Indonesian Journal of Electrical Engineering and Computer Science
Vol. 8, No. 1, October 2017, pp. 27 ~ 35
DOI: 10.11591/ijeecs.v8.i1.pp27-35

Optimisation of Biochemical Systems Production using Hybrid of Newton method, Differential Evolution Algorithm and Cooperative Coevolution Algorithm

Mohd Arfian Ismail*[1], Vitaliy Mezhuyev [1], Kohbalan Moorthy [1], Shahreen Kasim [2], and Ashraf Osman Ibrahim [3,4]
[1]Faculty of Computer Systems and Software Engineering, Universiti Malaysia Pahang, Pahang, Malaysia
[2]Soft Computing and Data Mining Centre, Faculty of Computer Science and Information Technology, Universiti Tun Hussein Onn, Johor, Malaysia
[3]Faculty of computer Science and Information Technology, Alzaiem Alazhari University, Khartoum North 13311, Sudan
[4]Arab Open University, Khartoum, Sudan
*Corresponding author, e-mail: arfian@ump.edu.my

Abstract

This paper present a hybrid method of Newton method, Differential Evolution Algorithm (DE) and Cooperative Coevolution Algorithm (CCA). The proposed method is used to solve the optimisation problem in optimise the production of biochemical systems. The problems are maximising the biochemical systems production and simultaneously minimising the total amount of chemical reaction concentration involves. Besides that, the size of biochemical systems also contributed to the problem in optimising the biochemical systems production. In the proposed method, the Newton method is used in dealing biochemical system, DE for optimisation process while CCA is used to increase the performance of DE. In order to evaluate the performance of the proposed method, the proposed method is tested on two benchmark biochemical systems. Then, the result that obtained by the proposed method is compare with other works and the finding shows that the proposed method performs well compare to the other works.

Keywords: *Newton method, Differential Evolution Algorithm, Cooperative Coevolutioan Algorithm, Biochemical systems, Computational Intelligence*

1. Introduction

Biomass is a good alternative to produce the biofuel. This is because the biomass is a plant-based resource that can be used to replace the limited biofuel. Nowadays, the demand of biomass is increase where it leads to competition of land and plant [1, 2, 3]. Recently, many researchers have focus on manipulating the microorganism activity in order to produce the biomass rather than really on increasing the land and plant. This is because manipulating the microorganism is far cheaper and reduce time rather than increase the land or plant. But, the biomass that extracted from manipulating the microorganism activity has a limitation where the production is low [4, 5]. Due to that, many researcher have focus on optimisation the production of biomass. One way to improve the biomass production is the optimisation of biochemical systems production by fine-tuning the reactions value in biochemical systems.

The optimisation of the production in biochemical systems can be performed because the biochemical system can be represented by a nonlinear equations system. In the nonlinear equations system, each variable is used to represent each reactions of biochemical systems. The process of fine-tuning the reactions value can be performed by change the variables value. Fine-tuning process of the variables in nonlinear equations system becomes a hard task if involves a large biochemical systems. This is because a large biochemical systems contains with many reactions and involves many interaction between reaction. In order to overcome this situation, this paper

Received May 6, 2017; Revised September 2, 2017; Accepted September 15, 2017

present an automated method to fine-tuning the variables in nonlinear equations system. The proposed method hybrid the Newton method, Differential Evolution Algorithm (DE) and Cooperative Coevolution Algorithm (CCA).

In optimisation of biochemical systems production, the biochemical systems can be modelled by mathematical model, which is generalised mass action (GMA) model. During the optimisation, there are several constraints involve which are steady state condition and reaction concentration constraint. The steady state condition make all the equations in GMA model equal to 0 where it make the optimisation process become the process of solving a nonlinear equations system. There are various methods that can be used in solving a nonlinear equations system such as Newton method, Secant method and Bisection method. In this study, Newton method is used because Newton method is fast in solving the system [6], simple to used [7, 8] and very widely used in solving nonlinear equations system [9, 10, 11].

For fine-tuning the reactions value in biochemical systems, an optimisation method is needed. The reason of fine-tuning is to discover the suitable value that produce the high production of biochemical systems. The fine-tuning process become complicated when involves a complex biochemical system where contains with many reactions and involves many interaction between them. Because of that, an optimisation method is need. There are various method can be applied such as genetic algorithm (GA), DE, and Particle Swarm Optimisation (PSO) algorithm. This study used DE because DE offer several advantages such as DE involves few parameters [12, 13] and DE is more robust on several problems when compare to other [14].

