Conference Proceeding Science and Technology, 3(1), 2020, 1–10

Conference Proceeding of 3rd International E-Conference on Mathematical Advances and Applications (ICOMAA-2020)

ISSN: 2651-544X
http://dergipark.gov.tr/cpost

An Extensive Statistical Study for the Leukemia Mathematical Model using the RVT Technique

Abdallah Hussein[1,*] *Howida Slama*[2] *Nabila. A. El-Bedwhey*[3] *Mustafa M. Selim*[2]

[1] *Department of Engineering and Applied Sciences, Community College, Umm Al-Qura University, Makkah, 715, Saudi Arabia, ORCID:0000-0001-5224-2544*
[2] *Department of Physics, Faculty of Science, Damietta University, New Damietta City 34517, Egypt, ORCID:0000-0002-0172-1550*
[3] *Department of Mathematics, Faculty of Science, Damietta University, New Damietta City 34517, Egypt, ORCID:0000-0003-3331-050X*
** Corresponding Author E-mail: ahmostafa@uqu.edu.sa*

Abstract: This paper provides a probabilistic study for the four compartmental leukemia mathematical model. Our study focuses on the randomized endemic equilibrium state considering the proliferation rate of the immune cells due to the cancer relapse is a continuous random variable. This treatment makes the presented model to be more realistic and efficient. Depending on the Random Variable Transformation (RVT) technique, the first probability density functions (1-PDFs) for the solution processes of susceptible blood cells, infected blood cells, cancer cells and immune cells are explicitly derived at the equilibrium state. These PDFs are general and valid for any probabilistic distribution of the input random variable. Relying on the obtained PDFs, the main statistical properties, specifically, the mean and the variance functions for the solution processes are conducted. To test the validity of the theoretical findings associated to the proposed randomized leukemia model, some numerical results are presented through an illustrative example.
Keywords: Leukemia mathematical model, Random Variable Transformation (RVT) technique, first probability density function (1-PDF), randomized endemic equilibrium state, random proliferation rate.

1 Introduction

Random (or stochastic) differential equations are established as one of the supportive ways to describe most of physical problems, in which the randomness arises, in various fields such as physics, chemistry, epidemiology, astrophysics, biology, engineering and social sciences. This type of differential equations can be solved via different methods and techniques such as Fokker-Planck equation [1], Wiener-Hermite expansion [2]-[3], and perturbation based methods [4], WHEP technique [5] and the random variable transformation (RVT) technique [6]-[7]-[8]-[9]-[10]-[11]-[12]-[13].

The Random Variable Transformation (RVT) technique is a powerful technique that helps to get a full probabilistic description of the stochastic solutions of some stochastic differential equations. The full stochastic solution means obtaining the first probability density function (1-PDF) of the solution process then the mean, variance, covariance ... etc. The RVT technique gives a general solution of the problem by allowing the input random variable to have any probabilistic distribution. It is also treating discrete or continuous random differential equations that have one or more random variables (RVs). In this paper, authors apply the RVT to study the statistical behavior of the randomized equilibrium state of the leukemia. Leukemia is a type of cancer that starts in the blood forming tissues, such as the bone marrow. It is usually beginning in the white blood cells and starts to make a lot of abnormal white blood cells which don't function properly. Large number of leukemia cells can enter the blood stream very quickly and crowd out the normal blood cells which may lead to Anemia, bleeding, and infections. Furthermore, leukemia can spread to the lymph nodes or other organs and cause swelling or pain.

The dynamics and spread of endemic diseases in biology and medicine can be, in general, described by nonlinear ordinary and partial differential equations. The dynamics of Leukemia can be modeled by such system of nonlinear differential equations. For more details on leukemia mathematical models as well as some recent developments the readers can refer to references [14]-[15]-[16]-[17] and the references within. However, in recent work, some new developments in modeling the nonlinear behavior of immunotherapeutic treatment of leukemia using Adoptive T cell are addressed [18]-[19]. This model consists of four nonlinear ordinary differential equations for susceptible, infective, cancer and immune cells. The stability theory of differential equations and numerical simulation are used to analyze this model and the analysis reveals that the external re-infusion of immune cells reduces the concentration of cancer cells and infected cells in the blood.

In this article we study the four component Leukemia model, at endemic equilibrium state, from a statistical point of view. Specifically, we consider the source of randomness is the proliferation rate of the immune cells due to the cancer relapse. It is considered as a continuous random variable. However, the argument of this paper can be applied if we generalize the randomness to the other parameters of the leukemia model.

The layout of the paper is as follows, in section 2, the theory of RVT technique is presented. The formulation of the four component mathematical model for leukemia and its deterministic solution at equilibrium point is given in section 3. Moreover, in section 4, the RVT technique is applied to obtain the 1-PDF, the mean and the variance functions. Finally, for clarification the results and conclusions are illustrated.

2 The random variable transformation (RVT) technique

The RVT technique is based on the following general theorem [7]-[13] when we have multi-random variable problems.

Theorem 1. *If we assume that $\boldsymbol{X} = (X_1, \ldots, X_n)$ is a random vector of dimension n with joint PDF, $f_{\boldsymbol{X}}(\boldsymbol{x})$, and consider a deterministic one-to-one mapping $\boldsymbol{g} : R^n \longrightarrow R^n$, where $\boldsymbol{Y} = \boldsymbol{g}(\boldsymbol{X})$, to be continuous with respect to each one of its arguments with continuous partial derivatives. Then, if we can define $\boldsymbol{s} : R^n \longrightarrow R^n$ such that $\boldsymbol{x} = \boldsymbol{g}^{-1}(\boldsymbol{y}) = \boldsymbol{s}(\boldsymbol{y})$, where $\boldsymbol{s}(\boldsymbol{y})$ is the vector of inverse transformation, then the random vector $\boldsymbol{Y}$ have a joint PDF $f_{\boldsymbol{Y}}(\boldsymbol{y})$ given by*

$$f_{\boldsymbol{Y}}(\boldsymbol{y}) = f_{\boldsymbol{X}}(\boldsymbol{s}(\boldsymbol{y}))|J_n|, \tag{1}$$

since, J_n is the jacobian of the transformation;

$$J_n = \det(\frac{\partial \boldsymbol{x}}{\partial \boldsymbol{y}}) = \begin{pmatrix} \frac{\partial x_1}{\partial y_1} & \cdots & \frac{\partial x_n}{\partial y_1} \\ \vdots & \ddots & \vdots \\ \frac{\partial x_1}{\partial y_n} & \cdots & \frac{\partial x_n}{\partial y_n} \end{pmatrix} \neq 0. \tag{2}$$

In (2), $X_i (i = 1, 2, 3, n)$ are called the input random variables while $Y_i (i = 1, 2, 3, n)$ are the output random variables. Hence, the joint PDF of the output random variables can be obtained if the joint PDF of the input random variables is defined in a closed form.

