Parameter Estimation for Simulation of Glycolysis Pathway by Using an Improved Differential Evolution

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Abstract. An improved differential evolution (DE) algorithm is proposed in this paper to optimize its performance in estimating the germane parameters for metabolic pathway data to simulate glycolysis pathway for *Saccharomyces cerevisiae*. This study presents an improved algorithm of parameter sensitivity test into the process of DE algorithm. The result of the improved algorithm is testifying to be supreme to the others estimation algorithms. The outcomes from this study promote estimating optimal kinetic parameters, shorter computation time and ameliorating the precision of simulated kinetic model for the experimental data.

Keywords: Parameter Estimation, Differential Evolution, Evolutionary Algorithm, Optimization, Metabolic Engineering.

1 Introduction

Current studies basically have concentrated on the modification of the computer readable data from the biological activity which allows the mean of analysis. Thus, studying in the metabolic pathway permits scientists to simulate the process inside the cell by a mathematical modeling. To develop a valid pathway model that functions as biological functions simulator is the goal for the study of system biology. Parameter estimation is one of the key steps in mathematical model. Regrettably, it has encountered a few problems such as increasing number unknown parameters and equations in the model which contributes to high complexity of the model [1] and low accuracy due to the existence of noise data [2]. Therefore, the aim of this study is to propose an intelligent algorithm of incorporate DE and parameter sensitivity test to resolve the rising unknown parameters which lead to the complexity of the model. The advantages of DE are effectiveness, speed, simplicity and ease of use as it consists of only few control parameters [3]. Moreover, parameter sensitivity test also plays an important role in generating a model with less irrelevant parameters which can minimize computational burden that leads to less computational effort and time.

2   Method

Parameters that are comprised of the glycolysis pathway model for *Saccharomyces cerevisiae* will first undergo parameter sensitivity test to identify relevant parameters. Next, these identifiable parameters will undergo DE to estimate its optimal value.

2.1   Parameter Sensitivity Test [4]

I.   Model checking and retrieve necessary information (parameters, states and reactions).
II.   Determine steady-state for nominal model.
III.   Determine steady-state for perturbed model.
IV.   Output steady-state sensitivity in graph.

2.2   Differential Evolution Algorithm [5]

I.   Generate random population of m x n solutions for the problem within the higher and lower bound where m = number of identifiable parameters and n= number of generation. Solutions are presented in the form of floating points.
II.   Evaluate the fitness function f(x) of each individual for n solution where each individual represents a candidate parameter value.
III.   Create new population by repeating the following steps until new population is complete:

  o   Randomly select three parent individuals from a population for each n by the following formula where *i* is the parent index.

$$individual\_i= floor(rand() * population\ size) + 1 . \tag{1}$$

  o   New generation mutate by the following formula for each population size.

$$temp\_population(i)=Pop(individual3)+F*(Pop(individual1)-Pop(individual2)) . \tag{2}$$

  Where F is differentiation constant and Pop is the original population matrix.

  o   If randb(j)<CR or j=rnbr(i)

    Crossover occurs and generated new population.

  Else

    No crossover and original population remain.

  Where Randb(j)= jth random evaluation of a uniform random number generator [0,1] and Rnbr = random chosen index {1,2, …D}.

IV.   If end condition is satisfied stop and return optimal parameter in current population else go to step II.

3   Result and Discussion

Execution times with 87 unknown parameters shown in Table 1 are greater than the execution time shown in Table 2 with 4 unknown parameters. It is shown that the lesser the execution time needed when the smaller the number of parameters for the

Table 1. Execution time (without parameter sensitivity test with 87 unknown parameters)

	Nelder-Mead	SA	GA	DE
Execution time	3:42:57	5:44:43	0:08:53	0:07:52

Table 2. Execution time (with parameter sensitivity test with 4 unknown parameters)

	Nelder-Mead	SA	GA	DE
Execution time	0:07:13	0:09:48	0:08:52	0:07:17
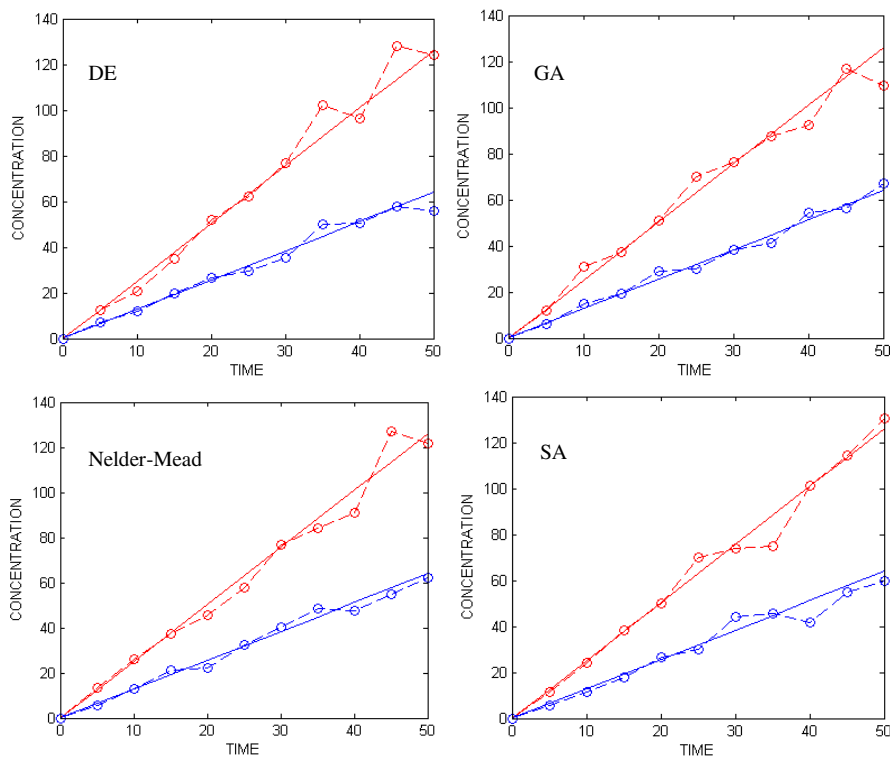
Fig. 1. Measurement data versus simulated data (-o simulated result, -- measurement result; red line- species 4, blue line – species 10)

algorithm. In Table 2 Nelder-Mead and DE are the two algorithms that required less execution time. Unfortunately for Nelder-Mead as the number of unknown parameters increase, the execution time increases dramatically whereas this is not occurs in DE. DE is shown need a minimum execution time even with bigger population size. Even though the execution time of DE is short consistently, the result that generated by DE are almost similar with the other estimation algorithms respectively which shown in Figure 1. Thus, the proposed method of the incorporation of parameter sensitivity test and DE solves the parameter estimation problems which reduces the number of unknown parameters and the computational time and raises the accuracy of the simulated model with the actual model.

4   Conclusion and Future Work

In conclusion, DE is shown outperform than other stochastic optimization algorithms in this study but regrettably it may easily be captured in local minima. Basically, the concentration will be on global minima rather than local minima. To evade being captured in local minima, DE is required for large population. Wang and Chiou showed that DE needs larger population and more computational time in order to produce the optimal result [6]. State observer which acts as initiator for the starting point such as Kalman Filter can be implemented into the DE algorithm to improve its performance in the future. DE seems to be very sensitive to control parameters: population size, crossover constant and differentiation constant. Therefore self adapting approach to these control parameters can be used to optimize the performance of the traditional as well as the proposed DE algorithm.

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