In the optimisation of biochemical systems production, two factors that need to be considered which are the production and the total of chemical reaction concentrations involves. In addition, a large of biochemical systems that content with many reactions and interaction between them also contribute to the difficulty in optimisation process. Because of these factors, this make the representation of the solution become complex. This make the optimisation proses become hard and complicated. In order to overcome these issues, this study use CCA in order to simplify the representation of the solution by dividing the complete into multiple sub-solutions.

In this paper, the hybrid of Newton method, GA and CCA is proposed and discuss in detail. The aim of the proposed method is to solve the problems in optimisation of biochemical systems production which are to improve the biochemical systems production and at the same time reduce the total of chemical reaction concentrations involves. In the proposed method, the function of Newton method is to solve the nonlinear equations system, DE is used in optimisation process where DE is used to fine-tuning process while CCA is utilised to improve the performance of DE. In the following section, the explanation of the proposed method is discussed in detail. Then, the model and experimental data is describe in detail where two benchmark biochemical systems are used namely the *Saccharomyces cerevisiae* (*S.cerevisiae*) pathway and the *Escherichia Coli* (*E.coli*) pathway. After that, the experimental result and discussion is presented before this paper was conclude in conclusion.

2. A Hybrid Method of Newton Method, Differential Evolution Algorithm and Cooperative Coevolution Algorithm

This section is about the discussion of the proposed method. The proposed method hybrid Newton method, DE and CCA. In the proposed method, Newton method is utilised to deal with nonlinear equations system, DE is used in optimisation process and CCA is embodied into DE in order to improve the performance of DE by simplifies the chromosome representation. Figure 1 shows the proposed method in flowchart form. The detail steps in the proposed method are as follows:

Step 1: Generate the initial solution. In the first step, the first generation of m solution is generated separately in n sub-population (the number of sub-population is equal to the number of variables that need to be tuned). The variable (in nonlinear equations system) is represented by sub-chromosome. The sub-chromosome is in binary format. The sub-chromosome is generated randomly and in a specific format (depends on the value of chemical reaction concentration).

Step 2: Form the complete chromosome. The complete solution is form in this step by combine all

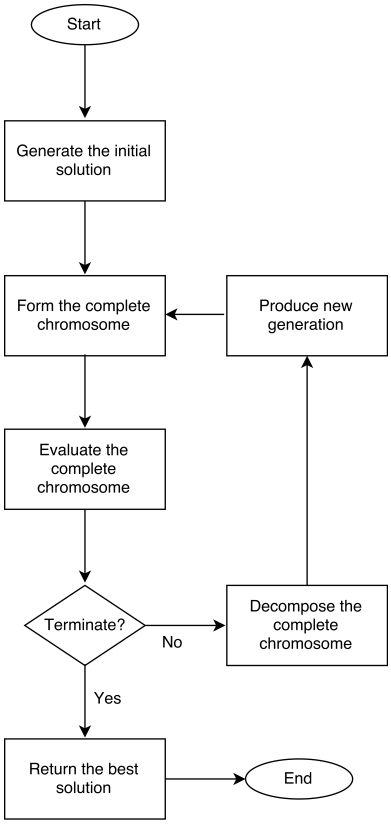

Figure 1. The flowchar of the proposed method

sub-chromosomes from all sub-populations. The sub-chromosome is selected based on their fitness value where the sub-chromosome that has lowest fitness value is selected and then combine with other sub-chromosome from each sub-population. This is because the selection process is intended to minimise the total amount of chemical reaction concentration involves. Figure 2 depicted the generation of sub-chromosome until the formation of complete chromosome.
Step 3: Evaluate the complete chromosome. In this step, the complete chromosome is decoded into variables form. At this stage, the Newton method is used in solving the nonlinear equations system. Besides that, two termination conditions are applied which are; the maximum number of generation is reach and all the chemical reaction concentration value is in their range. The process move forward to Step 6 if these conditions are meet, otherwise the process enter the next step.
Step 4: Decompose the complete chromosome. In this step, the complete chromosome is decomposed into multiple sub-chromosomes. After that, all sub-chromosomes went back into their own sub-population for reproduction process.
Step 5: Produce new generation. This step is intended to improve the solution by producing the next generation of the solution. This step happens in all sub-population. The mutation and crossover process are applied on all sub-chromosome.
Step 6: Return the best solution. This is the final step. In this step, the best solution is given.

