



# Mathematical Modelling of Chemical Kinetics with Model Dashboards

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# Chapter 1

## Introduction

From a real world problem, we identify the processes in that problem and then we formulate a mathematical model. This model describes the real world problem in mathematical terms. Analysing and simplifying that model can give us a mathematical solution. Interpreting our mathematical solution gives us a result that helps us to better understand the real world problem.

Some models like the ones we will look at are derived based on fundamental mechanisms of the physics or chemistry involved. These are sometimes called physics-based, mechanistic or first-principles models. On the other hand some people use data-driven or empirical models. These models rely fully on having experimental data.

There are advantages and disadvantages to the two kinds of models. Data-driven models use information from previously collected data (training data) to identify the characteristics of the current trend and to predict the future trend [1]. Data-driven models are completely reliant on getting a substantial amount of good data. As a result, it can be harder to understand what is happening physically from a data model. For example, chemical reactions can be complex and take a lot of time. If we were relying on data driven models to model the reaction, it would be hard to pinpoint how much data we would need to be representative of the entire reaction. It may not even be possible to get sufficient experimental data over a long time frame. It would be easier to draw the wrong conclusions from the data driven model, because of the lack of information.

In these situations, mechanistic models work best. Mechanistic models work outside of where the data is collected. They use physical or chemical laws of nature and are not based on experimental data. So the mechanisms are known and understandable. For a chemical reaction, we may have some physical knowledge about how the reaction will proceed. However for more complex reactions, we may need to collect experimental data to fit the model and improve it.

Interestingly, combining the two makes for very accurate models. Experimental data can improve the accuracy of mechanistic model. Data-driven models that are generated from mechanistic models can be trained using both simulation and field data[1].

In this report, we plan to model chemical kinetics mathematically using known physics and chemistry laws. Chemical kinetics is just one application of modelling interacting species. Some other applications are predator prey relationship models and disease dynamics models [2].

The objectives of this report are:

1. To detail the mathematics needed to model chemical reactions, specifically the reaction rates. This includes demonstrating how to derive the equations for a given reaction.

2. To outline the various ways to analyse and solve these mathematical modelling. This will introduce non-dimensionalisation and asymptotic solutions.
3. To explore complex cases of chemical reactions. This is where chemical oscillations and catalytic reactions will be analysed.
4. To create model graphical user interfaces, in the form of dashboards or apps using MATLAB. This would allow non-experts to explore model outputs, different parameters, and to fit model parameters without having to edit code.

In Chapter 2 we introduce chemical kinetics and outline the important concepts and fundamentals necessary to model chemical reactions. In Chapter 3 we outline the simple rate laws for modelling basic chemical reactions. Chapter 4 introduces successive and reversible reactions. In Chapter 5 the process of nondimensionalisation is discussed. Chapter 6 considers the mathematical modelling of chemical oscillations. Chapter 7 discusses catalytic chemical reactions.

## Chapter 2

# Chemical Kinetics

In this chapter, the basic theories of chemical kinetics necessary for modelling are introduced. Chemical kinetics is the branch of physical chemistry that is concerned with understanding the rates of chemical reactions [3]. Chemical reactions constantly occur in everyday life. Photosynthesis, oxidation (more commonly known as rusting), and fermentation are everyday examples of chemical reactions. Chemical reactions are achieved by kinetic energy and they occur when molecules collide in their environments.

A molecule is a group of two or more atoms held together by chemical bonds. As molecules collide, they break down into smaller particles, and form products. This is known as a chemical reaction. If we can predict the number of collisions, we can in turn predict the rate of reaction. The rate of a chemical reaction is the change in the amount of a reactant or product per unit time. The study of how collisions between molecules affect the rate of chemical reactions is chemical kinetics. With chemical kinetics, we aim to model and analyse these interactions between molecules.

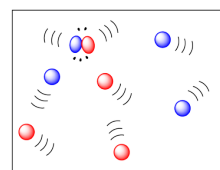


Figure 2.1:  
Molecules Moving  
and Colliding[4]

## 2.1 History of Chemical Kinetics

Chemical kinetics was first developed in 1864. Two Norwegian chemists, Peter Waage and Cato Guldberg, investigated the forces that drive chemical reactions. They found a relationship between the mass of the reactant and the rate it undergoes a chemical reaction. This became known as the Law of Mass Action. This law states that the speed of a chemical reaction is proportional to the quantity of the reacting substances. We will introduce this law in more detail in Section 2.5.

## 2.2 Kinetic Energy

As atoms and molecules move around their environments, they often collide with each other. Not all collisions are effective. If there is a sufficient amount of kinetic energy in these collisions, and the collision is oriented properly, a chemical reaction takes place. These collisions are depicted in Figure 2.2. A product is a substance that is formed as the result of a chemical reaction. As many collisions and reactions take place, the concentration of the reacting molecules goes down, while the concentration of the product goes up. There is not always enough energy between the molecules to make a reaction. There has to be enough energy in a collision. The activation

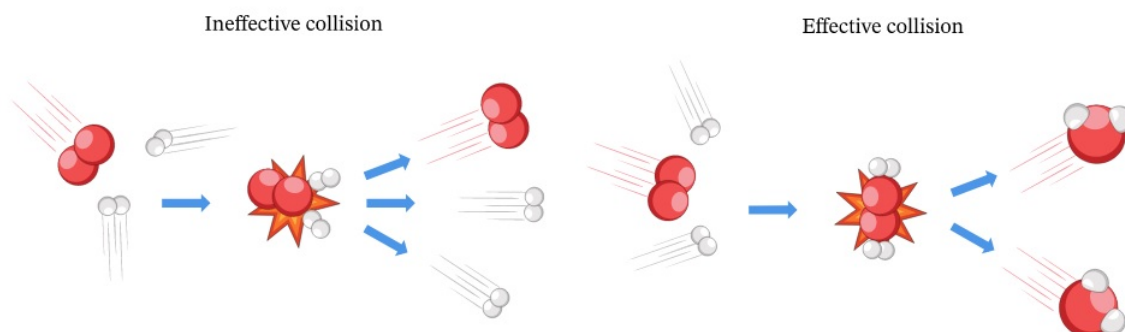


Figure 2.2: Depiction of ineffective and effective collisions [5]

energy is the energy threshold that must be overcome to produce a chemical reaction. Molecules need this much energy to hit other molecules hard enough to break them apart, and knock atoms off them. They then reform the atoms in different ways and eventually a product is formed. Activation energy is kinetic energy. The faster the molecules move the harder the collision will be. Once energy requirements are met, and the molecules collide in the right way, the reaction will proceed, but the rate of the reaction varies.

## 2.3 Elementary Reactions

An elementary reaction is a chemical reaction where reactants, or molecules, form products in a single step with a single transition state [6]. It focuses specifically on the collisions between the molecules. An elementary reaction is one step in an overall reaction mechanism. Elementary reactions may combine to form complex or nonelementary reactions. There are many types of elementary reactions. Some of them are:

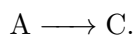
- Unimolecular
- Bimolecular
- Termolecular

Let us first define some elements of these reactions. The concentration of a reactant or product could either be the mass concentration or molar concentration. Molar concentration is measured by the amount of moles per unit volume. A mole is defined as  $6.02214076 \times 10^{23}$  of some chemical unit, be it atoms, molecules, ions, or others [7]. In this paper we will assume the concentration to be the molar concentration. This will be represented by square brackets, i.e.  $[A]$  is the concentration of A. The rate of reaction will be denoted as  $r$  for simplicity, and  $k$  is the reaction rate coefficient. Let us now examine the different types of elementary reactions.

A **unimolecular** reaction is a chemical reaction with just reactant one molecule. As there is only one reactant, unimolecular reactions are first order. For a first-order reaction, the rate of reaction is proportional to the concentration of one reactant and can be written as

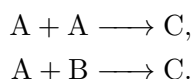
$$r = k[A].$$

In a unimolecular reaction, a molecule rearranges itself and forms one or more products. This is shown as



An example of this is radioactive decay. This is the spontaneous process through which an unstable atomic nucleus breaks into smaller, more stable fragments.

A **bimolecular** reaction is when two molecules collide with each other and form one or more products. This is represented as

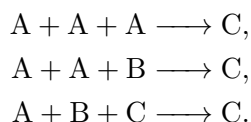


As there are two reactants, or two of the same reactants colliding, bimolecular reactions are second order. A second-order reaction has a rate proportional to the concentration of the square of a single reactant or the product of the concentration of two reactants, so that

$$\begin{aligned} r &= k[A]^2, \\ r &= k[A][B]. \end{aligned}$$

This is a common type of reaction in Organic Chemistry [6].

A **termolecular** reaction is when three molecules collide at once and react together. This is shown as



It is rare to see a termolecular reaction. This is because it is an unlikely event that three molecules will collide simultaneously with enough energy at the same place and time.

## 2.4 Stoichiometry and Rate Laws

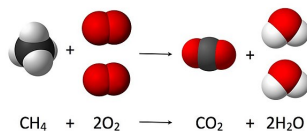


Figure 2.3: A stoichiometric diagram of the combustion reaction of methane [8].

**Stoichiometry** is the measure of the quantitative relationship between the products and reactants of a chemical reaction in terms of their relative ratios of mass or volume. Stoichiometry uses the laws of conservation of mass which states that mass cannot be created or destroyed, it can only be converted from one form to another. This law tells us that every elementary reaction needs to be balanced. The mass at the beginning of the reaction must equal the mass at the end. As a result of this law, we can predict the products of an elementary reaction. Figure 2.3 depicts the reaction of methane ( $\text{CH}_4$ ) with oxygen ( $\text{O}_2$ ). The amount of oxygen (red), hydrogen (white) and carbon (black) atoms stay the same before and after the reaction, they have just been rearranged. The mass before and after the reaction stays the same. Using stoichiometry, we can already know the outcome of a collision. If we know the amount of a reactant, we can calculate the amount of the product.



But with stoichiometry, we cannot predict how fast a reaction occurs or how fast the product is formed. We have to measure each reaction using rate laws. If we know exactly how many molecules are hitting each other, then the rate of reaction becomes quite predictable.

## 2.5 Law of Mass Action

The Law of Mass Action states that the speed of a chemical reaction is proportional to the quantity of the reacting substances.

To examine this we will follow the definition of the law of mass action given by Holmes [9]. Let A and B be reactants, and C and D be products of the reaction. Let us consider the general reaction



where  $\alpha, \beta, \gamma$ , and  $\delta$  are the stoichiometric coefficients used to balance out the equation. Basically,  $\alpha$  moles of reactant A react with  $\beta$  moles of reactant B and form  $\gamma$  moles of product C and  $\delta$  moles of product D.

The Law of Mass Action has three assumptions: First, the rate of the reaction is proportional to the product of the reactant concentrations, where each concentration is raised to the power of its respective coefficient. The rate of reaction is given as

$$r = k[A]^\alpha[B]^\beta. \quad (2.2)$$

Equation (2.2) is the law of mass action.

The second assumption is that the rate of change of the concentration of each element in the reaction is the product of its coefficient with the rate of the reaction. This is positive for a product and negative for a reactant, so that

$$\begin{aligned} \frac{dA}{dt} &= -\alpha r, \\ \frac{dC}{dt} &= \gamma r. \end{aligned}$$

Note that for the rest of this report,  $A$  and  $[A]$  will be used interchangeably to denote concentration.

Thirdly, for a system of reactions, the rates add.

Combining these assumptions, we can get the following:

$$\begin{aligned} \frac{dA}{dt} &= -\alpha r = -\alpha k A^\alpha B^\beta, \\ \frac{dB}{dt} &= -\beta r = -\beta k A^\alpha B^\beta, \\ \frac{dC}{dt} &= \gamma r = \gamma k A^\alpha B^\beta, \\ \frac{dD}{dt} &= \delta r = \delta k A^\alpha B^\beta. \end{aligned}$$

We assume the initial concentrations for the products and reactants to be known. We will refer to them as  $A_0$ ,  $B_0$ ,  $C_0$  and  $D_0$ .

These equations are not the easiest to solve. But we can combine the differential equations to find conserved quantities. Basically combine the time derivatives in some way to get them equal to 0. We can do this in the following way:

$$\beta \frac{dA}{dt} - \alpha \frac{dB}{dt} = -\alpha\beta k A^\alpha B^\beta + \alpha\beta k A^\alpha B^\beta = 0.$$

So from this it follows that,

$$\begin{aligned}\beta A(t) - \alpha B(t) &= \text{constant}, \\ \beta A_0 - \alpha B_0 &= \text{constant}, \\ \beta A(t) - \alpha B(t) &= \beta A_0 - \alpha B_0.\end{aligned}\tag{2.3}$$

Continuing this for each substance in the general reaction 2.1, we get the following conservations:

$$\begin{aligned}\beta A(t) - \alpha B(t) &= \beta A_0 - \alpha B_0 \\ \gamma A(t) + \alpha C(t) &= \gamma A_0 + \alpha C_0 \\ \delta A(t) + \alpha D(t) &= \delta A_0 + \alpha D_0\end{aligned}\tag{2.4}$$

Equations (2.4) are conservation laws. These are useful, when studying kinetic equations, because they reduce the number of equations that need to be solved. In the end, we can get the following equations in terms of  $A(t)$ :

$$B(t) = \frac{\beta}{\alpha}(A(t) - A_0) + B_0\tag{2.5}$$

$$C(t) = \frac{\gamma}{\alpha}(A_0 - A(t)) - C_0\tag{2.6}$$

$$D(t) = \frac{\delta}{\alpha}(A_0 - A(t)) - D_0\tag{2.7}$$

A steady state in the system occurs at constant concentrations which satisfy the kinetic equations. Such solutions can be found by setting all the time derivatives to zero and solving for equilibrium concentrations.

$$\begin{aligned}\frac{dA}{dt} &= -\alpha k A^\alpha B^\beta = 0 \\ \frac{dB}{dt} &= -\beta k A^\alpha B^\beta = 0 \\ \frac{dC}{dt} &= \gamma k A^\alpha B^\beta = 0 \\ \frac{dD}{dt} &= \delta k A^\alpha B^\beta = 0\end{aligned}$$

For this to be satisfied, either  $A(t) = 0$  or  $B(t) = 0$ . If  $A(t) = 0$  then using the equations (2.5) - (2.7),

$$\begin{aligned}A(t) &= 0 \\ B(t) &= B_0 - \frac{\beta}{\alpha}(A_0) \\ C(t) &= \frac{\gamma}{\alpha}A_0 - C_0 \\ D(t) &= \frac{\delta}{\alpha}A_0 - D_0\end{aligned}$$

If  $B(t) = 0$  then

$$B(t) = 0$$

$$A(t) = A_0 - \frac{\alpha}{\beta} B_0$$

$$C(t) = \frac{\gamma}{\beta} B_0 - C_0$$

$$D(t) = \frac{\delta}{\beta} B_0 - D_0$$

These are the steady states.

## Chapter 3

# Basic Models of Chemical Kinetics: Simple Rate Laws

The Law of Mass Action only applies to elementary reactions. However, for more complex reactions where the reaction pathway may be unknown, the rate of reaction for a general reaction is often written as  $r(t) = k[A]^m[B]^n$ . The exponents  $m$  and  $n$  have to be found experimentally. In simple cases this leads to simple rate laws. To understand simple rate laws, we first need to introduce the differential rate law.

Let us look at a reactant component we will call A. Over time the molecules in A decrease and the concentration of A goes down. Let  $A(t)$  be the concentration of A at time  $t$  and let  $r(t)$  be the rate of reaction of A at time  $t$ . The rate of reaction of A over the small time period, is equal to the change in the concentration of A divided by the change in time. From this we can form an expression for  $r(t)$ :

$$-r(t) = \frac{\Delta A}{\Delta t}, \quad (3.1)$$

where  $\Delta A$  represents the change in A, and  $\Delta t$  represents the change in time. More precisely:

$$-r\left(t + \frac{\Delta t}{2}\right) = \frac{A(t + \Delta t) - A(t)}{\Delta t}$$

Take the limit as  $\Delta t \rightarrow 0$  and we get,

$$\begin{aligned} \lim_{\Delta t \rightarrow 0} -r\left(t + \frac{\Delta t}{2}\right) &= \lim_{\Delta t \rightarrow 0} \frac{A(t + \Delta t) - A(t)}{\Delta t}, \\ -r(t) &= \lim_{\Delta t \rightarrow 0} \frac{A(t + \Delta t) - A(t)}{\Delta t}. \end{aligned} \quad (3.2)$$

We get the formal definition of a derivative. So,

$$-r(t) = \frac{dA}{dt}. \quad (3.3)$$

We can conclude that the rate of reaction of A is equal to the change in concentration of the reactant A. This is known as the differential rate law. Similar differential equations can be written down for all reactants and products in a reaction.

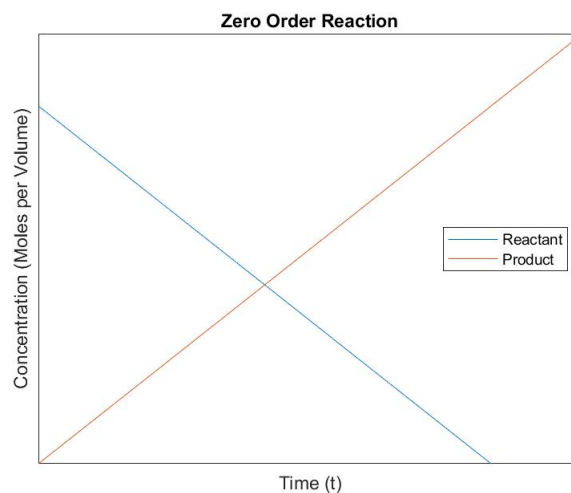


Figure 3.1: Zero Order Reaction

### 3.1 Zero Order Reaction

In a zero order reaction, the rate of reaction is independent of the concentration of the reactant. This is depicted in Figure 3.1.

The reaction rate is written as:

$$r = k[A]^0 = k \quad (3.4)$$

The reaction rate is constant. An example of this type of reaction is the decomposition of ethanol in human blood. The concentration of ethanol decreases linearly with time.

We can use the reaction rate (3.4) to derive an equation for the reactant and the product in a zero order reaction.

Let  $A(t)$  be the concentration of reactant A at a time  $t$ , and let  $B(t)$  be the concentration of product B at time  $t$ .

The initial conditions are

$$\begin{aligned} A(0) &= a_0, \\ B(0) &= b_0 = 0, \end{aligned} \quad (3.5)$$

where  $a_0$  is the initial concentration of A and where  $b_0$  is the initial concentration of B.

