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# STOCHASTIC MODELLING OF TIME LAG FOR SOLVENT PRODUCTION BY *C. ACETOBUTYLICUM* P262 (PEMODELAN STOKASTIK DENGAN MASALENGAHAN BAGI PENGHASILAN PELARUT OLEH *C. ACETOBUTYLICUM* P262)

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**Abstract :**This work is carried out to model jointly time delay and unknown disturbances of gelatinised sago starch to solvent production by C. *acetobutylicum* P262. The proposed model of C. *acetobutylicum* P262 proliferation is formulated as stochastic delay logistic model. Moreover, Luedeking-Piret equations were used to model the solvent production of acetone and butanol by C. *acetobutylicum* P262, whose number of living cell, $x(t)$ is subjected to time delay and beyond deterministic behaviour. The strong solution of the resulting models was simulated numerically via numerical method of Euler-Maruyama (EM). Their respective root mean square errors (RMSE) were calculated by comparing the simulated and experimental data so that the prediction quality of the model can be assessed.

**Abstrak** :Penyelidikan ini dijalankan bagi memodelkan lengahan masa dan hingar rawak yang terdapat dalam proses penghasilan pelarut oleh C. *acetobutylicum* P262. Model yang dicadangkan bagi mengkaji kadar pertumbuhan sel C. *acetobutylicum* P262 adalah stokastik logistic model yang melibatkan masa lengahan. Persamaan Luedeking-Piret digunakan untuk memodelkan pembentukan pelarut acetondanbutanol oleh C. *acetobutylicum* P262. Kepekatan sel hidup, $x(t)$ tertakluk kepada masa lengahan dan bukan lagi tertentu. Penyelesaian hampiran bagi model tersebut dihitung menggunakan kaedah berangka Euler-Maruyama (EM). Ralat min punca kuasadua dihitung bagi menentukan kepersisan model yang dibentuk.

**Keywords:**Stochastic delay differential equations (SDDEs), Delay Differential Equations (DDEs), Stochastic Ordinary Differential Equations (SODEs), Euler-Maruyama (EM).

## 1. Introduction

Modelling of physical phenomena and biological system using ordinary differential equations (ODEs) and stochastic ordinary differential equations (SODEs) has become an intensive research over last few years. In both types of equations the unknown function and its derivatives are evaluated at the same instant time, *t*. However, it was generally acknowledge that many of the natural phenomena around us do not have an immediate effect from the moment of their occurrence. For instance, the growth of the microbe is not instantaneous but responds only after some time lag, $\tau > 0$. In such cases, ODEs and SODEs which are simply depending on the present state are inadequate to describe the process that involves time delay. The modelling of such phenomena, leading to what is called delay differential equations (DDEs) and stochastic delay differential equations (SDDEs). Indeed, DDEs are unsatisfactory to model the process with the presence of random effects. Definitely the dynamical systems whose evolution in time is governed by uncontrolled fluctuationsas well as the unknown function is depending on its past history can often be modelled via SDDEs.

Our main concern in this paper is to model jointly time delay and unknown disturbances of gelatinised sago starch to solvent production by C.*acetobutylicum*P262 of batch process. In typical batch fermentation, there are two important features that control the mechanism of the process namely time delays and the system is continually subjected to the effects of random or uncontrolled fluctuations which are referred as noise. The presence of time delay is a consequence of the simple fact that initially, microbial are in the process of adapting themselves to the new environment, thus no growth occur. They are in the situation to synthesis the new enzymes in response to change in the availability of substitutable substrates [2]. The microbe in this position is said to be in a lag phase. At the end of the lag phase, the population of microorganisms is well-adjusted to the new environment, cells multiply rapidly and cell mass doubles regularly with time. Microbe subsequently enters a period called an exponential phase. As time evolves, the system is subjected to an intrinsic variability of the competing within species and deviations from exponential growth arise. It happens as a result of the nutrient level and toxinconcentration achieves a value which unable to sustain the maximum growth rate. This phase is recognized as a stationary phase. By taking into account all the phases involve in batch fermentation, modellers should aware that mathematical models for the dynamic of this process take the form of SDDEs. In many problems, analytical solution for SDDEs is not available and numerical methods provide a suitable way to approximate their solutions. In the present article,the strong solution of the proposed model is approximated via EM method. It was [4] who proposed a numerical method of EM for SDDE. This method has order of convergence of 0.5, yet it is the simplest to be implemented in C.

This paper is organized as follows; Section 2.0 reviewed the latest mathematical model of ODEs, DDEs and SODEs used to describe the cell growth and solvent production of batch fermentation. Then, we incorporate a slow microbial adaptation and unknown disturbances of the system via SDDE model. A description of numerical methods and numerical algorithm for SDDEs is carried out in Section 3.0. We present the values of kinetic parameter model in Section 4.0 and the results of solvent production by C. *acetobutylicum*P262 are demonstrated. Lastly, the root mean square error (RMSE) is computed in order to assess the validity of the stochastic model with time lag.

## 2. Reviews on Mathematical Modelling of Cell Growth & Solvent Production

The classical logistic ODE used to describe the cell growth of C. *acetobutylicum* P262 is given below

$$\frac{dx(t)}{dt} = \mu_{\max}\left[1-\frac{x(t)}{x_{\max}}\right]x(t), \quad t\in[-\tau,T] \tag{1}$$

The constant $x_{\max}$ denotes the maximum cell concentration (*g/L*), $\mu_{\max}$ correspond to maximum specific growth rate ($h^{-1}$) and $T$ is the terminal point of time $(h)$. In natural environment $x_{\max}$ is limiting population determined by carrying capacity of the environment. This model has been used by [18] to model the cell growth of C. *acetobutylicum* in batch system. The production of acetone and butanol were formulated as Luedeking-Piret equation of

Acetone: $$\frac{dA}{dt} = a\left(\frac{dx}{dt}\right) + b\,x \tag{2}$$

Butanol: $$\frac{dB}{dt} = c\left(\frac{dx}{dt}\right) + e\,x \tag{3}$$

where

$x$ = concentration of cell mass (g/L),
$A$ = acetone concentration (g/L)
$a$ = growth associated coefficient for acetone formation (g substrate/g cell)
$b$ = non-growth associated coefficient for acetone formation (g substrate/g cell)
$B$ = butanol concentration (g/L)

$c$ = growth associated coefficient for butanol formation (g substrate/g cell)
$e$ = non-growth associated coefficient for butanol formation (g substrate/g cell)

The differential equations (1), (2) and (3) had been used to model the solvent production by C. *acetobutylicum* in [9]. As aforementioned in [9], the production of acetone and butanol was non-growth associated system. Therefore, the values of growth associated coefficient for product formation was zero. The exact solution of (1) and Luedeking-Piret equations of (2) and (3) can be written in the following form

Cell growth: $$x(t) = \frac{x_{\max} \exp(\mu_{\max} t)}{\left(\frac{x_{\max}}{x_0}\right) - 1 + \exp(\mu_{\max} t)} \tag{4}$$