3. Model and Experimental Data

In order to test the performance of the proposed method, two benchmark biochemical systems are used which are the optimisation of the ethanol production in *S. cerevisiae* pathway and the optimization of the *trp* biosynthesis in *E. Coli*. A Java program based on JAMA version 1.0.3 and jMetal [15] are used. The JAMA program is used in dealing with nonlinear equations system while

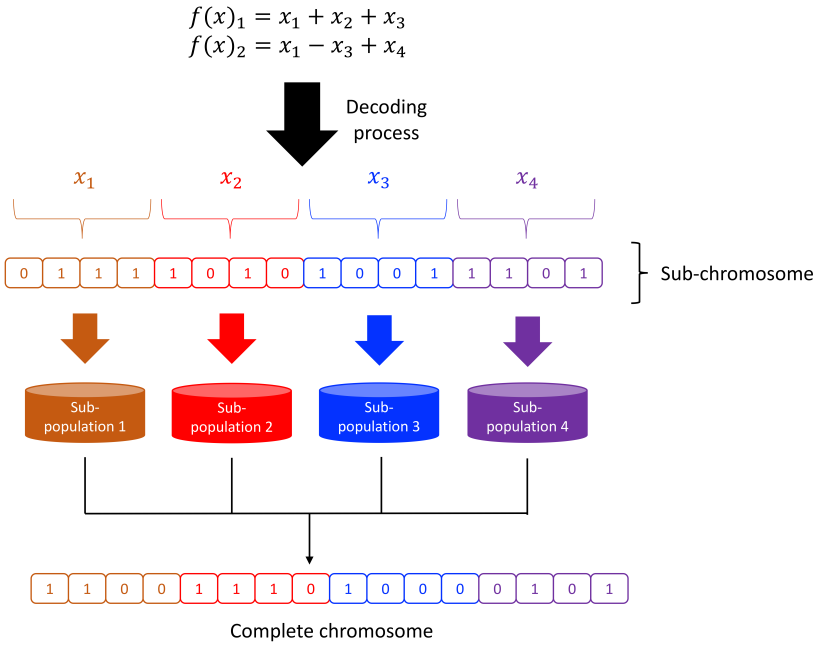

Figure 2. The process of formation the complete chromosome

jMetal for optimisation process. The JAMA can be obtained from http://math.nist.gov/javanumerics/jama/ and jMetal can be downloaded from http://jmetal.sourceforge.net. The detail description of two benchmark biochemical systems are describe in the next sub section.

3.1. Optimisation of the ethanol production in *Saccharomyces cerevisiae* pathway

The proposed method is used to optimise the ethanol production in *S.cerevisiae* pathway. The detail description of this pathway can be found in [16]. In this pathway, the nonlinear equations system can be represented as follows:

$$\begin{aligned} V_{in} - V_{HK} &= 0 \\ V_{HK} - V_{PFK} - V_{Carb} &= 0 \\ V_{PFK} - V_{GAPD} - 0.5V_{Gro} &= 0 \\ 2V_{GAPD} - V_{PK} &= 0 \\ 2V_{GAPD} + V_{PK} - V_{HK} - V_{Carb} - V_{PFK} - V_{ATPase} &= 0 \end{aligned} \tag{1}$$

where at steady state conditions, these chemical reaction concentrations (denoted by V) have the following value:

$$\begin{aligned} V_{in} &= 0.8122X_2^{-0.2344}Y_1 \\ V_{HK} &= 2.8632X_1^{0.7464}X_5^{0.0243}Y_2 \\ V_{PFK} &= 0.5232X_2^{0.7318}X_5^{-0.3941}Y_3 \\ V_{Carb} &= 8.904 \times 10^{-4}X_2^{8.6107}Y_7 \\ V_{GAPD} &= 7.6092 \times 10^{-2}X_3^{0.6159}X_5^{0.1308}Y_4 \\ V_{Gro} &= 9.272 \times 10^{-2}X_3^{0.05}X_4^{0.533}X_5^{-0.0822}Y_8 \\ V_{PK} &= 9.471 \times 10^{-2}X_3^{0.05}X_4^{0.533}X_5^{-0.0822}Y_5 \\ V_{ATPase} &= X_5Y_6 \end{aligned} \tag{2}$$