2.1 The case of one input random variable

Suppose the following one-to-one map between the input and output random variables,

$$Y = u(X), \tag{3}$$

and $f_X(x)$ is the 1-PDF of the scalar input random variable X. Then the 1-PDF of output random variable Y can be given, in view of (1), as:

$$f_Y(y) = f_X(u^{-1}(y))|J|, \tag{4}$$

where J is the Jacobian of the inverse transformation $x = u^{-1}(y)$, i.e.

$$J_n = \frac{\partial x}{\partial y} = \frac{\partial u^{-1}(y)}{\partial y} \neq 0. \tag{5}$$

3 The leukemia model formulation and its solution in equilibrium state

The aim of this section is to present the leukemia model in the form of mathematical equations. In this model, there are four compartments. Those compartments are the population of susceptible blood cells, s, the population of infected blood cells, i, the population of leukemic cells (abnormal cells), c, and the population of white blood cells or immune cells, w, [18]-[19].
The leukemia mathematical model is formed by the following system of ordinary differential equations:

$$\frac{ds}{dt} = A - a_0 s - \beta sc, \tag{6a}$$

$$\frac{di}{dt} = \beta sc - \beta_0 i - \beta_1 ci, \tag{6b}$$

$$\frac{dc}{dt} = k - k_0 c - k_1 cw, \tag{6c}$$

$$\frac{dw}{dt} = B + bc - b_0 w - b_1 cw. \tag{6d}$$

In (6a)-(6d), A represents the source term of susceptible blood cells compartement entering into the circulatory blood from the bone marrow, lymph nodes and thymus. The natural death rate of susceptible, infected, cancer, and immune blood cells are a_0, β_0, k_0, and b_0 respectively. There is a loss of susceptible blood cells due to being infected by the cancer cells represented by the parameter, β. In addition, the parameter β_1, is the decay rate of infected cells because of the interaction with cancer cells. In (6c) the first term k represents the constant recruitment rate of cancer cells into the blood system, while the parameter k_1 is the lack rate of cancer cells due to the effect of immune cells. The parameter b_1 is the decay rate of some immune cells due to the existence of cancer cells in the blood. Immune cells in cancer patients have an external infusion at a rate of B. If cancer relapses, the immune cells will be proliferated at a rate, b. The solution of the leukemia model, (6a)-(6d), in the disease-free equilibrium (DFE) point or endemic equilibrium point can be performed as follows:

$$S^* = \frac{A(1+\frac{k_1 w^*}{k_0})}{a_0 + \frac{a_0 k_1 w^*}{k_0} + \frac{\beta k}{k_0}}, \tag{7a}$$

$$I^* = \frac{\beta}{\beta_0 + \frac{\beta_1 k/k_0}{1+k_1 w^*/k_0}} (\frac{A}{a_0 + \frac{a_0 k_1 w^*}{k_0} + \frac{\beta k}{k_0}}) \frac{k}{k_0}, \tag{7b}$$

$$C^* = \frac{k/k_0}{1 + k_1 w^*/k_0}, \tag{7c}$$

$$W^* = \frac{-(k_0 b_0 + k b_1 - B k_1) + \sqrt{(k_0 b_0 + k b_1 - B k_1)^2 + 4 b_0 k_1 (k b + B k_0)}}{2 b_0 k_1}. \tag{7d}$$

Here, S^*, I^*, C^* and W^* are the population of susceptible, infected, leukemic and immune cells in DFE point (or endemic equilibrium point), respectively.

4 Stochastic Leukemia model

In this section, we will treat the above mentioned leukemia model in DFE point and endemic equilibrium case by considering the random nature in a significant parameter which is the proliferate rate, b. In this context, we use the RVT technique, discussed in Sec.2, in order to get the stochastic solution which is represented by the 1- PDF, the mean and the variance functions of the solution process. This is the target of the following subsections.

4.1 The statistical study of the population of susceptible blood cells, S^*

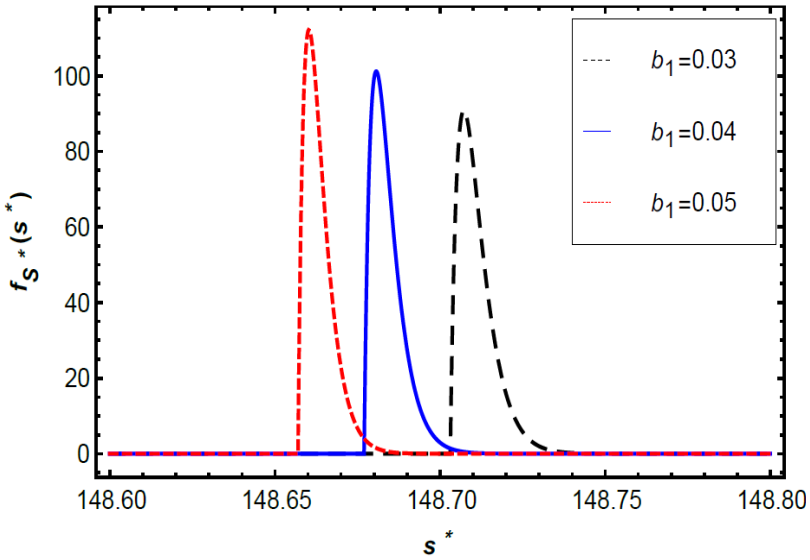

Fig. 1: The profile of the 1-PFD, $f_{S^*}(s^*)$, for different values of the decay rate, b_1.