Product formation

Acetone: $$A(t) = A(t_0) + b\int_{t_0}^{t} x(s)ds \tag{5}$$

Butanol: $$B(t) = B(t_0) + e\int_{t_0}^{t} x(s)ds \tag{6}$$

where $x_0 = x(t_0)$, $A(t_0)$ and $B(t_0)$ represent the initial cell, acetone and butanol concentration respectively. It is reasonable to model the cell growth via DDEs by assumption that initially cells are inactive and once it is activated the cell division is not instantaneous [3]. Early attempt to model the population growth using logistic DDE has been made in [6]. He proposed a classical delay logistic model by assuming biological self-regulatory reaction represented by the factor $1 - \frac{x(t)}{x_{\max}}$ in (1) is not instantaneous but responds only after some time lag, $\tau > 0$. The original motivation of [6] by introducing time delay in classical logistic ODE is to model the oscillations observed in *Daphnia* populations, on the ground that fertility of the pathogenetic female influenced by the density of past population. An obvious distinction between DDEs and ODEs is in specifying the initial value, $x(t_0)$. For DDE, it is not enough to determine the solution for $t \geq 0$ by having $x(t_0)$ alone. We need to have initial function, to specify the history of $x(t)$ for $t \in [-\tau, 0]$. Thus, the corresponding classical logistic DDE of (1) is

$$\begin{aligned} x'(t) &= \mu_{\max}\left[1 - \frac{x(t-\tau)}{x_{\max}}\right]x(t), \quad t \in [-\tau, T] \\ x(t) &= \Phi(t), \ t \in [-\tau, 0] \end{aligned} \tag{7}$$

The time delay $\tau$ models the length of the time period between the initial time and maturing time wherein the division of the cell begins. The presence of internal and external noise in batch system ultimately linked with the theory of SODEs. The deterministic model of (1) and (7) do not accommodate random variations of metabolism. An alternative stochastic model would result from the hypothesis that the process itself is not smooth. The cell growth of C. *acetobutylicum* P262 is subjected to a variety of internal and external influences, which change over time. Therefore, it is necessary to add suitable system variability to the deterministic model (1). In [1] the parameter $\frac{\mu_{\max}}{x_{\max}}$ is allowed to vary randomly by introducing a white noise perturbation that is

$$b \to b + \sigma \frac{dW(t)}{dt}, \tag{8}$$

where $b = \frac{-\mu_{\max}}{x_{\max}}$, $\sigma$ is a diffusion coefficient and $W(t)$ is a one dimensional stochastic process having scalar Wiener process components that is the increment $\Delta W(t) = W(t+\Delta t) - W(t)$ are independent Gaussian random variables with mean zero and variance the increment of the time, $\Delta t$. Model (1) with perturbation (8) is an Itô SODE of the following

$$dx(t) = \mu_{\max}\left(1 - \frac{x(t)}{x_{\max}}\right)x(t)dt + \sigma x^2(t)dW(t), \tag{9}$$

or more accurately as an integral equation

$$x(t) = x_0 + \int_0^T \mu_{\max}\left(1 - \frac{x(s)}{x_{\max}}\right)x(s)ds + \int_0^T \sigma x^2(s)dW(s). \tag{10}$$

The second integral in (6) is stochastic integral with respect to a Wiener process, $W(t)$. The Wiener process is nowhere differentiable and its continuous sample path are not bounded variation. So, it cannot be interpreted as Riemann-Stieltjes integral. The stochastic integrals can be interpreting either as Itô or Stratonovich integral depending on the evaluation points of the integrand. Model (9) is formulated in [13] to model cell proliferation of the microbe in batch fermentation. The strong solution of SODE (9) was approximated using EM. Model (9) can be transformed into Stratonovich form and vice-versa by means of the following formula

$$\bar{f}(t, x_t) = f(t, x_t) - \frac{1}{2} g(t, x_t) \frac{\delta g}{\delta x}(t, x_t). \tag{11}$$

where $f(t, x_t)$ is drift coefficient and $g(t, x_t)$ is known as diffusion coefficient. By employing (11) to drift coefficient in (9) we obtain the stochastic model in Stratonovich form of

$$dx(t) = \left(\mu_{\max}\left(1 - \frac{x(t)}{x_{\max}}\right)x(t) - \sigma^2 x^3(t)\right)dt + \sigma x^2(t) \circ dW(t), \tag{12}$$

or in the integral form

$$x(t) = x_0 + \int_0^T \left(\mu_{\max}\left(1 - \frac{x(s)}{x_{\max}}\right)x(s) - \sigma^2 x^3(s)\right)ds + \int_0^T \sigma x^2(s) \circ dW(s). \tag{13}$$

The symbol $\circ$ is used to indicate the Stratonovich SODE (i.e. $\circ dW(t)$). SODE (12) has been formulated in [17] to model the cell growth in batch culture and the strong solution of SODE is simulated via SRK2. In the acetone-butanol biosynthesis process by C. *acetobutylicum* P262, a more sophisticated insight into physical phenomena may be achieved if we consider problems with both time-lag and assume that the observed biological system operate in noisy environment. In such a case, it is practical to model the cell division in batch culture via SDDE. Therefore, the model we derive in the present article is in the form of (13) with random perturbation to $\frac{\mu_{\max}}{x_{\max}}$. It means that, the mathematical model of SDDE is formulated to describe the cell growth of C. *acetobutylicum*P262. SDDE can be approached either as SODE with added delay or DDE with noise [14]. The second approach shall be considered here. We assume that our model is in autonomous form. Therefore, a general formulation of autonomous SDDE is

$$\begin{aligned} dx(t) &= f(x(t), x(t-\tau))dt + g(x(t), x(t-\tau)) \circ dW(t), \qquad t \in [-\tau, T] \\ x(t) &= \Phi(t), \quad t \in [-\tau, t_0], \ \tau > 0 \end{aligned} \tag{14}$$

or in integral form it can formulated rigorously as

$$x(t) = \int_{t_0}^{t} f(x(s), x(s-\tau))ds + \int_{t_0}^{t} g\big(x(s), x(s-\tau)\big) \circ dW(s), \qquad t \in [-\tau, T]$$
$$x(t) = \Phi(t), \quad t \in [-\tau, t_0], \ \tau > 0 \tag{15}$$

where $f : R \times R \to R$ and $g : R \times R \to R$. The functions $f$ and $g$ need to satisfy the local Lipchitz condition and linear growth condition in order to ensure the existence and uniqueness solution [11]. In applied problems the initial function, $\Phi(t)$ for $-\tau \le t \le 0$ is found experimentally and also may be

determined from another equation without deviating argument. For our purpose $\Phi(t)$ is determined experimentally. Let we have the delay logistic equation of (13) in the form of

$$x'(t) = \frac{\mu_{\max}}{x_{\max}}\big[x_{\max} - x(t-\tau)\big]x(t), \quad t \in [-\tau, T] \tag{16}$$

Then, perturbation through parameter $\frac{\mu_{\max}}{x_{\max}} \to \frac{\mu_{\max}}{x_{\max}} + \sigma \frac{dW(t)}{dt}$, leading to the following differential equation

$$dx(t) = \mu_{\max}\left(1 - \frac{x(t-\tau)}{x_{\max}}\right)x(t)dt + \sigma\, x(t)x(t-\tau)dW(t). \tag{17}$$

Thus, a simplified batch fermentation kinetic model for cell growth of C. *acetobutylicum*P262 is in the form of (17). The mathematical model of solvent production in terms of $x(t)$ are given as below

$$\text{Acetone } \frac{dA}{dt} = b\, x(t) \tag{18}$$

$$\text{Butanol } \frac{dB}{dt} = d\, x(t) \tag{19}$$

where $x(t)$ is subjected to time delay and no longer deterministic. Kinetic parameter model of $\mu_{\max}, b, d$ and $\sigma$ need to be estimated.