In this biochemical system, the ethanol production is given by V_{PK} and it became the fitness function of complete chromosome. This lead to the improving the production as follows:

$$max\, F_1\ (v) = V_{PK} \tag{3}$$

For the total of chemical reaction concentrations involves, it can be formulated as follow:

$$min\, F_2 = \sum_{j=1}^{5} X_j + \sum_{j=6}^{6} Y_j \tag{4}$$

where the range of X is set between 0.2 to 1.2 and Y in the range of 0 to 50 [17, 18].

3.2. Optimisation of the *tryptophan* biosynthesis in *Escherichia Coli* pathway

In this pathway, the proposed method is used to optimise the *trp* production. Xiu *et al.* has explained in detail of this pathway[19]. For this pathway, the nonlinear equations system can be formulated as follows:

$$\begin{aligned} V_{11} - V_{12} &= 0 \\ V_{21} - V_{22} &= 0 \\ V_{31} - V_{32} - V_{33} - V_{34} &= 0 \end{aligned} \tag{5}$$

All reaction concentration (denoted by V) has the following values at steady state condition:

$$\begin{aligned} V_{11} &= 0.6403 X_3^{-5.87\times10^{-4}} X_5^{-0.8332} \\ V_{12} &= 1.0233 X_1 X_4^{0.0035} X_{11}^{0.9965} \\ V_{21} &= X_1 \\ V_{22} &= 1.4854 X_2 X_4^{-0.1349} X_{12}^{0.8651} \\ V_{31} &= 0.5534 X_2 X_3^{-0.5573} X_6^{0.5573} \\ V_{32} &= X_3 X_4 \\ V_{33} &= 0.9942 X_3^{7.0426\times10^{-4}} X_7 \\ V_{34} &= 0.8925 X_3^{3.5\times10^{-6}} X_4^{0.9760} X_8 X_9^{-0.0240} X_{10}^{-3.5\times10^{-6}} \end{aligned} \tag{6}$$

The *trp* production is given by reaction V_{34} thus it become the fitness function of the complete chromosome. This lead to the improving the production as follows:

$$max\, F_1\ = V_{34} \tag{7}$$

For the total of chemical reaction concentrations involves, it can be formulated as follow:

$$min\, F_2\ = \sum_{j=1}^{6} X_j + X_8 \tag{8}$$

where the range of X_1 to X_3 is between 0.8 to 1.2, X_4 between 0 to 0.00624, X_5 between 4 to 10, X_6between 500 to 5000 and between X_8 0 to 1000 [17, 18].

4. Experimental results and discussions

In producing the best result, several experiments are performed. Table 1 list the DE parameters setting used. For CCA, the number of sub-populations depend on the variables in nonlinear equations system the need to be tuned. For the *S.cerevisiae* pathway, the number of sub-populations is 11 while for *E.coli* pathway, the number of sub-populations is 7. For the Newton

Table 1. The DE parameters

Parameter	*S.cerevisiae* pathway	*E.coli* pathway
Mutation (Scaling factor)	0.8	0.7
Crossover	0.2	0.2

method, fixed parameter used for both pathway; the number of iteration is 100 and the tolerance value is 10^{-6}.

In *S.cerevisiae* pathway, the best result obtained by the proposed method is 52.7269 in maximising the ethanol production while 295.2405 in minimising the total of chemical concentration involves. The detail result, average result and comparison with other methods are listed in Table 2. From Table 2, it can be observed that the performance of the proposed method is outperform the result from other works in maximising the ethanol production and at the same time minimising the total amount of chemical reaction concentration involves.