The rate of change in A can be given by the equation

$$\frac{dA}{dt} = -k. \quad (3.6)$$

Integrate equation (3.6) to get an equation for  $A(t)$

$$\begin{aligned} \int dA &= -k \int dt \\ \Rightarrow A(t) &= -kt + c_1. \end{aligned}$$

Recall (3.5) and solve for initial condition at  $t = 0$  which leads to,

$$\begin{aligned} A(0) &= -k(0) + c_1, \\ \Rightarrow a_0 &= c_1. \end{aligned}$$

Now we have an equation for  $A(t)$ :

$$A(t) = a_0 - kt. \quad (3.7)$$

To get an equation for the concentration of the product,  $B(t)$ , we use the conservation laws we introduced on the outset:

$$A(t) + B(t) = a_0 + b_0$$

So we get an equation for  $B(t)$ :

$$\begin{aligned} B(t) &= a_0 - A(t) \\ \Rightarrow B(t) &= a_0 - a_0 + kt \\ \Rightarrow B(t) &= kt \end{aligned} \quad (3.8)$$

We can use (3.7) and (3.8) to determine the concentrations of reactant A and product B for known values of  $k$  and  $a_0$ . The reaction is complete when,

$$A(t) = a_0 - kt = 0,$$

at time,

$$t = \frac{a_0}{k}.$$

The half-life of a substance, is the time required for the concentration of the substance to reduce to half of its initial value. The half life for  $A(t)$  will occur when

$$A(t) = \frac{a_0}{2} = a_0 - kt,$$

at time,

$$t = \frac{a_0}{2k}.$$

## 3.2 First Order Reaction

In a first order reaction the rate of reaction is dependent on the concentration of one reactant. This is depicted in Figure 3.2. The reaction rate is written as:

$$r = k[A]^1 = k[A]$$

Let us examine a reactant A, and a product B. Let  $A(t)$  be the concentration of A at a time  $t$ , and let  $B(t)$  be the concentration of B at time  $t$ . We define the initial conditions as,

$$\begin{aligned} A(0) &= a_0, \\ B(0) &= b_0 = 0, \end{aligned} \quad (3.9)$$

where  $a_0$  is the initial concentration of A and  $b_0$  is the initial concentration of B.

The rate of change in A can be given by the equation

$$\frac{dA}{dt} = -k. \quad (3.10)$$

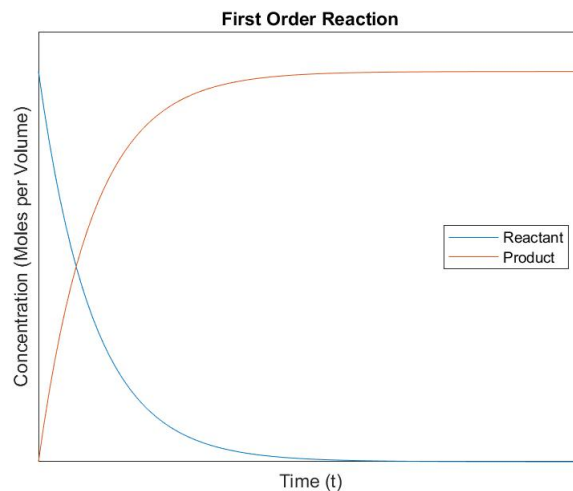


Figure 3.2: First order reaction

Integrate equation (3.10):

$$\int \frac{dA}{A} = -k \int dt$$

$$\ln(A) = -kt + c.$$

We get an equation for  $A(t)$ ,

$$A(t) = e^{-kt+c} \quad (3.11)$$

Let  $e^c$  be a constant  $K_1$  which we substitute  $K_1$  into equation (3.11):

$$A(t) = K_1 e^{-kt}. \quad (3.12)$$

We then solve for initial condition at  $t = 0$  and we get

$$A(0) = K_1 e^{-k(0)},$$

$$A(0) = K_1. \quad (3.13)$$

Recall (3.9) and substitute in

$$A(0) = a_0 = K_1.$$

Now we have the following equation for  $A(t)$ :

$$A(t) = a_0 e^{-kt} \quad (3.14)$$

We use the Equation (3.14) for  $A(t)$  to find an equation for  $B(t)$ . We can do this by recalling Equation (2.4), the conservation laws. So the equation for  $B(t)$  can be derived this way:

$$A(t) + B(t) = a_0 + b_0,$$

$$B(t) = a_0 - A(t),$$

$$B(t) = a_0(1 - e^{-kt}). \quad (3.15)$$

The steady states for this system is when:

$$\begin{aligned}\frac{dA}{dt} &= -kA = 0, \\ A(t) &= 0 \\ B(t) &= a_0\end{aligned}$$

The half life of the reaction is time required for half the initial concentration of A to react. This is when,

$$A(t) = \frac{a_0}{2} = a_0 e^{-kt},$$

at time

$$t = -\frac{\ln(\frac{1}{2})}{k}.$$

The half-life here is independent of the initial concentration. This means that it takes the same time for half the concentration to deplete no matter what the initial concentration is. The reaction is complete when the concentration of A is equal to 0.

We can use equations (3.14) and (3.15) to determine the concentrations of A and B for known values of  $a_0$  and  $k$ . On the otherhand, we can use experimental data to determine the reaction rate coefficient  $k$ .

### 3.2.1 First Order Reaction Example

As an example, we will examine the reaction of Aspirin to form Salicylic Acid.

Time (h)	Aspirin (M)	Salicylic Acid (M)
0	$5.55 \times 10^{-3}$	0.00
2	$5.51 \times 10^{-3}$	$0.040 \times 10^{-3}$
5	$5.45 \times 10^{-3}$	$0.10 \times 10^{-3}$
10	$5.35 \times 10^{-3}$	$0.20 \times 10^{-3}$
20	$5.15 \times 10^{-3}$	$0.40 \times 10^{-3}$
30	$4.96 \times 10^{-3}$	$0.59 \times 10^{-3}$
40	$4.78 \times 10^{-3}$	$0.77 \times 10^{-3}$
50	$4.61 \times 10^{-3}$	$0.94 \times 10^{-3}$
100	$3.83 \times 10^{-3}$	$1.72 \times 10^{-3}$
200	$2.64 \times 10^{-3}$	$2.91 \times 10^{-3}$
300	$1.82 \times 10^{-3}$	$3.73 \times 10^{-3}$

Table 3.1: Data from [10]

Using the data from Table 3.1 we plot Aspirin and Salicylic Acid against time, and join the points together to aid visualisation. The result is Figure 3.3.

Our goal is to build the equation of this reaction, using the equation (3.14) we previously derived. We are missing  $k$ , reaction rate coefficient.

We can find a value for  $k$  by fitting a linear model to equation (3.14), using linear regression. Linear regression builds an equation that models the linear relationship between a dependent and independent variable. It finds a straight line that best fits the data.



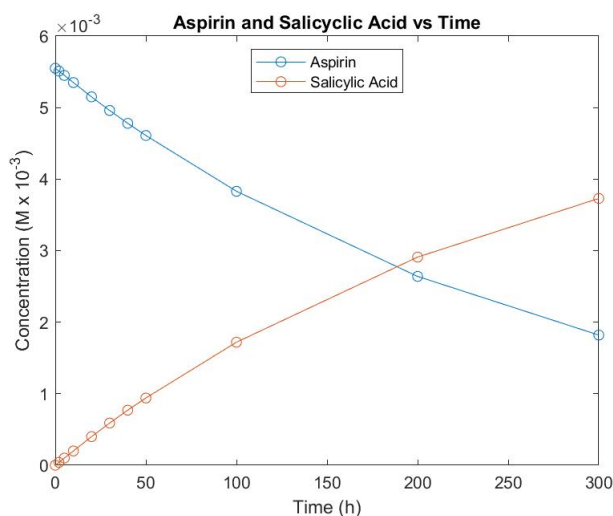


Figure 3.3: Time vs Aspirin and Salicylic Acid

From figure 3.3 its clear to see that a straight line would not best represent the concentrations of Aspirin and Salicylic Acid. So, we transform the data to see if we can find a linear relationship to time. An appropriate transformations would be taking natural log of the concentrations.

Time (h)	$\ln(\text{Aspirin})$ (M)	$\ln(\text{Salicylic Acid})$ (M)
0	-5.19395735122379	$-\infty$
2	-5.20119065581731	-10.1266311038503
5	-5.21213967030699	-9.21034037197618
10	-5.23065871807422	-8.51719319141624
20	-5.26875856430649	-7.82404601085629
30	-5.30634953824530	-7.43538802106451
40	-5.34331473247877	-7.16912004311654
50	-5.37952742197358	-6.96963068270023
100	-5.56489047578958	-6.36543098815678
200	-5.93697636182391	-5.83960219779874
300	-6.30891877789343	-5.59134704532641

Table 3.2: Natural Log Transformation of Aspirin and Salicylic Acid

Table 3.2 is a table of the natural log transforms of the data in Table 3.1

From figure 3.4 it is clear to see that the natural log of the concentration of Aspirin is linear. This identifies the reaction as first order. If a plot of the natural log of reactant concentration versus time is linear, then the reaction is first order in that reactant. We can use this information to find the value of  $k$ .

Using the `fitlm` function in Matlab, we find the equation of the line to be:

$$\ln(A(t)) = -0.0037t - 5.1940 \quad (3.16)$$

From the equation (3.16) we get that the slope of the line is -0.0037. This is our reaction rate coefficient  $k$ .

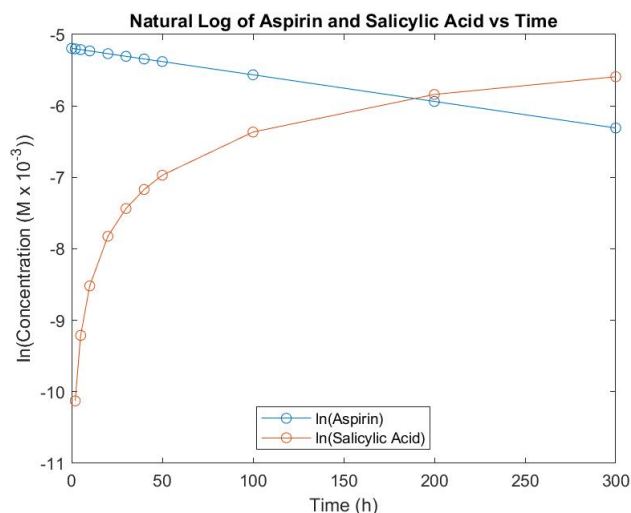


Figure 3.4: Natural Log of Aspirin and Salicylic Acid against Time

To evaluate how good the model is, we can calculate the Adjusted R-Squared ( $R^2$ ) and Root Mean Square Error (RMSE) values. The formulas for these are:

$$\text{Adjusted } R^2 = 1 - \left( \frac{SS_R}{SS_T} \right) \left( \frac{N-1}{N-p-1} \right),$$

$$RMSE = \sqrt{\sum_{i=1}^N \frac{(\hat{y}_i - y_i)^2}{N}},$$

where  $SS_R$  is the sum of squares of residuals,  $SS_T$  is the total sum of squares,  $N$  is the total sample size,  $p$  is the number of independent variables,  $\hat{y}$  are the predicted values, and  $y$  are the actual values. The Adjusted  $R^2$  value is the amount of variability that is explained by the regression model. It determines how well the model fits the data after taking into account the number of variables in the regression model. The closer the value is to 1, the better the model fits. The RMSE shows how far the model predictions are from the actual true values. The Adjusted  $R^2$  value is only used to evaluate the fit for linear regression models, whereas the RMSE can be used for both linear and non-linear regression models.

Both the Adjusted  $R^2$  and the RMSE values, show our model is a perfect fit. So we can substitute our reaction rate coefficient -0.0037 into our equations (3.14) and (3.15) to get equations for the concentrations in Aspirin and Salicylic Acid:

$$A(t) = 5.1940e^{-0.0037t}$$

$$S(t) = 5.1940(1 - e^{-0.0037t})$$

where  $A(t)$  and  $S(t)$  are the concentrations of Aspirin and Salicylic Acid at time  $t$ .

Figure 3.5 shows the data points from Table 3.1 and the computed equations plotted on a graph. The data points align excellently with our computed equation.

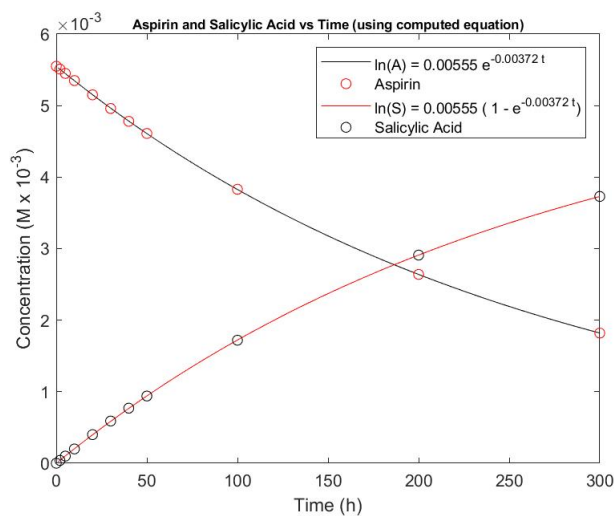


Figure 3.5: Computed equation for Aspirin and Salicylic Acid against time

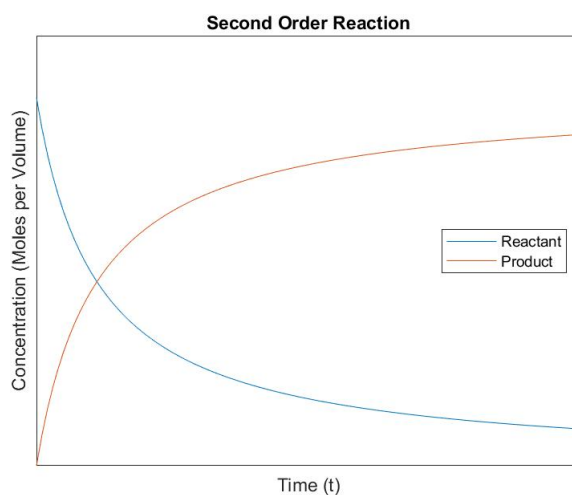


Figure 3.6: Second Order Reaction

### 3.3 Second Order Reaction

In a second order reaction, the rate of reaction is dependent on the concentration of two reactants. In some cases these two reactants are the same. The reaction rate is written as:

$$\begin{aligned} \text{rate of reaction} &= k[A][B] \\ \text{rate of reaction} &= k[A]^2 \end{aligned} \quad (3.17)$$

We will be focusing on (3.17), where the reactants are identical.

Let  $A(t)$  be the concentration of reactant A at a time  $t$ , and let  $P(t)$  be the concentration of product P at time  $t$ .

$$\begin{aligned} A(0) &= a_0, \\ P(0) &= p_0 = 0, \end{aligned} \quad (3.18)$$

where  $a_0$  is the initial concentration of A and where  $p_0$  is the initial concentration of B.

The rate of change in A can be given by the equation,

$$\frac{dA}{dt} = -kA^2. \quad (3.19)$$

Integrate equation (3.19)

$$\begin{aligned} \int \frac{1}{A^2} dA &= -k \int dt \\ \Rightarrow -\frac{1}{A} &= -kt + c_1. \\ \Rightarrow \frac{1}{A} &= kt - c_1. \end{aligned} \quad (3.20)$$

We get an expression for  $A(t)$

$$A(t) = \frac{1}{kt - c_1} \quad (3.21)$$

Solving for initial conditions we get:

$$\begin{aligned} A(0) &= \frac{1}{k(0) - c_1} \\ \Rightarrow a_0 &= -\frac{1}{c_1} \\ \Rightarrow -c_1 &= \frac{1}{a_0} \end{aligned} \quad (3.22)$$

New equation for  $A(t)$ :

$$A(t) = \frac{1}{kt + \frac{1}{a_0}} \quad (3.23)$$

Writing this equation as,

$$\frac{1}{A(t)} = kt + \frac{1}{a_0},$$

and plotting  $\frac{1}{A(t)}$  against  $t$  gives a linear relationship.

The equation for  $P(t)$  can be derived this way using conservation laws:

$$\begin{aligned} A(t) + P(t) &= a_0 + p_0 \\ \Rightarrow P(t) &= a_0 - A(t) \\ \Rightarrow P(t) &= a_0 - \frac{1}{kt + \frac{1}{a_0}} \\ \Rightarrow P(t) &= \frac{a_0 kt}{kt + \frac{1}{a_0}} \end{aligned} \quad (3.24)$$

The steady states for this system occur when,

$$\begin{aligned}A(t) &= 0, \\P(t) &= a_0.\end{aligned}$$

The half life for this reaction is when,

$$A(t) = \frac{a_0}{2} = \frac{1}{kt + \frac{1}{a_0}},$$

at time

$$t = \frac{1}{a_0 k}.$$

## Chapter 4

# More Complex Reactions

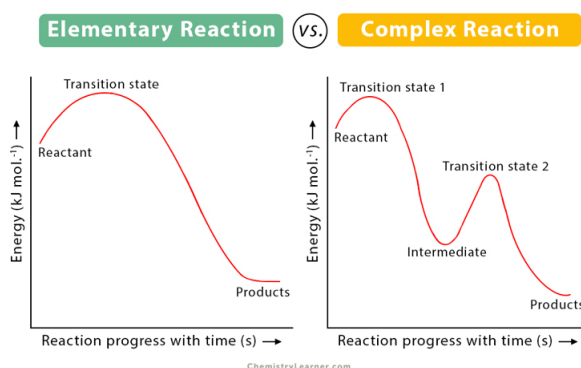


Figure 4.1: Elementary versus Complex Reactions[11]

An elementary reaction is a chemical reaction that takes a single step. A complex reaction is a chemical reaction involving many steps.

Figure 4 shows the difference between an elementary reaction and a complex reaction. The energy levels for each reaction are graphed. The spikes in the graph are labelled as the transition states. The transition state is the phase of the reaction where the reaction attains the highest energy. It is a very short-lived stage, where the original chemical bonds of the reactants are broken down to form new ones [11]. There is more than one transition state in a complex reaction. This means there are many stages in a complex reaction unlike the one stage in an elementary reaction. In an elementary reaction, reactants directly form the products without any intermediates. In contrast, in a complex reaction, reaction intermediates form the final products [11].

Complex reactions can be understood by breaking them up into elementary steps. We will now look at some examples of complex reactions.

### 4.1 Successive Chemical Reactions

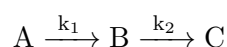


Figure 4.2 depicts the evolution of components A, B and C in a successive reaction. Here a reactant A is converted into a product C through an intermediate B. From the figure 4.2 we see

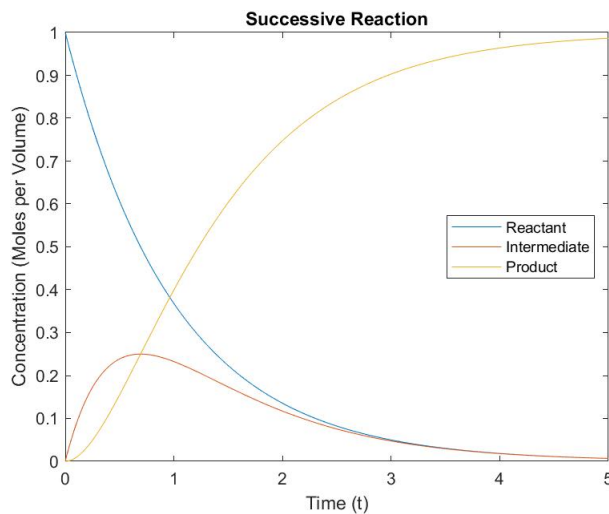


Figure 4.2: Successive Reaction

the concentration of the intermediate goes up, then goes back down to 0 again. In this case we are going to assume that the two reaction rate constants are different, i.e  $k_1 \neq k_2$ .

