Computer Simulations of Elementary Reversible Reactions: Product Distributions and Stability Analysis

Kal Renganathan Sharma*

PE Electrical Program, San Jacinto College Central Campus, USA

*Corresponding Author: Kal Renganathan Sharma, PE Electrical Program, San Jacinto College Central Campus, Pasadena, TX 77505.

Received: September 28, 2015; Published: November 19, 2015

Abstract

The scheme of elementary consecutive reactions both reversible were studied using computer simulations. Numerical solutions were obtained using the method of Runge Kutta of the third order. The dimensionless concentrations of species A, R and S were obtained in MS Excel for Windows 2013. The results for different values of the reaction rate ratios $\omega$, $\kappa$, $\epsilon$ are presented. The intermediate product R undergoes a maximum. Sometimes more of the species S is formed. The species dimensionless concentration as a function of dimensionless time as well the species concentrations as a function of conversion of species A are shown as Figures. Taylor series solutions were obtained. Truncation of fourth and higher order terms were found not to be sufficient for accurate predicting the species concentration for mature times. Cross-over from more R to more S was seen under some conditions at later times. The stability of the system can be studied by obtaining the Eigen values and Eigen vectors of the rate matrix.

Keywords: Reversible Consecutive Reactions; Runge Kutta Method; Product Distributions; Taylor Series Solution; Intermediate Product Yield; Eigen Stability

Introduction

Products that are made from petrochemicals such as automobile tires, clothing, and athletic shoes and diapers are going to be manufactured from raw materials that stems from botanical plants. Principles of enzyme catalysis are used in this endeavor. The PCR study of microorganism or host cell or polynucleotide that serves as catalyst can be performed using microarray analysis [2]. Cloning can be confirmed using sequencing studies. Mutagenesis and molecular cloning methods needed to achieve the desired outcome of higher yields can be designed using the information using microarray analysis. Engineered microbes and development of biocatalysts has led to the commercialization of biobased polymers. The environmentalists’ concerns about air and water pollution can be allayed using manufacturing processes that are scaled-up from tube studies of bioprocess technologies. Plants can be used as source of raw materials for common polymers such as polyester, spandex, synthetic rubber and nylon. Energy sustainability is another benefit obtained using this route. Plants as a source for raw materials make them renewable feed stocks.

Invista and Genomatics [2] have made the News for the investments in setting up manufacturing plants in order to prepare nylon intermediates from sugar. Acrylic acid for superabsorbent polymers is going to be manufactured using a bio-based method by BASF, Cargill and Novozymes. A 100% biobased soda bottle is under development at Coca Cola and its partner Virent is going to supply the raw material. P-xylene is used as a precursor to terephthalic acid that is used in condensation polymerization with ethylene glycol in order to make PET, polyethylene terephthalate. Raw material supply and cost can be a critical factor in determination of the Present Worth of these manufacturing plants. Invista’s Lycra brand spandex is 70% from dextrose that is derived from corn. The CO$_2$ emissions from these processes are low. These fibers are stretchy. Bioprocess based BDO was sourced from BASF. BASF had licensed this technology from Genomatica. Genomatica has demonstrated a bioprocess route to butadiene the monomer that is used to make polybutadiene that is used

to make automobile tires. Engineered microbes have been developed in order to make caprolactum used in the preparation of nylon 6 and adipic acid and hexamethylene diamine used in nylon 6.6. Virent has the technology that can be used to convert sugars catalytically into gasoline and diesel. Virent along with Shell has a vision to build biorefineries. Products from biorefineries are expected to become attractive by cost when the oil reserves become depleted. Acrylic acid production by biotechnology is a goal of a partnership of conglomerates such as BASF, Cargill and Novozymes, in the fields of agriculture, enzymes and chemicals. The group earlier this 2014 year reported 3-hydroxypropionic acid from sugar. 3-Hp was converted to glacial acrylic acid. This is used in order to make diapers that are super absorbent. Commercial biobased products are likely in the next decade to make:

a. Succinic acid, fumaric acid, malic acid from bacterial fermentation of glucose, chemical oxidation of 1,4-butanediol
b. 2,5-Furandicarboxylic acid from chemical dehydration of glucose, oxidation of 5-hydroxymethylfurfural
c. 3-hydroxypropionic acid from glycerol or glucose by bacterial fermentation
d. Glycerol from vegetable oils by catalytic transesterification
e. Sorbitol from glucose from corn syrup by hydrogenation of xylose
f. Xylitol from xylose by bacterial fermentation.

