DYNAMICAL ANALYSIS OF CHEMOSTAT MODELS INCORPORATING VARIABLE YIELD COEFFICIENT AND SUBSTRATE INHIBITION WITH RECYCLING PROCESS

UMMAL AISHA FARHANA BINTI MOHD SADIQ

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Universiti Tun Hussein Onn Malaysia

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Dedication to

This research report is dedicated to my family members, my parents

Mohd Sadiq bin S A Sahul Hamid,

Basiral Beevi Shaik Dawood Alim,

my siblings

Mohamed Mubeen bin Mohd Sadiq,

Mohamed Hussain bin Mohd Sadiq

and my husband

Mohammad Faiz Bin Abdul Latiff

Thanks for your endless support, love and prayers.

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ABSTRACT

This research analyses chemostat models for microbial production. Chemostat is a tool that can be used for the continuous production of microbes under controlled conditions such as pH, temperature, light, and nutrients. This ability makes chemostat promising for the applications of microbes as renewable resources, microbial products and wastewater treatment. The dynamics of the chemostat can be described using the chemostat mathematical model. The microbial growth in the chemostat can be interpreted mathematically using the specific growth rate model. The growth of microbes chiefly depends on the concentration of the nutrient. However, the growth of microbes can be inhibited under a high concentration of nutrients. Therefore, in this thesis, Andrew's growth model was considered to describe the inhibitory effect of high substrate concentration on the microbial growth in the chemostat model. The dependency of product yield towards the substrate concentration was also incorporated into the chemostat model. The performance of chemostat was also investigated with the influence of the recycling process. The stability and bifurcation analyses of the chemostat models were conducted to examine the dynamical behaviour of the steady-state of the chemostat system to identify the regions of parameters that generate oscillations of microbe population in the chemostat which occurs due to any changes in the stability of the steady-state of the system. There are two types of steady-states found which are washout steady-state and no washout steady-state. Washout steady-state means there is no growth of microbes occur in the reactor while no washout steady-state means there is growth of microbe occur in the chemostat. The steady-state solutions and their stability were determined as a function of residence time. The studies revealed the conditions to avoid the situation where no growth of microbes occurred in the chemostat. It was identified that there exists a parameters' region that can generate stable limit cycle and also region of bistability of steady-states. The high value of recycling parameter increases the cell mass concentration in the chemostat.

ABSTRAK

Kajian ini menganalisis model matematik kemostat yang digunakan untuk mengaggarkan penghasilan mikrob. Kemostat adalah satu alat yang digunakan untuk penghasilan mikrob secara berterusan dengan mengawal nilai pH, suhu, cahaya, dan nutrien dalam kemostat. Keupayaan ini menjadikan kemostat sebagai alat yang boleh menghasilkan mikrob sebagai sumber yang boleh diperbaharui, produk mikrob dan rawatan air kumbahan. Dinamik kemostat boleh diterangkan dengan menggunakan model matematik kemostat. Pertumbuhan mikrob dalam kemostat boleh ditafsirkan secara matematik menggunakan model kadar pertumbuhan. Pertumbuhan mikrob sangat bergantung kepada kepekatan nutrien. Walau bagaimanapun, pertumbuhan mikrob boleh terhalang jika kepekatan nutrien yang digunakan adalah terlalu tinggi. Oleh itu, dalam tesis ini, model pertumbuhan Andrew digabungkan dengan model kemostat untuk menggambarkan kesan menggunakan kepekatan nutrien yang tinggi terhadap pertumbuhan mikrob. Pergantungan hasil produk terhadap kepekatan nutrien juga diambil kira dalam model kemostat. Pengaruh proses kitar semula terhadap prestasi kemostat juga disiasat dalam kajian ini. Analisis kestabilan dan pencabangan model kemostat dijalankan untuk mengkaji dinamik keadaan mantap sistem kemostat dan untuk mengenal pasti rantau-rantau parameter yang boleh menghasilkan variasi populasi mikrob dalam kemostat di mana berlakunya perubahan terhadap kestabilan keadaan mantap sistem kemostat. Terdapat dua jenis keadaan mantap yang dijumpai dalam kajian ini iaitu keadaan mantap *washout* yang bermaksud tiada pertumbuhan mikrob dalam kemostat dan keadaan mantap bukan *washout*, keadaan di mana pertumbuhan mikrob berlaku dalam kemostat. Penyelesaian keadaan mantap dan kestabilannya ditentukan dalam fungsi waktu kediaman. Kajian mendedahkan syarat untuk mengelak keadaan di mana tiada pertumbuhan mikrob berlaku di dalam kemostat. Rantau parameter yang menjana had kitaran yang stabil dan rantau yang membolehkan dua keadaan mantap stabil telah dikenal pasti. Nilai parameter kitar semula yang tinggi dapat meningkatkan kepekatan mikrob dalam kemostat.