Let us separate the reaction into two parts:



The rate of reactions for the reactant and concentration for the first part (4.1) are:

$$\begin{aligned} \frac{dA}{dt} &= -k_1 A \\ \frac{dB}{dt} &= k_1 A \end{aligned}$$

The rate of reactions for the reactant and concentration for the second part (4.2) are:

$$\begin{aligned} \frac{dB}{dt} &= -k_2 B \\ \frac{dC}{dt} &= k_2 B \end{aligned}$$

As B is involved in the two parts of the reaction, we combine the reaction rates and get:

$$\frac{dB}{dt} = k_1 A - k_2 B \quad (4.3)$$

So the reaction rates for the three elements of this reaction is:

$$\begin{aligned} \frac{dA}{dt} &= -k_1 A \\ \frac{dB}{dt} &= k_1 A - k_2 B \\ \frac{dC}{dt} &= k_2 B \end{aligned}$$

Initial conditions:

$$\begin{aligned}A(0) &= a_0 \\B(0) &= b_0 = 0 \\C(0) &= c_0 = 0\end{aligned}$$

A is a first order reaction:

$$\begin{aligned}\frac{dA}{dt} &= -k_1 A \\A(t) &= a_0 e^{-k_1 t}\end{aligned}\tag{4.4}$$

Substitute into the reaction rate for B,

$$\begin{aligned}\frac{dB}{dt} &= k_1 A - k_2 B, \\ \frac{dB}{dt} &= k_1 a_0 e^{-k_1 t} - k_2 B.\end{aligned}\tag{4.5}$$

We use the integrating factor method to solve for  $B(t)$ :

$$\begin{aligned}e^{\int k_2} &= e^{k_2 t} \\ \frac{d}{dt}(e^{k_2 t} B) &= e^{(k_2 - k_1)t} k_1 a_0 \\ e^{k_2 t} B &= k_1 a_0 \int e^{(k_2 - k_1)t} dt, \\ e^{k_2 t} B &= k_1 a_0 \left( \frac{e^{(k_2 - k_1)t}}{k_2 - k_1} + K \right) \\ B(t) &= \frac{k_1 a_0}{k_2 - k_1} e^{-k_1 t} + K_1 e^{-k_2 t}\end{aligned}$$

Solving for initial conditions and getting a value for constant  $K$ :

$$\begin{aligned}b_0 = 0 &= \frac{k_1 a_0}{k_2 - k_1} + K_1 \\ K_1 &= -\frac{k_1 a_0}{k_2 - k_1}\end{aligned}\tag{4.6}$$

We get an equation for  $B(t)$ :

$$\begin{aligned}B(t) &= \frac{k_1 a_0}{k_2 - k_1} e^{-k_1 t} - \frac{k_1 a_0}{k_2 - k_1} e^{-k_2 t} \\ B(t) &= \frac{k_1 a_0}{k_2 - k_1} (e^{-k_1 t} - e^{-k_2 t})\end{aligned}\tag{4.7}$$

Adding the three equations we find the conservation law:

$$\begin{aligned}\frac{dA}{dt} + \frac{dB}{dt} + \frac{dC}{dt} &= 0 \\ \Rightarrow A(t) + B(t) + C(t) &= a_0.\end{aligned}\tag{4.8}$$



We can use this conservation law to get an equation for  $C(t)$ .

$$C(t) = a_0 - A(t) - B(t)$$

$$C(t) = a_0 \left( 1 + \frac{k_1 e^{-k_2 t} - k_2 e^{-k_1 t}}{k_2 - k_1} \right).$$

The steady states for a successive reaction occurs when the rate of reaction for the intermediate and the other two derivatives are equal to 0. This takes the form,

$$\frac{dB}{dt} = k_1 A - k_2 B = 0.$$

So the steady states are:

$$B = \frac{k_1}{k_2} A$$

$$C = a_0 - A \left( 1 + \frac{k_1}{k_2} \right)$$

Using the steady states, we can simplify  $C(t)$  again:

$$C(t) = a_0 - \left( 1 + \frac{k_1}{k_2} \right) a_0 e^{-k_1 t}$$

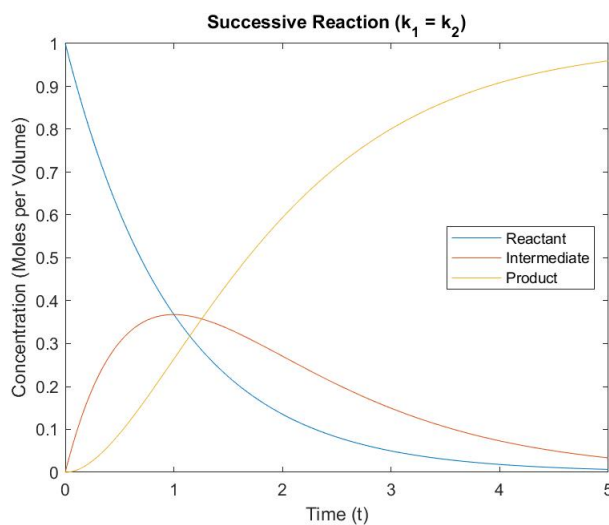


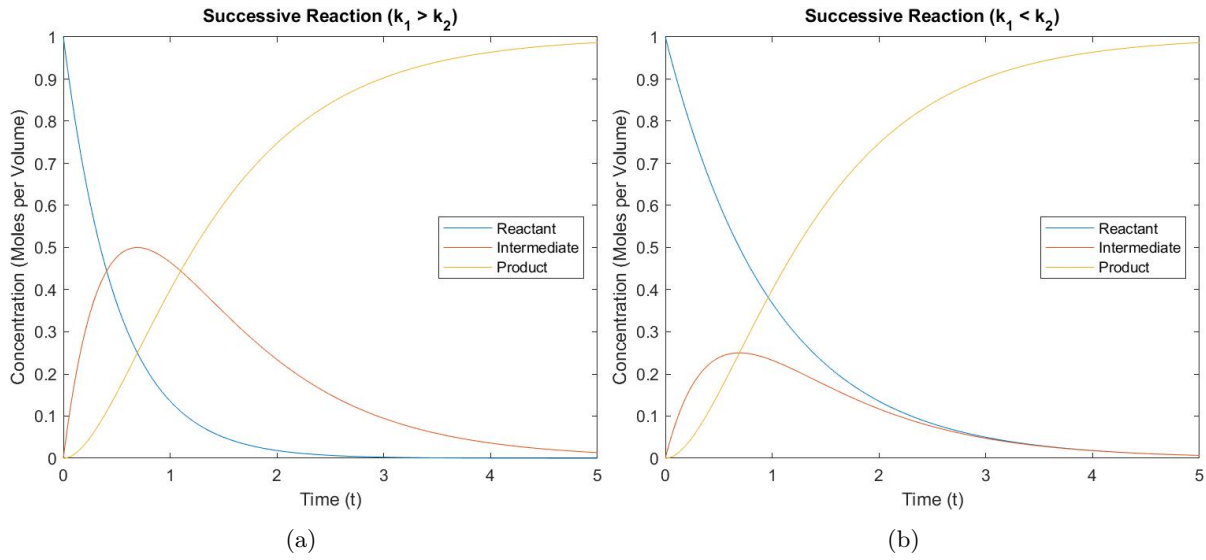
Figure 4.3: Successive Reaction with equal rates

If we look at the case when  $k_1 = k_2 = k$ , as shown in Figure 4.3 then

$$\frac{dA}{dt} = -kA,$$

$$\frac{dB}{dt} = kA - kB,$$

$$\frac{dC}{dt} = kB.$$



So using the conservation law in equation (4.8) and the initial conditions, we get the following results:

$$\begin{aligned} A(t) &= a_0 e^{-kt}, \\ B(t) &= a_0 k t e^{-kt}, \\ C(t) &= a_0 - a_0 e^{-kt} - a_0 k t e^{-kt}. \end{aligned}$$

When  $\varepsilon = 1$ , that is when  $k_1 = k_2$ , we can just solve the equations exactly, using the solutions derived in section 4.1.

## 4.2 Reversible Chemical Reactions

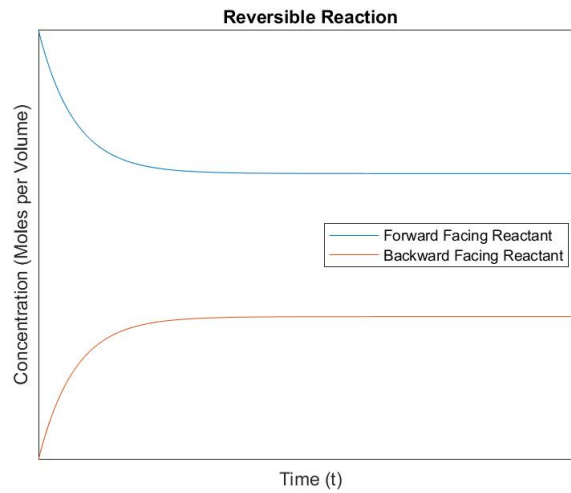
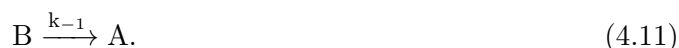


Figure 4.4: Reversible Reaction

All of the reactions we have looked at so far have been forward facing, but this is not always the case. We can have forward and back facing reactions. Figure 4.4 shows a reversible reaction. This reaction is written as:



where  $k_1$  is the forward facing rate constant, and  $k_{-1}$  is the backwards facing rate constant. A and B take turns being the reactant and the products. An example of this type of reaction in organic chemistry is the dissociation of hydrogen iodides. Let us first look at this as two separate first order reactions:



Let us get an expression for the rate of reaction 4.10. This is a first order reaction and takes the form:

$$\begin{aligned} \frac{dA}{dt} &= -k_1 A \\ \frac{dB}{dt} &= k_1 A \end{aligned}$$

And for the rate of reaction 4.11:

$$\begin{aligned} \frac{dB}{dt} &= -k_{-1} B \\ \frac{dA}{dt} &= k_{-1} B \end{aligned}$$

Combining these we get the following expressions for the reaction rates:

$$\frac{dA}{dt} = k_{-1} B - k_1 A \quad (4.12)$$

$$\frac{dB}{dt} = k_1 A - k_{-1} B \quad (4.13)$$

$A(t)$  and  $B(t)$  are the concentrations of A and B respectively at time  $t$ . We assume the initial conditions are known and given by:

$$\begin{aligned} A(0) &= a_0, \\ B(0) &= b_0 = 0. \end{aligned}$$

We can get the following conserved quantity by combining 4.12 and 4.13:

$$\begin{aligned} \frac{dA}{dt} + \frac{dB}{dt} &= 0 \\ A(t) + B(t) &= a_0 \end{aligned} \quad (4.14)$$

Combining 4.12 and 4.14:

$$\begin{aligned} \frac{dA}{dt} &= k_{-1}(a_0 - A) - k_1 A \\ \frac{dA}{dt} + (k_{-1} + k_1)A &= k_{-1}a_0 \end{aligned} \quad (4.15)$$

We solve this by using the integrating factor  $e^{\int k_{-1}+k_1}$ :

$$\begin{aligned}
 e^{\int k_{-1}+k_1} &= e^{(k_{-1}+k_1)t} \\
 \Rightarrow \frac{d}{dt}(e^{(k_{-1}+k_1)t} A) &= e^{(k_{-1}+k_1)t} k_{-1} a_0 \\
 \Rightarrow e^{(k_{-1}+k_1)t} A &= k_{-1} a_0 \int e^{(k_{-1}+k_1)t} dt \\
 \Rightarrow A(t) &= \frac{k_{-1} a_0}{k_{-1} + k_1} + C e^{(k_{-1}+k_1)t}.
 \end{aligned} \tag{4.16}$$

We get a value for  $C$ , the constant of integration, by solving for the initial condition. We then sub it back into our equation 4.16 for  $A(t)$ :

$$\begin{aligned}
 a_0 &= \frac{k_{-1} a_0}{k_{-1} + k_1} + C \\
 \Rightarrow A(t) &= a_0 \left( \frac{k_{-1}}{k_{-1} + k_1} + \left(1 - \frac{k_{-1}}{k_{-1} + k_1}\right) e^{(k_{-1}+k_1)t} \right) \\
 \Rightarrow A(t) &= a_0 \left( \frac{k_{-1} + k_1 e^{(k_{-1}+k_1)t}}{k_{-1} + k_1} \right)
 \end{aligned} \tag{4.17}$$

We use the conservation law 4.14 to get an equation for  $B(t)$ :

$$\begin{aligned}
 B(t) &= a_0 - A(t) \\
 \Rightarrow B(t) &= a_0 \left( 1 - \frac{k_{-1} + k_1 e^{(k_{-1}+k_1)t}}{k_{-1} + k_1} \right)
 \end{aligned} \tag{4.18}$$

The steady states for this system are when:

$$\begin{aligned}
 \frac{dA}{dt} &= k_{-1} B - k_1 A = 0, \\
 \frac{dB}{dt} &= k_1 A - k_{-1} B = 0.
 \end{aligned}$$

For this to occur:

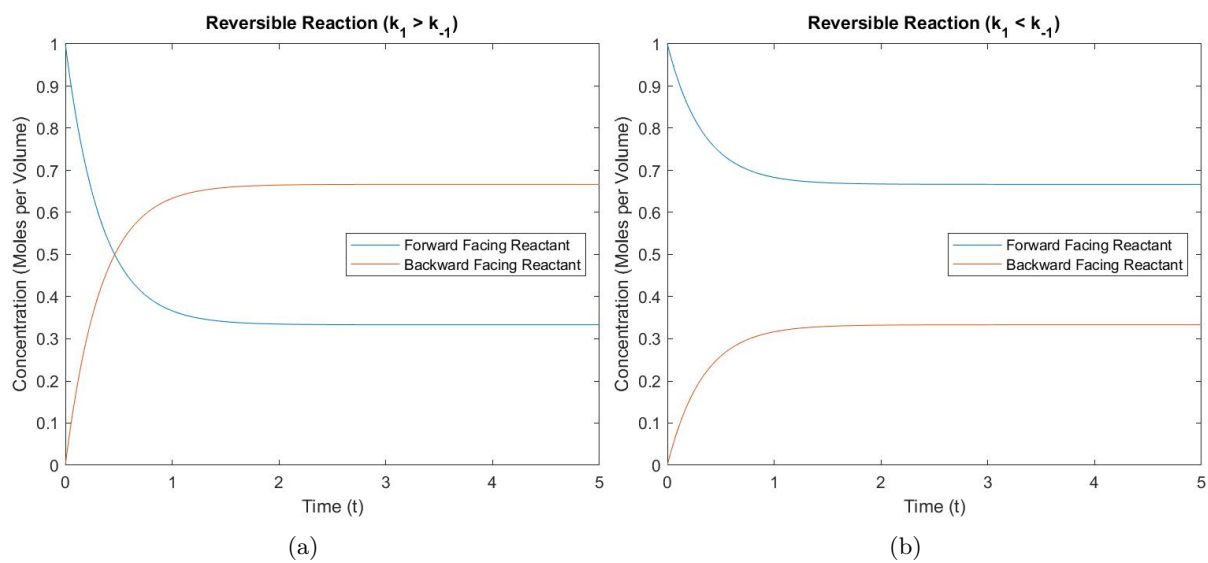
$$\begin{aligned}
 k_1 A &= k_{-1} B \\
 \Rightarrow A &= \frac{k_{-1}}{k_1} B
 \end{aligned}$$

Chemical equilibrium is the condition of a reversible reaction taking place where the rate of forward reaction is equal to the rate of backward reaction [12]. The equilibrium equation is:

$$\frac{B}{A} = \frac{k_1}{k_{-1}}.$$

We use the conservation law 4.14 to calculate the equilibrium states:

$$\begin{aligned}
 B &= a_0 - A \\
 \frac{a_0 - A}{A} &= \frac{k_1}{k_{-1}} \\
 A_{\text{equilibrium}} &= \frac{a_0 k_1}{k_1 + k_{-1}} \\
 B_{\text{equilibrium}} &= \frac{a_0 k_1}{k_1 + k_{-1}}
 \end{aligned}$$



If the forward reaction is faster than the backward reaction there should be more B present in equilibrium.

## Chapter 5

# Nondimensionalisation

The models and solutions we have derived so far have been in dimensional form. In this chapter we will introduce a process to simplify models called nondimensionalisation. This is the process will be applied when analysing the complicated models in Chapters 6 and 7.

Nondimensionalisation is defined as the partial or full removal of physical dimensions from an equation involving physical quantities by a suitable substitution of variables [13]. Nondimensionalisation simplifies models where measured units are involved. Dimensional variables are variables that have units. For example the concentration of a reactant  $A$  would have the units moles per volume. The goal of nondimensionalisation is to convert dimensional variables into dimensionless ones. Basically meaning that don't have units. The dimensionless or scaled model is still accurate, and the original model can be derived again by substituting back in the variables that were nondimensionalised.

As stated in the reference [14], the purpose of the technique is three-fold:

1. Make independent and dependent variables dimensionless.
2. Make the size of independent and dependent variables about unity.
3. Reduce the number of independent physical parameters in the model.

The number one represents a single entity and it is our unit of counting.[15]. When nondimensionalising, each variable is scaled by a typical or reference value[16]. The scale used becomes the unit of measurement.

Nondimensionalisation is very important, especially in systems with many parameters. It helps simplify the system, as the number of parameters in scaled models may be much less than the number of physical parameters in the original model. In doing so it allows us to explore and analyse the properties of the model better. We can find out which terms are small, and which ones have a big effect on the system, or in our case, the chemical reaction. The parameters in scaled models are also dimensionless and express ratios of physical effects rather than levels of individual effects. Setting meaningful values of a few dimensionless numbers is much easier than determining physically relevant values for the original physical parameters[14]. This in turn allows us to try and compare the sizes of different terms and come up with reduced model.

So, how are the scales or reference values chosen? The choice of scales is highly problem-dependent and requires knowledge of the characteristic features of the solution or the physics of the problem [14]. As an example, say we want to convert a variable  $X$  into its dimensionless counterpart  $\bar{X}$ , we would divide  $X$  by a scaling factor or reference value  $X_c$ , i.e  $\frac{X}{X_c} = \bar{X}$ . From

our knowledge of the problem, we might be able to define a parameter  $X_0$  as the initial value for  $X$ .  $X_0$  could then be used as a scale for  $X$ . So  $X = X_0\bar{X}$ . It is important that the scales used are realistic, this is where previous knowledge about the physics of the problem is important. Choosing a scale that is too big might not make sense in a scenario where the original physical variable would never reach that size.

Scaling can also be a challenge in situations where there are many scales that can be used. For example if we wanted to scale time in the reversible reaction discussed in section 4.2, we might scale it by the time it takes for the forward facing part of the reaction to finish. There would also be the option to scale the time by the backward reaction. The different timescales can be combined and analysed using asymptotic solutions. This is expanded on later on in section 5.1.1.

It is important to note that the scaling factor must have the same dimensions as the dimensional variable. So the scaling factor could also be a combination of different parameters in the system.