Downstream chemicals of these products include 1,4 butanediol, THF, tetrahydrofuran, γ-butyrolactone, maleic anhydride, pyrrolidones, 1,3-propane diol, acrylic acid, methyl acrylate, acrylamide, propylene glycol, ethylene glycol, 1,3-propanediol, glyceric acid, lactic acid, acetol, acrolein, epichlorohydrin, isosorbide, propylene glycol, ethylene glycol, glycerol, lactic acid, alkanes, propylene glycol, ethylene glycol, glycerol, xylaric acid, furfural, 2,5-dihydroxymethylfuran.

In vista is setting up a $100 million manufacturing plant at Orange, TX in order to make AND, adiponitrile using next generation technology. They also have novel biotechnology process to make butadiene a raw material in the manufacture of automobile tires. Geomatics has posted on their websites 18 proprietary patents on bio based polymer technology. They prepare 6-ACA, 6-aminocaproic acid from 5-formylvaleric acid [3] using a biocatalyst. The 6-ACA is then converted into caprolactum. They discuss a host cell or polynucleotide used to catalyze the reaction. Nylon 6 can be made from caprolactum. Nylon 6, 12 is a copolymer of caprolactum and laurolactum. Caprolactum has been made from compounds obtained from mineral oil in current industrial practice. Plasmids carrying the different genes were identified by genetic, biochemical and phenotypic means. PCR diagnostic analysis of transformed or purified plasmid DNA and DNA sequence analysis may be used. The genes that encode the biocatalyst were amplified from g DNA using PCR methods. PCR reactions were analyzed using agarose gel electrophoresis. PCR products were purified and cloned. The sequence of genes cloned by PCR was verified by DNA sequencing. Escherichia Coli was grown in 96 well plates with 940 µl media containing 0.02% L-arabinose. Protein expression was studied. Cells for small scale growth were obtained by centrifugation and supernatant was decanted. Centrifugation of 6000g was operated at 4°C for 20 minutes.

Cells in living species contain many chemical compounds. How the chemicals are manufactured, how some reactants combine at moderate temperature and pressure, how some decompose is governed by enzyme catalysis. Enzymes are globular proteins. They have been found to catalyze more than 5000 biochemical reactions types. Buchner first extracted certain enzymes from living cells in 1897. E. Fisher proposed in 1894 that both the enzyme and substrate take complementary geometric shapes that fit into each other admirably and presented their 'lock and key' model. One weakness of this model is it does not explain the intermediates that are now known to form in different pathways. The set of enzymes made in a cell can determine which metabolic pathways occur in that cell. Enzymes are said to convert substrates into products. They act as a catalyst. A catalyst, by definition, is a substance that is known to increase the rate of a chemical reaction without undergoing permanent chemical change. It affects the rate of the reaction without undergoing chemical change. It does not affect the chemical equilibrium of the reactants and products. During enzymatic action the activation energy of the reaction undergoes a reduction in value. This can be seen in the synthesis of glucose 6 phosphate from glucose 1 phosphate. The number of 'hot molecules' that can participate in the reaction [5] is larger when the activation of energy of the reactions in lowered on account of enzymatic action.
Catalysts that are found to be active within the living cell can be made to be active outside the living cell such as in a bioreactor. Sumner isolated the first enzyme in 1926. Since then the number of known enzymes are greater than 1500. Microarray analysis and NGS, next-generation sequencing machines [1] can be used to study gene transcription and gene translation processes and other biochemical reactions with increased accuracy. Potentially 3000-4500 enzymes may be present in the human anatomy. Enzyme Commission, EC, identified 6 classes of reactions that are known to be catalyzed by enzymes. These are:

a. Hydrolases
b. Transferases
c. Lyases
d. Ligases
e. Oxidoreductases
f. Isomerases

The enzyme urease for example catalyzes the decomposition of urea. Oxidative dehydrogenation of alcohol is catalyzed by alcohol dehydrogenase. Familiar names among enzymes are pepsin, trypsin that are found in the human digestive tract, rennin used in cheese factories and 'old yellow enzyme' causes browning of sliced apples.