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LIST OF SYMBOLS AND ABBREVIATIONS

C	-	Reycle concentration factor
D	-	Dilution rate (hr^{-1})
F	-	Flowrate ($L\,hr^{-1}$)
I	-	Dimensionless inhibition constant ($I = K_S / K_I$)
K_d	-	Death coefficient (hr^{-1})
K_I	-	Inhibition constant ($g\,L^{-1}$)
K_S	-	Half saturation constants for nutrient ($g\,L^{-1}$)
R	-	Recycle ratio based on volumetric rates
R^*	-	Dimensionless recycle ratio parameter ($R^* = (C-1)R$)
S	-	Substrate concentration ($g\,L^{-1}$)
S^*	-	Dimensionless substrate concentration ($S^* = S / K_S$)
S_0	-	Initial substrate concentration ($g\,L^{-1}$)
S_0^*	-	Dimensionless initial substrate concentration ($S_0^* = S_0 / K_S$)
t	-	Time (hr)
t^*	-	Dimensionless time ($t^* = t\mu_{\max}$)
V	-	Volume of the reactor (L)
X	-	Cell mass concentration ($g\,L^{-1}$)
X^*	-	Dimensionless cell mass concentration ($X^* = X / \alpha K_S$)
X_0	-	Initial cell mass concentration ($g\,L^{-1}$)
X_0^*	-	Dimensionless initial cell mass concentration ($X_0^* = X_0 / \alpha K_S$)
Y	-	Cell mass yield coefficient
$\mu(S)$	-	Microbial specific growth rate (hr^{-1})
$\mu_{\max}$	-	Maximum microbial specific growth rate (hr^{-1})

τ	-	Residence time (hr)
τ^*	-	Dimensionless residence time ($\tau^* = \mu_{\max} V / F$)
α	-	Constant in yield coefficient
β	-	Constant in yield coefficient ($L\, g^{-1}$)
β^*	-	Dimensionless yield coefficient constant ($\beta^* = \beta K_S / \alpha$)

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CHAPTER 1

INTRODUCTION

1.1 Background of research

In recent years, biofuel which is a product of microbes has gained interest as an alternative fuel that substitutes both petrol and diesel. The increase in the demand for biofuel is due to its environmentally friendly property of reducing pollution caused by crude oil products. Besides that, the demand for other microbial products such as vitamins, antibiotics, vaccines and pharmaceutical drugs have also increased. The production of microbes can also be used for wastewater treatment. Hence, to fulfill these demands, the production of microbes needs to be improved by understanding the mechanism of microbial growth which can be studied using an experimental apparatus called continuous stirred tank reactor (CSTR) or chemostat.

The chemostat is a tool that has been widely used for the continuous production of cell mass or microbes over a period of time (Monod, 1950, Novick & Szilard, 1950). Chemostats can be used to study the growth of microbes under controlled environments such as pH, temperature, light and nutrients so that a maximized product yield can be generated in the bioreactor over a long period (Vazquez, 2018). Chemostats have an inlet to allow substrates or nutrients to enter the reactor at a constant flow rate and the microbes' growth process takes place in the reactor. Then, the culture is drained out of the reactor at the same rate to keep the volume in the reactor constant. The efficiency of the chemostat is based on understanding the growth rate of the microbes in the reactor (Alqahtani *et al*., 2012).

The growth process of microbes in the chemostat is usually modelled by using microbial growth kinetic models that explain the relationship between microbes and substrates such as from the Monod (1949), Tessier (1936), Moser (1958) and Contois

(1959) models. Most of these models express the growth of microbes by consuming the substrate or nutrient. However, some substrates may inhibit the growth of microbes under high concentrations since more than one substrate molecule bind to an active site of the enzyme which deactivates the enzyme and hence reduces the metabolism of the cell and the viability of the microbe (Tan *et al*., 1996; Thatipamala *et al*., 1992). Hence, the growth rate model that expresses the substrate concentration inhibitory effects towards the microbial growth is required to estimate the growth of the microbial population in the chemostat.

