Turk. J. Math. Comput. Sci.
5(2016) 8–18

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Mathematical Modeling of Biochemical Reactions Under Random Effects

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Received: 27-09-2016 • Accepted: 24-11-2016

Abstract. In this study, random effects are added to the parameters of the deterministic Biochemical Reaction Model (BRM) to form a system of random differential equations. A random model is built with these equations to describe the random behavior of biochemical reactions. Gaussian and Beta distributions are used for the random effect terms. Numerical characteristics of the random model are investigated using the simulations of the random equation system. Characteristics of the model components under Gaussian and Beta distributed effects are compared and comments are made on the difference in these two cases. The results are also used to explore the differences in the deterministic and random models of BRM and to study the random behavior of the model components.

2010 AMS Classification: 34F05, 82B80, 92C45, 60K37

Keywords: Random Differential Equation, Biochemical Reaction Model, Beta Distribution, Gaussian Distribution, Random Effect, Runge Kutta Method.

1. Introduction

Mathematical modeling is the investigation of systems or events in physical, biochemical and social sciences through mathematical equations. The type of mathematical equations to be used for the model is determined according to the amount of information that is present on the system or event to be modeled. One possible classification of mathematical models is based on the randomness of the events. A mathematical model can be either deterministic or probabilistic. An event that produces the same result in every trial under the same conditions is called deterministic. Most of the models used in health and medical sciences are deterministic, i.e. not random. However, there are some events in nature that do not produce the same results under the same conditions, such as the flipping of a coin. The randomness in such events can be modeled in the mathematical equations by using random variables or stochastic processes. Stochastic models containing such random equations are frequently used in finance, insurance and etc.

The model used in this study, Biochemical Reaction Model (BRM), was introduced by Michaelis and Menten in 1913 [11]. BRM consists of nonlinear differential equations describing the changes in the amounts of the substrate, the enzyme, the enzyme-substrate complex and the product. Since the equations are nonlinear, numerical methods are used to obtain a numerical solution of this system.

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This work was supported by Research Fund of the Karadeniz Technical University. Project Number: FBA-2016-5394.

Some of the parameters of BRM describe the rates of reactions. The reaction rate is mostly used as a constant value in deterministic models. However, it is known that a reaction is effected by pressure and temperature. Consequently, a change in these factors would also change the value of the rates of the reactions. In this study, the parameters describing random events are added random effects with both Gaussian (normal) and Beta distributions to form a random model. Numerical solutions of the random model are simulated in MATLAB to investigate the numerical characteristics of the random BRM, such as expected value, variation, moments and etc. Numerical characteristics for both distributions are found and compared to each other to comment on the random behavior of the model and the influence of the distributions on the results.

2. Biochemical Reaction Model

Among some models used for describing the dynamics of chemical reactions catalyzed by enzymes, the Biochemical Reaction Model of Michaelis and Menten is one of the simplest and most effective. It provides a useful tool for analyzing the reaction through the Michaelis-Menten rate constant $K_m = (k_{-1} + k_2)/k_1$. The model describes the flow of chemical reactions under the catalysis of enzymes as:

$$E + A \underset{}{\overset{k_{-1}}{\longleftarrow}} \overset{k_1}{\longrightarrow} Y \xrightarrow{k_2} E + X$$

where E is the enzyme, A is the substrate, Y is the enzyme-substrate complex and X is the product. k_1,k_{-1} and k_2 are the rate constants of the first forward reaction, backward reaction and the second forward reaction, respectively [11]. Considering this flowchart, the following system of differential equations are given for BRM [16]:

$$\begin{aligned} \frac{dA}{dt} &= -k_1 EA + k_{-1} Y, \\ \frac{dE}{dt} &= -k_1 EA + (k_{-1} + k_1) Y, \\ \frac{dY}{dt} &= k_1 EA - (k_{-1} + k_1) Y, \\ \frac{dX}{dt} &= k_2 Y \end{aligned} \tag{2.1}$$

along with the initial conditions

$$A(0) = A_0,\ E(0) = E_0,\ Y(0) = Y_0,\ X(0) = X_0.$$

The variables of system (2.1) describing the amounts of the substrate, enzyme, complex and substrate can be changed to scaled variables describing the concentrations. By reducing the system (2.1) to a system of equations for the dimensionless form of concentrations of the substrate and the enzyme-substrate complex which are denoted by x and y, we get

$$\begin{aligned} \frac{dx}{dt} &= -x + (\alpha + \beta) y + xy, \\ \frac{dy}{dt} &= \frac{1}{\epsilon}(x - \beta y - xy) \end{aligned} \tag{2.2}$$

along with the initial conditions

$$x(0) = 1,\ y(0) = 0.$$

The new dimensionless parameters of system (2.2) and their values for the numerical simulations are as follows [16]:

$$\alpha = \frac{k_2}{k_1 A_0},\ \beta = \frac{(k_{-1} + k_2)}{k_1 A_0},\ \epsilon = \frac{E_0}{A_0}.$$

$$\alpha = 0.375,\ \beta = 1,\ \epsilon = 1.$$

The equations are nonlinear and hence many studies in the literature concentrate on the approximate solutions of the model: Yildirim et. al. used multi-step differential transform method in [16], Sen used Adomian decomposition method in [12], Goh et. al. compared the results obtained from the multistage variational iteration method and Runge-Kutta method in [4]. Additional literature can be found on the application of other schemes to the BRM [1, 9].

