Chapter 4

Second-order differential equations: A simple bioreactors model

4.1 Introduction

In this chapter we apply the techniques and idea from chapter 3 to a simple model for the growth of microorganisms. The microorganism (X) grows by consuming a substrate, or nutrient, (S), to produce more cells and a product (P). This model arises in a variety of applications.

- In microbiology it models experiments on microbial growth in a continuous flow reactor.
- In bioprocess and chemical engineering it arises as a model for a bioreactor, one use of which is to manufacture products using genetically altered microorganisms.
- It is the simplest model for the biological oxidation of wastewaters.
- It provides the underpinning of a model that has been used to study the mammalian large intestine [8].
- In ecology it arises as a model for a lake.

4.2 Model equations

4.2.1 The dimensional model

$$V\frac{\mathrm{d}S}{\mathrm{d}t} = F\left(S_0 - S\right) - VX\frac{\mu\left(S\right)}{\alpha}, \tag{4.1}$$

$$V\frac{\mathrm{d}X}{\mathrm{d}t} = F\left(X_0 - X\right) + VX\mu\left(S\right), \tag{4.2}$$

Specific growth rate

$$\mu\left(S\right) = \frac{\mu_m S}{K_s + S}, \tag{4.3}$$

Residence time

$$\tau = \frac{V}{F}, \tag{4.4}$$

where the specific growth defined by equation (4.3) is known as the Monod model.

In these equations F is the flowrate through the bioreactor $\left(\mathrm{dm}^3\,\mathrm{hr}^{-1}\right)$, K_s is the Monod constant $\left(\mathrm{g}\,\mathrm{dm}^{-3}\right)$, S is the substrate concentration within the bioreactor $\left(\mathrm{g}\,\mathrm{dm}^{-3}\right)$, S_0 is the concentration of substrate flowing into the reactor $\left(\mathrm{g}\,\mathrm{dm}^{-3}\right)$, V is the volume of the bioreactor, X is the concentration of cell-mass $\left(\mathrm{g}\,\mathrm{dm}^{-3}\right)$, X_0 is the concentration of cell-mass flowing into the reactor $\left(\mathrm{g}\,\mathrm{dm}^{-3}\right)$, t is time $\left(\mathrm{hr}^{-1}\right)$, α is the yield factor (–), μ is the specific growth rate model, μ_m is the maximum specific growth rate $\left(\mathrm{hr}^{-1}\right)$, and τ is the residence time (hr). The main experimentally controllable parameters are the substrate concentration in the feed (S_0) and the flow-rate (F). Experimental results are often presented as a function of the residence time $(\tau = V/F)$.

The yield factor (α) is the quotient of weight of bacteria formed to weight of substrate used, in simple models that is assumed constant.

This model is an example of an unstructured biological growth model. Although such models have been criticised, they are frequently used to analyse experimental data due to their simplicity.

A number of assumptions have made in deriving this model. They include: the bioreactor is sufficiently well stirred to approximate to the ideal of complete mixing, operating conditions such as the pH and temperature are held constant, and that flow through the reactor is sufficiently fast that cell-growth does not occur on the walls of the reactors. Assumptions have also been made regarding the nature of the interaction between the cellmass and the substrate.

4.2.2 The dimensionless model

By introducing dimensionless variables for the substrate concentration $(S^* = S_1/K_s)$, the cell mass concentration $(X^* = X_1/\left(\alpha K_s\right))$ and time $(t^* = \mu_m t)$ the system of differential equations (4.1) & (4.2) can be written in the dimensionless form

$$\begin{aligned}\frac{\mathrm{d}S^*}{\mathrm{d}t^*} &= \frac{1}{\tau^*}\left(S_0^* - S^*\right) - \frac{X^*S^*}{1+S^*},\\ \frac{\mathrm{d}X^*}{\mathrm{d}t^*} &= \frac{1}{\tau^*}\left(X_0^* - X^*\right) + \frac{X^*S^*}{1+S^*}.\end{aligned} \tag{4.5}$$

In these equations S_0^* is the dimensionless substrate concentration in the feed $(S_0^* = S_0/K_s)$, X_0^* is the dimensionless cell mass concentration in the feed $(X_0^* = X_0/\left(\alpha K_s\right))$, τ^* is the dimensionless residence time $(\tau^* = \mu_m \tau_1)$. The main experimentally controllable parameter is the dimensionless residence time.

Note that whilst equations 4.1–(4.3) contains six sets of parameters $(F/V, K_s, S_0, X_0, \alpha$ & $\mu_m)$ the dimensionless system defined by equation (4.5) only contains three sets $(S_0^*$, X_0^* & $\tau*)$. The reduction in the number of parameters is one reason to non-dimensionalise models prior to their analysis.

Question 4.1 *Show that by introducing dimensionless variables for the substrate concentration* $[S^* = S/K_s]$*, the cell mass concentration* $[X^* = X/\left(\alpha K_s\right)]$ *and time* $[t^* = \mu_m t]$ *the system of differential equations* (4.1) *&* (4.2) *can be written in the form of system* (4.5) *Check all the dimensionless groupings in the model in terms of dimensional parameters.*

Solution See example C.1. □

4.3 Analysis of the model with $X_0^* = 0$

In most applications it can be assumed that the concentration of biomass flowing into the reactor is zero, i.e. $X_0 = X_0^* = 0$. In this section we analyse the system (4.5) making this assumption.