One of the models that incorporate the substrate concentration inhibition is Andrew's (1968) model. Andrew's growth kinetics model is an extension of the Monod model where an additional substrate inhibition term has been taken into account. This model has been widely used for many applications since it provides a good fit for experimental data, especially for wastewater treatment systems (Abdi et al., 2013; Costa & Quintelas, 2011; Economou *et al*., 2011; Goudar *et al*., 2000; Halmi *et al*., 2014; Krishnan *et al*., 2017).

Previous experimental studies of chemostats by Dorofeev *et al.* (1992) and Lee *et al.* (1976) have found that the oscillatory behaviour of microbe population in the chemostat can be explained when the yield coefficient dependent on the substrate concentration and not when the yield coefficient is constant. Hence, the yield coefficient cannot be assumed as a constant where several theoretical studies have been done to study the consequence of this assumption (Alqahtani *et al.*, 2012, Alqahtani *et al.*, 2015b, Nelson & Sidhu, 2005, Nelson & Sidhu, 2007, Nelson & Sidhu, 2009). The oscillation of microbes in the reactor happens when a stable steady-state of the system loses its stability and periodic solution arise. This is called the bifurcation process, where a slight change in the parameter value can change the stability of the steady-state of a system. It has been proven by several previous studies where the productivity of microbe is improved by natural oscillation of microbes in the chemostat. The natural oscillation of microbes produces more microbes compared to a stable chemostat system (Alqahtani *et al*., 2015b, Balakrishnan & Yang, 2002; Nelson & Sidhu, 2005, 2009; Yang & Su, 1993).

It was also found that the productivity of the microbes can be improved when the cell mass leaving the reactor is recycled back into the reactor by using a tool called a settling unit. The microbes are recycled back to the chemostat after it has been settled down in the settling unit. There are studies that have been conducted to investigate the effect of the recycling process of the microbes which are found to be effective in improving the microbe production (Ajbar *et al.*, 1997; Alqahtani *et al*., 2015a; Bhowmik & Alqahtani, 2018; Cao *et al.*, 2015; Nelson *et al.*, 2012; Nelson *et al.*, 2008; Vanavil *et al.*, 2014).

Therefore, in this research, the chemostat model with a variable yield coefficient and Andrew's growth model was analysed to explain the growth of microbes in the chemostat. The effect of the recycling process towards the growth of microbial with variable yield coefficient and substrate inhibition kinetic model was also studied. The dynamical behaviours of the steady-state solutions with and without the recycling process were discussed by doing the stability analysis. The conditions for the washout of cell mass which means no growth of microbes occurring in the reactor and the condition for maximising the cell mass concentration in the reactor were identified by performing the stability analysis. The range of parameters that generates oscillations of microbes in the chemostat was determined by conducting the bifurcation analysis. The effect of natural oscillation of microbes in the chemostat was also included in this research.

1.2 Problem statement

The improvement of microbe production in a chemostat can be achieved by analysing the mathematical models of the chemostat. The chemostat model should be able to describe the mechanism of microbes so that the microbe production can be enhanced. It is known that the efficiency of the chemostat relies on the growth rate of microbes and the product yield. Hence, the growth rate of microbes and the product yield should be estimated precisely. The growth rate depends mainly on the concentration of the nutrient in the chemostat. However, a high concentration of substrate will inhibit the growth of microbes by deactivating the enzyme of the microbes. Hence, the growth rate model that expresses the substrate concentration's inhibitory effects towards the microbe growth is required to estimate the growth of the microbe population in the chemostat. The product yield that depends on the substrate concentration should be considered to define the actual process.

Previously, many analyses have been performed by considering the Monod model as the growth rate model and a few works were done using Andrew's substrate inhibition model. There are also analyses that considered variable yield coefficient and there are studies that considered recycling process into the chemostat model. However, there is no analysis yet has been done to the chemostat model with the Andrew's growth model, variable yield coefficient and recycling process. Therefore, in this research, the chemostat models with Andrew's growth model, a substrate inhibition model and variable yield coefficient with and without recycling process were analysed to study the dynamical behaviour of the steady-states of the chemostat systems. The stability and bifurcation analyses were performed to prevent the washout situation from occurring in the reactor and to identify the parameter range that generates oscillation of microbe population in the chemostat to improve the production of microbes.