The proliferate rate, b, can be obtained in terms of s^* by substituting (7d) into (7a) as

$$\begin{aligned} b(s^*) = \frac{1}{k_1(A - a_0 s^*)^2}(&-A^2 b_1 k_0 + 2A a_0 b_1 k_0 s^* - a_0^2 b_1 k_0 s^{*2} + A b_1 k s^* \beta - A b_0 k_0 s^* \beta \\ &- A B k_1 s^* \beta - a_0 b_1 k s^{*2} \beta + a_0 b_0 k_0 s^{*2} \beta + a_0 B k_1 s^{*2} \beta + b_0 k s^{*2} \beta^2), \end{aligned} \tag{8}$$

Then the jacobian is given by

$$J_{s^*} = \frac{\partial b}{\partial s^*} = \frac{A\beta((b_1 k - b_0 k_0 - B k_1)(A - a_0 s^*) + 2 b_0 k s^* \beta)}{k_1 (A - a_0 s^*)^3}. \tag{9}$$

According to eq.(4) the 1-PDF of s* is given by

$$\begin{aligned} f_{S^*}(s^*) = &|\tfrac{A\beta((b_1 k - b_0 k_0 - B k_1)(A - a_0 s^*) + 2 b_0 k s^* \beta)}{k_1 (A - a_0 s^*)^3}| \tfrac{1}{\Gamma[\alpha_1]} exp(A^2 b_1 k_0 + A s^* (-2 a_0 b_1 k_0 + (-b_1 k + b_0 k_0 + B k_1)\beta) \\ &+ s^{*2}(a_0^2 b_1 k_0 + a_0(b_1 k - b_0 k_0 - B k_1)\beta - b_0 k \beta^2)/k_1 (A - a_0 s^*)^2 \gamma_1)(\tfrac{1}{k_1 (A - a_0 s^*)^2} \\ &(-A^2 b_1 k_0 + A s^* (2 a_0 b_1 k_0 + (b_1 k - b_0 k_0 - B k_1)\beta) + s^{*2}(-a_0^2 b_1 k_0 + a_0(-b_1 k + b_0 k_0 + B k_1)\beta + b_0 k \beta^2)))^{-1+\alpha_1}. \end{aligned} \tag{10}$$

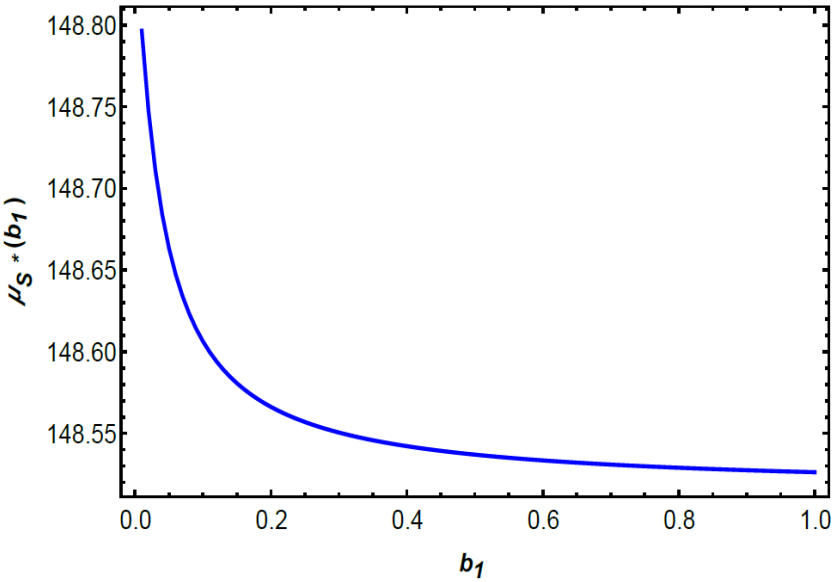

Fig. 2: The variation of the mean, $\mu_{S^*}(b_1)$, versus the decay rate, b_1.

4.2 *The statistical study of the population of infected blood cells, I^**

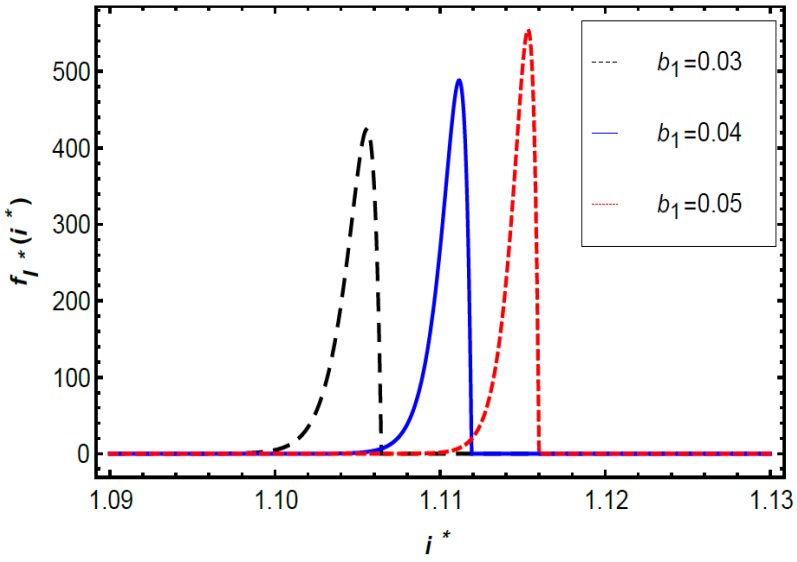

Fig. 3: The profile of the 1-PFD, $f_{I^*}(i^*)$, for different values of the decay rate, b_1.