4.3.1 Invariant region

Question 4.2 *Show that the region bounded by*

$$\begin{aligned} 0 &\le S^* \le S_0^*, \\ 0 &\le X^*, \end{aligned}$$

is invariant.

This region makes 'sense' physically. The variables S^* and X^* are related to the concentrations of the substrate and biomass in the reactor. Concentrations are non-negative quantities. Thus the positive quadrant should be invariant $(S^* \ge 0, X^* \ge 0)$. Furthermore, the substrate is flowing into a reactor where it is being consumed by biomass and there are no processes producing substrate within the reactor. Thus the substrate concentration inside the reactor should be no greater than the concentration of substrate flowing into the reactor $(S^* \le S_0^*)$.

At time $t = 0$ when the reactor starts up the initial value for the dimensionless biomass concentration will be positive $(X^*(t^*) > 0)$. The value for the dimensionless substrate concentration will usually be zero $(S^*(t^* = 0) = 0)$. If it is not zero it can be made very small before the reactor starts, so we can assume at the $t^* = 0$ that $0 \le S(t^*) \le S_0^*$. Therefore at time $t^* = 0$ the initial condition is always inside the invariant region. Thus the solution of system (4.5) is always within the invariant region.

Solution Left for the student. ☐

Question 4.3 *Can you find a way to 'close-up' the invariant region?*

Solution I don't know the answer to this question. So bonus marks if you can do it! ☐

4.3.2 Steady-state solutions

Question 4.4 *Show that the steady-state solutions of* (4.5) *are given by the 'washout' state*

$$(S^*, X^*) = (S_0^*, 0) \tag{4.6}$$

and the 'no washout' state

$$(S^*, X^*) = \left(\frac{1}{\tau_1^* - 1}, \frac{S_0^* \tau_1^* - (1 + S_0^*)}{\tau_1^* - 1} \right) \tag{4.7}$$

The 'washout' state is so-named because the steady-state value of the cellmass concentration is zero. As new cellmass does not flow into the reactor $(X_0^* = 0)$ this means that all the original cellmass present in the system has been literally 'washed-out' of the reactor.

Solution Left for the student to do. ☐

We are only interested in 'physically meaningful' steady-state solutions. That is to say, we are only interested in steady-state solutions with $S^* \ge 0$ and $X^* \ge 0$.

Question 4.5 *Show that the no-washout branch is physically meaningful when*

$$\tau^* \ge 1 + \frac{1}{S_0^*}.$$

Solution We require $S^* \ge 0$ and $X^* \ge 0$. From equation (4.7) the former is true when

$$\tau^* > 1. \qquad \textbf{C1}$$

Given that $S^* > 0$ the requirement for $X^* \geq 0$ is given by

$$S_0^* \left(\tau^* - 1\right) - 1 \geq 0.$$

This condition requires

$$\tau^* \geq 1 + \frac{1}{S_0^*}. \quad \mathbf{C2}$$

Now if condition **C2** holds then condition **C1** holds. Thus the condition for the no-washout branch to be physically meaningful is

$$\tau^* \geq 1 + \frac{1}{S_0^*}.$$

□

4.3.3 Stability of the steady-state solutions

In this section we investigate the stability of the washout and no-washout solutions as a function of the dimensionless residence time (τ^*). The dimensionless residence time is the main experimentally controllable parameter in the model, i.e. it is the primary bifurcation parameter.

To investigate the stability of the solution branches we need to know the Jacobian of system (4.5).

Question 4.6 *Show that the Jacobian of system* (4.5) *is given by*

$$J = \begin{pmatrix} \frac{-1}{\tau^*} - \frac{X^*}{(1+S^*)^2} & -\frac{S^*}{1+S^*} \\ \frac{X^*}{(1+S^*)^2} & \frac{-1}{\tau^*} + \frac{S^*}{1+S^*} \end{pmatrix} \tag{4.8}$$

Solution Left as an exercise for the student. □

4.3.3.1 Stability of the washout branch

Example 4.1

1. *Evaluate the Jacobian matrix along the washout branch and find its eigenvalues.*
2. *State the range of residence times for which the washout branch is stable.*

Solution

When the Jacobian matrix (4.8) is evaluated at the washout state we obtain

$$J\left(S^* = 0, X^* = 0\right) = \begin{pmatrix} \frac{-1}{\tau_1^*} & -\frac{S_0^*}{1+S_0^*} \\ 0 & \frac{-1}{\tau_1^*} + \frac{S_0^*}{1+S_0^*} \end{pmatrix}$$

The eigenvalues of this matrix are

$$\lambda_1 = -\frac{1}{\tau_1^*}$$
$$\lambda_2 = \frac{-1}{\tau_1^*} + \frac{S_0^*}{1+S_0^*}.$$

