ABSTRACT
Microbial strains can be manipulated to improve product yield and improve growth characteristics. However, the complexities of the metabolic networks which lead to data ambiguity have made the effects of genetic modification on the desirable phenotypes hard to predict. A vast number of reactions in cellular metabolism lead to combinatorial problem in obtaining optimal gene deletion strategy. Consequently, as the size of the problem increases the computational time will increase exponentially with the size. Another problem is the lack of rational strategies based on predictive analysis tools causes low accuracy of the results. Optimization algorithms are developed to identify the effects of gene knockout on the results. However, this process is often faced the problem of being trapped in local minima and slow convergence due to repetitive iterations of algorithm. In this research, Bees Hill Flux Balance Analysis (BHFBA) is proposed, it is a hybrid of Bees Algorithm, Hill Climbing Algorithm and Flux Balance Analysis, to solve the problems and improve the performance in predicting optimal sets of gene deletion for sustaining the growth rate meanwhile maximizing production yield of desired metabolite. The proposed algorithm is tested with the model organism from Biochemical Genetic and Genomic (BiGG) database. BHFBA performed better in term of computational time, stability and production yield. The algorithm is tested with 8 benchmark function to prove the robustness and reliability of the algorithm. The non-intuitive gene knockout strategies are identified by the proposed algorithm that may be a useful reference for solving metabolic engineering problems.

KEYWORD
Bees Algorithm, Hill Climbing, Flux Balance Analysis, Microbial Strains, Optimization