## 3. Euler-Maruyama Scheme and Numerical Coding

We have considered strong Euler-Maruyama approximations with a fixed step size, *h* on the interval $[0, T]$, for $h = \frac{T}{N}$, $t_n = (n-1)\cdot h$, $n = 1, \ldots, N$. We assumed that, there is an integer number $N_\tau$ such that the delay can be expressed in terms of the step size $\tau = N_\tau \cdot h$. For SDDE (14), the Euler-Maruyama scheme has the following form

$$x(t_{n+1}) = x(t_n) + hb(x(t_n), x(t_n - \tau)) + g(x(t_n), x(t_n - \tau))(\Delta W_n) \tag{20}$$

with $\Delta W_n = W(t_{n+1}) - W(t_n)$, denoting independent $N(0,h)-$ distributed Gaussian random variables. The Euler discretization for the process given in (17) looks like

$$x(t_{n+1}) - x(t_n) = \mu_{\max}\left(1 - \frac{x_{n-N_\tau}}{x_{\max}}\right)x(t_n)\cdot h + \sigma\, x_n x_{n-N_\tau} \cdot (\Delta W_n) \tag{21}$$

We generate a code to simulate the solution of discretization process (15) using the language of C. The resulting algorithm is presented below;

1) Define the fixed step size, $h = \frac{T}{N}$, $t_n = (n-1)\cdot h,\ n = 1,\ldots,N$
2) Define an integer number $N_\tau$ such that the delay can be expressed in terms of the step size $\tau = N_\tau \cdot h$.
3) Define the step, such as the end of the step is $\frac{T}{\tau}$.
4) Do initial function evaluation $\Phi([step][n-1])$ at the initial interval $t \in [-\tau, 0]$. It is needed for the first EM step. Print the solution $x(t) = \Phi([step][n-1])$ for $t \in [-\tau, 0]$.
5) Do drift function evaluation. If $step = 1$ , the drift function is $f(y[step][n-1], \Phi[step][n-1])$ else the drift function is computed as $f(y[step][n-1], y[step][(n-1)-N_\tau])$.
6) Do diffusion function evaluation, $g(y[step][n-1])$.
7) Perform a random number generator, $randn$.
8) If $step = 1$ and for $n = 1; n <= N_\tau; n++$ , perform an explicit EM step,
$$y[step][n] = \Phi[step][n-1] + h\, f(y[step][n-1], \Phi[step][n-1]) + \sqrt{h} * randn * g(y[step][n-1])$$
9) If $step = 2,3,\ldots$ and for $n = 1; n <= N_\tau; n++$ , perform an explicit EM step,
$$y[step][n] = y[step][(n-1)-N_\tau] + h\, f(y[step][n-1], y[step][(n-1)-N_\tau]) + \sqrt{h} * randn * g(y[step][n-1])$$
10) Print the solution, $y[step][n]$.

In $step = 1$, the history of $x(t) = \Phi(t)$ for $t \in [-\tau, 0]$ is used to compute the strong solution of $x(t)$ for $t \in [0, \tau]$. Meanwhile, the numerical solution in $\text{step} = 2,3,\ldots$ is computed iteratively using method of steps. Once the numerical solution of $x(t)$ for $t \in [0, \tau]$ is known, we can proceed this argument to simulate the strong solution of $x(t)$ for $t \in [\tau, 2\tau], [2\tau, 3\tau]$ and so on.

## 4. Results and Discussion

Three sets data of cell growth of *C. acetobutylicum* P262 were observed in [9] at $t \in [0, 288]$, where *t* is a time measured in hour. The experiment was carried out to investigate the effect of different inorganic nitrogen source to yeast extract, YE. YE1, YE2 and YE3 represent the control medium (no inorganic source), medium with Ammonium Chloride ($NH_4CL$) and medium with Ammonium Nitrate ($NH_4NO_3$) respectively. For ODE (1) the kinetic parameter of $\mu_{\max}, b$ and $d$ were estimated using Levenberg Marquardt algorithm [9], while for SDE (12) the values of $\mu_{\max}$ and $\sigma$ were estimated using Levenberg Marquardt algorithm in [6] respectively, whereas *b* and *d* were approximated using Simplex method in [17]. The estimation parameters in SDDEs are very infancy.

The method up to date only considered the SDDEs where their respective diffusion coefficient is in unitary form, means that in the form of additive noise. In the present article, due to the small value of time lag, $\tau$ , the estimated values of $\mu_{\max}$ and $\sigma$ in SDDE (27) is based on SDE (12). The kinetic parameter models *b* and *d* for Luedeking-Piret equation (18) and (19) were estimated using Simplex method. The initial values of $x(t_0), A(t_0), B(t_0)$ and the maximum cell concentration, $x_{\max}$ were observed from the experimental data [9]. The initial values of $x(t_0), A(t_0), B(t_0)$ are given in Table 1.

**Table 1**. Initial values of $x(t_0)$, $A(t_0)$, $B(t_0)$ for YE1, YE2 and YE3

| **Initial values** | **YE1** | **YE2** | **YE3** |
|---|---|---|---|
| $x(t_0)\ (g/L)$ | 0.0031 | 0.002 | 0.0025 |
| $A(t_0)$(g substrate / g cell) | 0.068 | 0.02096 | 0.02799 |
| $B(t_0)$ (g substrate / g cell) | 0 | 0 | 0 |

The estimated values of kinetic parameter for YE1, YE2 and YE3 are presented below.