In our previous examples,  $A$  and  $B$  are concentrations measured in moles per volume. So we would want to compare  $A$  and  $B$  to a known concentration measured the same way. One such concentration would be  $a_0$  often used to denote the initial concentration for  $A$ . So  $a_0$  can be used as the scaling factor for  $A$  and  $B$ , becoming “measuring stick” for all concentrations in the model.

We will demonstrate this technique of nondimensionalisation using the successive reactions discussed in Section 4.1.

## 5.1 Nondimensionalisation of Successive Reactions

In this section we will nondimensionalise the successive reaction we derived in section 4.1.

From section 4.1 we recall,

$$\begin{aligned}\frac{dA}{dt} &= -k_1A, \\ \frac{dB}{dt} &= k_1A - k_2B, \\ \frac{dC}{dt} &= k_2B,\end{aligned}$$

with initial conditions  $A(0) = a_0$ ,  $B(0) = 0$ , and  $C(0) = 0$ .

We rescale the independent and dependent variables using the following substitutions:

$$A = \bar{A}a_0, \quad B = \bar{B}a_0, \quad C = \bar{C}a_0, \quad t = \bar{t}t_c \quad (5.1)$$

where  $t_c$  is the time scaling factor that will be determined later. The initial conditions will become

$$\bar{A}(0) = 1, \quad \bar{B}(0) = 0, \quad \bar{C}(0) = 0$$

The system of differential equations now become:

$$\begin{aligned}\frac{d\bar{A}}{d\bar{t}} &= -t_c k_1 \bar{A}, \\ \frac{d\bar{B}}{d\bar{t}} &= t_c k_1 \bar{A} - t_c k_2 \bar{B}, \\ \frac{d\bar{C}}{d\bar{t}} &= t_c k_2 \bar{B}.\end{aligned}\tag{5.2}$$

There are many possible choices for a timescale and dimensionless parameter. To analyse the system, we will consider different timescales and dimensionless parameters. To start, we can choose our time scale  $t_c$  to equal  $\frac{1}{k_2}$ . This allows the change in concentration of  $\bar{C}$  to depend only on  $\bar{B}$ . We can also introduce a new dimensionless parameter  $\alpha = \frac{k_1}{k_2}$ . The parameter  $\alpha$  is the ratio of the reaction rates of the first reaction ( $A \longrightarrow B$ ) to the second ( $B \longrightarrow C$ ). When  $\alpha$  is large, it means the first reaction is much quicker and its reaction rate is much larger than the second reaction. The system of equations then becomes:

$$\begin{aligned}\frac{d\bar{A}}{d\bar{t}} &= -\alpha \bar{A}, \\ \frac{d\bar{B}}{d\bar{t}} &= \alpha \bar{A} - \bar{B}, \\ \frac{d\bar{C}}{d\bar{t}} &= \bar{B}.\end{aligned}$$

We can get our conservation law:

$$\begin{aligned}\frac{d\bar{A}}{d\bar{t}} + \frac{d\bar{B}}{d\bar{t}} + \frac{d\bar{C}}{d\bar{t}} &= 0, \\ \bar{A}(\bar{t}) + \bar{B}(\bar{t}) + \bar{C}(\bar{t}) &= 1.\end{aligned}\tag{5.3}$$

Solving the equations we get

$$\begin{aligned}\bar{A} &= e^{-\alpha \bar{t}}, \\ \bar{B} &= \frac{\alpha}{1 - \alpha} (e^{-\alpha \bar{t}} - e^{-\bar{t}}), \\ \bar{C} &= 1 - \frac{\alpha}{1 - \alpha} e^{\bar{t}} - \frac{1}{1 - \alpha} e^{-\alpha \bar{t}}.\end{aligned}$$

We have reduced the number of parameters to from 3 to 1.

### 5.1.1 Asymptotic Solution

We have already gotten the analytic dimensional solution for this in section 4.1.

Another option would be to use asymptotic expansions to get approximate solutions for the successive reactions. Approximate solutions are very important if an analytic solution cannot be found. For much more complicated models, the ability to construct asymptotic or reduced solutions that we can write down the solutions to is useful. We can get the solution without solving the whole thing numerically. While it is unnecessary here, approximate solutions are a flexible tool that can help in understanding the behaviour of the system.



Recalling the equations 5.2, we have two choices for the time scale  $t_c$ ,  $t_c = \frac{1}{k_1}$  and  $t_c = \frac{1}{k_2}$ . The time scale  $\frac{1}{k_1}$  is the time over which the reactant  $A$  transforms into  $B$ . The time scale  $\frac{1}{k_2}$  is the time over which the intermediate  $B$  transforms into the product  $C$ . We will choose  $t_c = \frac{1}{k_1}$ , and define  $\varepsilon = \frac{k_2}{k_1}$ .

Assume  $\varepsilon$  is a small value, i.e  $k_1 \gg k_2$

$$\begin{aligned}\frac{d\bar{A}}{d\bar{t}} &= -\bar{A} \\ \frac{d\bar{B}}{d\bar{t}} &= \bar{A} - \varepsilon\bar{B} \\ \frac{d\bar{C}}{d\bar{t}} &= \varepsilon\bar{B},\end{aligned}$$

In this case, we are going to assume that  $\varepsilon$  is much less than 1. ( $\varepsilon \ll 1$ )

Just looking at the system, we can see that provided  $\bar{A}$  and  $\bar{B}$  are both order 1 the effect of  $\bar{B}$  is small compared to  $\bar{A}$  in the differential equation for  $\bar{B}$ . So if we neglect it, the rate of reaction for  $\bar{B}$  would depend only on  $\bar{A}$ . We could assume that if  $\varepsilon$  is very small, the concentration of  $\bar{B}$  is increasing exponentially. But this approximation is only true for a short time at the beginning of the reaction. This means we will need another approximate solution for later on in the reaction. We will derive this later, but for now at the initial part of the reaction, we look for a solution for  $\bar{A}$  and  $\bar{B}$  in the form of a regular expansion:

$$\begin{aligned}\bar{A}(\bar{t}) &= \bar{A}_0(\bar{t}) + \varepsilon\bar{A}_1(\bar{t}) + \varepsilon^2\bar{A}_2(\bar{t}) + \dots \\ \bar{B}(\bar{t}) &= \bar{B}_0(\bar{t}) + \varepsilon\bar{B}_1(\bar{t}) + \varepsilon^2\bar{B}_2(\bar{t}) + \dots\end{aligned}$$

We can find  $\bar{C}$  by using the conservation law 5.1. For this approximation, we need the terms to be well ordered. This means that each term is smaller than the previous one.

Substituting the expansions into our differential equations give us:

$$\begin{aligned}\frac{d}{d\bar{t}}(\bar{A}_0(\bar{t}) + \varepsilon\bar{A}_1(\bar{t}) + \varepsilon^2\bar{A}_2(\bar{t}) + \dots) &= -(\bar{A}_0(\bar{t}) + \varepsilon\bar{A}_1(\bar{t}) + \varepsilon^2\bar{A}_2(\bar{t}) + \dots) \\ \frac{d}{d\bar{t}}(\bar{B}_0(\bar{t}) + \varepsilon\bar{B}_1(\bar{t}) + \varepsilon^2\bar{B}_2(\bar{t}) + \dots) &= (\bar{A}_0(\bar{t}) + \varepsilon\bar{A}_1(\bar{t}) + \varepsilon^2\bar{A}_2(\bar{t}) + \dots) \\ &\quad - \varepsilon(\bar{B}_0(\bar{t}) + \varepsilon\bar{B}_1(\bar{t}) + \varepsilon^2\bar{B}_2(\bar{t}) + \dots).\end{aligned}\tag{5.4}$$

Matching like terms, the initial conditions for the system becomes:

$$\begin{aligned}\bar{A}_0(0) + \varepsilon\bar{A}_1(0) + \varepsilon^2\bar{A}_2(0) + \dots &= 1 & \Rightarrow & \bar{A}_0(0) = 1, \bar{A}_1(0) = 0, \dots \\ \bar{B}_0(0) + \varepsilon\bar{B}_1(0) + \varepsilon^2\bar{B}_2(0) + \dots &= 0 & \Rightarrow & \bar{B}_0(0) = 0, \bar{B}_1(0) = 0, \dots\end{aligned}$$

We can put  $\bar{C}$  aside for now as it only depends on  $\bar{B}$ , and we will use the conservation law to solve for it.

Looking at  $\mathcal{O}(1)$  terms

$$\begin{aligned}\frac{d\bar{A}_0}{d\bar{t}} &= -\bar{A}_0(\bar{t}), \\ \frac{d\bar{B}_0}{d\bar{t}} &= \bar{A}_0(\bar{t}).\end{aligned}$$

We solve for  $\bar{A}_0$  and  $\bar{B}_0$ , recalling that  $\bar{A}_0(0) = 1$  and  $\bar{B}_0(0) = 0$

$$\begin{aligned}\bar{A}_0(\bar{t}) &= e^{-\bar{t}} \\ \bar{B}_0(\bar{t}) &= 1 - e^{-\bar{t}}\end{aligned}$$

Looking next at  $\mathcal{O}(\varepsilon)$  terms

$$\begin{aligned}\frac{d\bar{A}_1}{d\bar{t}} &= -\bar{A}_1(\bar{t}), \\ \frac{d\bar{B}_1}{d\bar{t}} &= \bar{A}_1(\bar{t}) - \bar{B}_0(\bar{t}),\end{aligned}$$

and solving for  $\bar{A}_1$  and  $\bar{B}_1$  we get,

$$\begin{aligned}\bar{A}_1(\bar{t}) &= 0, \\ \bar{B}_1(\bar{t}) &= 1 - \bar{t} - e^{-\bar{t}}.\end{aligned}$$

We can continue solving for many orders of  $\varepsilon$  i.e.,  $\mathcal{O}(\varepsilon^2), \mathcal{O}(\varepsilon^3), \dots$  to get a more accurate approximation. For now the approximate solution for  $\bar{A}, \bar{B}$  and  $\bar{C}$  are:

$$\begin{aligned}\bar{A}(\bar{t}) &= e^{-\bar{t}} + \mathcal{O}(\varepsilon^2), \\ \bar{B}(\bar{t}) &= 1 - e^{-\bar{t}} + \varepsilon(1 - \bar{t} - e^{-\bar{t}}) + \mathcal{O}(\varepsilon^2), \\ \bar{C}(\bar{t}) &= -\varepsilon(1 - \bar{t} - e^{-\bar{t}}) + \mathcal{O}(\varepsilon^2)\end{aligned}\tag{5.5}$$

As we said in the outset of this example, this approximation requires the terms to be well ordered. This can only be true when  $\bar{t} < \frac{1}{\varepsilon}$ . This then suggests we have picked inappropriate scales for larger times and so we need to rescale.

We can re-scale time by this larger time period  $\frac{1}{\varepsilon}$  and get another approximation for  $\bar{A}(\bar{t}), \bar{B}(\bar{t})$  and  $\bar{C}(\bar{t})$ . This will become the outer solution or the long time solution.

The previous solution we found can be called the inner solution. In this example it can be described as the short or early time solution.

We begin by setting our time scale

$$\bar{t} = \frac{1}{\varepsilon}\tau,$$

and so

$$\bar{A}\left(\frac{1}{\varepsilon}\tau\right) = \tilde{A}(\tau) \text{ and } \bar{B}\left(\frac{1}{\varepsilon}\tau\right) = \tilde{B}(\tau).$$

The system of differential equations then becomes:

$$\begin{aligned}\varepsilon \frac{d\tilde{A}}{d\tau} &= -\tilde{A} \\ \varepsilon \frac{d\tilde{B}}{d\tau} &= \tilde{A} - \varepsilon\tilde{B}\end{aligned}$$

We again put the equation for  $\bar{C}$  aside, as it relies solely on  $\bar{B}$ , and can be derived using the conservation law. Our goal is to get approximate solutions for  $\tilde{A}(\tau)$  and  $\tilde{B}(\tau)$  in the form

$$\begin{aligned}\tilde{A}(\tau) &\approx \tilde{A}_0(\tau) + \varepsilon\tilde{A}_1(\tau) + \varepsilon^2\tilde{A}_2(\tau) + \dots, \\ \tilde{B}(\tau) &\approx \tilde{B}_0(\tau) + \varepsilon\tilde{B}_1(\tau) + \varepsilon^2\tilde{B}_2(\tau) + \dots\end{aligned}$$

Adding these into the system of equations, we get

$$\begin{aligned}\varepsilon \frac{d}{d\tau}(\tilde{A}_0(\tau) + \varepsilon \tilde{A}_1(\tau) + \varepsilon^2 \tilde{A}_2(\tau) + \dots) &= -(\tilde{A}_0(\tau) + \varepsilon \tilde{A}_1(\tau) + \varepsilon^2 \tilde{A}_2(\tau) + \dots) \\ \varepsilon \frac{d}{d\tau}(\tilde{B}_0(\tau) + \varepsilon \tilde{B}_1(\tau) + \varepsilon^2 \tilde{B}_2(\tau) + \dots) &= (\tilde{A}_0(\tau) + \varepsilon \tilde{A}_1(\tau) + \varepsilon^2 \tilde{A}_2(\tau) + \dots) \\ &\quad - \varepsilon(\tilde{B}_0(\tau) + \varepsilon \tilde{B}_1(\tau) + \varepsilon^2 \tilde{B}_2(\tau) + \dots).\end{aligned}\tag{5.6}$$

To get the approximate solutions, we look at each order of  $\varepsilon$  and get a solution at each order. First look at  $\mathcal{O}(1)$  terms:

$$\tilde{A}_0(\tau) = 0.\tag{5.7}$$

This is because there are no other  $\mathcal{O}(1)$  terms other than  $\tilde{A}_0$ .

Next look at  $\mathcal{O}(\varepsilon)$  terms:

$$\begin{aligned}\frac{d\tilde{A}_0}{d\tau} &= -\tilde{A}_1 \\ \frac{d\tilde{B}_0}{d\tau} &= -\tilde{A}_1 - \tilde{B}_0\end{aligned}$$

We already got a value for  $\tilde{A}_0$  so we use it here and then get,

$$\begin{aligned}\tilde{A}_1(\tau) &= 0 \\ \tilde{B}_0(\tau) &= b_1 e^{-\tau},\end{aligned}$$

Where  $b_1$  is an unknown constant.

$\mathcal{O}(\varepsilon^2)$  terms:

$$\begin{aligned}\frac{d\tilde{A}_1}{d\tau} &= -\tilde{A}_2 \\ \frac{d\tilde{B}_1}{d\tau} &= -\tilde{A}_2 - \tilde{B}_1\end{aligned}$$

Using the previous values we get,

$$\begin{aligned}\tilde{A}_2(\tau) &= 0 \\ \tilde{B}_1(\tau) &= b_2 e^{-\tau},\end{aligned}$$

where  $b_2$  is an unknown constant.

So our approximate solutions for  $\tilde{A}(\tau)$  and  $\tilde{B}(\tau)$  become:

$$\begin{aligned}\tilde{A}(\tau) &= 0 + \mathcal{O}(\varepsilon^2) \\ \tilde{B}(\tau) &= b_1 e^{-\tau} + \varepsilon b_2 e^{-\tau} + \mathcal{O}(\varepsilon^2)\end{aligned}$$

Both  $\tilde{A}(\tau)$  and  $\bar{A}(\bar{t})$  are approximations of the function  $A(t)$ .  $\bar{A}(\bar{t})$  is the inner solution and  $\tilde{A}(\tau)$  is the outer solution. So, in the transition region between the inner and outer solution, we should expect the two expansions to give the same result. This is accomplished by requiring that the value of  $\bar{A}(\bar{t})$  as  $\bar{t} \rightarrow \infty$  is equal to the value of  $\tilde{A}(\tau)$  as  $\tau \rightarrow 0$ . This is called matching.

Matching  $\tilde{A}(\tau)$  and  $\bar{A}(\bar{t})$  we get:

$$\begin{aligned}\lim_{\bar{t} \rightarrow \infty} \bar{A}(\bar{t}) &= \lim_{\tau \rightarrow 0} \tilde{A}(\tau) \\ \lim_{\bar{t} \rightarrow \infty} e^{-\bar{t}} &= \lim_{\tau \rightarrow 0} 0 = 0\end{aligned}$$

We can find values for  $b_1$  and  $b_2$  by matching  $\bar{B}(\bar{t})$  and  $\tilde{B}(\tau)$  in the same way:

$$\begin{aligned}\lim_{\bar{t} \rightarrow \infty} \bar{B}(\bar{t}) &= \lim_{\tau \rightarrow 0} \tilde{B}(\tau) \\ \lim_{\bar{t} \rightarrow \infty} 1 - e^{-\bar{t}} + \varepsilon(1 - \bar{t} - e^{-\bar{t}}) &= \lim_{\tau \rightarrow 0} b_1 e^{-\tau} + \varepsilon b_2 e^{-\tau}\end{aligned}$$

The limit here goes to infinity, so we will use another matching method called Van Dyke's method to find the value for the two unknown constants.

Van Dyke Matching is relatively simple to use [17]. The outer solution is written in terms of the inner variable which is then expanded in terms of  $\varepsilon \ll 1$  to the order the solution is at. Taylor's theorem can be used to expand the solution. This is called the inner expansion of the outer solution. we repeat the process again for the inner solution. The inner solution is written in terms of the outer variable, and then expanded. Matching the inner and outer solution requires that the outer expansion of the inner solution is equal to the inner expansion of the outer solution.