3. Random Modeling of Biochemical Reaction Model

A considerable portion of the studies on mathematical modeling of real-life events are carried out with a deterministic approach. However, many of the events that are modeled deterministically have stochastic components. Hence a probabilistic modeling study is more suitable for these types of events. Biochemical Reaction Model is one of these models which consist of deterministic equations. Some of the parameters of BRM are dependent on the rate constants k_1,k_{-1} and k_2, whose values may vary according to the conditions in which the reaction is performed. Hence, there is a certain level of randomness in the nature of biochemical reactions [5, 7]. There are a number of modeling studies on biochemical reactions that take the stochasticity of the reactions into account [7, 8]. In this study, we model the random nature of these reactions by changing the deterministic coefficients of the BRM into random coefficients to form a random model consisting of random differential equations.

Equation system (2.2) has three parameters α, β and ϵ. The parameters α, β are dependent on the reaction rates k_1,k_{-1} and k_2, while the third parameter is defined as $\epsilon = E_0/A_0$ for the initial values of the enzyme and the product. Since the values of the reaction rates may vary according to the values of the temperature and pressure, transforming the parameters α, β to random variables would provide a better modeling approach for these reactions [10, 13, 16]. We use two different probability distributions to describe the possible variations in the values of these parameters: Gaussian (normal) distribution and Beta distribution.

3.1. Gaussian Distributed Parameters.

The parameters α and β are assumed to be constant values ($\alpha = 0.375, \beta = 1$) for deterministic numerical studies. In this part, they will be considered as normally distributed random variables. A random variable X is said to be Gaussian (normal) distributed with parameters (μ, σ^2) and denoted as $X \in N(\mu, \sigma^2)$ if its probability density function is of the form

$$f(x) = \frac{1}{\sigma\sqrt{2\pi}} e^{-\frac{1}{2}\left(\frac{x-\mu}{\sigma}\right)^2}, \ x \in \mathbb{R}.$$

where μ is the mean of the distribution and σ^2 is the variance. The mean values of the distributions of α and β will be chosen as the values of the parameters in the deterministic models, so that the possible variations of the parameters around their average values can be described properly in the random variables:

$$\alpha \in N(\mu_1, \sigma_1^2) = N(0.375, \sigma_1^2),$$

$$\beta \in N(\mu_2, \sigma_2^2) = N(1, \sigma_2^2).$$

A normally distributed random variable $X \in N(\mu, \sigma^2)$ can be shown as

$$X = \mu + \sigma Z,$$

where $Z \in N(0, 1)$. Using this property, we denote the parameters α and β as

$$\alpha = 0.375 + \sigma_1 Z_1,$$

$$\beta = 1 + \sigma_2 Z_2$$

where σ_1, σ_2 are the standard deviations of the distributions of α and β, respectively, and Z_1, Z_2 are independent and standard normally distributed random variables. The third parameters ϵ is not dependent on the reaction rates, so it is assumed to be constant on its value $\epsilon = 1$. It is known that approximately 99.7% of the values of a Gaussian distributed random variable are within 3 standard deviations of its mean value, i.e. the interval $[\mu - 3\sigma, \mu + 3\sigma]$. Hence, the values of σ_1 and σ_2 are determined as $\sigma_1 = 1/24$ and $\sigma_2 = 1/30$ to set similar domains for the random parameters with both Gaussian and Beta distributions (see Figure 1). The random model under Gaussian random effects is given using the new parameters (for independent and $N(0, 1)$ distributed random variables Z_1, Z_2):

$$\begin{aligned} \frac{dx}{dt} &= -x + \left(1 + \frac{1}{30}Z_2 - \left(0.375 + \frac{1}{24}Z_1\right)\right)y + xy, \\ \frac{dy}{dt} &= \left(x - \left(1 + \frac{1}{30}Z_2\right)y - xy\right) \end{aligned} \tag{3.1}$$

along with the initial values

$$x(0) = 1, \ y(0) = 0.$$

Random variables that are expected to be sum of independent quantities often have normal distribution. Considering the central limit theorem, normal distribution is used for sufficiently large numbers of random variables whose distributions are not known. Normal distribution was used for the random effects in this study since the exact distributions of the random values of the parameters are not known and their values depend on the variations of the temperature and pressure. Assuming 10^5 simulations will be produced for the random model, normal distribution would be an appropriate choice to model the distribution of the parameters.

Random variables are measureable functions from the space of possible outcomes to real numbers. Hence, system (3.1) would produce a system of deterministic differential equations with the values of the parameters α and β differing for every trial of the event. Since these are deterministic equations with variant parameters in every trial, the numerical solution methods will be applied using the deterministic schemes. The deterministic numerical results of the simulations of the model are used to find the random numerical characteristics of the model components.

3.2. **Beta Distributed Parameters.** A random model similar to the system (3.1) above will be made using random effects with Beta distribution. Beta distribution is widely used in modeling problems where the probability of success in a probabilistic experiment is unknown. Beta distribution has been used in statistical description of sunshine data [14], soil property variability [6] and the variability in the probability of HIV transmission [15]. In this part, Beta distribution will be used as the probability distributions of the parameters α and β, since the real specific distributions of the values of these parameters are not known.