**Table 2**.Estimated Parameters for Equations (1), (12) and (17)

| **Model** | **Experimental Data** | **Parameter Estimation** | | | | |
|---|---|---|---|---|---|---|
| | | $\hat{\mu}_{\max}\ (h^{-1})$ | $\hat{x}_{\max}\ (g/L)$ | $\hat{\sigma}$ | $\hat{a}$ | $\hat{b}$ |
| ODE (1) | YE1 | 0.4 | 3.525 | - | 0.025 | 0.082 |
| | YE2 | 0.7 | 0.9490 | - | 0.025 | 0.082 |
| | YE3 | 0.55 | 4.295 | - | 0.025 | 0.082 |
| SDE (12) | YE1 | 0.4848 | 3.525 | 0.0028 | 0.2596 | 0.1076 |
| | YE2 | 0.5056 | 0.9490 | 0.0127 | 0.0072 | 0.0414 |
| | YE3 | 0.6354 | 4.295 | 0.0052 | 0.2431 | 0.0835 |
| SDDE (17) | YE1 | 0.4848 | 3.525 | 0.0028 | 0.2529 | 0.1046 |
| | YE2 | 0.5056 | 0.9490 | 0.0127 | 0.0077 | 0.0430 |
| | YE3 | 0.6354 | 4.295 | 0.0052 | 0.2613 | 0.0872 |

The results of SDE (12) and SDDE (17) together with their experimental data for YE1, YE2 and YE3 were presented in Figure 1a), Figure 1b) and Figure 1c) respectively.

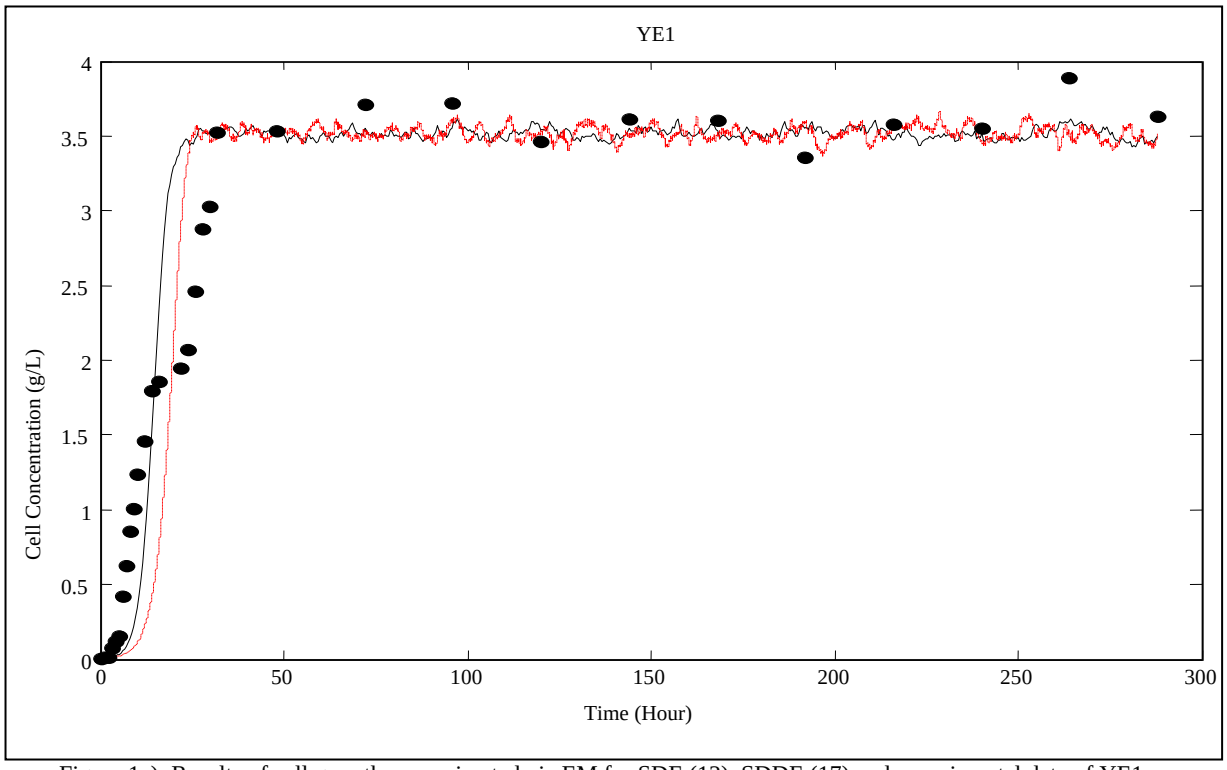


Figure 1a): Results of cell growth approximated via EM for SDE (12), SDDE (17) and experimental data of YE1.

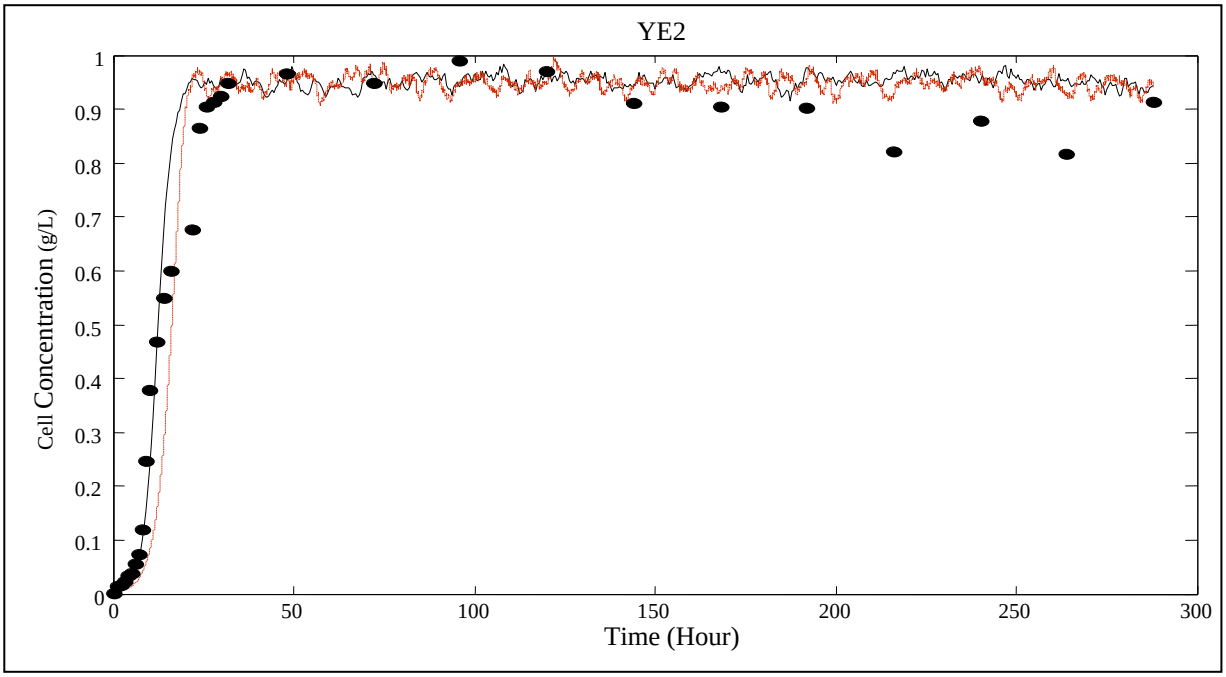


Figure 1b): Results of cell growth approximated via EM for SDE (12), SDDE (17) and experimental data of YE2.