We recall our inner and outer solutions for  $B$ :

$$\begin{aligned}\bar{B}(\bar{t}) &= 1 - e^{-\bar{t}} + \varepsilon(1 - \bar{t} - e^{-\bar{t}}) + \mathcal{O}(\varepsilon^2), \text{ (inner solution),} \\ \tilde{B}(\tau) &= b_1 e^{-\tau} + \varepsilon b_2 e^{-\tau} + \mathcal{O}(\varepsilon^2) \text{ (outer solution).}\end{aligned}$$

First we look at the outer expansion, of the inner solution, i.e, the inner solution written in terms of the outer variable:

$$\bar{B}(\bar{t}) = \bar{B}\left(\frac{\tau}{\varepsilon}\right) = 1 - e^{\frac{\tau}{\varepsilon}} + \varepsilon\left(1 - \frac{\tau}{\varepsilon} - e^{\frac{\tau}{\varepsilon}}\right)$$

$e^{\frac{\tau}{\varepsilon}}$  is an exponentially small term. So we can treat it as 0 and remove it from the equation.

$$\begin{aligned}\bar{B}\left(\frac{\tau}{\varepsilon}\right) &= 1 + \varepsilon\left(1 - \frac{\tau}{\varepsilon}\right) \\ \bar{B}\left(\frac{\tau}{\varepsilon}\right) &= 1 - \tau + \varepsilon + \mathcal{O}(\varepsilon^2)\end{aligned}$$

Next we look at the inner expansion of the outer solution:

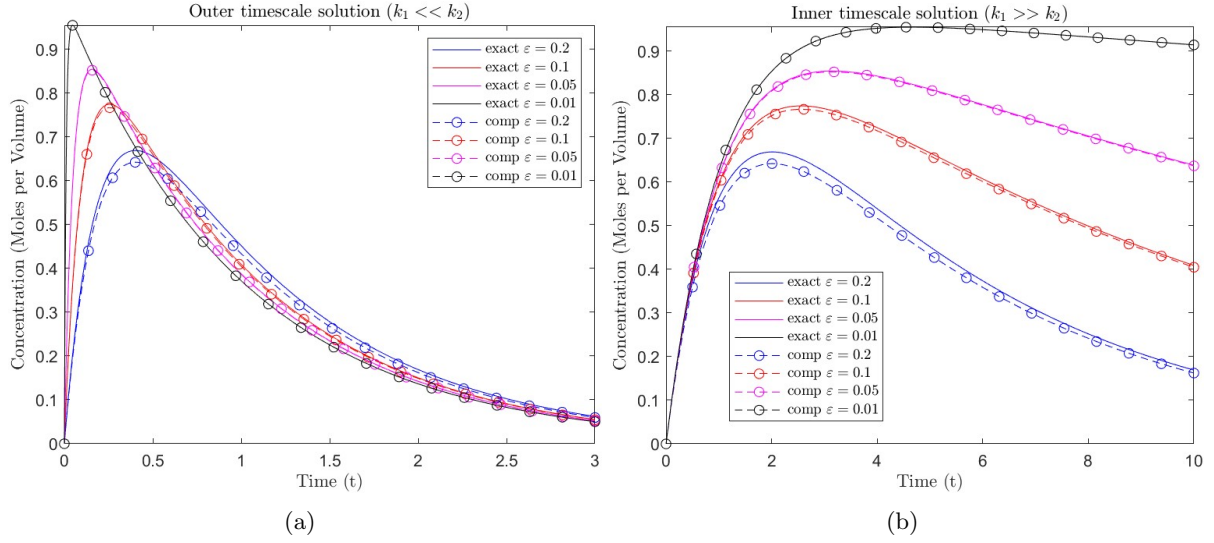
$$\tilde{B}(\tau) = \tilde{B}(\varepsilon \bar{t}) = b_1 e^{-\varepsilon \bar{t}} + \varepsilon b_2 e^{-\varepsilon \bar{t}}$$

Substitute  $e^{-\varepsilon \bar{t}}$  with the Taylor expansion of  $e^{-\varepsilon \bar{t}}$ :

$$\begin{aligned}\tilde{B}(\varepsilon \bar{t}) &= b_1(1 - \varepsilon \bar{t}) + \varepsilon b_2(1 - \varepsilon \bar{t}) \\ \tilde{B}(\varepsilon \bar{t}) &= b_1 - \varepsilon(b_1 \bar{t} - b_2) + \mathcal{O}(\varepsilon^2)\end{aligned}$$

Van dyke matching requires that the outer expansion of the inner solution,  $\bar{B}(\frac{\tau}{\varepsilon})$  should be equal to the inner expansion of the outer solution,  $\tilde{B}(\varepsilon \bar{t})$ .

$$\begin{aligned}\bar{B}\left(\frac{\tau}{\varepsilon}\right) &= \tilde{B}(\varepsilon \bar{t}) \\ 1 - \tau + \varepsilon &= b_1 - \varepsilon(b_1 \bar{t} - b_2)\end{aligned}$$

Figure 5.1: Outer and Inner solutions for  $B$ 

Using the same terms for the solutions by replacing  $\tau$  with  $\varepsilon\bar{t}$  we get

$$\begin{aligned} 1 - \varepsilon\bar{t} + \varepsilon &= b_1 - \varepsilon(b_1\bar{t} - b_2) \\ 1 - \varepsilon(\bar{t} - 1) &= b_1 - \varepsilon(b_1\bar{t} - b_2) \end{aligned}$$

Match the terms by order  $\varepsilon$ :

$$\begin{aligned} b_1 &= 1 & \bar{t} - 1 &= b_1\bar{t} - b_2 \\ \bar{t} - 1 &= \bar{t} - b_2 \\ 1 &= b_2 \end{aligned}$$

Now we have the values for our constants ( $b_1 = b_2 = 1$ ).

The solutions for the species now consists of two pieces, the inner and outer solution.

$$\begin{aligned} \bar{B}(\bar{t}) &= 1 - e^{-\bar{t}} + \varepsilon(1 - \bar{t} - e^{-\bar{t}}) + \mathcal{O}(\varepsilon^2) \text{(inner solution),} \\ \tilde{B}(\tau) &= e^{-\tau} + \varepsilon e^{-\tau} + \mathcal{O}(\varepsilon^2) \text{(outer solution).} \end{aligned}$$

The inner solution approximates the reaction when  $k_1 \gg k_2$ , and the outer solution when  $k_1 \ll k_2$ . Inputting small and large values of  $k_1$  and  $k_2$  into the exact solution, will give us a good idea of how accurate the approximates solutions are. Figure 5.1.1 show the two solutions plotted for different values of  $\varepsilon$ . As  $\varepsilon$  gets smaller, the approximation is more accurate to the exact solution.

Combining the two approximate solutions forms a composite solution. To get the composite solution, we add the inner and outer solutions, and then take away the parts common to both. The common parts would be the matched solution. From van dyke's method this would be inner expansion of the outer solution and the outer expansion of the inner solution. Since these are

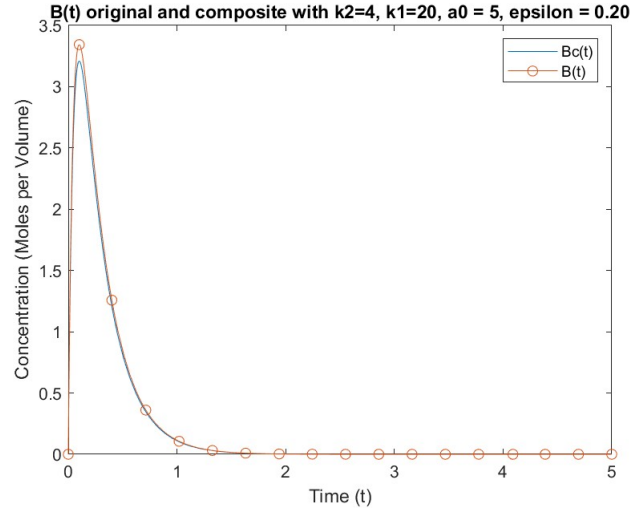


Figure 5.2: B and B composite solution

equal, we just take away one of them. We can now get a composite solution for  $\bar{B}(\bar{t})$ .

$$\begin{aligned}\bar{B}_c(\bar{t}) &= \bar{B}(\bar{t}) + \tilde{B}(\varepsilon\bar{t}) - \bar{B}\left(\frac{\tau}{\varepsilon}\right) \\ \bar{B}_c(\bar{t}) &= 1 - e^{-\bar{t}} + \varepsilon(1 - \bar{t} - e^{-\bar{t}}) + e^{-\varepsilon\bar{t}} + \varepsilon e^{-\varepsilon\bar{t}} - 1 + \varepsilon\bar{t} - \varepsilon + \mathcal{O}(\varepsilon^2) \\ &= e^{-\varepsilon\bar{t}} - e^{-\bar{t}} + \varepsilon(e^{-\varepsilon\bar{t}} - e^{-\bar{t}}) + \mathcal{O}(\varepsilon^2)\end{aligned}$$

The composite solutions for all three of the species are:

$$\begin{aligned}\bar{A}_c(\bar{t}) &= e^{-\bar{t}} + \mathcal{O}(\varepsilon^2) \\ \bar{B}_c(\bar{t}) &= e^{-\varepsilon\bar{t}} - e^{-\bar{t}} + \varepsilon(e^{-\varepsilon\bar{t}} - e^{-\bar{t}}) + \mathcal{O}(\varepsilon^2) \\ \bar{C}_c(\bar{t}) &= 1 - e^{-\varepsilon\bar{t}} - \varepsilon(e^{-\varepsilon\bar{t}} - e^{-\bar{t}}) + \mathcal{O}(\varepsilon^2)\end{aligned}$$

The composite expansion gives a very good approximation to the solution over the whole time interval. This is demonstrated in Figure 5.2.

## Chapter 6

# Chemical Oscillations: Lotka-Volterra

In section 2.5 we introduced the Law of Mass Action. This is an integral law in Chemical kinetic. This law led chemists to believe that reactions approach equilibrium steadily. While this is true for most chemical reactions, chemists are now very familiar with chemical oscillations.

Chemical oscillations puzzled chemists for a long time. Chemical oscillation are seen as the periodic depletion of the reactants and surge of products [18].

The Lotka Volterra model is the earliest proposed explanation for why a chemical reaction may oscillate [19]. It is the simplest mathematical model which exhibits such oscillations [20].

This model was proposed by American biophysicist Alfred Lotka and Italian mathematician, Vito Volterra. Lotka developed a model for chemical reactions, whereas Volterra developed a model for oscillations found in population dynamics[20].

In 1920 Lotka proposed the following reaction mechanism [19]:



A single chemical reaction is said to be autocatalytic if one of the reaction products is also a catalyst for the same or a coupled reaction. Steps 1 and 2 in 6.1 are autocatalytic as X and Y accelerate their own production. This is also known as a predator-prey model. We will discuss this in more detail.

The rate laws for the reactant A, the product B, and the intermediates X and Y are:

$$\begin{aligned}\frac{dA}{dt} &= -k_1 AX \\ \frac{dX}{dt} &= k_1 AX - k_2 XY \\ \frac{dY}{dt} &= k_2 XY - k_3 Y \\ \frac{dB}{dt} &= k_3 Y\end{aligned}\tag{6.2}$$

The initial conditions are:

$$A(0) = a_0 \quad X(0) = x_0 \quad Y(0) = y_0 \quad B(0) = 0$$

The conservation law for the system is

$$\begin{aligned} \frac{dA}{dt} + \frac{dB}{dt} + \frac{dX}{dt} + \frac{dY}{dt} &= 0 \\ A(t) + B(t) + X(t) + Y(t) &= a_0 + x_0 + y_0 \end{aligned} \quad (6.3)$$

This model is most commonly applied in the context of predator prey relations. For simplicity, we will look at the model from this angle. In this context  $X$  represents the prey population.  $Y$  represents the predator population.  $B$  is basically a counter for the amount of deceased predators.  $A$  represents the amount of resources available. This is always assumed to be infinite or constant.

Looking at the equations 6.2 in this scenario, we assume  $A$  to be held constant. So  $A$  is always equal to  $a_0$ . We will now write as  $A(t)$  as  $a$ . So its rate of change does not need to be considered as it is equal to 0. Since we can get  $B(t)$  from the conservation law, we only need to focus on two equations,

$$\begin{aligned} \frac{dX}{dt} &= -k_1AX + 2k_1AX - k_2XY, \\ \frac{dY}{dt} &= 2k_2XY - k_2XY - k_3Y. \end{aligned}$$

where the initial values are

$$X(0) = x_0 \text{ and } Y(0) = y_0$$

Let us look at the steady states for this system. At the steady state, there is no change with time so,

$$\begin{aligned} \frac{dX}{dt} &= k_1aX - k_2XY = 0 \\ \frac{dY}{dt} &= k_2XY - k_3Y = 0 \end{aligned}$$

We get the following expressions for the steady state:

$$\begin{aligned} k_1aX &= k_2XY & k_2XY &= k_3Y \\ y_s &= \frac{ak_1}{k_2} & x_s &= \frac{k_3}{k_2} \end{aligned}$$

We use the steady state values to nondimensionalise the systems. The scales we choose are,

$$X = \bar{X} \frac{k_3}{k_2} \quad Y = \bar{Y} \frac{k_3}{k_2} \quad t = \bar{t} \frac{1}{k_3}$$

$\frac{1}{k_3}$  is the time scale over which the predators die off. We also define a new dimensionless parameter  $\alpha = a \frac{k_1}{k_3}$ .



They system of equations then becomes:

$$\begin{aligned}\frac{d\bar{X}}{dt} &= \alpha\bar{X} - \bar{X}\bar{Y} \\ \frac{d\bar{Y}}{dt} &= \bar{X}\bar{Y} - \bar{Y}\end{aligned}$$

The steady states points are

$$\bar{x}_s = 1 \text{ and } \bar{y}_s = a$$

There is another steady state when  $\bar{X} = \bar{Y} = 0$ . As the result is trivial, we will focus on the other steady state.

Before solving the equations, we want to understand the behaviour of the system around the steady state. Around the steady state we can assume that functions of  $\bar{X}$  and  $\bar{Y}$  take the form,

$$\begin{aligned}\bar{X}(\bar{t}) &= 1 + \varepsilon(\bar{t}), \text{ and} \\ \bar{Y}(\bar{t}) &= a + \delta(\bar{t}),\end{aligned}\tag{6.4}$$

$\varepsilon(\bar{t})$  and  $\delta(\bar{t})$  being small distances in both directions from the equilibrium position.

Next we define:

$$\begin{aligned}\frac{d\bar{X}}{dt} &= f(\bar{X}, \bar{Y}) = \alpha\bar{X} - \bar{X}\bar{Y} \\ \frac{d\bar{Y}}{dt} &= g(\bar{X}, \bar{Y}) = \bar{X}\bar{Y} - \bar{Y}\end{aligned}$$

We use Taylor expansions to approximate the function around the steady state:

$$\begin{aligned}\frac{d\varepsilon}{dt} &= f(1, a) + f_x(1, a)\varepsilon + f_y(1, a)\delta \\ \frac{d\delta}{dt} &= g(1, a) + g_x(1, a)\varepsilon + g_y(1, a)\delta\end{aligned}$$

In matrix form this is written as:

$$\frac{d}{dt} \begin{pmatrix} \varepsilon \\ \delta \end{pmatrix} = \begin{pmatrix} f_x(1, a) & f_y(1, a) \\ g_x(1, a) & g_y(1, a) \end{pmatrix} \begin{pmatrix} \varepsilon \\ \delta \end{pmatrix}\tag{6.5}$$

Following the steps are presented in the references [21] and [22], we see that the solution takes the form

$$\begin{pmatrix} \varepsilon \\ \delta \end{pmatrix} = e^{\lambda t} \mathbf{v},\tag{6.6}$$

where  $\lambda$  is the eigenvalue and  $v$  is the corresponding eigenvector.

We define  $J$  to be the Jacobian matrix evaluated at the steady state,

$$J = \begin{pmatrix} f_x(1, a) & f_y(1, a) \\ g_x(1, a) & g_y(1, a) \end{pmatrix}$$

Putting these back into 6.5 we get,

$$\mathbf{J}\mathbf{v} = \lambda\mathbf{v}.\tag{6.7}$$

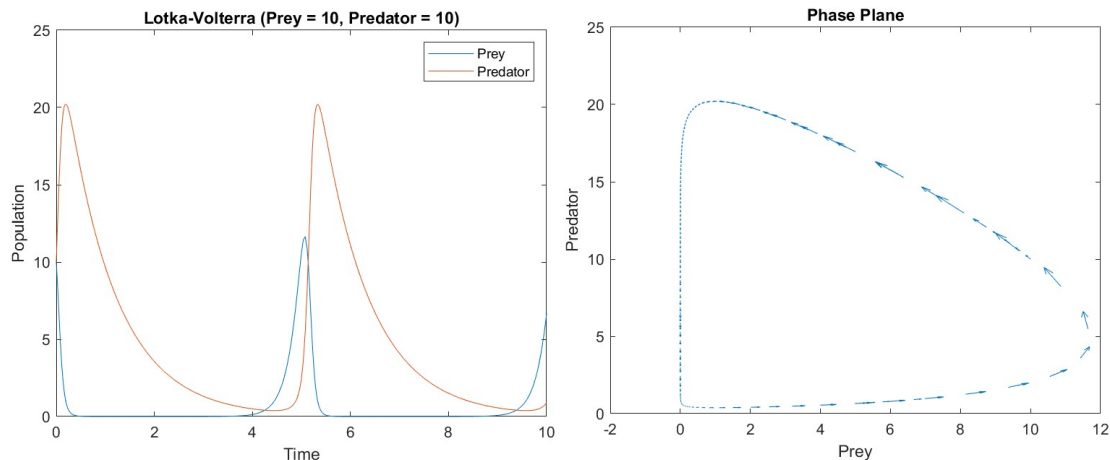


Figure 6.1: Predator Prey model with equal initial values

We determine the eigenvalues by solving the characteristic equation

$$\det(\mathbf{J} - \lambda \mathbf{I}) = 0$$

$$\lambda^2 + \alpha = 0$$

The eigenvalues for the system are all imaginary.

$$\lambda = \pm i\sqrt{a}$$

This shows that around the steady state, it is stable, but not asymptotically stable. The system starts near the steady state but never actually approaches it. Continuing on we arrive at

$$\begin{pmatrix} \varepsilon \\ \delta \end{pmatrix} = c_1 \begin{pmatrix} \frac{i}{\sqrt{a}} \\ 1 \end{pmatrix} e^{i\sqrt{a}t} + c_2 \begin{pmatrix} \frac{1}{i\sqrt{a}} \\ 1 \end{pmatrix} e^{-i\sqrt{a}t}.$$

De Moivre's Theorem from mathematics indicates that the exponential terms can be written as

$$\begin{pmatrix} \varepsilon \\ \delta \end{pmatrix} = c_1 \begin{pmatrix} \frac{i}{\sqrt{a}} \\ 1 \end{pmatrix} (\cos(\sqrt{a}t) + i \sin(\sqrt{a}t)) + c_2 \begin{pmatrix} \frac{1}{i\sqrt{a}} \\ 1 \end{pmatrix} (\cos(\sqrt{a}t) - i \sin(\sqrt{a}t)),$$

where  $c_1$  and  $c_2$  are unknown constants.

From this we can see that the oscillation frequency about the steady state is  $\sqrt{a}$ . And the oscillation period is  $\frac{2\pi}{\sqrt{a}}$ .

Figures 6.1 to 6.3 depict the lotka volterra model and phase planes for different initial values for predators and prey with  $\alpha = 5$ .