1.3 Research objectives

This research consists of three main objectives which are

i. to reformulate the chemostat model by taking into account variable yield coefficient and Andrew's growth function with and without the recycling process.
ii. to perform the stability and bifurcation analyses of chemostat model by incorporating variable yield coefficient and Andrew's growth function with and without the recycling process.
iii. to investigate the performance of the reactor with and without the recycling process.

1.4 Scope of research

There are many types of microbial growth kinetic models that can be used to estimate the growth rate of microbes in a chemostat. In this research, Andrew's growth model was applied to express the substrate inhibitory effect on the microbes' growth rate. The chemostat model that was analysed in this research is a model that considers the growth of a single cell consuming a single substrate in a single reactor. A single reactor was considered so that the output from the single reactor can be set as a benchmark before comparing the output of two or more reactors. The feed was assumed to be a sterile feed where no initial amount of cell mass is supplied into the chemostat. The chemostat has an inlet to supply initial amounts of substrates and cell mass concentration into the reactor. However, no initial amount of cell mass was introduced into the chemostat to study the growth of microbes under sterile conditions.

There are two types of steady-states found in this study which are washout and no washout steady state. Washout steady-state means no growth of microbes occur in the chemostat while the no washout steady-state means there are growth of microbes occur in the chemostat. The stability and bifurcation analyses of this steady states were performed as the analysis done by Nelson & Sidhu (2005). The bifurcation analysis in this research is the local bifurcation analysis which can be analysed entirely through changes in the local stability of the steady-states, periodic orbits and other invariant sets. The phase plane and bifurcation diagrams of the chemostat model were visualised using *Mathematica* software.

1.5 Significance of research

The findings of this research will be a good contribution to microbial studies by improving the production of microbes using a chemostat system. Theoretically, the analysis of the chemostat model with substrate inhibition and variable yield coefficient will aid researches in choosing better parameter values for a high production of microbe. The stability analysis will present the steady-state solutions and the dynamical behaviour of those steady states. The condition for the washout of cell mass in the reactor (which means no growth of microbes occurring) was identified, hence, this situation can be avoided. Next, the condition for the cell mass in the reactor being maximised can be determined by using optimization method and the condition should be satisfied to produce a maximum amount of cell mass concentration. The condition for the oscillation of microbes to occur, which refers to the condition that makes the steady-states of the system becomes unstable, was determined by performing the bifurcation analysis. The parameter values should be chosen according to the condition since it has been proven that oscillation of microbe population that occurs in the chemostat can improve the productivity of the microbes in previous studies.

Therefore, the growth of microbes in the chemostat can be maximised continuously and the high demand for the microbe population can be fulfilled.

1.6 Framework of research

This thesis consists of six chapters. The first chapter discusses the background of research, problem statement, objectives of research, scopes of research and framework of research.

In Chapter 2, the literature review of this research is presented. The first topic in this chapter is the introduction of the chemostat where the characteristics and applications of the chemostat are discussed. This chapter also provides a discussion about existing chemostat models to estimate the production of microbes. The variable yield coefficient function and the substrate inhibited growth rate model are also addressed in this chapter. Finally, the existing chemostat models with the recycling process are described.

In Chapter 3, the methodology of this research is provided. The derivation of the basic chemostat model is presented and the process of recycling microbes into the chemostat is discussed in this chapter. The model involved in performing the stability and bifurcation analyses is provided in this chapter in order to analyse the chemostat model.

Next, Chapter 4 analyses the chemostat model with variable yield coefficient and substrate inhibition. The dynamical behaviour of the system is presented, and the bifurcation point is obtained in this chapter. The results are estimated and plotted by using the *Mathematica* software.

The fifth chapter presents the analysis of chemostat model with variable yield coefficient, substrate inhibition and recycling process. The dynamical behaviour and the range of parameters for oscillation occurrence are identified. The effect of recycling parameter is studied and the performance of the chemostat system with the recycling process is investigated.

Finally, in Chapter 6, the summary of this research and some recommendations for future work are prepared. The framework of this research is summarised in Figure 1.1.

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