Often times the reaction mechanism occurring within the cell is not well known. Experiments are conducted. At first, a guess is made of the elementary reactions taking place. The reaction intermediates that are formed are noted. Then an expression for the overall reaction rate is developed. This expression is checked against the experimental observations made. The iterative process of guess and estimation and verification can continue till a reasonable fit is obtained. Cofactors add on to apoenzyme that are not active and become catalytically active halo enzyme active complex. Metals and coenzymes can be cofactors. The Michaelis and Menten kinetics discussed in earlier section is applicable in order to describe enzymatic processes.

In this study, elementary consecutive reactions, both reversible are considered. These reactions are often encountered during enzyme catalytic transformations. Numerical solutions are obtained. This system has not been quantitatively explained in the literature but has been qualitatively discussed in [6]. Studies of intermediate product yield improvement by mass transfer of intermediate product in situ, was presented by [7].

Computer Simulation of Kinetics of Elementary Reversible Reactions in Series
The scheme of reactions shown in Figure 1 is elementary and reversible [8].

![Figure 1: Elementary Reactions in Series, Both Reversible.](image)

Both the consecutive reactions in Figure 1 in series are reversible. These types of reactions are found to occur during cyclic deracemizations reactions. The order of the four reactions is assumed to be of the first order. The kinetics of the four reactions can be written as follows:

---

The rate expressions can be written in the state-space form as follows:

\[
\frac{d}{dt} \begin{pmatrix} C_A \\ C_R \\ C_S \end{pmatrix} = \begin{pmatrix} -k_f & +k_r & 0 \\ k_f & -(k_r + k_2) & -k_2 \\ 0 & k_2 & -k_r \end{pmatrix} \begin{pmatrix} C_A \\ C_R \\ C_S \end{pmatrix}
\]  \tag{2}

The stability of the system can be studied by obtaining the Eigen values and Eigen vectors of the rate matrix. The characteristic equation can be written as follows:

\[
(-k_f - \lambda)(k_r - \lambda)(k_r + k_2 - \lambda) - k_f k_r k_2 - k_f (-k_f - k_r - \lambda) = 0
\]  \tag{3}

From the eigenvalue of the rate matrix the stability of the system can be studied. The rate expressions can be made dimensionless using the following substitutions:

\[
u_A = \left( \frac{C_{A_0}}{C_{A_0}} \right) u_A = \left( \frac{C_{A_0}}{C_{A_0}} \right) u_A = \left( \frac{C_{A_0}}{C_{A_0}} \right) \tau \equiv \left( k_f t \right) \phi = \left( k_f t \right) \kappa = \left( \frac{k_1}{k_f} \right) \varepsilon = \left( \frac{k_2}{k_f} \right)
\]  \tag{4}

The rate expressions can be seen to become:

\[
\begin{align*}
\frac{du_A}{d\tau} &= -u_A + \omega u_A \\
\frac{du_R}{d\tau} &= u_A + \omega u_A - (\phi + \kappa) u_R \\
\frac{du_S}{d\tau} &= \omega u_S - \omega u_A \\
\end{align*}
\]  \tag{5}

Runge Kutta method of the third order was used in order to obtain the solution for the Equations (5).

This method is described in [9]. The weighting factors and the recursive relations used are given as follows:

\[
y_{i+1} = y_i + \frac{1}{6} (k_1 + 4k_2 + k_3) h
\]  \tag{6}

Where,

\[
k_1 = f(x_i, y_i) \\
k_2 = f(x_i + 0.5h, y_i + 0.5k_1h) \\
k_3 = f(x_i + h, y_i + k_2h + 2k_3h)
\]  \tag{7}