In a similar manner we can substitute from (7d) in (7b) to get b in terms of i^* as

$$
\begin{aligned}
b(i^*) = {} & \frac{1}{2a_0^2 i^{*2} k_1^2 \beta_0^2} - k_1(-Ab_0 k\beta - a_0 b_1 i^* k\beta_0 + a_0 b_0 i^* k_0 \beta_0 + a_0 B i^* k_1 \beta_0 + b_0 i^* k\beta\beta_0 + a_0 b_0 i^* k\beta_1) \\
& \sqrt{A^2\beta^2 - 2Ai^*\beta^2\beta_0 + i^{*2}\beta^2\beta_0^2 - 2Aa_0 i^*\beta\beta_1 - 2a_0 i^{*2}\beta\beta_0\beta_1 + a_0^2 i^{*2}\beta_1^2} k_1(-A^2 b_0 k\beta^2 - Aa_0 b_1 i^* k\beta\beta_0 + \\
& Aa_0 b_0 i^* k_0 \beta\beta_0 + Aa_0 B i^* k_1 \beta\beta_0 + 2Ab_0 i^* k\beta^2\beta_0 + 2a_0^2 b_1 i^{*2} k_0 \beta_0^2 + a_0 b_1 i^{*2} k\beta\beta_0^2 - a_0 b_0 i^{*2} k_0 \beta\beta_0^2 - \\
& a_0 B i^{*2} k_1 \beta\beta_0^2 - b_0 i^{*2} k\beta^2\beta_0^2 + 2Aa_0 b_0 i^* k\beta\beta_1 + a_0^2 b_1 i^{*2} k\beta_0\beta_1 - a_0^2 b_0 i^{*2} k_0\beta_0\beta_1 - \\
& a_0^2 B i^{*2} k_1 \beta_0\beta_1 - a_0^2 b_0 i^{*2} k\beta_1^2),
\end{aligned}
\tag{11}
$$

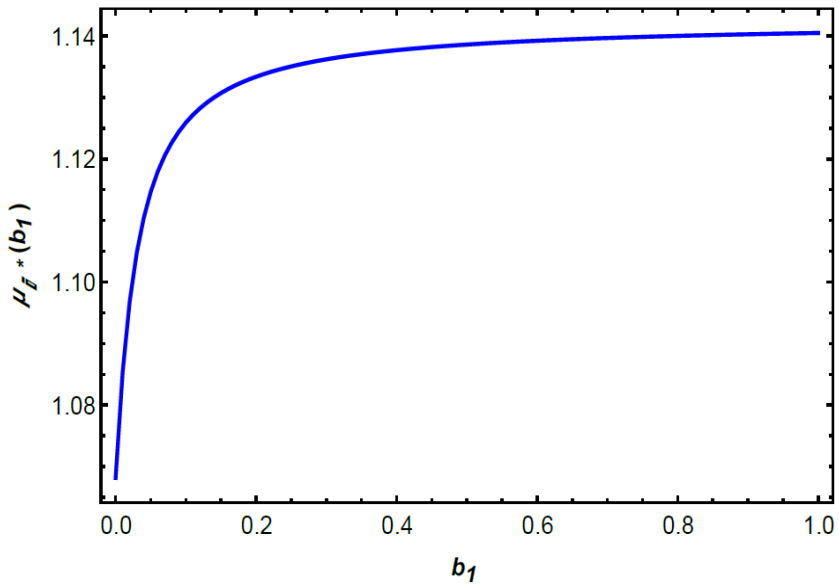

Fig. 4: The variation of the mean, $\mu_{I^*}(b_1)$, versus the decay rate, b_1.

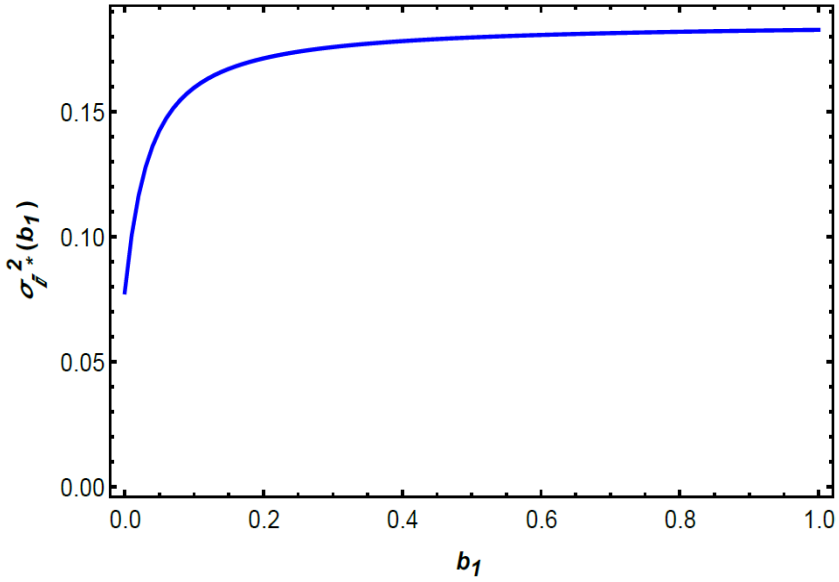

Fig. 5: The variation of the variance, $\sigma^2_{I^*}(b_1)$, versus the decay rate, b_1.

Then the jacobian can be evaluated as

$$
\begin{aligned}
J_{i^*} = (&A\beta(-2A^2b_0k\beta^2 + A\beta(a_0i^*(-b_1k\beta_0 + b_0k_0\beta_0 + Bk_1\beta_0 + 4b_0k\beta_1) - 2b_0k(-2i^*\beta\beta_0 + \\
&\sqrt{\beta^2(A - i^*\beta_0)^2 - 2a_0i^*\beta(A + i^*\beta_0)\beta_1 + a_0^2i^{*2}\beta_1^2})) - i^*(a_0^2i^*\beta_1(-b_1k\beta_0 + b_0k_0\beta_0 + Bk_1\beta_0 + 2b_0k\beta_1) + 2b_0k\beta\beta_0(i^*\beta\beta_0 - \\
&\sqrt{\beta^2(A - i^*\beta_0)^2 - 2a_0i^*\beta(A + i^*\beta_0)\beta_1 + a_0^2i^{*2}\beta_1^2}) + a_0(i^*(-b_1k + b_0k_0 + Bk_1)\beta\beta_0^2 \\
&+ b_1k\beta_0\sqrt{\beta^2(A - i^*\beta_0)^2 - 2a_0i^*\beta(A + i^*\beta_0)\beta_1 + a_0^2i^{*2}\beta_1^2} \\
&- b_0k_0\beta_0\sqrt{\beta^2(A - i^*\beta_0)^2 - 2a_0i^*\beta(A + i^*\beta_0)\beta_1 + a_0^2i^{*2}\beta_1^2} - Bk_1\beta_0\sqrt{\beta^2(A - i^*\beta_0)^2 - 2a_0i^*\beta(A + i^*\beta_0)\beta_1 + a_0^2i^{*2}\beta_1^2} \\
&- 2b_0k\beta_1\sqrt{\beta^2(A - i^*\beta_0)^2 - 2a_0i^*\beta(A + i*\beta_0)\beta_1 + a_0^2i^{*2}\beta_1^2}))))/(2a_0^2i^{*3}k_1\beta_0^2 \\
&\sqrt{A^2\beta^2 + i^{*2}(\beta\beta_0 - a_0\beta_1)^2 - 2Ai^*\beta(\beta\beta_0 + a_0\beta_1)}),
\end{aligned}
\tag{12}
$$

