorithms and with dynamic programming by Roubos, van Straten, and van Boxtel (1999). The optimization of feeding profile for ethanol and penicillin production was applied by Kookos (2004) using Simulated Annealing while the optimization of protein production in *E. coli* was applied using Ant Algorithms by Jayaraman, Kulkarni, Gupta, Rajesh, and Kusumaker (2001). Chiou and Wang (1999) used Differential Evolution (DE) for the optimization of the *Zymomonas mobilis* fed-batch fermentation while Wang and Cheng (1999) used the same algorithm for ethanol production in *Saccharomyces cerevisiae*. Sarkar and Modak (2004) used a genetic algorithm based technique to address fed-batch bioreactor application problems with single or multiple control variables.

A recent study shows DE is a better solution for bio-process applications (Banga, Moles, & Alonso, 2004). Da Ros et al. (2013) have even suggested DE hybrids for these applications after showing DE as the better method in the estimation of the kinetic parameters of an alcoholic fermentation model. Rocha, Mendes, Rocha, Rocha, and Ferreira (2014) compared the performance of EAs, DE and Particle Swarm Optimization (PSO) on four different bioprocess case studies taken from the scientific literature and found that DE had better performance when compared to other algorithms.

In recent years, many new nature-inspired algorithms have emerged such as Particle Swarm Optimization (PSO) (Kennedy & Eberhart, 1995), Artificial Bee Colony Optimization (ABC) (Basturk & Karaboga, 2006), Cuckoo Search (CS) (Yang & Suash, 2009), Firefly Algorithm (FA) (Yang, 2010) and Artificial Algae Algorithm (AAA) (Uymaz, Tezel, & Yel, 2015). A detailed discussion on the proliferation of search algorithms can be seen in Sörensen (2015) and an overview of some of the most widely used can be seen in Burke and Kendall (2014). These algorithms were applied to various problems and have shown improved performance compared to classical algorithms. One of these algorithms, the Backtracking Search Optimization Algorithm (BSA) was recently proposed by Civicioglu (2013). It was developed for solving real-valued numerical optimization problems based on the behaviour of living creatures in social groups revisiting at random intervals to preying areas enriched by food source. BSA was developed based on DE and has many elements similar to DE. However, it improved upon DE by incorporating new elements such as improved mutation and crossover operators and the utilization of a dual population. BSA also has only one control parameter compared to DE which requires two parameters for fine-tuning. With these improvements, it is expected that BSA will perform better than DE. BSA has shown promising results in solving boundary-constrained benchmark problems. Due to its encouraging performance, several studies have been done to investigate BSA's capabilities in solving various engineering problems (Askarzadeh & Coelho, 2014; Das, Mandal, Kar, & Ghoshal, 2014; El-Fergany, 2015; Guney, Durmus, & Basbug, 2014; Song, Zhang, Zhao, & Li, 2015).

BSA uses a unique mechanism for generating trial individual by controlling the amplitude of the search direction through mutation parameter,  $F$ . This enables a balanced global and local search, thus enhances its problem solving ability. BSA also consults its historical population which is stored in its memory to generate more efficient trial population, resulting in improved searching ability. Other algorithms such as PSO, DE and DE Covariance Matrix Adap-

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