The dimensionless concentrations of the species A, R and S, \( u_A, u_R \) and \( u_S \) as a function of dimensionless time, \( \tau = k_f t \) is shown in Figure 2. The step size used in the computer simulations was \( h = 0.01 \). The distribution of products R and S as a function of conversion of reactants A, \( X_A = 1 - u_A \) is shown in Figure 3. Figure 2 and Figure 3 were obtained for reaction rate constant ratio values of \( \kappa = \varepsilon = \omega = 0.333 \).
The dimension less concentrations of the species $A$, $R$, and $S$, $u_A$, $u_R$, and $u_S$ as a function of dimensionless time, $\tau = k/t$ is shown in Figure 4. The step size used in the computer simulations was $h = 0.01$. The distribution of products $R$ and $S$ as a function of conversion of reactants $A$, $X_A = 1 - u_A$, is shown in Figure 5. Figure 4 and Figure 5 were obtained for reaction rate constant ratio values of $\kappa = \epsilon = \omega = 0.2$. It can be seen that after 70% conversion of reactant $A$ the concentration of product species $R$ formation decreases. At about 88% conversion of reactant $A$ the concentration of species $S$ also decreases. At higher conversions the reactant $A$ species concentration is lower and hence the rate of the reaction decreases.
The dimensionless concentrations of the species A, R and S, $u_A$, $u_R$ and $u_S$, as a function of dimensionless time, $\tau = k \cdot t$ is shown in Figure 6. The step size used in the computer simulations was $h = 0.01$. The distribution of products R and S as a function of conversion of reactants A, $X_A = 1 - u_A$ is shown in Figure 7. Figures 6 and 7 were obtained for reaction rate constant ratio values of $\kappa = 0.92$, $\varepsilon = 0.7$ and $\omega = 0.05$.

Figure 6: Product Distribution for Species A, R and S at $\kappa = 0.92$, $\varepsilon = 0.7$, $\omega = 0.05$.

Figure 7: Distribution of Product Materials R and S, $u_R$ and $u_S$ as a Function of Conversion of Species A at $\kappa = 0.92$, $\varepsilon = 0.7$, $\omega = 0.05$.

For the special case of Equation (5) when \( \omega = 0 \) and \( \epsilon \) is high and \( \kappa \) the intermediate product yield of species R is seen to further increase. This can be seen in Figure 8. The product distribution as a function of conversion of A is shown in Figure 9. This is when conversion of species A to intermediate species R is irreversible and the more of the species S by a reverse reaction forms species R. This in addition to formation of species R from species A can lead to more species R. The rate matrix for Equation (5) in the special case when \( \omega = 0 \) can be seen to be:

\[
K = \begin{pmatrix}
-1 & 0 & 0 \\
1 & -\kappa & \epsilon \\
0 & \kappa & -\epsilon
\end{pmatrix}
\]  

(8)

Where: \( K \) is the rate matrix in the kinetic rate equations for species A, R and S for the special case when \( \omega = 0 \). The rate equation in state space form can be written as follows:

\[
\frac{d}{d\tau} \begin{pmatrix} u_A \\ u_R \\ u_S \end{pmatrix} = \begin{pmatrix}
-1 & 0 & 0 \\
1 & -\kappa & \epsilon \\
0 & \kappa & -\epsilon
\end{pmatrix} \begin{pmatrix} u_A \\ u_R \\ u_S \end{pmatrix}
\]  

(9)

The Eigen values for Equation (9) can be calculated using the characteristic equation:

\[-(1 + \lambda)(\kappa + \lambda(\epsilon + \lambda) - \kappa \epsilon) - 1*0 = 0\]  

(10)

The solutions to Equation (10) can be seen to be \( \lambda_1 = -1, \lambda_2 = 0 \) and \( \lambda_3 = -(\kappa + \epsilon) \).

\[\text{Figure 8: Product Distributions of Species A, R and S for } \kappa = 3, \epsilon = 0 \text{ and } \omega = 0.3333.\]
Taylor Series Solution

Numerical solution was obtained for the system of consecutive reactions in series, both steps reversible by the method of Runge Kutta of the third order. Here a Taylor series solution is obtained for the system of ODEs given in Equation (5) in dimensionless form. This is another method to obtain the solution to the model equations.

\[
\begin{align*}
\frac{du_A}{d\tau} &= -u_A + \omega u_R \\
\frac{du_R}{d\tau} &= u_A - (\varepsilon + \kappa)u_R + \omega u_S \\
\frac{du_S}{d\tau} &= \kappa u_R - \omega u_S \\
\end{align*}
\]