According to (4) the 1-PDF of i^* is given by

$$f_{I^*}(i^*) = |j_{i^*}|\frac{1}{\Gamma[\alpha_1]}2^{(}1-{}_1)exp(-A^2b_0k\beta^2 - Aa_0b_1i^*k\beta\beta_0 + Aa_0b_0i^*\beta\beta_0 + Aa_0Bi^*k_1\beta\beta_0 + 2Ab_0i^*k\beta^2\beta_0$$
$$+ 2a_0^2b_1i^{*2}k_0\beta_0^2 + a_0b_1i^{*2}k\beta\beta_0^2) - a_0b_0i^{*2}k_0\beta\beta_0^2 - a_0Bi^{*2}k_1\beta\beta_0^2 - b_0i^{*2}k\beta^2\beta_0^2 + 2Aa_0b_0i^*k\beta\beta_1$$
$$+ a_0^2b_1i^{*2}k\beta_0\beta_1 - a_0^2b_0i^{*2}k_0\beta_0\beta_1 - a_0^2Bi^{*2}k_1\beta_0\beta_1 - a_0^2b_0i^{*2}k\beta_1^2$$
$$- \sqrt{A^2\beta^2 + i^{*2}(\beta\beta_0 - a_0\beta_1)^2 - 2Ai^*\beta(\beta\beta_0 + a_0\beta_1)}(Ab_0k\beta - i^*(b_0k\beta\beta_0 + a_0(-b_1k\beta_0 + b_0k_0\beta_0 + Bk_1\beta_0 + b_0k\beta_1)))$$
$$/2a_0^2i^{*2}k_1\beta_0^2\gamma_1(1/(a_0^2i^{*2}k_1\beta_0^2)(A^2b_0k\beta^2 + Aa_0b_1i^*k\beta\beta_0 - Aa_0b_0i^*k_0\beta\beta_0 - Aa_0Bi^*k_1\beta\beta_0 - 2Ab_0i^*k\beta^2\beta_0 - 2a_0^2b_1i^{*2}k_0\beta_0^2 -$$
$$a_0b_1i^{*2}k\beta\beta_0^2 + a_0b_0i^{*2}k_0\beta\beta_0^2 + a_0Bi^{*2}k_1\beta\beta_0^2 + b_0i^{*2}k\beta^2\beta_0^2 - 2Aa_0b_0i^*k\beta\beta_1 - a_0^2b_1i^{*2}k\beta_0\beta_1 + a_0^2b_0i^{*2}k_0\beta_0\beta_1 + a_0^2Bi^{*2}k_1\beta_0\beta_1$$
$$+ a_0^2b_0i^{*2}k\beta_1^2 + (A^2\beta^2 + i^{*2}(\beta\beta_0 - a_0\beta_1)^2 - 2Ai^*\beta(\beta\beta_0 + a_0\beta_1))(Ab_0k\beta - i^*(b_0k\beta\beta_0 + a_0(-b_1k\beta_0 + b_0k_0\beta_0 + Bk_1\beta_0$$
$$+ b_0k\beta_1)))))^{-1+\alpha_1}\gamma_1^{-\alpha_1}. \tag{13}$$

4.3 *The statistical study of the population of the cancer cells, C^**

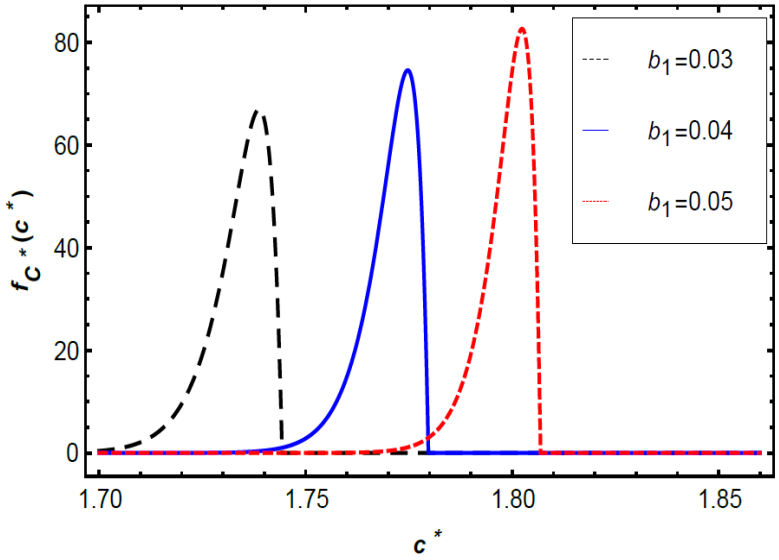

Fig. 6: The profile of the 1-PFD, $f_{C^*}(c^*)$, for different values of the decay rate, b_1.