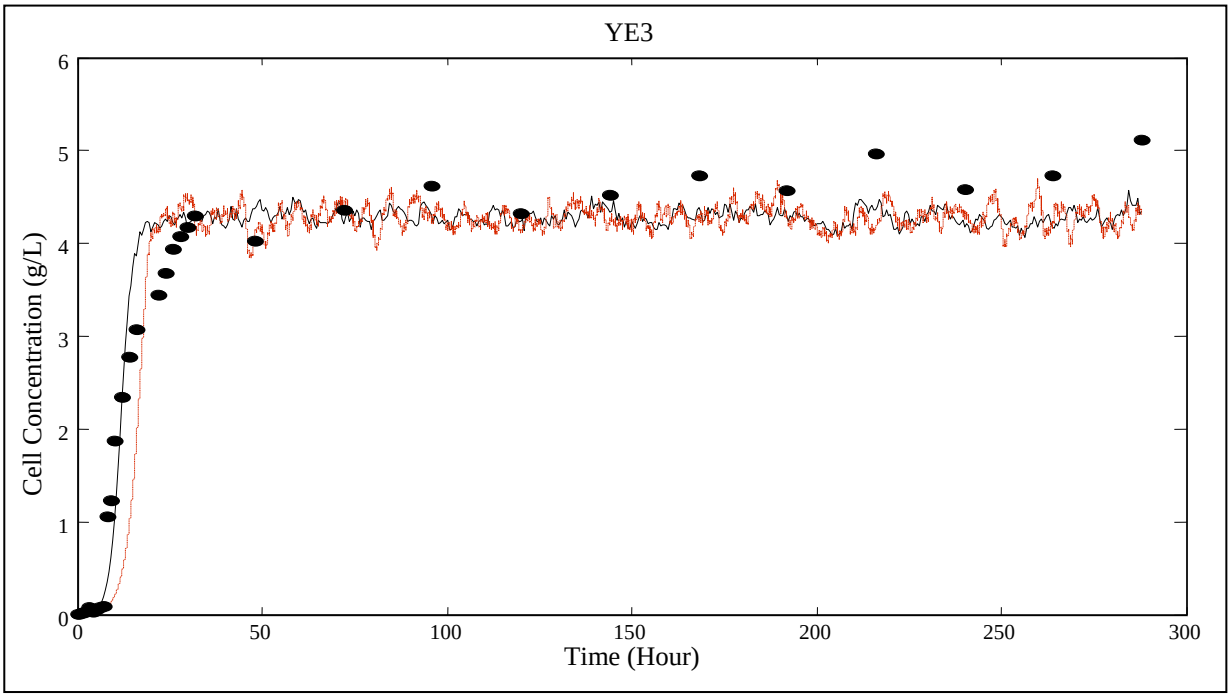


Figure 1c): Results of cell growth approximated via EM for SDE (12), SDDE (17) and experimental data of YE3.

| | |
|---|---|
| – – | Stochastic model (SDE) |
| ——— | Stochastic model with after-effect (SDDE) |
| ● | Experimental data |

From the results obtained in Figure 1a)-1c), we can summarize that stochastic model with after-effect (SDDE) described the experimental data more adequate compare to stochastic model (SDE). Please found the root mean square error (RMSE) in Table 3, which showed the low value when the model

based on SDDE were employed. The results of Luedeking-Piret equation for Acetone concentration whose $x(t)$ was described by ODE (1), SDE (12) and SDDE (17) together with their experimental data for YE1, YE2 and YE3 were presented in Figure 2a), Figure 2b) and Figure 2c) respectively.

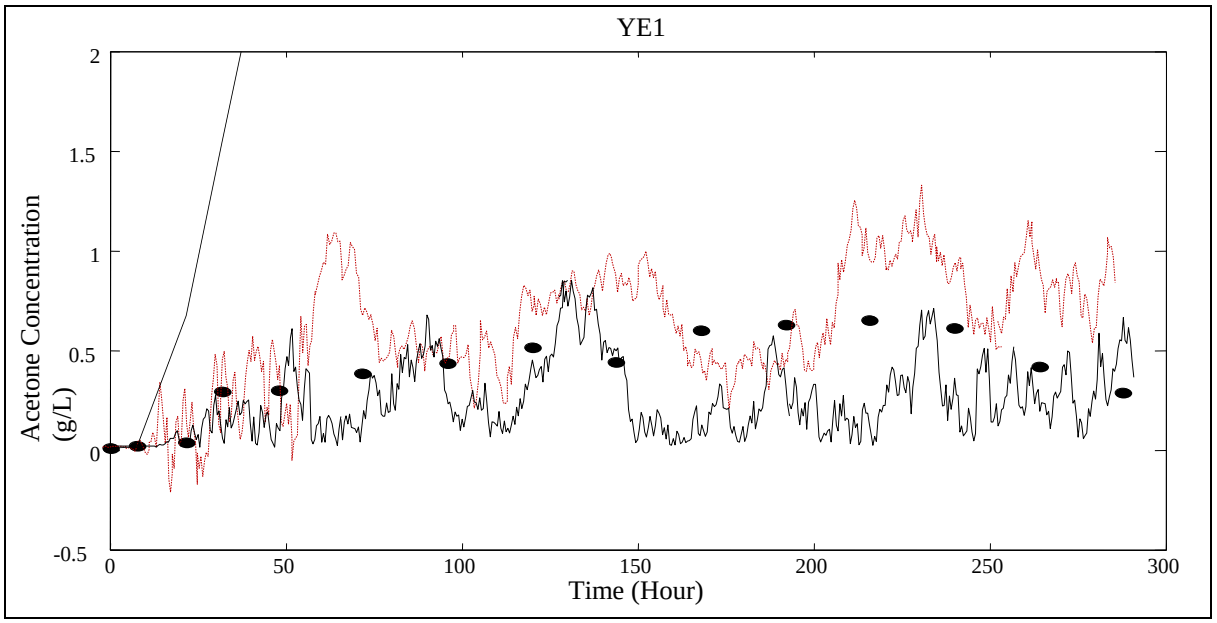


Figure 2a): Results of acetone concentration using deterministic model, stochastic model, stochastic model with after-effect and experimental data for YE1.