The standard beta distribution is a continuous probability distribution on $(0, 1)$ with the shape parameters (a, b) for $a > 0, b > 0$. A random variable Z^* is said to be standard beta distributed with parameters (a, b) in the interval $(0, 1)$ and denoted as $Z^* \in Beta(a, b)$ if its probability density function has the form

$$f(x) = \frac{1}{B(a,b)} x^{a-1}(1-x)^{b-1}, \ x \in (0,1), \ a > 0, \ b > 0,$$

where a is the left shape parameter and b is the right shape parameter [3]. Beta distribution has a symmetrically curved shaped probability distribution function if the shape parameters satisfy the condition $a = b > 1$, which would be useful for comparing the results with normal distribution which has a similarly symmetrically curved shaped probability density function. $X^* = c + dZ^*$ has a 'general' beta distribution function in the interval (c, d) and it is denoted as $X^* \in Beta(c, d, a, b)$ if its probability density function has the form

$$f(x) = \frac{1}{B(a,b)d^{a+b-1}} (x-c)^{a-1}(c+d-x)^{b-1}, \ c < x < c+d, \ a > 0, \ b > 0,$$

where c is the location parameter, d is the scale parameter and a, b are the left and right shape parameters, respectively.

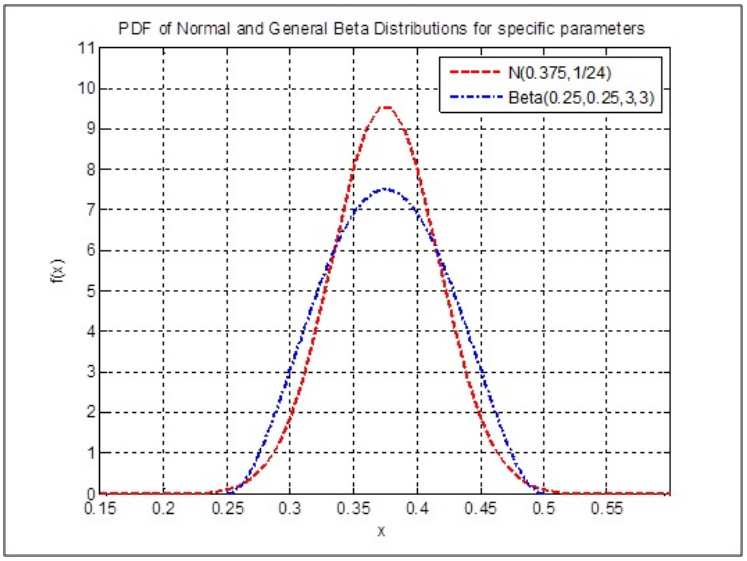

FIGURE 1. Probability Density Functions of the distributions used for α.

It can be seen in Figure 1, that a random variable with a general Beta distribution takes values from the interval (c, d), while a normally distributed random variable takes values from the interval $(-\infty, \infty)$. Hence, the variation of the normal distribution is larger than the variation of the general Beta distribution. In this part, we will assume the coefficients of the model (2.2) are beta distributed and compare the results with the normally distributed results. If $\alpha \in Beta(0.25, 0.25, 4, 4)$, then the mean value of α is: $E(\alpha) = 0.375$. Similarly, if $\beta \in Beta(0.9, 0.2, 3, 3)$ then the mean value of β is $E(\beta) = 1$. Since a general beta distributed random variable X^* can be shown as $X^* = c + dZ^*$ using a standard $Beta(a, b)$ distributed random variable Z^*, we define the parameters of the model (2.2) as

$$\alpha = 0.25 + 0.25Z_1^*,$$

$$\beta = 0.9 + 0.2Z_2^*$$

where Z_1^*, Z_2^* are independent and standard $Beta(3, 3)$ distributed random variables. Replacing these random variables in the system (2.2), we obtain:

$$\begin{aligned} \frac{dx}{dt} &= -x + (0.9 + 0.2Z_2^* - (0.25 + 0.25Z_1^*))\, y + xy, \\ \frac{dy}{dt} &= (x - (0.9 + 0.2Z_2^*)\, y - xy) \end{aligned} \tag{3.2}$$

along with the initial values

$$x(0) = 1,\ y(0) = 0.$$

4. Results

A random variable is a measurable function from the set of possible outcomes to the real numbers. Hence for every trial of the event, systems (3.1) and (3.2) produce deterministic differential equations with different coefficients. These systems of differential equations are simulated in MATLAB and Runge-Kutta method is used to obtain numerical results of these nonlinear differential equations. The results are used to obtain numerical characteristics of the model components which are given for both cases.

4.1. **Results for Normally Distributed Random Effects.**

In this part, the solution curves, expected values, variances, standard deviations and confidence intervals of the model components under normally distributed random effects are given [2].

4.1.1. *Solution Curves.*

The solution curves of $x(t)$ and $y(t)$ are given in Figure 2.