The Lotka Volterra model is an oscillating system. As we have seen, it is most commonly used when discussing predator and prey relations. The lotka volterra model gives the tools to analyse more complicated system such as the belousov-zhabotinsky oscillating reaction. The Belousov reaction consists of the oxidation of malonic acid ( $\text{CH}_2(\text{COOH})_2$ ) by bromate ions ( $\text{BrO}_3^-$ ) in a medium of sulphuric acid [24]. The Belousov-Zhabotinsky reaction was the first oscillating reaction to be reported and studied systematically. This is also the first chemical

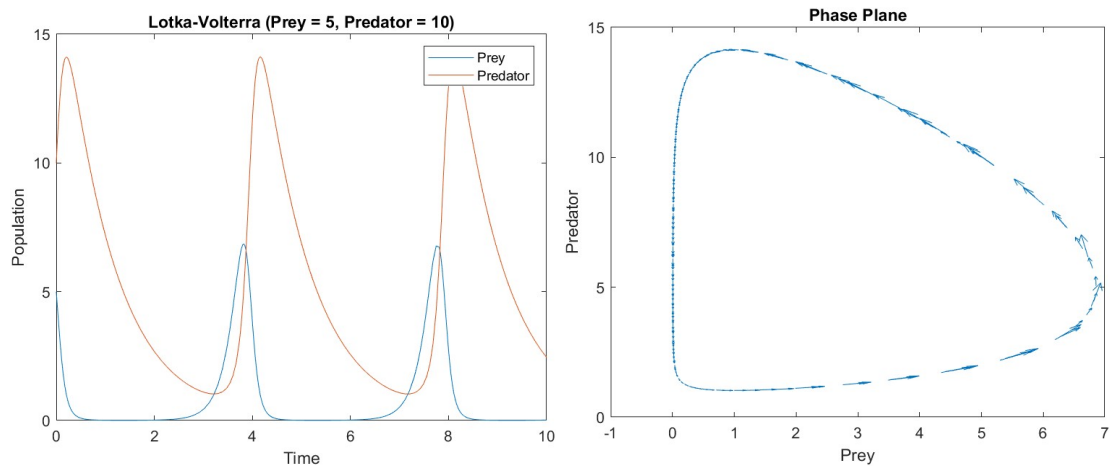


Figure 6.2: Predator Prey model where initial Predators are larger than Prey

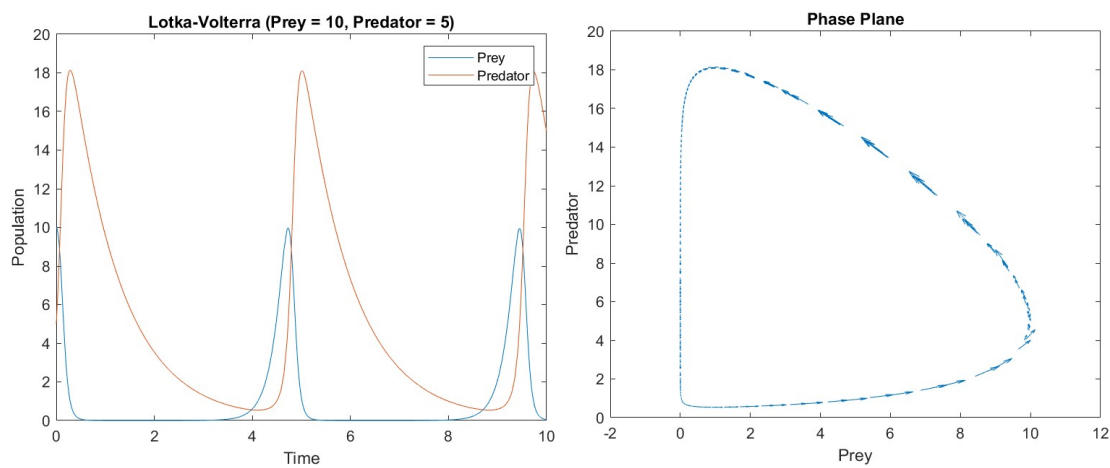


Figure 6.3: Predator Prey model where initial Predators are smaller than Prey

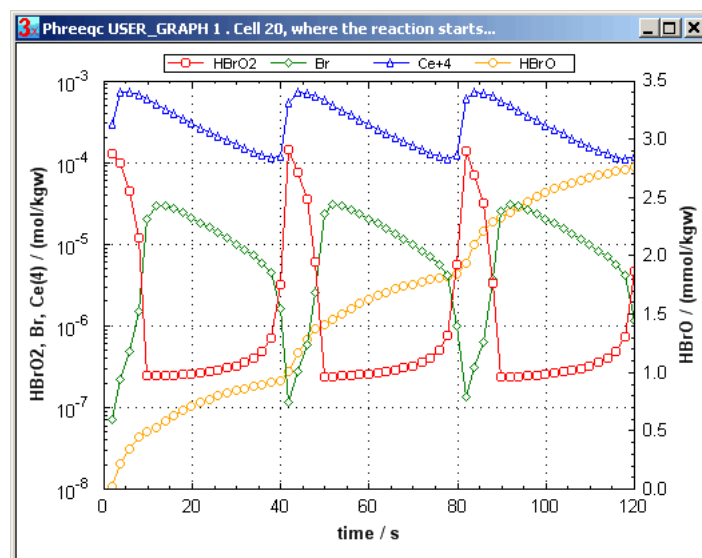


Figure 6.4: Belousov-Zhabotinsky oscillating chemical reaction [23]

reactions found to exhibit oscillations both in time and space. Figure 6.4 shows a graph of this reaction. The Belousov-Zhabotinsky oscillating chemical reaction is used in practice for an oscillating system. Similar steps used for the Lotka Volterra model, can be used to analyse this more complicated reaction.

## Chapter 7

# Enzyme Substrate Reaction: Michaelis-Menten Equations

A catalyst speeds up a reaction. An enzyme is a type of catalyst. Enzymes are biological molecules used to speed up reactions. Substrates are reactant molecules that the enzyme binds with to catalyse the reaction.

Chemical reactions in biological systems are often catalyzed or sped up by enzymes. They are highly specific and react only with particular substrates. They are very effective at very low concentrations. An example of this is the enzyme pepsin that breaks down the substrate protein into the product amino acids. Often the exact mechanisms are not well understood and can involve very complicated pathways with multiple enzymes and other catalysts [9]

In this chapter, we will consider the simplest enzyme reaction called the Michaelis Menten model:



S is the substrate and E is the Enzyme. The enzyme binds to a substrate and combine to form an enzyme-substrate intermediate or complex which we call C. The complex then breaks down the final product P and returns the enzyme E unchanged.

We will use square brackets to represent their concentration, e.g  $[P]$  is the Product concentration.

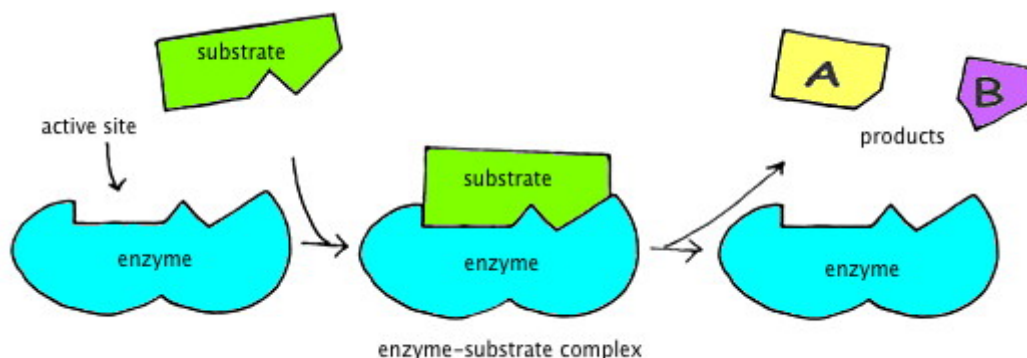


Figure 7.1: Enzyme Substrate Reaction [25]

So applying to the Law of Mass Action discussed in Section 2.5, we derive the following equations:

$$\begin{aligned}\frac{d[S]}{dt} &= -k_1[S][E] + k_{-1}[C] \\ \frac{d[E]}{dt} &= -k_1[S][E] + k_{-1}[C] + k_2[C] \\ \frac{d[C]}{dt} &= k_1[S][E] - k_{-1}[C] - k_2[C] \\ \frac{d[P]}{dt} &= k_2[C]\end{aligned}$$

with initial conditions,

$$[S](0) = S_0; [E](0) = E_0; [C](0) = 0; [P](0) = 0.$$

From these equations we see two conservation laws:

$$\begin{aligned}\frac{d[E]}{dt} + \frac{d[C]}{dt} &= 0 & \frac{d[S]}{dt} + \frac{d[C]}{dt} + \frac{d[P]}{dt} &= 0 \\ \Rightarrow [E] + [C] &= E_0 & \Rightarrow [S] + [C] + [P] &= S_0\end{aligned}$$

This first conservation law makes sense as  $E$  is only a catalyst. The free enzyme  $E$  plus the combined enzyme  $C$  is always constant.  $E$  turns into  $C$  and  $C$  turns back into  $E$ .

From these laws, we can write  $[E]$  in terms of  $[C]$ . Since  $[P]$  only depends on  $[C]$ , we can ignore it for now and only focus on the equations for  $S$  and  $C$ .

$$\begin{aligned}\frac{d[S]}{dt} &= -k_1 E_0 [S] + k_1 [S][C] + k_{-1}[C] \\ \frac{d[C]}{dt} &= k_1 E_0 [S] - k_1 [S][C] - k_{-1}[C] - k_2[C]\end{aligned}$$

We nondimensionalise by choosing the following scales:

$$[S] = S_0 S \qquad [C] = E_0 C \qquad t = \frac{1}{k_1 E_0} \bar{t}$$

We choose to scale  $[C]$  by the initial value of  $[E]$ , because of the conservation laws. The law that  $[E] + [C] = E_0$  indicates that the concentration of  $[C]$  can range up to  $E_0$  [9]. The parameter  $k_{-1}$  is the rate of reaction caused by the spontaneous breakdown of the enzyme-substrate complex. This is not usually large, so  $k_{-1}$  will not be used as a time scale in this example.

The dimensionless equations are:

$$\begin{aligned}\frac{dS}{d\bar{t}} &= -S + SC + \frac{k_{-1}}{k_1 S_0} C \\ \frac{dC}{d\bar{t}} &= \frac{S_0}{E_0} (S - SC) - \frac{k_{-1} + k_2}{k_1 E_0} C\end{aligned}$$

with initial constants

$$S(0) = 1 \text{ and } C(0) = 0. \tag{7.2}$$

In this system,  $k_{-1}$  and  $k_2$  reduces the complex, while  $k_1$  increases the complex. Michaelis Constant ( $K_M$ ) is a ratio of the breakdown of the complex  $C$  to the formation of the complex. We can use this constant to define more dimensionless parameters:

$$K_M = \frac{k_{-1} + k_2}{k_1} \quad \alpha = \frac{K_M}{S_0} \quad \lambda = \frac{k_2}{k_1 S_0} \quad \varepsilon = \frac{E_0}{S_0}$$

$\varepsilon$  is assumed to be very small, as only a small amount of enzyme is needed to react with a substrate and catalyse a reaction.  $\varepsilon$  tells us about the relative rates at which the substrate and the complex are transformed due to the forward reaction. When  $\varepsilon$  being small means that the time for the complex to accumulate, will be much shorter than the time it takes the substrate to deplete. The dimensionless model becomes

$$\begin{aligned} \frac{dS}{dt} &= -S + C(S + \alpha - \lambda) \\ \varepsilon \frac{dC}{dt} &= S - C(S + \alpha) \end{aligned}$$

We can now analyse the system behaviour based on just 3 parameters instead of 5.

There are a couple of ways to analyse this system. We can arrive at a numerical solution using parameter values from experimental data. Another way is to use asymptotic expansions to find approximate solutions for this system. The expansions we will use are

$$\begin{aligned} S &\approx S_0(\bar{t}) + \varepsilon S_1(\bar{t}) + \dots \\ C &\approx C_0(\bar{t}) + \varepsilon C_1(\bar{t}) + \dots \end{aligned}$$

Inserting these expansions into the equations gives us,

$$\begin{aligned} \frac{d}{d\bar{t}}(S_0(\bar{t}) + \varepsilon S_1(\bar{t}) + \dots) &= -(S_0(\bar{t}) + \varepsilon S_1(\bar{t}) + \dots) \\ &\quad + (C_0(\bar{t}) + \varepsilon C_1(\bar{t}) + \dots)((S_0(\bar{t}) + \varepsilon S_1(\bar{t}) + \dots) + \alpha - \lambda), \end{aligned} \quad (7.3)$$

$$\begin{aligned} \varepsilon \frac{d}{d\bar{t}}(C_0(\bar{t}) + \varepsilon C_1(\bar{t}) + \dots) &= (S_0(\bar{t}) + \varepsilon S_1(\bar{t}) + \dots) \\ &\quad - (C_0(\bar{t}) + \varepsilon C_1(\bar{t}) + \dots)((S_0(\bar{t}) + \varepsilon S_1(\bar{t}) + \dots) + \alpha). \end{aligned} \quad (7.4)$$

We now solve the equations for each order of  $\varepsilon$ . Starting with the  $\mathcal{O}(1)$  terms:

$$\begin{aligned} \frac{dS_0}{d\bar{t}} &= -S_0 + C_0(S_0 + \alpha - \lambda) \\ 0 &= S_0 - C_0(S_0 + \alpha) \end{aligned}$$

We get the following expressions for  $C_0$  and  $S_0$

$$\begin{aligned} C_0 &= \frac{S_0}{S_0 + \alpha} \\ S_0 + \alpha \ln(S_0) &= -\lambda \bar{t} + A \end{aligned}$$

where  $A$  is a constant that will be determined later. The initial conditions,  $S(0) = 1$  and  $C(0) = 0$  cannot apply here which indicates that this is the outer solution. We find the inner solution that does incorporate the initial conditions. We will match the two solutions and get a value for the constant  $A$ .

To find the inner solution, we need to rescale the time. The scales we now choose are

$$\bar{t} = \tau \frac{1}{\varepsilon}. \quad (7.5)$$

And for the inner time solution, we rename  $S(\bar{t})$  and  $C(\bar{t})$  to  $\tilde{S}(\tau)$  and  $\tilde{C}(\tau)$ .

The differential system becomes,

$$\begin{aligned} \frac{d\tilde{S}}{d\tau} &= \varepsilon(-\tilde{S} + C(S + \alpha - \lambda)), \\ \frac{d\tilde{C}}{d\tau} &= S - C(S + \alpha). \end{aligned}$$

Now we produce an asymptotic solution for the inner time scale:

$$\begin{aligned} \frac{d}{d\tau}(S_0 + \varepsilon S_1 \dots) &= \varepsilon(-(S_0 + \varepsilon S_1 \dots) + (C_0 + \varepsilon C_1 + \dots)((S_0 + \varepsilon S_1 \dots) + \alpha - \lambda)) \\ \frac{d}{d\tau}(C_0 + \varepsilon C_1 + \dots) &= (S_0 + \varepsilon S_1 \dots) - (C_0 + \varepsilon C_1 + \dots)((S_0 + \varepsilon S_1 \dots) + \alpha) \end{aligned}$$

Taking one order of  $\varepsilon$  at a time, for  $\mathcal{O}(1)$ ,

$$\begin{aligned} \frac{dS_0}{d\tau} &= 0, \\ \frac{dC_0}{d\tau} &= S_0 - C_0(S_0 + \alpha). \end{aligned}$$

It then follows by integrating and solving for initial conditions

$$S_0(\tau) = 1.$$

Integrating the second equation by using integrating factor and applying the initial condition for  $C_0$ , we find

$$\begin{aligned} \frac{dC_0}{d\tau} &= 1 - C_0(1 + \alpha) \\ C_0 &= \frac{1}{1 + \alpha}(1 - e^{-(1+\alpha)\tau}) \end{aligned}$$

Now we can match the inner and outer solutions together. We recall the two solutions

Outer solution:	Inner solution:
$S(t) = A - \lambda t - \alpha \ln(S(t))$	$\tilde{S}(\tau) = 1$
$C(t) = \frac{S(t)}{S(t) + \alpha}$	$\tilde{C}(\tau) = \frac{1}{1 + \alpha}(1 - e^{-(1+\alpha)\tau})$

We match by getting the limits for the two solutions as  $t \rightarrow 0$  and as  $\tau \rightarrow \infty$  Matching  $S(t)$  and  $\tilde{S}(\tau)$  gives a value to the constant  $A$ :

$$\begin{aligned} \lim_{t \rightarrow 0} S(t) &= \lim_{\tau \rightarrow \infty} \tilde{S}(\tau), \\ \lim_{t \rightarrow 0} A - \lambda t - \alpha \ln(S(t)) &= \lim_{\tau \rightarrow \infty} 1, \\ A &= 1. \end{aligned} \quad (7.6)$$



Matching  $C(t)$  and  $\tilde{C}(\tau)$ :

$$\begin{aligned}\lim_{t \rightarrow 0} C(t) &= \lim_{\tau \rightarrow \infty} \tilde{C}(\tau) \\ \lim_{t \rightarrow 0} \frac{S(t)}{S(t) + \alpha} &= \lim_{\tau \rightarrow \infty} \frac{1}{1 + \alpha} (1 - e^{-(1+\alpha)\tau}) \\ \frac{S(0)}{S(0) + \alpha} &= \frac{1}{1 + \alpha} \\ \frac{1}{1 + \alpha} &= \frac{1}{1 + \alpha}\end{aligned}$$

Now we can combine the inner and outer solutions and remove the parts common to both and get a composite solution. We will use the inner expansion for the solution. The composite solution for  $S$ :

$$\begin{aligned}S_c(t) &= S(t) + \tilde{S}(\tau) - 1 \\ S_c(t) &= A - \lambda t - \alpha \ln(S(t) + 1) - 1 \\ S_c(t) &= 1 - \lambda t - \alpha \ln(S(t))\end{aligned}$$

Composite solution for  $C$ :

$$\begin{aligned}C_c(t) &= \frac{S(t)}{S(t) + \alpha} + \frac{1}{1 + \alpha} (1 - e^{-(1+\alpha)\tau}) - \frac{1}{1 + \alpha} \\ C_c(t) &= \frac{S(t)}{S(t) + \alpha} - \frac{1}{1 + \alpha} e^{-(1+\alpha)\frac{t}{\varepsilon}}\end{aligned}$$

Notice that the composite solution  $S_c(t)$  is the same as the outer solution  $S(t)$ .

Values for  $S(t)$  can be found using implicit and explicit iterative methods. The numerical solution can be calculated using methods such as the Forward Euler method. The `ode15s` function in MATLAB is a stiff differential equations solver based on the numerical differentiation formulas. We can use this function to arrive at a numerical solution. We will use values from a model of the transport of P-glycoprotein. P-glycoprotein is a protein that pumps many foreign substances out of cells. The parameter values used are the ones used in Holmes' book [9]:

$$k_1 = 10^9 M^{-1} s^{-1} \quad k_{-1} = 7.5 \times 10^5 s^{-1} \quad k_2 = 10^3 s^{-1} \quad E_0 = 10^{-5} M \quad S_0 = 100 E_0 M$$

where  $M$  is 1 mole per litre.

The numerical solutions are plotted in Figure 7.2. The concentrations in these figures are normalised as they are easier to analyse. The complex decreases as the substrate. At the beginning of the reaction, the enzyme substrate quickly increases in concentration and the substrate stays close to its initial concentration. When most of the enzyme is used up, the complex breaks down as the reaction product is formed. Both the substrate and the complex deplete, while the product concentration increases along with the unchanged enzyme.

It is clear to see how beneficial it is to look at a small time period. In Figure 7.2, the second graph (b) shows the complete reaction. Even though this particular reaction is complete in half a second, by only focusing on the long time scale we miss out on a lot of information regarding the formation of the complex. In the first graph (a) in Figure 7.2, it is clear to see the reversible reaction between the enzyme and complex.

Figure 7.3 depicts the composite solution and the numerical solution. As  $\varepsilon$  is very small in this example, there is little to no difference between the composite and numerical solution. The composite solution explains both the inner and outer timescales very well.

