CHAPTER 1

INTRODUCTION

1.1 RESEARCH BACKGROUND

Differential equations play a crucial role in formulation and analysis of many biological and physical systems (Jones et al., 2011). They relate the function of one or more variables with its derivative. The differential equations are called ordinary differential equations (ODEs) if the unknown function also known as dependent variable is a function of single independent variable t (Abell and Braselton, 2004). ODEs which explicitly allow the perturbation of random fluctuations are classified as stochastic differential equations (SDEs). In various range of applications SDEs have a richer mathematical framework compared with ODEs. SDEs incorporate the uncontrolled fluctuation into the biological and physical phenomenon, hence it provides a realistic mathematical model for the analysis of underlying systems than their deterministic counterpart do (Hale, 1993). However, ODEs and SDEs which are simply depending on the present state are unable to illustrate the physical processes which involve time delay. In both types of equations the unknown function and its derivative are evaluated at instant time t.

In most of natural phenomenon, a delayed-feedback is introduced when they are some hidden variables and processes which are not well understood but are known to cause a time-lag (Bocharov and Rihan, 2000). A patient, for example, shows symptoms of an illness days or even weeks after the day in which she/he was infected. ODEs and SDEs can be improved by incorporating time delay into both equations. Deterministic differential equation with delayed-feedback is called delay differential equations (DDEs). However, DDEs are inadequate to model the process with the presence of both time delay and random effects. The process that involves the incorporation of both time delay and random effects can be modelled via stochastic delay differential equations (SDDEs). SDDEs are a generalization of DDEs and SDEs (Mohammed, 1984).

One of the most important systems that subject to the presence of noise and time delay is batch fermentation process. Fermentation is a process of converting sugar to solvents (acetone, butanol and ethanol) under anaerobic condition by using yeast undergoes (Madihah, 2002). There are two important features that control the mechanism of this process, namely time delay and the system is continually subject to the effects of random which is referred to as noise. The presence of time delay is a consequence of the simple fact that microbes are in the process of adapting themselves to the new environment. Thus, there is no growth occur. The microbes, synthesize the new enzymes in response to the changes in the availability of substrate. Microbes at this stage are assumed to be in a lag phase. Obviously, at the end of lag phase the microorganism is well adjusted and cells multiply rapidly. Cell mass doubles regularly with time. This period is recognized as an exponential phase. As time evolves the intrinsic variability of competing within species occur and deviations from exponential growths arise. It happens as a result of the nutrient level and concentration of toxin reach as a value which is unable to sustain the maximum growth rate. This phase is the most frequently known as a stationary phase. The production of solvent occurs in two different phases which are acidogenic and solventogenic phases. Acetyl-CoA and butyryl-CoA function as the intermediates key for solvent production. Acetylaldehyde and butyraldehyde are produced in this stage. The production of solvents (acetone and butanol) happens in solventogenic phase. As aforementioned, cell growth of *Clostridium Acetobutylicum* P262 is subjected to delayed-feedback and noise. The presence of these two features will influence the concentration of acetone and butanol that will be produced in batch fermentation process. To understand the behaviour of this physical system it is necessary to develop a mathematical model that incorporates both of the delayed-feedback and noisy environment. Thus, this research is carried out to model jointly time delay and stochasticity of the microbial growth and solvents production of acetone and butanol in batch fermentation process.

1.2 PROBLEM STATEMENTS

All biological and physical processes need time to complete. In batch fermentation process, time delay occurs due to the fact that initially cells are in the position of adapting themselves to the new environment. Hence, the biological regulatory reaction of the cell growth is not instantaneous. Cells only respond after some time lag, $r > 0$. The process indicates an intrinsic variability in the stationary phase. Cells compete with each other for space and food due to the exhausted of nutrient level and toxin concentration. Bearing in mind, all the phases involve in batch fermentation, it is necessary to model the process via SDDEs. Hence, the research problems were set as below;

(i) Will the stochastic model with time delay be an efficient model to describe the solvent production of acetone and buthanol by *Clostridium Acetobutylicum* P262 in batch fermentation process?

(ii) How to develop the algorithm to approximate the solutions of stochastic model in (i)?

(iii) How to estimate the kinetic parameter and simulate the solutions of stochastic model with delayed-feedback?