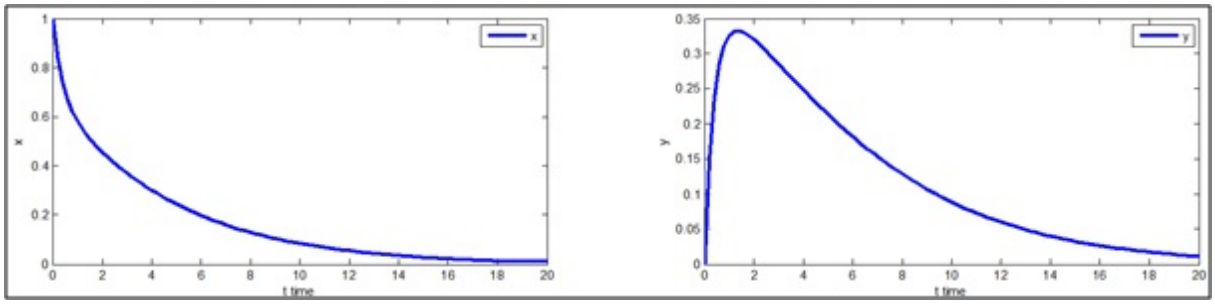

Figure 2. The solution curves of $x(t)$ and $y(t)$.

It can be seen from the graph that the value of x, which represents the concentration of the substrate decreases through the process meaning that the amount of substrate constantly decreases and finally reaches a very low value, as expected. The value of y, which represents the concentration of substrate-enzyme complex increases in the beginning and then decreases in a similar manner to the decrease of x. This behavior shows the mixture of the enzyme and product in the beginning and the decrease in the amount of mixture in the second phase where the substrate is turning into the product. Both graphs show that the behaviors of the variables under random effects are in compliance with the real life occurrence of the process.

The maximum and minimum values obtained for x and y are as follows: x reaches its maximum value $max(x(t)) = 1$ at $t = 0$ and its minimum value $min((x(t)) = 0.009749$ at $t = 20$, while y reaches its maximum value $max(y(t)) = 0.3325$ at $t = 1.4$ and its minimum value $min(y(t)) = 0$ at $t = 0$. It should also be noted that $y(t) = 0.01136$ for $t = 20$.

Note that the results for the solution curves only depend on the 10^5 trials of the reaction simulated by MATLAB. While the expected values, variances and confidence intervals will be valid for all trials of the event, these solution curves may show slight variations in other simulations.

4.1.2. *Expected Values.* The expected values $E(x(t))$ and $E(y(t))$ are given in Figure 3.

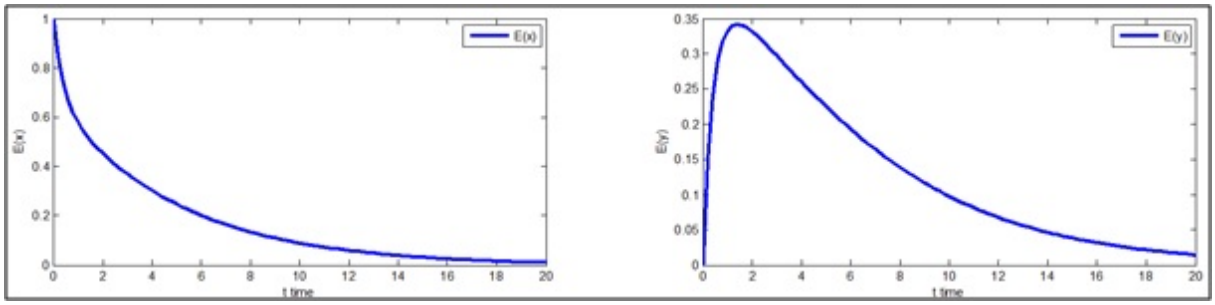

FIGURE 3. The expected values of $x(t)$ and $y(t)$.

The graphs for the expected values represent similar changes to the graphs of the solution curves, as expected. Since the expected values are valid for all possible trials of the reaction under random effects, it can be said that the reaction is expected to proceed in accordance to the deterministic case. The concentration of the substrate is expected to have a maximum value of 1 at $t = 0$ and a minimum value of 0.01205 at $t = 20$, while the concentration of the enzyme-substrate complex is expected to have a maximum value of 0.3418 at $t = 1.4$ and a minimum value of 0 at $t = 0$. Thus, the substrate concentration is expected to drop to approximately 0.01 at $t = 20$, while the complex concentration is expected to reach approximately 0.34 at $t = 1.4$ and then drop to approximately 0.01 at $t = 20$.

4.1.3. *Variances.* The variances $var(x(t))$ and $var(y(t))$ are given in Figure 4.