Table 2. The detail result obtained by the proposed method in *S.cerevisiae* pathway

Parameter	This work	Work by [20]	Work by [18]	Work by [21]
X_1	1.113	1.14	1.102	1.11
X_2	1.053	1.05	1.046	1.03
X_3	1.127	1.15	1.141	1.13
X_4	1.164	1.17	1.171	1.18
X_5	0.92	1.12	1.113	51.14
Y_1	49.972	49.97	50	49.99
Y_2	49.810	44.77	45.953	45.83
Y_3	49.90	49.89	50	49.92
Y_4	47.333	47.26	47.772	47.97
Y_5	48.062	48	48.366	48.30
Y_8	49.792	49.75	50	49.79
F_1	**52.727**	52.084	52.512	52.57
F_2	**295.241**	295.28	297.664	297.384

Meanwhile, the best result produce by the proposed method in *E.coli* pathway is 3.9988 in maximising the *trp* production and 6015.5871 in minimising the total of chemical concentration involves. The detail result, average result and comparison with other methods are listed in Table 3. Same observation with *S.cerevisiae* pathway, the performance of the proposed method also perform better when it compare to other works.

Table 3. The detail result obtained by the proposed method in *E.coli* pathway

Parameter	This work	Work by [22]	Work by [23]	Work by [18]	Work by [21]
X_1	1.191	1.19	1.2	1.2	1.11
X_2	1.119	1.15	1.15	1.12	1.114
X_3	0.8	0.8	0.8	0.8	0.8
X_4	0.0054	0.0041	0.004	0.0054	0.0054
X_5	4.037	4	4	4.011	4.75
X_6	5000	5000	5000	5000	5000
X_8	1000	1000	1000	1000	1000
F_1	**3.999**	3.06	3.06	3.95	3.98
F_2	**6015.5871**	6016.38	6016.57	6016.57	6016.22

Besides that, the comparison between multi sub-population that used in this study with single population (dont use CCA). The purpose of CCA is to enhance the performance of DE in minimising the total amount of chemical reaction concentration involves. Several experiments are

conducted using parameters setting in Table 1. Figure 3 and Figure 4 depicted the bar graph of the comparison between multi sub-population with single population in *S.cerevisiae* pathway and *E.coli* pathway. From that figures, it can be seen clearly that all the results of multi sub-population are lower compare to the results obtained by single population. It can be concluded that, the CCA able to improve the performance of DE in minimising the total amount of chemical reaction concentration involves.

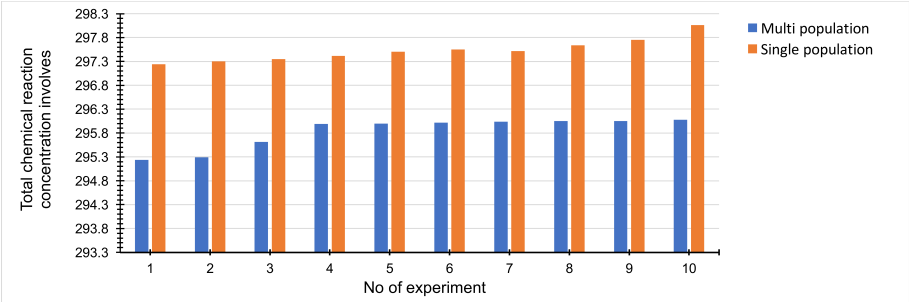

Figure 3. The comparison of multi population and single population in *S.cerevisiae* pathway

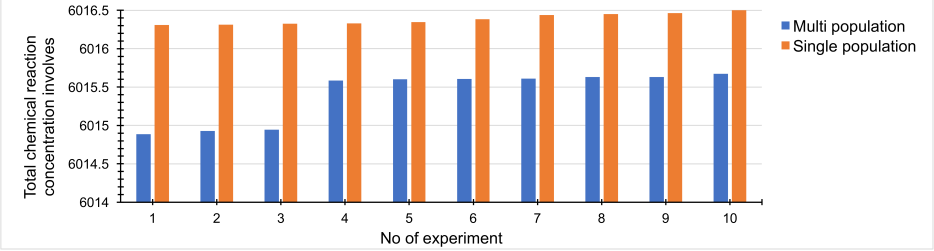

Figure 4. The comparison of multi population and single population in *E.coli* pathway

In order to show the consistency in apply CCA, the proposed method is compared with the method that not use CCA (only use Newton method and DE). About 100 independent experiments are performed. Figure 5 and Figure 6 show the comparison in box plot form. Figure 5 show the ethanol production in *S.cerevisiae* pathway while Figure 6 show the *trp* production in *E.coli* pathway. From the figures, the result produce by the proposed method are not too wide compare to the result that not use CCA. From this observation, it can be explained that the propose method able to produce a consistent result if the experiment run several times.