Thus the washout state is *stable* if

$$\tau_1^* < 1 + \frac{1}{S_0^*}. \tag{4.9}$$

4.3.3.2 Stability of the no-washout branch

Question 4.7

1. *Evaluate the Jacobian matrix along the washout branch. Do not substitute the values for S^* and X^* into the Jacobian matrix.* ***Hint.*** *You can simplify expressions of the form $S^*/(1+S^*)$ by considering the steady-state equation arising from the derivative $\dfrac{dX^*}{dt^*}$.*
2. *Show that any physically meaningful solution is stable.*
3. *State the conditions for the no-washout solution to be stable.*

Solution Using the hint we note that along the no-washout steady-state branch

$$\frac{S^*}{1+S^*} = \frac{1}{\tau^*}.$$

The Jacobian matrix can therefore be written in the form

$$J = \begin{pmatrix} \frac{-1}{\tau^*} - \frac{X^*}{(1+S^*)^2} & -\frac{1}{\tau^*} \\ \frac{X^*}{(1+S^*)^2} & 0 \end{pmatrix} \tag{4.10}$$

Along the no-washout branch we therefore have that

$$\det J = \frac{1}{\tau^*} \cdot \frac{X^*}{(1+S^*)^2},$$
$$\det J > 0 \Rightarrow \frac{X^*}{(1+S^*)^2} > 0$$

which is true provided $X^* > 0$ and $S^* > 0$.

From our earlier work we know that $X^* > 0$ when

$$\tau^* > 1 + \frac{1}{S_0^*},$$

and that when this inequality holds that $S^* > 0$. From equation (4.10) we have

$$\operatorname{tr} J = -\frac{1}{\tau^*} - \frac{X^*}{(1+S^*)^2}$$

and by assumption we have

$$X^* \geq 0,$$
$$S^* > 0.$$

Thus for physically meaningful solutions the condition $\operatorname{tr} J < 0$ automatically holds.

Thus the no-washout steady-state solution is stable provided that

$$\tau^* > 1 + \frac{1}{S_0^*}$$

We know that the simple bioreactor model has two solution branches. We have determined the stability of these solution branches as a function of the residence time and therefore can now draw steady-state diagrams.

Question 4.8 *Draw steady-state diagrams showing how the dimensionless cell mass concentration (X^*) and the dimensionless substrate concentration (S^*) change as the dimensionless residence time (τ^*) is varied. Identify the type of bifurcation occurring in your diagrams. (Only plot physically meaningful solutions).*

Solution Left as an exercise for the student. □

We have found the conditions under which the no-washout branch is stable. We can therefore answer questions such as the following, which are useful in practical operation of bioreactors.

4.3.4 Large residence time approximations

It is sometimes useful to know the performance of bioreactors at large residence times.

Question 4.9 *Obtain asymptotic formula for the dimensionless substrate and cell-mass concentrations.*

Solution Left as an exercise for the student. But the answers are

$$\begin{aligned} S^* &\approx \frac{1}{\tau^*} + O\left(\frac{1}{\tau^{*2}}\right), \\ X^* &\approx S_0^* - \frac{1}{\tau^*} + O\left(\frac{1}{\tau^{*2}}\right). \end{aligned}$$

4.3.5 Characterising the performance of a bioreactor

Example 4.2 *What residence time is required if the concentration of the substrate leaving the reactor is 90% of the substrate concentration entering the reactor?*

Solution The substrate concentration entering the reactor is S_0^*. If the substrate concentration leaving the reactor is 90% of the substrate concentration entering the reactor then the steady-state value for the substrate concentration is given by $S^* = 0.1S_0^*$. Thus

$$\begin{aligned} 0.1S_0^* &= \frac{1}{\tau^* - 1}, \\ \Rightarrow \tau^* &= 1 + \frac{10}{S_0^*}. \end{aligned}$$

□

Question 4.10 *The efficiency of the process in utilizing substrate is given by*

$$\mathcal{E} = 100 \cdot \frac{S_0^* - S^*}{S_0^*}.$$

What residence time should be used to:

(a) utilize 90% of the substrate?

(b) utilize 95% of the substrate?

(c) maximise utilization of the substrate?

Solution Left as an exercise. □

Question 4.11 *When a continuous bioreactor is used as a production process, its performance may be judged by the quantity of bacteria produced in unit time, which is sometimes called the output rate. In dimensional terms this is defined by*

$$\mathcal{O} = q \cdot X,$$

or in dimensionless terms by

$$\mathcal{O}^* = \frac{X^*}{\tau^*}.$$

(a) How is $\mathcal{O}^*$ related to $\mathcal{O}$?

(b) Find the value of:

(i) the dimensionless residence time, τ^*_{max} *that maximises the value of the dimensionless output.*

(ii) The value of the dimensionless biomass concentration when the residence time is given by $\tau^* = \tau^*_{\text{max}}$.

(iii) The maximum value of the dimensionless output.

Solution Left as an exercise. □

4.3.6 Miscellaneous

Questions that we have not yet covered.

1. By undertaking a phase-plane analysis of (4.5) find all possible types of behaviour exhibited by this system.
2. Can you find a Dulac function for this system? Hence, or otherwise, determine if sustained oscillations are possible for this system.
3. Product formation.

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