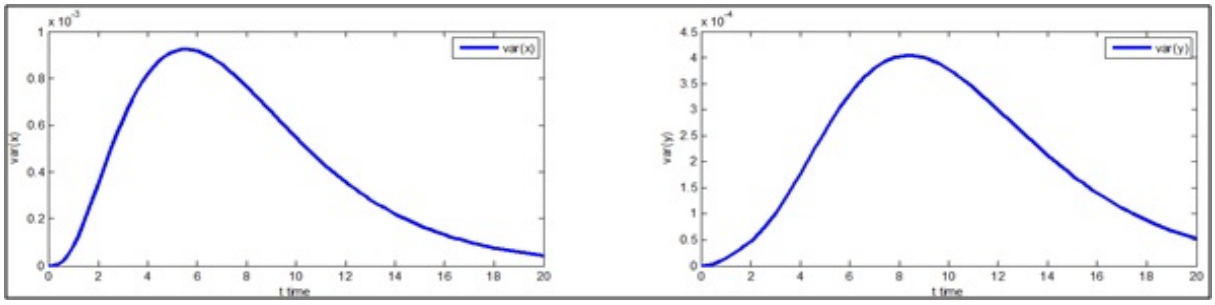

FIGURE 4. The variances of the variables $x(t)$ and $y(t)$.

Variance is a measurement of the deviation from the mean value of a random variable. A rise in the value of a variance implies more deviations from the average value of the random variable. Since the random variable in this case is the parameter and the mean of the random variable corresponds to the value of the parameter in the deterministic case, the rise in the values of the variances show the deviations of the random results from the deterministic results. It can be seen from the graphs that the random case produces results that are considerably different from the results of the deterministic case.

The variance of the concentration of the substrate reaches its maximum value 0.000924 at $t = 5.6$ and its minimum value 0 at $t = 0$, while the variance of the concentration of the complex reaches its maximum value 0.0004038 at $t = 8.4$ and its minimum value 0 at $t = 0$.

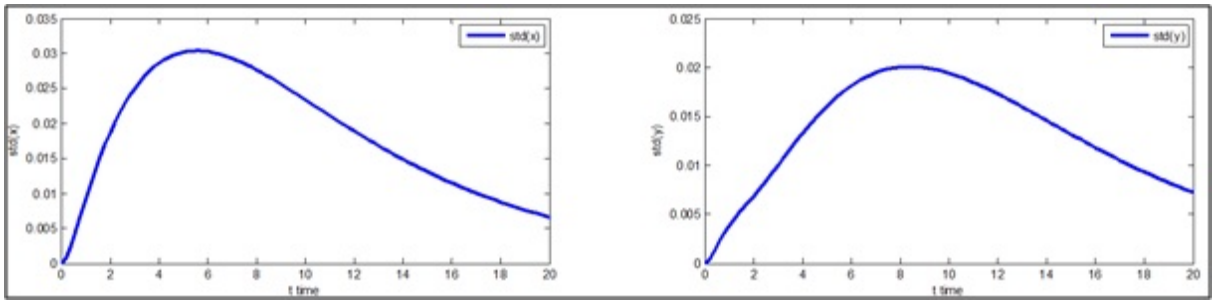

FIGURE 5. The standard deviations of $x(t)$ and $y(t)$.

4.1.4. *Standard Deviations.* The standard deviations $std(x(t))$ and $std(y(t))$ are given in Figure 5.

The standard deviations of the variables show similar behavior to the variations of the variables, as expected. Standard deviation, which by definition is the square root of variance, describes the deviations from the mean of the random variable, just like the variance. However with the standard deviations, we can also see the amount of these deviations and the graphs show that the random case produces up to 3% deviated results from the deterministic case under these conditions of the reaction.

The standard deviation of the substrate reaches its maximum value 0.0304 at $t = 5.6$ and its minimum value 0 at $t = 0$, while the standard deviation of the enzyme-substrate intermediate complex reaches its maximum value 0.0201 at $t = 8.4$ and its minimum value 0 at $t = 0$.

4.1.5. *Confidence Intervals.* The confidence intervals for mean values $[E(x(t)) - K\sigma(x(t)), E(x(t)) + K\sigma(x(t))]$ and $[E(y(t)) - K\sigma(y(t)), E(y(t)) + K\sigma(y(t))]$ are given in Figure 6.

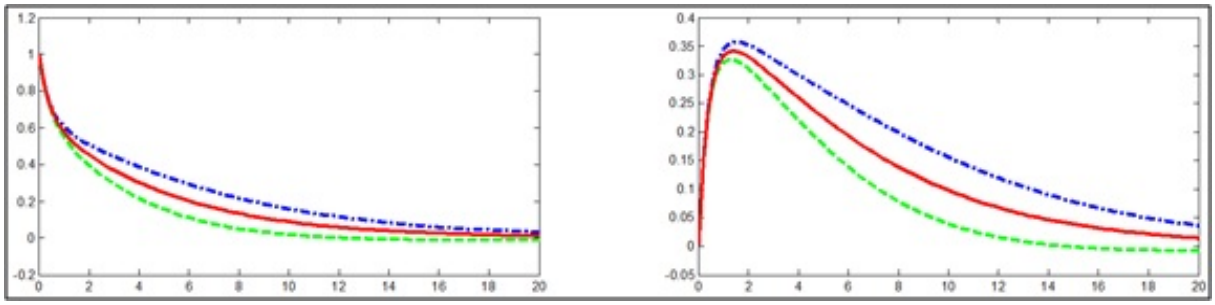

FIGURE 6. The confidence intervals of $x(t)$ and $y(t)$.