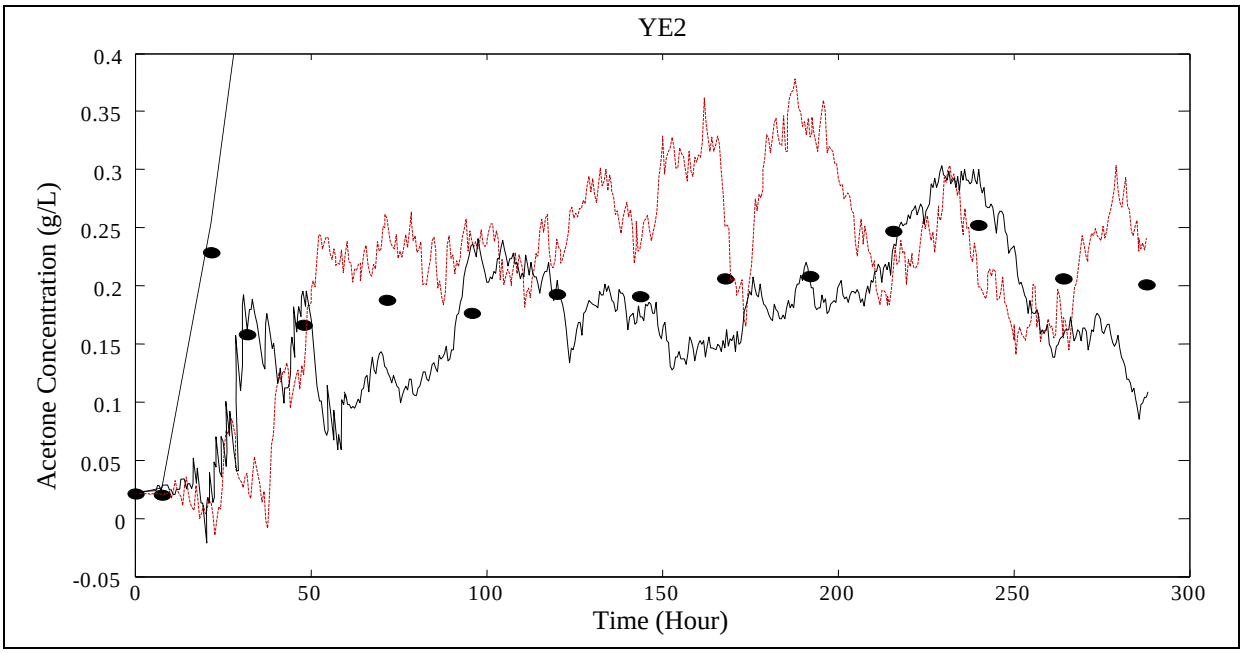


Figure 2b): Results of acetone concentration using deterministic model, stochastic model, stochastic model with after-effect and experimental data for YE2.

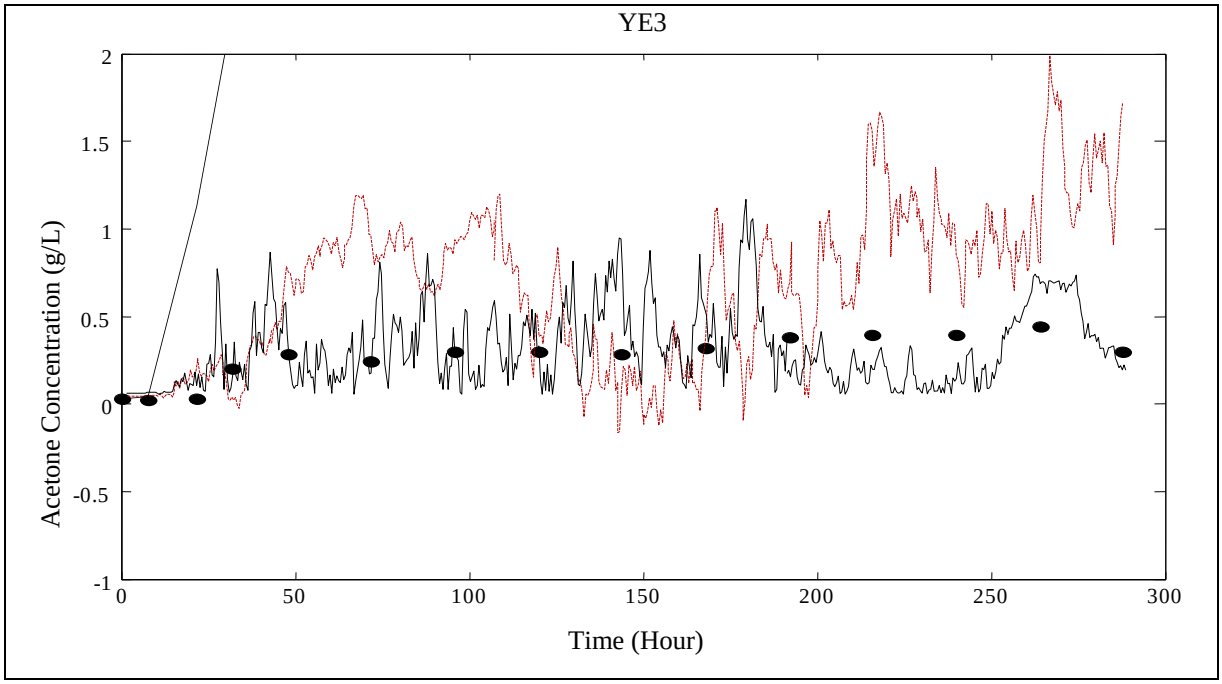


Figure 2c): Results of acetone concentration using deterministic model, stochastic model, stochastic model with after-effect and experimental data for YE3.

Meanwhile, the results of Luedeking-Piret equation for Butanol concentration whose $x(t)$ was described by ODE (1), SDE (12) and SDDE (17) together with their experimental data for YE1, YE2 and YE3 were demonstrated in Figure 3a), Figure 3b) and Figure 3c) respectively.

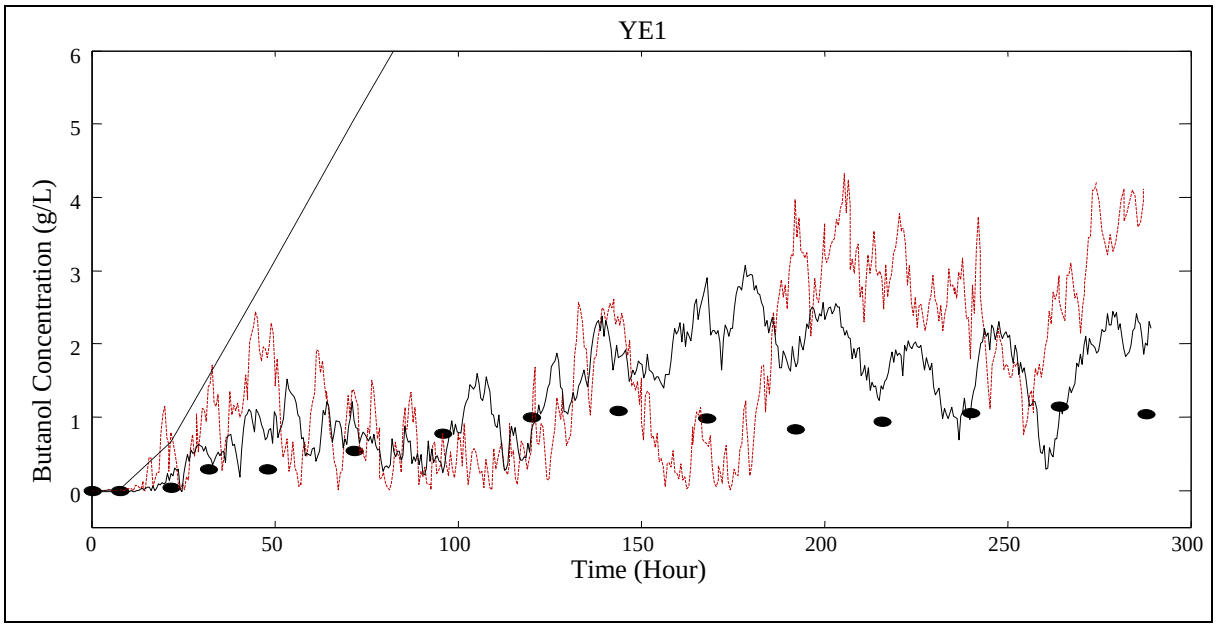


Figure 3a: Results of butanol concentration using deterministic model, stochastic model, stochastic model with after-effect and experimental data for YE1.