Similarly, substitute from (7d) in (7c) to get c^* as a function of b, then we can evaluate b as follows

$$b(c^*) = \frac{b_0k + b_1c^*k - b_0c^*k_0 - b_1c^{*2}k_0 - Bc^*k_1}{c^{*2}k_1}. \tag{14}$$

Then the jacobian is given by

$$J_{c^*} = \frac{\partial b}{\partial c^*} = \frac{-2b_0k - b_1c^*k + b_0c^*k_0 + Bc^*k_1}{c^{*3}k_1}, \tag{15}$$

According to (4) the 1-PDF of C^* is given by

$$f_{C^*}(c^*) = |\frac{-2b_0k - b_1c^*k + b_0c^*k_0 + Bc^*k_1}{c^{*3}k_1}|\frac{1}{\Gamma[\alpha_1]}exp(\frac{b_0(-k + c^*k_0) + c^*(-b_1k + b_1c^*k_0 + Bk_1)}{c^{*2}k_{11}})$$
$$(\frac{b_0(k - c^*k_0) - c^*(-b_1k + b_1c*k_0 + Bk_1)}{c^*k_1})^{-1+\alpha_1}\gamma_1^{-\alpha_1} \tag{16}$$

4.4 *The statistical study of the population of the immune cells, W^**

As we have done in the previous subsections, the proliferate rate, b, can be obtained in terms of w^* from (7d) as

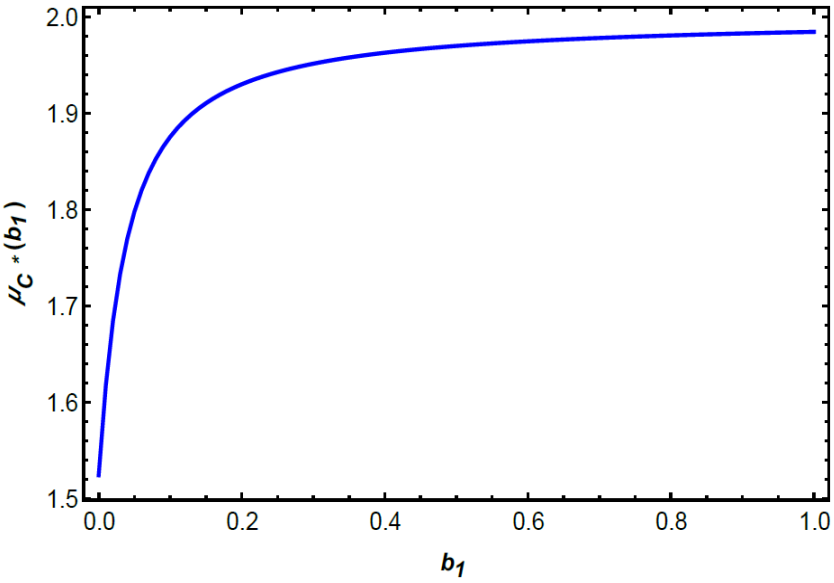

Fig. 7: The variation of the mean, $\mu_{C^*}(b_1)$, versus the decay rate, b_1.

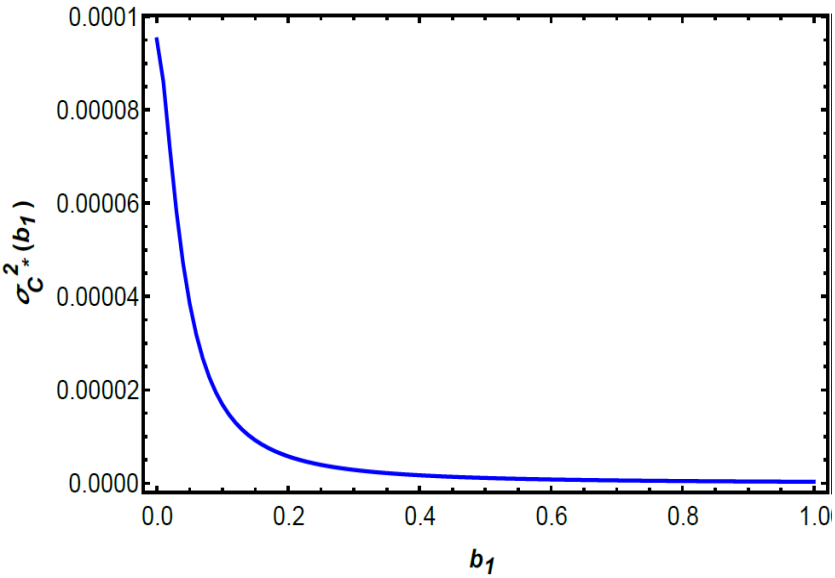

Fig. 8: The variation of the variance, $\sigma^2_{C^*}(b_1)$, versus the decay rate, b_1.

$$b(w^*) = \frac{b_1 k w^* - (B - b_0 w^*)(k_0 + k_1 w^*)}{k}. \tag{17}$$

The jacobian is given by

$$J_{W^*} = \frac{\partial b}{\partial w^*} = \frac{b_1 k + b_0 k_0 - B k_1 + 2 b_0 k_1 w^*}{k}, \tag{18}$$

According to (4) the 1-PDF of W^* can be developed as

$$\begin{aligned} f_{W^*}(w^*) = & |\frac{b_1 k + b_0 k_0 - B k_1 + 2 b_0 k_1 w^*}{k}|((b_1 k w^* - (B - b_0 w^*)(k_0 + k_1 w^*)/k)^{-1+\alpha_1} \gamma_1^{-\alpha_1} \\ & exp(\frac{-b_1 w^* + \frac{(B - b_0 w^*)(k_0 + k_1 w^*)}{k}}{\gamma_1})/\Gamma[\alpha_1]). \end{aligned} \tag{19}$$

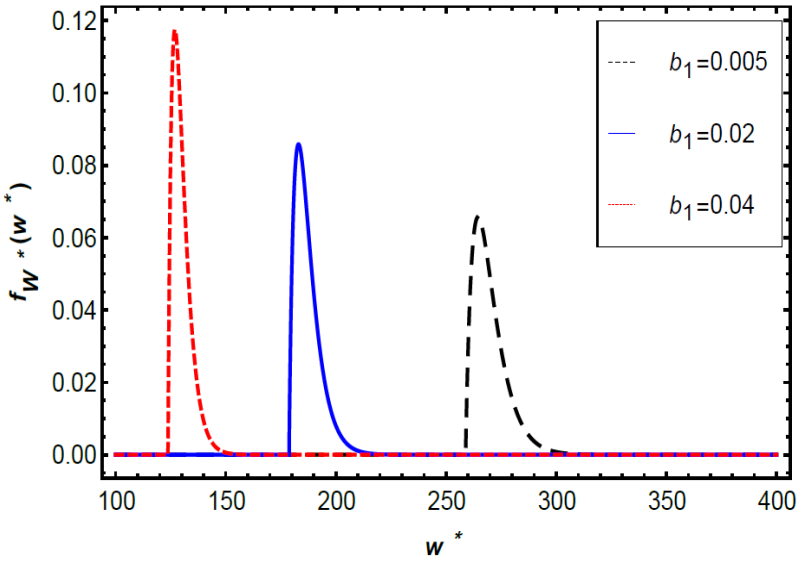

Fig. 9: The profile of the 1-PFD, $f_{W^*}(w^*)$, for different values of the decay rate, b_1.