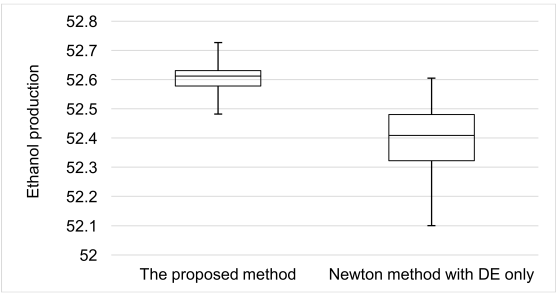

Figure 5. The boxplot of the ethanol production

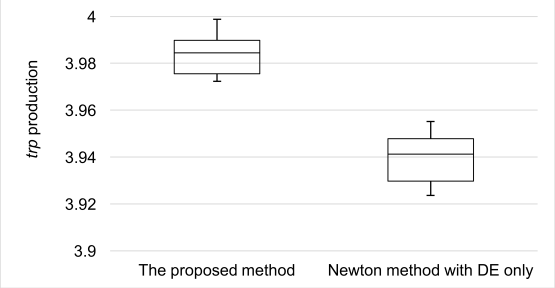

Figure 6. The boxplot of the *trp* production

5. Conclusion

This paper has proposed a hybrid method of Newton method, DE and CCA. The proposed method is proposed to overcome the problems in optimisation of biochemical systems where the problems are to maximise the biochemical systems production and simultaneously minimise the total amount of chemical reaction concentration involves. The proposed method works by view the biochemical systems as nonlinear equation system. Firstly, the Newton method is used to solve the nonlinear equations system. Then, DE is used in optimisation process. The performance of DE is drop when applied on alrge and complex biochemical systems and CCA is utilised to improve the performance of DE. The proposed method is applied on benchmark biochemical systems and the experimental result show that the performance is outperform the other works.

Acknowledgement

Special thanks and appreciation to the editor and anonymous reviewers that reviewed this paper. The author also would thanks to the sponsor from RDU Grant Vot No. RDU1603115 form Universiti Malaysia Pahang.

References

[1] A. Ajanovic, "Biofuels versus food production: Does biofuels production increase food prices?" *Energy*, vol. 36, no. 4, pp. 2070–2076, 2010.
[2] M. Harvey, "The new competition for land: Food, energy, and climate change," *Food Policy*, vol. 36, no. 1, pp. S40—-S51, 2010.
[3] S. Haus, S. Jabbari, T. Millat, H. Janssen, R.-J. Fischer, H. Bahl, J. R. King, and O. Wolkenhauer, "A systems biology approach to investigate the effect of pH-induced gene regulation on solvent production by Clostridium acetobutylicum in continuous culture," *BMC Systems Biology*, vol. 5, no. 10, 2011.
[4] M. Caspers, U. Brockmeier, C. Degering, T. Eggert, and R. Freudl, "Improvement of Sec-dependent secretion of a heterologous model protein in Bacillus subtilis by saturation mutagenesis of the N-domain of the AmyE signal peptide." *Applied microbiology and biotechnology*, vol. 86, no. 6, pp. 1877–85, may 2010.
[5] Y.-S. Jang, J. Lee, A. Malaviya, D. Y. Seung, J. H. Cho, and S. Y. Lee, "Butanol production from renewable biomass: Rediscovery of metabolic pathways and metabolic engineering," *Biotechnology Journal*, vol. 7, no. 2, pp. 186–198, 2011.
[6] C.-S. Liu, "A modified Newton method for solving non-linear algebraic equations," *Journal of Marine Science and Technology*, vol. 17, no. 3, pp. 238–247, jun 2009.
[7] M. Al-Towaiq and Y. A. Hour, "Two Improved Methods Based on Broyden's Newton Methods for the Solution of Nonlinear System of Equations," *Journal of Engineering and Applied Sciences*, vol. 11, pp. 2344–2348, 2016.
[8] C.-S. Liu and S. N. Atluri, "A novel time integration method for solving a large system of non-linear algebraic equations," *Computer Modeling in Engineering and Sciences*, vol. 31, no. 2, pp. 71–83, jan 2008.