The formula for confidence interval of the mean of the random variable $x(t)$ has the form:

$$[E(x(t)) - K\sigma(x(t)), E(x(t)) + K\sigma(x(t))].$$

For $K = 1, 2, 3$ this formula gives approximately 68%, 95% and 99.7% confidence intervals for the mean value of the random variable. Using the standard deviations above approximately 99.7% confidence intervals are obtained for the mean values of the model components (upper limit: dash-dotted line, lower limit: dashed line). It can be seen from the graphs that in certain stages of the reaction process, the results can be considerably different from the mean values. The confidence interval for $x(t)$ has a maximum value of 1 at $t = 0$ and a minimum value of -0.007953 at $t = 17.8$, while the confidence interval for $y(t)$ has a maximum value of 0.3577 at $t = 1.6$ and a minimum value of -0.007953 at $t = 20$.

4.2. **Results for Beta Distributed Random Effects.** In this part, the solution curves, expected values, variances, standard deviations and confidence intervals of the model components under beta distributed random effects are given.

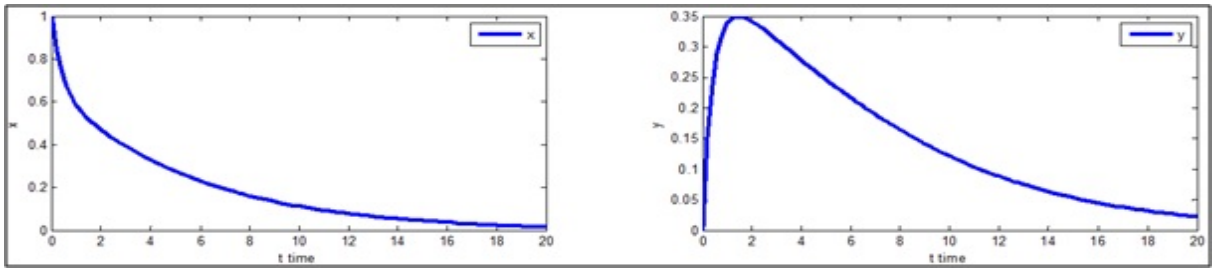

FIGURE 7. The solution curves of $x(t)$ and $y(t)$.

4.2.1. *Solution Curves.* The solution curves of $x(t)$ and $y(t)$ are given in Figure 7.

It can be seen from the graphs that the variables $x(t)$ and $y(t)$ under beta distributed random effect show similar behavior the both the deterministic case and the case with normally distributed random effects. The solution curve for the concentration of the substrate decreases throughout the process while the solution curve for the concentration of the complex decreases accordingly after hitting its maximum value. $x(t)$ has its maximum value 1 at $t = 0$ and its minimum value 0.0183 at $t = 20$, whereas $y(t)$ has its maximum value 0.3492 at $t = 1.4$ and its minimum value 0 at $t = 0$.

4.2.2. *Expected Values.* The expected values $E(x(t))$ and $E(y(t))$ are given in Figure 8.

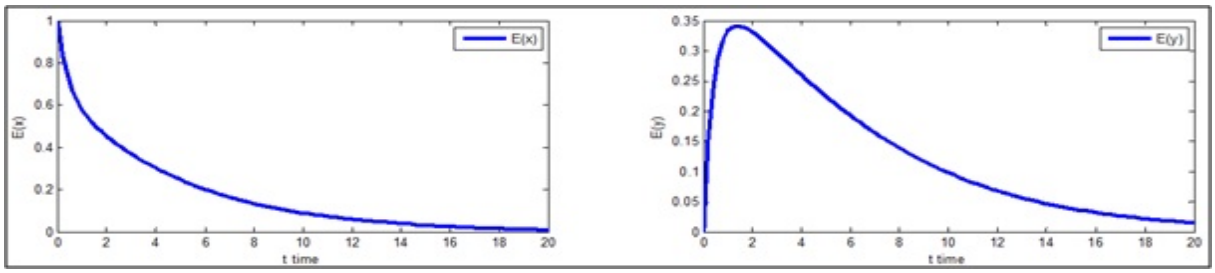

FIGURE 8. The expected values of $x(t)$ and $y(t)$.

The graphs for the expectations of $x(t)$ and $y(t)$ under beta distributed random effects are in compliance with the solution curves, as expected. The concentration of the substrate is expected to have a maximum value of 1 at $t = 0$ and a minimum value of 0.01246 at $t = 20$, while the concentration of the complex is expected to have a maximum value of 0.3419 at $t = 1.4$ and a minimum value of $t = 0$. Note that the expected value, variance, standard deviation and confidence intervals under beta distributed random effects are valid for all possible trials of the event, while the solution curves only describe the changes of the variables in the trials simulated by MATLAB for these calculations.

4.2.3. *Variances.* The variances $var(x(t))$ and $var(y(t))$ are given in Figure 9.