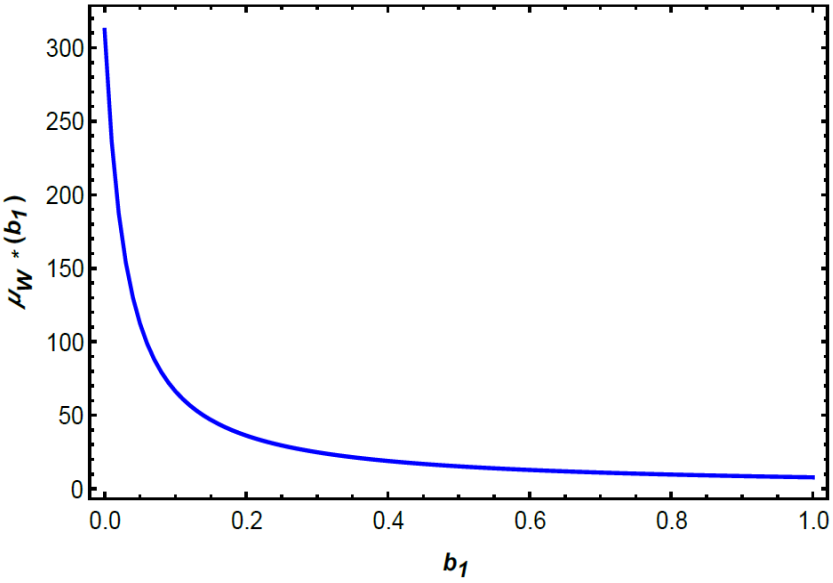

Fig. 10: The variation of the mean, $\mu_{W^*}(b_1)$, versus the decay rate, b_1.

The 1-PDFs that obtained before help us to find the main statistical quantities such as the mean and variance functions of each compartments (S^*, I^*, C^* and W^*) from the following relations respectively,

$$E[H] = \mu_H = \int_{-\infty}^{\infty} h f_H(h) dh, \tag{20a}$$

$$V[H] = (\sigma_H)^2 = \int_{-\infty}^{\infty} h^2 f_H(h) dh - (\mu_H)^2, \tag{20b}$$

where H stands for S^*, I^*, C^* or W^* and h stands for the arguments: s^*, i^*, c^* or w^*, respectively. The 1-PDFs $f_H(h)$ are given by (10), (13), (16) and (19) in each case.

5 Numerical results and discussions

In this section, we introduce a numerical example to check the validity of our theoretical findings obtained in previous sections. In all results, the random variable, b, is considered to obey a Gamma distribution, i.e b ~Gamma (α, β), with shape parameter $\alpha = 2.0$ and rate parameter $\beta = 0.2$. Also, the model deterministic parameters are taken, for clarification, as, $k = 10$; $k_0 = 5$; $k_1 = 0.005$; $B = 15$; $b_0 = 0.05$; $\beta = 0.00005$; $\beta_0 = 0.003$; $\beta_1 = 0.005$; $A = 1.5$; $a_0 = 0.01$. Moreover, to assess our model, we discuss the effect of the decay rate of immune cells due to the existence of cancer cells in the blood, b_1, on the statistical behviour of the equilibrium states for all compartments. However, the effect of other model parameters can be discussed in the same way.

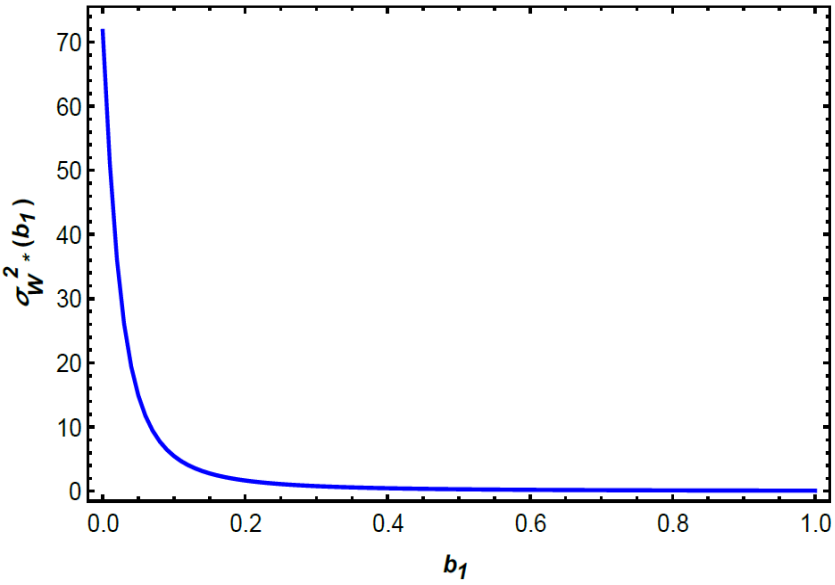

Fig. 11: The variation of the variance, $\sigma^2_{W^*}(b_1)$, versus the decay rate, b_1.

In Figs. 1, 3, 6 and 9, the 1-PDFs, of the equilibrium states for all compartments are presented at different values of the decay rate of immune cells due to the existence of cancer cells in the blood, b_1. Figs. 2,4,7 and 10 are plotted to show the behavior of the mean value of each compartment as the decay rate, b_1 increases. Finally, the same behavior for the variance values of each compartment is studied in Figs. 5,8 and 11.

In Fig.1, the profiles of 1-PDFs, $f_{S^*}(s^*)$, at different values of the decay parameter, b_1, show the decrease of mean value of the equilibrium state for the susceptible compartment as the value of b_1 increases. This behavior can be noticed more clearly in Fig.2 where the mean μ_{S^*} is plotted versus b_1.

In Fig. 3 the 1-PDF, $f_{I^*}(i^*)$, as given by (13), are also plotted at different values of b_1. It is observed that the mean value and the dispersion around the mean of the infected compartment increases as the decay rate increases. This can be observed more clearly from Fig. 4 (for the mean behavior) and Fig. 5 (for the variance behavior).