[9] C. Grosan and A. Abraham, "A New Approach for Solving Nonlinear Equations Systems," *Systems, Man and Cybernetics, Part A: Systems and Humans, IEEE Transactions on*, vol. 38, no. 3, pp. 698–714, 2008.
[10] Y. Mo, H. Liu, and Q. Wang, "Conjugate direction particle swarm optimization solving systems of nonlinear equations," *Computers {&} Mathematics with Applications*, vol. 57, no. 11-12, pp. 1877–1882, 2009.
[11] M. A. Ismail, S. Deris, M. S. Mohamad, and A. Abdullah, "A newton cooperative genetic algorithm method for in silico optimization of metabolic pathway production," *PloS one*, vol. 10, no. 5, p. e0126199, 2015.
[12] S. Das, S. S. Mullick, and P. N. Suganthan, "Recent advances in differential evolution-An updated survey," *Swarm and Evolutionary Computation*, vol. 27, pp. 1–30, 2016. [Online]. Available: http://dx.doi.org/10.1016/j.swevo.2016.01.004
[13] F. Peñuñuri, C. Cab, O. Carvente, M. A. Zambrano-Arjona, and J. A. Tapia, "A study of the Classical Differential Evolution control parameters," *Swarm and Evolutionary Computation*, vol. 26, pp. 86–96, 2016. [Online]. Available: http://dx.doi.org/10.1016/j.swevo.2015.08.003
[14] S. T. Suganthi, D. Devaraj, and S. H. Thilagar, "An improved differential evolution algorithm for congestion management considering voltage stability," *Indian Journal of Science and Technology*, vol. 8, no. 24, 2015.
[15] J. J. Durillo and A. J. Nebro, "jMetal: A Java framework for multi-objective optimization," *Advances in Engineering Software*, vol. 42, no. 10, pp. 760–771, 2011.
[16] J. L. Galazzo and J. E. Bailey, "Fermentation pathway kinetics and metabolic flux control in suspended and immobilized Saccharomyces cerevisiae," *Enzyme and Microbial Technology*, vol. 12, no. 3, pp. 162–172, 1990.
[17] H. Link, J. Vera, D. Weuster-Botz, N. T. Darias, and E. Franco-Lara, "Multi-objective steady state optimization of biochemical reaction networks using a constrained genetic algorithm," *Computers and Chemical Engineering*, vol. 32, no. 8, pp. 1707–1713, 2008.
[18] G. Xu, "Steady-state optimization of biochemical systems through geometric programming," *European Journal of Operational Reseach*, vol. 225, no. 1, pp. 12–20, 2013.
[19] Z.-L. Xiu, A.-P. Zeng, and W.-D. Deckwer, "Model analysis concerning the effects of growth rate and intracellular tryptophan level on the stability and dynamics of tryptophan biosynthesis in bacteria," *Journal of Biotechnology*, vol. 58, no. 2, pp. 125–140, 1997.
[20] F. Rodriguez-Acosta, C. M. Regalado, and N. V. Torres, "Non-linear optimization of biotechnological processes by stochastic algorithms: Application to the maximization of the production rate of ethanol, glycerol and carbohydrates by Saccharomyces cerevisiae," *Journal of Biotechnology*, vol. 65, no. 1, pp. 15–28, 1999.
[21] M. A. Ismail, S. Deris, M. S. Mohamad, and A. Abdullah, "A Hybrid of Newton Method and Genetic Algorithm for Constrained Optimization method of the Production of Metabolic Pathway," *Life Science Journal*, vol. 11, no. 9s, pp. 409–414, 2014.
[22] A. Marin-Sanguino, E. O. Voit, C. Gonzalez-Alcon, and N. V. Torres, "Optimization of biotechnological systems through geometric programming," *Theoretical Biology and Medical Modelling*, vol. 4, pp. 38–54, 2007.
[23] J. Vera, C. Gonzalez-Alcon, A. Marin-Sanguino, and N. Torres, "Optimization of biochemical systems through mathematical programming: Methods and applications," *Computers {&} Operations Research*, vol. 37, no. 8, pp. 1427–1438, 2010.