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 which is used 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 testified to be better than the other estimation algorithms. The outcomes from this study promote estimating of optimal kinetic parameters, shorter computation time and ameliorating the precision of the simulated kinetic model for 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. Thus, the studies of metabolic pathway permit scientists to simulate the process inside the cell by a mathematical modeling. Developing a valid pathway model that acts as a biological function's simulator is the goal for the study of system biology. Parameter estimation is one of the key steps in the mathematical model. Unfortunately, it has encountered some problems such as increasing number of unknown parameters and equations in the model which contributes to the 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 incorporating DE and parameter sensitivity test to resolve the rising unknown parameters. 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 fewer irrelevant parameters which can minimize the computational burden that leads to less computational effort and time.

2 Method

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 $m \times n$ 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:

- Randomly select three parent individuals: individual1, individual2, individual3 from a population for each n by the following formula where i is the parent index.

  $$\text{individual\_}i = \text{floor}(\text{rand}(\,) * \text{population size}) + 1 \qquad (1)$$

- New generation is mutated by the following formula for each population size.

  $$\text{temp\_population}(i) = \text{Pop}(\text{individual\_3}) + \text{F}*(\text{Pop}(\text{individual\_1}) - \text{Pop}(\text{individual\_2})) \qquad (2)$$

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

- If Randb(j) < CR or j = Rnbr(i)
  Crossover occurs and generates 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

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

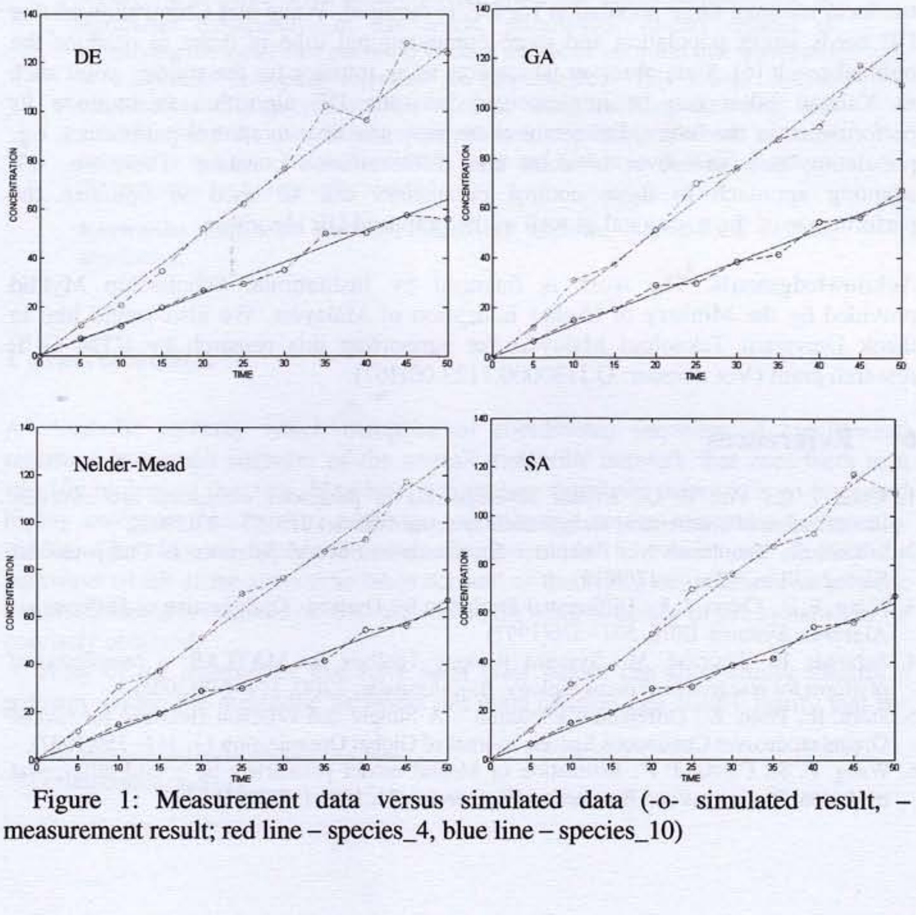

Figure 1: Measurement data versus simulated data (-o- simulated result, – measurement result; red line – species_4, blue line – species_10)

Execution times with 87 unknown parameters (Table 1) are far greater than those with 4 unknown parameters (Table 2). It is shown that the execution time is directly proportional to the number of unknown parameters; this time increases when the number of unknown parameters increases. In Table 2 Nelder-Mead and DE are the two algorithms that required less execution time. However, the performance of Nelder-Mead decreases as the number of unknown parameters increases. DE is shown to have the least execution time even with a larger population size. Even though the process time required by DE is consistently short, the results generated by DE are almost similar with other estimation algorithms respectively (Figure 1). Thus, the proposed method of incorporating the parameter sensitivity test with DE solves the parameter estimation problems whereby the number of unknown parameters and the computational time are reduced, and the accuracy of the simulated model is improved.

5 Conclusion and Future Work

In conclusion, DE is shown to outperform other estimation algorithms in this study but regrettably it may easily be trapped in local minima. Basically, the concentration will be on the global minima rather than the local minima. To evade being trapped in the local minima, large population for DE is required. 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 an 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, e.g. 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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