CHAPTER 3

METHODOLOGY

3.1 Introduction

This chapter describes the methodology used in this research which contains five sections. The first section is about the framework and it described the following in details; the pathways, metabolites, enzyme and kinetic equation, and kinetic parameters. The second section is about the sensitivity analysis method and their application in this research. The third section is about the Particle Swarm Optimization (PSO) method which was applied to correct the kinetic parameters of the model under study. The last section is about validation, which describes how to prove that the sensitivity analysis and optimization algorithm methods are highly sufficient in order to achieve our goals in this research.

3.1.1 The condition used in the sensitivity and optimization methods

Based on the method of one at a time sensitivity measures we define the degree of sensitivity to measure the sensitivity among kinetics, there are 194 kinetics involved, for 0.1 dilution rate each kinetic is increased by 10%, 20%, 40% and 80% then quantify the changes using the Highest Mean for each kinetic parameters on the model response it will be described in the sensitivity analysis method. Moreover, in dilution rate 0.2 each kinetic parameter increased by 10% and 20% then quantifies the changes using the Highest Variance.

The PSO factors used in this study in order to reach our objectives are fitness function, dimension problem, population size, upper and lower values, c1&c2 they

represent the exploitation coefficient, r1 & r2 are random numbers between 0 and 1 with weight constant ω which are explained PSO part. The metabolite concentration of (Hoque et al., 2005) are Fructose 1,6-biophosphate *FDP* (0.67 mM), Phosphoenol-pyruvate *PEP* (1.04 mM), Isocitrate *ICIT* (0.21 mM) and 2-Keto-D-gluconate *2KG* (0.134 mM) are used in PSO algorithm execution in order to fit the optimization result closely with that experimental data picked-up from (Hoque et al., 2005) by test the optimization result in (Kadir et al., 2010) model.

3.2 Framework of the research

In order to achieve large-scale kinetic parameters optimization of metabolic network of *E. coli*, this framework in Figure 3.1 was employed to describe the 4th phase in this chapter for the purpose of solving large scale kinetic parameters.

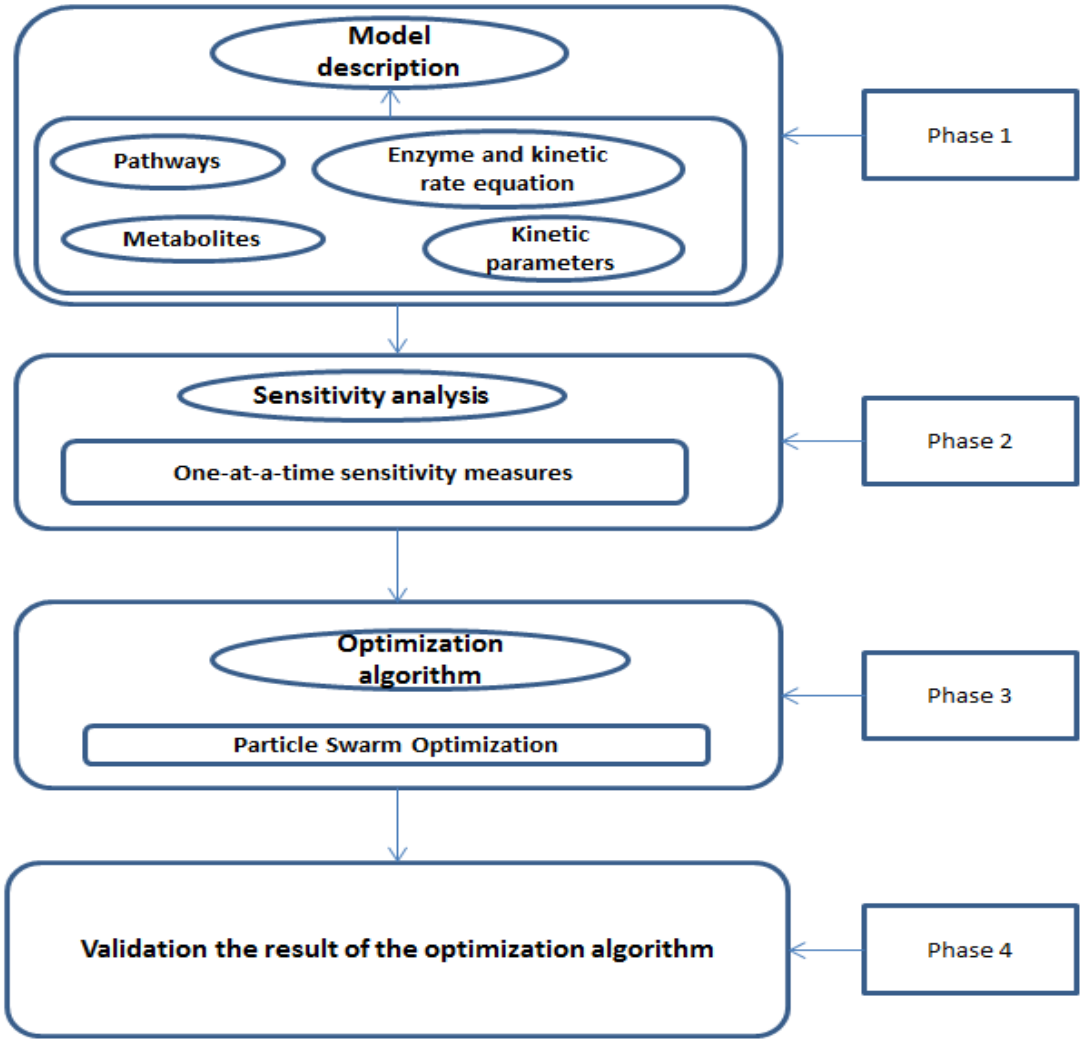
The first phase is describing the model that used in this study which contains pathways, conditions, equations, kinetic values, enzymes and metabolite concentrations.

The second phase is the method of sensitivity analysis technique that we are going to use for the analyization of the model under study, and it contains the implementation of the sensitivity analysis algorithm in dilution rate of 0.1 and 0.2 using One-At-A-Time Sensitivity Measures.

The third phase is the optimization algorithm of PSO which is proposed to optimize the sensitivity analysis result and their implementation to the sensitivity analysis result of 0.1 dilution rates in order to achieve optimization for large-scale kinetic parameters.

The validation is proposed in the fourth phase by replacing the kinetic sensitivity analysis result with optimum values founded by PSO then run the simulation if the output is close to real experimental data we accept the optimization result if not it will be repeated till our result got close to experimental data. The criteria to prove our result is more close to experimental data than the model output result under study by measure

the percentage errors between our result, the model under study result with real experimental data.



Figuer 3.1: Framework of the study

3.3 Model description

The metabolic network model under study was used as a case study in order to achieve a large-scale kinetic parameters optimization of the metabolic network of *E. coli*. Identification of the pathways, metabolites, enzyme and kinetic rate equations, and kinetic parameters involves in this model has to be done so as to realize the goal.