Also, in Fig.6 the profiles of 1-PDFs, $f_{C^*}(c^*)$ as given by (16), at different values of b_1, show an increase of mean value while the dispersion around the mean decreases at the equilibrium state for the cancer cells as the value of b_1 increases. This behavior is presented more clearly in Figs.7 and 8 where the mean μ_{C^*} and the variance, $\sigma^2_{C^*}$, are respectively plotted versus b_1.

In Fig.9 we presented the profile of the 1-PDF, $f_{W^*}(w^*)$, as given by (19), at different values of b_1. One can observe the decrease in both of the mean and the variance values of the equilibrium state for the immune cells as b_1 increases which is confirmed in Figs.10 and 11 where the mean μ_{W^*} and the variance $\sigma^2_{W^*}$ are plotted versus b_1.

The above studied bahviours of the four compartments of the model are consistent with the physical nature of the problem, where, if the decay rate of the immune cells increases, the susceptible population will decrease and consequently the susceptible cells will transform rapidly to the infected cells. So, the infected cells will increase. In addition, the cancer cells will increase due to the decrase of immune cells. This confirms the reliability of our proposed model.

6 Conclusion

In this article, one of the interesting models in biology, the so called Leukemia model, has been discussed in a randomized phase. To study the randomized equilibrium state for each compartment of the model, the proliferation rate of the immune cells due to the cancer relapse is considered as a continuous RV. A full probabilistic description of susceptible blood cells, infected blood cells, cancer cells and immune cells, governed by this model, at the equilibrium state are developed. This description is based on the application of the RVT technique to get the 1-PDF, the mean and variance functions of the above mentioned random quantities. The numerical results show a consistency with the available published results. This study may help doctors to diagnose, more accurately, Leukemia disease which is one of the most common types of blood cancer among children.

Finally, we expect that our proposed model is a good realistic model since it considers the probabilistic behavior of one of the important rates in the model. However, the methodology in this paper can be applied if we generalize the randomness to the other rates associated to the leukemia model. It is also possible to assign arbitrary statistical distributions for these rates according to the nature of randomness in the model. This matter is our goal in the future research.

7 References

1 I. Gihman, A. Skorohod, *One-dimensional stochastic differential equations of first order*, Springer-Verlag, 1972.
2 E. Abdel Gawad, M. El-Tawil, *General stochastic oscillatory systems*, Appl. Math. Model. (AMM) **17**(6) (1993), 329-335.

3 A. Jahedi, G. Ahmadi, *Application of Wiener-Hermite expansion to non stationary random vibrations of a Duffing oscillator*, J. Appl. Mech. **50** (1983), 436-442.
4 A. Nayfeh, *Problems in perturbation*, John Wiley, New York, 1993.
5 M. El-Tawil, *The application of WHEP technique on stochastic partial differential equations*, Int. J. Differ. Equ. **7**(3) (2003), 325-337.
6 R. Walpole, R. Myers, S. Myers, *Probability and statistics for engineers and scientists*, sixth ed., Prentice-Hall, New Jersey, 1998.
7 A. Papoulis, S. U. Pillai, *Probability, random variables and stochastic processes*, 4th Edition, McGraw-Hill, New York, 2002.
8 M.-C. Casabán, J.-C. Cortés, J.-V. Romero, M.-D. Roselló, *Probabilistic solution of random SI-type epidemiological models using the Random Variable Transformation technique*, Commun. Nonlinear Sci. Numer. Simul. **24**(1) (2015), 86-97.
9 M.-C. Casabán, J.-C. Cortés, A. Navarro-Quiles, J.-V. Romero, M.-D. Roselló, R.-J. Villanueva, *A comprehensive probabilistic solution of random SIS-type epidemiological models using the random variable transformation technique*, Commun. Nonlinear Sci. Numer. Simul. **32** (2016), 199-210.
10 H. Slama, A. Hussein, N.A. El-Bedwhey, M.M. Selim, *An approximate probabilistic solution of a random SIR-type epidemiological model using RVT technique*, Appl. Math. Comp. **361** (2019), 144-156.
11 J.-C. Cortés, S.K. El-Labany, A. Navarro-Quiles, H. Slama, *A comprehensive probabilistic analysis of approximate SIR-type epidemiological models via full randomized discrete-time Markov chain formulation with applications*, Math. Meth. Appl. Sci. **43**(14) (2020), 8204-8222.
12 A. Hussein, M.M. Selim, *A general probabilistic solution of randomized radioactive decay chain (RDC) model using RVT technique*, Eur. Phys. J. Plus **135**(418) (2020), 1-16.
13 A. Hussein, Mustafa M. Selim, *A complete probabilistic solution for a stochastic Milne problem of radiative transfer using KLE-RVT technique*, J. Quant. Spect. Spectrosc. Radiat. Transf. **232** (2019), 54-65.
14 A.S. Forkas, J.B Keller,B.D. Clarkson, *Mathematical model of granulocytopoiesis and chronic myelogenous leukemia*, Cancer Res. **51**(8) (1991), 2084-2091.
15 J.M. Goldman, J.V. Melo, *Chronic myeloid leukemia-advances in biology and approaches to treatment*, New Engl. J. Medic. **349**(15) (2003), 1451-1464.
16 M. Mamat, Subiyanto, A. Kartono, *Mathematical model of cancer treatments using immunotherapy, Chemotherapy and bio chemotherapy*, Appl. Math. Sci. **7**(5) (2013), 247-261.
17 M.C. Mackey, L. Pujo-Menjouet, *Contribution to the study of periodic chronic myelogenous leukemia*, Comptes Rendus Biologies **327**(3) (2004), 235-244.
18 M. Agarwal, A. S. Bhadauria, *Mathematical modeling and analysis of leukemia: effect of external engineered T cells infusion*, Appl. Appl. Math. **10**(1) (2015), 249-266.
19 S. Khatun, H.A. Biswas, *Modeling infectious disease in healthcare problems for the medical systems improvement in Bangladesh*, Proceedings of the 2^{nd} European Conference on Industrial Engineering and Operations Management (IEOM) Paris, France, (2018), 3024-3031.