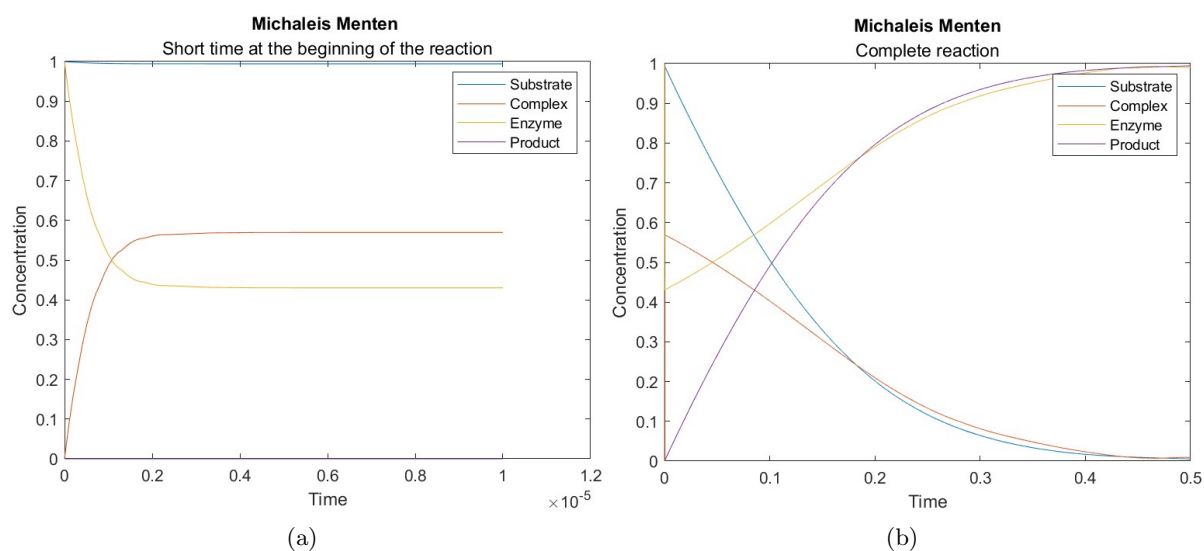


Figure 7.2: Michaelis Menten Reaction: Numerical Solution

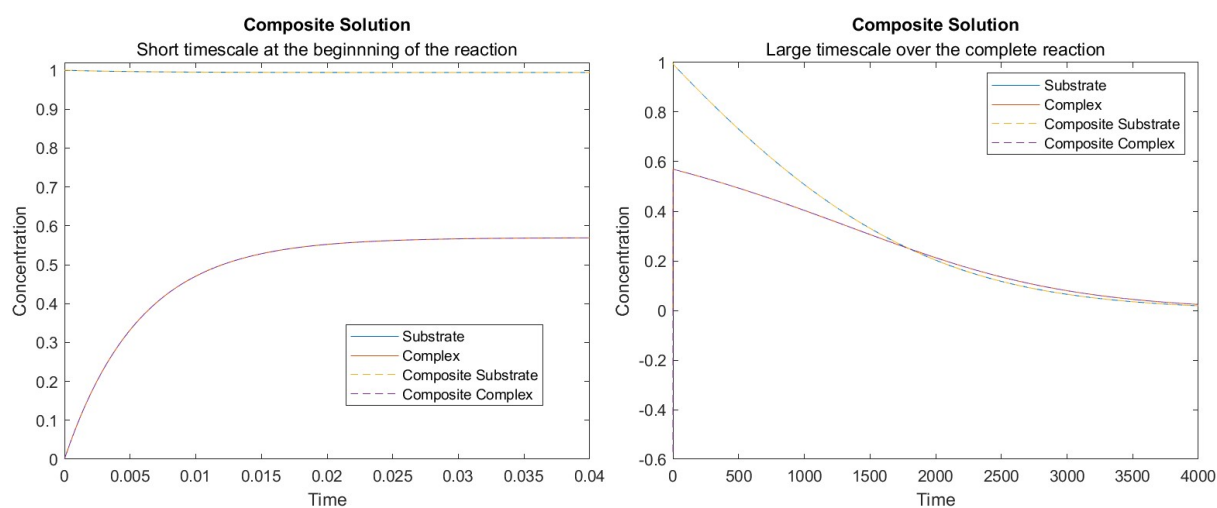


Figure 7.3: Composite solution compared with Numerical Solution

## Chapter 8

# Dashboard Application: Modelling Chemical Kinetics

A dashboard is a visual display of the most important information needed to achieve one or more objectives; consolidated and arranged on a single screen so the information can be monitored at a glance [26]. An important part of this project is to represent the chemical kinetic models we have derived using a MATLAB dashboard application.

With the overwhelming amounts of data and information available at our fingertips, and with the fast development of technology, the need for dashboards has increased. Dashboard applications give users the freedom to play around with and visualise data, without needing to evaluate models or to code everything themselves. They are adaptable to changes in inputs and variables. Similarly, these tools can also help ensure that operational decision-makers in organizations are not overwhelmed by the avalanche of data when trying to use information effectively[26]. Using dashboards, large amounts of information can be arranged and summarised. When created properly, the user or reader can have the confidence that the dashboard output is correct. They can then use the information to influence their decision making and even go on to create something more. Advancement of technology has made complex mathematics accessible to more people in a way they can understand. This has given rise to many dashboard solution providers in the market[26]. Popular ones include Power BI, Tableau, RShiny and Python, to name a few.

To choose what software to use for our application, we had to focus on what we wanted as the main functionality of the app. The application was to demonstrate chemical reactions, and to output the mathematical model associated with it. Most of the software were just for data presentation, and were not really built for solving or extracting mathematical models. The obvious choice was MATLAB. It is used in industry and academia and was designed specifically for engineers and scientists to analyze and design systems and products [27]. MATLAB App Designer allows the a user to create professional applications without having to be a professional developer. The capabilities of MATLAB are quite impressive. One feature that stands out when creating an app is the drag and drop feature. Buttons, plots, tables, text boxes, panels and so much more can quickly arranged together to make a neat graphical user interface (GUI). Applications made using MATLAB App designer allows for a lot of user interaction.

The App designer also brings along all of Matlab's core functionality. MATLAB functions such as ode45 and ode15s used to solve differential equations, can be run in the background, and its results shown on the app. Packages such as the Statistics and Machine Learning Toolbox,

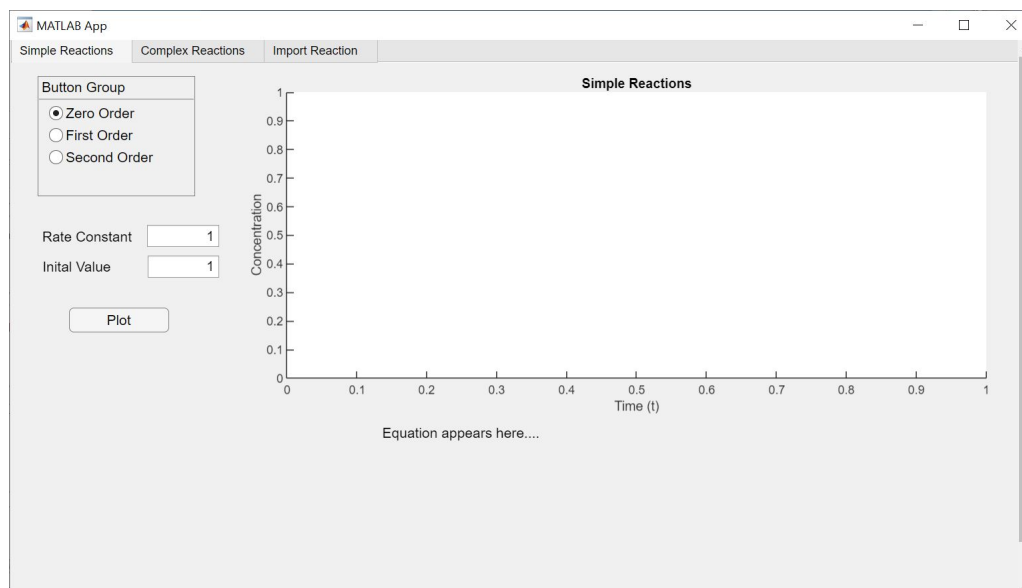


Figure 8.1: Simple Reaction tab

and the Symbolic Math Toolbox can be imported and used as well.

Text in Matlab can also be written using a Latex interpreter. This is especially useful in this application when writing mathematical expressions.

An integral attribute of dashboards is that they are easy to share. Unfortunately, one drawback of using MATLAB App designer is that the application created are not easily shared with those who do not have MATLAB. So at the moment the app can be found as a package on GitHub at the following link: <https://github.com/ChetachiNwarié/Final-Year-Project-19244355>. However in the future we want this app to be available to many whether they have the Matlab environment installed or not. Hopefully this functionality will come about in a later update of Matlab.

## 8.1 Dashboard Application Features

The dashboard application “Modelling Chemical Kinetics” was created so the user could understand what is happening in a system. It was especially to be of use to those who do not have a background in mathematics, but still want to explore chemical kinetic models.

The main features of this application are to:

- Demonstrate different types of chemical reactions using parameters given by the user
- Import a reaction dataset and output the mathematical model associated with the reaction

As of this report, dashboards to visualise simple reactions and complex reactions has been implemented. There is also an option to fit reactions from the data imported.

Figure 8.1 is the typical user interface used for the simple and complex reactions. There is the option to pick the desired reaction order, and the option to choose parameters for the system for the user to explore. This information is used to plot the graph for the concentrations of the species in the reaction. Figure 8.2 is an example of a more complicated interface. There

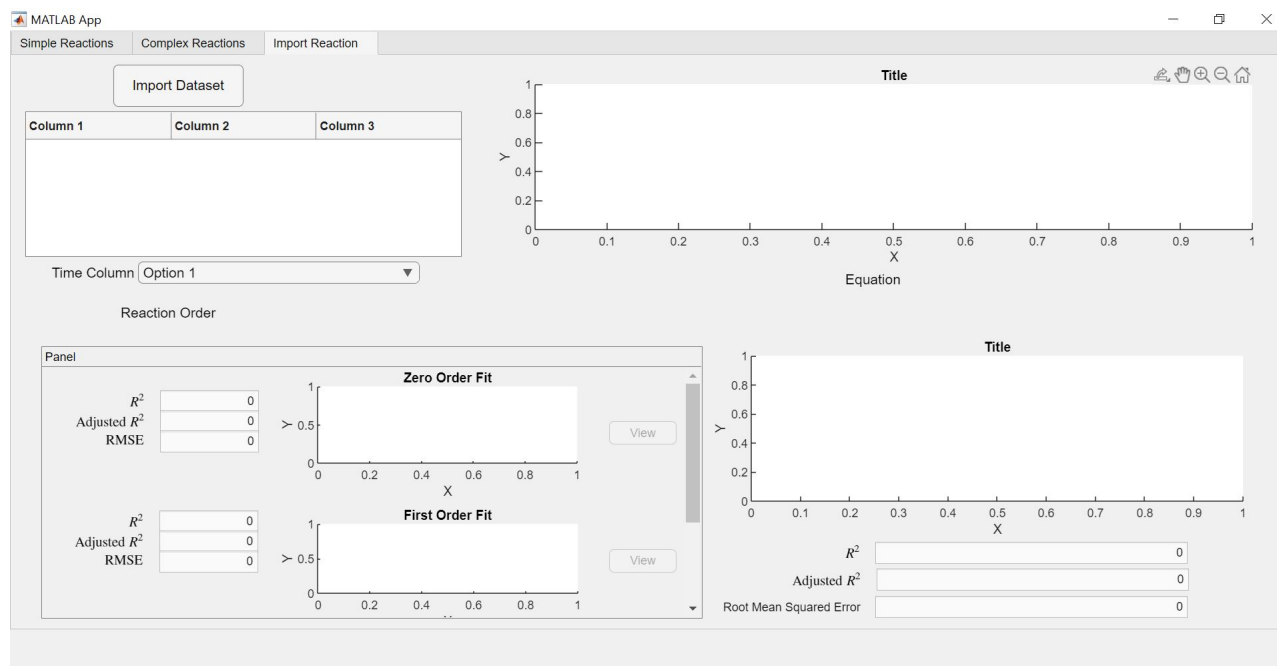


Figure 8.2: Import Reaction tab

are many plots and panels that can be used to analyse the system. So as not to cram too much information on one screen, scrollable panels are used to show the desired information. In this interface the user can import a data set and be shown 3 different possible reaction order fits. And then the user can decide depending on the parameters, what fit they want to use. The equation governing the reactant is also output.

## 8.2 Dashboard Application User Guide

Figure 8.3 is a screenshot of the application demonstrating a successive reaction. The user has the option to choose between a reversible reaction and a successive reaction. The can also choose the initial conditions and reaction rates for the system. Note that in the context of a reversible reaction, the rate constant 2 is the reverse reaction rate. By default, the rate constants and initial value is set to 1, until the user changes them. Figure 8.4 demonstrates the “Import Reaction” tab. For demonstration purposes, the data used in section 3.2.1 was imported into the application as a csv file. The application is built to accept excel and csv files. The data from the file is converted into a MATLAB table. The column headings and values are clearly seen in the table. The time column drop down that allows the user to identify which column holds the time variable. The time column values have to start from zero for the application to work. By default, the application assumes the first column to be the time column. And the first column with a nonzero initial value is assumed to be the reactant.

The data is graphed directly on the plot at the top right of the window. The axes and legend titles are automatic. The equation for the reactant appears below the graph.

The reaction order is determined from the reactant data. As demonstrated in section 3.2.1, the data is transformed using log and inverse transformations, and a linear fit is made. The

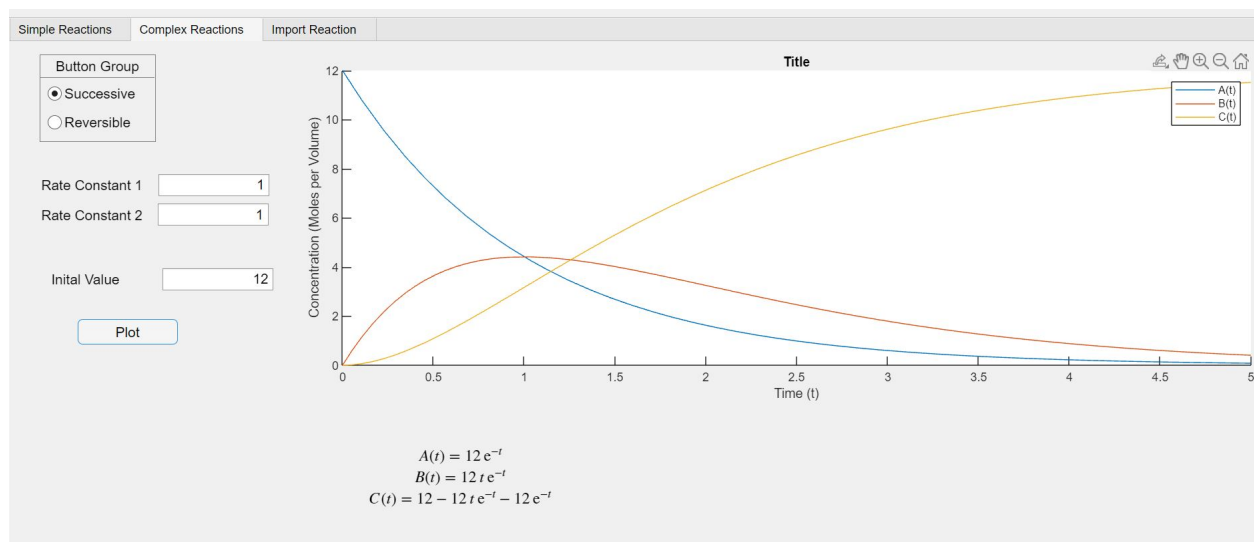


Figure 8.3: Example for Complex Reaction tab

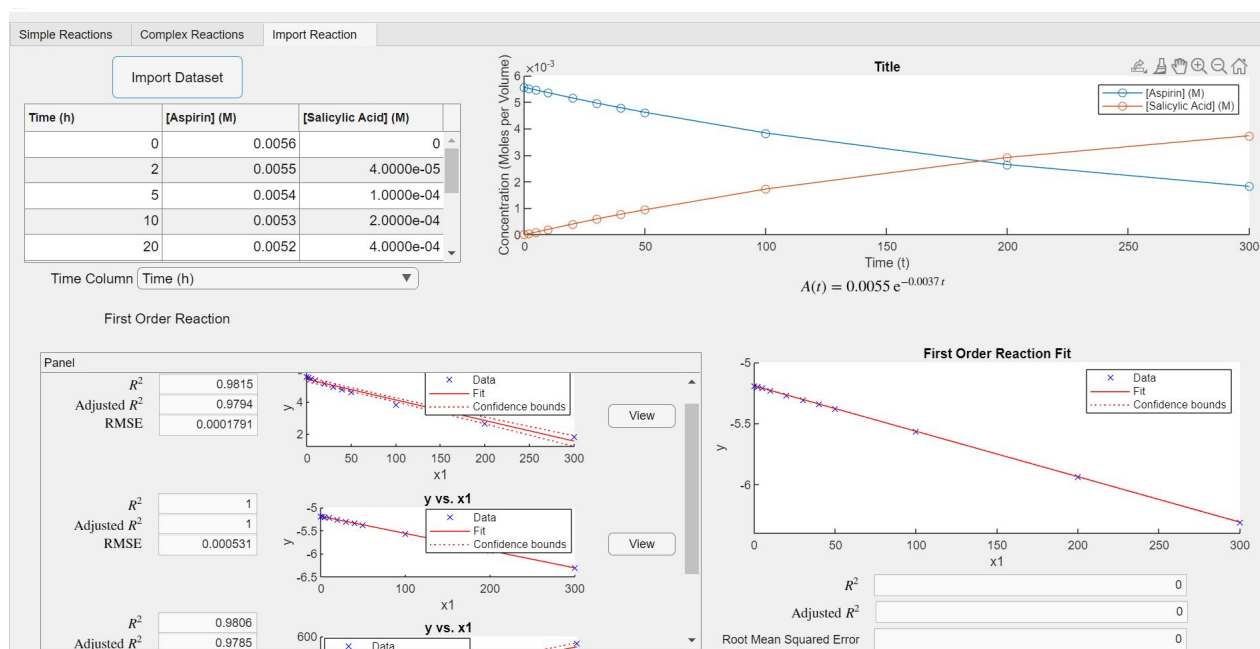


Figure 8.4: Importing First Order Reaction from Section 3.2.1

### 8.3. FUTURE UPDATES TO THE APPLICATIONModelling Chemical Kinetics

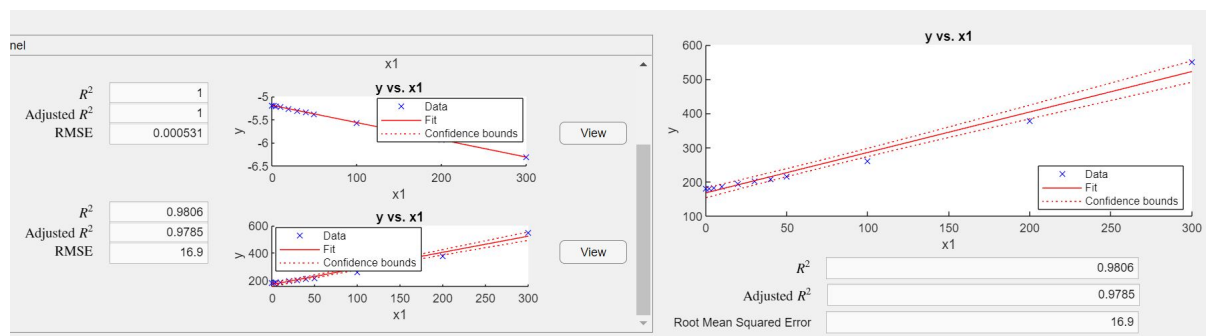


Figure 8.5: Linear fit to different transforms of the reactant

“Reaction Order Fits” panel shows all three of the fits. This is magnified in Figure 8.5. The three fits represent, zero order, first order and second order. The “best fit” is determined by the  $R^2$  value. This fit is also used to derive the equation for the reactant. The “View” buttons project the graphs to the plot frame on the right. The  $R^2$ , Adjusted  $R^2$  and RMSE values are also shown there.