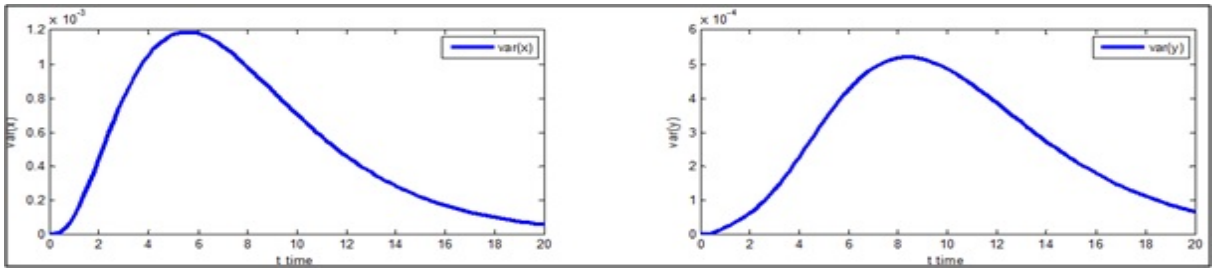

FIGURE 9. The variances of the variables $x(t)$ and $y(t)$.

The variances of $x(t)$ and $y(t)$ seem to reach their maximum value somewhere around the midpoint of the simulated interval and decrease after this stage. This means that the variables show different behavior than their mean values, i.e. the values used for the deterministic case, in the middle of the process. The variance of the substrate has its maximum value 0.001189 at $t = 5.6$ and its minimum value 0 at $t = 0$, while the complex has its maximum value 0.0005197 at $t = 8.4$ and its minimum value 0 at $t = 0$.

4.2.4. *Standard Deviations.* The standard deviations $std(x(t))$ and $std(y(t))$ are given in Figure 10.

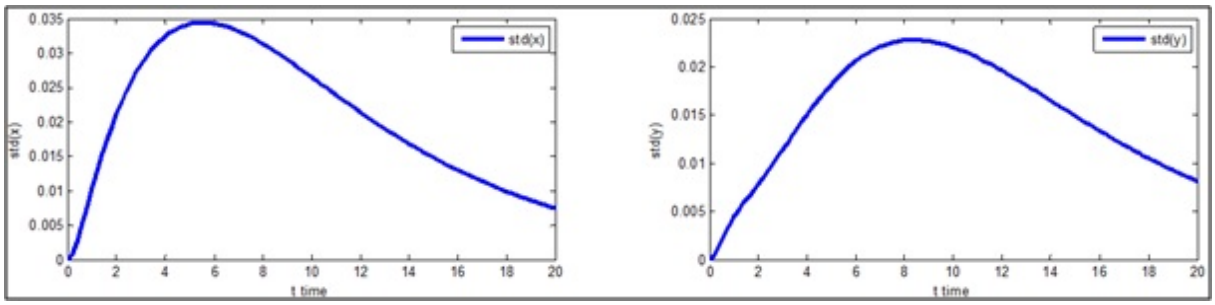

FIGURE 10. The standard deviations of $x(t)$ and $y(t)$.

The changes of the standard deviations of the variables are in compliance with changes of the variables, as expected. The standard deviation of $x(t)$ has its maximum value 0.03448 at $t = 5.6$ and its minimum value 0 at $t = 0$, while the standard deviation of $y(t)$ has its maximum value 0.0228 at $t = 8.4$ and its minimum value 0 at $t = 0$. These results show that there is at most (approximately) 3.5% difference between the random case and the deterministic case.

4.2.5. *Confidence Intervals.* The confidence intervals for mean values $[E(x(t)) - K\sigma(x(t)), E(x(t)) + K\sigma(x(t))]$ and $[E(y(t)) - K\sigma(y(t)), E(y(t)) + K\sigma(y(t))]$ are given in Figure 11.

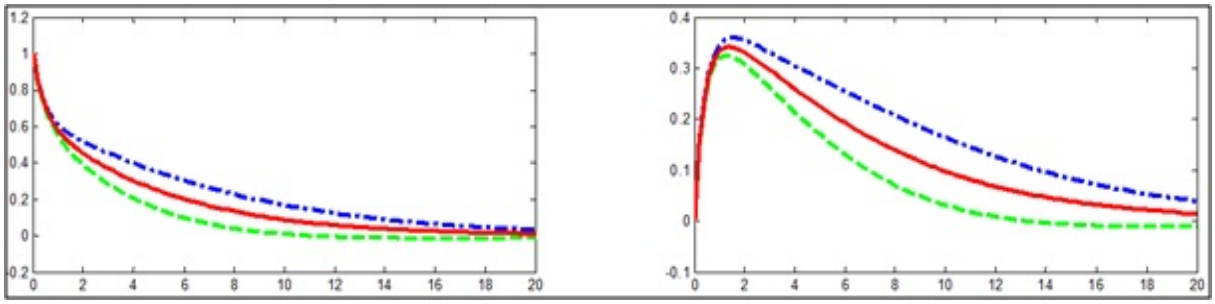

FIGURE 11. The confidence intervals of $x(t)$ and $y(t)$.

The standard deviations found above for the beta distributed random effects create the 99.7% (approximately) confidence intervals for the mean values of the variables. The dash-dotted line represents the upper limit of the confidence interval while the dashed line represents the lower limit of the interval. The possible variations in the second variable represent how different the random case can occur in the real life reaction procedure. The confidence interval for $x(t)$ has a maximum value of 1 at $t = 0$ and a minimum value of -0.01159 at $t = 16.4$, while the confidence interval for $y(t)$ has a maximum value of 0.3598 at $t = 1.6$ and a minimum value of -0.009465 at $t = 18.8$.