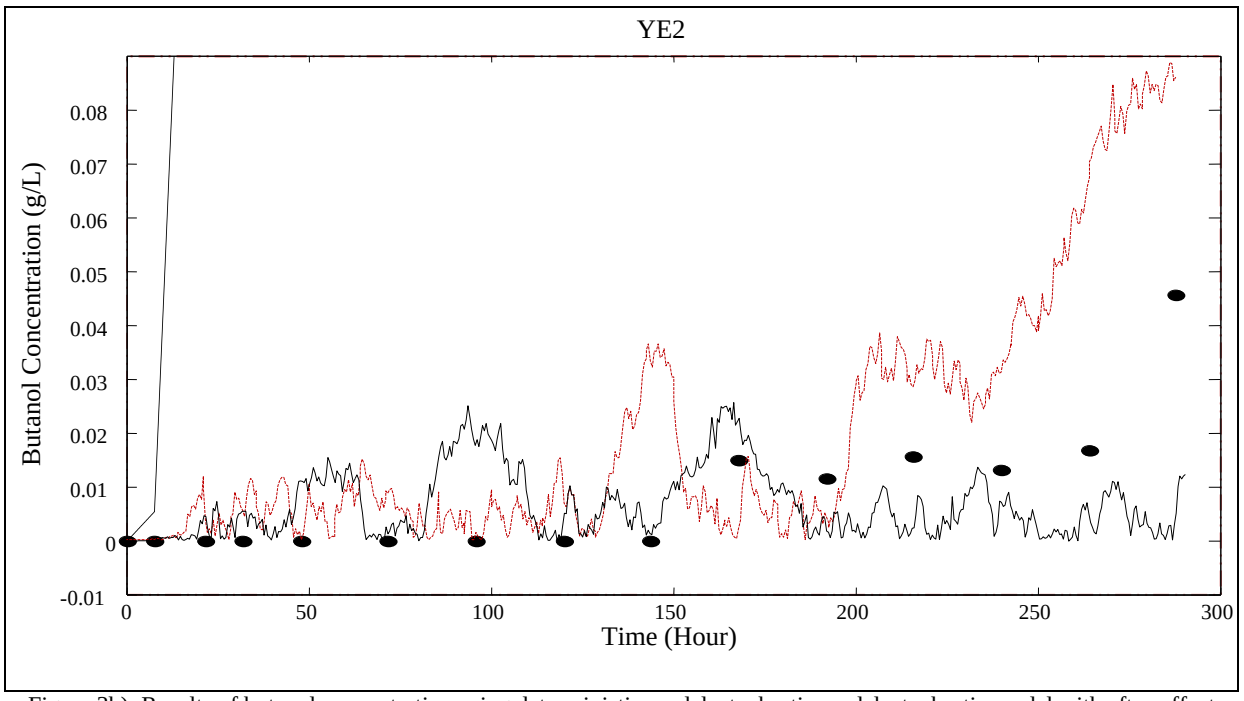


Figure 3b): Results of butanol concentration using deterministic model, stochastic model, stochastic model with after-effect and experimental data for YE2.

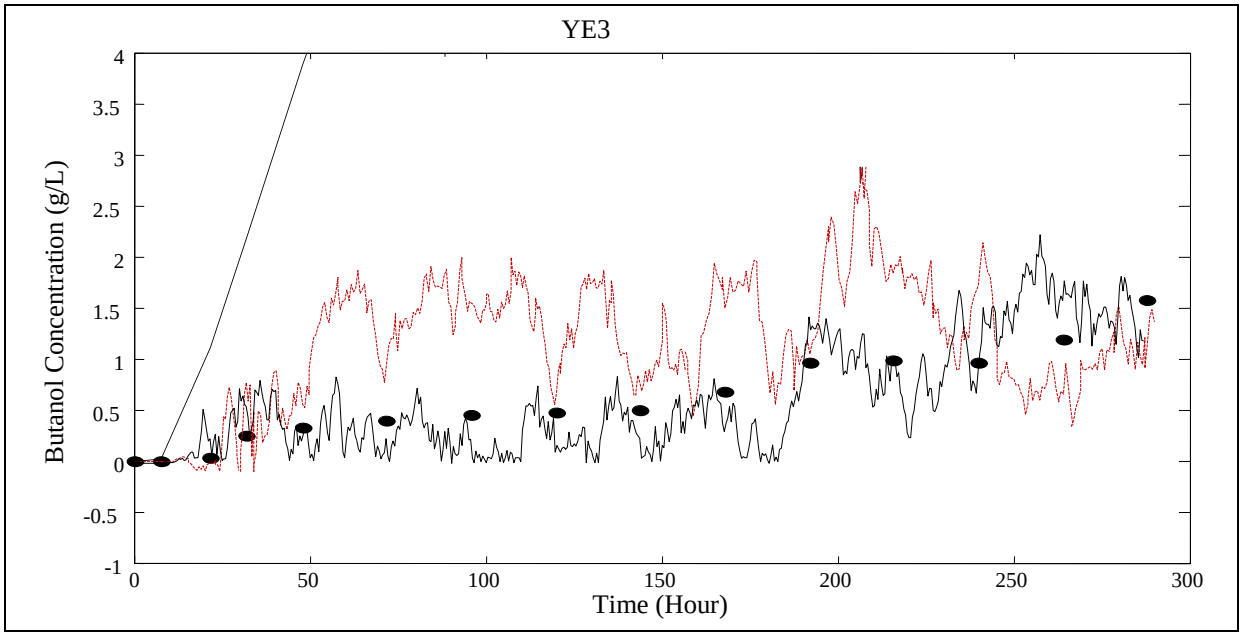


Figure 3c): Results of butanol concentration using deterministic model, stochastic model, stochastic model with after-effect and experimental data for YE3.

| | |
|---|---|
| ..... | Deterministic model (ODE) |
| – – | Stochastic model (SDE) |
| —— | Stochastic model with after-effect (SDDE) |
| ● | Experimental data |

From the illustration given in Figure 2a)-2c), it can be seen clearly that the production of acetone based on SDDE describe the experimental data adequately compare to SDE. Furthermore Figure 3a)-3c) also showed that the production of butanol based on SDDE describe the experimental data more adeqaute compare to SDE.