### 8.3 Future Updates to the Application

There are endless ways to improve the app. An effort was made to not overload the application with too much functionality to begin with, and to work efficiently within time constraints. If its development was rushed, and all possible functions were included, it would have made the application confusing and awkward to use. There are ideas of a lot more functionality that can be implemented into this application and will hopefully be done in the future.

One such idea is allowing users to generate graphs from chemical equations written in the standard form. The user would input the number of species in the system and then outline the reaction path or paths. The rough idea is to get MATLAB to then generate the differential equations, and then use ode45 or ode15 to solve and graph the system.

Another anticipated update is to implement reactions with chemical oscillations and catalytic reactions. For the chemical oscillations, phase planes will be used to determine the stability of the system. The user would also be able to control the parameters used for the system.

As these methods used to model chemical kinetics can also be used in modelling population interactions and disease models, a future application should be able to handle that data, and produce results and summaries depending on the context of the data.

## Chapter 9

# Conclusions

In this report, we explored the theory behind chemical kinetics. We described the basic mathematics required to model chemical reactions. We have looked at the law of mass action and some simple rate laws. We have also looked how to derive differential laws from elementary reactions. We have used this knowledge to understand some more complex reactions, such as reversible reactions and successive reactions. We have derived models for different chemical reactions, and looked into the important features for these models such as conservation laws and steady states.

We also emphasised the importance of nondimensionalisation in analysing a mathematical model. Asymptotic solutions were also derived to analyse models over small and big time scales.

We built on this knowledge by examining more complex reactions. The Lotka-Volterra model introduced us to chemical oscillations. We saw that even if getting an exact solution was difficult, we could learn a lot about the model by observing its behaviour about a steady state. The Michaelis-Menten model introduced us to catalytic reactions in the form of enzyme-substrate reactions. Here we saw the usefulness of asymptotic solutions in measuring very small time scales.

A dashboard application was created using MATLAB App Designer. It demonstrated some of models discussed in this report. It allowed for user input to generate models and graphs based on the desired parameters and imported datasets.

Before starting this report, I knew very little about chemistry and chemical reactions. Researching and looking into chemical kinetics from a mathematical standpoint has been a good opportunity to learn about the world of chemistry. While compiling this report, I gained a lot of experience in deriving mathematical models. I appreciated this as I have seen that deriving mathematical models is a very important skill to have.

I have also improved my skills in MATLAB and even used the App Designer to build an application for this report. The skills I have learned in automating and packaging models in dashboards will be useful, not only in the application of chemical kinetics, but also more widely in the presentation of any statistical or mathematical modelling in industry.



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## Appendix A

# First Order Reaction Example

The following is MATLAB code from the first order reaction example in section 3.2.1.

```
1 clear all;
2 close all;
3
4 t = [
5 0;
6 2;
7 5;
8 10;
9 20;
10 30;
11 40;
12 50;
13 100;
14 200;
15 300
16 ];
17
18 a = [
19 5.55e-3;
20 5.51e-3;
21 5.45e-3;
22 5.35e-3;
23 5.15e-3;
24 4.96e-3;
25 4.78e-3;
26 4.61e-3;
27 3.83e-3;
28 2.64e-3;
29 1.82e-3];
30
31 b = [
32 0.00;
```

```
33 0.040e-3;
34 0.10e-3;
35 0.20e-3
36 0.40e-3;
37 0.59e-3;
38 0.77e-3;
39 0.94e-3;
40 1.72e-3;
41 2.91e-3;
42 3.73e-3];
43
44 figure;
45 plot(t,a, '-o')
46 hold on
47 plot(t,b, '-o')
48 legend({'Aspirin', 'Salicylic Acid'}, 'Location', 'north')
49 xlabel('Time (h)');
50 ylabel('Concentration (M x 10-3)');
51 title('Aspirin and Salicylic Acid vs Time')
52 hold off
53
54
55 lna = log(a);
56 lnb = log(b);
57
58 figure;
59 plot(t,lna, '-o')
60 hold on
61 plot(t,lnb, '-o')
62 legend({'ln(Aspirin)', 'ln(Salicylic Acid)'}, 'Location', 'south')
63 xlabel('Time (h)');
64 ylabel('ln(Concentration (M x 10-3))');
65 title('Natural Log of Aspirin and Salicylic Acid vs Time')
66 hold off
67
68 model = fitlm(t,lna);
69 h = model.Coefficients.Estimate;
70
71 p = 1:0.1:300;
72
73 A = a(1)*exp(h(2)*p);
74 B = a(1) - A;
75 figure;
76 plot(p,A, '-k')
77 hold on
78 plot(t,a, '-or')
```

```
79 hold on
80 plot(p,B, '—r ')
81 hold on
82 plot(t,b, 'ok ')
83 line = sprintf('ln(A) = %.5f e^{%.5f t}',a(1),h(2));
84 line2 = sprintf('ln(S) = %.5f ( 1 - e^{%.5f t})',a(1),h(2));
85 legend({line, 'Aspirin',line2, 'Salicylic Acid'},'Location','north east
      ')
86 xlabel('Time (h)');
87 ylabel('Concentration (M x 10^{-3})');
88 title('Aspirin and Salicylic Acid vs Time (using computed equation)',
      'FontSize', 8)
89 hold off
```

## Appendix B

# Asymptotic Solution to the Successive Reaction

The following MATLAB code generates the plots from Successive reaction in section 5.1.1.

```
1 %% Plots
2
3 %% Tidy up workspace
4 clear;
5 close("all");
6
7 %% Declare symbolic functions
8 syms B(t) Bc(t)
9
10 %%Taking random values for k1 and k2
11 k1 = 20;%Taking k1 bigger to show better agreement.
12 k2 = 4;
13 a0 = 5;
14
15 e = (k2/k1);
16
17
18 B(t) = ((k1*a0)/(k2-k1))*(exp(-k1*t) - exp(-k2*t));
19
20 %%
21
22 %Dimensionless composite solution is \bar{B}(\bar{t}) = exp(-e*\bar{t})
    - exp(-\bar{t}) + e*(exp(-e*\bar{t}) - exp(-\bar{t}))
23 %Time has been scaled with 1/k1 and e = (k2/k1). So dimensionaless
    time =
24 %k1*dimensional time or \bar{t} = k1*t. Also multiplying by a0, the
    dimensional solution is then:
25 % B(t) = a0*(exp(-e*(k1*t)) - exp(-k1*t) + e*(exp(-e*k1*t) - exp(-k1*
    t))) and subbing
```

```

26 % for e: B(t) = a0*(exp(-(k2*t)) - exp(-k1*t) + (k2/k1)*(exp(-k2*t) -
    exp(-k1*t)))
27
28 %Composite solution for B
29 Bc(t) = (a0)*(exp(-k2*t) - exp(-k1*t) + e*(exp(-k2*t) - exp(-k1*t)));
    %"Dimensionalised" version (small error is rescaling initially)
30 %Bc(t) = exp(-e*t) - exp(-t) + e*(exp(-e*t) - exp(-t)); %Non-
    dimensionalised version
31
32 figure;
33 fplot(B)
34 tle = sprintf("B(t) original with k2=%f, k1=%f, a0 = %f, epsilon =
    %.2f", k2, k1, a0, e);
35 title(tle)
36 xlabel('Time (t)');
37 ylabel('Concentration (Moles per Volume)');
38 axis('auto')
39 xlim([0 5])
40 hold off
41
42
43 figure;
44 fplot(Bc)
45 tle = sprintf("B(t) composite with k2=%f, k1=%f, a0 = %f, epsilon
    = %.2f", k2, k1, a0, e);
46 title(tle)
47 xlabel('Time (t)');
48 ylabel('Concentration (Moles per Volume)');
49 axis('auto')
50 xlim([0 5])
51 hold off
52
53
54 figure;
55 fplot(Bc)
56 hold on
57 fplot(B, '-o')
58 tle = sprintf("B(t) original and composite with k2=%f, k1=%f, a0 =
    %f, epsilon = %.2f", k2, k1, a0, e);
59 title(tle)
60 xlabel('Time (t)');
61 ylabel('Concentration (Moles per Volume)');
62 legend("Bc(t)", "B(t)")
63 axis('auto')
64 xlim([0 5])
65 hold off

```

```

66
67
68 %% Some things to try
69
70 %% Dimensionaless solutions (accurecy of asymptotic solution)?
71
72 %The following is really just to show the asymptotic solution gets
    more
73 %accurate for smaller epsilon.
74 %Note I choose outer timescale for comparison, as it is easier here
75 syms Bnond(eps,tau) Bnondc(eps,tau)
76
77
78 Bnond(eps,tau) = (1/(eps-1))*(exp(-tau/eps) - exp(-tau)); %Non
    dimensionalised version (check solution)
79 Bnondc(eps,tau) = exp(-tau) - exp(-tau/eps) + eps*(exp(-tau) - exp(-
    tau/eps));
80
81
82 xmax= 3;
83 figure;
84 fplot(Bnond(0.2,tau),[0,xmax],'b')
85 hold on
86 fplot(Bnond(0.1,tau),[0,xmax],'r')
87 hold on
88 fplot(Bnond(0.05,tau),[0,xmax],'m')
89 hold on
90 fplot(Bnond(0.01,tau),[0,xmax],'k')
91
92
93 fplot(Bnondc(0.2,tau),[0,xmax],'b—o')
94 hold on
95 fplot(Bnondc(0.1,tau),[0,xmax],'r—o')
96 hold on
97 fplot(Bnondc(0.05,tau),[0,xmax],'m—o')
98 hold on
99 fplot(Bnondc(0.01,tau),[0,xmax],'k—o')
100
101 legend(["exact $\varepsilon = 0.2$", "exact $\varepsilon = 0.1$", "
    exact $\varepsilon = 0.05$", "exact $\varepsilon = 0.01$", "comp $
    \varepsilon = 0.2$ ", "comp $\varepsilon = 0.1$", "comp $\varepsilon
    = 0.05$", "comp $\varepsilon = 0.01$"], "interpreter", "latex")
102 title("Outer timescale solution ($k_1 \ll k_2$)", "Interpreter", "latex
    ")
103 xlabel('Time (t)', "Interpreter", "latex");
104 ylabel('Concentration (Moles per Volume)', "Interpreter", "latex");

```



```

105
106 %On the innertime scale the corresponding plots are
107
108 xmax= 10;
109 figure;
110 fplot(Bnond(0.2,0.2*t),[0,xmax], 'b')
111 hold on
112 fplot(Bnond(0.1,0.1*t),[0,xmax], 'r')
113 hold on
114 fplot(Bnond(0.05,0.05*t),[0,xmax], 'm')
115 hold on
116 fplot(Bnond(0.01,0.01*t),[0,xmax], 'k')
117
118
119 fplot(Bnondc(0.2,0.2*t),[0,xmax], 'b—o')
120 hold on
121 fplot(Bnondc(0.1,0.1*t),[0,xmax], 'r—o')
122 hold on
123 fplot(Bnondc(0.05,0.05*t),[0,xmax], 'm—o')
124 hold on
125 fplot(Bnondc(0.01,0.01*t),[0,xmax], 'k—o')
126
127 legend(["exact  $\epsilon = 0.2$ ", "exact  $\epsilon = 0.1$ ",
        "exact  $\epsilon = 0.05$ ", "exact  $\epsilon = 0.01$ ", "comp  $\epsilon$ 
         $\epsilon = 0.2$ ", "comp  $\epsilon = 0.1$ ", "comp  $\epsilon$ 
         $\epsilon = 0.05$ ", "comp  $\epsilon = 0.01$ "], "interpreter", "latex")
128 legend('Location', 'south')
129 title("Inner timescale solution ( $k_1 \gg k_2$ )", "Interpreter", "latex
    ")
130 xlabel('Time (t)', "Interpreter", "latex");
131 ylabel('Concentration (Moles per Volume)', "Interpreter", "latex");

```

## Appendix C

# Michaelis Menten Equatons

The following MATLAB code generates the plots from the enzyme substrate reaction in chapter 7.

```
1  close all;
2
3  k1 = 1e9;
4  k_1= 7.5e5;
5  k2 = 1e3;
6  E0 = 1e-5;
7  S0 = 100*E0;
8
9  a = (k_1 + k2)/(S0*k1);
10 l = k2/(S0*k1);
11 eps = E0/S0;
12
13
14
15
16
17 %% Short time dimensionless solution first
18 tspan = linspace(0,0.04,100);%more points for better plots
19 y0 = [1; 0];
20 [t,y] = ode15s(@(t,y) odefun(t,y,a,l,eps), tspan,y0);
21 figure;
22 plot(t,y)
23 tle = sprintf("Michaelis Menten ", y0(1),y0(2));
24 title(tle, "(Short time/Inner Solution)")
25 xlabel("Time")
26 ylabel("Concentration")
27 legend("Substrate", "Complex")
28
29 figure;
30 plot(y(:,1),y(:,2), '—')
```

```

31 q = quiver(y(:,1),y(:,2),gradient(y(:,1)),gradient(y(:,2)));%Arrows
    are not great visually.
32 q.ShowArrowHead = 'off';
33 q.Marker = '.';
34 title("Phase Plane for inner solution")
35 xlabel("Substrate")
36 ylabel("Complex")
37 %axis([0.95 1 0 1]) %could change axis range
38
39 figure;
40 plot(t,y(:,2))
41 title("Enzyme-Substrate Complex ", "(Short time/Inner solution)")
42 xlabel("Time")
43 ylabel("Concentration")
44
45 %% Long time dimensionless
46
47 tspan = linspace(0,4000,8000);%more points for better plots
48 y0 = [1; 0];
49 [t,y] = ode15s(@(t,y) odefun(t,y,a,l,eps), tspan,y0);
50 figure;
51 plot(t,y)
52 tle = sprintf("Michaelis Menten", y0(1),y0(2));
53 title(tle, "(Long time/Outer Solution)")
54 xlabel("Time")
55 ylabel("Concentration")
56 legend("Substrate", "Complex")
57
58 figure;
59 plot(y(:,1),y(:,2),'-')
60 q = quiver(y(:,1),y(:,2),gradient(y(:,1)),gradient(y(:,2)));%Arrows
    are not great visually.
61 q.ShowArrowHead = 'off';
62 q.Marker = '.';
63 title("Phase Plane for long timescale")
64 xlabel("Substrate")
65 ylabel("Complex")
66 %axis([0.95 1 0 1]) %could change axis range
67
68 figure;
69 plot(t,y(:,2))
70 title("Enzyme-Substrate Complex", "(Long time/Outer Solution)")
71 xlabel("Time")
72 ylabel("Concentration")
73
74

```

```

75 %% Dimensional (short time)
76 tspan = linspace(0,1e-5,100);
77 y1 = [S0; 0; E0; 0];
78 [t,yd] = ode15s(@(t,y) odef(t,y,k1,k_1,k2,E0), tspan,y1);
79 %Plot normalised concentrations, easier to analyse
80 figure;
81 plot(t,yd(:,1)/S0)
82 hold on
83 plot(t,yd(:,2)/E0)
84 plot(t,yd(:,3)/E0)
85 plot(t,yd(:,4)/S0)
86 tle = sprintf("Michaleis Menten ");
87 title(tle,"Short time at the beginning of the reaction")
88 xlabel("Time")
89 ylabel("Concentration")
90 legend("Substrate", "Complex", "Enzyme", "Product")
91
92 figure;
93 plot(t,yd(:,2))
94 title("Enzyme-Substrate Complex","Short time at the beginning of the
      reaction")
95 xlabel("Time")
96 ylabel("Concentration")
97
98 %We can see initial transition in phase plane
99 figure;
100 plot(yd(:,1),yd(:,2),'-')
101 q = quiver(yd(:,1)/S0,yd(:,2)/E0,gradient(yd(:,1)/S0),gradient(yd
      (:,2)/E0));%Arrows are not great visually.
102 q.ShowArrowHead = 'off';
103 q.Marker = '.';
104 title("Phase Plane at the start of the reaction")
105 xlabel("Substrate")
106 ylabel("Complex")
107
108 %% Dimensional (long time)
109 tspan = linspace(0,0.5,10000);
110 y1 = [S0; 0; E0; 0];
111 [t,yd] = ode15s(@(t,y) odef(t,y,k1,k_1,k2,E0), tspan,y1);
112 %Plot normalised concentrations, easier to analyse
113 figure;
114 plot(t,yd(:,1)/S0)
115 hold on
116 plot(t,yd(:,2)/E0)
117 plot(t,yd(:,3)/E0)
118 plot(t,yd(:,4)/S0)

```

```

119 tle = sprintf("Michaleis Menten");
120 title(tle, "Complete reaction")
121 xlabel("Time")
122 ylabel("Concentration")
123 legend("Substrate", "Complex", "Enzyme", "Product")
124
125 figure;
126 plot(t,yd(:,2))
127 title("Enzyme-Substrate Complex", "Complete reaction")
128 xlabel("Time")
129 ylabel("Concentration")
130
131 %Now very hard to see initial transition
132 figure;
133 plot(yd(:,1),yd(:,2),'-')
134 q = quiver(yd(:,1)/S0,yd(:,2)/E0,gradient(yd(:,1)/S0),gradient(yd
    (:,2)/E0));%Arrows are not great visually.
135 q.ShowArrowHead = 'off';
136 q.Marker = '.';
137 title("Phase Plane over the complete reaction")
138 xlabel("Substrate")
139 ylabel("Complex")
140
141 %% Functions
142 function dydt = odefun(t,y,a,l,eps) %Outer solution (Long time scale)
143     dydt = zeros(2,1); %number of species
144     dydt(1) = -y(1) + y(2)*(y(1) + a - l);
145     dydt(2) = (y(1) - y(2)*(y(1) + a))/eps;
146 end
147
148
149 function dydt = odef(t,y,k1,k_1,k2,E0)
150     dydt = zeros(4,1); %number of species
151     dydt(1) = -k1*y(1)*E0 + k1*y(1)*y(2) + k_1*y(2);
152     dydt(2) = k1*y(1)*E0 - k1*y(1)*y(2) - k_1*y(2) - k2*y(2);
153     dydt(3) = -dydt(2);
154     dydt(4) = -dydt(1) - dydt(2);
155 end

```