4.3. **Review of the Results.** In this part, reviews on the chemical process and the effects of normal and beta distributions on the random behavior are given.

4.3.1. *Reviewing the Reaction.* Considering the assumptions we used for the nondimensionalization of the 4-equation system to a 2-equation system, we can find the results for all of the 4 components (substrate, enzyme, enzyme-substrate complex, product) using the results of the simulations above [12]. We switch from the set of variables x, y which denote the concentrations of the substrate and enzyme-substrate complex, respectively, to the set of E, A, Y, X describing the amounts of the enzyme, substrate, enzyme-substrate complex and product, respectively to deduce a more clear conclusion from the results. In particular, the concentrations of the 4 components satisfy

$$E^* + Y^* = 1,\ A^* + X^* + \epsilon Y^* = 1$$

where the starred variables are the concentrations of the variables of the model (2.1). The value of ϵ was taken as 1 for the calculations. Considering these, the following conclusions can be made for the model from the simulations: (i) Both the enzyme and enzyme substrate complex have entered the reaction and are consumed at the end of the procedure ($E(x(t)) \cong 0.00125$, $E(y(t)) \cong 0.01483$ at $t = 20$) (ii) Since the enzyme is not consumed in the chemical reaction and $A^* + X^* + \epsilon Y^* = 1$,

$$E(A^* + X^* + \epsilon Y^* = 1) \rightarrow E(X^*) = 1 - E(A^*) - E(Y^*).$$

Considering $x(t)$ and $y(t)$ stood for A^* and Y^*, at $t = 20$, $E(X^*) \cong 1 - 0.00125 - 0.01483$. Thus

$$E(X^*) \cong 0.98392.$$

This means that at the end of the simulated interval, the product concentration is very close to 1, as expected since the substrate and the intermediate complex concentrations are very close to 0. Thus, it can be said that the reaction takes place in a natural way under both beta distributed and normally distributed random effect.

4.3.2. *Reviewing the Distributions.* If the graphs of the results for both distributions are examined, it can be seen that the model components show similar behavior under both normally distributed and beta distributed random effects. The only difference that can be spotted between these two sets of results is the difference in the variances in these two cases. The variances in the results of the beta distribution seem to be larger than the variance in the normally distributed case. The reason behind this difference lies in the nature of the distributions used for the random effects. The parameters used for the random effects with normal distribution were:

$$\alpha \in \left(0.375, \left(\frac{1}{24}\right)^2\right), \beta \in \left(0.375, \left(\frac{1}{30}\right)^2\right).$$

Similarly, the parameters for the beta distributions used for the random effects were:

$$\alpha \in Beta(0.25, 0.25; 3, 3), \beta \in Beta(0.9, 0.2; 3, 3).$$

The variance of a $N(\mu, \sigma^2)$ distributed random variable is σ^2. Hence, the variances for α and β (with normal distribution) would be approximately $(1/24)^2 = 0.001736$ and $(1/30)^2 = 0.001111$, respectively. On the other hand, the variance of a general beta distributed ($Beta(c, d, a, b)$) random variable (with location parameter c and scale parameter d) would be $d^2 \frac{ab}{((a+b)^2(a+b+1))}$. Hence the variances for α and β (with beta distribution) would be approximately $\left(\frac{1}{4}\right)^2 \frac{3,3}{(6)^2(7)} = 0.002232$ and $\left(\frac{1}{5}\right)^2 \frac{3,3}{(6)^2(7)} = 0.001428$, respectively. It can be seen for the chosen parameters, the Beta distribution has a larger variance than the normal distribution, which is the reason behind the difference of the variances of the results. Note that these results are found only for the distributions with the chosen parameters and the use of other parameters could result in a different situation.

4.3.3. *Reviewing the Results.* The results in [16] prove that the random behavior of the model is similar to the estimations from the deterministic analysis, with minor numerical differences. If the concentration of the enzyme-substrate intermediate complex is examined as an example, it can be seen that the referred study gives the deterministic result for $y(t)$ at $t = 20$ as 0.01317264, while the expectation of this value is around 0.01483 in the random case. The nature of the distribution used for the random effects in constructing a random model affects the amount of this difference between the deterministic and random results.

5. Conlusion

The parameters of the deterministic Biochemical Reaction Model (BRM) were added random effects with both normal and beta distributions. The results show that the random reaction proceeds in accordance to the deterministic case. While the behaviors of the random components are very similar to their deterministic counterparts, there are some small numerical differences in the random results, which are as expected. Small differences in the variances of the cases with normally distributed random effects and beta distributed random effects were also spotted, which was a consequence of the differences in the variances of the distributions used. Further analysis can be made on the model by studying the stability conditions of the model or sensitivity of the parameters of the model. Various other probability distributions could be used with different parameters to analyze the effects of these distributions on the result. A stochastic model could also be formed for BRM by adding stochastic noise terms to the equations. Analysis of various models from both deterministic and stochastic cases could give useful insights on the stochasticity of the event. All of the mentioned additional studies could be done to reaction models or other mathematical models on arbitrary events or systems. Such additional analysis could provide a better understanding of the reaction dynamics.

6. Acknowledgements

This work was supported by Research Fund of the Karadeniz Technical University. Project Number: FBA-2016-5394.

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