At \(t=0\), \(u_A = 1\), \(u_A'(0) = -1\), \(u_R(0) = 0\), \(u_S(0) = 0\), \(u_R'(0) = 1\), \(u_S'(0) = 0\)

\[
\begin{align*}
\frac{d^2 u_A}{d\tau^2} &= (1 + \omega)u_A - (1 - \omega - \kappa)\omega u_R + \omega \omega u_S \\
\end{align*}
\]

\[
\begin{align*}
u_A'(0) &= (1 + \omega)
\end{align*}
\]
The Taylor series written about the dimensionless time, $\tau = 0$ for dimensionless species A and R after truncation of fourth and higher order terms are:

$$\frac{d^4 u_A}{d\tau^4} = -u_A(1 + \omega + \kappa) + u_A(\omega + (\omega + \kappa)^2 + \varepsilon \kappa) - \omega u_A (\omega + \kappa + \varepsilon) \quad (17)$$

$$u_A(0) = (1 + \omega + \kappa) \quad (18)$$

$$\frac{d^2 u_A}{d\tau^2} = \omega u_A (\kappa + \varepsilon - 1 - \omega) \quad (19)$$

$$u_A(0) = \kappa(\kappa + \varepsilon - 1 - \omega) \quad (20)$$

$$\frac{d^4 u_A}{d\tau^4} = u_A(1 - \kappa + \varepsilon(\omega + \kappa)^2 + u_A(\omega - 2\varepsilon \kappa - 2\omega \kappa - 2\varepsilon^2) - \omega u_A (\omega + 2\varepsilon \kappa + (\omega + \kappa)^2 + 2\varepsilon \kappa + \varepsilon^2) \quad (21)$$

$$u_A(0) = (1 + \omega + \kappa) \quad (21)$$

The Taylor series written about the dimensionless time, $\tau = 0$ for dimensionless species A and R after truncation of fourth and higher order terms are:

$$u_A(\tau) = 1 - \tau + (1 + \omega) \frac{\tau^2}{2!} + \frac{\tau^3}{3!} (1 + \omega \kappa + \omega^2) \ldots \quad (21)$$

$$u_A(\tau) = \tau - (1 + \omega + \kappa) \frac{\tau^2}{2!} + (\omega^2 + \kappa^2 + 2\omega \kappa + \varepsilon \kappa - \kappa - 1) \frac{\tau^3}{3!} + \ldots \quad (22)$$

$$u_A(\tau) = \kappa \frac{\tau^2}{2!} + \frac{\tau^3}{3!} (\varepsilon + \kappa - 1 - \omega) + \ldots \quad (23)$$

Conclusions

Elementary consecutive reactions are the building block of reactions observed to occur during enzyme catalytically and sustainable transformation of biomass into useful chemicals at the lowest cost. Computer simulations were used to study the elementary consecutive reactions, both reversible. Numerical solutions were obtained using the method of Runge Kutta of the third order. The dimensionless concentrations of species A, R and S were obtained in MS Excel for Windows 2013. The results for different values of the reaction rate ratios $\omega, \kappa, \varepsilon$ are shown in Figures 2-8. The intermediate product R undergoes maxima. Sometimes more of the species S is formed compared with species R. Other times equal amounts of species R and species S were found. This kind of distribution of materials R and S was seen at $\kappa = \varepsilon = \omega = 0.2$.

The species dimensionless concentration as a function of dimensionless time as well the species concentrations as a function of conversion of species A are shown as Figures. Taylor series solutions were obtained. Truncation of fourth and higher order terms was found not to be sufficient for highly accurate prediction of the species concentration for mature times. Cross-over from more R to more S was seen under some conditions at later times. The stability of the system was studied by obtaining the Eigen values and Eigen vectors of the rate matrix. The rate expressions was written in the state-space form in Equation. (2). the system was studies for the special case of $\omega = 0$. The solutions to Equation. (10), the characteristic Eigen value can be seen to be $\lambda_1 = -1, \lambda_2 = 0$ and $\lambda_3 = -(\kappa + \varepsilon)$. This would mean a stable system.

Bibliography