The prediction quality of the models can be assessed by using root mean square error (RMSE)

$$RMSE = \sqrt{\frac{\sum_{i=1}^{n}(y_i - x_i)^2}{n}} \tag{22}$$

where $y_i$ is the experimental data and $x_i$ is the predicted solution. The obtained RMSE for YE1, YE2, and YE3 are shown in Table 3.

**Table 3.** RMSE for YE1, YE2 and YE3

| **Strain and Solvent Production** | **Mathematical Model** | **RMSE** | | |
|---|---|---|---|---|
| | | **YE1** | **YE2** | **YE3** |
| Cell Growth of C.*acetobutylicum* P262 | Stochastic logistic with time delay (17) | 0.4352 | 0.0901 | 0.4160 |
| | Stochastic logistic equation (12) | 0.4451 | 0.0900 | 0. 4263 |
| | Logistic equation (1) | 0.5483 | 0.1058 | 0.5420 |
| Acetone | Luedeking-Piret equation (18) | 0.1852 | 0.03807 | 0.2051 |
| | | 0.2042 | 0.0666 | 0.2859 |
| | | 1.1262 | 0.6051 | 3.4364 |
| Butanol | Luedeking-Piret equation (19) | 0.1637 | 0.00542 | 0.1807 |
| | | 0.8401 | 0.0447 | 0.4540 |
| | | 3.4007 | 2.0022 | 9.4259 |

It can be seen that the numerical solution of stochastic logistic models with time delay describe the experimental data more adequately as indicated by low values of RMSE for YE1 and YE3, and almost same for YE2. Since the cell growth of *C. acetobutylicum* P262 is subjected to time delay and no longer deterministic, the production of acetone and butanol shall be described by stochastic delay logistic model and Luedeking-piret equation, indicating that $x(t)$ in (18) and (19) is a stochastic process. We can see that, the simulated data according to the models (18) and (19) for YE1, YE2 and YE3 fitted well to the experimental data as shown in Figure 2a)-Figure 2c) and Figure 3a)-Figure 3c). Furthermore, RMSE of product formation for acetone and butanol as presented in Table 3 are much smaller than deterministic model, thus indicates that stochastic delay Luedeking-piret equation is more adequate to describe the solvent production by C. *acetobutylicum*P262.

## 5. Conclusion

The models based on logistic and Luedeking-Piret equation were inadequate to describe direct fermentation of sago starch to solvent by *C. acetobutylicum* P262 [7]. Moreover, from the value of RMSE provided in Table 3, we can conclude that the stochastic logistic and Luedeking-Piret equations are insufficient to describe the fermentation process considered here. However, this process can be described adequately via stochastic logistic and Luedeking-Piret equations with time delay. Thus, in this paper we were used stochastic logistic with time delay and Luedeking-Piret equations equipped with EM and found that the resulting model describes the experimental data more adequately than its deterministic and ordinary stochastic counterpart.

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## References


[1] Arifah B. (2005). Applications of Stochastic Differential Equations and Stochastic Delay Differential Equations in Population Dynamics. PhD Thesis, University of Strathclyde.

[2] Bailey, J. E. & Ollis, F. D. (1986). *Biochemical Engineering Fundamentals*, 2nd Edition, McGraw-Hill.

[3] Baker, C. T. H. and Buckwar, E. (2000). 'Numerical Analysis of Explicit One-Step Methods for Stochastic Delay Differential Equations.'*London Mathematical Society Journal Comput. Math.*, 3: 315-335.

[4] Buckwar, E. (2000). 'Introduction to the numerical analysis of stochastic delay differential equations.'*Journal of Computational and Applied Mathematics*, 125: 297-307.

[5] Haliza A. R., Arifah B, Mohd Khairul Bazli, Norhayati R., Madihah M. S. (2009). 'Nonlinear Parameter Estimation of Stochastic Differential Equations.'*2nd International Conference and Workshops on Basic and Applied Sciences and Regional Annual Fundamental Science Seminar*, 44-48.

[6] Hutchinson, G. E. (1948). 'Circular causal system in ecology.'*Ann. NY Acad. Sci.* 50: 221-246.

[7] Hu, Y. Mohammed, S. E. A. and Yan, F. (2004).'Discrete time approximation of stochastic delay equations: the Milstein scheme.'*Ann. Probab. 32* (1A): 265-314.

[8] Kuchler, U. and Platen, E. (2000). 'Strong discrete time approximation of stochastic differential equations with time delay.'*Mathematics and Computers in Simulation*, 54: 189-205.

[9] Madihah M. S. (2002). Direct Fermentation of Gelatinised Sago Starch to Solvent (Acetone Butanol-Ethanol) by Clostridium Acetobutylicum P262. PhD Thesis, University Putra Malaysia.

[10] Madihah M.S., Liew S. T. and Arbakariya A. (2008). The Profile of Enzymes Relevant to Solvent Production during Direct Fermentation of Sago Starch by Clostridium saccharobutylicum P262 Utilizing Different pH Control Strategies. *Biotechnology and Bioprocess Engineering*, 13, 33-39.

[11] Mao, X. (2008). *Stochastic Differential Equations and Applications*, 2nd Edition, Horwood Publishing.

[12] Mohd. KhairulBazli M. A., Arifah B., Madihah M. S. &Haliza A. R. (2009). 'Stochastic Growth of *C. acetobutylicum*,'*2nd International Conference and Workshops on Basic and Applied Sciences and Regional Annual Fundamental Science Seminar*, 146-149.

[13] Mohd. KhairulBazli M. A., Stochastic Modeling of The C. Acetobutylicum and Solvent Productions in Fermentation.' preprint.

[14] Mohammed, S.E.A. (1984). *Stochastic Functional Differential Equations.* Pitman Advanced Publishing.

[15] Norhayati R., Arifah B., Yeak S. H., Haliza A. R., Madihah M. S. and MohdKhairulBazli (2009). 'The Performance of Euler-Maruyama and 2-stage SRK in Approximating the Strong Solution of Stochastic Model.'*2nd International Conference and Workshops on Basic and Applied Sciences and Regional Annual Fundamental Science Seminar*, 138-141.

[16] Norhayati R., Arifah B., Yeak S. H., Haliza A. R. and Madihah M. S. (2010). 'The Performance of Euler-Maruyama, 2-Stage SRK and 4-Stage SRK in Approximating the Strong Solution of Stochastic Model.'*JurnalSainsMalaysiana*39(5): 851–857

[17] Norhayati R., Arifah B., Yeak S. H., Haliza A. R., Madihah M. S. and MohdKhairulBazli (2010).**'**Stochastic Model of Gelatinised Sago Starch to Solvent Production by C. *acetobutylicum* P262.' Regional Conferences on Statistical Sciences 2010 (RCSS'10).

[18] Yerushalmi, L., Volesky, B. And Votruba, J. (1986).'Modelling of culture kinetics and physiological for *Clostridium acetobutylicum.*' *Journal of Canadian Chemical Engineering*, 64: 607-616.